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GLOBAL HEPATITIS SUMMIT 2023

The 18th International Symposium on
Viral Hepatitis and Liver Disease (ISVHLD)

ABSTRACTS

#GHS2023

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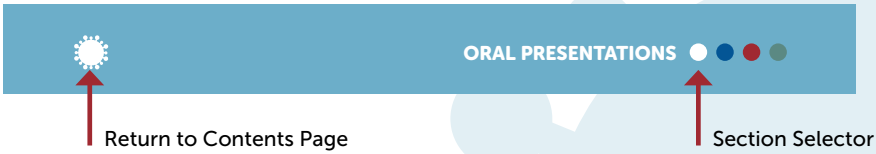

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O01

DEMONSTRATION OF HCV RNA METHYLATION IN CLINICAL ISOLATES AND COMPARISON WITH CELL CULTURE-DERIVED VIRUS

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Background: Recently, N6-methyladenosine (m6A) modification of viral RNA has been observed in HIV and flaviviruses, including Hepatitis C Virus (HCV). This post-transcriptional modification affects translation (5'UTR), viral particle production (E1) and innate immune recognition (NS5B). To date, HCV RNA methylation has only been detected in vitro using the HCV genotype 2a JFH-1 infectious clone in liver cancer cell lines (Huh7 and HepG2). Given its varied effect on HCV infection, studying methylation in clinical samples will help us determine if it actually occurs in natural infection and will shed light on the importance of methylation at specific sites. We analyzed the reported methylation sites in E1 of HCV RNA from patient-derived plasma of different HCV genotypes (1-4) using an optimized RT-PCR approach that allows for site specific detection and low amount of input material.

Purpose: Validation of RT-PCR protocol for m^6A detection

Detection of m^6A modification in E1 from HCV RNA derived from patient samples

Comparison of HCV methylation in E1 in plasma-derived and cell-culture derived virus

Methods: Reverse Transcription enzymes BstI and MRT, were used for cDNA synthesis of HCV-RNA from plasma from patients with chronic HCV infection (genotypes 1-4) and JFH1, followed by quantitative PCR. BstI activity is hindered by the presence of m6A on RNA, whereas MRT is not. The ratio of BstI to MRT product can therefore be used to infer methylation, where the threshold value >0.5 suggests methylation. Genes with known methylation (SON) and no methylation sites (HPRTI1) were used as controls. RT-PCR protocol was validated by immunoprecipitation of methylated RNA (Me-RIP) in cell-culture derived HCV using m^6A-specific antibodies.

Results: The RT-PCR approach was validated with the gold standard MeRIP in cell culture derived HCV (JFH-1) supporting previous evidence that methylation in E1 prevents particle production shown by no pull down of m^6A E1 from supernatant RNA compared to enrichment of methylated E1 in intracellular RNA (Fig1a,c). However methylation in E1 was observed in plasma-derived HCV from genotypes 1-4 by RT-PCR, in contrast to what was seen in HCV from supernatant (Fig1b).

Conclusion: We were able to confirm the presence of HCV RNA methylation in clinical HCV samples. Glycoprotein E1 was methylated in all plasma samples from G1-4, whereas results from JFH1 (RT-PCR and Me-RIP) showed methylation of only intracellular RNA, suggesting that E1 methylation prevents particle production. Further studies will focus on specific sites of methylation in E1 to understand the apparent discrepancy between results using JFH1 and clinical samples.

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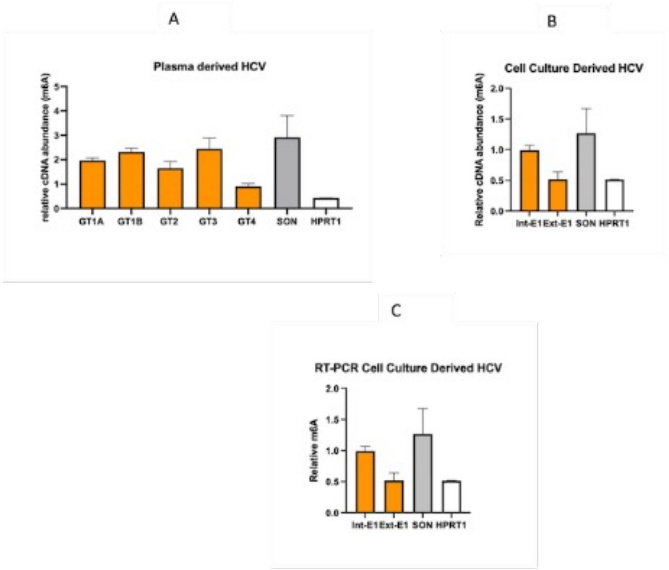

Figure 1. Relative detection and quantification of m6A sites in glycoprotein envelope E1 in HCV. A. m6A detection in E1 from plasma derived viral RNA of clinical HCV samples. B. m6A detection in E1 from intracellular (Int) RNA and extracellular (Ext) RNA from cell culture derived virus (JFH-1) compared to positive SON and negative control HPRT1. C. Detection of Methylation from JFH-1 by MeRIP, HCV RNA was isolated and pulled down by anti-m6A or IgG. Recovered RNA was quantified by qPCR and is reported as a % of input RNA showing methylation of HCV RNA in the E1 regions. Representing genotypes GT1A,1B,2,3 and 4. n=3 replicas

Disclosure of Interest: None Declared

O02

EVALUATION OF HEPATITIS C VIRUS TRANSMITTED/ FOUNDER VARIANTS OBTAINED FROM OBSERVED HCV INFECTION THROUGH LUNG TRANSPLANTATION FROM HCV-INFECTED DONORS TO UNINFECTED RECIPIENTS

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Background: In contrast to the large diversity seen in chronic Hepatitis C virus (HCV) infection, samples taken from acute HCV infection have shown only a small number of viral lineages, suggesting the presence of a limited number of Transmitted/Founder (T/F) variants that are able to efficiently expand and establish infection in a new host. Characterization of T/F variants in HCV infection has been limited due to the difficulty of obtaining samples from early HCV infection and in identification of the donor virus. Using samples from lung transplant recipients who received organs from HCV-infected donors, we evaluated the presence of T/F variants in observed HCV infection.

Aims: To compare viral diversity in donors and recipients and evaluate sequence-dependent functional characteristics of founders compared to non-founder populations

Methods: Using Illumina MiSeq, 250bp reads we obtained the sequences of donors and their respective recipients from day 7 post-transplant. ShoRAH, a bioinformatics tool used for haplotype reconstruction, was then used to identify haplotypes in the Core-E2 region of one recipient/donor pair RA/DA. We used maximum likelihood phylogenetic trees (PhyML) to identify founders and non-founders and used Highlighter plot to compare silent and non-silent mutations in founders and non-founders.

Results: In HVR1, non-synonymous mutations were more frequent in non-founders than founders from the DA population. Selection of hydrophobic and basic residues especially in position 3 (R/H) was seen in founders, which aligns with non-selection acidic residue (Q), which was enriched in the of non-founders in the DA population (fig.1). Previous reports have indicated that HVR1 position 3 is almost always hydrophobic and basic (R/H) which allows it to interact with different host molecules involved in entry.

Conclusion: Our preliminary data show that at the time of transmission, there exists a decrease in population diversity and selection of founder variants for their enhanced infectivity and absence of non-founder variants that may be less fit at establishing infection, as evidenced by the transmission of HVR1 variant with basic residues at position 3 and the absence of variants with acidic residues in our lung transplant RA. More analysis is in progress to track founder evolution in longitudinal recipient samples and assess functional characteristics in vitro.

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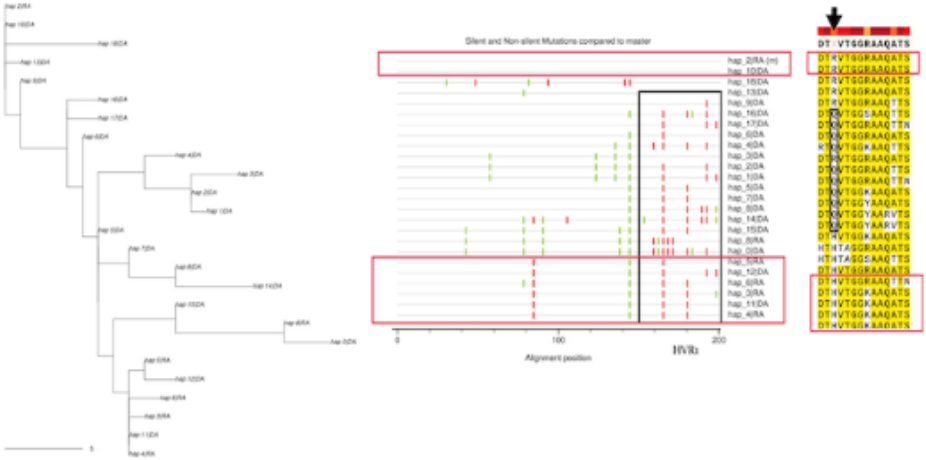

Figures 1. A. Maximum likelihood phylogenetic tree (PhyML) of haplotypes in E1-E2 region in RA and DA. B. Highlighter plot showing silent (green) and non-silent(red) mutations in aligned DA and RA haplotypes. Red boxes represent the dominant haplotype in RA and DA and black box indicates increase of mutations especially non-silent in HVR1 region. Alignment of translated HVR1 shown on the right indicating non silent mutation in position 3 in 10 donor haplotypes (boxed in black) which are absent from all RA haplotypes including the dominant RA and DA haplotypes (boxed in red)

Disclosure of Interest: None Declared

O03

VIROLOGICAL CHARACTERIZATION OF TREATMENT FAILURES AND RETREATMENT OUTCOMES IN PATIENTS INFECTED WITH "UNUSUAL" HCV GENOTYPE 1 SUBTYPES

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Introduction: Among the so-called "unusual" HCV genotypes, genotype 1, non-1a/1b subtypes are common in patients of African origin. Among them, GT-1l has recently been suggested to be less responsive to NS5A inhibitor-containing regimens than GT-1a or GT-1b. Here, we used shotgun metagenomics based on deep sequencing and/or Sanger sequencing to characterize amino acid substitutions present at baseline and selected by DAA therapy in regions targeted or not targeted by DAAs in non-1a/1b subtypes infected patients who failed to achieve SVR.

Methods: Sequence determination was based on Sanger sequencing, deep sequencing, or both, according to the availability of the methods upon reception of the samples. Deep sequencing was performed by means of NextSeq500 (Illumina). Full-length HCV sequences were analyzed using our original in-house MetaMIC® software (1% cutoff).

Results: Among 640 patients with HCV infection treated with an NS5A inhibitor-containing regimen who experienced a virological failure, 285 (44.5%) were infected with GT-1, and 47 of them (7.5%) with "unusual" GT-1 subtype, including: 1d (n=8), 1e (n=13), 1f (n=1), 1g (n=2), 1i (n=2), 1k (n=1), 1l (n=18) and 1-undetermined (n=2). 41/44 (93.2%) were born in Africa. Treatment regimens were NS5B inhibitor + NS5A inhibitor (80.9%), NS3 protease inhibitor + NS5A inhibitor (9.1%), NS3 protease inhibitor + NS5A inhibitor + NS5B inhibitor (4.3%). At baseline, in the NS5A region, 2 to 4 polymorphisms known to be associated with reduced susceptibility to NS5A inhibitors were present as dominant species (>99%) by deep sequencing in 5 patients, including 3 infected with GT-1l and 2 with GT-1e. The most frequent polymorphisms were K24G/R, L31M, H58P and A92T. At treatment failure, 35/36 (97%), 30/36 (83.3%), 16/36 (44.4%) and 4/36 (11.1%) patients harbored 1, 2, 3 or 4 NS5A RASs, respectively. The majority of patients harbored NS5A RASs at positions L31, H58 and Y93. One NS5B polymerase RAS (C316Y) was present at failure in a GT-1e-infected patients who received dasabuvir. All patients treated with a triple combination of DAAs or with the combination of glecaprevir and pibrentasvir achieved SVR.

Conclusion: We report the largest cohort of patients infected with "unusual" GT-1 subtypes failing DAAs thus far. The large number of NS5A RASs present at baseline explains lower SVR rates with NS5A inhibitor-based therapies in these patients. Our results emphasize the need for identifying this subtype and other "unusual" subtypes (e.g. GT-4r) in Africa where they are common, and the urgent need to guarantee equal access to last-generation DAA therapies in Africa.

Disclosure of Interest: None Declared

O04

A STEP-WISE ADAPTATION OF HEPATITIS C VIRUS LEADS TO A HIGH RATE OF INFECTION IN PRIMARY MOUSE HEPATOCYTES.

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Background and Aims: HCV is well adapted to its host, in such a way that only Humans and Chimpanzees hold a robust infection. Cross-species transmission is limited by host factor incompatibilities and restriction factors. However, HCV replication is error-prone giving rise to a vast spectrum of variants, facilitating viral adaptation to changing environments. Herein, we exploited this property for the adaptation and generation of a virus population with high replication fitness in primary mouse hepatocytes (PMH) and improved in vivo infection.

Method: We first adapted HCV through several steps including, culturing the virus between human (Huh-7.5) and mouse liver cells expressing HCV entry factors (MLT-5H). Eventually we passaged the virus to primary mouse hepatocytes (PMH) from entry factor transgenic mice with blunted IFN signalling (hOC^{hep} $IFN^{-/-}$). The replication kinetics of the final viral population (Mouse adapted HCV; MadHCV) and a clone derived from the population were compared to its parental virus in mouse and human cells. Finally, The MadHCV clone was used to infect hOC^{hep} $IFNAR^{-/-}$ mice.

Results: The HCV adaptation led to increased infectious virus release in the MLT-5H and hOC^{hep} $IFNAR^{-/-}$ PMH by more than 3 logs compared to the parental virus. In contrast, infection of primary human hepatocytes, human pluripotent stem cell-derived hepatocytes, and primary macaque hepatocytes remained similar to parental HCV. This suggested that adaptation was specific to mouse and did not compromise fitness in human cells. The MadHCV population remained susceptible to telaprevir and interferon and depended on the expression of human hCD81 and hOccludin for infection. The MadHCV clone had similar replication and infection kinetics to the population, but an increased susceptibility to neutralisation. However, exchanging the coding region of the E1/E2 proteins back to the parental sequence (MadHCV-WTE1E2) reverted the neutralisation properties without losing infectivity. Finally, in vivo inoculation rendered several mice with detectable viremia 4 weeks after inoculation. Infection efficacy was higher for MadHCV-WTE1E2 than MadHCV. Correlating with this difference, only inoculation of MadHCV-WTE1E2 induced detectable HCV antibody responses in the blood plasma.

Conclusion: This step-wise adaptation has enabled us to broaden the HCV tropism to infect human entry factor transgenic mice with blunted IFN signalling. The MadHCV clones provide new opportunities for development of an immune competent mouse model for HCV, which in turn should facilitate HCV vaccine research and development.

Disclosure of Interest: None Declared

O05

COMPARISON OF HAV AND HCV INFECTIONS IN VIVO AND IN VITRO REVEALS DISTINCT PATTERNS OF INNATE IMMUNE EVASION AND ACTIVATION

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Background: Despite strong similarities in terms of biology and replication, Hepatitis A (HAV) and Hepatitis C (HCV) viruses cause opposing infection outcomes. Previous reports show that HAV does not induce an innate immune response in infected chimpanzees, in contrast to HCV (Lanford et al., 2011). This lack of response has been imputed to strong counteraction by HAV proteases 3CD and 3ABC (Yang et al., 2007; Qu et al., 2011).

Purpose: In order to solve the controversy in literature, we aimed at elucidating in vivo and in vitro the mechanisms of induction and counteraction of innate immunity by HAV and HCV.

Methods: Looking for an in vivo model allowing a side-by-side comparison of the virus interplay with the host innate immune response, we infected uPA-SCID mice with humanized liver with HAV and HCV. We then moved to appropriate cell culture models, in order to inquire how efficiently HAV and HCV were sensed by the endoplasmic Toll-Like-Receptor 3 (TLR3) and the cytoplasmic Rig-I-Like-Receptors (RLRs) RIG-I and MDA5. Furthermore, we investigated potential hindering of these pathways by HAV and HCV, detecting proteolytical cleavage of the TLR3 adaptor TRIF and the RLR adaptor MAVS, through transient and stable expression of HAV and HCV viral proteases.

Results: We detected similar levels of Interferon stimulated genes (ISGs) induction in hepatocytes of HAV and HCV infected human liver chimeric mice. In cell culture, HAV induced ISGs exclusively upon sensing by MDA5 and dependent on LGP2. TRIF and MAVS were only partially cleaved by HAV 3ABC and 3CD, not sufficiently to abrogate signalling. In contrast, HCV NS3-4A efficiently degraded MAVS, as previously reported, whereas TRIF was not cleaved.

Conclusion: We show that HAV induces an innate immune response in hepatocytes via MDA5/LGP2, with limited control of both pathways by proteolytic cleavage. HCV activates TLR3 and lacks TRIF cleavage, suggesting that this pathway mainly contributes to HCV induced antiviral response in hepatocytes. Our results shed new light on induction and counteraction of innate immunity by HAV and HCV and their potential contribution to clearance and persistence.

Disclosure of Interest: None Declared

O06

RISING TREND OF SYMPTOMATIC INFECTIONS DUE TO HEPATITIS A VIRUS INFECTION IN ADOLESCENT AND ADULT AGE GROUP: AN OBSERVATIONAL STUDY FROM A TERTIARY CARE LIVER INSTITUTE IN INDIA

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Background: Hepatitis A virus (HAV) is the most common cause of acute viral Hepatitis (AVH) in children and is hyper endemic in India. It causes self-limiting illness and rarely acute liver failure (ALF) especially in adults. There is a definite shift in clinical presentation and age of occurrence in low income countries in the last decade.

Purpose: To find out the incidence, clinical presentation and outcome of HAV infection in both pediatric and adult age group.

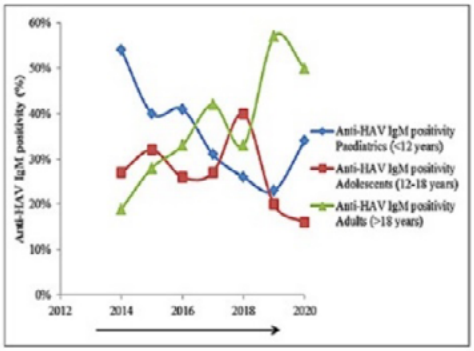
Methods: In this retrospective study data search was done from January 2014 to December 2020 of 10,717 cases of AVH described by acute onset and 4 times the upper limit of normal levels of serum ALT. HAV infection was detected by Anti-HAV IgM positivity.

Results: Confirmed HAV infection was seen in 748 (7%).Out of them symptomatic cases requiring hospitalization were 410(55%). Males were more as compared to females; 2.6: 1 and median age of infection was 15(IQR: 9-21) years. Out of 410 cases 272(66%) were AVH and 138 were ALF (34%) as per clinical criteria. We divided all the cases into 3 age-groups: pediatric (<12 years), adolescent (12-18 years) and adults > 18 years. AVH occurrence was seen equal amongst all the 3 age-groups: 94, 34% pediatric; 89,33% adolescent and 89,33% adults (p value = 0.43). Occurrence of HAV related ALF was significantly more in adults : 43,31% pediatric; 43,31% adolescent and 52,38% adults(p value 0.02).Mortality was seen in 24 (6%) which was much higher in ALF 23,96% cases and in the adult age group: 10,44%(p value = 0.001). Overall total bilirubin levels were 8.9(IQR: 5.7-22.5)mg/dl. In pediatric it was: 7.3(4.7-19.2) mg/dl, in adolescent 7.4(5.3-21.1) mg/dl and in adults 12.5(6.7-27.6)mg/dl. ALT levels were overall 1016(217-2222) IU/L: in pediatric 968(389-2018) IU/L, adolescent : 1133(236-2353) IU/Land in adults 1002(118-2459)IU/L.

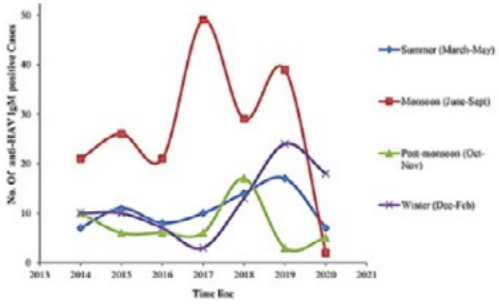
HAV IgM positivity in pediatric age group was 35.5(23-54)% ,adolescents 26.8(16-40)% while in adults it was 37.4(19-57)% and showed a rising trend of positivity on year wise comparison(Figure 1) . Looking at the seasonal trend, infection was predominantly seen during the post-monsoon season (June to September) across all the age groups (Figure 2).

Conclusions: Symptomatic cases of HAV infection in adults are rising and are associated with ALF and high mortality in low income countries like India. High degree of suspicion in adult ALF cases for HAV infection should be there and transplant options should be offered earlier.

Image/Table:



Rising trend of HAV IgM antibody positivity



Seasonal trend of HAV infection

Disclosure of Interest: None Declared

O07

HIGH HCV INCIDENCE IS ASSOCIATED WITH SOCIAL AND SPATIAL NETWORK STRUCTURES AMONG PEOPLE WHO INJECT DRUGS IN NEW DELHI

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Background: People who inject drugs (PWID) account for some of the fastest growing HCV epidemics globally. While individual risk factors for infection are well understood, less is known about network and spatial factors.

Methods: 2512 PWID in New Delhi, India were recruited (2017-20) into a cohort using a network referral approach. Index participants were asked to name and recruit people they injected with in the past month (egocentric network of the index). Each recruit was asked to name and recruit their recent injection network members (egocentric network of recruit; sociometric network of index). Biometrics were used to identify duplicates and cross-network linkages. Participants underwent a survey and blood draw semi-annually. Blood was tested for HCV antibodies and HCV RNA. Network analyses and Poisson regression were used to identify predictors of incident HCV.

Results: Baseline HCV RNA+ prevalence was 46.8%.Before the study was paused in March 2020 due to COVID-19, we observed 92 HCV seroconversions over 382.25 person-years of follow-up, equating to an incidence rate of 24.1 cases per 100 person-years (95% CI: 19.6 – 29.5). Individual-level factors significantly associated with incident HCV included age, sexual activity, needle sharing, and injection frequency (Table). Of the 92 incident HCV infections, 67% (62) were directly connected to at least one HCV RNA+ person, and all 92 were within one degree of separation of an HCV RNA+ person. Participants with incident HCV reported injecting at 140 unique injection venues. The median number of venues participants reported injecting at in the 6 months prior to seroconversion was 3 (IQR: 2 – 5.5). We found the majority of incident infections reported injecting at two particular venues, geographically adjacent to one another; 45% (41) reported injecting at venue #40 and 32% reported injecting at venue #39. Incident HCV infections were also significantly clustered by network community and had significantly higher degree and betweenness. Even after accounting for individual risk factors, HCV incidence was significantly associated with the number of HCV RNA+ alters (adjusted incidence rate ratio [AIRR] = 1.30) and injecting at venue #40 (AIRR = 2.53). This spatial association extended out to indirect ties, with 17% reduced odds of incident HCV for each additional person separating a participant from venue #40 (AIRR = 0.83).

Conclusions: We observed a fast-growing HCV epidemic driven by viremia not only within egocentric but also sociometric and spatial networks, highlighting the importance of achieving broad SVR and expanding “treat a friend” approaches to key venues. Expanding treatment and prevention efforts in PWID populations is critical for epidemic control.

Image/Table:

Table. Risk factors for HCV incidence by multivariable Poisson regression.

Factors Associated with Incident HCV	Univariable Model IRR (95% CI)	Multivariable Model 1 AIRR (95% CI)	Multivariable Model 2 AIRR (95% CI)	Multivariable Model 3 AIRR (95% CI)	Multivariable Model 4 AIRR (95% CI)	Multivariable Model 5 AIRR (95% CI)
Age (per 5-year increase)	0.74 (0.66 – 0.84)	0.78 (0.69 – 0.88)	0.77 (0.68 – 0.87)	0.77 (0.68 – 0.87)	0.75 (0.66 – 0.85)	0.76 (0.67 – 0.86)
Sexual Activity (vaginal or anal sex in prior 6 months)	0.48 (0.31 – 0.75)	0.56 (0.36 – 0.89)	0.58 (0.37 – 0.91)	0.58 (0.37 – 0.91)	0.62 (0.39 – 0.97)	0.59 (0.36 – 0.93)
Shared Syringes (prior 6 months)	3.72 (2.17 – 6.37)	2.38 (1.35 – 4.18)	2.49 (1.41 – 4.39)	2.46 (1.39 – 4.35)	2.22 (1.27 – 3.87)	2.35 (1.34 – 4.13)
Injection Frequency (per 50 injections in prior 6 months)	1.09 (1.06 – 1.12)	1.07 (1.04 – 1.11)	1.07 (1.04 – 1.11)	1.07 (1.03 – 1.11)	1.06 (1.03 – 1.10)	1.06 (1.03 – 1.10)
Number Actively Infected Injection Partners (HCV RNA-positive)	1.18 (0.93 – 1.50)	-	1.30 (1.02 – 1.66)	1.19 (0.85 – 1.67)	-	-
Network Distance from an Actively Infected participant (HCV RNA-positive)	0.78 (0.56 – 1.09)	-	-	0.85 (0.56 – 1.28)	0.77 (0.56 – 1.05)	0.82 (0.59 – 1.13)
Injecting at a Venue #40	2.64 (1.75 – 3.98)	-	-	-	2.53 (1.66 – 3.85)	-
Network Distance from Venue #40	0.87 (0.77 – 0.99)	-	-	-	-	0.83 (0.73 – 0.94)

Note: Columns represent a regression and depict the adjusted incidence rate ratio (AIRR) and 95% confidence intervals for the included variables. A dash signifies that the variable was not included in the model for that column.

Disclosure of Interest: None Declared

O08

AN UNEXPECTEDLY HIGH HEPATITIS C VIRUS PREVALENCE IN SOUTHERN LAOS LED TO THE IDENTIFICATION OF RISK PRACTICES AND SUGGESTED THAT EXTENSIVE TESTING AND TREATMENT ARE REQUIRED

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Abstract Content: There are only few studies that describe the epidemiology of Hepatitis C virus (HCV) infection in the Lao People's Democratic Republic (PDR). A study in blood donors in 2003-2005 found an HCV prevalence of 1.1%(Jutavijittum et al.,2007). Studies in healthcare workers and garment factory workers reported that 3.9% and 2% had anti-HCV antibodies, respectively (Black et al.,2015; Xaydalasouk et al.,2018). The studies were primarily conducted in Central Lao PDR, with the exception of the study in healthcare workers, which also included a Northern province. We used samples from a cross-sectional, hospital-based study conducted in 2017-2019 in Saravan province(Xaydalasouk et al.,2021) to investigate the prevalence of HCV infection. Saravan is located in the South and characterized by a largely rural population, ethnic diversity and poor health indicators.

For the original study, participants aged 5-90 years were asked to participate during hospital visits. After informed consent, blood samples were taken. Left-over samples were tested for anti-HCV antibodies by ELISA. Positive samples were subjected to reverse transcription PCR to obtain sequences for phylogenetic analyses.

Among 753 samples, 11.7% were positive for HCV antibodies. The HCV seroprevalence was higher in participants >30 years ($p<0.001$), married participants ($p=0.04$) and in those practising animism ($p=0.02$). Participants from the Pako ethnic group were more likely to be positive ($p<0.001$). The Pako make up most of the population in Samuoi district, where the HCV prevalence was the highest (24.4%). Sequencing data showed considerable diversity within genotype 6.

Our results indicated that a high proportion of the population living in Saravan could face liver-related complications and suggested that an investigation into risk-practices was needed. Therefore, we conducted a follow-up study in Samuoi district in 2022. In total, 402 participants were recruited (160 HCV infected cases and 242 controls; age-matched $\pm$5 years).

Among the cases, 58.8% had detectable viral load. These participants were referred to the district hospital for clinical assessment and treatment. While the prevalence of some risk factors, such as tooth filing was relatively low (9.5%), more than half (58.0%) of the participants stated to have received parenteral medicine, and among those, 72% reported re-use of syringes. Tattooing was frequent (33.1%) and associated with having higher odds for being positive (adjusted odds ratio (aOR)=1.8(95% CI 1.2-2.8); $p=0.01$). In addition, accidental blood exposure for example when assisting people during accidents was also associated with HCV seropositivity (aOR=1.9(1.2-2.9); $p<0.01$).

We identified an unexpectedly high HCV prevalence in Southern Lao PDR and associated risk factors. Our findings underline that the HCV epidemiology in the Lao PDR is not yet well-understood and that extensive community-based testing for exposure and ongoing infection and treatment for HCV are warranted.

Disclosure of Interest: None Declared

O09

PREDICTION OF HBV-RELATED CIRRHOSIS COMPLICATIONS WITH MACHINE LEARNING ALGORITHMS USING ELECTRONIC HEALTH RECORDS

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Background: There is still a significant prevalence of chronic Hepatitis B (CHB) infection in Taiwan. Many of these patients further develop liver cirrhosis which can be irreversible and life-threatening. While decompensated cirrhosis greatly increases the burden of disease for patients, it can be effectively prevented with timely interventions and disease management.

Purpose: In this study, we aim to establish a prediction model for predicting decompensation in patients with CHB-related cirrhosis and to identify useful signals that can aid in clinical decision-making.

Methods: Using retrospective data from electronic health records (EHRs) of CHB patients with cirrhosis between 2003-2017 at a medical center in central Taiwan, we adopted machine learning techniques to construct and train decompensation prediction models. Out of 5,125 cirrhosis patients, 3,330 were included in the final training dataset. We excluded those under age of 20 and with insufficient data from blood tests (alanine transaminase (ALT), aspartate aminotransferase (AST), total bilirubin, albumin, prothrombin time (PT) etc.) and antiviral treatment (lamivudine (LAM), entecavir (ETV)) which we used as model features. Complications measured were ascites, variceal bleeding, jaundice, hepatic encephalopathy, spontaneous bacterial peritonitis, hepatorenal syndrome, and hepatocellular carcinoma. They were considered individually and collectively in the prediction models. Ten-fold cross-validation was performed to enhance the performance of our models.

Results: We used support vector machine (SVM), logistic regression (LR), decision tree (DT), and random forest (RF) algorithms to detect incident decompensation. Of all models, the LR model that predicts ascites in patients under ETV therapy gave the best results, with an area under receiver operating characteristic (AUROC) of 0.93 (95% confidence interval (CI): 0.86-0.99), and an accuracy of 0.88. Total bilirubin, albumin, and PT were the most significant among the ten examined features. For patients under LAM treatment, our RF model was able to predict jaundice with an AUROC of 0.91 (95% CI: 0.80-0.99) with an accuracy of 0.87. In patients with multiple complications, our SVM model was able to achieve AUROC of 0.85 (95% CI: 0.77-0.93) and an accuracy of 0.77.

Conclusions: Our machine learning algorithms demonstrated acceptable performance for predicting ascites, jaundice, and multiple complications in patients with CHB-related cirrhosis. Results of this study may provide important information as to which patients are likely to advance to decompensated cirrhosis, potentially enabling clinicians to intervene in time.

Disclosure of Interest: V. C.-R. Hsieh Grant / Research support from: This study is supported by grants: MOST 107-2314-B-039 -065-MY3 and MOST 110-2410-H-039-003., M.-Y. Liu: None Declared, H.-C. Lin: None Declared

O10

SPATIAL TRANSCRIPTOMICS REVEALS WIDESPREAD INTRAHEPATIC HEPATITIS B VIRUS INTEGRATION IN CHRONIC INFECTED PATIENTS

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Background & Aim: Hepatitis B virus (HBV) can integrate into the chromosomes of infected hepatocytes, contributing to oncogenesis and the production of Hepatitis B surface antigen (HBsAg). In this study, we aimed to explore whether HBV integration events could spread throughout the liver tissue in different phases of chronic HBV infection and their correlation with clinical characteristics.

Methods: We constructed high-resolution spatial transcriptomes of liver biopsies containing 13,059 tissue spots from 18 patients with chronic HBV infection to analyze the occurrence and relative distribution of transcriptionally active viral integration events.

Results: Spatial transcriptome sequencing identified the presence of 13,154 virus-host chimeric reads in the liver biopsies of all patients, including three patients who achieved HBsAg seroclearance. These HBV integration sites were randomly distributed on chromosomes and could localize in host genes involved in hepatocarcinogenesis, such as ALCAM, MBL2, and SH2D5. HBV integration events could be detected in 7.85% (1,026 of 13,059) of tissue spots. Patients who were receiving or had received antiviral treatment had a significantly lower percentage of spots with viral integration and significantly fewer chimeric reads compared with treatment naïve patients. Besides, HBeAg-positive patients tended to have higher levels of viral integration.

Conclusions: Transcriptionally active HBV integration occurred in different phases of chronic HBV infection, including in patients with limited HBV reservoirs. HBV could integrate into cancer-related genes, and antiviral treatment may reduce the number and extent of viral integrations.

Disclosure of Interest: None Declared

O11

HEPATITIS B SURFACE ANTIGEN KINETICS DURING AND AFTER NUCLEOS(T)IDE ANALOGUES DESCRIBED BY MATHEMATICAL MODELING

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Abstract Content:

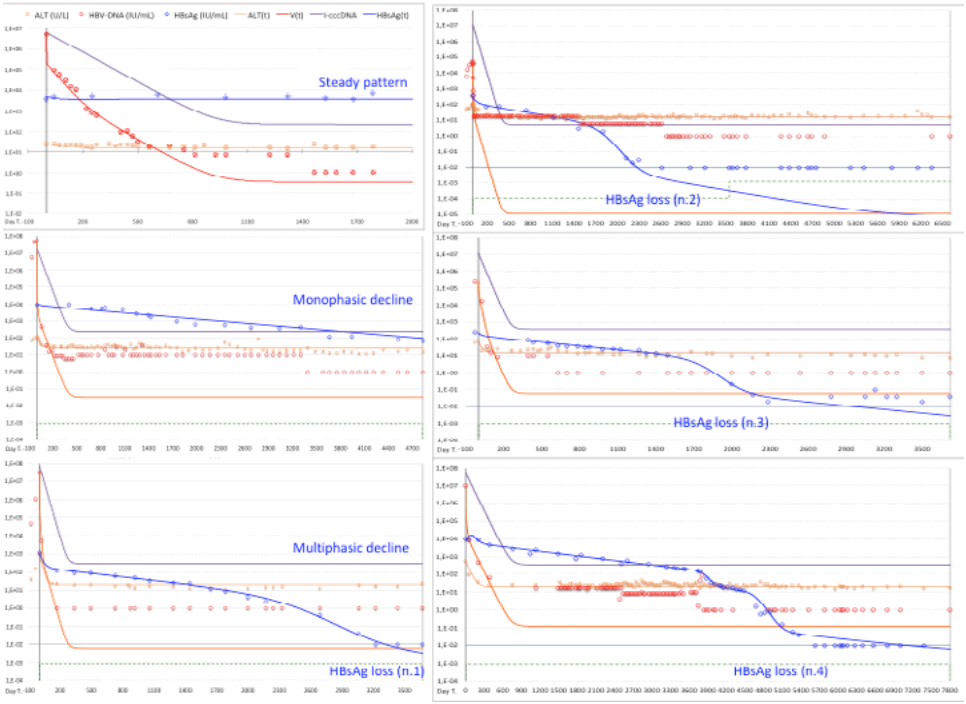
Background: HBsAg clearance (functional cure) is the optimal endpoint of chronic Hepatitis (CHB) treatment. Nucleo(s)tide analogues (NAs) have a limited impact on HBsAg serum levels (HBsAgsl), however achieving low HBsAgsl during treatment correlates with HBsAg loss after discontinuation (DC). We studied on therapy HBsAgsl kinetics to uncover the mechanisms underlying its decline that may help to predict functional cure at the individual level.

Methods. We set up a mathematical model to describe by ordinary differential equations the: 1) dynamics of replication competent infected hepatocytes (with cccDNA >1 copy) producing HBsAg by either cccDNA or integrated DNA (intDNA); 2) cccDNA turnover; 3) dynamics of not replication competent infected hepatocytes (which lost cccDNA by cell division) still producing HBsAg by intDNA. Baseline (BL) infected cells (I0-cccDNA) and their immune mediated clearance rate were determined according to our previous model upon NAs block of HBV replication. The cccDNA lifetime was computed by fitting ALT, HBV-DNA and HBsAgsl. HBsAg production rate constants by I0-cccDNA and I0-intDNA, BL I0-intDNA and their lifetime by fitting HBsAg only. We applied the model in 31 pts: 29 HBeAg-neg and 2 HBeAg-pos at BL, median age 56.1y (range 30-76.6), 21 (65.6%) males, and 17 (54.8%) with liver cirrhosis. Median NAs treatment was 123.1 months (range 41.2-260.1). HBV-DNA was tested by COBAS TaqMan assay (Roche) and HBsAg by Architect HBsAg assay system (Abbott).

Results. HBsAgsl during NAs therapy showed 3 major patterns: steady (S=3), monophasic (M1=18) and multiphasic (M2=10) decline. Mean ALT at BL were lower in M1 than M2 (121±95 vs 666±565 U/L, p=0.0004), as well as HBsAgsl (4,421.9±2,876,2 vs 18,846.8±22,861.3 IU/mL, p=0.0272). Overall, 6 (19.4%) pts lost HBsAg: 5 (17.2%) HBeAg-neg (4 during NAs, 1 after DC) and 1 (50%) HBeAg-pos (after DC). All pts who lost HBsAg had a multiphasic decline. The model fitted HBsAgsl in all pts with each pattern (Figure). $I_{0\text{-}cccDNA}$ were lower in M1 than in M2 pts (22.0%±15.4% vs 54.8%±27.3%, p=0.0159), as well as the proportion of BL HBsAg produced by cccDNA (1.7%±2.3 vs 53.3%±27.3%, p<0.0001). The cccDNA lifetime was similar in M1 and M2 pts (52±52 vs 31±14 days, p=0.2288), whereas I_{intDNA} lifetime was longer in M1 than M2 pts (3,938±2,681 vs 1,340±875 days, p=0.0065). All pts who lost HBsAg during NAs had accelerations of HBsAg decline preceding clearance.

Conclusions. Mathematical modeling showed that faster HBsAg decline after NAs was associated with higher disease activity and prevalent HBsAg production from cccDNA, whose lifetime was shorter than that of intDNA. HBsAg loss was characterized by multiphasic declines during NAs therapy.

Image/Table:



Disclosure of Interest: P. Colombatto Conflict with: AbbVie, L. Civitano: None Declared, B. Coco: None Declared, D. Cavallone: None Declared, F. Oliveri: None Declared, G. Ricco: None Declared, M. Santucci: None Declared, F. Damone: None Declared, V. Romagnoli: None Declared, A. Salvati: None Declared, L. Surace: None Declared, P. Bleve: None Declared, F. Bonino: None Declared, M. Brunetto Conflict with: Gilead, Janssen, Speakers bureau of: Abbvie, Gilead, Janssen, EISAI-MSD, Roche

O12

THE LONG-TERM PROGNOSIS AND THE NEED FOR HISTOLOGIC ASSESSMENT IN CHRONIC HEPATITIS B IN SEROLOGICAL IMMUNE-TOLERANT PHASE

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Abstract Content: Background/Aims: The effect of histologic status of immune-tolerant (IT) phase of chronic Hepatitis B on long-term outcomes is yet unclear. The aim of this study is to find out how well serological criteria currently used corresponds to the histologic criteria in determining IT phase and to suggest the indication for liver biopsy.

Methods: Patients in serological IT phase, defined by criteria of positive Hepatitis B e antigen, HBV-DNA $\geq 10^6$ IU/mL and normal or minimally elevated alanine aminotransferase (ALT) $\leq$ 60 IU/L, who underwent liver biopsy at three different hospitals were included. The distribution of histologic IT phase, defined as fibrosis of stage 1 or less and inflammation of grade 1 or less, was compared with that of serological IT phase. The risk factors for the incidence of liver-related events, such as hepatocellular carcinoma, liver cirrhosis, liver transplantation and death, were also analyzed.

Results: Eighty-two (31.7%) out of 259 clinically suspected IT phase patients belonged to histologic IT phase. Age over 35, high AST and low albumin were useful for ruling out histologic IT phase. Risk factors predicting liver-related events were age and significant fibrosis stage. There was no significant difference in the proportion of histologic IT phase and clinical prognosis between normal ALT and mildly elevated ALT groups. However, even in patients with normal ALT, age was an important factor in predicting the presence of histologic IT phase.

Conclusions: A significant number of patients who belonged to serological IT phase were not in histologic IT phase. Patients over 35 years and those with high AST, low albumin and low HBV DNA levels were more likely to experience poor long-term clinical outcomes. Therefore, additional histologic assessment should be considered.

Disclosure of Interest: None Declared

O13

SWITCHING TENOFOVIR DISOPROXIL FUMARATE (TDF) TO TENOFOVIR ALAFENAMIDE FUMARATE (TAF) IN HEPATITIS B/HIV CO-INFECTION: A FEASIBILITY STUDY

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Abstract Content: Background: Tenofovir alafenamide (TAF) delivers the active metabolite more efficiently to target cells compared with the original prodrug (tenofovir disoproxil fumarate, TDF) and has a more favourable side-effect profile. Recent studies suggest that TAF is highly efficacious in HBV/HIV co-infection and may have superior effects on HBV suppression; however, few studies have explored the safety and efficacy of switching between different tenofovir formulations in this population.

Purpose: This open-label study (IN-UK-311-3056) explored the feasibility of switching from TDF to TAF in HBV/HIV co-infection.

Methods: The study was conducted at two centres in the United Kingdom, namely King's College Hospital and Chelsea & Westminster Hospital. Co-infected individuals on stable TDF-based antiviral therapy for the previous twelve months were eligible to take part. All participants recorded undetectable viral levels (HIV RNA, HBV DNA) at their screening visit and were converted to a TAF based treatment regimen (TAF + emtricitabine + third agent) for 48 weeks. The primary endpoint was the feasibility of this approach, as determined by safety parameters, tolerability and study retention rates. Secondary endpoints included the emergence of detectable HBV (DNA $\geq$20 IU/ml) or HIV viremia ($\geq$40 copies/ml), as well as the trajectory of renal function, bone mineral density and viral biomarkers. Clinical review, venepuncture and urinalysis were performed at baseline, weeks 4, 12, 24 and 48.

Results: Twenty-seven individuals were invited to take part in the screening process; three met the exclusion criteria and a further four withdrew consent prior to enrolment. The remaining participants were predominantly male (70%), non-cirrhotic (95%) and of Afro-Caribbean ethnicity (60%). All were co-infected with HIV-1 and established on long term antiretroviral treatment prior to enrolment (median 6.5 years). One individual withdrew from the study at week 24, but the remaining participants (95%) completed 48 weeks of follow-up. No adverse or serious adverse events related to the study drug were observed. Most patients (18/19, 94.7%) maintained undetectable HIV RNA and HBV DNA throughout the follow-up period, with one individual achieving HBsAg seroconversion (from a screening HBsAg titre of 680.81 IU/ml). By week 48, there was a significant increase in HDL cholesterol levels (p=0.001) but no change in LDL cholesterol (p=0.218), estimated glomerular filtration rate (p=0.588) or bone mineral density (p=0.472 at hip).

Conclusion: Switching from TDF to TAF in HBV/HIV co-infection appears safe, well tolerated and maintains virological suppression. Further studies are needed to confirm these findings in larger, multi-ethnic populations.

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O14

EARLY OFF-TREATMENT KINETICS OF VIRAL AND HOST BIOMARKERS AFTER DISCONTINUATION OF NUCLEOS(T)IDE ANALOGUES AMONG CHRONIC HEPATITIS B PATIENTS (RETRACT-B STUDY)

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Abstract Content: Background: While discontinuation of nucleos(t)ide analogues (NAs) among chronic Hepatitis B (CHB) patients may be beneficial for specific patient groups with respect to functional cure or HBsAg loss, characteristics and early off-treatment kinetics of biomarkers among patients who remain off-treatment without HBsAg loss have not been well characterized. We aim to describe this group and analyze early off-treatment kinetics.

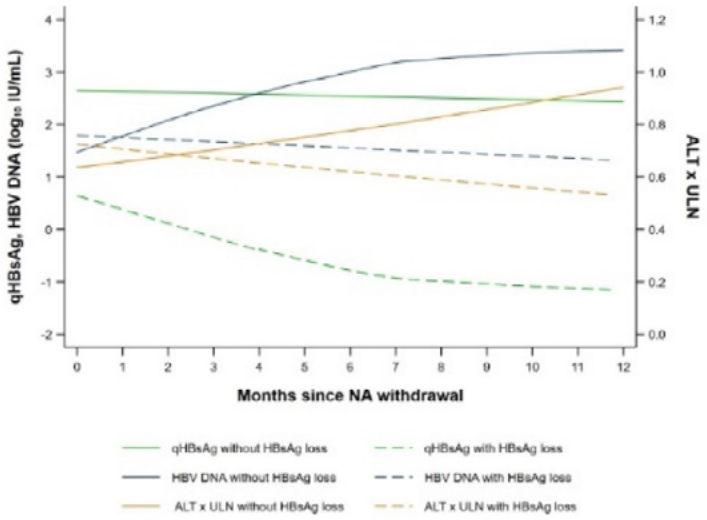
Methods: Cohort study of CHB patients who were virally suppressed, non-cirrhotic and HBeAg negative at NA discontinuation. Patients with coinfection, prior interferon therapy, or prior HCC diagnoses were excluded. Mixed-effects regression was used to analyze HBsAg, HBV DNA, and ALT kinetics among patients who remained off-treatment at the end of 1 year; only patients with follow-up $\geq$1 year were included.

Results: Among 804 patients (mean age 52$\pm$12 years, 71% male, 84% start of NA HBeAg negative), 29 (3.6%) achieved HBsAg loss and 775 (96%) remained off-treatment without HBsAg loss at 1 year. Patients with HBsAg loss (vs without) had a higher proportion of Caucasians (vs Asians) (31% vs 8.3%, p<.001), tenofovir-treated patients prior to cessation (vs entecavir-treated) (50% vs 32%, p=.04), and lower median HBsAg at end of treatment (0.4 [-0.6-1.6] vs 2.7 [2.2-3.1] $\log_{10}$IU/mL, p<.001). Median ALT at end of treatment among the whole group was 0.6x ULN (0.4-0.8). Patients with HBsAg loss showed a rapid decline in mean HBsAg in the first 6 months while those without HBsAg loss showed a modest decrease. There was a decreasing trend in mean HBV DNA among patients with HBsAg loss while HBV DNA increased steadily for the first 6mos among those without HBsAg loss; however, it stabilized thereafter. Patients with HBsAg loss (vs without) had a lower proportion of virological relapses (HBV DNA>2,000 IU/mL: 21% vs 59%; p<.001) in the first year. Patients with HBsAg loss experienced a higher proportion of flares (ALT>5x ULN: 21% vs 10%, p=.07; ALT>10x ULN: 10% vs 4.5%, p=.15) in the first year but mean ALT decreased over time for that group and increased for those without HBsAg loss. Mean ALT remained normal in both

groups. Among those without HBsAg loss, 4 had HBeAg reversions, and 1 patient decompensated in the first year.

Conclusion: Early viral and host kinetics were good indicators of outcomes among patients who remained off-treatment at 1 year. Patients without HBsAg loss showed increases in HBV DNA and ALT with worse clinical outcomes and only minimal decreases in HBsAg compared to those who achieved HBsAg loss.

Image/Table:



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Sciences, Merck Sharp and Dohme, Springbank Pharmaceuticals, Sysmex Corporation, Roche, Conflict with: AbbVie, Aligos Therarpeutics, Arbutus Biopharma, Bristol Myers Squibb, Dicerna Pharmaceuticals, Finch Therapeutics, GlaxoSmithKline, Gilead Sciences, Janssen, Merck Sharp and Dohme, Clear B Therapeutics, Springbank Pharmaceuticals, Roche, M. Sonneveld Grant / Research support from: Roche, Bristol Myers Squibb, Gilead Sciences, Fujirebio, Speakers bureau of: Roche, Bristol Myers Squibb, Gilead Sciences, Fujirebio, T. Vanwolleghem Grant / Research support from: Gilead Sciences, Roche, Bristol Myers Squibb, Conflict with: Janssen Pharmaceuticals, Gilead Sciences, Abbvie, Bristol Myers Squibb, Speakers bureau of: W.L. Gore, Gilead Sciences, Bristol Myers Squibb, X. Forns Conflict with: AbbVie, Gilead Sciences, G. Papatheodoridis Grant / Research support from: Abbvie, Gilead Sciences, Conflict with: Abbvie, Dicerna, Gilead Sciences, GlaxoSmithKline, Ipsen, Janssen, Merck Sharp and Dohme, Roche, Spring Bank, Takeda, J.-H. Kao Conflict with: Abbvie, Roche, Gilead Sciences, Speakers bureau of: Abbvie, Fujirebio, Gilead Sciences, Y.-C. Hsu Conflict with: Gilead, Speakers bureau of: Abbvie, Bristol Myers Squibb, Roche, Novartis, Gilead, M. Cornberg Grant / Research support from: Roche, Conflict with: Abbvie, Gilead Sciences, Merck Sharp and Dohme, GlaxoSmithKline, Janssen-Cilag, Spring Bank Pharmaceuticals, Novartis, Swedish Orphan Biovitrum, Falk Foundation, W.-J. Jeng: None Declared, H. Janssen Grant / Research support from: AbbVie, Gilead Sciences, Janssen, Roche, Conflict with: AbbVie, Bristol Myers Squibb, Gilead Sciences, Janssen, Merck, Roche, Arbutus, Vir Biotechnology Inc

O15

TENOFOVIR DISOPROXIL FUMARATE (TDF) VERSUS TENOFOVIR ALAFENAMIDE (TAF) OR TDF/EMTRICITABINE (TDF/FTC) TO TREAT HEPATITIS B: META-ANALYSIS OF 2914 PATIENTS IN 11 RANDOMISED CLINICAL TRIALS

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Abstract Content: Introduction: Current WHO guidelines recommend tenofovir for the treatment of chronic Hepatitis B infection. There are 2 forms of tenofovir: disoproxil fumarate (TDF) is widely available as a generic, while the alafenamide prodrug (TAF) is branded and more expensive in middle- and high-income countries. There are large differences in cost between branded TAF and generic TDF in the US, UK and elsewhere.

Methods: We conducted a systematic search of clinical trial databases (www.clinicaltrials.gov), and EMBASE / PUBMED, to identify randomised trials comparing TAF versus TDF and TDF/FTC versus TDF. The primary efficacy parameter was HBV DNA negativity after the longest follow up time available. Additionally, we evaluated HBeAg loss, HBeAg seroconversion and ALT normalisation. Safety parameters were adverse events, serious adverse events, grade 3/4 adverse events and grade 3/4 abnormalities in low-density lipoprotein cholesterol (LDL). Results were analysed using the Mantel-Haenszel random effects model in REVMAN. Differences between drugs were shown as Odds Ratios (OR) with 95% confidence intervals.

Results: In the meta-analysis, we included 6 randomised trials of TAF versus TDF in 2256 patients. One trial of HIV-HBV coinfection (Alliance) showed evidence of imbalanced randomisation. For comparison of TAF with TDF monotherapy, there was no significant difference in HBV DNA negativity (OR: 1.27 [95% C.I. 0.88-1.83], p=0.21), HBeAg loss (OR: 1.34 [95% C.I. 0.94-1.92], p=0.10), any adverse events (OR: 1.15 [95% C.I. 0.95-1.39], p=0.16), grade 3/4 adverse events (OR: 1.13 [95% C.I. 0.73-1.74], p=0.58) and serious adverse events (OR: 0.79 [95% C.I. 0.41-1.53], p=0.48). There were significant differences between TAF and TDF in ALT normalisation (OR: 1.73 [95% C.I. 1.38-2.17], p<0.00001), HBeAg seroconversion (OR: 1.58 [95% C.I. 1.05-2.37], p=0.03) and grade 3/4 elevations in LDL cholesterol (OR: 4.17 [95% C.I. 1.74-10.02], p=0.001). In the meta-analysis comparing TDF/FTC and TDF (5 RCTS, 658 patients), there was no significant difference in HBV DNA negativity (OR: 1.55 [95% C.I. 0.87-2.76], p=0.14), ALT normalisation (OR: 1.75 [95% C.I. 0.86-3.55], p=0.12), HBeAg loss (OR: 0.77 [95% C.I. 0.41-1.45], p=0.42), HBeAg seroconversion (OR: 0.64 [95% C.I. 0.26-1.58], p=0.34), serious adverse events (OR: 1.36 [95% C.I. 0.48-3.83], p=0.56), any adverse events (OR: 0.84 [95% C.I. 0.38-1.82], p=0.65) and grade 3/4 adverse events (OR: 1.24 [95% C.I. 0.48-3.22], p=0.66). In the UK, the price of TDF monotherapy was $6/month, versus $18/month for TDF/FTC and $420/month for TAF.

Conclusion: In this meta-analysis of 11 trials, there was no significant difference between TAF and TDF, or between TDF/FTC and TDF, for the primary efficacy outcome of HBV DNA negativity. TAF was associated with higher risks of Grade 3 or 4 elevations in LDL cholesterol. Large differences in price between TAF and TDF cannot be justified by differences in safety and efficacy.

Image/Table:

Table 1: Efficacy and safety of TAF. TDF and TDF/FTC in randomised trials

	TAF vs. TDF		TDF/FTC vs. TDF	
	TAF	TDF	TDF/FTC	TDF
HBV DNA negativity	974/1341 (73%)	629/911 (69%)	247/307 (80%)	230/314 (73%)
ALT normalisation	478/986 (48%)	198/548 (36%)	88/121 (73%)	71/117 (61%)
HBeAg loss	107/733 (15%)	53/460 (12%)	22/197 (11%)	27/195 (14%)
HBeAg seroconversion	85/785 (11%)	37/516 (7%)	9/145 (6%)	14/142 (10%)
Any adverse events	823/1230 (67%)	495/799 (62%)	234/298 (78%)	246/303 (81%)
Serious adverse events	64/1343 (5%)	55/911 (6%)	26/174 (15%)	19/179 (11%)
Grade 3/4 adverse events	61/1230 (5%)	37/799 (5%)	37/236 (16%)	31/239 (13%)
Grade 3/4 LDL elevations	54/1200 (5%)	7/783 (1%)	-	-

Disclosure of Interest: None Declared

O16

FXR AGONISTS ALONE OR IN COMBINATION WITH IFNA INHIBIT HBV REPLICATION AND HDV PROPAGATION IN FUNCTIONAL HEPATOCYTES

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Abstract Content: The nuclear farnesoid X receptor (FXR) is a master regulator of hepatocyte differentiation and functions. Some agonists/ligands of FXR were shown to inhibit the replication of HBV and the propagation of HDV. Here, using seven different FXR agonists with different structures (GW4064, Tropifexor, Vonafexor, Cilofexor and Nidufexor) we further characterized these inhibitory phenotypes in relevant in vitro models (PHH an dHepaRG), thus confirming a FXR-dependent class effect.

IFNa (in its pegylated form) is yet often used as the first line treatment in HBV and HDV patients, despite its low tolerance and subsequent relative limited efficacy. The combination of Peg-IFNa with Vonafexor, a non-steroidal non-bile acid, and highly selective FXR agonist, has been shown, in an open-label phase II trial (NCT04365933), to significantly reduce HBsAg levels in HBe-negative HBV-infected patients. This stronger combination inhibitory phenotype has been recapitulated in our models with various FXR agonists against HBV and HDV replication in the absence of any drug toxicity. The inhibitory phenotype was particularly strong on HBV RNA and HBsAg biogenesis, as well as on the propagation of HDV by affecting the specific infectivity of secreted particles.

FXR agonists show antiviral activity on both HBV and HDV viruses, with a much better efficacy when combined with low/less toxic doses of IFNa. This study provides support for the existence of a mechanism of action underlying the antiviral activity of FXR agonists, alone or in combination with IFNa, details of which should be explored further to assist on the identification of efficacy predictive factors for clinical evaluations.

Disclosure of Interest: None Declared

O17

ACCEPTABILITY AND USABILITY OF ORAL FLUID HCV SELF-TESTING FOR HEPATITIS C TESTING: A SYSTEMATIC REVIEW

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Abstract Content: Background: The use of Hepatitis C virus self-testing (HCVST) is strategy to increase HCV testing in key populations. Studies that reported data on the acceptability and usability of HCVST using oral-fluid tests had limited sample size.

Purpose: To estimate the pooled rates of acceptability/feasibility and agreement of HCVST using oral-fluid test by conducting a systematic review (PROSPERO CRD42022349874).

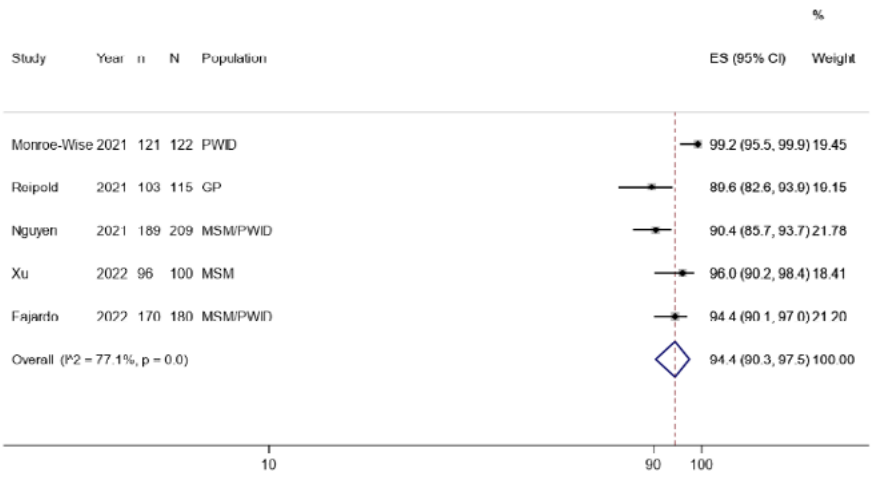
Methods: We searched online databases (PubMed, Embase, Web of Science, Scopus, LILACS) for studies that evaluated acceptability, usability, inter-reader and/or inter-operator (re-testing) variability for HCVST using oral-fluid tests. Two independent reviewers screened the titles and abstracts and extracted data from full-texts. Pooled rates of correct sample collection, HCVST without need of assistance, re-reading/re-testing agreement and perspectives of HCVST after testing were estimated. Sensitivity analyses were performed in men who have sex with men (MSM) and people who inject drugs (PWID). Between-study heterogeneity was assessed using the I^2 statistics.

Results: We screened 229 articles, and the full text was assessed in 9 identified documents. A total of 6 studies [5 manuscripts and 1 conference abstract] comprising 870 individuals from six countries [United states (n=95 - Hepatology Clinic), Kenya (n=150 PWID), Egypt (n=116 - general population), Vietnam (n=104 MSM and n=105 PWID), China (n=100 MSM) and Georgia (n=100 MSM and n=100 PWID)] were included. All studies used OraQuick® HCV Rapid Antibody Test. The pooled overall rates for correct sample collection and for people who performed HCVST without needing assistance in any step [95% confidence interval (CI)] were 87.2% [76.0-95.3] (5 studies; n=755; I^2=93.7%) and 62.6 [95%CI 37.2-84.8] (5 studies; n=755; I^2=98.0%), respectively. The pooled rate of agreement for re-reading was 95.0% [95%CI 91.5-97.6] (6 studies; n=831; I^2=74.0%) and for re-testing (excluding invalid tests) was 94.4% [95%CI 90.3-97.5] (5 studies; n=726; I^2=77.1%) (Figure 1). The pooled rate of those who would be willing to test again was 92.6% [95%CI 86.7-97.0] (5 studies; n=775; I^2=86.4%). The pooled rates of those who would recommend HCVST and of those who prefer HCVST at home were 94.4% [95%CI 84.7-99.6] (I^2=93.7%) and 69.9% [95%CI 57.5-79.8] (I^2=89.1%). Pooled rates (95%CI) of correct sample collection [72.8% (95%CI 63.3-81.5) vs 90.8% (85.9-94.8)] and HCVST without assistance [44.1% (14.1-76.7) vs 78.1% (53.4-95.3)] was lower in PWID compared to MSM.

Conclusion: HCV testing with oral-fluid HCVST is feasible and well-accepted. HCVST using oral-fluid kits should be considered in key-populations for increasing the number of identification of people with HCV infection.

Image/Table:

Figure 1. Pooled overall rates of agreement for re-testing excluding invalid tests



Disclosure of Interest: None Declared

O18

THERAPEUTIC VACCINATION FOR CHRONIC HEPATITIS B USING ADJUVANT-LOADED PARTICULATE HEPATITIS B CORE ANTIGEN

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Background and Aims: HBV core protein spontaneously assembles to HBV capsids or particulate Hepatitis B core antigen (HBcoreAg) and acts as a powerful immunogen representing a unique vaccine carrier platform. We have developed a therapeutic Hepatitis B vaccine, TherVacB, which employs particulate HBcoreAg and Hepatitis B S antigen (HBsAg) for prime, and a recombinant modified vaccinia virus Ankara (MVA) for boost. The recombinant HBcoreAg is produced in E.coli and encapsulates bacterial RNA (bRNA). In the present study, we aimed to explore whether the bRNA content is affecting the immunogenicity of HBcoreAg, and to substitute bRNA by well-characterized RNA-based adjuvant poly I:C or DNA-based adjuvant CpG. Therefore, we compared the humoral and cellular responses induced by TherVacB immunization with empty, bRNA-, poly I:C- and CpG-containing capsids.

Methods: bRNA was removed from HBcoreAg by LiCl precipitation following disassembly in GuHCl. Afterwards, HBcoreAg can be reassembled with or without specific nucleic acid: poly I:C or CpG adjuvant. The morphology and structure of empty, bRNA-, and adjuvant-containing capsids were characterized by electron microscopy (EM) and solid-state nuclear magnetic resonance (NMR) analyses. Efficacy of TherVacB regimens with different capsids was assessed in HBV-naïve and AAV-HBV infected mice developing persistent HBV replication.

Results: Empty HBcoreAg allowed highly efficient incorporation of poly I:C or CpG. The EM and solid-state NMR analyses showed that the empty, poly I:C- and CpG-containing capsids exhibited comparable morphology, secondary and tertiary structure as bRNA-containing capsids. In both HBV- naïve and AAV-HBV mice, TherVacB immunization with empty HBcoreAg elicited significant lower B- and T-cell responses compared to bRNA-containing HBcoreAg. By contract, immunization with poly I:C- or CpG-capsids induced very high levels of anti-HBc and anti-HBs, and vigorous HBcoreAg- as well as co-administered HBsAg-specific T-cell responses, which were even comparable with those in the groups of bRNA-containing HBcoreAg with respective poly I:C, CpG adjuvants externally. Of note, the amounts of adjuvants encapsidated in HBcoreAg were significantly lower than those using in the groups with external adjuvants. Moreover, more than 50% reduction in level of serum HBeAg and numbers of HBV-positive hepatocytes was observed by the end of the study after TherVacB vaccination with poly I:C- and CpG-containing HBcoreAg, indicating long-term control of persistent HBV replication.

Conclusion: The adjuvant-loaded HBcoreAg stays intact in vitro and shows strong immunogenicity in vivo, representing a novel encouraging candidate for therapeutic Hepatitis B vaccines.

Disclosure of Interest: None Declared

O19

COMBINED COVID-19 VACCINATION AND HEPATITIS C VIRUS SCREENING INTERVENTION IN MARGINALISED POPULATIONS IN SPAIN

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Background: The COVID-19 pandemic has hindered efforts to address the Hepatitis C virus (HCV) and HIV by reducing testing, particularly in marginalised groups, who have some of the highest rates of these conditions and lowest rates of COVID-19 vaccination.

Purpose: This pilot study aimed to assess the acceptability of combining HCV testing with COVID-19 vaccination in a centre for addiction services (CAS) in Barcelona and a mobile testing unit (MTU) in Madrid, Spain.

Methods: From 28/09/2021-30/06/2022, 187 adults from marginalised populations (i.e., people experiencing homelessness, those with substance use and/or mental disorders, sex workers, refugees, undocumented migrants) were offered HCV antibody (Ab) testing along with COVID-19 vaccination. If HCV Ab+, they were tested for HCV-RNA. MTU participants were also screened for HIV, per the standard of care. HCV-RNA+ and HIV+ participants, not on antiretroviral therapy (ART), were offered treatment.

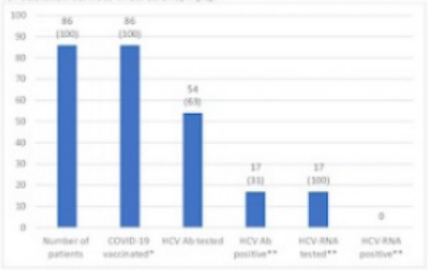
Results: Of the 86 CAS participants (mean age 47 [SD: 10]), 77% were male, all had a substance use disorder (SUD), 21% had mental health disorders and 14% were HIV+. Of everyone, 15% had a previous COVID-19 diagnosis, 93% had been previously vaccinated for COVID-19, of whom 90% had received the full first round schedule but none had received a COVID-19 vaccine booster, and all received a COVID-19 vaccine during the study intervention (Figure 1). Of all participants, 54 (63%) were tested for HCV Ab, of whom 17 (32%) were positive, of whom all were tested for HCV-RNA and none were positive. Of the 101 MTU participants (mean age 36 [SD: 11]), 69% were male, 59% had a SUD and 10% had mental health disorders. Of everyone, 12% had a previous COVID-19 diagnosis, none had been previously vaccinated for COVID-19 and all received a COVID-19 vaccine during the study intervention (Figure 2). Everyone was tested for HCV Ab and HIV and 15 (15%) and 9 (9%) were positive, respectively. Of those HCV Ab+, all were tested for HCV-RNA, of whom 9 (60%) were positive. Of those HCV-RNA+, 33% were HIV coinfected, 56% reported that the most likely route of HCV transmission was injecting drug use and 8 (89%) have started HCV treatment. Of those HIV+, none were new diagnoses and 5 (56%) had abandoned ART, of whom 3 (60%) have restarted it.

Conclusions: The intervention had an acceptability rate of 63% at the CAS and 100% at the MTU, was safe and optimised the use of time, while serving to reach marginalised populations with a critical vaccine and needed testing services. This integrated model of care, which also

linked participants to HCV and HIV care, should be considered for future healthcare intervention planning, such as when providing COVID-19 vaccine boosters.

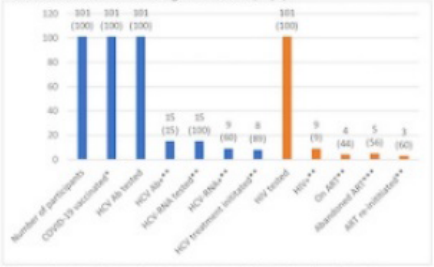
Image/Table:

Figure 1. Analysis of the combined COVID-19 vaccination and HCV screening intervention at the centre for addiction services in Barcelona, n (%).



Unless otherwise indicated, percentages are of the total n of participants.
*Vaccinated during the study intervention.
**Denominator is equal to the n of the prior column.
Abbreviations: Ab, antibody; HCV, hepatitis C virus.

Figure 2. Analysis of the combined COVID-19 vaccination and HCV and HIV screening and linkage to care intervention at the mobile testing unit in Madrid, n (%).



Unless otherwise indicated, percentages are of the total n of participants.
*Vaccinated during the study intervention.
**Denominator is equal to the n of the prior column.
***Denominator is equal to the n of HIV+ participants.
Abbreviations: Ab, antibody; ART, antiretroviral therapy; HCV, hepatitis C virus.

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Lundbeck and Esteve, outside of the submitted work. , G. Cuevas: None Declared, J. L. Espada: None Declared, W. Morón: None Declared, R. F. Palma-Álvarez Speakers bureau of: Speaker honorariums from Angelini, Casen Recordati, Exeltis, Lundbeck, MSD, Mundipharma, Servier and Takeda, outside of the submitted work. , J. Feld Grant / Research support from: Research support from Gilead Sciences and AbbVie, outside of the submitted work. , Conflict with: Consulting fees from Gilead Sciences and AbbVie, outside of the submitted work. , J. Valencia Speakers bureau of: Speaker fees from Gilead Sciences, AbbVie and ViiV, outside of the submitted work.

O20

CLASS A CAPSID ASSEMBLY MODULATORS INDUCE CELL DEATH THROUGH HBV CORE PROTEIN AGGREGATION AND POTENTIALLY ACTIVATE THE INNATE IMMUNE RESPONSE

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Background & Aims: Despite a preventive vaccine, almost 300 million people suffer of HBV chronic infection. Therapies controlling HBV replication exist but do not lead to functional cure of chronic Hepatitis B. HBV core protein (HBc) is the building block of HBV nucleocapsid and it modulates almost every step of the HBV life cycle. Class A capsid assembly modulators (CAM-As) represent attractive direct antiviral agents (DAAs). They impair HBV replication by blocking pgRNA encapsidation and inducing HBc aggregation due to aberrant nucleocapsid structures. We already showed that CAM-A RG7907 treatment leads to an unexpected sustained HBsAg reduction in a mouse model. In this study we present the latest insights about the mechanism of action (MoA) of the CAM-A RG7907.

Methods: We investigated the impact of RG7907 treatment on core aggregation, cell survival, and transcriptomic reprogramming in HBc-expressing hepatoma cell lines (HepG2) and primary human hepatocytes (PHH) as well as in the HBV-replicating cell line HepAD38.

Results: RG7907 induced extensive HBc-aggregation-dependent cell death both in hepatoma cells and in primary hepatocytes. Transcriptomic analyses revealed the activation of specific host pathways such as apoptosis, inflammation, and interferon response. The induction of apoptosis-related gene expression was validated in HBc-expressing HepG2 and PHH as well as in HepAD38. We also observed an upregulation of Interferon lambda1 (INFL1) in HepAD38 suggesting the potential reactivation of the innate immunity upon CAM-A treatment.

Conclusions: CAM-A-dependent HBc aggregation drives cell death via activation of host specific pathways such as the inflammatory and innate immunity responses. These results shed light on a yet unknown MoA specific of CAM-A compounds.

Disclosure of Interest: V. TAVERNITI Grant / Research support from: Aligos Belgium BV , D. B. KUM Employee of: Aligos , H. VANRUSSELT Employee of: Aligos Belgium BV, L. HEYDMANN: None Declared, Y. DEBING Employee of: Aligos Belgium BV, T. F. BAUMERT Grant / Research support from: Aligos Belgium BV , E. VERRIER Grant / Research support from: Aligos Belgium BV

O21

A NATIONAL PROGRAM TO SCALE-UP DECENTRALIZED HEPATITIS C VIRUS POINT-OF-CARE TESTING AND TREATMENT IN AUSTRALIA

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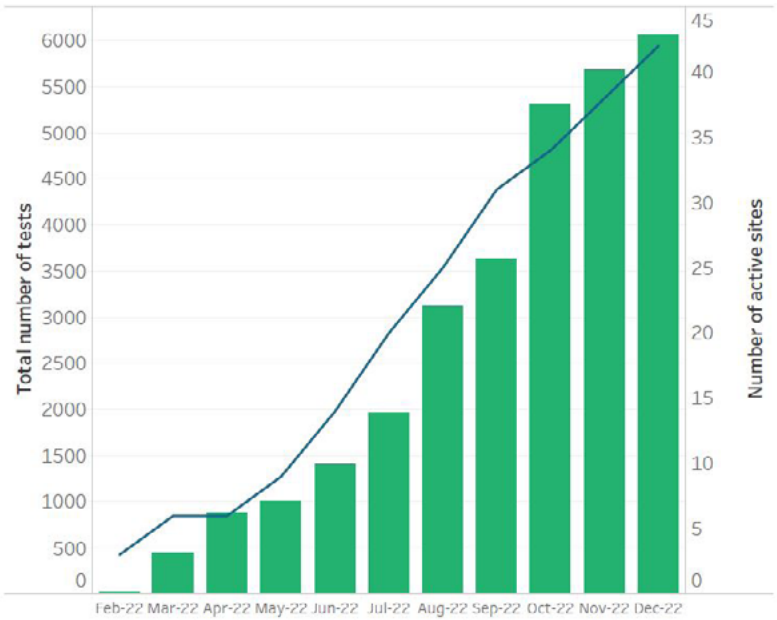
Background: Fingerstick point-of-care HCV RNA testing enables diagnosis and treatment in a single-visit, increases testing acceptability, and reduces loss to follow-up, addressing the drop-off in the HCV care cascade. This analysis evaluated HCV testing and RNA prevalence in a national program to scale-up point-of-care HCV testing.

Methods: The National Australian HCV Point-of-Care Testing Program is evaluating the scale-up of point-of-care HCV testing (antibody: Bioline HCV test; RNA: Xpert HCV Viral Load Fingerstick test) at 89 sites in Australia, including drug treatment clinics, needle and syringe programs, prisons, mental health services, homelessness services, Aboriginal Community Controlled Health Organisations, and mobile outreach clinics through an observational study. The program facilitates point-of-care testing for anyone at risk of HCV or attending a service providing care for people at risk of HCV. The program also includes standardised operator training for non-laboratory staff and quality assurance program. Immediate HCV RNA testing is performed in settings with high HCV antibody prevalence (>15%, drug treatment, needle syringe programs and prisons). HCV antibody testing with reflex RNA testing is performed in settings with low HCV antibody prevalence (<15%, mental health, homelessness).

Results: Between January and December 2022, 40 sites (community, n=27; prison, n=13) have been established in five states/territories (107 operators trained) with 5,391 HCV point-of-care tests performed (antibody, n=485; RNA, n=3,606) in the community (n=1,758) and prisons (n=3,606) (Figure 1). Among those receiving HCV RNA testing (n=5,106), 644 people (13%) have current HCV infection (community, 10%; prison, 14%). The overall treatment uptake is 73% (468 of 644), including 84% in the prison (408 of 485).

Conclusion: This program is one of the first internationally to evaluate scale-up of point-of-care HCV testing in different settings, providing critical information on this approach towards reducing HCV prevalence. Standardised operator training and quality assurance have been critical for success. Facilitators and barriers to testing, scale-up and treatment uptake will be identified, informing the feasibility of HCV point-of-care testing scale-up in other global settings.

Image/Table:



Disclosure of Interest: J. Grebely Grant / Research support from: AbbVie, Biolytical, Cepheid, Gilead Sciences, Hologic, Conflict with: AbbVie, Cepheid, Gilead Sciences, Speakers bureau of: AbbVie, Cepheid, Gilead Sciences, C. Markus: None Declared, L. Causer: None Declared, D. Silk: None Declared, S. Comben: None Declared, S. Hosseini-Hooshyar: None Declared, A. Lloyd: None Declared, M. Martinez: None Declared, I. Shaw: None Declared, P. Cunningham: None Declared, C. Fowlie: None Declared, E. Cunningham: None Declared, A. Marshall: None Declared, M. Byrne: None Declared, C. Treloar: None Declared, S. Shih: None Declared, R. Gray: None Declared, V. Wiseman: None Declared, T. Applegate: None Declared, R. Guy: None Declared, M. Martinello: None Declared, B. Hajarizadeh: None Declared, L. Lafferty: None Declared, W. Dimech: None Declared, L. Cabuang: None Declared, S. Kerr: None Declared, P. Read: None Declared, A. Pedrana: None Declared, Y. Sheehan: None Declared, T. Alex: None Declared, J. O'Loan: None Declared, M. O'Flynn: None Declared, G. Dore: None Declared, S. Matthews: None Declared

O22

A GENE EDITING APPROACH FOR CHRONIC HEPATITIS B: ELIMINATION OF HEPATITIS B VIRUS IN VIVO BY TARGETING CCCDNA AND INTEGRATED VIRAL GENOMES WITH A SEQUENCE-SPECIFIC ARCUS NUCLEASE

E. Harrison[1,*], C. L. Gorsuch[1], P. Nemec[1], M. Yu[2], S. Xu[2], D. Han[2], J. Smith[1], J. Lape[1], N. V. Buuren[2], R. Ramirez[2], R. C. Muench[2], M. M. Holdorf[2], B. Feierbach[2], G. Falls[1], J. Holt[1], W. Shoop[1], E. Sevigny[1], F. Karriker[1], R. Brown[1], A. Joshi[1], T. Goodwin[1], Y. Tam[3], P. Lin[3], S. Semple[3], N. Leatherbury[1], W. E. Delaney 4th[2], D. Jantz[1], A. R. Smith[1]

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Background: ARCUS nucleases can be engineered to recognize conserved DNA sequences in the Hepatitis B virus (HBV) genome. Delivery of ARCUS mRNA to hepatocytes with lipid nanoparticles (LNPs) provides a strategy for chronic Hepatitis B (CHB) treatment. Persistence of CHB is attributed to maintenance of the intrahepatic pool of viral covalently closed circular DNA (cccDNA) and expression of immunosuppressive Hepatitis B surface antigen (HBsAg) from integrated HBV. Current nucleos(t)ide therapies for CHB prevent virus production and spread but have no direct impact on cccDNA or expression of HBsAg from integrated virus. ARCUS nucleases expressed in hepatocytes can cut both cccDNA and integrated viral genomes leading to removal of cccDNA and inhibition of viral gene expression.

Purpose: We describe a potential curative approach for CHB using a highly specific engineered ARCUS nuclease (ARCUS-POL) targeting the HBV genome.

Methods: Through iterative rounds of nuclease engineering, ARCUS-POL nucleases were optimized to exhibit high levels of on-target editing with minimal off-target activity. Efficacy and specificity were then tested in vitro in primary human hepatocytes (PHHs) infected with HBV and a HepG2 cell line with an integrated partial HBV genome. To evaluate ARCUS-POL in vivo, novel episomal adeno-associated virus (AAV) mouse and non-human primate (NHP) models were developed containing a portion of the HBV genome serving as a surrogate for cccDNA. Clinically relevant delivery was achieved through systemic administration of LNPs containing ARCUS-POL mRNA.

Results: Transient ARCUS-POL expression in HBV-infected PHHs produced >75% reductions in both cccDNA and HBsAg. Importantly, ARCUS-POL produced no detectable translocations in PHHs using hybrid capture followed by long-read sequencing. After transient delivery of ARCUS-POL into cells containing integrated HBV DNA, >80% on-target editing was achieved with subsequent HBsAg reductions. In both mouse and NHP AAV models, a significant decrease in total AAV copy number and high on-target indel frequency was observed. In the case of the mouse model, which supports HBsAg expression, circulating surface antigen was durably reduced by 96%.

Conclusions: ARCUS-Pol nucleases were able to eliminate cccDNA and reduce HBsAg expression from integrated HBV without inducing translocations. Together, these data support a potential gene editing approach and cure for CHB.

Disclosure of Interest: E. Harrison Employee of: Precision BioSciences Inc., C. Gorsuch Employee of: Precision BioSciences Inc., P. Nemec Employee of: Precision BioSciences Inc., M. Yu Employee of: Gilead Sciences Inc., S. Xu Employee of: Gilead Sciences Inc., D. Han Employee

of: Gilead Sciences Inc., J. Smith Employee of: Precision BioSciences Inc., J. Lape Employee of: Precision BioSciences Inc., N. Buuren Employee of: Gilead Sciences Inc., R. Ramirez Employee of: Gilead Sciences Inc., R. Muench Employee of: Gilead Sciences Inc., M. Holdorf Employee of: Gilead Sciences Inc., B. Feierbach Employee of: Gilead Sciences Inc., G. Falls Employee of: Precision BioSciences Inc., J. Holt Employee of: Precision BioSciences Inc., W. Shoop Employee of: Precision BioSciences Inc., E. Sevigny Employee of: Precision BioSciences Inc., F. Karriker Employee of: Precision BioSciences Inc., R. Brown Employee of: Precision BioSciences Inc., A. Joshi Employee of: Precision BioSciences Inc., T. Goodwin Employee of: Precision BioSciences Inc., Y. Tam Employee of: Acuitas Therapeutics, P. Lin Employee of: Acuitas Therapeutics, S. Semple Employee of: Acuitas Therapeutics, N. Leatherbury Employee of: Precision BioSciences Inc., W. Delaney 4th Employee of: Gilead Sciences Inc., D. Jantz Employee of: Precision BioSciences Inc., A. Smith Employee of: Precision BioSciences Inc.

O23

TREATMENT ELIGIBILTY AND PERFORMANCE OF THE WHO TREATMENT CRITERIA IN CHRONIC HEPATITIS B PATIENTS IN TANZANIA

N. A. Adam[1*], E. V. Quang[2 3], J. U. Kim[4], E. Lord[5], Y. Shimakawa[6], J. C. Rwegasha[1], M. Lemonie[7]

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Background and aims: In sub-Saharan Africa (sSA), the proportion of patients with chronic Hepatitis B virus infection (CHB) in need of antiviral therapy and the concordance between treatment eligibility established by the World Health Organisation (WHO) and that by the European Association for the Study of the Liver (EASL) are poorly described. This study aimed to assess i.The proportion of patients eligible for antivirals according to the EASL. ii.The performance of the WHO treatment criteria to indicate the EASL's criteria in CHB patients in Tanzania.

Methods: We prospectively enrolled consecutive HBV-monoinfected patients, non heavy drinkers, HBV treatment-naïve without hepatocellular carcinoma, referred to hepatology clinic at Muhimbili National Hospital, Tanzania. HBV viral load (Cobas AmpliPrep/Cobas TaqMan (CAP/CTM) assay), Hepatitis B e antigen (HBeAg) (Architect assay), liver enzyme levels (ALT/AST) and liver stiffness measurement (LSM) using Fibroscan, were performed on the same day for each participant. Significant liver fibrosis and cirrhosis were defined as LSM ≥7.8 and ≥9.5 kPa, respectively[1].

Using LSM as a reference, we assessed the performance of APRI to detect cirrhosis and using the 2017 EASL treatment criteria as a gold standard, we evaluated the performance of the WHO treatment criteria to identify patients eligible for antiviral therapy.

Results: Between 2020 and 2021, we recruited 257 consecutive patients, of them only 41 (16%) knew about their infection and 152 (59%) expressed fear about their diagnosis. Participants were mainly males (183/257 (71%)), median age 35 years (IQR: 30–43), 66 (28%) with BMI ≥ 30 kg/m2, 11 (4.7%) with positive HBeAg, median HBV DNA 734 IU/ml (98-4,836), median ALT 25 IU/L (18-35), median LSM 6.0 kPa (5.0-7.9). Out of 257 patients, 64 (25%) had significant liver fibrosis including 36 (14%) cirrhosis. Sensitivity and specificity of APRI >0.5 to detect significant liver fibrosis was 0.28 and 0.83, respectively. None of the enrolled patients had an APRI > 2 although 36 had suspected cirrhosis. Among 225 patients with complete data, 49 (21.8%) fulfilled the 2017 EASL treatment criteria and only 8 (3.6%) the WHO criteria. Using the EASL guidelines as reference, the performance of the WHO criteria to select patients for treatment was poor with a sensitivity of only 0.08 but an excellent specificity of 0.98.

Conclusion: Our study reports about 20% of CHB patients in need of immediate antiviral therapy and found poor performance of APRI to detect fibrosis and cirrhosis as well as unsatisfactory performance of the current WHO criteria to identify patients eligible for treatment. Revised guidelines adapted to sSA are needed.

[1] Lemoine et al. Gut 2016

Disclosure of Interest: None Declared

O24

THE TLR8 AGONIST SELGANTOLIMOD MODULATES KUPFFER CELL DIFFERENTIATION STATUS AND INDIRECTLY IMPAIRS HBV ENTRY INTO HEPATOCYTES VIA AN IL-6-DEPENDENT MECHANISM

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Background: Chronic HBV infection affects close to 300 million people worldwide and is one of the major etiologies for the development of cirrhosis and liver cancer. In spite of universal vaccination programs, HBV remains a global burden due to the limited therapeutic options available. Therefore, achieving the goal of HBV cure will require a continuous effort in the development of novel molecules and combination therapies. In this context, the TLR8 agonist Selgantolimod (SLGN) has shown promising results during its clinical evaluation as an immunomodulatory agent against HBV.

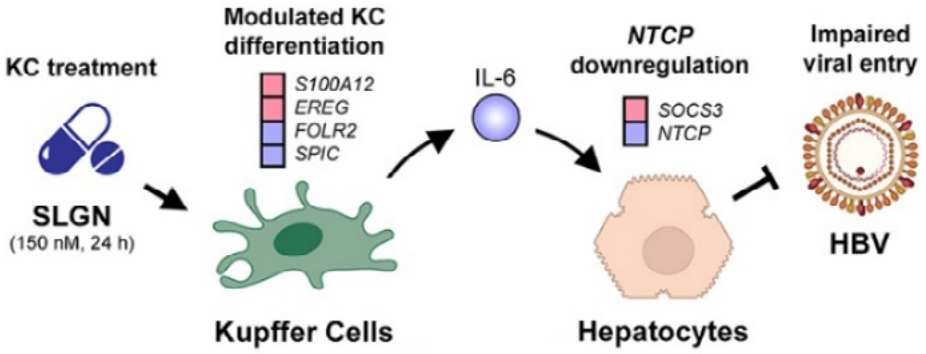
Purpose: Although the effect of SLGN has been explored in the peripheral immune compartment, little is known regarding its intrahepatic response. Therefore, we aimed to characterize the transcriptomic changes and intercellular communication events associated with the action of SLGN in the liver microenvironment.

Method: We analyzed publicly available single-cell RNA-seq (scRNA-seq) data in order to identify TLR8-expressing cell types in the human liver and optimized a method for their isolation. We characterized the transcriptomic and cytokine profiles of this population in response to SLGN. The indirect effect of SLGN was evaluated by RNA-seq in primary human hepatocytes (PHH) treated with SLGN-conditioned media (CM) and the quantification of viral parameters following HBV infection. Identified signaling pathways mediating this effect were validated by the analysis of liver transcriptomic data from HBV-infected patients.

Results: Our analysis determined that TLR8 is predominantly expressed in the myeloid compartment of the liver. Therefore, we established a method for the isolation of Kupffer cells (KCs) from human liver resections. Using this model, we found that in vitro treatment of KCs with SLGN induces the upregulation of markers that characterize monocyte populations (e.g., EREG, S100A12) and the downregulation of genes associated with the KC identity (e.g., SPIC, FOLR2). Interestingly, a similar prolife was observed in response to LPS, suggesting this to be part of the general changes associated with an inflammatory response. Moreover, treatment of PHH with SLGN-CM produced in KCs led to the downregulation of NTCP and an impaired HBV entry into hepatocytes. Finally, co-treatment with SLGN-CM and an IL-6-inhibitory antibody identified IL-6 as the cytokine mediating this reduced HBV entry.

Conclusions: Our results suggest that in addition to its previously described therapeutic antiviral activity in HBV-infected hepatocytes, SLGN also has a prophylactic effect via an IL-6-dependent mechanism. Furthermore, our characterization of SLGN sheds light into the general transcriptional programs regulating KC activation and underscores the importance of considering cell states when annotating hepatic cell populations based on scRNA-seq data.

Image/Table:



Disclosure of Interest: None Declared

O25

EFFECTIVENESS OF REFLEX HCV VIRAL LOAD SAMPLE COLLECTION IN IMPROVING TURN-AROUND TIME FOR HCV DIAGNOSTICS IN NASARAWA STATE NIGERIA

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Background: Achieving the WHO targets of eliminating viral Hepatitis as a public health threat by 2030, will require implementation of the WHO endorsed best practices for simplified service delivery, which includes decentralization, integration, and task sharing[1]. Viral Hepatitis is a major public health concern in Nasarawa state with findings from a cross-sectional study and program data, showing average seropositive rate of 13.2% for both mono and HCV/HIV co-infected populations higher than the National prevalence of 1.1% for both populations. Clinton Health Access Initiative is currently supporting the Nasarawa State Government-led HCV elimination program through the simplified treatment algorithm – screening, viral load diagnostic testing, and treatment. This is targeted to improve access to Hepatitis C services,however uptake of these services resulted in long turnaround times (TAT) or loss to follow up (LTFU) hence delays in clinical action.

Purpose: This abstract aims to highlight the impact of reflex viral load sample collection following antibody screening as a approach to reduce TAT to viral load testing and (TAT) amongst People Living with HIV in 4 facilities.

Method: Using lab registers, PLHIV screening data from January 2021 to March 2022 was collected and triangulated with the viral load data using the patient unique numbers to ensure accuracy . Healthcare workers across ART clinics were trained on management of Hepatitis. "Patient Navigators" who primarily are HIV program defaulter trackers were trained on sample collection techniques and equipped with the requisite data tools to document screening outcomes. Unscreened PLHIV were tracked and screened for HCV antibodies using rapid diagnostic tests. Positive patients were identified, and samples were instantly collected for HCV viral load testing on the GeneXpert near POC platform. Viremic patients were linked to HCV curative treatments. Post-reflex phase data was collected from April 2022 to November 2022.

Results: In the pre-reflex phase 2,368 patients were screened in the facility across GH Awe Doma, Wamba, and Uke. 397 patients were identified seropositive (seropositivity rate 16.7%) and 281 were linked to viral load testing (71% linkage to care rate) with an average TAT of 214 days. In the post-reflex phase, 2,504 were screened at the community across the earlier listed sites. 100 patients were identified seropositive (seropositivity rate 4%)

Conclusion: The design and deployment of innovative service delivery models such as WHO recommended reflex HCV viral load sample collection following a positive antibody RDT result significantly improved HCV viral load testing turn-around time and further aid clinical decision.

Disclosure of Interest: None Declared

O26

DRIED BLOOD SPOT (DBS): A NEW TOOL FOR SCREENING, DIAGNOSIS AND MONITORING HEPATITIS D VIRUS (HDV) INFECTION

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Background: Hepatitis D virus (HDV) infection is one of the major public health concerns around the world. Globally, an estimated 5 to 10% of chronic HBsAg carriers are co-infected with HDV. HDV infection can lead to a rapid disease progression towards cirrhosis and hepatocellular carcinoma. The diagnosis of HDV infection is crucial for its management. The dried blood spot (DBS) technique can be used to collect, store, and ship whole blood specimens. The objective of the present study is to assess the performance of standardized HDV diagnostic and monitoring tools in the analysis of DBS.

Methods: Paired plasma and whole blood specimens collected using the DBS technique from 97 patients were tested for virological markers used to diagnose and monitor HDV infection.

Results: Immunological assay detection of anti-HD antibodies in specimens from DBS was reliable after establishment of a new signal-to-cutoff ratio. HDV RNA was detected from DBS in the vast majority of patients with active replication, but HDV RNA levels were substantially lower than in plasma specimens. The mean HDV RNA detected in whole blood were 1.6 Log IU/disk less than those in plasma. HDV genotype determination was possible in DBS with a 100% concordance with results from plasma specimens.

Conclusion: This study showed that whole blood specimens collected can be used to diagnose and to monitor HDV infection. DBS sampling is a clinically relevant tool to improve access to Hepatitis D worldwide.

Disclosure of Interest: None Declared

O27

HEPATITIS B CORE RELATED ANTIGEN (HBCRAG), NOT AS GOOD AS IT SEEMS?: A CRITIQUE AND SYSTEMATIC REVIEW

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Background: Hepatitis B core-related antigen(HBcrAg) is a new biomarker for Chronic Hepatitis B(CHB) but its performance has not been critically or systematically appraised.

Methods: We evaluated the biological pathway of HBcrAg, and performed a systematic review of PubMed for clinical trials, cohort studies, and case-control studies that evaluated the clinical utility of HBcrAg. The effectiveness of HBcrAg in predicting HBV-specific clinical events (e.g. HBeAg seroconversion, phases of CHB, HBsAg loss, treatment response, and relapse after stopping therapy) was examined using receiver operating characteristic(AUROC) curves. The correlation coefficients of HBcrAg with HBV DNA, quantitative HBsAg (qHBsAg), HBV RNA, and cccDNA were summarised from published studies. Median values were used as estimates.

Results: HBcrAg consists of three precore/core protein products: Hepatitis B core antigen(HBcAg), HBeAg, and 22kDa precore protein(p22cr). In HBeAg(+) CHB, HBeAg contributed 72±10%, HBcAg 17±8% and p22cr 15±9%, but in HBeAg(-) CHB contributions were unquantifiable. The false-positive rate was 9.3% with a false negative rate between 12-35%. The new iTACT-HBcrAg is more sensitive but does not resolve false positive performance. A PubMed search found 248 papers on HBcrAg but after exclusions, 59 were suitable for analysis. The clinical performance was evaluated using AUROC, with median AUROC for HBeAg seroconversion 0.860, predicting HBeAg(-) Hepatitis 0.867, HBsAg loss 0.645, treatment response 0.757, and relapse after stopping therapy 0.688. The median correlation coefficient(r) with HBV DNA was 0.630, qHBsAg 0.414, HBV RNA 0.619 and cccDNA 0.550. Correlation decreased during antiviral therapy but combined biomarkers improved performance.

Conclusions: HBcrAg has a mixed performance and has a poor correlation with HBsAg loss and antiviral therapy, hence HBcrAg results should be interpretated with caution.

Disclosure of Interest: None Declared

O28

DEVELOPMENT AND CLINICAL UTILITY OF HIGH-THROUGHPUT HBCAG-SPECIFIC IMMUNOASSAYS FOR THE MANAGEMENT OF HBV THERAPIES

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Background: Hepatitis B core antigen (HBcAg) has been proposed as a surrogate marker to reflect transcriptional activity of HBV covalently closed circular DNA (cccDNA) during active infections and may be a valuable tool to monitor the efficacy of antiviral therapies. However, HBcAg-specific immunoassays are unavailable, and current assays that measure Hepatitis B core-related antigen (HBcrAg) cannot distinguish between HBcAg, HBeAg, and precore (PreC) proteins.

Here, we describe the development of two fully automated assays to specifically detect phosphorylated HBcAg (P-HBcAg, representing non-HBV DNA-containing particles) and non-phosphorylated HBcAg (HBcAg, representing HBV DNA-containing particles) in single timepoint patients with active infections, three acute HBV infection panels, and in chronic Hepatitis B (CHB) patients ontherapy.

Methods: The P-HBcAg and HBcAg assays are chemiluminescent microparticle immunoassays (CMIA) on a fully automated platform (ARCHITECT i2000SR) that use specific monoclonal antibodies to capture and detect either phosphorylated or non-phosphorylated HBcAg circulating in HBV infected patients. P-HBcAg and HBcAg signals are measured as relative light units (RLUs). For both assays the time to first result is ~36 min. Using these assays, we analyzed 124 single timepoint specimens from HBV infected patients with viral load ranges from 10^3 to 10^9 HBV DNA copies/ml, longitudinal specimens from three patients with acute HBV infections, and four HBeAg-negative patients from the REP 401 study receiving antiviral therapy (TDF - tenofovir disoproxil fumarate, pegIFN - pegylated interferon, NAPs - nucleic acids polymers).

Results: The assays showed a limit of quantification (LOQ) of 4 pg/ml for P-HBcAg and 14 pg/ml for HBcAg. Analyzing acute infections revealed that P-HBcAg/HBcAg levels correlate more closely than HBcrAg to HBV DNA. Notably, HBeAg and HBcrAg kinetics radically differ from P-HBcAg and HBcAg following peak viral levels. 42-67 days after peak HBV DNA levels, HBeAg and HBcrAg levels declined at a much slower rate than P-HBcAg and HBcAg. During antiviral treatment of CHB patients, HBcAg correlates well with HBV DNA and indicates a therapeutic response to the treatment at the beginning of the therapy. In contrast, P-HBcAg tracks more closely to HBV RNA. Importantly, in these patients on-therapy P-HBcAg is detectable several months after HBcAg became undetectable indicating that cccDNA is still present and transcriptionally active in hepatocytes.

Conclusion: Overall, the ability to specifically distinguish between the various states of HBcAg (phosphorylated and non-phosphorylated) provides additional insights for disease staging, drug development, and management of HBV therapies.

Disclosure of Interest: R. Geissler Shareholder of: Abbott Laboratories, Employee of: Abbott Laboratories, M. Patel Employee of: Abbott Laboratories, M. Anderson Shareholder of: Abbott Laboratories, Employee of: Abbott Laboratories, A. Vaillant Shareholder of: Replicor Inc., Employee of: Replicor Inc., X. Qiu Shareholder of: Abbott Laboratories, Employee of: Abbott Laboratories, G. Cloherty Shareholder of: Abbott Laboratories, Employee of: Abbott Laboratories

O29

CIRCULATING HBV RNA CORRELATES WITH INTRAHEPATIC COVALENTLY CLOSED CIRCULAR DNA (CCCDNA) TRANSCRIPTIONAL ACTIVITY IN UNTREATED AND NUC-TREATED CHRONIC HEPATITIS B (CHB) PATIENTS

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Abstract Content: Quantification of Hepatitis B virus (HBV) RNA in blood circulation (cirB-RNA) across chronic Hepatitis B (CHB) phases and during long-term nucleos(t)ide analogues (NUC) treatment and its correlation with intrahepatic viral markers and HBcrAg, the other emerging biomarker of cccDNA transcription, is still lacking.

122 untreated and 30 NUC-treated CHB patients with paired liver biopsy and serum sample, were analyzed for serum HBV DNA, quantitative (q)HBsAg and HBcrAg. Liver cccDNA and 3.5Kb RNA were assessed by qPCR and droplet digital PCR (ddPCR). cirB-RNA was quantified by the Roche HBV RNA investigational assay for use on the cobas® 6800 System (LLOQ 10 cp/ml; linearity range 10 to 10^7cp/ml; LLOD ~3cp/mL).

All untreated HBeAg(+) patients, 74% of HBeAg(-) chronic Hepatitis (CH) and 21% of HBeAg(-) chronic infection (CI) patients had detectable cirB-RNA. The 39 cirB-RNA(-) patients had lower cccDNA, 3.5Kb RNA and 3.5Kb RNA/cccDNA as compared to the cirB-RNA(+) ones. No significant difference was found in qHBsAg levels, while both HBcrAg and serum HBV DNA were significantly higher in cirB-RNA(+) patients. In HBeAg(-) patients, cirB-RNA significantly correlated with serum HBV DNA, HBcrAg, intrahepatic 3.5Kb RNA and cccDNA transcriptional activity, but not with HBsAg and cccDNA levels. A subgroup of cirB-RNA(+) patients with increased cccDNA, serum HBV DNA levels and fibrosis score was identified among HBeAg(-) HBcrAg(-) patients.

All NUC-treated patients (median treatment duration of 2.6 years) had detectable intrahepatic cccDNA and RNA by ddPCR, albeit at low levels. HBcrAg was quantifiable in 77% and cirB-RNA in 40% of patients. cirB-RNA(+) patients showed higher 3.5Kb RNA and cccDNA transcriptional activity levels compared to cirB-RNA(-) ones, but no significant difference in cccDNA amount.

Our results support the notion that cirB-RNA detected by Roche HBV RNA investigational assay reflects the transcriptional activity of intrahepatic cccDNA in both untreated and NUC-treated CHB patients.

This work is supported by the French National Research Agency Investissements d'Avenir program (CirB-RNA project – ANR-17-RHUS-0003)

Disclosure of Interest: None Declared

O30

THE USE OF LIMAX IN PREDICTING CLINICALLY RELEVANT MILESTONES IN CHRONIC LIVER DISEASE OF DIFFERENT AETIOLOGIES

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Background: LiMAx is a novel non-invasive tool that measures the metabolic capacity of hepatocytes function by measuring the ratio of $^{13}CO_2$ to $^{12}CO_2$ exhaled over a maximum period of 60 minutes. It's ability to diagnose and stage steatosis and fibrosis, both milestones in the development of established cirrhosis, alongside its ability to predict 90-day mortality will be assessed in this systematic review to look at its role in chronic liver disease (CLD).

Methods: Search for available literature was carried out on Embase and Medline accessed via Ovid and Web of Science and Cochrane. Literature onwards of 1946 to March 2022 was accessed. The inclusion criteria were case control or cohort studies and there was no language restriction applied. Statistical analysis for the diagnostic accuracy of LiMAx in comparison to the diagnostic accuracy of other available tests for clinically relevant milestones in CLD was carried out by pooling AUROCs and correlation coefficients.

Results: Data from the 7 studies was extracted into Excel tables with the total number of 1623 participants. LiMAx performed significantly better than TE, FIB- 4, AAR, Spleen size and APRI at predicting 90- day mortality (AUROC=0.82). The CLD review demonstrated the superiority of LiMAx in detecting cirrhosis (AUROC=0.92). LiMAx has a predictive accuracy of 0.77 and was the best at identifying fibrosis for patients with non-NAFLD aetiology. Furthermore, results also showed that LiMAx had the strongest (negative) correlation with liver histopathology (r = -0.75).

Conclusion: The LiMAx test is promising for detection of cirrhosis and fibrosis of non- NAFLD aetiology as it outperforms other conventional scores. Largescale validation studies, need to be done prior to introduction in clinical practice, so that several subgroup analyses according to etiology and stage of disease can be carried out.

Key words: LiMAx; Liver Maximum Functional Capacity; Chronic Liver Disease; Cirrhosis; Fibrosis; Steatosis; MELD; CPS; Mortality

Disclosure of Interest: None Declared

O32

THE CCAAT/ENHANCER-BINDING PROTEIN BETA - SERPINB3 AXIS INHIBITION AS A NOVEL STRATEGY FOR NON-ALCOHOLIC STEATOHEPATITIS TREATMENT

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Introduction: The liver has an established key role in maintaining metabolic homeostasis. The serine protease inhibitor SerpinB3 has been described as critical mediator of liver inflammation and fibrosis. 1-Piperidine Propionic Acid (1-PPA) has been recently proposed as a specific SerpinB3 inhibitor.

Aim: To assess a targeted therapeutic strategy for NASH, using 1-PPA in in vitro and in vivo models of NASH.

Methods: SerpinB3-transgenic (TG) and SerpinB3-KO mice were fed on MCD and CDAA diets to induce experimental NASH. Starting from the second month, mice were injected with 1-PPA (70 ng/g) and at sacrifice liver specimens were analyzed for histological parameters and for molecular and protein gene expression. Fibrosis and inflammation genes were assessed in LX2 and THP1 cell lines, exposed to human SerpinB3 (100ng/ml) alone or with 1-PPA (100ng/ml) after 24 hours incubation. The expression of CCAAT Enhancer Binding Protein Beta (CEPB-b), a SerpinB3 transcriptor factor, also involved in metabolic disturbances and inflammatory response, was assessed in different cell lines with or without 1-PPA and in mouse livers in relation to SerpinB3 expression.

Results: SerpinB3-KO mice showed significantly lower steatosis, inflammation and fibrosis after both dietary regimens, while opposite findings were observed in SerpinB3-TG mice, where treatment with 1-PPA reverted these features. This effect was associated to a parallel reduction of genes involved in adipogenesis, inflammation and fibrosis. These findings were confirmed in LX2 or THP1 cells exposed to SerpinB3. At mechanistic level C/EBP-β induced SerpinB3 and was in turn induced by this serpin, generating a positive loop. 1-PPA was able to inhibit the C/EBP-β-SerpinB3 axis.

Conclusions: SerpinB3 - C/EBP-b axis could be relevant in the development of NASH and the SerpinB3 inhibitor 1-PPA is effective in the control of adipogenesis, inflammation and fibrosis in vitro and in NASH models, supporting this approach for a targeted therapy of NASH.

Disclosure of Interest: None Declared

O33

DYRK1B INDUCES FATTY LIVER DISEASE AND ITS DISRUPTION IS PROTECTIVE AGAINST LIVER STEATOHEPATITIS AND LIVER FIBROSIS

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Abstract Content: We have identified multiple independent gain of function mutations in the DYRK1B gene that underlie early-onset diabetes, metabolic syndrome, and fatty liver disease(NAFLD) (NEJM, 2014). DYRK1B levels are increased in the liver of patients with non-alcoholic liver steatoHepatitis (NASH) and mice with a Western diet-induced NASH, indicating its global role in the pathogenesis of NASH. Increasing Dyrk1b levels in the mouse liver by viral vector delivery enhances lipogenesis (DNL), FA uptake, and TG secretion and causes hyperlipidemia and NASH. Conversely, the knockdown of Dyrk1b was significantly protective against high-calorie-induced hepatic steatoHepatitis, fibrosis, and hyperlipidemia. Mechanistically, Dyrk1b increases DNL by dislocating mTOR inhibitors, Deptor, and Fkbp, directly activating mTORC2, bypassing AKT. Dyrk1B also increases plasma membrane sn-1,2-diacylglycerol levels and increases PKCε-mediated IRKT1150 phosphorylation, which results in impaired activation of hepatic insulin signaling and reduced hepatic glycogen storage

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O34

GLECAPREVIR/PIBRENTASVIR IS SAFE AND EFFECTIVE IN ITALIAN PATIENTS WITH CHRONIC HEPATITIS C AGED 75 YEARS OR OLDER: A MULTICENTER STUDY

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Background: Glecaprevir and Pibrentasvir (G/P) determines high rates of sustained virologic response (SVR) with optimal safety profile in patients with chronic Hepatitis C virus (HCV) infection. The efficacy and safety of G/P in Caucasian patients aged 75 years and older has not been widely analyzed. Methods: This is a retrospective multicenter real-world study enrolling all consecutive patients 75 years and older who received G/P between October 2017 and January 2022 at 5 referral centers in Italy. SVR was analyzed by Intention to Treat (ITT) and Per Protocol analysis (PP). Results: 570 patients met the inclusion criteria and were analyzed: mean age was 80 (75-97) years, 356 were females, 52% (298/570) had HCV-1 and 44% (252/570) had HCV-2. 137 (24%) patients had liver cirrhosis. 463 (81%) patients were taking at least 1 concomitant drug, with 144 (25%) taking ≥5 concomitant drugs. G/P was given for 8 weeks in 488 patients (86%). During treatment 48 patients (8%) reported side effects, with 10 (2%) patients discontinuing treatment prematurely. Two patients developed treatment unrelated serious adverse events. Overall, the SVR rate was 97.9% (558/570) by ITT analysis and 99.6% (558/560) by PP analysis. SVR rates remained consistently high among subgroup analysis stratified by genotype, treatment duration, fibrosis stage and concomitant medications. Conclusions: Treatment with G/P achieved 97.9% SVR rates in HCV patients older than 75 years of age. Safety was optimal with only 2% of patients discontinuing early.

Disclosure of Interest: None Declared

O35

REAL-LIFE STUDY OF RESISTANCE-ASSOCIATED SUBSTITUTIONS TO NS5A AND NS5B INHIBITORS IN HCV INFECTED PATIENTS FROM ARGENTINA

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Introduction: Treatment with direct-acting antivirals (DAA) achieves a sustained virologic response (SVR) in >95% of patients infected with HCV. Selection of viral variants carring resistance-associated substitutions (RAS) to NS3, NS5A and NS5B inhibitors is one of the main causes of therapeutic failure.

Objective: Characterize pre-existing NS5A- and NS5B-RAS (basal RASs) in patients infected with HCV genotype 1 and 3. Evaluate their impact on treatment outcome.

Characterize NS5A- and NS5B-RAS in patients without SVR.

Methodology: Sixty-six patients form 2 public hospitals with chronic HCV treated with DAA during 2018-2020 were analyzed. The majority of patients (84.8%) were treatment-naïve patients and 81.8% were treated with Sofosbuvir+Daclatasvir with or without Ribavirin.

Basal RAS as well as therapeutic failure RAS in NS5A and NS5B were determined by Sanger sequencing. Phylogeny studies were done using IQ-tree software.

Results: 77,3% (51/66) of patients achieved a SVR; 4,5% (3/66) resulted in treatment failure. 12,1% of pre-treatment samples (8/66) had RAS in NS5A (7/8) and NS5B (1/8). The frequency of basal RAS in NS5A was as follows: K24R (1/8), R30Q (2/8), L31M (2/8), A62L (2/8), Y93H (2/8), which mostly were unique except for one patient with the combination R30Q+L31M+Y93H. In NS5B, the combination L159F+C316N (1/8) was also observed. 75% of patients with basal RAS (6/8) showed a SVR, one was deceased while the remaining did not respond to treatment with the emergence of 3 new NS5A-RAS (Q30K+L31V+K24R). Among the remaining patients without SVR, one showed emergence RAS in NS5A (Y93H), whereas the other there was neither basal nor post-treatment RAS. No association between the phylogenetic profile and the RAS-related sequences was observed.

Conclusion:

-Pre-existing RAS frequency was low (12,1%) and it did not have an impact on the treatment response since most patients achived a SVR.

-Non-responding patients had diverse RAS in NS5A.

-RAS detection and analysis may be useful in patients with DAA-treatment failure.

Disclosure of Interest: None Declared

O36

EFFICACITY OF TWO LAST-GENERATION DAA IN INFREQUENT HEPATITIS C GENOTYPES/SUBTYPES: REAL-WORLD DATA FROM THE CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL

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Introduction: Patients with infrequent Hepatitis C virus (HCV) genotypes/subtypes are characterized by resistance-associated substitution (RAS) profiles that have been associated with lower sustained virological responses (SVR). Real-world data regarding efficacy of direct-acting antiviral (DAA)-based regimens are needed in order to optimize HCV therapy and to further support expert recommendations.

Aims: The aim of this study was to evaluate the efficacy of DAA-based regimens in patients infected with infrequent HCV genotypes/subtypes in a real-world cohort at the Centre hospitalier de l'Université de Montréal (CHUM).

Method: A retrospective analysis of every patient referred to the CHUM was performed. Between 2014 and 2021, patients with an infrequent HCV genotype/subtype according to the EASL guidelines definition were identified. Patients treated with at least 1 DAA-based regimen were included. Patients enrolled in clinical trials were excluded. Liver fibrosis was assessed prior to DAA therapy by means of liver elastography or by histological evaluation of liver biopsy. SVR was defined as an undetectable HCV RNA 12 weeks after the end of treatment (SVR12). The choice of the DAA combination was made at the physician's discretion.

Results: Among the 801 patients treated with at least 1 DAA-based regimen, 108 (13.5%) had an infrequent genotype/subtype. Median age was 64 (17 – 96), 54 (50.9%) were of male gender, 54 (50.9%) had F3-F4 fibrosis.

Figure 1 shows the overall successes and failures by generation of DAA. The overall SVR12 rate with at least one DAA-based regimen was 87.0% (94/108). In a subgroup analysis, the overall SVR12 rate of patients treated with 2 last-generation DAA was 91.1% (51/56).

Twelve patients received additional DAA-based regimens. Before retreatment, 75.0% had F3-F4 fibrosis. SVR12 was 91.7% (11/12). One cirrhotic genotype 1k patient failed 4 DAA-based regimens (SOF/SIM; SOF/LDV 24/48 weeks; SOF/LDV/RBV).

Conclusion: Our real-world data show that in patients with infrequent HCV genotypes/subtypes treated with 2 last-generation DAA the SVR rate is 91.1%. Although the data are limited, these results support the efficacity of initially treating them with 2 last-generation DAA. More data are needed to determine optimal treatment regimen by genotype/subtype and the benefits of a rational approach based on RAS determination.

Image/Table:

Fig 1. DAA-based regimens and outcomes by genotypes/subtypes

Regimen	Genotypes/subtypes (n)									
The successes (SVR12)										
Last generation DAA										
SOF/VEL	2 (1)	2c (4)	2i (1)	4 (1)	4c (2)	4h (1)	4k (1)	4l (1)	4r (1)	4s (1)
	5a (7)	6 (2)	6a (3)	6e (1)	6h (2)	6l (1)	6o (1)	6xc (1)	7 (1)	7a (1)
SOF/VEL/RBV	1d (1)	2l (1)	4k (4)							
GLE/PIB	2c (1)	4h (1)	4k (1)	6a (2)	6f (1)					
SOF/VEL/VOX	1 (1)	1l (1)	3b (1)	3i (1)	4r (5)	6p (1)				
Past generation DAA										
SOF/PegIFN/RBV	1e (1)	2 (1)	4 (1)	5a (1)	7a (1)					
SOF/RBV	2 (6)	2c (2)	2i (4)	2k (1)	4c (1)	4l (1)	4r (1)	4v (1)	6a (1)	
SOF/SIM	1d (1)									
SOF/LDV	4 (2)	4r (1)	5a (3)	6a (4)	6e (1)	6o (1)				
SOF/LDV/RBV	1g (1)	5a (1)	6a (1)	6e (1)						
SOF/DCV/RBV	1d (1)	2 (1)								
EBR/GRZ	4c (1)	4k (1)	6o (1)							
EBR/GRZ/RBV	4c (1)	4k (1)								
OBV/PTV/R/RBV	4k (1)									
The failures										
Last generation DAA										
SOF/VEL	3i (1)	4b (1)	4r (1)	6p (1)						
SOF/VEL/RBV	3b (1)									
Past generation DAA										
SOF/PegIFN/RBV	1d (1)									
SOF/RBV	2 (2)	2i (1)								
SOF/SIM	1k (1)									
SOF/LDV	1 (1)	1l (1)	1k (1)	4r (1)	6a (1)					
SOF/LDV/RBV	1k (1)									
OBV/PTV/R/RBV	4k (1)									

Disclosure of Interest: None Declared

O37

INTRODUCING AFFORDABLE, GENERIC SECOND-LINE TREATMENT FOR HEPATITIS C ELIMINATION IN RWANDA: PRELIMINARY RESULTS

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Introduction: A 5-year national program for the elimination of viral Hepatitis C was launched in Rwanda in 2018. Of the 7 million people who have received Hepatitis C screenings to date, 60,000 have been treated with first-line directly acting antivirals (DAAs). About 95% of patients respond well to DAAs, although some patients have DAA failure and need a second-line regimen. Sofosbuvir-Velpatasvir-Voxilaprevir (SOF-VEL-VOX), the second regimen recognized by the World Health Organization, is expensive and unaffordable in low- and middle-income nations. We conducted an observational cohort study on the feasibility, side effects, and patient outcomes of Hepatitis C treatment with Sofosbuvir/Velpatasvir + Ribavirin (SOF/VEL+RBV), as a possible alternate second-line regimen to SOF-VEL-VOX.

Methodology: Patients who have failed on first-line DAAs were recruited from 44 hospitals since November 2021 and consented to participate in a 24-week second-line treatment using SOF/VEL+RBV. Participants were counseled on pregnancy prevention and offered modern contraceptives and clinical and laboratory assessments were performed at baseline and during treatment for profiling the safety of the second-line regimen. An electronic data system, District Health Information System (DHIS2 tracker) was used for patient records and follow-up. Every patient was closely monitored by a trained healthcare provider from treatment initiation to the date of the sustained virologic response test (SVR12).

Result: 234 patients were enrolled in this ongoing study. Of them, 152 (65.2%) were female, (170), 71.7% were aged 60+ years, 23 (9.8%) were living with HIV, and 15 (6.4%) were cirrhotic (defined by APRI). The most commonly reported side effects were fatigue (26, 11.1%), loss of appetite (20, 8.6%), headache (19, 8.1%), and nausea (18, 7.7%). 6 (2.5%) discontinued treatment due to anemia or side effects, and 1 (0.4%) lost to follow-up after initiating treatment. The most commonly reported laboratory abnormality was anemia (17, 7.2%). So far, only 88 out of 234 enrolled patients have outcomes such as cured, discontinuity, or loss to follow-up, while the remaining patients completed treatment and are waiting for SVR 12 results. Of the 81 patients who completed treatment and received SVR12 results, 70 (86.4%) were cured, and 11 (14.5%) failed treatment.

Conclusion: SOF/VEL+RBV is an affordable and safe generic regimen with relatively high efficacy. Based on the observed cure rate, this therapy could be a potential alternative to SOF/VEL/VOX in LMIC.

Disclosure of Interest: None Declared

O38

EX VIVO IMMUNOLOGICAL ASSAYS HAVE THE POTENTIAL TO PREDICT RESPONSE TO PD-1 TARGETING THERAPIES IN CHRONIC HEPATITIS B PATIENTS

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Background and Aims: HBV-specific T cells are functionally exhausted in chronic Hepatitis B virus (HBV) infection. Immune checkpoint blockade targeting PD-1/PD-L1 can rescue HBV-specific T cells and potentially achieve functional cure. Our study aimed to identify an ex vivo assay that might predict chronic Hepatitis B (CHB) patients responsive to checkpoint inhibitor therapy.

Methods: We enrolled immunotolerant (IT), HBeAg+ immune-active (IA+), HBeAg- immune-active (IA-), inactive carriers (IC) and functionally cured (FC) patients to test ex vivo PD-1 blockade on HBV-specific T cell functionality. PBMCs were stimulated with overlapping peptides covering HBV proteins +/- anti-PD-1 blocking. Functional T cells were measured using a 2-color FluoroSpot assay for IFN-gamma and IL-2. We measured ISG15 induction in CD4 T cells from patients who did or did not have greater IL-2 responses after PD-1 blockade, which has been shown to predict overall survival in cancer patients treated with checkpoint inhibitors.

Results: Ex vivo IFN-gamma+ responses did not differ across phases. IL-2+ responses were significantly higher among IC and FC patients. PD-1 blockade restored IL-2+ responses across all patient cohorts but HBeAg negative status was associated with significantly higher functional restoration. Antigen-specific T cell responses differed by stage of disease. IC patients had significantly higher functional Core-specific T cell responses that were highly responsive to PD-1 blockade compared to IT patients. Ex vivo frequencies of Env-specific T cells were not significantly different between IT and IC patients, and represented a smaller proportion of the total HBV-specific responses among IC patients. CHB patients that showed increased IL-2 production after PD-1 blockade also displayed significantly lower induction of ISG15, which was in line with checkpoint inhibitor responses in cancer patients that had better overall survival

Conclusion: We demonstrate that IL-2 production was superior to IFN-gamma as a marker of T cell restoration across the clinical phases. Ex vivo PD-1 blockade enhanced HBV-specific T cell functionality and this restoration was primarily observed in patients with HBeAg negative disease. The ability to predict patients who are likely to respond to PD-1 therapy, either through an antigen specific assay or the IFN response capacity, could select/exclude patients for checkpoint inhibitor therapy, which carries a significant risk of adverse events.

Disclosure of Interest: None Declared

O39

ACUTE HEPATITIS OF UNKNOWN ETIOLOGY (AHUA) IN ISRAELI CHILDREN: HUMAN HERPESVIRUS 6 (HHV6) AS A POSSIBLE TRIGGER FOR THE DISEASE

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Background and aim: An increase in the number of cases of acute Hepatitis of unknown etiology (AHUA) in children has been observed since October 2021. As of 24 November 2022, the European Centre for Disease Prevention and Control reported 572 such cases in 22 countries. Among different viruses that were tested, SARS-Cov-2, adenovirus and adeno-associated-virus 2 (AAV2) have been suggested as possible triggers in numerous cases. However, the causal relationship between AHUA and any potential etiology is still unclear. Here we report virological findings in the Israeli patients.

Methods: Samples (whole blood, sera, feces) from 23 children <18 years old with acute unexplained Hepatitis, collected between October 2021 and September 2022, were analyzed. Demographic and Clinical data, laboratory tests and SARS-Cov-2 status were collected. Adenovirus, enteroviruses, human herpesvirus 6 (HHV6) and AAV2 were all tested.

Results: Median age was 4 years (IQR 2-13), 15/23 were females; none required liver transplantation. Adenovirus was found in 2/19 of whole blood samples and in 5/12 of fecal samples, one of which was subtyped as T-2. AAV2 was detected in 4/18 patients. Past SARS-Cov-2 exposure (infection or vaccination) could be verified in 14/22 cases. HHV6 reactivation (detected by PCR or by rise in serum IgG) in 14/21. Nearly all patients (22/23) were exposed to at least one of these viruses.

Conclusions: Our results suggest that in Israel, HHV6 is a plausible cause for the outbreak of acute Hepatitis in children. In view of the SARS-Cov-2 pandemic, it may be that combination of reactivation or active infection with specific viruses could be a trigger for this outbreak.

Disclosure of Interest: None Declared

O40

SEVERE ACUTE HEPATITIS OF UNKNOWN ETIOLOGY PRESENTING AS ACUTE LIVER FAILURE IN CHILDREN: OUTCOMES FROM THE LIVER INTENSIVE CARE UNIT

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Background & Objectives: A sudden surge of severe acute Hepatitis of unknown etiology has been reported from around the world with over 1000 cases reported from 35 countries since March 2022. Cases of severe acute Hepatitis developing acute liver failure (ALF) have poor outcomes with only 25% native liver survival (NLS). We describe the workup, clinical course, and outcome of children with severe acute Hepatitis presenting as ALF.

Methods: After ethical approval, we collected the restrospective data of cases presenting with severe acute Hepatitis over 4 months (May-August 2022) at a tertiary care pediatric hepatology and liver transplant referral center. Severe acute Hepatitis (with ALF) was defined as per the recent WHO definition to include children up to 16 years of age presenting with severe acute Hepatitis (serum transaminases >500 IU/L) and ALF (INR > 2) of unknown etiologies. All cases underwent diagnostic evaluation for hepatotropic viruses (Hepatitis A, B, and E), autoimmune Hepatitis, fulminant Wilson disease, and rigorous history of drug intake. Patients where no etiology could be found were subjected to second-line tests which included IgM CMV, EBV, parvovirus DNA, adenovirus DNA PCR in blood and stool, SARS-COV2 PCR from the respiratory sample, SARS-COV2 IgG antibody, IgM dengue, and HHV-6 DNA PCR.

Results: A total of 178 children presented with acute Hepatitis during May-August 2022, including 28 presenting as ALF. Of the 28 patients with ALF, 18 (64.3%) were HAV-induced ALF, while 8 (28.6%) had an unknown etiology. Table 1 describes the clinical presentation and outcome of the 8 children with severe acute Hepatitis of unknown etiology presenting as ALF. The median age of presentation was 4 years (range: 1.5 – 15 years); 6 (75%) were males. All extended panel viral markers were negative in 7 cases and one girl had detectable IgM parvovirus antibody (Parvovirus PCR negative). Six (75%) of these children had SARS-COV2 IgG antibodies (5 unvaccinated). Adenovirus DNA PCR was negative in all 8 cases. Two children (25%) survived with their native liver, while 4 (50%) died and 2 (25%) received living donor LT. Most had a fulminant course with the median time from admission to death/LT being 2.5 days (range 1 – 14 days). Compared to HAV-induced ALF, these children were younger (4 years vs 13 years), had higher INR (6.31 vs 2.9), had a greater prevalence of GI symptoms (62.5% vs 11.1%) and worse outcomes (NLS: 25% vs 50%).

Conclusion: Children with severe acute Hepatitis of unknown etiology are younger, have shorter jaundice to HE interval, a predominance of GI symptoms, and have a rapidly progressive liver failure with low NLS, thus requiring expedited evaluation and referral to an LT center.

Image/Table:

Table 1: Clinical presentation, course, and outcome of children presenting with severe acute hepatitis of unknown etiology (with acute liver failure) from May to August 2022

Sl No	Age (years) / Gender	Jaundice to HE interval (Days)	Grade of HE	Other Symptoms	Bilirubin (total/ direct) (mg/dl)	Peak INR	AST (IU/L)	ALT (IU/L)	Ammonia (µg/dl)	Adenovirus PCR	SARS-COV2 Ab S/CO	IgG/ AI markers	HVP/ CRRT	KCH criteria for LT	Outcome	Duration of ICU stay (Days)
1	14/F	10	2→3	--	29.8/ 19.8	2.44	656	588	144	-ve	5.28	18.2/ ANA, ASMA, LKM1, SLA -ve	HVP x 3 sessions	3	LT	8
2	1.5/M	HE prior to jaundice	1→ 2	GI symptoms	1/0.5	3.8	8158	5317	154	-ve	3.05	6.8/ ANA, ASMA, LKM1, SLA –ve	No	2	Survived	7
3	3/M	HE prior to jaundice	2→ 3	GI symptoms	3.3/2	5.92	6976	5442	1785	-ve	3.24	12.8/ ND	HVP x 1 session	3	Death	1
4	15/M	8	4	Previous Acute hepatitis	13.6/7. 6	6.7	3377	3540	346	-ve	2.26	23.3/ ANA, ASMA, LKM1, SLA –ve	HVP x 3 sessions	3	Death	3
5	1.5/M	1	2→ 3	GI symptoms	19.4/7. 6	6.8	636	900	256	-ve	2.8	12.2/ ANA, ASMA, LKM1, SLA –ve	No	3	Death	2
6	4/M	1	3	GI symptoms	2.8/1.9	11.5	7800	7775	943	-ve	-ve	5.89/ ANA, ASMA, LKM1, SLA –ve	CRRT	2	Death	1
7	4/M	7	3	GI symptoms	23.8/ 13	7.2	3341	1966	146	-ve	-ve	12.2/ ANA, ASMA, LKM1, SLA -ve	HVP x 3 sessions CRRT	3	LT	14
8	8/F	2	1	--	5.8/3.8	4.78	3198	2881	121	-ve	2.93	14.3/ ANA 1:20 +ve, ASMA, LKM1		3	Survived	11

Disclosure of Interest: None Declared

O41

A NOVEL TECHNOLOGY FOR DIAGNOSIS OF HCV VIREMIA USING THERMO-SENSITIVE SMART POLYMER: PILOT STUDY OF A POINT OF CARE TEST OF HCV COMPARED TO POLYMERASE CHAIN REACTION TEST (PCR)

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Introduction: Chronic Hepatitis C virus (HCV) infection represents a major global health problem with 71 million chronically infected individuals worldwide. Many infected people remain undiagnosed and unaware of their infection and may progress to cirrhosis and hepatocellular carcinoma. The current diagnostic algorithm is based on using two steps; rapid diagnostic tests (RDTs) and viral load confirmation which are expensive, and require advanced laboratory facilities and qualified lab personnel. Thus, there is a need for one step, and accurate Point of Care (POC) test for HCV viremia. We reported that Thermo-sensetive smart polymer, "NIPAAm-co-HIPAAm-co-SAKIPAAm"(Patent:2019/2002) was able to extract and enrich HCV antigens but detection was done using the thermocycler of PCR machine [1] Detection of the extract could by done using colloidal gold nanoparticles for detection of the HCV smartpolymer extract to have a complete test (extraction , enrichment and detection) without the need of PCR machine

Aim: To evaluate this novel technology for extraction and enrichment of HCV antigens using the thermo-sensitive smart polymer and also detection by colloidal gold nanoparticles as (POC) for comparison with the gold standard PCR.

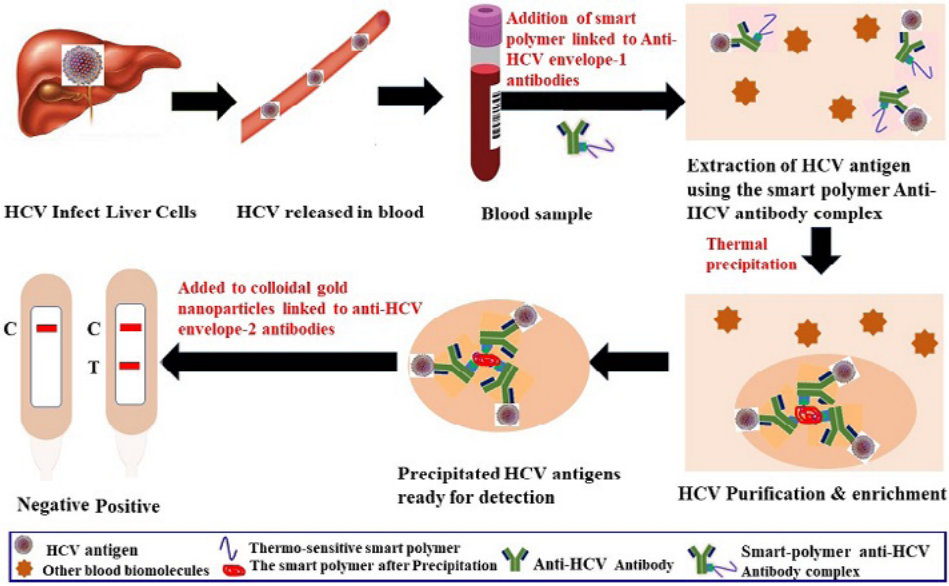
Methods: 46 serum samples: 37 positive HCV and 9 Negative samples were used for diagnosis of HCV viremia using the novel thermo-sensitive smart polymer technology and the results are compared to the gold standard PCR (Cobas ampliprep/TaqMan®, Roche). Extraction and enrichment: Anti-hcv antibodies for envelope protein-1 are added to thermo-sensitive smart polymer for extraction and enrichment of HCV antigens in serum samples. Detection: The enriched precipitate is added to colloidal gold nanoparticles (AuNPs) which binds to anti-HCV antibodies for envelope protein-2 to form colored complex for positive samples.

Results: HCV antigens extracted by thermo-sensitive smart polymer then detected by gold nanoparticles yield the same results for positive and negative samples as detected by HCV RNA PCR. The sensitivity and specificity are both100%.

Conclusion: The novel thermo-sensitive smart polymer technology is simple, one step test and has the same diagnostic accuracy as the gold standard PCR but does not require expensive facilities or highly qualified lab personnel. It could be considered a point of care test (POC) for HCV viremia if validated in multicenter studies.

References: 1. A Nabil, E Yoshihara, K Hironaka, A Hassan, R Soliman, G Shiha and M Ebara, A novel technology for extraction and enrichment of hcv antigen using temperature-sensitive smart polymer: a comparison with pcr, a pilot study. Hepatology 2022, 1316, s402.

Image/Table:



Disclosure of Interest: None Declared

O42

INNOVATIVE APPROACH USING CLINICAL METAGENOMICS FOR THE DIAGNOSIS OF NON-ELUCIDATED LIVER DISEASES

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Background and Aims: Diagnosis of acute and chronic liver diseases (CLD) may be challenging when main etiologies are absent. Liver histology usually provides hints but often fails to accurately identify the etiologic factor. Clinical metagenomics (CMg) is a new technique based on sequencing of nucleid acids allowing the identification of microorganisms in an exhaustive manner. Our aim was to evaluate the performance of CMg for the diagnosis of non-elucidated liver diseases.

Methods: All patients seen between 2019 and 2022 in a single tertiary centre for a non-elucidated liver disease were included. Inclusion criteria were elevated biochemical liver tests with no definite diagnosis after a comprehensive work-up including a liver biopsy. The cut-off of 6 months discriminated acute and chronic profiles. Shotgun metagenomics was performed on each liver biopsy specimen with the aim to detect unexpected microorganisms.

Results: 67 patients (mean age ±SD: 53.8±16.3, male: 65.2 %) were included. Their clinical presentations consisted of acute pattern in 39 patients (58.2 %, median ALT: 126 IU/l, median ALP: 230 IU/l) whose cytolysis with or without jaundice in 14 (73.7 %) , cholestatic in 21 (50 %) or mixed pattern in 4 (66.7%). The presentation was chronic in 21 patients (41.8%, %, median ALT: 46 IU/l, median ALP: 133 IU/l) whose cytolysis in 5 (26.3 %), cholestasis in 21 (50%) or mixed pattern in 2 (33.3 %). 42 patients (62 %) had immunosuppression: 16 (23.9 %) due to solid organ transplantation, 6 to HIV infection (9 %), 10 to hematopoietic or other cancer (14.9%), and 8 (11.9%) had immunosuppressive treatment for autoimmune diseases. Results of CMg were positive in 14 (20.9%), including false positive due to contamination in 4 (6 %). Pathogens identified were adenovirus in one patient presenting with acute Hepatitis, HCV in one seronegative liver solid-transplant recipient (SOT) with recently acquired infection, HEV in one liver SOT patient with unexplained cytolysis and negative HEV serology, HDV in 1 seronegative HBsAg(+) patients, Mycobacterium spp in a immunocompetent patient with unexplained liver granulomatosis, HEV serotype C in SOT patient with non-detectable viral load, and Sphingobium spp in a cirrhotic patient presenting with uncommon ACLF. Additionally, 3 patients had positive results that were considered as putative cofactors. Pathogens were EBV in one HIV-infected patient with tuberculosis, and TTV in two patients, one on immunotherapy for hematopoietic cancer and the other on Rituximab treatment for inflammatory bowel disease. Taking the whole population, a definite diagnosis was made after a comprehensive work-up in 48 patients (71.6%) including 7 (10.4%) infectious diseases diagnosed by CMg.

Conclusions: CMg performed on liver tissue is technically feasible and may bring etiologic diagnostic in patients with non-elucidated acute or chronic liver disease.

Disclosure of Interest: None Declared

O43

HIGH MOLECULAR DIVERSITY AND REMARKABLE GEOGRAPHICAL DISTRIBUTION OF HEPATITIS DELTA VIRUS STRAINS, THAT ARE SPREADING IN CAMEROON

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Abstract Content: Cameroon, located in central Africa, is known to be a country of high prevalence of Hepatitis B (HBV) and Delta (HDV) virus infections, along with a high genetic variability of the circulating strains. In this study, we aimed to carry out a study on the molecular diversity of HDV strains that spread all over the Country. Due to limited access to analysis laboratories, almost all patients' clinical samples are referred to the Pasteur Center in Yaoundé. All HBsAg-positive samples collected between January 2018 and December 2020 from most regions of the country were considered. Age, gender, and city of residence were recorded. HDV diagnosis was performed by total HDV antibody (HDV-Ab) screening by a commercial enzyme like immunosorbent assay. HDV-RNA viral load (HDV-VL) was performed on all positive samples using a validated HDV quantification kit capable of properly quantify all HDV strains whatever the genotype. HDV genotyping was performed using the Sanger sequencing method of the well-described R0 amplicon of the HDV genome followed by phylogenetic analyses. A total of 402 samples positive for HDV-Ab could be considered in this study. were. Among them 105 (26.1%) were HDV-VL negative. The remaining 297 (73.9%) showed detectable HDV-VL titers ranging around the lower limit of detection (LOD) of the assay to more than 8 log IU/ml. Genotype could be obtained for 237 (79.8%) of the HDV-RNA positive samples. HDV-1 genotype was predominant (75.1%). HDV-5, -6, -7 and -8 were also found, with a proportion of 2.9%, 8%, 12.6% and 1.3% respectively. Interestingly, most HDV-1 strains were found in the Northern part of the country, whereas only HDV-6 and -7 strains were isolated in the East region. In the North-West / West regions, HDV-1, -5, -7 and -8 were identified, while in the South-West HDV-6 but not HDV-5 was found. In the Central region, all genotypes were present, whereas only HDV-1 and -7 were identified in the South. Of note, no new subgenotypes were found by analyzing the complete genome sequence of one strain among each cluster of the phylogenetic tree.

In summary, HDV-1, and HDV-5 to -8 are spreading in Cameroon, with a remarkable geographical distribution. Such diversity argues for the emergence of the human HDV in this part of the world. Additional studies are needed to further assess this genetic variability over the whole genome sequences of these strains.

Disclosure of Interest: None Declared

O44

CLINICAL CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH CIRRHOSIS AND HEPATOCELLULAR CARCINOMA IN THE GAMBIA, WEST AFRICA

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Background: Chronic liver disease is a major cause of premature death in sub-Saharan Africa (sSA). However, due to lack of curative treatment for cirrhosis and hepatocellular carcinoma (HCC), clinical relevance of screening and surveillance of cirrhosis and HCC in sSA remains unclear. We described the clinical characteristics and outcomes of patients with cirrhosis and HCC in The Gambia and assessed the impact of Tenofovir Disoproxil Fumarate (TDF) on survival.

Methods: We prospectively followed up adults consecutively diagnosed with cirrhosis or HCC between 2012-2015 in The Gambia, West Africa. HBV-positive patients with cirrhosis, without HCC, were offered TDF. Primary outcome was overall survival estimated using the Kaplan-Meier method. Multivariable Cox proportional hazards models with the inverse probability of treatment weighted (IPTW) were performed to determine the effect of TDF.

Findings: Of 529 patients enrolled in this study, 336 patients (252 with HCC and 84 with cirrhosis) were analysed. Patients were predominantly male (75.3%) with median age 42 years (IQR: 33-55). HBV, HCV and HDV serologies were positive in 84.4%, 9.9% and 9.9%, respectively. Sixty-four percent of HCC patients had multifocal tumour, with a median size of 7.5 cm (IQR: 5.4-10.8). Median survival was 17.1, 11.3 and 1.5 months among patients with compensated cirrhosis, decompensated cirrhosis, and HCC, respectively (log rank p<0.0001).

In HBV-positive patients with cirrhosis, median turnaround time between cirrhosis diagnosis and TDF initiation was 4.9 months. TDF treatment was associated with improved survival in patients with HBV-related cirrhosis (IPTW-adjusted Cox analysis HR: 0.14; 95%CI: 0.06-0.34, p<0.001). Ascites (HR: 1.83, 95%CI: 1.09–3.09) and portal thrombosis (HR: 3.81, 95%CI: 1.99–7.30) were independent risk factors of mortality in HCC cases.

Interpretation: Early screening and treatment programs of cirrhosis and HCC alongside simplified treatment guidelines are urgently required in Africa.

Disclosure of Interest: None Declared

O45

UPDATED PREVALENCE OF CHRONIC HEPATITIS B AND HEPATITIS DELTA INFECTION AMONG FOREIGN-BORN INDIVIDUALS IN THE UNITED STATES IN 2021

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Background: Suboptimal awareness and testing for both chronic Hepatitis B (CHB) and Hepatitis delta virus (HDV) infections among adults contributes to poor understanding of the true prevalence of CHB and HDV infections in the United States (US). Foreign-born (FB) persons contribute to the majority of the clinical burden of both CHB and HDV infections in the U.S., given higher prevalence of CHB and HDV in other countries, particularly Asia and Africa. This study aims to provide an updated estimate of both CHB and HDV prevalence among FB adults in the US.

Methods: We comprehensively evaluated CHB prevalence among FB adults in the US by performing systematic reviews and meta-analyses (surveys published from 1980 to 2021) that combined country-specific CHB prevalence rates with number of FB living in the US in 2021 by country of birth from the US Census Bureau. Among adults with CHB, estimates of HDV prevalence were analyzed by combining country-specific HDV prevalence rates (anti-HDV or HDV RNA positive) for persons with CHB from meta-analyses and applied these estimates to the number of FB with CHB in the US in 2021 by country of birth to estimate the number of FB CHB patients with combined HDV infection.

Results: In 2021, the overall FB population in the US was 48.8 million, among which the overall estimated prevalence of CHB was 3.10% (95% CI 2.53–3.67), resulting in 1.51 million (95% CI 1.24–1.79) FB adults with CHB. While the prevalence of CHB was highest among FB individuals from Africa (pooled prevalence, 8.56%, 95% CI 6.87-10.25), followed by Asia (pooled prevalence, 5.84%, 95% CI 5.28-6.40), given immigration patterns, the actual number of FB individuals with CHB was predominantly from Asia (~873,000), followed by the Americas (~286,000), then Africa (~239,000) (Figure 1). Among FB adults with CHB, overall estimated pooled prevalence of HDV infection was 9.33% (95% CI 4.94–15.88), resulting in ~141,000 FB adults with HDV (95% CI 75,000–240,000). World region-specific estimates of HDV infection among adults with CHB were 8.75% in Asia, 7.47% in the Americas, 20.83% in Oceania, 10.94% in Africa, and 14.38% in Europe, representing ~76,000 (Asia), ~21,000 (Americas), ~2,600 (Oceania), ~26,000 (Africa), and 14,000 (Europe) FB CHB adults with HDV infection in the US (Figure 2).

Conclusion: This analysis provides an updated estimate of the number of FB adults with CHB (~1.51 million) as well as those with combined CHB-HDV infections (~141,000) living in the US in 2021. Accurate estimates of both CHB and HDV infections are critical to understand as they would help guide healthcare resource planning as well as appropriate public health policy development.

Image/Table:

Figure 1. CHD Prevalence Among Foreign-Born Adults in the U.S. by World Region of Birth

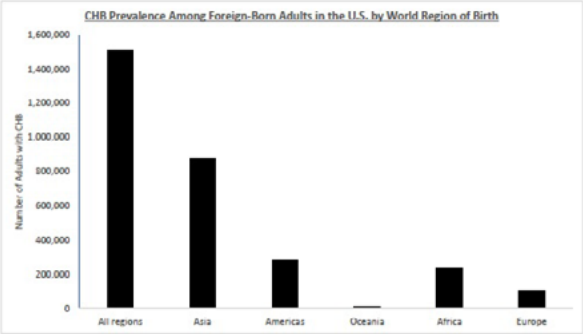
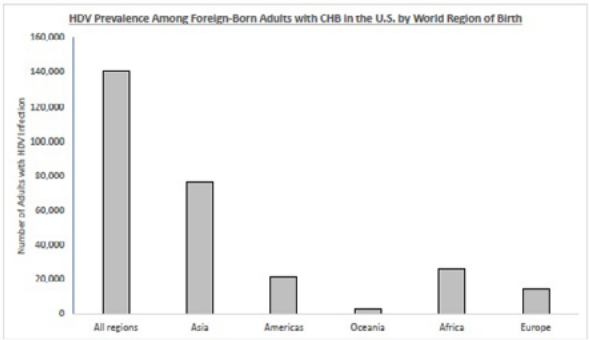


Figure 2. HDV Prevalence Among Foreign-Born Adults with CHB in the U.S. by World Region of Birth



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O46

NATIONAL PREVALENCE AND RISK FACTORS OF HEPATITIS DELTA VIRUS INFECTION IN HBSAG POSITIVE SUBJECTS IN CAMEROON, CENTRAL AFRICA

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Background: A recent systematic review and meta-analysis summarized current knowledge of Hepatitis delta virus (HDV) in the continent: high prevalence in Central Africa (26% in persons with chronic HBV infection, 38% among those with liver disease), intermediate prevalence in West Africa (respectively 7% in general population with chronic HBV infection and 10% in liver-disease population), and low prevalence in East and Southern Africa (only 0.05% in chronic HBV infection). However, this assessment was based on a small number of studies in a few countries, which generally used samples of convenience. The reasons for this huge variation in HDV prevalence between regions (and between countries within a given region) are unknown. Unmet needs include a better description of the epidemiology of the virus, its natural history and the modes of transmission in Africa. Demographic Health Surveys (DHS) offer a unique opportunity for the mapping of various pathogens on a very large nationwide representative sample.

Objective: To investigate the national distribution and risk factors of HDV infection in Cameroon.

Method: We tested for Hepatitis B virus (HBV) surface antigen (HBsAg) and anti-HDV antibodies 14 150 capillary blood samples collected during the 2011 Demographic and Health Survey, whose participants were representative of the Cameroonian population aged 15-49 (both genders) and 50-59 years (men only). Historical data on exposure to medical care as well as socio-demographic data were collected and factors associated with HDV assessed through logistic regression and geospatial analyses. The samples had already been tested for Hepatitis C virus and HIV antibodies.

Results: Overall, 1621/14 150 (weighted prevalence=11.9%) participants were HBsAg positive, among whom 224/1621 (10.6%) were anti-HDV positive. In 2011, the estimated numbers of HBsAg positive and HDV seropositives were 1 160 799 and 122 910 in the 15-49 years age group, respectively. There were substantial regional variations in prevalence of chronic HBV infection, but even more so for HDV (from 1% to 54%). In multivariable analysis, HDV seropositivity was independently associated with living with an HDV-seropositive person (OR=8.80; 95% CI: 3.23 to 24.0), being HIV infected (OR=2.82; 95% CI: 1.32 to 6.02) and living in the South (latitude <4°N) while having rural/outdoor work (OR=15.2; 95% CI: 8.35 to 27.6, when compared with living on latitude ≥4°N and not having rural/outdoor work).

Conclusion: We found evidence for effective intra-household transmission of HDV in Cameroon. We also identified large differences in prevalence between regions, with cases concentrated in forested areas close to the Equator, as described in other tropical areas. The reasons underlying these geographical variations in HDV prevalence deserve further investigation.

Disclosure of Interest: None Declared

O47

THE BURDEN OF HEPATITIS B VIRUS (HBV) INFECTION IN CHILDREN AND WOMEN OF REPRODUCTIVE AGE IN NIGERIA, 2018

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Abstract Content: The WHO global target to eliminate mother to child transmission(MTCT) of Hepatitis B virus(HBV) by 2030 requires achievement of Hepatitis B surface antigen(HBsAg) prevalence of ≤0.1% among children and ≥90% coverage with timely Hepatitis B vaccine birth dose(HepB-BD) and 3 additional doses(HepB3). Hepatitis B(HepB) vaccination including hepB-BD has been in the immunization schedule in Nigeria since 2004 but coverage is low. To assess the impact of vaccination and the current risk of HBV MTCT, we tested residual specimens from a sample of children and women of reproductive age(WRA)[15-44 years] from the 2018 Nigeria AIDS Indicator and Impact Survey(NAIIS), a nationally representative serosurvey, for markers of HBV infection.

Methods: Plasma specimens from 6588 children 2-9 years of age were tested for HBsAg. Specimens from 311 WRA who tested positive for HBsAg in NAIIS were evaluated for HBeAg, HBV DNA and HBV genotype. We calculated HBV prevalence estimates weighted to reflect complex survey design and Wilson 95% confidence intervals (CI). Associations between HBV infection and demographic characteristics were evaluated by Rao-Scott^2 statistic and multivariable logistic regression. Descriptive statistics were calculated for other HBV markers.

Results: HBsAg prevalence among children was 5.8%(CI: 5.0%-6.6%). Prevalence among children 2-4 and 5-9 years of age was 6.4%(CI: 4.9%-7.9%) and 10.0%(CI: 8.1%-11.8%) respectively in the northern region compared to 1.3%(CI: 0.6%-2.1%) and 1.2%(CI: 0.6%-1.7%) in the southern region. Prevalence was inversely correlated with HepB vaccine coverage in those regions.

HBsAg prevalence among WRA was 6.3%(95%CI: 5.4%-7.3%). Prevalence in WRA was significantly higher in the north(7.8%, 95%CI: 6.4-9.4%) than the south(4.4%, 95%CI: 3.4-5.7%).

In multivariable logistic models, age, region, and wealth quintile were significantly associated with HBV infection among children; only region was significantly associated with HBV infection among WRA.

Among HBsAg+ WRA, 19% were HBeAg+ and 17% had HBV DNA levels≥200,000 IU/mL. The proportion who were HBeAg+ and/or had high HBV DNA levels was greater among women 15-29 years than those 30-44 years. Genotypes E and A accounted for 90% and 10% of specimens.

Conclusions: HBV prevalence among children in Nigeria remains high, particularly in the north correlating with low vaccine coverage in the region. Prevalence was lower in the south, but the similar burden in younger and older children suggests remaining infections are likely due to MTCT. Efforts are needed to address low HepB vaccine coverage across Nigeria including improving HepB3 vaccine coverage in the north while increasing coverage with timely HepB-BD nationwide.

Disclosure of Interest: None Declared

O48

EFFICACY AND SAFETY OF ALXN1840 VERSUS STANDARD OF CARE IN WILSON DISEASE: PRIMARY RESULTS FROM AN ONGOING PHASE 3, RANDOMIZED, CONTROLLED, RATER-BLINDED TRIAL

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Background and Aims: ALXN1840 is an oral, copper (Cu)-binding agent that forms a stable tripartite (tetrathiomolybdate-Cu–albumin) complex. This study investigated the efficacy and safety of ALXN1840 for treating Wilson disease (WD) using a novel plasma biomarker of Cu sequestration.

Method: Prior SoC for > 28 days and 0 – 28 days determined enrolment to Cohorts 1 and 2, respectively. Primary endpoint: mean daily area under the effect–time curve of directly measured non-ceruloplasmin-bound Cu 0 – 48W (dNCC $AUEC_{0-48W}$). Secondary endpoints: 0 – 48W change in neurological Unified WD rating scale (UWDRS) Part II and III scores, and Clinical Global Impression – Improvement (CGI-I) scores. A pre-specified hierarchical statistical testing method was used to control multiplicity across primary and key secondary endpoints. Adverse events(AEs) were summarized.

Results: 214 patients enrolled; all had preserved liver function and 79% had neurological symptoms. 207 were treated, 137 with ALXN1840 and 70 with SoC; mean age was 34.3 and 32.1 years, and 59.9% and 52.9% were male, respectively. Mean daily dNCC $AUEC_{0-48W}$ (µmol/L) was 3.2 times greater with ALXN1840 than with SoC overall (least-squares mean [LSM] difference, 2.18 [standard error (SE), 0.244], $p < 0.0001$), and 2.5 times greater with ALXN1840 for Cohort 1, despite a mean prior SoC duration of > 12 years (Figure). UWDRS scores reduced modestly from 0 to 48W (mean [95% confidence interval] change in Part III score for symptomatic patients: ALXN1840, −2.91 [−4.74, −1.09]; SoC, −1.17 [−3.20, 0.86]). No significant between-group differences occurred by 48W. Transformed CGI-I scores improved with ALXN1840 vs SoC at 48W; LSM difference, −0.3 [SE, 0.15], $p = 0.0316$; outside the multiplicity testing sequence). For 0 – 48W, 100.1 (ALXN1840) and 86.5 (SoC) patients experienced AEs per 100 patient-years. Most AEs (ALXN1840, 94.1%; SoC, 92.7%) were not serious. The most frequent AE with ALXN1840 was alanine aminotransferase increase (14.6%). Two deaths, considered unrelated to ALXN1840, were reported.

Conclusion: ALXN1840 treatment for 48W provided superior Cu control to SoC and was generally well tolerated. Future data analysis of the 60-month open-label extension of this study will evaluate long-term efficacy and safety of ALXN1840.

Previously presented at EASL 2022

Image/Table:

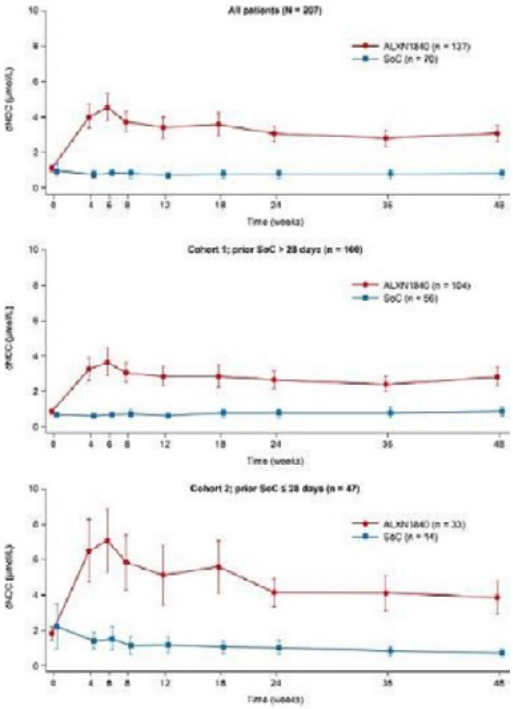

Figure: dNCC values by treatment group from 0 to 48 weeks.
dNCC, directly measured non-ceruloplasmin-bound copper; SoC, standard of care.

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Vivet Therapeutics, Conflict with: Alexion Pharmaceuticals, Deep Genomics and Ultragenyx. Participated on a Data Safety Monitoring Board or Advisory Board for Alexion Pharmaceuticals, Deep Genomics, Ultragenyx and Vivet Therapeutics., A. Ala Grant / Research support from: Alexion & Orphalan – Contracts for study to organization, Conflict with: Honoria payments and travel expenses from Alexion and Honoria from Orphalan, P. Ferenci Conflict with: Ambys, Mexbrain, Univar Solutions BV and Vivet Therapeutics; and and has a patent for WTX-101 (ALXN1840)., P. Ott Grant / Research support from: Alexion Pharmaceuticals, Orphalan and Univar Solutions BV, Conflict with: Honoraria payments from GMP-Orphan SA, D. Abdurakhmanov Conflict with: Nothing to disclose, F. Szalay Conflict with: Nothing to disclose, P. Socha Conflict with: Alexion Pharmaceuticals and honoraria payment and travel expense from Orphalan, N. Shimizu Conflict with: Nothing to disclose, J. Bronstein Conflict with: Nothing to disclose, D. Bega Conflict with: Alexion Pharmaceuticals and Ultragenyx Pharmaceuticals., S. Hahn Conflict with: consulting fees and travel expenses from Alexion Pharmaceuticals, E. Swenson Shareholder of: Own stocks in Alexion Pharmaceuticals., Employee of: Alexion Pharmaceuticals, Y. Chen Shareholder of: Own stocks in Alexion Pharmaceuticals., Employee of: Alexion Pharmaceuticals., A. Poujois Conflict with: honoraria payment and travel expenses from Alexion Pharmaceuticals and participated on a Data Safety Monitoring Board or Advisory Board for Alexion Pharmaceuticals.

O49

OBESITY IS ASSOCIATED WITH A LATE-STAGE HEPATOCELLULAR CARCINOMA AT DIAGNOSIS DESPITE ADEQUATE ULTRASOUND SURVEILLANCE

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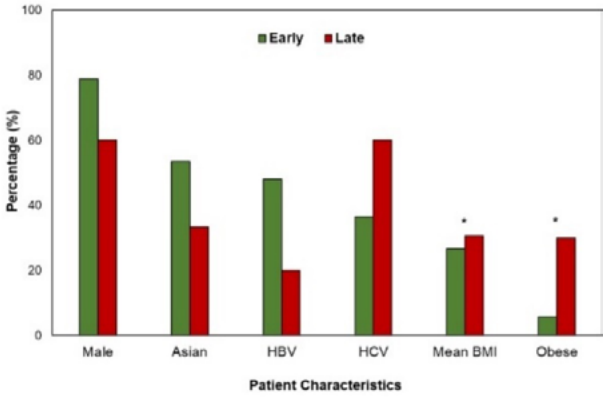
Background: Surveillance for hepatocellular carcinoma (HCC) is key to early diagnosis and access to potentially curative therapy. Despite surveillance, some patients are found to have advanced HCC at diagnosis. Understanding the factors associated with failed surveillance may offer potential new strategies for surveillance. We aim to describe characteristics of patients diagnosed with HCC at an advanced stage compared to those diagnosed with curable HCC from a large, prospective study evaluating ultrasound (US) alone compared to US plus serum biomarkers (BM) for HCC surveillance.

Method: Patients with cirrhosis or high-risk HBV infection (REACH-B score $\geq$9) followed at the Toronto Centre for Liver Disease (n=1208) were randomized to HCC surveillance with US alone (Group A) or US+BM (Group B) with measurement of alpha-fetoprotein (AFP), lectin-reactive fraction of AFP (AFP-L3) and des-gamma-carboxy prothrombin (DCP). Elevated BM levels and/or findings on US triggered CT/MRI for confirmation of HCC diagnosis. Using the Barcelona Clinic Liver Cancer (BCLC) staging system, HCC stage at diagnosis was categorized as early (BCLC stages 0, A) or late (BCLC stages B, C).

Results: Among 62 patients diagnosed with HCC (age 62$\pm$10 years, 76% male, 50% Asian, 84% viral Hepatitis, 97% cirrhosis), 84% were diagnosed at an early stage and 16% were diagnosed at a late stage, with no difference seen between the US and US+BM strategies. Late HCC occurred only in cirrhotic patients and compared to those diagnosed early, there was a lower proportion of males (60% vs 79%, p=0.20), lower proportion of Asians (33% vs 53%, p=0.27), a lower proportion with HBV (20% vs 48%, p=0.10) and a greater proportion with HCV (60% vs 37%, p=0.17) as the underlying liver disease (Figure). Patients diagnosed with late HCC had higher BMI (31$\pm$2 vs 27$\pm$0.5 kg/m^2, p=0.02) and thus, were more likely to be obese (30% vs 6%, p=0.02), than those diagnosed with early disease. There were no differences in the time since prior surveillance or the reported quality of the previous US.

Conclusion: In this large prospective study, obesity was associated with a diagnosis of late-stage HCC among adult patients with cirrhosis. Alternative surveillance modalities to ultrasound may be required for obese patients with cirrhosis.

Image/Table:



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O50

TARGETING CD63 AS A NOVEL FIBROGENIC IMMUNE TARGET FOR THE TREATMENT OF HEPATOCELLULAR CARCINOMA AND THE REVERSION OF HEPATIC FIBROSIS

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Background: Hepatocellular Carcinoma (HCC) is the most common type of primary liver cancer and accounts for 75% of all hepatic malignancies. While the main etiology is unknown, 90% of HCC cases arise from fibrotic livers. NASH is also a consequence of hepatic fibrosis ultimately leading to HCC. Numerous studies have demonstrated that NASH leads to advanced fibrosis and cirrhosis, thereby increasing the risk of developing HCC. While NASH and HCC incidence are significantly higher, patients are diagnosed in advanced stages which contributes to poor prognosis. Currently there are no effective treatments for resolving hepatic fibrosis in NASH. Therefore, there exists an unprecedented need to develop novel, effective therapeutic modalities to treat hepatic fibrosis and revert its progression to HCC. CD63, also known as lysosome-associated membrane glycoprotein 3, has been described to have critical roles in multiple biological processes, including tumorigenesis and metastasis in other cancers.

Purpose: The goal of our studies was to identify a novel immune target that could be mechanistically blocked for the reversion of the fibrotic phenotype in the liver and prevent its progression to NASH and HCC.

Method: We used next generation sequencing technologies like Mass Spectrometry to identify CD63 as a novel immune protein enriched in patients with HCC and NASH. Further, we validated our discoveries using single cell RNA sequencing and Spatial Transcriptomic profiling of > 200 targets on pathogenic patient livers of fibrotic origin. Finally, using in vitro cell culture assays and din vivo animal models, we have mechanistically described c-JUN as a key upstream regulator of CD63 and demonstrate that CD63 regulates key cytokines thus promoting the pro-fibrogenic signaling cascade in the liver.

Results: Our data demonstrate that CD63 overexpression drives NASH mediated fibrogenesis to develop HCC. We have evaluated CD63 as an effective drug target in NASH and HCC with the goal of developing an effective monoclonal antibody to block the pro-fibrogenic signaling of CD63 and target pathogenic cells for immune clearance. Here, we validate the effect of CD63 as a target for the treatment of NASH and its progression to HCC.

Conclusion: We have identified a key protein target that can be effectively blocked for the reversion of fibrosis in the liver. Our studies point to an exciting mechanism where an interplay between genetic regulators of fibrosis and the innate immune landscape can be altered to enhance therapy for patients with hepatic fibrosis leading to NASH and HCC. In sum, our results show for the first time that a tetraspanin like CD63 can be mechanistically modulated to treat liver fibrosis and we have developed a blocking antibody for the treatment of the same. Results from our studies will be of significant clinical value in for the treatment of HCC and NASH.

Disclosure of Interest: None Declared

O51

EXPRESSION OF THE AXONAL GUIDANCE CUE NETRIN-1 ASSOCIATES WITH NEONEUROGENESIS OF DRUGGABLE CHOLINERGIC ORIENTATION AND AGGRESSIVE HCC FEATURES

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Background & Aims: The unexplained interpatient variation in hepatocellular carcinoma (HCC) remains a major challenge. We aimed at addressing the under-explored association between the disease and neural regulations in the liver.

Methods & Results: We in-depth characterized the innervation of French biobanks HCC samples by conventional biochemistry methods. We also applied bioinformatics approaches to the TCGA dataset in order to stratify samples according to neural features and molecular correlates. We highlighted the predominant parasympathetic polarity of HCC nerves, and demonstrated that clinical HCC samples are netrin-1 rich and host liver neurogenesis with cholinergic features. Using the TCGA dataset, we then defined an HCC neural signature, derived from adrenergic and cholinergic receptor levels, that allowed patient stratification into two classes (Figure 1). Cholinergic tumors correlated with TP53 mutations ($p \leq 0.05$), shorter progression-free interval (PFI) and overall survival (OS), displayed more pathogenic molecular traits (e.g., AFP-rich, proliferative tumors, mitotic functions including DNA repair, EMT, Ras, and Akt/mTOR pathways), aggressive HCC signatures and B cell accumulation (Figure 2), as well as enriched expression of immune checkpoints inhibitors in the immune active class. Instead, adrenergic tumors, predominant in patients aged >60 and with mutated CTNNB1, were correlated with better OS and PFI ($p < 0.05$), and numerous immune pathways (Figure 3). In vitro rigorous synergy assays (Chou-Talalay) assays on five rationally selected HCC lines also indicated that standard-of-care HCC-relevant TKIs strongly synergy with cholinergic drugs. Last, targeting cholinergic pathways could impede anchorage-independent growth in these cell lines.

Conclusions: Our results depict neural features of HCC and how the existing tumor classification may also be shaped by neural inputs. Altogether, we show that the parasympathetic branch of the autonomic nervous system (ANS) is integrated into the pathobiology of HCC, and advocate for the use of ANS-targeting drugs in HCC research, many of which being clinically safe and well characterized.

Figure 1. Sample distribution after dimensional reduction (PCA) based on the 10 per cent most variable genes (normalized values). Cholinergic class in blue and adrenergic class in red are contrasted.

Figure 2. ssGSEA scores were calculated for each sample. Pathways comparison between neural classes was performed with the Wilcoxon Test and significant pathways (padj < 0.05) selected.

Figure 3. Upper panels: from up-regulated (derived from adrenergic tumors) and down-regulated (derived from cholinergic tumors) transcripts obtained by differential gene expression analysis, enriched pathways were identified. Pathways with adjusted p-value < 0.01 were selected. Lower panel: Kaplan-Meier representation of the predictive value of both classes with respect to overall survival (OS).

Image/Table:

Figure 1

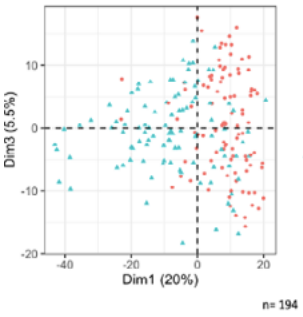


Figure 3

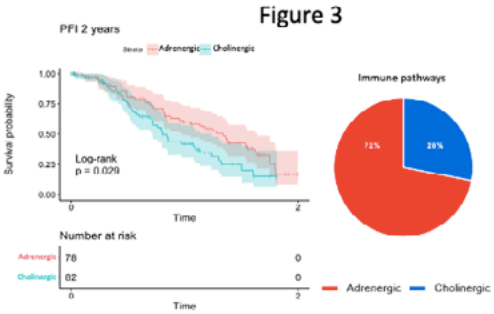
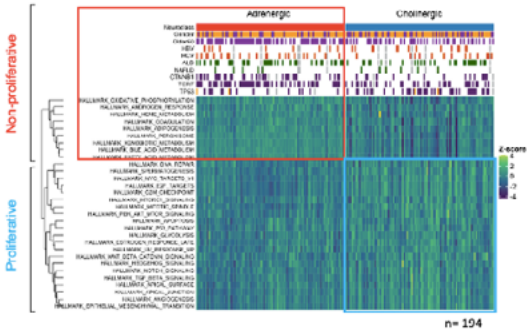


Figure 2



Disclosure of Interest: None Declared

O52

ENHANCER OF ZESTE HOMOLOG 2 (EZH2) AND O-GLCNAC TRANSFERASE (OGT) MODULATE CELL CYCLE AND CANCER-ASSOCIATED PATHWAYS IN HEPATOCELLULAR CARCINOMA

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Abstract Content: Despite recent improvements, treatment options for hepatocellular carcinoma (HCC) remain largely unsatisfactory. Epidrugs are currently being evaluated as cancer therapy and a first inhibitor of the histone methyltransferase Ezh2 obtained FDA approval. As the catalytic subunit of PRC2, Ezh2 is responsible for H3K27 di- and trimethylation associated with gene repression. In additional to this canonical activity, Ezh2 can also activate gene transcription. Ezh2 is frequently upregulated in HCC tissues and increased Ezh2 expression correlates with HCC aggressiveness and/or poor prognosis. Ezh2 knockdown in HCC cells reverses tumorigenicity in a nude mouse model, suggesting a potential therapeutic value of Ezh2 inhibition in HCC. Ezh2 activity is regulated by post-translational modifications, including glycosylation by OGT. We have previously shown that OGT expression is increased in tumor tissue from HCC patients. Interestingly, it has been reported that OGT and Ezh2 co-repress a defined tumor suppressor genes in breast and colon cancer cells. The aim of our project is to assess whether OGT and EzH2 can regulate cancer-associated pathways in HCC. Using a French cohort of 152 HCC patients and the TCGA LIHC cohort, we showed that OGT and Ezh2 are upregulated in tumor tissue as compared to peri-tumor tissue. RNA-seq and ChIP-seq analysis of human hepatoma cells indicate that OGT and Ezh2 co-modulate the expression of > 200 genes, among which genes involved in cell cycle and cancer pathways. Notably, only a minority of co-regulated genes appear to be co-repressed by Ezh2 and OGT. Our data suggest that Ezh2/OGT mostly promote gene expression in hepatoma cells. Furthermore, stabilization of O-GlcNAcylation increased the number of Ezh2/OGT target genes. Taken together, our data uncovered that Ezh2 and OGT modulate cell cycle and cancer pathways in transformed liver cells and provide important insights for epigenetic strategies as potential future anti-HCC therapies.

Disclosure of Interest: None Declared

O53

GENE EXPRESSION ANALYSIS OF DISEASED AND CONTROL LIVER TISSUE TO EXPLORE PATHOGENIC PATHWAYS IN INFLAMMATION

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Background: Liver diseases such as Non-alcoholic fatty liver disease (NAFLD) and Non-Alcoholic SteatoHepatitis (NASH) are extremely prevalent worldwide and carry a poor prognosis. Gaining insight into the transcriptional profiles of these conditions is therefore crucial for understanding their pathogenesis. We therefore aimed to compare hepatocyte transcriptomic data in control and diseased states using differential expression analysis. We hypothesised that different drivers of inflammation are present in distinct liver diseases, and that gender impacts expression.

Methods: We made use of data from two large studies which had retrieved liver biopsies. The first study looked at 195 Hepatitis C (HCV) infected individuals, while the second took samples from obese (12), control, (14), NAFLD (15) and NASH-affected (16) individuals. We analysed the second study independently, comparing gene expressions for all states against the controls and then merged the datasets to compare HCV-infected gene expression to control. The impact of gender on gene expression was also compared. Multiple R software packages and Gene-set enrichment analysis (GSEA) were used to analyse the data.

Results and Discussion: All studied liver diseases (NAFLD, NASH, HCV-infection) resulted in upregulation of inflammatory markers compared to control, with the biggest difference noted in HCV-infection. Meanwhile, obesity did not alter gene expression significantly. GSEA confirmed these findings, further revealing that complement dysregulation is present in all these conditions. We also demonstrated that gender drives differences in gene expression in HCV infection, but not necessarily in the other conditions. Further research is ongoing to delineate the specific pathogenic drivers of each of these conditions.

Conclusion: Differential expression analysis of diseased and control liver tissue reveals a host of inflammatory markers that are upregulated. Gaining a better understanding of these inflammatory drivers could help in the development of therapeutic targets, for example in the form of complement or IL-2 blockade, which could potentially assist in the halting of hepatocyte inflammation.

Disclosure of Interest: None Declared

O54

AUTO-AGGRESSIVE CD8 T CELLS REPRESENT COMMON EFFECTORS OF LIVER DAMAGE ACROSS STAGES OF CHRONIC HEPATITIS B.

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Background: Liver damage mediated by CD8 T cell activation is the primary driver of disease progression in chronic Hepatitis B (CHB) patients. Our previous study defined an auto-aggressive CD8 T cell population that killed hepatocytes through a Fas ligand dependent mechanism in the liver of patients with active Hepatitis. The objective of this study was to determine if the auto-aggressive CD8 T cell population was specific to stages of Hepatitis and identify the precursor population.

Methods: We obtained four single cell RNA sequencing (scRNAseq) datasets from CHB patients. We used bioinformatics analysis to identify auto-aggressive CD8 T cells and measured their frequency and changes in gene expression in CHB patients with different degrees of liver damage. Precursor populations were identified using overlapping T cell receptor clonotypes between clusters and by performing trajectory analysis of scRNAseq data.

Results: In a cross-sectional analysis that stratified patients by alanine aminotransferase (ALT) levels, auto-aggressive CD8 T cells could be detected in patients with ALT as low as 2 x upper limit normal (ULN). Interestingly, gene expression did not change in auto-aggressive CD8 T cells between 2xULN to 50xULN ALT, indicating that these cells arise as a marker of liver damage and did not change based on the degree of damage. Using the additional CHB datasets, we confirmed auto-aggressive CD8 T cells were present only in patients with active Hepatitis: HBeAg+ Hepatitis, HBeAg- Hepatitis and acute Hepatitis. They were not detected in HBeAg+/- infection or in patients with functional cure. Precursor analysis indicated that auto-aggressive CD8 T cells arise from a liver-resident CD8 T cell population.

Conclusions: Auto-aggressive CD8 T cells were a signature of liver disease progression, found only in patients with active liver damage.

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O56

THE COMMUNITY POP-UP CLINIC (CPC): A UNIQUE STRATEGY TO ENGAGE THE INNER CITY IN HCV ELIMINATION - AND MORE

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Abstract Content: Several strategies have been proposed to identify Hepatitis C Virus(HCV) infected inner-city residents, engage them in care, provide them with antiviral therapy, establish conditions to maximize treatment completion and cure achievement. Elimination of HCV infection as a public health concern by the end of this decade will require a concerted effort in all target populations, including vulnerable inner-city population, many of whom are actively using drugs and facing other issues more challenging than HCV infection:housing and financial insecurity, untreated mental illness and active addiction. In Vancouver, engagement in healthcare for this population is critical, especially in light of a critical opioid crisis with 7 overdose deaths(OD)/day, largely among individuals disengaged from care.

We have evaluated a novel approach of Community Pop-Up Clinics(CPCs) and its ability to promote access to care, uptake of HCV therapy and its outcome, with additional analyses of HCV reinfection rate and opioid-related death. We hypothesized that by implementing this CPC program, we will optimize engagement in care of vulnerable population, increase successful HCV therapy uptake and reduce reinfection and mortality.

From January2021–November2022, we conducted 80 weekly CPCs at various locations(mainly single room occupancy buildings) and evaluated 1378 individuals. 465 individuals(33.7%) were found to carry HCV antibodies. Of 465 individuals, 327 individuals(70.3%) were found to be viremic. We attempted to engage all in care to treat their HCV infection. HCV engagement has been secured in 321 cases(99.1%). 278(86.6%) individuals have started treatment and 42 are in the pre-treatment phase, and 1 had died of OD in the pre-treatment phase. The median time from CPC attendance to HCV treatment initiation was 6 weeks. Of 278, 258 have completed treatment, 19 are currently on treatment and 1 died of OD during treatment. Of 258 subjects who have completed treatment, 210 are confirmed as cured (SVR12), 45 are awaiting SVR4, 1 documented virologic relapse and 2 documented to be reinfected, a rate of 0.54/100 person-years. By mITT, cure rate is 210/213(98.6%). Overall, in this vulnerable population with 6-7 opioid overdose deaths/day, we only documented 2 ODs over 367 PY of overall follow-up.

Taken together, our data validates the development of multidisciplinary programs such as ours aimed at treating HCV in vulnerable populations that must be engaged in care for HCV elimination to become a reality and documents additional societal benefits that could be achieved. Our program can easily be reproduced, expanded and optimized to enhance efforts for HCV elimination in this key group of core transmitters.

Disclosure of Interest: None Declared

O57

ACHIEVING MICRO-ELIMINATION OF HEPATITIS C HYPERENDEMIC ABORIGINAL TOWNSHIPS IN TAIWAN: A SUCCESSFUL MODEL

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Background/Aims: The Hepatitis C virus (HCV) infection and replication vary among individual hepatocytes in chronic HCV infection by identifying hepatocytes with different HCV viral RNA. In Taiwan, some hyperendemic townships with a prevalence of anti-HCV of more than 10% have been explored, including Tau-Yuan Township in the Kaohsiung area in southern Taiwan. With the WHO goal to eliminate chronic Hepatitis by 2030, the Ministry of Health and Welfare (MOHW) in Taiwan has declared to achieve the goal by 2025, and first launched the micro-elimination of the hyperendemic aboriginal townships in August 2018. The aim of the study is to evaluate the results of the project in Tau-Yuan township (TYT) in Kaohsiung, Taiwan.

Methods: In TYT, the project underwent with the goals: For the registered residents aged 30-75 years who live in TYT for more than 6 months in a year, the screening rate of more than 80%, the viral test rate for positive anti-HCV patients more than 80%; and more than 80% of the definitely diagnosed viremic patients receiving DAAs therapy. The accessible clinical care including door-by-door screening, (on-site) diagnosis, and treatment is supported by the MOHW, the Health Center of TYT, and Kaohsiung Medical University Hospital.

Results: Of overall 4317 registered residents, 2516 aged 30-75 years and 1073 fulfill the criteria of living in TYT more than 6 months in a year as the target population. The clinical data were collected and screening was launched for patients who are unawareness the status of the anti-HCV status. Total of 1072 residents (100%, one died) receive screening. Of the patients with viremia, they may receive treatment by the regional hospitals or the medical centers in Kaohsiung city and the remaining patients receive therapy in the Health Center of TYT. The 127 anti-HCV positive patients were all tested for HCV RNA (100%) and 72 (55.8%) of the 129 patients were positive for HCV RNA. 44 and 25 patients were treated in the Health Center of TYT, and other hospitals, respectively, with a treatment rate of 98.6% (two viremic patients died before treatment and one refused treatment). All 44 patients treated on-site achieved SVR12.

Conclusions: In this real-world micro-elimination project of a Hepatitis C hyperendemic aboriginal township in Taiwan, the goal of elimination of Hepatitis C have achieved by improving the accessibility of care in the local Health Centers. This model is believed to represent a standard of care cascade in hyperendemic areas in Taiwan with the cooperation of Governments and non-government organizations.

Disclosure of Interest: None Declared

O58

ELIMINATING HEPATITIS B: ANTICIPATING COMMUNITY AND PUBLIC HEALTH IMPLICATIONS FOR ANY HEPATITIS B CURATIVE INTERVENTIONS

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Background: Hepatitis B elimination as a global public health threat will only occur with sustainable and tolerable curative treatments. While substantial activity is being conducted to identify the constituent elements of cure interventions, challenges in the public health response to Hepatitis B remain.

Purpose: Current global Hepatitis B elimination challenges include unsystematic and poor-quality testing and diagnosis processes, where linkage to clinical management is rare, and significant social implications related to the infection. This social research uses data gathered from an interdisciplinary range of key stakeholders to explore issues related to implementing curative Hepatitis B interventions.

Methods: An interdisciplinary advisory committee oversaw a process of exploratory semi-structured qualitative interviews with 31 key stakeholders, several of whom are living with Hepatitis B. Participants had responsibilities or contributed to global, regional, or local public health policy/program development, scientific and/or clinical investigation or translational research, or engagement with populations most affected by Hepatitis B. Interview prompts identified understandings of the social, political, economic and ethical issues related to cure implementation, including structural barriers to equitably implementing the cure at global, regional, national, or local levels with an inductive thematic analysis used to identify themes.

Results: Key themes included identifying that the descriptions and priorities of cure science reflected the individual and professional frameworks of participants; recognition that preparation and re-orientation of health systems will be required, and identifying the clinical infrastructure needed to effectively implement the cure. Other implications included the need for global or regional resourcing given the economic realities of the countries with a greater burden of the infection, cure affecting the impact of social impact and marginalisation resulting from disclosure of Hepatitis B.

Conclusions: While work continues on curative treatments, it will be for naught without the decentralization and simplification of current clinical and public health approaches to Hepatitis B, and determining country level barriers to Hepatitis B clinical management. The social impact of Hepatitis B is often as significant as the clinical implications, with curative treatments being more impactful than the removal of a virus from the body. Curative treatments will not only benefit individuals, but will fundamentally affect families where Hepatitis B occurs across generations, and often across multiple countries.

Disclosure of Interest: None Declared

O59

ELIMINATING HEPATITIS C IN AUSTRALIA: SUCCESS THROUGH WORKFORCE AND HEALTH SERVICE DELIVERY INNOVATION

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Background: Eliminate Hepatitis C Australia (ECA) is a partnership between researchers, implementors, government, health services and community organisations. ECA was philanthropically funded ($12M AUD) to create a national framework for Hepatitis C elimination. ECA aimed to stimulate catalytic change by fostering coordination and collaboration. One (of six) ECA components is workforce development and health service delivery (WDHSD), which funded programs that aimed to increase Hepatitis C testing and treatment. Purpose: The WDHSD component trialled innovative Hepatitis C programs, with the overall objective of generating and sharing robust evidence about which programs worked and why.

Methods: ECA began with a national consultation that identified funding priorities. Locally prioritised programs, which met ECA guiding principles, were subsequently funded in 2019. From the outset, funded programs worked collaboratively with ECA and tailored support including project, stakeholder, and people management; evaluation best practice; reporting and dissemination was provided. Crucially, ECA facilitated relationships between stakeholders, funders, ECA partners, and funding recipients. This promoted the dissemination of program findings and strategic thinking regarding project sustainability and ongoing funding.

Results: All 20 ECA funded programs were successfully implemented and evaluated; seven trialled workforce development initiatives, five implemented models of care, five projects delivered client engagement strategies and three projects focused on linking people to care using passive surveillance systems. Evidence from evaluation suggests nurse-led, nurse-peer partnerships, community-outreach, and community justice models of care were highly successful, in that marginalised clients were reached with HCV RNA test positivity ranging from 10–30%, and the workforce was expanded beyond medical-based clinicians, and ongoing funding was secured. Financial reimbursement to clients for testing and treatment were also effective in reducing loss-to-follow with key lessons being the need for flexibility in amounts and delivery. Finally, whilst there was extensive reach with workforce development programs, the effect on testing and treatment was mixed or difficult to quantify.

Conclusions: The ECA partnership is a transferable and scalable model. ECA demonstrated that success comes from injecting catalytic funding under a flexible model that allows for innovative models of care and creative thinking in what constitutes the Hepatitis C workforce. By adopting a flexible approach, fostering a culture of innovation, and sharing resources and findings, ECA has successfully changed the Hepatitis C landscape in Australia.

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O60

GILEAD LIVER COMMITMENT AND LOCAL ELIMINATION PROGRAMS LEADING TO GLOBAL ACTION IN HCV(LEGA-C) : THE OUTCOME AND IMPACT FROM LATE PHASE STUDIES

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Background: Since 2016 Gilead Sciences, Inc., has committed to support studies and grants for programs focused on Hepatitis C virus (HCV) elimination under LEGA-C (Local Elimination programs leading to Global Action in HCV) initiative. Focusing on Investigator Sponsored Studies (ISR) and collaborative studies under LEGA-C initiative, >120 studies in >30 countries were funded from Gilead until now. Here we aim to report the relative impact of these studies.

Methods: We describe the types of studies supported, the populations and the treatment patterns emerging from the studies. To assess the potential impact on providers' HCV awareness, we catalogued the number, types, and impact factors (IF) of studies' publications and the numbers of citations of study papers. To gauge potential impacts, we reviewed recent guidelines to identify mentions of LEGA-C supported studies.

Results: The studies were conducted in 6 continents ; North America (n=59), Europe (n=33), Asia (n=24), Africa (n=7), Australia (n=5), and South America (n=3). 76 studies have completed, 43 are enrolling/ongoing, and 1 is planned. The types of study were test and treat (n=38), screening and linkage to care (n=37), epidemiology (n=12), outreach/callback (n=10), modeling/ cost effectiveness (n=9), and patient/HCP education (n=4). 42 studies linked patients to treatment: 278,088 persons were screened, and 29,378 (10.6%) had confirmed HCV infection and enrolled in a study. Of those enrolled, 15,570 (53.0%) received treatment, and of those, 12,945 (83.1%) received direct-acting antivirals (DAAs). Of the 120 studies, 66 (55%) focused on special populations such as persons who inject drugs (n=33), men who have sex with men (n=8), persons with concomitant HIV infection (n=8), and homeless population (n=4). Publications include 76 journal articles, 30 oral presentations, 123 posters at conferences and 26 abstracts, presentation type not specified. Median IF of study journals was 5.2, and 40 papers were cited a total of 254 times. The AASLD 2019 HCV screening guidance and the EASL 2020 acute HCV treatment guideline cited the LEGA-C–supported paper on cost-effectiveness of universal screening of pregnant women for HCV infection, recommending that such screening be adopted.

Conclusions: Over 6 years on 6 continents, the LEGA-C initiative has supported >120 studies that enrolled ~29,000 HCV+ persons and treated >12,000 with DAAs. Special populations among whom HCV incidence is high were well represented. Supported studies have yielded 76 fully published articles in 47 different journals and have achieved high rates of citation. The ongoing LEGA-C initiative is demonstrably contributing to the understanding, treatment, and ultimate elimination of HCV.

Disclosure of Interest: K. M. Kwon: None Declared, B. Kreter Shareholder of: Holds Gilead stocks, Employee of: Current employee of Gilead, S. Garson Shareholder of: Gilead stock holder, Employee of: Current Gilead employee, R. A Bam Shareholder of: Gilead stock holder, Employee of: Current Gilead employee

O61

UNEQUAL ACCESS TO HBV DIAGNOSTICS IN RESOURCE LIMITED SETTINGS CAN HINDER PROGRESS TOWARDS THE WHO 2030 VIRAL HEPATITIS ELIMINATION TARGETS: INTERNATIONAL COALITION TO ELIMINATE HEPATITIS B VIRUS (ICE-HBV) SURVEY RESULTS

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Background: Increased HBV screening and treatment is needed to achieve the WHO 2030 targets. Without the necessary human and infrastructural resources, HBV transmission will continue, exacerbating inequity in the global response to HBV elimination.

Purpose: To determine the perceived priorities for HBV elimination among healthcare providers and evaluate the availability of diagnostic modalities and antiviral therapy for chronic Hepatitis B in resource limited settings (RLS).

Methods: In 2021, ICE-HBV launched a global online survey in three languages to understand better the availability of diagnostic tests and barriers to treatment in RLS. The survey had 53 items addressing the priorities for reaching the goal for HBV elimination, and the availability of diagnostic tests and therapies.

Results: 178 health care workers responded to the survey. Specialists accounted for about half, which included hepatologists (33%), gastroenterologists (6.9%), and infectious disease physicians (12.2%). The majority of respondents worked in sub-Saharan Africa (SSA) (37%), with 22% in South/South East Asia (SEA) and 15% in Europe (EU). About 80% of the respondents considered increased HBV screening and diagnosis, optimizing strategies to prevent mother-to-child-transmission (MTCT) as the highest priorities in achieving HBV elimination, followed by increased access to treatment (73%). Universal HBV screening of pregnant women at antenatal visit were routinely practiced in 59% of SSA and 66% of SEA regions. HBsAg ELISA testing was reported to be available in all regions outside SSA, but in only 51.4% of SSA settings. Similarly, HBV-DNA quantification with PCR were available in >80% of SEA and European regions but in only 54% of SSA settings. Unlike HBsAg ELISA, HBsAg rapid tests were accessible in >90% of SSA settings. However, 60% of respondents believed that only WHO pre-qualified HBsAg rapid tests should be used for screening and >55% of all respondents strongly agreed that an affordable Point-of-care (POC) HBV DNA test is necessary in their settings if HBV DNA is in the treatment

algorithm. Access to antiviral therapy was highly variable across the regions; tenofovir DF (83%) was most available followed by lamivudine (57%).

Conclusions: SSA has high HBV prevalence but has the least access to basic HBV screening assays. While most of the survey respondents considered increased HBV screening and optimizing strategies to prevent MTCT the highest priorities in achieving the WHO 2030 goal for HBV elimination. However, universal antenatal HBV screening of pregnant women was unavailable in 40% of SSA and 34% of SEA regions. Improved HBV screening strategies are urgently needed in RLS.

Disclosure of Interest: None Declared

O62

RXR-MEDIATED REGULATION OF SURFACE NTCP EXPRESSION AND ITS EFFECT ON NTCP-MEDATED HEPATITIS B AND HEPATITIS D VIRUS ENTRY

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Abstract Content: Chronic HBV infection remains a global public health problem. If left untreated, chronic HBV infection can progress to end-stage liver disease, such as liver cirrhosis and hepatocellular carcinoma (HCC). There are no curative treatment for HBV that can eliminate viral infection so far. To identify the host factors incorporating in HBV life cycle, and can be targeted as novel anti-HBV therapeutic we performed human genome siRNA library screening using HBV/NLuc (HBV/NL) reporter virus infection in HepG2-hNTCP. We identified the Kinesin motor protein KIF4 to be an important factor which facilitates Hepatitis B virus (HBV), and its satellite Hepatitis D virus (HDV), entry into human hepatocytes. We found that KIF4 play an important role in the transport of NTCP towards the cell surface where it become exposed to HBV and HDV infection. Cellular fractionation and immunofluorescence analysis (IF) showed that transient KIF4 depletion reduced surface and raised intracellular NTCP levels leading to the suppression of both HBV and HDV infection. Overexpression of wild-type KIF4 but not ATPase-null KIF4 mutant restored surface localization of NTCP and significantly improved cell permissiveness to HBV. Furthermore, we found that RXR agonists (Bexarotene, and Alitretinoin) down-regulated KIF4 expression resulting in a substantial decrease in HBV-Pre-S1 protein binding to HepG2-hNTCP cell surface and HBV infection in primary human hepatocyte (PXB) (Bexarotene, IC_{50} 1.89 $\pm$ 0.98 µM) cultures. Overall, we showed that KIF4 is a key regulator of NTCP surface localization, and NTCP-mediated HBV/HDV entry. Small molecules that suppress KIF4 expression are potential antiviral candidates targeting HBV and HDV entry.

Disclosure of Interest: None Declared

O63

IDENTIFICATION AND CHARACTERIZATION OF JANUS KINASE JAK1 AS AN HDV-RELATED HOST FACTOR AND ANTIVIRAL TARGET

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Abstract Content: The therapeutic strategies against HDV, including bulevirtide, demonstrated the potential of host targeting agents. This approach requires a comprehensive understanding of the molecular interactions between HDV and hepatocyte host factors. In this context, using a loss-of-function screen, we previously identified 191 HDV-related candidate host factors,including Janus kinase 1 (JAK1) (Verrier et al., Gut 2020). Although JAK1 plays a key role in the innate immune response against viral infection, we observed an unexpected proviral effect of this kinase on HDV infection. Validation assays in different in vitro systems, including primary human hepatocytes (PHH) in parallel to quantification of interferon stimulated gene expression suggests that JAK1 proviral activity is independent of the MDA5-mediated induction of the innate immune response upon HDV infection. CRISPR/Cas9-based Knockout-rescue assays confirmed the importance of JAK1 in the HDV life cycle. Notably, the restoration of JAK1 expression using a mutant version of the protein unable to bind ATP does not rescue the HDV infectious phenotype in JAK1-KO cells, thus demonstrating the key role of JAK1 kinase activity in the viral life cycle. Furthermore, through functional assays including analysis of HDAg phosphorylation, we demonstrated that JAK1 depletion is indirectly responsible for a loss of S-HDAg phorpshorylation, known to stimulate HDV replication. The infection phenotype could be rescued by IL-6 treatment in JAK1-KO cells, suggesting the involvement a intermediate kinase responsible for HDAg phosphorylation. Finally, JAK1-specificic inhibitors, including the FDA-approved molecule Upadacitinib, exhibit a dose-dependent antiviral effect in both NTCP-expressing hepatoma cells, PHH and differenciated HepaRG cells, confirming the targetability of JAK1 for anti-HDV treatments. Taken together, we uncovered JAK1 as a key host factor for HDV infection and a putative target for new antiviral treatment. The characterization of JAK1-HDV interactions will pave the way to a better understanding of the HDV life cycle and the development of new antiviral therapies.

Disclosure of Interest: None Declared

O64

SINGLE CELL RESOLVED ANALYSIS OF THE INNATE IMMUNE RESPONSE OF HDV INFECTED STEM CELL DERIVED HEPATOCYTES

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Background: Human pluripotent stem cell (hPSC)-derived hepatocyte-like cells (HLCs) are a valuable model to investigate host-pathogen interactions of Hepatitis viruses in a mature and authentic cellular environment. For example, we recently described that HLCs react to HCV and HBV infections similarly to adult hepatocytes.

Purpose: We investigated the susceptibility of HLCs to the HDV and analysed their innate immune response to the infection at the single cell level.

Methods: We differentiated hPSCs into HLCs, and inoculated them with infectious HDV produced in Huh7NTCP. We confirmed HDV infection by RTqPCR for the HDV RNA and immunostaining for the HDV antigen (HDAg). We then assessed activation of the HLCs innate immune response by RTqPCR and single cell RNA sequencing (scRNAseq).

Results: Cells undergoing hepatic differentiation became susceptible to HDV after acquiring expression of the viral receptor NTCP during hepatic specification. Inoculation of HLCs with HDV lead to increasing amounts of intracellular HDV RNA and accumulation of the HDAg in the cells. Upon infection, the HLCs mounted an innate immune response based on induction of the interferons IFNB and L, and upregulation of interferon-stimulated genes. The intensity of this immune response positively correlated with the level of viral replication and was dependent on both the JAK/STAT and NFκB pathway activation. Neither this innate immune response nor an exogenous IFNα2b treatment inhibited HDV replication. However, pre-treatment with IFNα2b reduced viral infection, suggesting that ISGs may limit early stages of infection and thus HDV spreading.

We then applied scRNAseq analysis on our HLCs. HDV RNA could be specifically captured and quantified in single HLCs. HLCs from the HDV inoculated population were then sorted based on their intracellular HDV RNA titre. We then assessed the innate immune genes activation in the various sub-population: Highly HDV replicating HLCs, low HDV replicating HLCs, and HDV RNA negative "bystander" HLCs were compared to control non inoculated HLCs. By analysing a panel of ~400 IRGs, we show that HDV replication drives a specific antiviral program in the infected HLCs, proportional to the level of replication of the virus. However, we observed only a very limited paracrine effect on bystander non-infected HLCs.

Conclusions: The in vitro HDV mono-infection of HLCs represents a new tool to study HDV replication, its host-pathogen interactions in cells displaying mature hepatic functions. Moreover, applying scRNAseq allows us to visualize the antiviral cellular response at unprecedented resolution.

Disclosure of Interest: None Declared

O65

HIRA SUPPORTS HEPATITIS B VIRUS MINICHROMOSOME ESTABLISHMENT AND TRANSCRIPTIONAL ACTIVITY IN INFECTED HEPATOCYTES

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Abstract Content: Despite the existence of safe and effective prophylactic vaccines, Hepatitis B virus (HBV) infection remains the most common chronic viral infection in the world. Current first-choice treatments for chronic Hepatitis B (CHB) achieve efficient viral suppression, but do not eradicate the virus. Thus, life-long therapy is needed in the majority of patients to maintain infection under control.

Upon HBV infection, covalently-closed-circular (ccc)DNA, the long-lived genomic reservoir, acquires an epigenetically regulated chromatin structure built by the HBV core (HBc) protein and host histones which allows its persistence and transcription in infected hepatocytes. The histone regulator A (HIRA) complex is a H3.3 histone chaperone. It promotes H3.3 deposition and nucleosome assembly independently of DNA synthesis by exploiting its capacity to bind to H3.3-H4 histone dimers and naked DNA. HIRA works in a complex with ubinuclein 1 (UBN1) and calcineurin-binding protein 1 (CABIN1) proteins.

Using cccDNA-specific chromatin immunoprecipitation after HIRA loss/gain of function, detailed molecular studies of host chromatin-associated factors in cell culture models of natural infection, i.e. HepG2-hNTCP cells and primary human hepatocytes (PHH), we demonstrated that HIRA is a crucial pro-viral factor essential for the formation of cccDNA and for maintaining its transcriptional activity. Indeed, cccDNA formation required the deposition of the histone variant H3.3 via the HIRA-dependent pathway and this occurred simultaneously with repair of the cccDNA precursor and independently from de novo viral protein expression. Interestingly, H3.3 in its S31 phosphorylated form appeared to be the preferential H3 variant found on transcriptionally active cccDNA in infected cultured cells and human livers. Moreover, association of the viral HBc protein with both cccDNA and HIRA suggested a possible interaction between the two proteins.

Altogether, we generated new insight on cccDNA biology that may help identifying novel strategies to specifically target the HBV minichromosome for degradation or functional silencing.

Disclosure of Interest: None Declared

O66

LIMITED IMPACT ON THE FUNCTIONS OF NF-κB ESSENTIAL MODULATOR (NEMO) IN HEPATITIS A VIRUS-INFECTED HEPATOCYTES

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Background: Hepatitis A virus (HAV), a member of Picornaviridae, is a positive-strand RNA (+ssRNA) virus. During its replication, double-stranded RNA (dsRNA) is formed and potentially sensed by host innate immunity through pattern-recognition receptors (PRRs), including toll-like receptor 3 (TLR3) and rig-I-like-receptors (RLRs). This leads to the activation of nuclear factor-κB (NF-κB) and interferon regulatory factors (IRFs), further inducing type-I interferon (IFN) and IFN-stimulated genes (ISGs) expression. Existing literature suggests that, despite the high replication rate in vivo, HAV tends to induce only limited ISGs. This is partly attributed to the action of the viral protease 3C, which proteolytically cleaves important innate immune adaptors, as NF-κB essential modulator (NEMO). Controversially, other studies show that in HAV-infected hepatocytes the IFN signaling is still intact.

Purpose: In this study, we sought to clarify the mechanisms of innate immune counteraction by HAV through the detection of 3C-mediated cleavage of NEMO and analysis of its potential impact on the NF-κB pathway.

Methods: Firstly, through transient overexpression of HAV 3C, we detected NEMO cleavage biochemically. Then, we assessed the degree of counteraction of the NF-κB pathway by HAV 3C in liver-derived cell lines, measuring mRNA levels of ISGs and chemokines upon ectopic expression of the 3C protease in cells treated with NF-κB stimulants. Next, we detected ISGs and chemokines in stimulated cells either harboring a HAV subgenomic replicon or infected with HAV. Lastly, to further understand the importance of NEMO in human hepatocytes, we knocked down NEMO and determined its impact on the NF-κB function, as well as on HAV replication and HAV-induced innate immune response.

Results: We detected incomplete cleavage of NEMO by HAV 3C. Moreover, mRNA expression of ISGs, inflammatory chemokines, and NF-κB-downstream specific genes was not downregulated in our models. Strikingly, we found that knock-down (KD) of NEMO did not downregulate ISGs expression, indicating that NEMO can still function at very low expression levels. Furthermore, the lack of NEMO did not have any impact either on HAV replication or the HAV-induced ISGs response.

Conclusion: Our findings demonstrated that HAV does not strongly counteract the NF-κB pathway. On the one hand, this might be due to the inefficient cleavage of NEMO by HAV 3C. On the other hand, we showed that minimal expression levels of NEMO already suffice to mount a full NF-κB-mediated response. Our study suggests that HAV might rely on alternative mechanisms, not based on NEMO cleavage, to evade innate immunity in hepatocytes.

Disclosure of Interest: None Declared

O67

THE PHOSPHATIDYLSERINE RECEPTOR T-CELL IMMUNOGLOBULIN MUCIN RECEPTOR 1 (TIM1) MEDIATES THE INFECTION OF ENVELOPED HEPATITIS E VIRUS

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Background: The Hepatitis E virus (HEV) is an underestimated RNA virus and currently the most common cause of acute viral Hepatitis. The viral life cycle and pathogenicity of the virus remain poorly understood and no specific therapies are currently available. Throughout their life cycle, viruses interact with cellular host factors, thereby determining host range, cell tropism, pathogenesis and ensuring their propagation. Unraveling these virus-host interactions will lead to novel fundamental insight and may identify potential antiviral targets.

Methods: Two related high-throughput mammalian two-hybrid approaches were used to screen for HEV interacting host proteins. Over 200 host proteins were identified that interacted with HEV ORF2-4 of two different genotypes (gts). Promising hits were examined on protein function, involved pathway(s), cellular expression and their relation to other viruses. Based on the annotation of biological function, the phosphatidylserine (PS) receptor T-cell Immunoglobulin Mucin receptor 1 (TIM1) was selected for further study. This protein showed an interaction in our assay with both gt-1 and gt-3 ORF3, and has previously been described as an attachment factor or receptor for a variety of viruses.

Results: We determined that HEV infection with particles derived from supernatants, which are cloaked by host-derived membranes (eHEV), is significantly impaired in absence or blockade of TIM1, demonstrated by using KO cells or TIM1 antibody neutralization respectively. eHEV particles resemble plasma-derived HEV and are possibly associated with ORF3 and PS. In contrast, infection with intracellular HEV particles (iHEV) was unaffected. iHEV was used as surrogate for feces-derived virus and is not associated with ORF3 and PS. Interestingly, eHEV infection could be restored by recombinantly expressing TIM1 in TIM1 knock-out cells. Additionally, we ectopically expressed this protein in cells that are TIM1 negative and showed that it increased infection. Moreover, immunostaining experiments show a co-localization of TIM1-expressing cells and HEV infection. Additionally we show that ORF3 colocalizes with TIM1 in HEV electroporated cells and that HEV replication is also influenced by TIM1.

Conclusions: Taken together, our findings support a role for TIM1 in eHEV-mediated infection, a strategy HEV may use to promote viral spread throughout the body. Future work will need to establish the exact, possibly combined, role of ORF3 and PS in the process of viral entry and the influence of TIM1 on viral trafficking or assembly.

Disclosure of Interest: None Declared

O68

THE HEPATITIS E VIRUS INFECTIOUS CYCLE – AN UPDATE

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Abstract Content: The Hepatitis E virus (HEV) is an enterically transmitted RNA virus and a major cause of acute Hepatitis worldwide. In recent years, cases of persistent HEV infection in immunocompromised inviduals have been rising which is alarming. HEV has a unusual life cycle in that it exists in two different virion forms: a naked form that is shed into the feces and an enveloped form that circulates in the bloodstream. The enveloped form, so called eHEV, is infectious, despite lacking virally encoded envelope proteins. While the biogenesis of eHEV is thought to be similar to that of exosomes, little is known about how these particles enter the cell and initiate an infection. Our recent study suggests that eHEV uses a novel entry mechanism involving the degradation of its membrane within late endosomes/lysosomes, as evidenced by a substantial loss of infectivity in cells depleted of the Niemann-Pick C1 protein or treated with an inhitor of lysosomal acid lipase. This novel entry mechanism may provide hints on the role of antibody in HEV infection. Neutralizing anti-capsid antibodies do not recognize the free eHEV particles, yet they effectively block eHEV-mediated spread in cell culture. Thus, antibodies may prevent eHEV uncoating in the late endosomes/lysosomes upon the degradation of the viral membrane. A better understanding of the eHEV entry and neutralization mechanisms is expected to advance our knowledge about this infection and may inform better strategies to prevent and treat HEV-associated diseases.

Disclosure of Interest: None Declared

O69

CHARACTERISATION OF A CELL CULTURE SYSTEM OF PERSISTENT HEPATITIS E VIRUS INFECTION IN THE HUMAN HEPARG HEPATIC CELL LINE

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Abstract Content: Hepatitis E virus (HEV) is considered as an emerging global health problem. The pathogen is responsible for more than 2 000 cases of acute Hepatitis in France every year resulting in majority from zoonotic infections associated with the consumption of raw or undercooked pork. In most cases, Hepatitis E is a self-limiting disease and the virus is cleared spontaneously without the need of antiviral therapy. However, immunocompromised individuals can develop chronic infection and liver fibrosis that can progress rapidly to cirrhosis and liver failure. For decades, the lack of efficient and relevant cell culture system and animal models has limited our understanding of the biology of HEV and the development of effective drugs for chronic cases. In the present study, we developed a model of persistent HEV infection in human hepatocytes in which HEV replicates efficiently. This HEV cell culture system is based on differentiated HepaRG cells infected with an isolate of HEV-3 derived from a patient suffering from acute Hepatitis E. Efficient replication was maintained for several weeks to several months as well as after seven successive passages on HepaRG naïve cells. Moreover, after six passages onto HepaRG, the virus was still infectious after oral inoculation into pigs. We also showed that ribavirin inhibited HEV replication in HepaRG cells. Using whole genome sequencing, 25 mutations including 8 non-synonymous mutations were detected in the genome of the virus recovered after 6 passages into HepaRG. This system represents a relevant and efficient in vitro model of HEV replication that could be useful to identify putative mutations within the viral genome than can occur in vitro in the context of prolonged Hepatitis E infection and to test antiviral drugs against chronic HEV infection. In addition, we are currently using this model to characterise the host antiviral response against HEV and identify antiviral molecules able to interfere with HEV replication.

Disclosure of Interest: None Declared

O70

A NOVEL CLASS OF GLYCAN-SENSITIVE HUMAN MONOCLONAL ANTIBODIES NEUTRALISING THE HEPATITIS E VIRUS (HEV)

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Background: Specific and effective therapies for infections with the Hepatitis E virus (HEV) are lacking in the clinic. As for other viral infections, neutralising antibodies may serve as novel therapeutic option for HEV infections. The protruding domain (p domain) of HEV's capsid protein, pORF-2, is the main epitope targeted by neutralising antibodies. However, the most abundant HEV antigen present in the sera of infected individuals are secreted pORF-2 dimers that are glycosylated in a specific site of the p domain. They are not infectious and serve as bait proteins capturing specific antibodies.

Methods: Memory B cells of two acutely infected individuals were selected by recognizing the p domain of pORF2. Heavy and light chain of the B cell receptor were sequenced and single chain variable fragments or monoclonal antibodies (mAb) were expressed in Expi293F cells. To analyse binding, ELISA and Biacore experiments were performed. Neutralisation assays were performed using different HEV strains and patient isolates. Selected scFvs in complex with HEV gt3 p domain were crystallised and structures were analysed. To confirm neutralisation in vivo, liver chimeric mice were treated with selected antibodies prior to HEV gt3 infection.

Results: Overall, we identified at least seven human mAbs neutralising both the naked and quasi-enveloped version of HEV gt3. Among the four most potent neutralisers, two showed glycan sensitivity. After pre-incubation of glycosylated pORF-2 dimers, glycan insensitive antibodies lost their neutralising ability in a dose dependant manner, whereas glycan-sensitive antibodies were unaffected. Structure analysis revealed that the p domains' glycosylation site lies within the very conserved epitope recognised by glycan-sensitive nAbs. The identified antibodies also recognized pORF-2 in the sera of HEV infected individuals. Additionally, 6 out of 11 patient isolates showing infection of human stem-cell derived hepatocytes were neutralised. Finally, we tested neutralisation in vivo using liver chimeric mice that develop HEV infection as observed by shedding of the virus in stool samples. Treatment with one nAb before and after infection with HEV prevented the development of HEV infection as HEV RNA was not detectable in the stool.

Conclusion: Here, we identified a novel class of human monoclonal antibodies potently neutralising HEV in vitro and in vivo. Glycan-sensitive antibodies are not inhibited by the presence of abundant glycosylated pORF-2 dimers. They show a broad neutralisation by recognizing a highly conserved epitope of pORF-2 and neutralisation of several patient isolates. These antibodies may serve as a novel therapeutic option for HEV infections.

Disclosure of Interest: None Declared

O71

OXYSTEROL BINDING PROTEIN (OSBP) IS NEEDED FOR HEPATITIS E VIRUS REPLICATION IN CULTURED HCELLSEPATOMA CELLS

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Background: Hepatitis E virus (HEV) is a single-stranded positive-sense RNA virus and can cause acute Hepatitis as well as chronic infections for some genotypes. The ORF1 of the HEV genome encodes a polyprotein around 190 kDa, which contains several putative domains, including helicase and RNA-dependent RNA polymerase. HEV helicase is a member of the superfamily 1 (SF1) helicase family and possesses multiple enzymatic functions, such as RNA 5'-triphosphatase activity, RNA unwinding, and nucleic acid-binding. It is thought to participate in viral RNA synthesis. However, the exact functions of the helicase and its interaction with cellular proteins remain unknown. During the dynamic activity of lipid metabolism, the members of the OSBP (oxysterol binding protein)-related proteins (ORPs) family shuffle among the intracellular membranous web, transporting sterols between the cellular membrane and intracellular compartments. OSBP is a lipid regulator that shuffles between the Golgi and ER for cholesterol and PI4P exchange and controls cholesterol efflux from cells. In addition, OSBP is exploited to facilitate the trafficking of lipid components to promote viral replication during the infection of some viruses.

Purpose: The objective of this study was to determine the role of OSBP in HEV replication and elucidate the mechanism of the OSBP effect.

Methods: Hepatoma cell line Huh7 was transfected with HEV RNA from replicon p6/luc, an HEV replicon of Kernow strain containing an insert encoding gaussia luciferase reporter replacing the 5' portion of ORF2. The luciferase in the culture supernatant was detected as it is secreted out of the cells after synthesis. The helicase from the HEV Kernow-C1 strain (GenBank Accession Number: JQ679013) was cloned. OSBP knockdown was conducted in Huh7 cells with shRNA and confirmed with Western blotting.

Results: Knockdown of OSBP significantly reduced the HEV replication from day 2 to 8 after transfection, as luciferase yield shows. To confirm the observation and exclude the possibility of an off-target effect, we transfected the OSBP-silenced cells with OSBP plasmid. Luciferase assay results showed that the ectopic expression of OSBP in the OSBP-silenced cells restored HEV replication. Further study showed that OSBP interacts with the HEV helicase, as shown in the co-immunoprecipitation assay. When over-expressed, OSBP preferentially localizes to the Golgi. However, co-transfection with plasmid encoding HEV helicase blocks the translocation of OSBP to Golgi.

Conclusions: Our results demonstrate that OSBP is required for HEV replication. HEV helicase interacts with OSBP and blocks its translocation to the Golgi apparatus. These data provide insights into HEV-cell interactions.

Disclosure of Interest: None Declared

O72

IMPLEMENTATION OF THE 'TORONTO PROTOCOL' GLECAPREVIR/PIBRENTASVIR+EZETIMIBE, FOR SOLID ORGAN TRANSPLANTATION FROM HCV NAT+ DONORS TO HCV-UNINFECTED RECIPIENTS: MOVING FROM RESEARCH TO STANDARD OF CARE

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Background: Increased use of HCV-infected donor organs (D+) for uninfected recipients (R–) is due to highly efficacious direct acting antiviral (DAA) therapy. We previously showed that an ultra-short course (7 days) of glecaprevir/pibrentasvir (G/P) combined with ezetimibe (EZE) prevented chronic infection in recipients across different organ types and HCV genotypes. This protocol has since been adopted as standard of care for HCV discordant transplants at our site. We report our results for two cohorts, one with extended follow-up for patients in the original study, and another describing patient outcomes since standard of care (SOC) adoption.

Methods: The population included all D+/ R– organ recipients who received the ultra-short therapy protocol with G/P+EZE x 1 dose pre- and daily for 7 days post-transplant. The follow-up period is reported until the last HCV RNA result or patient death. The primary endpoint is the establishment of chronic HCV infection, defined as positive HCV RNA 12-weeks post-transplant, or the need for retreatment after the initial protocol. Additional outcomes include graft rejection and patient survival.

Results: Since adoption of the protocol as standard of care, 35 additional patients received D+/R– organ transplant from 26 donors. The SOC cohort included 16 (46%) females and 19 (54%) males with a mean age of 53 years (range 21–79) with 21 kidney, 5 lung, 5 heart, 2 pancreas, 2 kidney-pancreas organ transplants. All patients completed the full treatment regimen before or shortly after hospital discharge with no dose reductions or treatment discontinuation. All patients had undetectable levels of HCV RNA at 2 weeks posttransplant and at the last follow-up visit with median follow-up of 51 weeks (range 2-111). The initial trial included 30 recipients from 18 donors. With extended follow-up to 165 weeks (IQR 89-182), no patients developed chronic HCV infection or relapsed. The 6-month patient survival rate was 93%. There was no graft loss, but 9 (21%) patients died from 7 to 165 weeks post-transplant with no HCV-related deaths. All patients in both groups achieved SVR with no breakthrough or retreatment. In the SOC group, three patient deaths unrelated to HCV treatment were reported at 11-, 188-, and 286-days post-transplant. Two episodes of acute rejection were reported.

Conclusion: An ultra-short course of G/P+E was safe with excellent graft and patient survival in D+/ R– solid organ transplant recipients. This approach is cost-saving, avoids complications of delayed therapy and can easily be operationalized into transplant protocols. These results support the current AASLD/IDSA recommendations to initiate prompt post-transplant treatment.

Image/Table:

	Initial trial (n=30)	Standard of care (n=17)	Total (n=47)
Age			
Median (IQR)	61 (48-66)	48 (26-72)	
Sex			
Male	23 (77%)	7 (41%%)	30 (64%)
Female	7 (23%)	10 (59%)	17 (36%)
Race			
White	22 (73%)	10 (59%)	32 (68%)
Asian	4 (13%)	5 (29%)	9 (19%)
Black	3 (10%)	0 (0%)	3 (6%)
Hispanic	1 (3%)	2 (12%)	3 (6%)
Transplanted organ			
Lung	13 (43%)	2 (12%)	15 (32%)
Kidney	10 (33%)	10 (59%)	20 (43%)
Heart	6 (20%)	2 (12%)	8 (17%)
Kidney/Pancreas	1 (3%)	2 (12%)	3 (6%)
Pancreas	0 (0%)	1 (6%)	1 (2%)
SVR			
	30 (100%)	17 (100%)	47 (100%)
Episodes of rejection			
	7 (23%)	3 (18%)	9 (19%)
Graft survival*^			
	21 (70%)	17 (100%)	38 (81%)
Patient survival^			
	21 (70%)	17 (100%)	38 (81%)
AEs related to treatment			
	1 (3%)	1 (6%)	2 (4%)
Complications of HCV			
	0 (0%)	0 (0%)	0 (0%)

*Graft loss only occurred in the event of patient death.
^The reported graft and patient survival rates in the initial trial are up to 147 weeks of follow-up. 6-month patient survival in the initial trial is 28 (93%).

Disclosure of Interest: None Declared

O73

TREATMENT OF PATIENTS WITH HEPATITIS C AFTER LIVER TRANSPLANTATION: EIGHT YEARS OF REAL-LIFE EXPERIENCE FROM THE CENTRE HOSPITALIER DE L'UNIVERSITE DE MONTREAL

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Introduction: Recurrence of Hepatitis C virus (HCV) infection is universal after liver transplantation. International societies recommend that all patients should be treated (1,2). Real-world data regarding efficacy of direct-acting antiviral (DAA)-based regimens are valuable for support recommendations in this population.

Aim: The aim of this study is to describe the clinic-virological characteristics and treatment efficacy of liver transplant recipients who were treated for HCV at a tertiary referral center in Montreal.

Material and methods: All HCV-infected patients, with or without cirrhosis, treated with a regimen of at least one direct-acting antiviral (DAA) were included. Patients enrolled in clinical trials were excluded.

Clinical and biological data were collected. Liver fibrosis was assessed before DAA therapy by liver elastography (FibroScan). Sustained virologic response was defined as undetectable HCV RNA (<12 IU/mL) 12 weeks after the end of treatment (SVR12). The choice of DAA combination was left to the discretion of the physician.

Results: Between 2014 and 2021, 800 patients were treated. Of these, 8.5% (68/800) were treated after liver transplantation. SVR12 was 92.6% (63/68). 83.8% were men, with a median age of 65 years (33-82), 22.1% had severe fibrosis/cirrhosis, and 5.8% developed fibrotic cholestatic Hepatitis.

Table 1 shows the 1st and 2nd line regimens and SVR12 by genotype. The 5 failures received a 2nd line with an SVR12 of 80.0% (4/5).

- P1: 67-year-old male, G2a, F0, treated with sofosbuvir(SOF)/velpatasvir(VEL) for 12 weeks. He developed fibrosing cholestatic Hepatitis and was retreated and cured with SOF/glecaprevir/pibrentasvir (GLE/PIB)/ribavirin(RBV) for 24 weeks.

- P2: 49-year-old male, G1a, F1, treated with SOF/simeprevir for 12 weeks. He was retreated and cured with SOF/ledipasvir(LDV) for 24 weeks.

- P3: 59-year-old female, G3a, F0, treated with GLE/PIB for 12 weeks. Resistance testing showed resistance-associated substitutions (RAS) in NS3 region, A156G; and in NS5A region, S24T and M28K. She was retreated and cured by SOF/GLE/PIB for 24 weeks.

- P4: 58-year-old male, G3b, F0, treated with SOF/VEL/RBV for 12 weeks, was retreated and cured with SOF/VEL/voxilaprevir (VOX) for 12 weeks.

- P5: 54-year-old male, G3a, F0-1, treated with SOF/daclatasvir for 24 weeks. Resistance test

showed Y93H in the NS5A region. He was retreated with SOF/VEL/VOX for 12 weeks without achieving SVR12. He developed a metastatic hepatocellular carcinoma.

Conclusion: In liver transplant patients treated for Hepatitis C, the SVR rate is 92.6%, confirming the efficacy of DAA treatment for Hepatitis C in liver transplant patients in our real-life experience.

Image/Table:

Table 1. Treatment regimens and SVR by genotype

1st line regime (n = 68)	n	%
Sofosbuvir/Velpatasvir/Voxilaprevir 12 weeks	1	1.5
Sofosbuvir/Velpatasvir 24 weeks	1	1.5
Sofosbuvir/Velpatasvir/Ribavirin 12 weeks	1	1.5
Sofosbuvir/Velpatasvir 12 weeks	9	13.2
Glecaprevir/Pibrentasvir 12 weeks	1	1.5
Sofosbuvir/Ledipasvir/Ribavirin 24 weeks	1	1.5
Sofosbuvir/Ledipasvir/Ribavirin 12 weeks	2	2.9
Sofosbuvir/Ledipasvir 12 weeks	23	33.8
Sofosbuvir/Daclatasvir 24 weeks	1	1.5
Sofosbuvir/Daclatasvir/Ribavirin 12 weeks	1	1.5
Sofosbuvir/Simeprevir/Ribavirin 12 weeks	1	1.5
Sofosbuvir/Simeprevir 24 weeks	1	1.5
Sofosbuvir/Simeprevir 12 weeks	15	22.1
Sofosbuvir/Ribavirin 24 weeks	7	10.3
Sofosbuvir/Ribavirin 12 weeks	1	1.5
Sofosbuvir/pegIFN/Ribavirin 12 weeks	1	1.5
Boceprevir/pegIFN/Ribavirin 12 weeks	1	1.5
2nd line regime (n = 5)	**n**	**%**
Sofosbuvir/Velpatasvir/Voxilaprevir 12 weeks	2	40.0
Sofosbuvir/Glecaprevir/Pibrentasvir 24 weeks	2	40.0
Sofosbuvir/Ledipasvir 24 weeks	1	20.0
Genotype (n = 68)	**n**	**SVR, % (n)**
1a	39	97.4% (38/39)
1b	7	100.0% (7/7)
2a	2	50.0% (1/2)
3a	13	84.6% (11/13)
3b	1	0.0% (0/1)
4a	1	100.0% (1/1)
4r	2	100.0% (2/2)
6a	2	100.0% (2/2)
6e	1	100.0% (1/1)

Disclosure of Interest: None Declared

O74

HCV MICRO-ELIMINATION IN MSM IN GERMANY: IMPACT OF DIRECTLY ACTING-ANTIVIRALS AND BEHAVIOR CHANGE DUE TO THE COVID 19 PANDEMIC

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Background: Recently acquired HCV infection is frequent in men who have sex men (MSM) with HIV coinfection, and more recently, in MSM taking pre-exposure prophylaxis. Since 2014, directly acting antiviral agents are broadly used for HCV in Germany, but label restrictions to chronic disease have hampered the use in the early phase of the infection. The impact of treatment and behavioral factors on HCV micro-elimination efforts is poorly studied in this population.

Methods: The NoCo cohort was established in April 2019 regrouping six German treatment sites for HIV and Hepatitis Care and HIV pre-exposure prophylaxis. The NoCo cohort is an ambidirectional cohort study, in which MSM were included if they had a diagnosis of recently acquired HCV infection since the year 2014 (beginning of universal DAA treatment in Germany) until December 2021.

Results: Overall, 237 men with recently acquired HCV infection were included between 2014 and 2021. Two hundred and six-teen (91%) occurred in HIV co-infected MSM, all but one on antiretroviral therapy. Of the 21 men without HIV, 15 (71%) were on HIV pre-exposure prophylaxis.

Most men were diagnosed through routine HCV testing (56.4%), followed by testing for ALT elevation (33.1%), 5.5% had an HCV-positive partner. The most common HCV genotype was 1a (58.7%), followed by 4d (16.5%), 3a (5.9%), or 4a (2.5%). Twenty patients (8.4%) had non-identifiable HCV subtypes. The median HCV viral load was 475,000 IU/mL (IQR 66955 to 3,01 $x10^6$), and the median ALT level was 224 U/L (IQR 86 to 521).

Between 2014-2019 26-36 patients were diagnosed with recently acquired HCV annually. In relation to all HIV-positive MSM under care, the incidence was 0.32 – 0.39% per year with no significant change over time. In 2020, a decline in HCV incidence to 0.28% was observed. In 2021 HCV incidence dropped to 0.02% (96% reduction compared to 2015 baseline).

A total of 88 reinfections (37.1%) were documented. Twenty-five men (31.3%) had multiple HCV infection episodes. Four reinfections occurred in Prep users. HCV reinfection was associated to older age (odds ratio, OR 1.04, p=0.005), the declared use of crystal methamphetamine (OR 5.3, p=0.032) and of ketamine (OR 7.1, p=0.042). HIV infection itself or HIV-associated variables were not linked to reinfection incidence.

Conclusions: The NoCo cohort demonstrated stable HCV incidence rates despite a broad use of DAAs. In 2021, however, micro-elimination goals were met, most likely due to behaviour changes related to the SARS-CoV-2 pandemic.

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O75

IMPACT OF TELEMEDICINE ACCESS TO HEPATITIS C SPECIALTY CARE ON THE CASCADE OF CARE: A RETROSPECTIVE COHORT STUDY

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Background: Direct-acting antivirals (DAAs) have revolutionized the HCV care cascade with their tremendous efficacy, which underscored the importance of optimizing HCV care accessibility to achieve the elimination goal. Telemedicine features the potential to increase healthcare access and has been utilized to mitigate the debilitating impact of COVID-19 pandemic on healthcare systems. However, rigorous studies of telemedicine services specifically used in HCV care remain in need to determine the effectiveness of telemedicine on the HCV care cascade.

Purpose: We aim to assess the effectiveness of telemedicine access to HCV specialty care on the HCV care cascade and outcomes.

Method: We utilized the Clinical Database of the Ottawa Hospital Viral Hepatitis Program (TOHVHP), a tertiary HCV specialty clinic, to retrospectively analyse medical records of adult patients (≥18 years old) initially assessed at the TOHVHP clinic between April 2018 and October 2022. The effectiveness of telemedicine was assessed in six-month intervals to illustrate the intersecting impact of the dynamic COVID-19 public health policies.

Result: A total of 926 patients were included in the study and 899 patients were successfully engaged in the HCV care cascade. The proportion of patients utilizing the telemedicine access (i.e., the Telemedicine (TM) group who only attended virtual appointments, and the Hybrid (HB) group who attended a mix of virtual and usual in-person appointments during the study period) trended up at each six-month interval chronologically when compared with UI (usual in-person appointments only) group (33.0%, 24.3%, 35.1%, 38.7%, 65.6%, 66.3%, 63.7%, 61.2%, p-value < 0.001). Lost-to-follow-up rates by groups were similar (HB:1.3%, TM:2.8%, UI:3.7%, p-value=0.189). HB group was associated with higher treatment initiation rates across the study period (HB:90.0%, TM:79.2%, UI:81.5%, p-value<0.001). No differences were identified in the treatment completion rate (HB:90.1%, TM:87.9%, 89.8%, p-value=0.908) or the SVR12 testing follow-up visit rate (HB:91.4%, TM:82.9%, UI=83.9%, p-value=0.055). By modified intent-to-treat analysis (mITT, defined as having received any DAA treatment but excluding those who were on treatment or within 12 weeks after treatment completion at the end of the evaluation period), HB and TM groups were associated with higher SVR rates than UI group (HB:88.5%, TM:81.7%, UI:78.4%, p-value=0.026). SVR rates among those who completed the SVR12 follow-up visit did not differ by group (HB:98.1%, TM:98.5%, UI:94.7%, p-value=0.137).

Conclusion: Telemedicine access to HCV specialty care was associated with higher treatment uptake and mITT SVR rate when compared with usual in-person outpatient services.

Disclosure of Interest: None Declared

O77

CLINICAL CHARACTERISTICS OF PATIENTS WITH SARS-COV-2 INFECTION AND PRE-EXISTING CHRONIC LIVER DISEASE

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Background : Since its emergence in 2019, the new Coronavirus SARS-CoV-2 has caused a global pandemic with high morbidity and mortality. Its profile in patients with pre-existing chronic liver disease (CLD) remains ill-defined. We aimed to determine the impact of COVID-19 on patients with pre-existing CLD.

Methods: We conducted a retrospective, descriptive study including all patients hospitalized for management of SARS-CoV-2 infection at the COVID-19 unit of the Hepato-Gastro-Enterology Department of Habib Thameur Hospital, in Tunisia, between October 2020 and February 2022. Patients who did not have liver chemistries during the hospitalization were not included. The clinical features and the characteristics of liver function in SARS-CoV-2-infected patients with pre-existing CLD were described.

Results: A total of 120 patients were included, mean age 59.46±15.35 years with a sex ratio (M/F) of 0.9. CLD was present in 11.7% of patients (n=14), of whom 8.3% had cirrhosis. Among the four patients without cirrhosis, two had chronic Hepatitis viral B on Entecavir and the other two had primary biliary cholangitis (PBC) on ursodeoxycholic acid (UDCA). In patients with cirrhosis, baseline Child-Pugh class was A in two, B in five and C in three patients. Acute hepatic decompensation was reported in six cases. It included new ascites in four cases, variceal haemorrhage in two cases and hepatic encephalopathy in three cases. Abnormal liver function tests was present in 11 patients with CLD, nine of them had cirrhosis. The presence of underlying CLD was independently associated with abnormal liver function (p=0.023; OR 11.8; CI [1.41-98.7]). The case fatality rate was significantly higher in patients with CLD at 0.14 and particularly in patients with cirrhosis at 0.2 (vs 0.03) (p=0.045).

Conclusion: Our study has shown that SARS-CoV-2 infection is associated with a poor prognosis in patients with CLD, especially in those with cirrhosis. Therefore, liver function should be taken seriously and evaluated more frequently in SARS-CoV-2-infected patients who have pre-existing CLD.

Disclosure of Interest: None Declared

O78

TREND OF TIMELY HEPATITIS B BIRTH DOSE VACCINE COVERAGE IN THE GAMBIA AND IMPACT OF THE COVID-19 PANDEMIC

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Background and Aims: Africa has the lowest coverage of timely Hepatitis B birth dose (HepB-BD) vaccination worldwide. In The Gambia, the first African country to introduce HepB-BD, we assessed the coverage of timely HepB-BD vaccination, the factors associated with delayed HepB-BD vaccination, and the impact of the COVID-19 pandemic on HepB-BD coverage.

Methods: Using data from the Gambian Health and Demographic Surveillance System, we computed the rate of timely (day 0-1) and delayed (days 2-7, 8-28, 28+) HepB-BD and assessed for change points in the average rate. From a logistic regression analysis, we determined the factors associated with delayed or no record of HepB-BD and assessed the impact of COVID-19 on timely HepB-BD.

Results: Out of 70,888 live births in three regions (Bansang, Basse and Farafenni) between 1st January 2015 and 31st December 2021, 4,513 (6.4%; 95% CI 6.2-6.5) received timely HepB-BD. Timely HepB-BD coverage increased from 1.8% in January 2015 to 20.7% in December 2021, peaking at 30.8% in October 2021.

Delayed HepB-BD, administered between days 2-7 and days 8-28, was observed in 3,946/70,888 (5.6%; 95% CI 5.4-5.7) and 32,157 (45.4%, 95% CI 45.0-45.7) babies, respectively. The median age at first dose of HepB vaccination was 20 days (IQR: 11-31 days).

Being born in a health facility [OR 0.76 (95% CI 0.68-0.84), p value <0.0001]; born after July 2018 [OR 0.47 (95% CI 0.41-0.53), p<0.0001]; or born to mother with Junior Secondary education [OR 0.50 (95% CI 0.34-0.77), p=0.001] increased chance of timely HepB-BD. Delayed or no record of HepB-BD vaccine was associated with being born on Friday [OR 3.27 (95% CI 2.74-3.92), p<0.0001] or Saturday [OR 6.14 (95% CI 4.89-7.81), p<0.0001]; born in Basse [OR 1.96 (95% CI 1.75-2.20), p<0.001] or Farafenni [OR 1.51 (95% CI 1.33-1.73), p<0.001]; or born during the rainy season [OR 1.12 (95% CI 1.03-1.22), p=0.008]. Increasing maternal age increased risk of delayed (or no record of) HepB-BD [OR 1.008 (95% CI 1.002-1.014), p=0.007) for every additional year.

Timely HepB-BD declined from 10.1% (CI 9.5-10.6) pre-COVID (from June 2019) to 5.4% (CI 4.5-6.3) during the first COVID-19 wave. After accounting for all other factors, the odds ratio of delayed HepB-BD among 3,187 babies born during the first COVID-19 wave was OR:1.4 (1.2-1.6, p=0.0002). Timely HepB-BD coverage improved immediately after the COVID-19 wave, reaching pre-COVID rates within 4-6 months.

Conclusion: Timely HepB-BD coverage improved marginally but remains low 25 years after its introduction in The Gambia. The negative impact of the COVID-19 pandemic on timely HepB-BD was transient. Strategies are urgently needed to achieve 90% HepB-BD coverage required to eliminate HBV by 2030.

Disclosure of Interest: None Declared

O79

INFANT HEPATITIS B VACCINATION IN AFRICA: URGENT NEED TO SUPPORT INFANT HEPATITIS B VACCINATION INCLUDING BIRTH DOSE VACCINE IN AFRICA

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Background: Two thirds of 6 million children <5 years old living with chronic Hepatitis B virus (HBV) infection are in Africa. Most chronic HBV infections occur during birth or in early childhood. Timely Hepatitis B birth dose vaccination (HepB-BD) followed by completion of 3 dose infant vaccine series (HepB3) are cost effective interventions. WHO set HepB-BD and HepB3 coverage targets of 50% and 90% for 2020. However, infant vaccination services were curtailed by COVID-19 response.

Purpose: We reviewed the status of HepB-BD policies and HepB vaccine coverage data for WHO Africa region to assess HepB vaccination status among children in Africa, including effects of COVID-19 on coverage.

Methods: WHO data on HepB-BD introduction for African countries were reviewed. Data reported by WHO and UNICEF were reviewed for HepB-BD and HepB3 coverage. WHO Africa's 2021 HepB-BD coverage estimates were compared with global and other WHO regional estimates. WHO Africa country HepB-BD coverage estimates were also evaluated. The 2021 coverage estimates for HepB-BD and HepB3 were compared with 2019 pre-COVID-19 coverage estimates for WHO Africa countries.

Results: By 2021, only 14 out of 47 (30%) WHO Africa countries had introduced HepB-BD. In 2021, global coverage for HepB-BD vaccine was 42%, below WHO 2020 target. WHO Africa had the lowest HepB-BD coverage (17%) while WHO Western Pacific had the highest coverage (78%). Of 14 WHO Africa countries with HepB-BD, nine (64%) had coverage data for 2021. Algeria (99%), Carbo Verde (96%) and Namibia (86%) had the highest while The Gambia (25%), Nigeria (52%) and Cote d'Ivoire (66%) had the lowest (Figure). Comparing 2021 with 2019 HepB-BD coverage, Cote d'Ivoire (57%) and Namibia (5%) had an increase whereas Sao Tome and Principe (26%) and Senegal (7%) had a decrease. HepB3 coverage was also lowest in the WHO Africa (71%) and was below global coverage of 80%. Comparing 2021 with 2019, HepB3 coverage decreased by 4% in WHO Africa and 5% globally. From 2019-2021, 10 countries in WHO Africa had HepB3 coverage increase ranging from 1–8%; 13 countries did not have a change and 24 counties had a decrease including eight with >10% decrease.

Conclusions: Despite high burden of HBV infections among children in WHO Africa, few countries have HepB-BD and HepB3 coverage declined in many countries after COVID-19 pandemic. Currently, less than one in five of African children receive timely HepB-BD. To assist countries in HepB-BD policy formulation, the Coalition for Global Hepatitis Elimination (CGHE) has developed a toolkit that provides policy makers a common resource of essential information to support HepB-BD introduction in Africa. The HepB-BD toolkit is available at *www.globalhep.org.*

Image/Table:

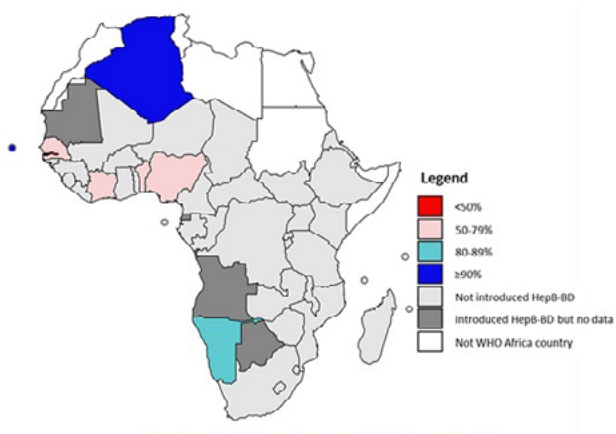

Figure. Hepatitis B birth dose vaccine coverage in WHO Africa countries, 2021

Disclosure of Interest: None Declared

O80

THE DEVELOPMENT OF A PAN-GENOTYPIC PROPHYLACTIC VIRAL VECTORED T CELL VACCINE AGAINST HEPATITIS C VIRUS

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Background: The significant genetic diversity of Hepatitis C virus (HCV) poses a major challenge for the development of an effective prophylactic vaccine. A previous promising vaccine candidate using recombinant chimpanzee adenovirus (ChAd) and modified vaccinia virus Ankara (MVA) vectors encoding the non-structural (NS) proteins of HCV genotype 1b (Gt1b) failed to prevent chronic infection in phase II clinical trials, despite producing high magnitude HCV specific T cells. The inability of T cells to cross recognise genotypes may have contributed to vaccine failure. To overcome this challenge, we have developed viral vectors encoding conserved segments of HCV genotypes 1–6 (ChAd-Gt1-6 and MVA-Gt1-6), ancestral 'Bole1a' HCV NS sequence (ChAd-Bole1a-NS), and Gt3a NS sequence (MVA-Gt3a-NS).

Methods: The immunogenicity and cross-reactivity of these vaccines were assessed in C57BL/6 or transgenic HLA-A*02:01 mice after a single dose (ChAd prime) and after heterologous prime-boost (ChAd-MVA). In prime experiments, mice were vaccinated intramuscularly (IM) with ChAd-Gt1-6 or ChAd-Bole1a-NS ($1x10^8$ IU). In prime-boost experiments, mice were vaccinated IM with ChAd-Gt1-6 or ChAd-Bole1a-NS ($1x10^8$ IU) followed 8-weeks later with MVA-Gt1-6 or MVA-Gt3a-NS ($5x10^7$ PFU) respectively. HCV-specific T cell magnitude and breadth was assessed 14-days post-vaccination using Gt-1a, -1b, and -3a peptides in ex vivo IFNγ ELISpot assays.

Results: Both ChAd-Gt1-6 and ChAd-Bole1a-NS induced HCV-specific T cell responses after a single dose. However, ChAd-Gt1-6 induced broader responses than ChAd-Bole1a-NS. Specifically, the response to ChAd-Bole1a-NS predominantly targeted the NS3 helicase, was highly specific to Gt-1, and had limited cross reactivity to Gt-3a. In contrast, the response to ChAd-Gt1-6 targeted multiple NS proteins and was cross reactive to all genotypes, with a significantly higher response to Gt3a compared to ChAd-Bole1a-NS ($p=0.026$). Prime-boost regimens increase the breadth of the response, such that when ChAd-Bole1a-NS was boosted with the heterologous MVA-Gt3a-NS vaccine the breadth of response was comparable to that induced by ChAd-Gt1-6 followed by MVA-Gt1-6, albeit with differences in specificity within the different genotypes.

Conclusion: The use of ChAd and MVA viral vectors in a prime-boost regimen is the optimum strategy to generate high magnitude T cell responses targeting multiple HCV genotypes. The use of viral vectors encoding the NS proteins from heterologous HCV genotypes, or viral vectors encoding conserved regions of HCV genotypes 1-6 are two novel approaches to generate cross-genotypic HCV vaccines. Phase-I human clinical trials would be required to select the optimal pan-genotypic strategy.

Disclosure of Interest: None Declared

O81

THE TIME INTERVAL FROM DIAGNOSIS OF CHRONIC HEPATITIS B TO INITIATION OF ANTIVIRAL THERAPY AND ITS ASSOCIATION WITH ADHERENCE TO TREATMENT IN THE GAMBIA

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Background and Aims: Assessment of liver disease and treatment eligibility criteria in people living with Hepatitis B virus is difficult in sub-Saharan Africa and represents a major obstacle to scale up treatment coverage in the region. This study aimed to estimate the time interval from first clinical assessment to antiviral treatment initiation in chronic Hepatitis B (CHB) infected patients in The Gambia and to assess the potential impact of delay in treatment initiation on adherence.

Methods: A retrospective analysis of CHB patients treated with tenofovir disoproxil fumarate (TDF) prospectively enrolled in the Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) programme in The Gambia. Patients were either screened in the community (group 1), referred to clinic with advanced chronic liver disease (ACLD) (group 2), screened in blood banks (group 3) or screened in the main outpatient department (OPD) at the Medical Research Council Unit in The Gambia (group 4).

For each participant we reviewed the dates of first positive Hepatitis B surface antigen screen (HBsAg), first clinical assessment for treatment eligibility (Fibroscan, alanine transaminase and viral load) and TDF dispensation. The primary time interval was calculated as the number of days between first clinical assessment and TDF dispensation. Adherence was measured using the Morisky questionnaire. Logistic regression was used to conduct bivariate and multivariate analyses, adjusting for age, sex, and cirrhosis status.

Results: We analysed a total of 183 patients (median age 35 years (interquartile range (IQR) 29.8-40), 155 male). Baseline characteristics were compared to the community group. The ACLD group had increased liver stiffness and cirrhosis prevalence ($p<0.0001$, $p<0.0001$). The prevalence of liver cirrhosis was also higher in the OPD group ($p=0.0003$). There were no other differences between the groups at baseline.

The median time interval from to treatment initiation was highest in the community group, 300.5 days (IQR 235.8-444.8), but was 185 days (IQR 84-378) when considering all patient groups. There was no significant association between delay in treatment initiation and adherence to TDF ($p=0.128$). The multivariate logistic regression identified no confounders.

Conclusion: The median time interval was estimated at 185 days. Although it did not impact on adherence to treatment, our results indicate that same day or rapid treatment initiation for hepatis B was difficult to achieve in The Gambia and this may impact the feasibility of HBV elimination goals in Sub-Saharan Africa.

Disclosure of Interest: None Declared

O82

A COMMUNITY-BASED INTERVENTION TO REDUCE MISSED OPPORTUNITIES IN PRIMARY CARE FOR VIRAL HEPATITIS SCREENING AMONG AT-RISK AFRICAN MIGRANTS IN CATALONIA, SPAIN

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Background: Africans in Europe migrating from high-endemic HBV and HCV areas may not know their disease status due to unreliable testing and vaccination in their home countries and underutilization of the host country health services. This delays diagnosis and linkage to care. In Catalonia, Spain, universal health coverage grants migrants access to health services, including primary care, which offers an entry point into the health system.

Purpose: We aimed to use point-of-care testing in community settings to identify and link to care or vaccinate West African migrants in the greater Barcelona area, Spain.

Methods: The community-based HBV screening program began in November 2020 and expanded to include anti-HCV OraQuick® testing and migration journey and health service utilization questions, in June 2022. From 21/11/20 to 4/12/2022, 636 people were offered HBV testing in community settings using an HBV surface antigen (HBsAg) rapid lateral flow test, DETERMINE® HBsAg 2, followed by whole blood sample collection using a plasma separation card (Roche Diagnostics), which analyzed HBV-DNA and anti-Hepatitis D virus (HDV) among those HBsAg+ and anti-HBc among those HBsAg-. HBsAg+ participants were immediately referred to a collaborating hospital for full assessment.

Results: 625 participants were included for analysis (mean age 42 [SD 10]). They were primarily from Ghana (81%) or Senegal (16%) and male (63%). Most participants had never been tested for HBV nor HCV (70%), while 15% were unsure if they had been. HBsAg+ prevalence was 10% (n=64) and no one was anti-HCV+. Of those participants enrolled since June 2022 (n=192), 72% reported having visited their primary care center in the past 12 months, of whom 66% had blood drawn during that visit. Of the latter, 11 participants were found to be HBsAg+ during the community-based screening program (of the 24 participants who tested HBsAg+ since 06/2022). Of those HBsAg+, 47% (n=30) had detectable HBV-DNA and one person was anti-HDV+. Of those who were HBsAg-, 35% were anti-HBc+. Overall, 76% (n=49) of those who were HBsAg+ had a first documented visit with a collaborating tertiary hospital; three preferred to visit their own physicians.

Conclusions: This community-based viral Hepatitis screening program provides an effective model for identifying and providing care to migrant populations at high risk of HBV infection who may otherwise not engage in care. Nearly 1/2 of the participants who received a new HBV diagnosis had visited their primary care center within the past 12 months, reflecting a missed opportunity for early screening and diagnosis in this population and reveals gaps in the current viral Hepatitis Care pathways in Catalonia.

Disclosure of Interest: None Declared

O83

ENGAGEMENT IN HEPATITIS C SCREENING AND TREATMENT AMONG PREGNANT AND POSTPARTUM INDIVIDUALS IN ONTARIO, CANADA: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

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Background: The opioid epidemic has led to increasing numbers of Hepatitis C virus (HCV) infections in younger populations and women of childbearing age. As a result, HCV among pregnant women has also increased. Prenatal care may be the only time when women engage in healthcare services, making it an opportune time to screen for and diagnose HCV, and link them to care. Currently, there is little known to describe trajectories of HCV care among pregnant or postpartum women in Canada or globally.

Purpose: Using health administrative data, we characterized engagement in HCV care among pregnant and postpartum individuals in Ontario, Canada identifying gaps in engagement and healthcare service delivery.

Method(s): We performed a population-based retrospective cohort study linking individuals who delivered between 1999 and 2018 to HCV testing records and health administrative datasets. We identified individuals who were alive and in Ontario as of Dec 31, 2018, with record of testing HCV antibody(Ab) or RNA positive and inpatient records of a delivery (livebirth or stillbirth). We determined whether individuals were positive before, within the prenatal care period (from estimated start of pregnancy) or after their earliest delivery date; as well as whether individuals had subsequent RNA testing, HCV care, and frequency of treatment through the provincial drug benefit program.

Result(s): On Dec 31, 2018, we identified 8389 individuals with an Ab or RNA positive test record and a delivery between 1999 to 2018. Of these individuals, 2384(28%) had their earliest positive test before or on their earliest delivery date, 682(8.1%) had their earliest positive test during the prenatal care period or on their earliest delivery date, and 370(4.4%) up to a year following delivery date. For individuals where their earliest positive corresponded to an Ab positive test result (N=8041(96%)), 6759(84%) had a subsequent RNA test, with median time to testing of 13(IQR:3-75) weeks and mean of 79(SD:149) weeks. Of these individuals, 4642 (69% of RNA tested) were RNA positive. Among all individuals with an RNA positive result (N=5147(61.4% of 8389)), 1575(30.6%) had a subsequent first treatment dispensation record with median time from RNA positive to treatment of 104(IQR:40-274) weeks and mean of 192.1(SD:205.5) weeks.

Conclusion(s): We observed delays between HCV testing and treatment among pregnant and postpartum individuals. The observed delay in treatment initiation calls for further investigation of the HCV cascade of care in the absence of reimbursement barriers including testing to subsequent follow-up data and timing. This work will shed light on the need for low barrier treatment models targeting postpartum linkage to care.

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O84

CHARACTERIZING OPERATIONAL MODELS OF HEPATITIS B AND C CARE FOR REFUGEE POPULATIONS: RESULTS OF A SYSTEMATIC REVIEW

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Background: Achieving the 2030 WHO Hepatitis B (HBV) and Hepatitis C (HCV) elimination targets will require equitable access to Hepatitis services in refugee populations. Previous systematic reviews and prevalence studies have found that refugees are at higher risk for HBV and HCV. Despite this increased risk, refugees are less likely to be screened and treated for HBV and HCV, and face unique barriers to care.

Purpose: The aim of this systematic review was to identify and characterize HBV and HCV prevention, testing, and treatment interventions targeting refugee populations globally.

Methods: A literature search was conducted on Embase, Cochrane, and PubMed databases using relevant keywords, including: HBV, hcv, intervention, program, educat*, support*, integrat*, campaign*, outreach, counsel*, engage*, train*, teach*, diagnos*, treat*, link*, Hepatitis b vaccin*, screen*, test*, opioid substitution, birth dose, needle syringe, needle exchange, direct acting antiviral, directly observed, harm reduction, refugee, and internally displaced. Research studies published in English between January 2010 to July 2022 were included if they described an HBV or HCV prevention, screening, or treatment intervention for refugee populations with details about program implementation.

Results: A total of 69 studies were included from Africa (n=7), the Americas (n=17), Eastern Mediterranean (n=4), Europe (n=30), South-East Asia (n=5), and the Western Pacific (n=6) (Table 1). 40 interventions targeted multiple diseases, which included HBV and/or HCV, 11 interventions targeted HBV and HCV, 16 interventions targeted HBV only, and 2 interventions targeted HCV only. Common interventions were testing only (n=19) and vaccination only (n=7). Of the 12 studies that reported funding sources, 50% reported governmental funding, 17% reported supplies donations, and 42% reported that refugees were included in the national health insurance scheme. Only 29 studies reported details about program impact.

Frequently reported program strengths were partnerships with community organizations, hospitals, and other stakeholders (n=19), bilingual care (n=13), and cultural mediators on staff (n=8). Common challenges included loss to follow up (n=5/30) in studies with linkage to care and uncompleted vaccination series (n=4/22) in studies with vaccination.

Conclusions: Models of HBV and HCV services for refugee populations remain limited, with most evidence from high-income countries. Across available studies, community stakeholder participation, language services, and governmental support appear key to Hepatitis service delivery. Best practices must be identified and disseminated to expand access to Hepatitis services for refugee populations.

Image/Table:

Table 1. Location of included interventions (n=69)

Country	Frequency (%)
African region	1 (1.4)
Australia	6 (8.7)
Bangladesh	1 (1.4)
Cameroon	1 (1.4)
Canada	1 (1.4)
Denmark	1 (1.4)
Ethiopia	1 (1.4)
Finland	1 (1.4)
France	2 (2.9)
Germany	5 (7.2)
Greece	2 (2.9)
India	1 (1.4)
Italy	14 (20.3)
Nigeria	1 (1.4)
Norway	1 (1.4)
Pakistan	4 (5.8)
Rwanda	2 (2.9)
South Sudan	1 (1.4)
Spain	1 (1.4)
Switzerland	1 (1.4)
Thailand	2 (2.9)
Thailand-Burma border	1 (1.4)
Turkey	1 (1.4)
United Kingdom	1 (1.4)
United States	16 (23.2)
Setting	**Frequency (%)**
Academic institution	1 (1.4)
Clinic or hospital	31 (44.9)
Community site	2 (2.9)
Refugee camp	11 (15.9)
Refugee/Immigration center	5 (7.2)
Refugee shelter/accommodations (not a refugee camp)	2 (2.9)
Multiple sites	4 (5.8)
Other	2 (2.9)
Not specified	11 (15.9)

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O85

PUTTING PEOPLE AT THE CENTRE: PROTOCOL FOR PATIENT JOURNEY MAPPING OF VIRAL HEPATITIS SERVICES IN VIET NAM AND THE PHILIPPINES

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Abstract Content: Chronic viral Hepatitis remains a major public health concern in the Western Pacific, including in Viet Nam and the Philippines. National health sector strategies have proliferated but services are not yet reaching the majority of people who need them. In order to accelerate progress, there is a critical need understand patients' experiences living with Hepatitis and navigating care. Patient journey mapping (PJM) is one research method that can provide valuable insight into what works well and where gaps exist from patients' perspectives, and indicate how the health system might better respond to their needs. PJM methods can be resource-intensive and are not yet consistently codified in the literature, resulting in few peer-reviewed studies from low-and-middle-income countries (LMICs). The Strengthening Integrated Treatment and Care for Hepatitis (StITCH) project will address this gap and inform the co-design of a new, people-centred model-of-care (MoC) for Hepatitis in Viet Nam and the Philippines. StITCH employs a PJM methodology that includes in-depth, retrospective and prospective interviews with approximately 30 patients living with Hepatitis B or C in each country. The purposive, quota-based sampling strategy aims to capture a longitudinal view of a diverse set of patient journeys. Data will be analyzed using a rapid, deductive qualitative approach adapted from previous studies with the intention of reducing the burden on in-country teams, allowing country comparison, and minimizing the time to actionable insights for co-design. Findings will be shared in narrative and visual formats using a new conceptual framework developed to explore individual, social and relational and health systems barriers and enablers of patients' journeys with Hepatitis. StItCH aims to generate a locally contextualised, patient-centric evidence base to inform the design and improvement of services for Hepatitis in Viet Nam and the Philippines. The approach can be replicated across other LMICs and for other disease areas to support achievement of Universal Health Care (UHC).

Disclosure of Interest: None Declared

O86

IMPACT OF HCV TESTING AND TREATMENT SERVICES ON HCV TRANSMISSION AMONG MEN WHO HAVE SEX WITH MEN AND WHO INJECT DRUGS IN SAN FRANCISCO: A MODELLING ANALYSIS

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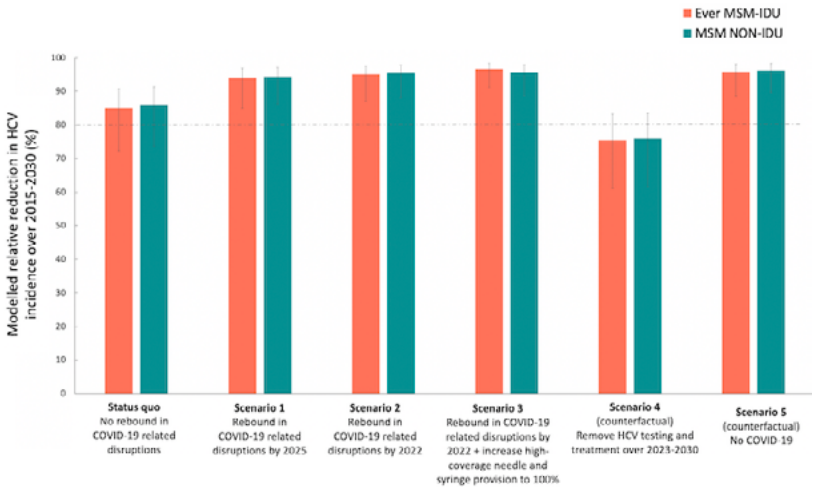
Background and Purpose: Men who have sex with men (MSM) carry a high burden of Hepatitis C virus (HCV), particularly MSM who ever injected drugs (ever MSM-IDU). Using modelling, we estimated whether current HCV testing and treatment in San Francisco (USA) can achieve the WHO HCV elimination target (80% reduction in HCV incidence over 2015-2030) among ever MSM-IDU.

Methods: We developed a dynamic HCV and HIV transmission model among MSM calibrated to San Francisco data, including proportion of ever MSM-IDU (stratified by recent and non-recent injection drug use: 6.0% and 6.7%, respectively), HCV antibody prevalence (15.5% and 2.3% among ever MSM-IDU and MSM who never injected (MSM non-IDU), 2011), HIV prevalence (32.8% and 17.3% among ever MSM-IDU and MSM non-IDU, respectively, 2017) and PrEP use (45% among all MSM, 2019). Based on data, we assumed high levels of ever HCV testing (79%-86%, 2011-2019) and ever HCV treatment (65% among diagnosed MSM, 2018). Following COVID-19 pandemic-related lockdowns, HCV testing and treatment rates decreased by 59%, HIV testing and treatment by 31% and PrEP initiation by 35%. We modelled the relative decrease in HCV incidence over several scenarios, including different trajectories of recovery in COVID-19 related disruptions, over 2015-2030.

Results: Among all MSM, 43.3% (95%CrI: 33.8-51.8%) of incident HCV infections were attributed to injection drug use in 2022. Among ever MSM-IDU, this estimate was 85.7% (95%CrI: 80.2-89.5%). By comparison, 2.8% (95%CrI: 1.8%-3.8%) and 20% (95%CrI: 14.5%-25.7%) of incident HIV infections were attributed to injection drug use among all MSM and ever MSM-IDU, respectively. Among ever MSM-IDU in 2015, HCV incidence was estimated at 1.2/100 person-years (0.8–1.6). Assuming COVID-19-related disruptions persist until 2030 (scenario status quo), we estimated that HCV incidence among ever MSM-IDU will decrease by 85% (72%-91%) over 2015-2030 (Figure). If COVID-19-related disruptions rebound (scenarios 1-3), HCV incidence would decrease by 94%-95%. Most of the declines in HCV incidence over 2015-2030 are due to the impact of HCV testing and treatment over this period (impact range over different scenarios: 76-85%) and, particularly, their scale-up since 2015 (54%-59%). If HCV testing and treatment would cease over 2023-2030 (scenario 4), then only a 74% decrease (95% CrI: 59%-83%) in HCV incidence would be achieved; this is the only scenario considered in which HCV incidence would increase.

Conclusions: Although injection drug use is only reported by a minority of MSM, it is estimated to account for nearly half of all incident HCV cases in this population. Despite COVID-19-related disruptions, we estimate that the WHO HCV incidence elimination target will be achieved among ever MSM-IDU in San Francisco, due to high HCV testing and treatment among MSM since 2015.

Image/Table:



Disclosure of Interest: None Declared

O87

RESCUE OF CIRRHOTIC CHRONIC HBV / HDV INFECTION FROM BULEVIRTIDE FAILURE BY SUBCUTANEOUS REP 2139-MG

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Background: REP 2139 blocks HBV subviral particle assembly and Hepatitis delta antigen function, driving HBsAg loss in HBV infection and HBsAg / HDV RNA loss in HBV / HDV co-infection. The safety and efficacy of SC injection of REP 2139-Mg in combination therapy is currently being assessed in cirrhotic patients with chronic HBV / HDV co-infection after failure or viral rebound to bulevirtide (BLV).

Methods: Compassionate access to REP 2139-Mg was approved by the ANSM in 8 patients with compensated cirrhosis having no response or viral escape in HDV RNA during 2 or 10mg BLV therapy. Existing TDF was supplemented with 48 weeks of QW SC 250mg REP 2139-Mg and either 90 or 180µg pegIFN. Weekly safety evaluations were accompanied by virologic assessment every 4 weeks.

Results: As this abstract is submitted, five patients have at least 4 weeks of REP 2139-Mg exposure.

One patient completed therapy with HDV RNA clearance at week 4, HBsAg clearance with seroconversion at week 12 and an asymptomatic self-resolving transaminase flare at week 9. Five months following removal of REP 2139-Mg and pegIFN, HDV RNA and HBsAg remain undetectable with HBsAg seroconversion (348 mIU/mL).

Central obesity likely prevents optimal liver accumulation of REP 2139 in one patient, with HDV RNA and HBsAg declines currently 2.2$\log_{10}$ and 0.7$\log_{10}$ IU/mL respectively from baseline. REP 2139-Mg administration was subsequently transitioned to IV infusion in this patient.

Two patients with significant REP 2139-Mg exposure have experienced HDV RNA clearance at weeks 13 and 16, with HBsAg loss (week 16) and HBsAg seroconversion (now 934.4 mIU/mL) in the first patient. HBsAg decline is > 2 $\log_{10}$ IU/mL in the second patient. Patient 5 has experienced a 0.5 $\log_{10}$ IU/mL decline in HDV RNA at week 4.

The administration of SC 250mg REP 2139-Mg with oral TDF and pegIFN has been well tolerated to date.

Conclusions: Subcutaneous REP 2139-Mg is safe, well tolerated, and effective against HBV and HDV infection in combination with TDF and low dose pegIFN in patients with compensated cirrhosis. REP 2139-Mg is also an effective salvage therapy in bulevirtide failure patients.

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O88

SAFETY AND EFFICACY OF REP 2139-MG IN ASSOCIATION WITH TDF IN PATIENTS WITH CHRONIC HEPATITIS DELTA AND DECOMPENSATED CIRRHOSIS

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Introduction: Chronic Hepatitis delta (CHD) typically leads to cirrhosis and hepatic decompensation. The only treatment option for CHD patients with decompensated cirrhosis is liver transplantation with associated short- and long-term complications. REP 2139-Mg is a nucleic acid polymer (NAP) that blocks the assembly and secretion of HBV subviral particles and Hepatitis delta antigen function, providing multiple effects against both HBV and HDV infection. The objective of this study is to describe the safety and efficacy of REP 2139-Mg in CHD patients with decompensated cirrhosis.

Patients & Methods: Compassionate use access in the first two European CHD patients with decompensated cirrhosis to receive REP 2139-Mg 250 mg QW subcutaneously (SC) and tenofovir disoproxil fumarate (TDF) 300 mg QD orally for a planned total duration of 48 weeks was approved in France by the ANSM. Clinical, biological, virological and imaging data were collected at baseline and every week for the first month, then every month. Safety and tolerance were continuously evaluated.

Results: Patient #1 is a Caucasian, 56-year old female, HDV treatment-naïve, with CHD decompensated cirrhosis (Child Pugh B8, portal hypertension and ascites) with HDV RNA 7.04 $\log_{10}$ IU/mL and HBsAg 1177 IU/mL at baseline. At week 4 of therapy, reversal of ascites was confirmed by ultrasound (minimal diuretic dose was maintained due to mild bilateral leg edema). HBsAg loss occurred at week 10 with HBsAg seroconversion (27 mIU/mL) at week 14 increasing to 168 mIU/mL at week 18. HDV RNA has been undetectable since week 20.

Patient #2 is an African, 56-year old female with arterial hypertension awaiting liver transplant. She experienced HDV relapse 1 year after discontinuing bulevirtide 2mg and pegIFN 180ug and progressed to decompensated cirrhosis (Child Pugh C11, portal hypertension, ascites and hepatocellular carcinoma) with accompanying edema, and pronounced fatigue. Baseline HDV RNA was 3.64 $\log_{10}$ IU/mL and HBsAg 4270 IU/mL. At Week 4, abdominal CT confirmed significant reduction of clinical ascites and peripheral edema and fatigue were markedly reduced.

Both patients have no side effects and present a good tolerance to subcutaneous injections of REP 2139-Mg to date.

Conclusions: REP 2139-Mg in association with TDF is safe and well tolerated in patients with CHD and decompensated cirrhosis. Liver function improvement with significant ascites reversal was rapid, occurring after only 4 weeks of treatment. HBV-HDV functional cure with HBsAg loss and HBs seroconversion appears achievable in this special population which could prevent the need for a future liver transplant

Disclosure of Interest: C. de Frietas: None Declared, C. Stern: None Declared, M. Bazinet Shareholder of: Replicor Inc., Employee of: Replicor Inc., V. Mackiewicz: None Declared, S. Brichler: None Declared, E. Gordien: None Declared, M. Bourlière: None Declared, A. Vaillant Shareholder of: Replicor Inc., Employee of: Replicor Inc.

O89

BULEVIRTIDE TREATMENT FOR HEPATITIS D IN DECOMPENSATED LIVER DISEASE – CLINICAL EXPERIENCE BASED ON REAL-WORLD CASE REPORTS

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Introduction: Hepatitis D is the most debilitating form of viral Hepatitis leading to liver cirrhosis and hepatocellular carcinoma. In 2020, the entry inhibitor bulevirtide was approved for the treatment of compensated liver disease in patients with chronic Hepatitis D. While patients with advanced but still compensated liver disease can be treated on-label, a treatment for the vulnerable collective of patients with decompensated liver disease is lacking.

Methods: In a joint effort we collected real-world data from 16 German centers treating patients with bulevirtide for chronic Hepatitis D. In a subset of special patients treatment was initiated in a state of decompensated liver disease. This subset was selected for a separate analysis. In addition, we analyzed a patient in which the treatment was continued after hepatic decompensation occurred under treatment.

Results: In five patients of the larger real-world cohort (n=114) treatment was initiated in a state of decompensated liver disease. Four patients were classified as Child-Pugh B, one case as Child-Pugh C. All five patients showed a virologic response (figure 1A). All but one patient showed decreasing ALT levels and rising platelet counts (figure 1B and C). In one patient with refractory ascites (shown in purple in figure 1) it came to a temporarily improvement of ascites. In another case (shown in green in figure 1) a significant hyperbilirubinemia of 72 mmol/l at baseline improved shortly after treatment initiation to 51mmol/l at week 2 and 38 mmol/l at week 32. During the displayed treatment periods there was no report of serious adverse events related to BLV.

A separate case had compensated liver disease at treatment initiation and developed hepatic decompensation with new ascites. In this individual case the risk of ALT flares due to treatment cessation with potential detrimental effects on the hepatic function was considered as to high. Under continued BLV treatment and optimized diuretic treatment hepatic recompensation was achieved.

Conclusion: Patients with decompensated liver disease due to chronic Hepatitis D are at great risk and represent a vulnerable collective. As of today, there is no approved treatment for these patients. In this summary of five case reports BLV treatment appeared to be safe and effective with virologic response in all cases. In addition, we reported a case in which de novo decompensation after initiation of BLV treatment improved under continued treatment. Large randomized controlled trials are urgently needed to address the unmet need of an effective and safe treatment in patients with Hepatitis D and decompensated liver disease.

Image/Table:

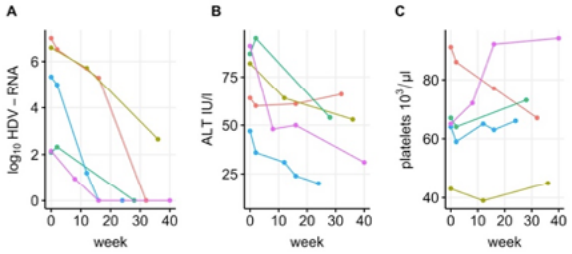

Figure 1. Viral kinetics, ALT and platelet dynamics in patient with decompensated liver disease at treatment initiation

Disclosure of Interest: None Declared

O90

EVALUATING DIFFERENCES IN ON-TREATMENT RISK OF HEPATOCELLULAR CARCINOMA AMONG A LARGE COHORT OF PREDOMINANTLY NON-ASIAN PATIENTS WITH NON-CIRRHOTIC CHRONIC HEPATITIS B INFECTION

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Background: Timely initiation of chronic Hepatitis B (CHB) therapy is associated with reductions in CHB-related hepatocellular carcinoma (HCC). However, disparities in long-term HCC risk remain despite treatment, and it remains unclear what are the drivers of these disparities in CHB-related HCC. We aim to evaluate differences in on-treatment risk of HCC among a large cohort of predominantly non-Asian patients with CHB in the United States (US).

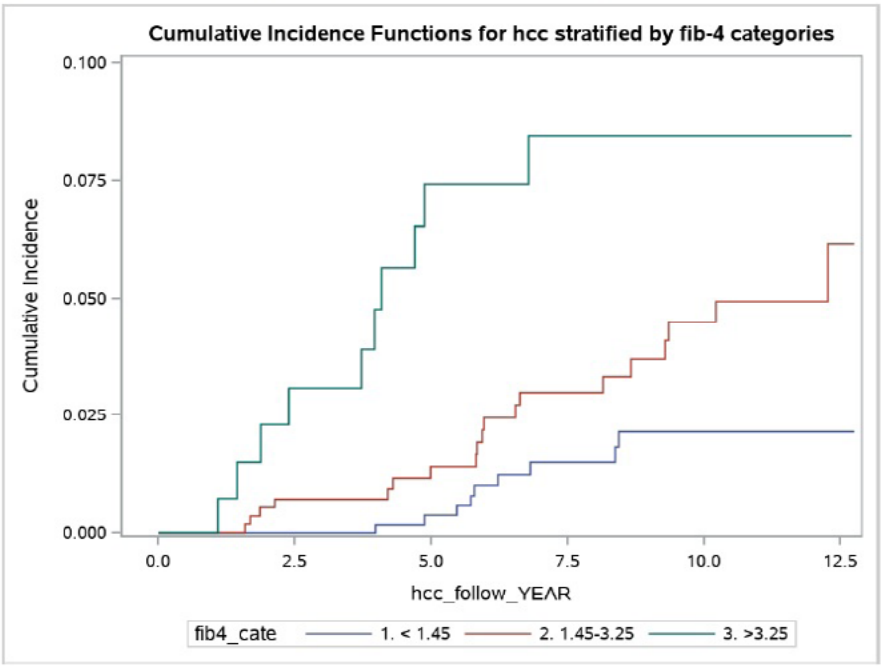
Methods: Adults with CHB were identified using the 2010-2022 Veterans Affairs (VA) Corporate Data Warehouse, which captures healthcare data on Veterans in the US. We excluded patients with concurrent HIV, Hepatitis C, or Hepatitis delta, as well as patients with cirrhosis or HCC at baseline or within 12 months of starting antiviral therapy. Cirrhosis and HCC were identified based on ICD-9/10 codes. Proportions of patients who developed HCC while on antiviral therapy were compared between groups using chi-square testing. Adjusted multivariable Cox proportional hazards competing risks models (death as censor) were utilized to evaluate for predictors of on-treatment risk of HCC.

Results: Among 2,510 non-cirrhotic CHB patients on antiviral therapy (94.2% men, 36.5% non-Hispanic white, 37.7% African American, 18.3% Asian, mean age 56.2 $\pm$ 13.4 years), 59.0% were on entecavir, 33.2% tenofovir disoproxil fumarate, and 7.8% tenofovir alafenamide. Over a median follow up of 6.3 years (IQR 3.5 – 10.0), 3.2% developed HCC. Compared to patients age 18-39 years, those age >60 years had higher rates of HCC (4.34% vs. 2.45%, p=0.02). Compared to patients with fibrosis-4 score (FIB-4)<1.45 at time of treatment initiation, those with FIB-4>3.25 had significantly higher rates of developing HCC (7.58% vs. 1.25%, p<0.001) (Figure). On multivariable regression, when compared to FIB-4 score < 1.45, CHB patients with FIB-4 > 3.25 had significantly higher on-treatment risk of HCC (HR 5.78, 95% CI 2.08-16.06, p<0.01). No significant differences in on-treatment risk of HCC were observed by race/ethnicity or age. When compared to patients on entecavir, no difference in risk of HCC was observed in those treated with tenofovir disoproxil fumarate (HR 1.12, 95% CI 0.56-2.23).

Conclusion: Among a large cohort of predominantly non-Asian patients with non-cirrhotic CHB, on-treatment HCC risk did not differ by antiviral therapy. While no sex-age-specific or race/ethnicity-specific differences in HCC risk were observed, patients with FIB-4 score>3.25 had significantly higher risk of on-treatment HCC compared to those with FIB-4<1.45. These data emphasize the importance of continued HCC surveillance despite being on treatment, especially when there is concern for significant hepatic fibrosis.

Image/Table:

Figure 1. Incidence of HCC among Non-Cirrhotic CHB Patients Stratified by FIB-4 Score at Baseline.



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O91

LONG TERM FOLLOW UP OUTCOME OF CHILDREN TREATED WITH PEGYLATED INTERFERON FOR HBEAG REACTIVE CHRONIC HEPATITIS B

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Objectives: We aim to evaluate the long term outcome of children with HBeAg reactive chronic Hepatitis B (CHB) treated with pegylated interferon (Peg-IFN) and to assess its effect on modification of natural course of disease in these children.

Methods: The cohort of HBeAg reactive children treated with sequential therapy - 8 weeks of nucleotide analogue (NA) followed by fixed duration (44 weeks) combination of NA and Peg-IFN were followed up every 6 monthly thereafter. HBe seroconversion was defined as HBeAg negative and anti-HBe reactive. HBs seroconversion was defined as HBsAg negative and anti-HBs reactive.

Results: A total of 32 children (Genotype D: 19; A: 6) with HBeAg reactive chronic Hepatitis B: 20 immunoactive (IA) and 12 immunotolerant (IT) received sequential combination therapy. The median follow-up period was 70 (Range: 42–96) months from last dose of Peg-IFN. A total of 8(25%) achieved HBe seroconversion during Peg-IFN therapy and another 8(25%) achieved HBe seroconversion at a median duration of 12 (Range: 6–62) months after stopping Peg-IFN. Transient HBe sero-reversion was seen in 1 child, 10 months after achieving HBe seroconversion. At a median FU of 58 months post completion of therapy, 16 children (50%) were HBeAg negative. HBs seroconversion was seen in 4 children during therapy and another 2 at 24 and 40 months after stopping Peg-IFN respectively [Table 1].

On subgroup analysis, 14/20 (70%) IA children were HBeAg negative at their latest FU, whereas 2/12 (16.67%) of IT children were HBeAg negative. 6/20 (30%) children in initial IA cohort were HBsAg negative at latest FU whereas 0/12 among IT group were HBsAg negative. Conclusion: There is sustained off treatment serological & virological response with use of Peg-IFN in IA phase of pediatric chronic Hepatitis B. 25% of children achieved HBe seroconversion after stopping Peg-IFN. HBe and HBs seroconversion occurred more frequently in those in IA phase and very rarely in those in IT phase.

Image/Table:

Table 1: Long term follow up results of HBeAg reactive children with chronic hepatitis B treated with Pegylated Interferon based combination therapy:

Group	HBe seroconversion		HBe sero-reversion	HBeAg negative at last FU	HBs seroconversion		HBs sero-reversion	HBsAg negative at last FU
	During ongoing Peg-IFN	After completing Peg-IFN			During ongoing Peg-IFN	After completing Peg-IFN		
Peg-IFN + NA (n = 32)	8 (25%)	8 (25%)	1/16 (6.3%)	16 (50%)	4 (12.5%)	4 (12.5%)	0	8 (25%)
IA group (n = 20)	8 (40%)	6 (30%)	1 (5%)	14 (70%)	4 (20%)	2 (10%)	0	6 (30%)
IT group (n = 12)	0	2 (16.7%)	0	2 (16.7%)	0	0	NA	0

IA: Immunoactive phase (HBeAg positive chronic hepatitis); IT: Immunotolerant phase (HBeAg positive hepatitis B infection); NA: Nucleos(t)ide Analogue; Peg-IFN: Pegylated Interferon

Disclosure of Interest: None Declared

O92

EFFECT OF ANTI-CD38 MONOCLONAL ANTIBODIES ON HEPATITIS C VIRUS REPLICATION IN CHRONICALLY INFECTED PATIENTS WITH MULTIPLE MYELOMA: A PROSPECTIVE SERIES

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Background: Daratumumab and isatuximab are anti-CD38 monoclonal antibodies (MoAbs) approved by the United States (US) Food and Drug Administration and European Medicines Agency for the treatment of patients with multiple myeloma (MM). Anti-CD38 MoAbs also target CD38-expressing T cells and natural killer cells. These agents have been associated with viral reactivation of Hepatitis B virus (HBV) and cytomegalovirus. However, data on the virologic changes of Hepatitis C virus (HCV) infection after anti-CD38 MoAbs are limited.

Purpose: To examine the effect of anti-CD38 MoAbs on HCV kinetics, we conducted this prospective study in chronically infected patients with MM receiving anti-CD38 MoAbs.

Method: Patients with chronic HCV infection and MM treated at MD Anderson Cancer Center, Houston, Texas, USA between January 4, 2013, and July 1, 2022, were enrolled in a prospective observational study. HCV-infected patients are defined as those with either active viremia or a history of HCV infection successfully treated (SVR). We analyzed the changes in HCV viremia in infected patients receiving anti-CD38 MoAbs. In patients with untreated HCV infection, serum HCV RNA levels are stable, varying only within 0.5 log IU/mL. HCV inhibition was defined as a decrease in HCV RNA level <1 log IU/mL from baseline following treatment with anti-CD38 MoAbs. HCV reactivation was defined as an increase in HCV RNA level ≥1 log IU/mL over baseline following treatment with anti-CD38 MoAbs.

Results: Of 37 HCV-infected patients enrolled, 6 received anti-CD38 MoAb therapy (daratumumab in all 6 cases). Most were male (4; 67%), were Black (3; 50%), did not have cirrhosis (5; 83%), and had HCV genotype 1 (6; 100%). Four patients (67%) were treated with direct-acting antiviral therapy before anti-CD38 MoAb therapy, and they all achieved sustained virologic response (SVR). None of these 4 patients experienced HCV relapse after receipt of daratumumab-containing therapy. HCV reactivation did not occur in the 2 patients (Figure 1A, Figure 1B) with active viremia during anti-CD38 MoAb therapy or even 6 months after its discontinuation.

Conclusion: These preliminary findings suggested that anti-CD38 MoAb therapy is not associated with enhanced HCV replication. Chronic HCV infection should not be considered a contraindication for anti-CD38 MoAb therapy. Our findings also suggest that the virologic cure (sustained virologic response) of HCV is not affected by anti-CD38 MoAbs.

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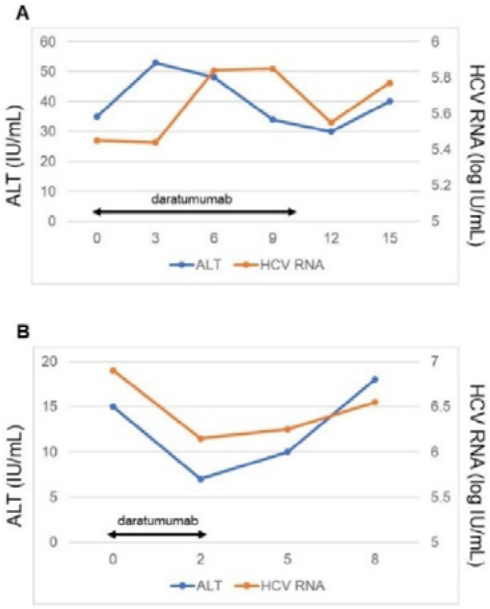

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LB/O93

DEPLETION OF DIPEPTIDYL PEPTIDASE 9 (DPP9) IN HEPATOCYTES INCREASES BECLIN-1 AND ACTIVATED CASPASE-1 PROTEIN LEVELS IN AN EXPERIMENTAL MODEL OF HEPATOCELLULAR CARCINOMA.

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Background and Aim: DPP9 is a ubiquitous intracellular peptidase that supresses NLRP1 inflammasome activation and BRCA2 activity. These actions of DPP9 suggest potential for this protease to influence tumourigenesis. Global DPP9 gene inactivation is lethal in mice and humans. Therefore, to study liver cancer generation, we produced mice in which DPP9 expression is knocked down only in liver epithelial cells. This was achieved by floxing exons 1 to 3 of DPP9 and crossing with an Albumin-Cre expressing mouse.

Results. This hepatocyte-specific DPP9 knockout mouse (Alb-DPP9-KO) was healthy at all ages. Alb-DPP9-KO mice and their littermate controls were treated with diethylnitrosamine (DEN) and thioacetamide (TAA) and given an atherogenic high fat diet (HFD) until they reached 28 weeks of age. The Alb-DPP9-KO mice had reduced liver mass and subcutaneous adipose tissue mass and had lower fasting plasma glucose. No differences were observed in the total number of macroscopic liver nodules, tumour burden, inflammation score or steatosis score between the two genotypes. However, the Alb-DPP9-KO mice had fewer small macroscopic liver nodules (<3 mm diameter) compared with littermate controls. Livers were assessed for immunological and autophagy markers. Alb-DPP9-KO mice had increased levels of active caspase-1 protein, indicative of increased inflammasome activity. Intrahepatic differential expression of the immune response genes *Nfkbib, Cxcl10 and Ccl5* was observed. However, there was no difference in the number of tumour infiltrating CD8+ T cells between genotypes. The Alb-DPP9-KO mice showed increased protein levels of Beclin1, an autophagy marker

Conclusion. Lifelong DPP9 depletion in hepatocytes led to reduced tumour sizes but not total tumour numbers at 28 weeks of age in this experimental model. Evidence for increased caspase-1 activation and autophagy regulation and a possible role in the regulation of energy metabolism was obtained in these mice. The latter result suggests that DPP9 might share with its sister protease DPP4 an ability to influence energy metabolism.

Disclosure of Interest: None Declared

LB/O94

MECHANISTIC PK/PD MODELING AND SIMULATION OF BEPIROVIRSEN PK, HBSAG AND ALT CHANGES FROM PHASE 2B STUDY TO INFORM PHASE 3 STUDY DESIGN AND DOSE SELECTION: B-CLEAR STUDY

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Background: Bepirovirsen (BPV; GSK3228836) reduced serum Hepatitis B surface antigen (HBsAg) in participants (pts) with chronic Hepatitis B infection in Phase 2 studies. Transient increases in alanine transaminase (ALT) were often observed after, or in parallel to, decreases in HBsAg.

A mechanistic pharmacokinetic/pharmacodynamic (PK/PD) model was developed to simultaneously capture the time course of HBsAg and ALT changes observed in BPV Phase 2 studies (Youssef A et al. Presented at EASL 2022 [abstract 3592). In this work, the model was used to simulate HBsAg responses to inform Phase 3 study design, dose regimen, and patient population selection.

Methods: The model was used to simulate BPV exposures and HBsAg levels for a range of dosing regimens (300 mg weekly and 300 mg weekly with dose reduction to 150 mg weekly), with and without loading doses in the first 2 weeks of treatment, and for dosing durations of 12 and 24 weeks. Simulations of end of treatment (EOT; Week 12 or 24) and end of study (EOS; 48 weeks post BPV treatment) responses (HBsAg <lower limit of detection [LLOD) were completed for different subpopulations based on significant covariates (eg, low baseline HBsAg [<3000 IU/mL). A sustained response HBsAg threshold of 0.000015 IU/mL reliably predicting EOS responses was identified, and used to simulate responses under potential Phase 3 study designs.

Results: Baseline HBsAg was a significant predictor of response to BPV treatment. In simulations, pts with low baseline HBsAg were more likely to achieve HBsAg <LLOD following administration of BPV compared with the overall population (range of predicted responses for pts with low baseline HBsAg: 34.8%–44.7% at EOT and 15.5%–19.2% at EOS; range of predicted responses for overall population: 23.3%–30.4% at EOT and 9.7%–12.3% at EOS) across different BPV dose regimens (Table). Similar response rates were predicted with and without loading doses. A higher proportion of pts were predicted to achieve a response with 24- versus 12-week BPV treatment (44.6% vs 34.8% at EOT and 19.1% vs 15.5% at EOS) in the low baseline HBsAg population (Table).

Conclusions: These modeling and simulation results support enrollment of pts with low baseline HBsAg in Phase 3 studies to maximize the benefit of BPV treatment. Simulation results will also be used to support BPV dose selection for the Phase 3 studies.

Table: Summary of simulation-based HBsAg response by dose regimen

			Participants with HBsAg response (%)	
Bepirovirsen dosing regimen	**Population**	**Outcome**	**EOT**	**EOS**
300 mg weekly x 24 weeks with loading dose on Day 4 and 11	Overall	HBsAg <LLOD	30.4	12.3
	Baseline HBsAg 35% <3000 IU/mL, 65% <1000 IU/mL*	HBsAg <LLOD	44.7	19.2
300 mg weekly x 24 weeks without loading dose	Overall	HBsAg <LLOD	30.3	12.2
	Baseline HBsAg 35% <3000 IU/mL, 65% <1000 IU/mL*	HBsAg <LLOD	44.6	19.1
300 mg weekly x 12 weeks, without loading dose	Overall	HBsAg <LLOD	23.3	9.7
	Baseline HBsAg 35% <3000 IU/mL, 65% <1000 IU/mL*	HBsAg <LLOD	34.8	15.5
300 mg weekly x 12 weeks, then 150 mg weekly x 12 weeks (without loading dose)	Overall	HBsAg <LLOD	26.1	11.0
	Baseline HBsAg 35% <3000 IU/mL, 65% <1000 IU/mL*	HBsAg <LLOD	39.3	17.5

*Phase 3 population simulated to include only patients with baseline HBsAg <3000 IU/mL, with 65% of them below 1000 IU/mL.

HBsAg LLOD = 0.05 IU/mL.

EOT, end of bepirovirsen treatment (Week 12 or Week 24); EOS, end of study (48 weeks post end of bepirovirsen treatment: Week 60 or Week 72); HBsAg, hepatitis B surface antigen; LLOD, lower limit of detection.

Disclosure of Interest: A. Youssef Shareholder of: GSK, Employee of: GSK, M. Ismail Conflict with: Clinical pharmacology and pharmacometrics consultant supporting EOP2 analysis, Employee of: Enhanced Pharmacodynamics, LLC, D. Mager Conflict with: Clinical pharmacology and pharmacometrics consultant supporting EOP2 analysis, Employee of: Enhanced Pharmacodynamics, LLC, A. Santulli Employee of: Enhanced Pharmacodynamics, LLC, M. Magee Shareholder of: GSK, Employee of: GSK, D. Theodore Shareholder of: GSK, Employee of: GSK, R. Elston Shareholder of: GSK, Employee of: GSK, M. Paff Shareholder of: GSK, Employee of: GSK, A. Nader Shareholder of: GSK, Employee of: GSK

LB/O95

PRECLINICAL ANTIVIRAL PROFILING OF AB-161, AN ORAL HBV INHIBITOR THAT DESTABILIZES HBV RNA AND SUPPRESSES HBSAG

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Background: One obstacle to a functional cure of chronic Hepatitis B (CHB) is the abundance of circulating surface antigen (HBsAg), which is produced from both covalently closed circular DNA (cccDNA) and integrated HBV DNA, and which is believed to play a role in maintaining HBV persistence. HBV RNA destabilizers target the non-canonical poly(A) RNA polymerase associated domain containing proteins 5 and 7 (PAPD5 and PAPD7), which are components of a virus-host complex essential for maintaining HBV RNA stability. Inhibition of PAPD5 and PAPD7 leads to degradation of HBV RNA and suppression of viral protein production including HBsAg. Since HBV replicates within hepatocytes, a liver-centric HBV RNA destabilizer would be expected to not only suppress viral replication but also mitigate potential toxicity associated with systemic exposures. Herein we report the preclinical profiling of AB-161, a potent small-molecule HBV RNA destabilizer.

Methods: Anti-HBV activity was assessed in HepG2.2.15 (HBV replication and HBsAg from stably transfected HBV genome) and PLC/PRF/5 (HBsAg from integrated HBV with a partial genome) cells, and in cells permissive to HBV infection including HepG2-NTCP and primary human hepatocytes (cccDNA-dependent replication and HBsAg production). Mechanism of action studies were conducted by analyzing intracellular viral markers and by reverse genetics using HBV constructs containing wild-type post-transcriptional regulatory element (PRE) or a partially deleted sequence within the PRE. AB-161 inhibition of PAPD5 and PAPD7 was determined using enzymatic assays. *In vivo* efficacy and pharmacokinetic and pharmacodynamic (PK/PD) correlation were conducted in mice infected with an adeno-associated virus (AAV) vector delivering an HBV genome.

Results: AB-161 is a potent HBV RNA destabilizer with differentiated anti-HBV effects compared to other classes of HBV inhibitors, including nucleos(t)ide analogs and capsid assembly modulators (CAM). AB-161 shows broad genotype coverage and reduces HBsAg with EC_{50} of 2.3 to 25.3 nM in HepG2.2.15, PLC/PRF/5, and HBV infected HepG2-NTCP and primary human hepatocytes. AB-161 promotes HBV RNA destabilization by inhibiting the catalytic activity of PAPD5 and PAPD7 (IC_{50} = 0.85 and 1.1 mM, respectively). Degradation of pgRNA becomes more pronounced when combined with an HBV CAM. In AAV-HBV infected mice, AB-161 reduces circulating HBsAg levels in a dose-dependent manner. PK/PD assessment reveals that reduction of HBsAg correlates with the liver concentration of AB-161.

Conclusion: AB-161 shows robust anti-HBV activity including suppression of HBV RNA and HBsAg production *in vitro* and *in vivo*. Results from these studies suggest that AB-161 could be an important component in combination therapy that may contribute to improving the functional cure rates in patients with CHB. AB-161 is currently being progressed into Phase 1 clinical studies.

Disclosure of Interest: None Declared

LB/O96

PHARMACOKINETICS AND SAFETY OF SINGLE-DOSE BEPIROVIRSEN IN ADULTS WITH MODERATE HEPATIC IMPAIRMENT AND HEALTHY MATCHED CONTROLS (B-ASSURED)

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Background: Bepirovirsen (BPV) is an anti-sense oligonucleotide (ASO) being studied for the treatment of chronic Hepatitis B (CHB). Patients with CHB are at an increased risk for progressive liver disease which may lead to cirrhosis, liver failure, and hepatocellular carcinoma. This phase 1, multicenter, open-label study was conducted to assess the effect of moderate hepatic impairment (HI) on the pharmacokinetics (PK) and safety of BPV.

Methods: The study design planned for enrollment in two parts: Part 1 in participants with moderate HI (Child-Pugh B; n=12) and Part 2 in mild HI. Part 2 was planned to start enrollment if a difference in PK was observed between participants with moderate HI and matched healthy controls; defined as the geometric mean ratio (GMR) of total plasma AUC (AUC0-•) or Cmax outside the prespecified clinical relevance range of 0.5 to 1.5. Participants were administered a single dose of 300 mg BPV subcutaneously and followed up to 50 days post-dose. PK parameters were estimated using noncompartmental analysis.

Results: The GMRs and related 90% confidence intervals of both AUC0-• and Cmax between participants with moderate HI and healthy controls were within the defined range (0.69 [0.59, 0.82 and 0.67 [0.52, 0.85, respectively). No clinically relevant differences were observed in geometric mean PK parameters between moderate HI and healthy participants, including AUC0-• (75.07 and 108.9 h*µg/mL), Cmax (6.57 and 9.83 µg/mL), $t_{1/2}$ (232.2 and 204.9 h), and apparent clearance (4.00 and 2.75 L/h). There were no serious adverse events reported and there were no emerging safety concerns.

Conclusions: Results from this study show no clinically relevant effect of moderate HI on BPV PK or safety. Mild hepatic impairment was not studied based on predefined criteria.

Funding: GSK (study 205871).

This abstract was previously presented as poster at ASCPT (American Society for Clinical Pharmacology and Therapeutics - 124th Annual Meeting, Mar 22-24, 2023).

Disclosure of Interest: K. Han Shareholder of: GSK, Employee of: GSK, N. Noormohamed Shareholder of: GSK, Employee of: GSK, T. Lukic Shareholder of: GSK, Employee of: GSK, T. Marbury Shareholder of: Orlando Clinical Research Center , Employee of: Orlando Clinical Research Center , E. Lawitz Conflict with: 89Bio Inc., AbbVie, Akero Therapeutics, Allergan, Alnylam Pharmaceuticals Inc., Amgen, Ascelia Pharma, Assemblybio, Astrazeneca, Axcella Health, Biocryst Pharmaceuticals, Bird Rock Bio Inc., Boehringer Ingelheim, Bristol-Myers Squibb, Conatus Pharmaceuticals, Cymabay Therapeutics, CytoDyn, DSM, Durect Corporation, Eli Lilly and Company, Enanta Pharmaceuticals, Enyo Pharma, Exalenz Bioscience, Galectin Therapeutics,

Galmed Pharmaceuticals, Genfit, Genentech, Gilead Sciences, GSK, Hanmi Pharmaceuticals, Hightide Biopharma, Intercept Pharmaceuticals, Inventiva, Janssen Pharmaceuticals, Laboratory for Advanced Medicine, Loxo Oncology, Madrigal Pharmaceuticals, Merck & Co., Metacrine, NGM Biopharmaceuticals Inc., Northsea Therapeutics, Novartis, Novo Nordisk Inc., Pfizer, Poxel Co., Roche, Sagimet Biosciences, Synlogic Therapeutics, Terns Pharmaceuticals, Viking Therapeutics, Zydus Pharmaceuticals, Paid Instructor of: Abbvie, Gilead Sciences, Intercept, An advisor for: Akero, Boehringer Ingelheim, BMS, Intercept, Novo Nordisk, Metacrine, Sagimet, Terns, H. Prescott Conflict with: FSP work with GSK, M. Magee Shareholder of: GSK, Employee of: GSK, R. Elston Shareholder of: GSK, Employee of: GSK, A. Nader Shareholder of: GSK, Employee of: GSK

LB/O97

EFFICACY AND SAFETY OF TALEN®-MEDIATED GENOME EDITING OF THE HEPATITIS B VIRUS CCCDNA AND INTEGRATED DNA IN VIVO

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Abstract Content: There are approximately 296 million individuals chronically infected with HBV worldwide with an increased risk of progressing to liver fibrosis, cirrhosis and/or hepatocellular carcinoma (HCC). Currently approved treatment options result in low functional cure rates, primarily because they are unable to target and eliminate the HBV covalently closed circular DNA (cccDNA) form or integrated HBV DNA sequences in infected hepatocytes. New treatment options currently in development do not directly target these aspects of the HBV biology. Thus, there remains a strong need for innovative mechanisms of action that directly target and silence HBV DNA sequences.

We have developed LUNAR®HBV, a genome editing therapeutic consisting of a pair of transcription activator-like effector nucleases (TALEN®s), delivered as mRNA encapsulated in our proprietary liver-directed LUNAR® lipid nanoparticles. TALEN®s translated in the liver are designed to specifically target and irreversibly inactivate both cccDNA and integrated HBV DNA by inducing targeted mutations, typically frameshift deletions.

In vitro assessment of HBV TALEN mRNA activity and specificity in multiple cell types demonstrated a strong reduction of HBsAg production with concomitant deletions in the HBV DNA targeted sequence. Using various HBV mouse models, LUNAR® HBV showed significant efficacy and targeting of both integrated and non-integrated HBV DNA in the liver of infected mice. LUNAR® HBV achieved greater than a two-log reduction of both HBV DNA and HBsAg levels in the plasma. Furthermore, these reductions directly correlated with the levels of edited HBV DNA observed in the livers of treated mice.

The specificity of LUNAR® HBV treatment was thoroughly evaluated using bioinformatic prediction tools, cell-based assays, and in vivo studies and exhibited a low off-target risk with a broad safety margin. The risk of inducing translocations across HBV DNA integration sites is being evaluated in vitro and in vivo and will be discussed.

Tolerability and biodistribution studies indicated that LUNAR® HBV was well tolerated and editing activity was only detected in the liver.

LUNAR®HBV is an efficient and highly specific genome editing approach with the potential to inactivate and reduce levels of both cccDNA and HBsAg from integrated HBV DNA. Furthermore, LUNAR®HBV was well tolerated in treated animals and showed a low potential risk of off-target gene editing activity in various pre-clinical models.

Disclosure of Interest: R. Diaz Trelles Employee of: Full time employee at Arcturus Therapeutics, N. El-Mecharrafie Employee of: Full time employee Arcturus Therapeutics, R. Yelin Employee of: Full time employee Arcturus Therapeutics, Y. Pei Employee of: Full time employee Arcturus Therapeutics, S. Sullivan Employee of: Full time employee Arcturus Therapeutics, A. Dukanovic Employee of: Full time employee, Q. Ruan Employee of: Full time employee, P. Limphong Employee of: full time employee Arcturus Therapeutics, L. Quirino Employee of: Full time employee Arcturus Therapeutics, G. Acharya Employee of: Full time employee Arcturus Therapeutics, S. Boheme Employee of: Full time employee Arcturus Therapeutics, S. Parker Employee of: Full time employee Arcturus Therapeutics, P. Chivukula Employee of: Full time employee Arcturus Therapeutics

LB/O98

BONE MARROW MONOCYTES SUSTAIN NK CELL DEVELOPMENT AND SURVIVAL DURING NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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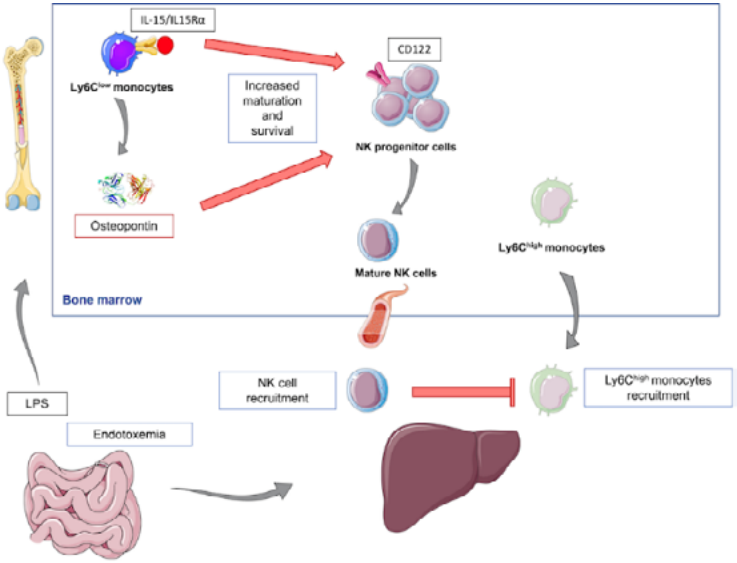
Abstract Content: In western countries where the unbalanced diets are causing a rise in obesity and metabolic disease incidence, the prevalence of non-alcoholic steatoHepatitis (NASH) is now skyrocketing. Yet, the pathogenesis of the different stages is still not fully known highlighting the need to further understand the cellular and molecular events underlying NASH evolution. Natural Killer (NK) cells are the predominant lymphocyte population in the liver. At the onset of NASH, an accumulation of activated NK cells has been observed in the liver in parallel with inflammatory monocyte recruitment and an increase in systemic inflammation.

Using *in vivo* and *in vitro* experiments, we show that NK cells are recruited to the liver where they restrict Ly6C^{high} monocyte recruitment and polarize them towards an M1 phenotype. We demonstrate that the NK cell recruitment is sustained by an IL-15-dependent increased NK cell-poiesis in the bone marrow. NK precursors are specifically stimulated through medullary monocytes that trans-present IL-15 and secrete osteopontin, a biomarker for patients with NASH. This cellular dialogue leads to increased survival and maturation of NK precursors. Endotoxemia is involved in this process and is responsible for the increase in osteopontin production by bone marrow monocytes.

We propose a tripartite gut-liver-bone marrow axis regulating the immune population dynamics and effector functions during liver inflammation.

Image/Table:



Disclosure of Interest: None Declared

LB/O99

48 WEEKS OF AB-729 + NUCLEOS(T)IDE ANALOGUE (NA) THERAPY RESULTS IN PROFOUND, SUSTAINED HBSAG DECLINES IN BOTH HBEAG+ AND HBEAG- SUBJECTS WHICH ARE MAINTAINED IN HBEAG- SUBJECTS WHO HAVE DISCONTINUED ALL THERAPY

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Background: AB-729 is a GalNAc-conjugated single trigger siRNA therapeutic that targets all HBV RNA transcripts, resulting in suppression of viral replication and all viral antigens. AB-729 is currently in Phase 2 clinical development in combination with other agents for the treatment of chronic Hepatitis B (CHB). Study AB-729-001 assessed different regimens of AB-729 for 48 weeks (W) in NA suppressed subjects. Here we report extended post-treatment follow-up (FU) data for all subjects from the dedicated HBeAg+ Cohort K and FU data up to 1 year post NA discontinuation (d/c) for the 9 HBeAg- subjects from other Cohorts who elected to stop NA therapy.

Methods: Cohort K was a dedicated HBeAg+ cohort (N=7) dosed with AB-729 90mg every 8W in combination with ongoing NA therapy. All subjects in the AB-729-001 study who received AB-729 for 48W were assessed for eligibility for NA d/c (ALT <2×ULN, HBeAg-, HBV DNA undetectable, and HBsAg <100 IU/mL on 2 consecutive visits) at least 24W after their last dose of AB-729. Safety and viral markers were assessed every 2-12W.

Results: In Cohort K, 5 of 7 subjects completed 48W of treatment (2 missed the last dose of AB-729 at W40), and all have completed 36W of a planned 48W of follow-up on ongoing NA therapy. The mean (SE) $\log_{10}$ change from baseline (N=5) in HBsAg was -2.57 (0.61) IU/mL at W48 and -2.14 (0.74) IU/mL at FU W36, with 2 subjects achieving HBsAg below the limit of quantitation (BLQ, <0.07 IU/mL). One has had sustained HBsAg BLQ from treatment W44 through FU W36 (baseline HBsAg 600.1 IU/mL) while the other has had HBsAg BLQ intermittently from W20 through the FU period (baseline HBsAg 545.2 IU/mL). Mean (SE) HBeAg declined from 19.64 (13.3) IU/mL to 1.73 (1.05) IU/mL by W48, with 2 subjects reaching HBeAg BLQ (<0.11 IU/mL). No subjects met NA d/c criteria within the protocol-defined window.

The 9 subjects from Cohorts E, F, G, and I who elected to stop NAs have completed at least 40W of FU off all HBV therapy. Key HBV DNA and HBsAg values are shown in the Table. Two subjects restarted NA therapy, one per Investigator request when HBV DNA reached 4670 IU/mL, and one who met the protocol defined HBV DNA restart criterion of >20,000 IU/mL; both subjects were asymptomatic and neither had ALT flares. The remaining 7 subjects continue to maintain low HBV DNA levels off all therapy, and HBsAg levels remain mean (SE) -1.55 (0.10) $\log_{10}$ below baseline levels up to 1½ years after the last dose of AB-729.

Conclusion: AB-729 treatment leads to marked HBsAg and HBeAg declines in HBeAg+ subjects, with 2 subjects each achieving HBsAg and HBeAg BLQ. NA d/c after NA+AB-729 treatment in

HBeAg- subjects who achieve HBsAg <100 IU/mL is well-tolerated and results in sustained low HBV DNA in 78% (7/9) of subjects and low HBsAg levels in all subjects up to a year off all therapy, suggestive of new viral set points via immune control.

Image/Table:

Table:

Timepoint	HBV parameter (IU/mL)	Pre-Study HBV DNA- (NA Suppressed)					Pre-Study HBV DNA+			
		Subject 46	Subject 52	Subject 51	Subject 53†	Subject 61	Subject 56	Subject 59	Subject 58*	Subject 60
Pre-study baseline	HBV DNA	TND	TND	TND	TND	TND	212,490	560	5840	9990
Pre-NA DC	HBV DNA	<LLOQ	<LLOQ	TND	TND	<LLOQ	<LLOQ	TND	<LLOQ	<LLOQ
NA DC FU W12	HBV DNA	10	30	<LLOQ	140	<LLOQ	4100	TND	970	<LLOQ
NA DC FU W24	HBV DNA	<LLOQ	50	80	20*	90	60	100	1590	10
NA DC FU W40	HBV DNA	60	60	110	TND*	810	510		190*	
NA DC FU W52	HBV DNA	50	80	390	-	90			-	
Pre-study baseline	HBsAg	1392	1888	6765	2368	2021	277.3	1338	1397	1128
Pre-NA DC	HBsAg	10.53	3.95	64.9	69.06	3.99	8.4	17.31	31.09	1.24
NA DC FU W12	HBsAg	33.12	6.61	113.5	128.7	7.16	8.56	6.78	65.06	5.45
NA DC FU W24	HBsAg	41.22	14.43	161.2	180.1*	29.79	4.53	42.33	77.26	20.34
NA DC FU W40	HBsAg	84.68	32.13	139.2	206.2*	73.36	6.58		181.1*	
NA DC FU W52	HBsAg	117.8	125.3	156.3	-	63.65			-	

HBV DNA lower limit of quantitation (LLOQ) = 10 IU/mL (Abbott Realtime HBV viral load assay); HBsAg LLOQ = 0.07 IU/mL (Roche Elecsys HBsAg II quant II); TND = target not detected; † subject restarted NA therapy; *value is post-NA restart.

Disclosure of Interest: M.-F. Yuen Grant / Research support from: Assembly Biosciences, Arrowhead Pharmaceuticals, Bristol Myers Squibb, Fujirebio Incorporation, Gilead Sciences, Immuncore, Merck Sharp and Dohme, Sysmex Corporation, and Roche, Conflict with: AbbVie, AligosTherapeutics, AntiosTherapeutics, Arbutus Biopharma, Arrowhead Pharmaceuticals, Assembly Biosciences, Bristol Myers Squibb, Clear B Therapeutics, DicernaPharmaceuticals, Finch Therapeutics, Fujirebio Incorporation, GSK, Gilead Sciences, Immunocore, Janssen, Merck Sharp and Dohme, Roche, Silverback Therapeutics, Sysmex Corporation, and VirBiotechnology, Speakers bureau of: AbbVie, DicernaPharmaceuticals, Fujirebio Incorporation, Gilead Sciences, Merck Sharp and Dohme, Roche, and Sysmex Corporation, J. Holmes: None Declared, S. Strasser Conflict with: Gilead, Speakers bureau of: Gilead, A. Leerapun: None Declared, W. Sukeepaisarnjaroen: None Declared, P. Tangkijvanich: None Declared, V. Sharma Shareholder of: Arbutus Biopharma, Employee of: Arbutus Biopharma, E. Medvedeva Shareholder of: Arbutus Biopharma, Employee of: Arbutus Biopharma, E. Thi Shareholder of: Arbutus Biopharma, Employee of: Arbutus Biopharma, G. Picchio Shareholder of: Arbutus Biopharma, Employee of: former employee of Arbutus Biopharma, T. Eley Shareholder of: Arbutus Biopharma, Employee of: Arbutus Biopharma, K. Sims Shareholder of: Arbutus Biopharma, Employee of: Arbutus Biopharma

LB/O100

ARE HEPATITIS C VIRUS CORE AND NS5A POLYAMOROUS? HOST INTERACTING PARTNERS IDENTIFIED IN AN INFECTION SYSTEM

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Background: Hepatitis C virus (HCV)-induced pathology can be driven both by direct and indirect mechanisms. The direct mechanisms are thought to be mainly mediated by two viral proteins, the capsid protein or Core and the nonstructural protein 5A (NS5A), which have been involved in the deregulation of several host pathways. However, this has mainly been studied in systems in which an isolated HCV protein was transiently over-expressed, and/or in non-hepatic cells.

Purpose: Our aim was to identify HCV Core and NS5A cellular interacting partners during HCV infection, that would be essential to the virus life cycle and/or linked to HCV-induced pathobiology.

Methods: A panel of tagged HCV Core or NS5A recombinant viruses was generated within the backbone of a JFH1-derived, highly cell culture-adapted strain. A twin strep tag (ST) was fused in frame for protein complex purification purposes, near the amino-terminus of Core or at either of two positions within the carboxy-terminal segment of NS5A, without significantly impacting viral replication and morphogenesis. Protein complexes were affinity-purified from three or five infection replicates in human hepatocarcinoma Huh-7.5 cells using magnetic streptactin beads. Interacting partners were identified by liquid nano-chromatography coupled to tandem mass spectrometry (Nano-LC-MS/MS). To discriminate strong protein interactions, we developed a novel scoring algorithm, incorporating statistical analyses of ST-derived hits with respect to non-binding V5-tagged controls, the Molecular Interaction Search Tool (MiST) and the Significance Analysis of INTeractome (SAINT) scores of the Nano-LC-MS/MS data.

Results: We identified 134 highly significant interacting partners of Core and 527 of NS5A, including some common hits. Using the CytoScape and STRING tools, pathways enriched within the groups of interacting partners were identified. For Core, the highest scored pathways were involved in the regulation of host transcription and gene expression, while NS5A partners mainly belong to intracellular transport, as well as metabolic processes, notably the TCA cycle and oxidative phosphorylation. In addition, we were able to identify domains of interaction of previously described NS5A cellular partners based on differential retrieval with NS5A fused to ST at the two different insertion positions.

Conclusion: In a highly relevant infection system, we found that Core is likely to be directly responsible for deregulation of host transcriptome. The predominant NS5A interacting partners suggest that this viral protein may contribute to the progression of HCV-induced liver damage by alterations in the host metabolism and/or intracellular transport processes. As these processes are essential to the virus life cycle, the functional significance of selected, previously unreported NS5A interactors is now being examined.

Disclosure of Interest: None Declared

LB/O101

NO RESISTANCE DETECTED TO BULEVIRTIDE MONOTHERAPY IN PARTICIPANTS WITH CHRONIC HEPATITIS D THROUGH 24 WEEKS OF TREATMENT FROM PHASE II AND PHASE III CLINICAL TRIALS

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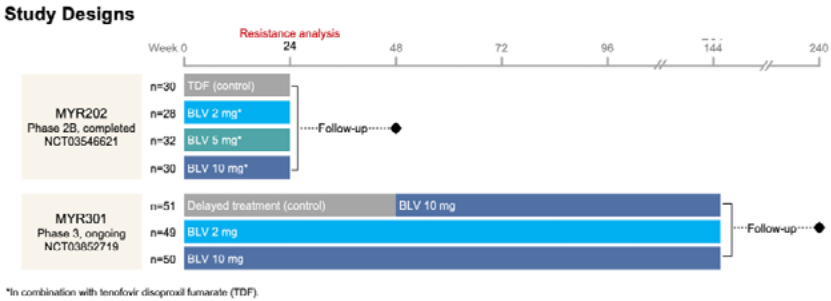
Background and Aims: Bulevirtide (BLV) is an entry inhibitor for HDV and HBV inhibiting the interaction between the HBV preS1 domain and the sodium taurocholate cotransporting polypeptide (NTCP) receptor on hepatocytes. BLV monotherapy has led to a substantial reduction of HDV RNA in phase II and phase III clinical trials. We report findings from a comprehensive virologic resistance analysis of patients with chronic Hepatitis D treated with BLV monotherapy at doses of 2mg, 5mg, or 10mg subcutaneously once daily for 24 weeks enrolled in phase 2 (MYR202, NCT03546621) and phase 3 studies (MYR301 NCT03852719).

Methods: Resistance analysis was performed for participants who experienced virologic non-response (NR) to BLV, defined as a decline in HDV RNA <1 $\log_{10}$ IU/ml from baseline (BL) at week 24 or virologic breakthrough (VB), defined as two consecutive increases in HDV RNA of ≥1 $\log_{10}$ IU/mL from nadir or two consecutive HDV RNA values ≥LOD if previously <LOD. Virologic partial response and virologic response were defined as HDV RNA decline ≥1 but <2 $\log_{10}$ IU/mL and decline ≥2 $\log_{10}$ IU/mL or HDV RNA <LOD at Week 24 respectively. The resistance analysis included deep sequencing of the HBV PreS1 BLV region and HDV HDAg region. Additionally, *in vitro* phenotypic testing was performed for clinical isolates at baseline and Week 24 for patients with NR and those with VB. For analysis control, sequencing and/or phenotypic analyses were performed for all available BL samples in the two studies.

Results: The resistance analysis was performed for 20 patients with NR and one participant with VB representing 11/77 (14%), 8/32 (25%), and 2/80 (2.5%) participants receiving BLV daily at 2mg, 5mg, and 10mg groups, respectively. These patients had no amino acid substitutions in the HBV PreS1 BLV region or HDV HDAg associated with resistance to BLV, neither at BL nor at week 24. Additionally, the detected amino acid substitutions were also present in patients experiencing virologic response and clinical isolates with these amino acid substitutions remained sensitive to BLV *in vitro* In the *in vitro* phenotypic analysis, we found no difference between the median EC_{50} values of BLV from 116 BL samples patients with NR (EC_{50} = 0.41 nM), partial response (EC_{50} = 0.41 nM) and virologic response (EC_{50} = 0.35 nM) regardless of the presence of HBV and HDV polymorphisms.

Conclusion: To our knowledge, this is the largest analysis to date showing no genotypic and phenotypic resistance to BLV monotherapy with 2 mg, 5 mg, and 10 mg in patients after 24 weeks of treatment.

Image/Table:



Disclosure of Interest: None Declared

LB/O102

UNDERSTANDING HEPATITIS C REINFECTION RATES AND FACTORS ASSOCIATED WITH HCV INFECTION IN NEW JERSEY, USA

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Introduction: Hepatitis C reinfection rates vary from different studies, obvious factors would include active drug use in a setting where community viral load of Hepatitis C is elevated. North Jersey Community Research Initiative (NJCRI) was interested in studying the widespread substance use and Hepatitis C reinfections in New Jersey, which effects the states HCV elimination efforts. By utilizing NJCRI's Mobile Hepatitis C Clinic, we travel to a variety of substance use disorder treatment facilities to bring the services to the patients. We study, screen, and treat those that have new infection, reinfections and those that never finished their treatments. This model reduces treatment barriers all throughout New Jersey.

Method: An observational study of Hepatitis C care and treatment across the state of New Jersey with looking at specific outcomes related to the number of viremic individuals at the end of the study and the number of those that had re-infection. The study duration was from 01/06/2022-1/27/2023. We parked our Mobile Hepatitis C Clinic in the proximity of a facility on an as needs basis by request of the facilities and added to our monthly Hepatitis C mobile clinic schedule. Clients were tested and blood was drawn on site, a week later they were invited to a telehealth visit with the healthcare provider who made assessment for therapy and sent their prescription to a specialty pharmacy, who in turn reached out to the clients and delivered their medications usually within one week of the telehealth visit. We defined re-infection as definite in a viremic patient with documented SVR in the past, or a patient with a new Hepatitis genotype and possible in a patient who was treated in the past with no documented SVR.

Results: Mean age of clients treated is 44 yrs of age (min, 22; max, 73). Six-hundred thirty-two clients were tested and treated for Hepatitis C viremia during the study period at 40 treatment facilities. Treatment completion rates are marked at 89% of 540, and those loss to follow up treatment are 11%. While the number among those reinfected with Hepatitis C viremia is approximately 3%, and treatment failure rates is slightly less 2%.

Conclusion: Our study supports the concept of mobile Hepatitis C treatment in order to prevent reinfection by bringing the services to the patients in a trusted community-based setting improved delivery of care and treatment and lowered reinfections, which supports the HCV state elimination efforts.

Disclosure of Interest: None Declared

LB/O103

TREATMENT FOR >12 WEEKS WITH THE CAPSID ASSEMBLY MODULATOR (CAM) ALG-000184 AND ENTECAVIR (ETV) DOSE DEPENDENTLY REDUCES HBSAG IN HBEAG+ SUBJECTS WITH CHRONIC HEPATITIS B (CHB)

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Background/Aims: Evaluate the safety and antiviral activity of dosing with ETV+ALG-000184, a prodrug of the CAM ALG-001075.

Methods: ALG-000184-201 is an ongoing multi-part, multi-country clinical trial (NCT04536337). Two cohorts are currently evaluating daily oral doses of ETV with 100 mg or 300 mg ALG-000184, respectively, for 48 weeks in untreated HBeAg+ CHB subjects. Described here are available data for subjects in these 2 cohorts that have dosed with the combination for >12 weeks.

Results: Among the 11 and 15 subjects enrolled in the 100 mg and 300 mg ALG-000184+ETV cohorts, 4 and 6, respectively, have dosed for >12-≤24 weeks. Both doses have been well tolerated: no serious adverse events (AEs) or premature discontinuations due to an AE have been reported. No AEs, laboratories, ECGs, or vital signs have been considered concerning to the study's safety review committee. Among the 4 and 6 subjects dosed >12 weeks, subjects have experienced multi-log maximum declines of HBV DNA (5.9-6.6 and 5.0-6.8 log10 IU/mL, respectively) and RNA (3.6-4.2 and 2.1-5.6 log10 copies/mL, respectively). Additionally, 4 and 4 of these subjects experienced HBsAg declines of ≥0.3 and ≥0.8 log10 IU/mL with maximum declines of 0.7 and 1.5 log10 IU/mL for the 100 mg and 300 mg cohorts, respectively.

Conclusions: In untreated HBeAg+ CHB subjects, dosing for >12 weeks with 100 or 300 mg ALG-000184+ETV was safe and resulted in substantial, dose-dependent reductions in antiviral markers, including HBsAg. Continued dosing to determine the longer term safety and antiviral activity of ALG-000184+ETV is warranted.

LB/O104

TOWARDS THE STRUCTURAL CHARACTERIZATION OF THE HEPATITIS DELTA VIRUS RIBONUCLEOPROTEIN COMPLEX BY NMR

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Abstract Content: Hepatitis D virus (HDV) is a defective, smallest RNA-negative virus that relies on co-infection with the Hepatitis B virus (HBV) to complete its replication cycle. The ribonucleoprotein complex (RNP) which constitutes the virus is composed of a single-stranded circular RNA with 1,678 nucleotides and the small and large delta-antigen isoforms (S-HDAg and L-HDAg). The structure of the RNP is yet to be determined. Here we report the initial steps towards such an analysis using wheat germ cell-free protein synthesis (WG-CFPS) combined with solid-state NMR (ssNMR) and solution-state NMR spectroscopy.

We synthesized using WG-CFPS both full-length S-HDAg and L-HDAg, as well as two subdomains of S-HDAg, corresponding to the oligomerization and RNA binding domains, and named $S^{1\text{-}60}$ and $S^{\Delta 60}$, respectively, in milligram amounts compatible with structural studies. On one hand, S- and L-HDAg were isolated on a density gradient and sedimented together for analysis by ssNMR. Both isoforms formed a complex with RNA as shown by ^{31}P spectra. Most of the signals of S- and L-HDAg are similar in the rigid and flexible parts of 2D ssNMR spectra. On the other hand, while $S^{1\text{-}60}$ is completely insoluble and therefore also analyzed by ssNMR, $S^{\Delta 60}$ is fully soluble and could be analyzed by solution NMR. Here, we experimentally determined the NMR structure of $S^{\Delta 60}$. We find $S^{\Delta 60}$ contains two intrinsically disordered protein segments separated by a helix-turn-helix motif spanning residues 96-142. This structured domain comprises parts of the two arginine-rich motifs (ARMs) of the protein. We show that the domain binds to different types of RNAs and that the residues involved in the binding are positioned around the start and end of the motifs. Our data allow to gain structural information about S-HDAg and L-HDAg in the context of the RNP, and about their interaction with nucleic acids.

Disclosure of Interest: None Declared

LB/O105

EXTENDED FOLLOW-UP IN THE REP 301 AND REP 401 STUDIES DEMONSTRATES DURABLE CLINICAL BENEFIT FROM NAP THERAPY

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Introduction: Nucleic acid polymers (NAPs) block the assembly of subviral particles in HBV infection and also inhibit viral replication and HDV envelopment in HBV / HDV co-infection. Previous studies combining NAPs with TDF and or pegIFN resulted in high rates of functional cure of HBV and HDV infection. These clinical endpoints have shown to be durable in follow-up in these previous studies ranging from 48 weeks(REP 401 study), 2.5 years (REP 102 study) to 3.5 years (REP 301 study). Recent follow-up visits of available participants in the REP 301 and REP 401 studies allowed evaluation of longer-term safety and antiviral responses with NAP-based combination therapy at 7.5 years and 5.5 years respectively.

Methods: All REP 301 and REP 401 participants were contacted. Follow-up visits for patients still residing in Moldova were conducted at the Toma Ciorba Hospital (Chisinau, Moldova) from December 2022 – Jan 2023 and included a liver ultrasound, fibroscan and a complete virological workup conducted on frozen serum at the Institute for Virology, University Hospital Essen (Essen, Germany) using Abbot Architect® qHBsAg and anti-HBs and Abbot Realtime® HBV DNA. HDV RNA was measured via Robogene 2.0 using the Instant Virus RNA/DNA extraction kit. These follow[1up visits constituted an average of 7.5 years of follow-up for REP 301 participants and 5.5 years of follow-up for REP 401 participants.

Results:A subset of participants was available for follow-up visits: 10/11 participants completing therapy in the REP 301 study and 21/40 participants completing therapy in the REP 401 study. Ultrasound examination of the liver did not detect any changes from baseline or development of HCC. Median liver stiffness continued to gradually decline in a majority of patients.

In the REP 301 study, functional cure of HDV achieved in 6 available participants at 3.5 years follow-up was maintained in all 6 participants, with functional cure of HBV maintained in 4 of these participants and partial cure maintained in the other two participants.

In the REP 401 study, the functional cure achieved in 8 available participants at 48 weeks follow-up was maintained in 6 participants, with transition to partial cure in the remaining two patients (HBsAg 0.68 and 1.07 IU/mL and HBV DNA 18 and < 10 IU/mL, respectively). Partial cure achieved in 9 available participants at 48 weeks follow-up transitioned to functional cure in 4 participants, was maintained in 4 participants and transitioned to formal rebound (HBV DNA 2825 IU/mL, normal ALT) in 1 participant.

Conclusions: NAPs are not associated with toxicity or liver complications atier completion of therapy. The immune control achieved (functional cure and partial cure of HBV and / or HDV) is durable for at least 7.5 years and appears to gradually improve in some patients.

Disclosure of Interest: A. Vaillant Employee of: Replicor Inc., Shareholder of: Replicor Inc., M. Bazinet Employee of: Replicor Inc., Shareholder of: Replicor Inc., V. Pantea: None Declared, G. Placinta: None Declared, L. Cojuhari: None Declared, V. Cebotarescu: None Declared, L. Larovoi: None Declared, V. Smesnoi: None Declared, C. Elsner: None Declared, U. Ditmer: None Declared

LB/O106

3-ANTIGEN HBV VACCINE, WITH PRE-S1, PRE-S2 AND S ANTIGENS, INDUCES A HIGHER AND MORE DURABLE IMMUNE RESPONSE COMPARED TO 1-ANTIGEN HBV VACCINE

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Background: 3-antigen HBV vaccine (3A-HBV) is produced in transfected mammalian CHO-cells and contains not only HBs antigen but also Pre-S2 and Pre-S1 antigens. These antigens are glycosylated and thus folded in mammalian environment, aiming to improve antigenic matching of wildtype HB virus and active, vaccine induced, protective anti HB antibodies. 3A-HBV is licensed in EU as PreHevbri®. In a pivotal trial 3A-HBV was compared with a single-antigen HBV vaccine (1A-HBV, yeast derived, Engerix-B®) in a multinational study (PROTECT) involving 1607 adult subjects of all ages. After 3 doses, 3A-HBV induced seroprotective levels of anti-HBs ≥ 10 IU/l in 91.4% as compared with 76.5% after 1A-HBV, the difference being 14.9% (95% CI: 11.2% to 18.6%) [Vesikari et al. Lancet Infect Dis 2021;21:1271.

Purpose: Anti-HBs levels, after initial vaccination course, are being checked in specific populations and seem to reflect the grade of protection. When anti HBs levels drop below a defined level, a boost vaccination is considered to reinstall protection. Longer persistence of immune response to Hepatitis B vaccination, usually measured by anti-HBs level, is of clinical relevance.

Method: A follow-up study on persistence of anti-HBs was conducted in Finland at 2.5 and now 3.5 years after basic vaccination schedule. Subjects who initially had achieved seroprotection in PROTECT, were eligible.

Results: After 2.5 years 465 subjects (mean age 59 years) participated and of the 3A-HBV recipients 88.1% were still seroprotected as compared with only 72.4% (1A-HBV). Now at 3.5 years after primary vaccination 344 subjects, who were still seropositive at 2.5 years, participated in the recent analysis. At this point 3 more subjects (1.5%) of the 3A-HBV group and 10 more subjects (6.9%) of the 1A-HBV group had lost seroprotection. The mean titers (GMC) of anti-HBs at 3.5 years were 1273 IU/L for 3A-HBV and 256.2 mIU/L for 1A-HBV participants. At the end of follow-up at 3.5 years anti-HBs levels of ≥ 100 IU/L were retained by 78.0% of the 3A-HBV recipients as compared to 39.6% of the 1A-HBV recipients.

Conclusion: In the PROTECT study, 3A-HBV induced 6x higher anti-HBs titers in all adults compared to 1A-HBV, with 5-8x higher titers in older adults, adults with diabetes, and adults with obesity (BMI > 30 kg/m2). This also resulted in more durable antibody titers and seroprotection rates, ≥ 10 mIU/mL and ≥ 100 mIU/mL, as observed in the 2.5 and 3.5 year follow-up study in Finland.

Disclosure of Interest: T. Vesikari Grant / Research support from: VBI Vaccines, A. Forstén Grant / Research support from: VBI Vaccines, V. Popovic Employee of: VBI, J. Spaans Employee of: VBI, L. Maubach Employee of: Syneos Health, F. Diaz-Mitoma Employee of: VBI

LB/O107

HEPATITIS ELIMINATION IN CONTEXT OF PANDEMIC PREPAREDNESS AND RESPONSE - OPPORTUNITIES TO STRENGTHEN HEALTH SYSTEMS

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Background: WHO has set global targets for elimination of HBV and HCV transmission and mortality by 2030. To achieve these goals, health systems must provide broad and equitable access to HBV and HCV prevention, testing and care services. With the emergence of the COVID-19 pandemic, countries re-directed Hepatitis programs resources to pandemic response. The transformations in public health and healthcare systems introduced by the COVID-19 response offer unique opportunities to drive progress towards Hepatitis elimination.

Purpose: To assist planning, we explored shared strategies and technologies of mutual benefit to the elimination of Hepatitis elimination and pandemic preparedness.

Methodology: Evidence was gathered in two ways. 1) a scoping literature review was conducted to identify case studies on the inter-relationships between the COVID-19 pandemic response and Hepatitis programs, 2) global survey and associated interviews of Hepatitis program managers and care providers were done to understand the role of Hepatitis programs in the pandemic response and the potential new capacities that can be leveraged to strengthen future Hepatitis elimination efforts.

Results: The survey, case studies and experts' opinions all found that the resources of Hepatitis programs were diverted to COVID-19 response; including: providers' time, clinical space, surveillance systems and, testing resources. Case studies identified countries with strong Hepatitis testing and treatment programs (Egypt, Georgia), community based initiatives (Spain) and surveillance (New Yok City, USA) where Hepatitis infrastructure was pivoted to the COVID-19 response. Countries reported that redirection of Hepatitis testing infrastructure contributed to lower COVID-19 case burden and shorter lockdowns. COVID-19 response improved vaccine supply chains (Georgia) and expanded laboratory capacity (Pakistan, Ethiopia) that can be put to dual use for Hepatitis testing. Moreover, the COVID-19 response expanded systemic use of telemedicine, at home testing strategies and adult vaccine delivery system.

Evidence did not indicate a clear plan for sustaining these investments.

Conclusion: The use of Hepatitis resources for COVID-19 response demonstrated that Hepatitis elimination programs build resilient health systems that can be repurposed to respond to pandemic threats. With the burden of COVID-19 diminishing, the investments run the risk of being shelved forgotten. Now is the time for public health leaders to repurpose the historic investments for other disease elimination efforts. Looking forward, the pandemic experience offers two-pronged transformative learning for health policymakers: 1) Invest in viral Hepatitis elimination to build sustainable infrastructure for preparedness and response against the emerging health threats 2) Leverage COVID-19 investments and innovations to accelerate Hepatitis elimination and demonstrate that services are in place and pandemic investments have long-term impact.

Disclosure of Interest: None Declared

LB/O108

CIRCULATING FIBROBLAST ACTIVATION PROTEIN ALPHA (FAP) AND DIPEPTIDYL PEPTIDASE 4 (DPP4) AS BIOMARKERS FOR FIBROSIS AND STEATOSIS

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Background: Metabolic associated fatty liver disease (MAFLD) is set to become one of the biggest healthcare burdens of modern society, currently affecting over two billion people worldwide. MAFLD begins with steatosis and can progress to fibrosis, cirrhosis and liver failure. The current gold standard to stage liver disease is liver biopsy scores. However, biopsies are invasive and subject to availability, affordability and sampling error. Thus, there is an urgent need to develop accurate, non-invasive tests. We have shown that in human cirrhosis, the unique post-proline protease fibroblast activation protein (FAP) is made at high levels by activated fibroblasts and a similar protease, dipeptidyl peptidase 4 (DPP4), is relocated from apical to basolateral domains of hepatocytes. Both enzymes are on cell surfaces and are released into the circulation.

Aim: Therefore, we investigated circulating FAP (cFAP) and DPP4 (cDPP4) as biomarkers of fibrosis and steatosis, respectively, in MAFLD. In-house enzyme assays for both proteases were applied to sera from two bariatric cohorts (n=342).

Results: A multi-variate model was developed combining cFAP with age, diabetes status and ALT to evaluate individuals who had an indeterminate diagnosis regarding liver fibrosis. The AUROC was 87.5% with a negative prediction value of 92% and a positive prediction value of 95%, indicating high accuracy. Accuracy increased when the cFAP model was combined with an established blood test - based algorithm; either FIB4 or NAFLD Fibrosis Score (NFS). In both cohorts, cDPP4 was associated with higher grades of steatosis, with the association strengthened when adjusted for diabetes status, ALP and AST:ALT.

Conclusions: Thus, we present novel, inexpensive diagnostic methods to assess whether an individual has severe MAFLD; using DPP4 for steatosis and FAP for fibrosis.

Disclosure of Interest: None Declared

LB/O109

INTRACELLULAR "IN SILICO MICROSCOPES" - FULLY 3D SPATIAL HEPATITIS C VIRUS REPLICATION MODEL SIMULATIONS

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Abstract Content: Virus pandemics and endemics cause enormous pain and costs. While the Covid19 pandemics induced obvious damages, the "silent" Hepatitis C virus (HCV) infection induced liver destruction is the main reason for liver transplants. Our framework aims to develop fully 3D resolved "in silico microscopes" to mirror in vitro / in vivo experiments by means of fully spatio-temporal resolved mathematical models describing the intracellular HCV viral RNA (vRNA) replication cycle which are evaluated at modern supercomputers.

HCV-generated virus genome replication factories are housed within virus-induced intracellular structures termed membranous webs (MW) which are derived from the Endoplasmatic Reticulum (ER). The ER is an interconnected intracellular membrane network and embedded within the cytosol. Up to now, the very advanced experimental data such as highly spatially resolved fluorescence and electro-tomography data in many cases do not enter computational vRNA cycle models.

To take advantage from such data, we model virus replication by means of mathematical diffusion-reaction partial differential equations (PDEs). The PDEs are evaluated upon realistic cell geometries which we reconstructed based on experimental data.

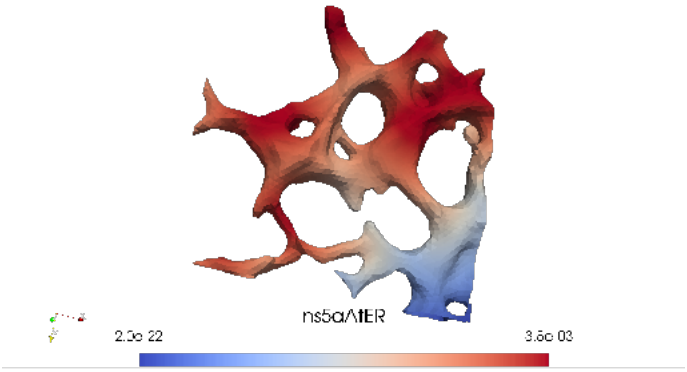
Our first models described the major components (vRNA, non-structural viral proteins - NSPs - and a host factor). Parameter sensitivity analysis allowed for new insights. The next steps incorporated different aggregate states of vRNA and NSPs, and population dynamics inspired diffusion and reaction coefficients instead of multilinear ones. The combination of these new concepts with spatial resolution provoked questions for advanced experiments. We further estimated realistic parameters such as NSP diffusion constants, which we integrate into our in silico framework.

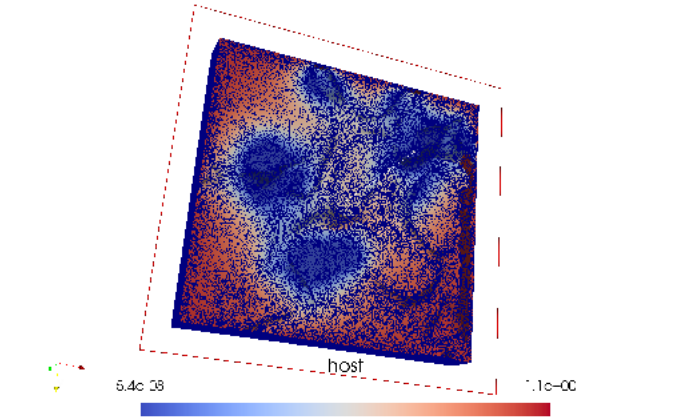
Presently, our work in progress (cf. figure) is merging effects restricted to the ER surface (e.g. NSP diffusion) with others taking place in the cytosol (e.g. host factor supply) to unveil quantitatively the interplay of virus components whose action is restricted to the 2D ER surface and of other virus components which act in the 3D volume cytosol.

Our simulations help understanding the relation of form and function of intracellular virus replication mechanisms. In the long run, our framework might help to facilitate the systematic development of efficient direct antiviral agents and vaccines.

References: doi:10.3390/ijerph16030513, doi:10.3390/v10010028, doi:10.3390/v9100282

Image/Table:





Disclosure of Interest: None Declared

LB/O110

UNDER-REPRESENTATION OF WHO AFRICA REGION IN HBV CLINICAL TRIALS: THE FIELD ADVANCES, BUT IN WHICH DIRECTION?

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Background and Aims: The WHO Africa region bears a disproportionate burden of morbidity and mortality related to chronic Hepatitis B Virus (HBV) infection. It currently represents 75 million chronic carriers and an estimated 70% of new worldwide HBV infections. Hence, in parallel with prevention, development of functional cure strategies is urgently needed. Host genetics, HBV genotypes, co-infections and distinct transmission patterns are associated with geographic location and can lead to different disease outcomes and drug susceptibility. Furthermore, acceptability, accessibility and affordability of interventions differ by setting according to local policy, culture, resources and infrastructure. We set out to determine the extent to which HBV clinical trials (CT) represent populations in the WHO Africa region, in order to highlight inequities and advocate for investment in better global coverage.

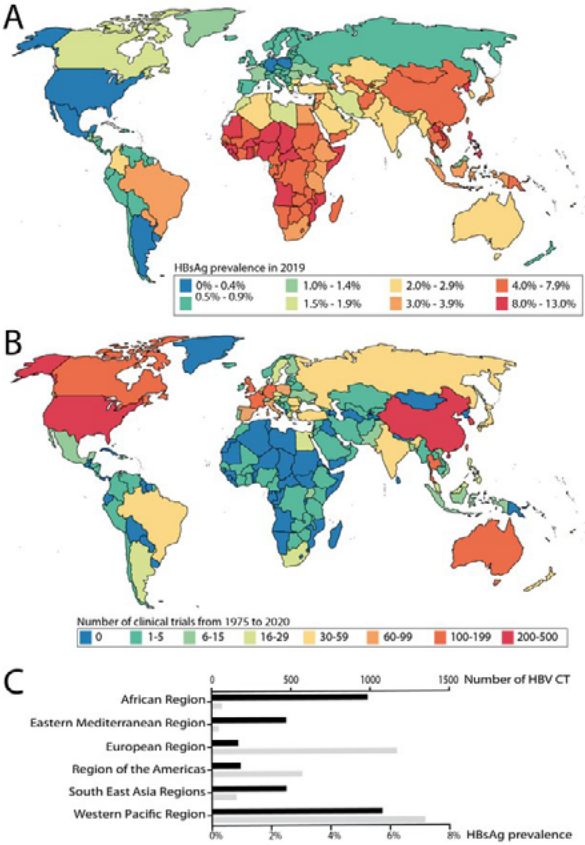
Methods: We screened the clinicaltrial.gov repository for 'Hepatitis B' related CT. We classified studies to investigate (1) location, (2) design (interventional/observational), (3) funding and (4) publication. P values were calculated using the Chi-Square test in Prism v. 8.0.

Results: We identified 1898 HBV CT that started between 1975 and 2020, of which 1429 (75.2%) were interventional studies. When compared to Hepatitis B surface Antigen (HBsAg) prevalence, distribution of HBV CT is biased ($p < 0.0001$) towards East Asia (41.0%), Europe (22.4%) and North America (25.3%), with the WHO African region representing only 2.6% (Figure 1). Focusing on the 40 WHO African region CT, 29 (72.5%) were interventional (representing 1.5% of the global total). In Africa, these interventional studies were mainly sponsored by academic institutes (17/29, 58.6%), and mostly focusing on prevention of vertical transmission and diagnosis (15/29, 51.7%). 27.5% (8/29) were investigating already approved drugs and 20.6% (6/29) novel antivirals, amongst which four were ongoing investigations of GSK3228836 (3) and Selgantolimod (1); the two others were terminated more than 8 years ago, without published results. As a comparison, studies in the U.S. are predominantly interventional CT (80%) with more than 50 molecules currently being investigated.

Conclusion: There is a clear neglect of investment in HBV-focused CT in Africa, particularly for interventions, to reduce the morbidity and mortality of chronic HBV infection. CTs in Africa are urgently needed to evaluate efficacy of newly discovered anti-HBV compounds and to ensure that new treatments can be distributed and deployed as they become available.

Figure 1: **Comparison of prevalence and clinical trials repartition related to HBV infection. A.** HBsAg prevalence in each country in 2019, Reproduced from GBD 2019 Hepatitis B Collaborators et al, 2020. **B.** Number of clinical trials per country from 1975 to 2020. **C.** Bar Chart representation of number of HBV CT (grey) vs HBsAg prevalence (dark) in WHO regions.

Image/Table:



Disclosure of Interest: None Declared

LB/O111

THE IMPACT OF COVID-19 OUTBREAK ON THE ELIMINATION OF HEPATITIS C IN TAIWAN

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Background: Taiwan government commit to pursuit Hepatitis C elimination by 2025 and has been put a lot of effort on it since 2017. However, the pandemic outbreak of Covid-19 during 2020 and 2022 has brought tremendous impact on public health and medical systems globally and may have influence on the progress of Hepatitis C elimination. This study aims at investigate the impact of Covid-19 outbreak on Hepatitis C elimination in Taiwan.

Methods: Four main Covid-19 outbreaks could be identified during January to April 2020, January to February 2021, May to August 2021, and April to July 2022. The scale of the latter two wave of outbreaks were much greater than the former two waves. To evaluate the impact of Covid-19 outbreak on Hepatitis C elimination, time trend of several indicators along the Hepatitis C virus (HCV) care cascade, including number of anti-HCV screening participants in the national screening program, proportion of HCV RNA testing among persons with anti-HCV positive results, number of patients receiving direct-acting antivirals (DAA) treatment, proportion of early withdrawal from DAA treatment, proportion of not completing sustained virologic response at 12 weeks after treatment (SVR12), and SVR12 rate, were examined. Both SVR12 rates among all patients receiving treatment, namely intention-to-treat (ITT) analysis, and among patients with known SVR12 testing results, namely per-protocol (PP) analysis, were included.

Results: The analysis of time trend among the above HCV care cascade indicators showed that the indicator which was most affected by the pandemic is the number of anti-HCV screening participants in the national screening program, however there seems no obvious impact on the proportion of HCV RNA testing among those with positive anti-HCV results and SVR12-PP rate. The rest of the HCV care cascade indicators were moderately affected by the pandemic. Moreover, the impact of the pandemic on the proportion of not completing SVR12 testing was greater than that on the proportion of early withdrawal from DAA treatment.

Conclusion: The impact of the Covid-19 outbreak has been investigated along the entire HCV care cascade. The pandemic has greater impact on the beginning and on the end of the HCV care cascade, namely attending screening and having SVR12 test after treatment. Once the patients have entered into the care cascade, the impact of the pandemic appears to be relatively small. Moreover, besides the impact of the Covid-19 outbreak, gradual downward trends were also observed on the proportion of early withdrawal from DAA treatment, proportion of completing SVR12, and SVR12-ITT rate, which brings warning signs.

Image/Table:

Table The time trend of the hepatitis C virus care cascade

Period	Monthly no. of anti-HCV screenees	% of HCV RNA testing among anti-HCV(+)	Monthly no. of patients with DAA	% of early withdrawal from DAA	% of patients not completing SVR12 testing	SVR12-ITT%	SVR12-PP%
2017/1-2019/12	--	--	2,080	2.6%	4.5%	93.6%	98.0%
2020/1-4 (Outbreak)	--	--	4,347	3.1%	6.1%	92.7%	98.8%
2020/5-12	82,092	46%	2,347	3.8%	6.0%	93.0%	99.0%
2021/1-2 (Outbreak)	159,086	48%	1,544	4.4%	8.7%	90.2%	98.8%
2021/3-4	185,705	49%	2,173	4.2%	9.5%	89.4%	98.7%
2021/5-8 (Major outbreak)	72,053	48%	1,513	4.4%	11.3%	87.7%	98.8%
2021/9-2022/3	80,169	47%	1,612	4.2%	11.9%	87.0%	98.7%
2022/4-7 (Major outbreak)	58,406	45%	1,358	5.4%	14.7%	84.2%	98.7%

HCV: hepatitis C virus; DAA: direct-acting antivirals; SVR12: sustained virologic response at 12 weeks after treatment; SVR12-ITT: the SVR12 rate among all patients receiving treatment, namely intention-to-treat (ITT) analysis; SVR12-PP: the SVR12 rate among patients with known SVR12 testing results, namely per-protocol (PP) analysis.

Disclosure of Interest: None Declared

LB/O112

REAL-TIME MONITORING SYSTEM FOR THE PROGRESS OF HEPATITIS C ELIMINATION: THE EXPERIENCE FROM TAIWAN NATIONAL HEPATITIS C ELIMINATION PROGRESS MONITORING INFORMATION NETWORK (TWNHCP-MIN)

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Background: Taiwan government has strong will to reach WHO's 2030 goal of Hepatitis C elimination by 2025. To timely monitor the progress of elimination, a real-time monitoring system, called 'Taiwan National Hepatitis C Elimination Progress Monitoring Information Network (TWNHCP-MIN)', was built by Taiwan National Hepatitis C Program Office (TWNHCP), the Ministry of Health and Welfare (MOHW). This study describes the structure of TWNHCP-MIN and the achievements and progress of Hepatitis C elimination in various subpopulations in Taiwan.

Method: The TWNHCP-MIN was built by connecting all available databases held by different departments under the MOHW including screening data from the Health Promotion Administration (HPA), claims data including diagnosis and treatment from the National Health Insurance Administration (NHIA), and other datasets pertaining to identifying various subpopulations including persons living with human immunodeficiency virus (HIV), persons on opioid substitution therapy (OST), patients with end stage renal disease (ESRD), patients with co-morbidity such as diabetes (DM), early chronic kidney disease (CKD), or pre-ESRD, etc from various sources. All of above data were updated on a daily basis. Based on the TWNHCP-MIN, the TWNHCP could perform real-time monitoring on the progress of Hepatitis C elimination for each subpopulations. Monthly progress reports of Hepatitis C elimination along the care cascade including screening coverage, linkage-to-care, treatment, etc. were generated and provided by the TWNHCP to identify the gaps and barriers of Hepatitis elimination. In combination of WHO's diagnosis and treatment goals, a micro-elimination goal of more than 72% (=90% diagnosis*80% treatment) of chronic Hepatitis C (CHC) patients were diagnosed and treated has been set up.

Results: By the end of July 2022, the proportion of CHC patients who were diagnosed and treated among patients with ESRD, HIV, persons on OST, prisoners, co-morbidity patients with DM, early CKD, and pre-ESRD were 81%, 77%, 61%, 28%, 39%, 42%, and 46%, respectively. The major gaps of the subpopulations which have not reached the elimination goal were mainly the

proportion of CHC patients been diagnosed, which comprising both anti-HCV testing rate and HCV RNA testing rate among those with positive anti-HCV results. The proportion of treatment among those diagnosed were satisfactory across all subpopulations.

Conclusions: The progress of Hepatitis C elimination has been successfully monitored by a timely monitoring system. The micro-elimination target of more than 72% of CHC patients were diagnosed and treated has been achieved in patients with ESRD and HIV in Taiwan. Based on the monitoring system, the major gaps of the subpopulations which have not reached the elimination goal were identified, and strategies to diminish the identified barriers were then discussed and developed.

Image/Table:

Table The hepatitis C cascade of care among various subpopulations

Sub-populations	(A) Infected: No. of estimated CHC	(B) Diagnosed: No. of CHC diagnosed	(C) Treated: No. of CHC treated	(D) % of diagnosed (=B/A)	(E) % of treatment among diagnosed (=C/B)	(F) % of treatment among estimated CHC (=C/A)
ESRD	6,174	5,283	5,015	85.60%	94.90%	81.20%
HIV	6,712	5,606	5,187	83.50%	92.50%	77.30%
OST	6,036	3,918	3,671	64.90%	93.70%	60.80%
Prisoners	7,143	2,410	2,303	33.70%	95.60%	32.20%
DM	50,126	20,044	19,515	40.00%	97.40%	38.90%
Early CKD	27,554	12,211	11,876	44.30%	97.30%	43.10%
Pre-ESRD	5,627	2,820	2,712	50.10%	96.20%	48.20%

ESRD: end stage renal disease; HIV: human immunodeficiency virus; OST: opioid substitution therapy; DM: diabetes mellitus; CKD: chronic kidney disease;

Disclosure of Interest: None Declared

LB/O113

UPDATE ON THE HEPATITIS C CARE CASCADE AND PROGRESS TOWARD HEPATITIS C ELIMINATION IN THE UNITED STATES IN 2021

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Background: Hepatitis C virus (HCV) infection, a major cause of cirrhosis and liver cancer, is targeted for elimination by the World Health Organization (WHO) globally and in the United States (US). Elimination efforts will require large scale HCV antibody (Ab) screening, followed by HCV RNA testing of HCV Ab + persons to detect current HCV infection followed by treatment with a highly effective direct acting antiviral regimen.

Purpose: The purpose of this study is to assess recent data on HCV testing and treatment in the US, to better understand the progress toward HCV elimination.

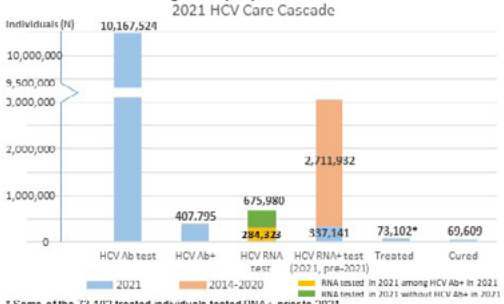
Methods: This study analyzed de-identified data from persons who were screened for HCV Ab and/or tested for HCV RNA by two large US commercial laboratories from 1/1/2014-12/31/2021. Validated imputation algorithms were used to characterize patients who initiated treatment and patients who achieved virological cure based on viral load decline and continued negative HCV RNA test results. The 3-digit ZIP code was used to map treatment rates by US state. HCV Ab with reflex to RNA tests were identified using available test numbers and test names.

Results: In 2021, HCV Ab tests were performed for a total of 10,167,524 persons, of whom 407,795 (4%) were Ab+, among which 284,323 (70%) were tested for HCV RNA. Including persons who tested HCV Ab+ in earlier years, a total of 675,980 persons had RNA tests performed in 2021, and 337,141 (50%) had a positive RNA test result. An estimated 73,102 HCV RNA+ persons were treated, of whom 69,609 (95%) were cured (Figure 1). In 2021, the number of persons screened for HCV Ab followed a bimodal age distribution, with age group 30-34 representing the largest number, and another peak around age group 50-54. The age of persons who tested positive for HCV RNA followed a similar distribution, with the highest among those aged 30-39 followed by 60-64 (Figure 2). From 2014 through 2021, the proportion of individuals who received reflex HCV RNA testing of HCV Ab+ specimens rose from 19% in 2014 to 35% in 2021. During this period, persons identified as HCV RNA+ by reflex testing were more likely to receive HCV treatment compared to individuals for whom Ab and RNA testing were ordered separately (43% vs 37%). Geographically in 2021, states in the northeast and the west coast had highest treatment rates (23-33%) whereas the south and mid-west regions had the lowest rates (11-20%) (Figure 3).

Conclusions: The bimodal age distribution of HCV RNA+ tests supports the current policy for HCV testing of all adults. Reflex testing for HCV RNA is associated with higher rates of linkage to care and treatment initiation. This procedure should be implemented across laboratories. However, treatment uptake across the US remains low, suggesting continued barriers to initiation of therapy and interruptions in care. The data suggest additional measures are needed to expand access to testing and treatment necessary to reach the WHO HCV elimination goals by 2030 in the US.

Image/Table:

Figure 1. HCV care cascade among adults (>18) in the US in 2021



* Some of the 73,102 treated individuals tested RNA+ prior to 2021.
Treated and cured individuals were identified using validated imputation algorithms.

Figure 2. Age distribution for HCV antibody screening and RNA-positive tests among adults in the US in 2021

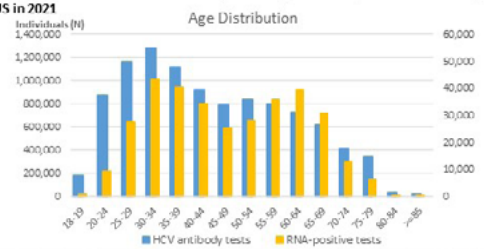
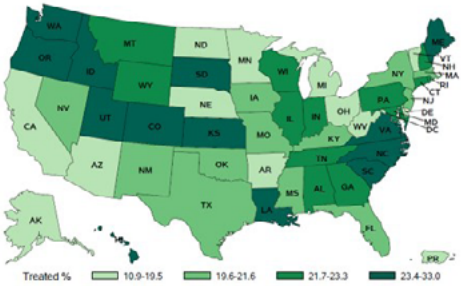


Figure 3. Heatmap of the percentage of HCV RNA+ patients that were treated in 2021 (national average = 21.1%)



Disclosure of Interest: J. Ward Employee of: The Task Force for Global Health, which receives funds for the support of the Coalition for Global Hepatitis Elimination from Abbott, Gilead, AbbVie, Merck, Siemens, Roche, Pharco, VBI Vaccines, Zydus-Cadila, governmental agencies, and philanthropic organizations., M. Ghany: None Declared, T. Morgan: None Declared, S. Marx Employee of: AbbVie and may own AbbVie stock, J. Kaur Employee of: AbbVie and may own AbbVie stock, N. Shukla Employee of: /contractor of AbbVie and may own AbbVie stock, S. Manthena Employee of: AbbVie and may own AbbVie stock, S. Jiao Employee of: AbbVie and may own AbbVie stock

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P001

FIRST REPORT OF NON PRIMATE HEPACIVIRUS (NPHV), HOMOLOGUE OF HEPATITIS C VIRUS (HCV), IN HORSES AND DOGS IN MOROCCO

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Background: In recent years, several homologs of the Hepatitis C virus (HCV) have been identified in different types of animals. Non-Primate Hepacivirus (NPHV), identified in dogs and horses, is considered to be genetically the closest homolog of HCV. The search for this virus in the equine population has been carried out in different parts of the world with the exception of the African continent. This study represents the first investigation of the prevalence of NPHV in dogs and horses in North Africa.

Methods: 208 animal plasma samples (172 horses and 36 dogs) were collected from different regions of Morocco. The search for the viral RNA of NPHV was carried out by nested PCR targeting two regions of the virus, the 5'UTR and NS3. Seroprevalence was detected by the GLIPS (Gaussia luciferase immunoprecipitation system) technique targeting anti-NS3 antibodies. Eight NS3 sequences isolated from the positive plasmas were subjected to phylogenetic analysis.

Results: Horses and dogs showed respective NPHV RNA positivity rates of 10.5% and 5.5%, and seroprevalences of 65.7% and 8.33%. Noted that juveniles appear to be more susceptible to NPHV infection with 23.5% NHPV RNA positivity rate. On the other hand, the seropositivity rate is very high in mares compared to stallions (77.14% via 46.27%, $p < 0.0001$). Phylogenetically, the strains of NPHV NS3 isolated in horses and dogs are very close to the strains isolated in Europe.

Conclusion: the circulation of NPHV is very common and evident in the Moroccan horse. Young age and female gender may be considered risk factors for NPHV infection. Additionally, there is proof that this virus affects both equine and canine populations, raising the prospect of interspecies transmission and posing the possibility that horses and dogs could act as possible vectors for the introduction of an ancestor of HCV to the human population.

Key words: Non-primate Hepacivirus, Equine, Canine, HCV, Seroprevalence.

Disclosure of Interest: None Declared

P002

HCV DIRECT ACTING ANTIVIRAL THERAPY NORMALIZES CIRCULATING LEVELS OF MICRORNAS IN HIV-1/HCV CO-INFECTED PATIENTS

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Background: Patients with Hepatitis C virus (HCV) infection who achieve a sustained virological response (SVR) on direct acting antivirals (DAAs) still need to be monitored for signs of liver disease. Thus, the identification of disease progression biomarkers is needed. We recently identified three plasma circulating microRNAs (miRNAs)—miR-100-5p_iso3p:-2, miR-122-5p, and miR-192-5p—that correlate highly with liver fibrosis progression in human immunodeficiency virus type 1 (HIV-1)/HCV co-infected patients.

Purpose: To investigate whether circulating levels of miR-100-5p_iso3p:-2, miR-122-5p, and miR-192-5p can be linked to liver disease progression in HIV-1/HCV co-infected patients who have achieved HCV SVR 12 weeks after finishing therapy.

Methods: Eighty-one chronic HIV-1/HCV co-infected patients were enrolled in a longitudinal study performed at baseline (T0) of DAA therapy and 12 weeks (T12) after concluding treatment. Circulating plasma levels of miR-100-5p_iso3p:-2, miR-122-5p and miR-192-5p were determined by real-time PCR at T0 and T12. Patient clinical parameters and liver fibrosis stage, determined by transient elastography, were controlled at T0, T12 and after two years of achieving SVR.

Results: Transient elastography at T0 showed that most of the study subjects were in an advanced stage of liver fibrosis (F0-1 9%, F2 11%, F3 32%, F4 48%). At T12, SVR was significantly associated with reductions in the levels of circulating miR-100-5p_iso3p:-2, miR-122-5p, and miR-192-5p ($P<0.0001$, $P<0.0001$, and $P=0.0008$, respectively) in the overall cohort and in patients with advanced (F3-4) liver fibrosis ($p<0.0001$, $p<0.0001$, and $P=0.0011$, respectively). Remarkably, at T12, no significant reduction in miRNA levels was observed in individuals who did not achieve SVR ($P=0.8750$, $P=0.1250$, and $P=0.1260$, respectively). Two years after reaching SVR, HCV-cured patients, but not non-responders, significantly reduced their liver stiffness ($p<0.0001$).

Conclusions: DAA-induced SVR is linked with a significant reduction in circulating levels of liver disease–associated miRNAs. Circulating miRNA levels may be valuable surrogate biomarkers of liver fibrosis progression in HIV-1/HCV co-infected patients following HCV cure with DAAs.

Disclosure of Interest: None Declared

P003

THE ASSOCIATION OF L-DOPA DECARBOXYLASE WITH AUTOPHAGY IN HEPATOCYTES AND ITS IMPLICATION IN THE LIFE CYCLE OF FLAVIVIRIDAE VIRUSES

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Abstract Content: L-Dopa Decarboxylase (DDC) is a major enzyme of catecholamine biosynthesis, converting L-Dopa to dopamine and 5-hydroxytryptophan to serotonin. Apart from its role in neurotransmitter biosynthesis, DDC has been isolated from a variety of peripheral organs, including the liver, where has been implicated in cell proliferation, apoptosis, and host cell immunity to viruses. Moreover, catecholamines have been involved in hepatocyte proliferation and the development of liver diseases, while in neuronal cells dopamine auto-oxidation have been associated with autophagy, a key process in maintaining cellular homeostasis and growth. Many viruses, among them Hepatitis C virus (HCV) and dengue virus (DENV), affect autophagy to favor their life cycle. Especially DENV has been shown to inhibit the fusion of autophagosome with the lysosome (completion of autophagy) at the late stage of infection. Our previous findings have showcased an inverse correlation of DDC expression and dopamine biosynthesis with HCV and DENV replication in cultured hepatocytes and in liver biopsies of HCV chronically infected patients. Moreover, viral infection downregulates DDC expression. Based on the above, HCV and DENV infection-related regulation of DDC could possibly mediate the effect of these viruses on autophagy. Here, we first investigated if DDC affects the induction and flux of the autophagy pathway in human hepatoma Huh7.5 cells, by silencing or overexpressing DDC. The autophagy levels were monitored by the detection of LC3B and p62, under starvation conditions or in the presence of lysosome inhibitors. DDC silencing prevented the autophagosome-lysosome fusion, while DDC overexpression promoted this process. Reversely, the induction of autophagy increased the expression of DDC, whereas the inhibition of autophagy - by Atg14L-knockout that inhibits both the formation of the autophagosome and the fusion with the lysosome, or by the use of the lysosomal inhibitor NH4Cl, or by the use of 3-MA which suppresses the initiation of autophagy through inhibition of PI3K-III- downregulated DDC. Next, we investigated the role of DDC on the DENV infection-related regulation of autophagy. For this, DENV-autophagy association was analyzed in Huh7.5 cells in the presence or not of DDC silencing, after treatment of cells with NH4Cl. Upon DDC silencing, the inhibitory effect of DENV in the completion of autophagy was more pronounced. Moreover, in DDC-silenced cells, no difference was observed in the virus propagation between the NH4Cl-treated and non-treated cells. In contrast, NH4Cl-treatment induced the virus proliferation in the control cells. This study suggested that the effect of DENV on DDC expression is at least part of the mechanism that the virus uses to inhibit the formation of autophagolysosomes. In total, our data highlighted an important role for DDC in metabolic and homeostatic processes, while at the same time augmented its previously reported significance in viral infections.

Disclosure of Interest: None Declared

P004

MTORC1 SIGNALING AS A MECHANISM OF M1 MACROPHAGE-DERIVED INTERFERON-GAMMA DYSFUNCTION IN CHRONIC HCV ADVANCED LIVER DISEASE

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Background: In response to pathogenic, inflammatory stimuli and metabolic cues, macrophages can differentiate into a pro-inflammatory (M1) phenotype, producing high concentrations of TNF-α, IL-12 and IL-6. The recent findings that human macrophages are an important source of interferon-gamma (IFN-γ) add some complexity to this picture. We have previously identified that IFN-γ secretion in M1 cells is regulated by the PI3k-mTOR activated p70S6K activated pathway. mTORC1 signalling has further been shown to regulate macrophage polarity and metabolism, making it a therapeutic target for regulating macrophage functions. It remains unclear the molecular mechanism by which human macrophages produce IFN-γ and its roles in advanced liver disease.

Purpose: We aim to determine the underlying mechanism of aberrant IFN-γ production by M1-like macrophages in HCV-mediated liver fibrosis and attempt to ameliorate their dysfunctional phenotype.

Methods: Blood monocytes were differentiated into macrophages using M-CSF for 6 days, then polarized into M1 macrophages from healthy and treatment-naïve HCV RNA^{+} individuals with varying degrees of fibrosis (F0-2 < 9.0 KPa, F3-4 > 11.0 KPa) and stimulated using lipopolysaccharide (LPS) or POLY I:C. The expression of IFN-γ and cell surface markers was determined by ELISA and multi-parameter flow cytometry. Rapamycin and AMPK-agonist treatments were applied to M1 cells to impair mTORC1 signalling. mTORC1 signalling by phosphorylation of RPS6 was evaluated using a methanol-based flow cytometry approach.

Results: M1 cells were confirmed to be the sole producer of IFN-γ *in vitro*, while M2 macrophages produced basal amounts. Furthermore, both LPS and POLY I:C stimulated M1 upregulated IFN-γ expression. Polarization and LPS stimulation further enhanced mTORC1 signalling in macrophages from healthy individuals. M1 surface markers CD80 CD86 expression and IFN-γ secretions were found to be impaired when cells were treated with rapamycin or AMPK-agonist ACAIR. In minimal fibrosis, we have observed a significant reduction of CD80, CD86 PD-L1, and IFN-γ production from M1 macrophages compared to healthy controls. In those with advanced liver fibrosis, M1 macrophages exhibit significant enhancement of CD80, CD163 and IFN-γ production. Early observations indicate that these M1 cells from HCV^{+} patients have enhanced mTORC1 signalling profiles.

Conclusions: We have identified that monocyte-derived macrophage polarity in chronic HCV infection is dependent on liver disease severity. Expression of M1 immunostimulatory markers and IFN-γ in advanced liver disease are enhanced and may contribute to the overall dysfunction of the innate/adaptative immune systems. mTORC1 inhibitors or AMPK-agonists may be a potential therapeutic target to counteract abberant inflammatory M1-polarization in advanced liver disease patients.

Disclosure of Interest: None Declared

P006

THE ANTIVIRAL EFFECT OF BLOCKING NEDDYLATION PATHWAY CAN PREVENT THE REPLICATION OF HEPATITIS B VIRUS

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Background: Hepatitis B virus (HBV) infection remains a major public health problem and the most frequent cause of chronic liver disease worldwide. Neddylation is a post-translational modification of ubiquitin-like proteins by its polypeptide NEDD8. In our work, we aimed to demonstrate whether blocking neddylation can cause an antiviral effect against HBV replication and confirm the role of NEDD8 in HBV viral replication.

Methods: We treated HepG2.2.15.7 and HepG2-hNTCP-30 cell lines with siNEDD8 and MLN4924, a potent and selective inhibitor of the NEDD8-activating enzyme. To assess proteins expression, we used western blot and immunofluorescence. We measured cellular viability, intracellular and extracellular HBV DNA, covalently closed circular DNA (cccDNA), HBsAg, HBeAg and HBcrAg to evaluate the consequences of different treatments on the viral replication.

Results: Our results showed an increase in NEDD8 expression in HepG2.2.15.7 cell line. We found that HBV replication in HepG2.2.15.7 and HepG2-hNTCP-30 cells decreased after NEDD8 was Knockdown by siRNA or MLN4924 treatments. In addition, HBsAg and HBeAg secretion was strongly suppressed in culture supernatants unlike HBcrAg. These results confirm that NEDD8 repression decreases HBV replication. However, no change was observed for cccDNA level confirming once again its persistence and longevity in chronic HBV infection.

Conclusions: The neddylation pathway plays an important role in HBV replication and persistence. Its modulation could thus provide new therapeutic strategies against chronic Hepatitis B.

Keywords: HBV, Neddylation, NEDD8, MLN4924, Chronic HBV infection.

Disclosure of Interest: None Declared

P007

ASSESSMENT OF NEUTRALIZING ACTIVITY OF ANTIBODIES AGAINST HEPATITIS B VIRUS SURFACE ANTIGEN IN THAI VACCINEES

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Abstract Content: Thailand has integrated the Hepatitis B (HB) vaccine into the national Expanded Program for Immunization since 1992. Although, this vaccination program has been proven very effective, leading to a decrease in Hepatitis B surface (HBs) antigen prevalence in the population, mother-to-child transmission of Hepatitis B virus (HBV) still occurs despite passive/active immunization at birth. A hypothesis to explain this residual transmission is that anti-Hepatitis B surface (anti-HBs) antibodies produced after vaccination or in Hepatitis B immunoglobulin (HBIG) have insufficient and/or inefficient neutralizing activity. Currently, neutralization activity cannot be measured with the ELISA tests that are commonly used to measure anti-HBs antibodies levels. An anti-HBs antibody level of ≥10 mIU/mL is usually considered as conferring protective immunity against HBV infection; however, this antibody level does not provide information on the level or extent of neutralizing activity. Therefore, this work aimed at assessing the relationship between the titer of anti-HBs antibodies and their neutralizing activity against different genotypes of HBV. Anti-HBsAg positive serum samples were selected from Thai students who received a booster dose of Heberbiovac HB recombinant vaccine, available in Thailand. Anti-HBs titers were measured using a commercial ELISA, and neutralizing activity was measured using the Hepatitis delta virus *in vitro* infection model as a practical surrogate to an HBV infection model. The titer of anti-HBs antibodies elicited by vaccine (362 – 113,740 mIU/ml) showed a correlation with neutralizing activity against HBV genotype D prototype at $r = 0.7763$, versus $r = 0.4344$ for genotype B prototype, the most prevalence genotype in Thailand. Furthermore, these antibodies neutralized more significantly HBV genotype D than genotype B ($p < 0.05$). These results imply that beside antibody titer measurement, the functionality of anti-HBs antibodies should be assessed especially with regard to HBV diversity in a define country. Our results suggest that passive and active HB immunoprophylaxis approaches could be improved by ensuring that the genotype/subtype of the HB vaccine matches that of the circulating HBV strain.

Disclosure of Interest: None Declared

P008

ANTI-HBC-NONREACTIVE OCCULT HEPATITIS B INFECTIONS WITH HBV GENOTYPES B AND C IN VACCINATED IMMUNOCOMPETENT ADULTS

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Background: Anti-HBc can persist for decades in HBV-infected individuals. However, lack of detectable anti-HBc has been reported in individuals with occult HBV infection (OBI) testing anti-HBs positive, especially in Southeast Asia. Isolated anti-HBs OBI remains uncharacterized. This unusual serological profiles in OBI carriers may lead to uncertainty in testing result interpretation or testing error suspicion.

Purpose: The prevalence and mechanisms underlying this condition were investigated over time in blood donors with OBI.

Methods: Isolated anti-HBs OBI status was identified from 466,911 donors from Dalian, China, and monitored by examining samples collected prior to the index diagnosis (lookback samples), at index, and during follow-up (mean: 27.1 months [range: 2.6-84.3]). Special attention was paid to the vaccination status.

Results: Of 451 confirmed OBIs (1:1,035), 43 (9.5%; 1:10,858) had anti-HBs as only serological marker. HBV genotype C was dominant (85%), while HBV genotype B was dominant (66%) in HBsAg+ donors. Isolated anti-HBs OBIs differed from anti-HBc-reactive OBIs by significantly younger age (median 24 years), higher HBV DNA (median: 20 IU/mL) and anti-HBs (median 60.5 IU/L) levels, paucity of mutations in HBV Core and S proteins, and higher vaccination rate (72%). Vaccinated isolated anti-HBs OBIs (n=31) differed from unvaccinated (n=11) by significantly younger age (22 vs 38 years), higher anti-HBs level at index (48% vs 9% with anti-HBs >100 IU/L), and higher frequency of anti-HBs response (44% vs 20%). Follow-up of 15 vaccinated and 5 unvaccinated OBIs showed that two individuals seroconverted to anti-HBc, 65% (8 vaccinated and 5 unvaccinated) became HBV DNA negative suggesting recent aborted infection, while 35% (7 vaccinated) had low persistent viremia 2 to 65 months post index with no evidence of anti-HBc or HBsAg conversion. No specific genetic feature was associated with altered antigenicity or core gene expression.

Conclusions: Rare occurrence and persistence over time of isolated anti-HBs OBI was confirmed in blood donors. Isolated anti-HBs OBI appears mainly associated with young, vaccinated, adults recently exposed to HBV one- or two-decades post-vaccination who remain largely protected from full blown HBV breakthrough infections, and develop low level aborted infection revealed by transient viremia and immune anti-HBs response. A subset of individuals still experienced low but persistent viral replication. The long-term outcome of this uncommon OBI condition is unclear. Unsuspected anti-HBc-negative viremic donors may be at risk of HBV reactivation if immunocompromised and may contribute to the HBV transfusion-transmission residual risk.

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P009

MOLECULAR AND SEROLOGICAL FOLLOW-UP OF ASYMPTOMATIC INDIVIDUALS WITH OCCULT HEPATITIS B VIRUS GENOTYPES B AND C INFECTION: PRELIMINARY ANALYSIS

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Background: Occult HBV infection (OBI) persists in asymptomatic individuals and remains potentially infectious. The viral mechanisms of OBI appear to be multifactorial but poorly understood, and the long-term clinical outcome is unknown.

Purpose: Blood donors with confirmed OBI were followed-up to study the evolution of HBV serological markers and genetic of HBV strains to assess the viral molecular mechanisms of OBI.

Methods: An OBI follow-up program is implemented in the Dalian blood center, China. Donors were called back at 6-months intervals and a whole blood sample was collected. Serological markers were tested with CLIAs. Viral load (VL) was measured with qPCR (LoQ: 20 IU/mL). HBV genome was amplified from plasma and sequenced.

Results: Sequential blood samples (2-7/donor) were collected from 45 OBI donors and 15 HBsAg+ controls over an average period of 32 months (range: 12-72). Both groups showed no change in HBsAg and anti-HBc profiles. Anti-HBs were detected in 32/45 (71%) OBIs at inclusion and/or during follow-up. No change over time in anti-HBs levels was observed in 17 (53%) donors (median: 28 IU/L; range: 10-202). Anti-HBs were transiently detected in 11 (34%) donors, and 4 (13%) had a transient increase (≥5-times) during follow-up. VL was undetectable in 14 (31%) OBIs and was transiently or continuously detected in 26 (58%) and 5 (11%; median: 20 IU/mL; range: 20-155), respectively. Median VL in controls was 117.5 IU/mL (range: 43-3x10^8). HBV sequence was available at index time and/or in follow-up for 38 (84%) OBIs and 13 (87%) controls. HBV genotypes were B (11%), C (83%), and D (6%) in OBIs, and B (85%) and C (15%) in controls. OBIs (n=34) showed a higher aa diversity in S proteins than controls (n=13): median 8.3% vs 3.2% (P=0.002). Pre-S/S aa sequences divergence in an individual at two time intervals was analyzed in 14 OBIs and 10 controls. No significant difference was observed between OBIs and controls. OBI sequences had 1 to 6 aa substitutions in pre-S1 domains involved in cellular receptor binding (12/34 [35%]) and virion formation (2/34 [6%]), and in the S major hydrophilic region at positions that were reported to negatively affect antigenicity (15/34 [44%]).

Conclusions: Anti-HBs level variations observed in some cases suggested a continuous balance between viral replication and host immune control. While OBI strains showed a higher genetic variability compared to non-OBIs, comparable rates of viral genetic changes over a relatively short period of time were observed in OBIs and non-OBIs. Mutations in critical domains of S proteins may participate to OBI genesis. Functional analysis and extended follow-up are needed to consolidate these preliminary data.

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P010

CHARACTERIZATION OF ACUTE PRIMARY OCCULT HEPATITIS B INFECTION IN ASYMPTOMATIC BLOOD DONORS INFECTED WITH HBV GENOTYPE C

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Background: Occult Hepatitis B virus infection (OBI) is categorized as seropositive (anti-HBc+ and/or anti-HBs+) or seronegative (anti-HBc-/anti-HBs-). Seronegative OBI carriers may have progressively lost anti-HBc and anti-HBs or have been negative for HBV antibody since the onset of infection. Few studies described acute primary OBI in subjects seroconverting to anti-HBc and/or anti-HBs without HBsAg reactivity. Viral mechanisms associated with this unusual condition remain elusive.

Purpose: Primary OBI was identified among HBV-infected blood donors. Serological and genetic characterization of the infecting HBV strains was performed to identify the mechanisms responsible for HBsAg non-detection.

Methods: OBI donors and HBsAg+ donors as controls were recalled and whole blood samples were collected. Serological markers were tested with CLIAs. Viral load was measured with qPCR (LoQ: 20 IU/mL). HBV genome was amplified and sequenced. Mutation-associated phenotypes were studied in transfected HuH7 cells.

Results: 497 out of 466,911 (0.11%) donors tested HBsAg-/HBV DNA+, and 184 (37%) were followed-up. Five seronegative donors aged 22-45y could be classified as acute primary OBI (2.7%) as they seroconverted to anti-HBc but never tested HBsAg reactive in 2-5 sequential blood samples collected over a period of 118 to 2202 days. They showed normal ALT levels (15-33 U/L) and intermittently detectable viral load (<20 IU/mL). Anti-HBc IgG were detected 91, 95, 118, and 160 days in four donors from index. One donor who has been vaccinated at the age of 20, had anti-HBs levels of 19 and 110 IU/L at 160 and 253 days post-index donation, respectively. One donor vaccinated at birth showed anti-HBs seroconversion (138 IU/L) but no anti-HBc at 180 days from index. Primary OBI strains were of genotype C and had a higher aa diversity in the S protein compared to HBsAg+ controls: median 11% vs 2.7 ($P<0.05$). No significant difference was observed compared to non-acute OBI strains. Two primary OBI S sequences showed 13 and 24 aa substitutions, including 9-10 unusual substitutions within the major hydrophilic region. No alteration of antigenic properties associated with mutations (positions s112-s120) was observed. Functional investigations of mutations in S promoters and in the s458 splicing donor site region are ongoing.

Conclusions: The existence of rare cases of primary acute OBI was confirmed. Preliminary genetic analysis suggested that mutations in S critical domains may participate to primary acute OBI genesis. Extremely low viral replication throughout the acute phase of the infection as the only factor accounting for undetectable HBsAg cannot be ruled out. Extended functional analysis is needed to consolidate the data.

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P011

DRIED BLOOD SPOT DBS: A NEW TOOL FOR THE DIAGNOSIS AND MONITORING OF HEPATITIS DELTA VIRUS INFECTION

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Background: Hepatitis D virus (HDV) infection is one of the major public health concerns around the world. Globally, an estimated 5 to 10% of chronic HBsAg carriers are co-infected with HDV. HDV infection can lead to a rapid disease progression towards cirrhosis and hepatocellular carcinoma. The diagnosis of HDV infection is crucial for its management. The dried blood spot (DBS) technique can be used to collect, store, and ship whole blood specimens. The objective of the present study is to assess the performance of standardized HDV diagnostic and monitoring tools in the analysis of DBS.

Methods: Paired plasma and whole blood specimens collected using the DBS technique from 97 patients were tested for virological markers used to diagnose and monitor HDV infection.

Results: Immunological assay detection of anti-HD antibodies in specimens from DBS was reliable after establishment of a new signal-to-cutoff ratio. HDV RNA was detected from DBS in the vast majority of patients with active replication, but HDV RNA levels were substantially lower than in plasma specimens. The mean HDV RNA detected in whole blood were 1.2 Log IU/disk less than those in plasma. HDV genotype determination was possible in DBS with a 100% concordance with results from plasma specimens.

Conclusion: This study showed that whole blood specimens collected can be used to diagnose and to monitor HDV infection. DBS sampling is a clinically relevant tool to improve access to Hepatitis D worldwide.

Disclosure of Interest: None Declared

P012

RIPK1 SCAFFOLDING PROPERTIES PROTECT HEPATOCYTES FROM TYPE-I-IFN-INDUCED APOPTOSIS IN A MOUSE MODEL OF HDV INFECTION

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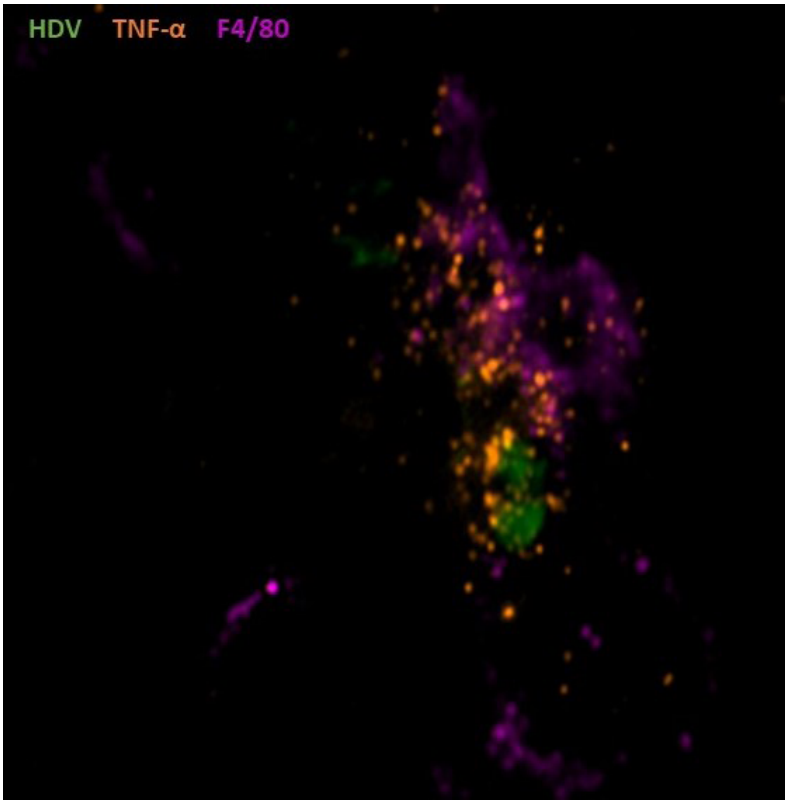
Background & Aims: Hepatitis delta virus (HDV) causes the most severe form of human viral Hepatitis. The underlying mechanisms involved in hepatocyte death or survival remain to be elucidated. We have recently developed a HDV mouse model that recapitulates most of the features of human infection including liver injury. Therefore, we took advantage of this model to investigate the role of different cellular/molecular players in HDV-induced liver damage.

Methods: The HDV mouse model was generated by the injection of adenoassociated viral vectors (AAVs) delivering both HBV and HDV genomes to the hepatocytes. *In situ* hybridization and immunohistochemistry were used to identify TNF-α producing cells and to detect HDV RNA. Molecular and cellular components potentially contributing to HDV-induced cell death or survival were identified using specific deficient or knockdown mice. Liver damage was determined by serological analyses, liver histology and immunohistochemistry analysis.

Results: Macrophages, which levels are significantly increased in HDV-infected mice, are the main source of TNF-α production. The scaffolding function of the receptor-interacting serine/threonine-protein kinase 1 (RIPK1) protects hepatocytes against caspase-8-mediated apoptosis, which we determined to be the main mechanism of liver cell death. Contrary to what we expected, neither TNF-α nor macrophages are involved in RIPK1-mediated protection. We found that type-I IFN plays a major role in HDV-induced apoptosis and that RIPK1 protects against this mechanism. Furthermore, in the absence of RIPK1, macrophage depletion resulted in HDV-induced severe liver damage and eventually death.

Conclusions: Here we show that HDV-induced type-I IFN production plays and important role in the induction of apoptosis in hepatocytes, and that RIPK1 scaffolding function plays a protective effect. Together with TNF-α, mainly produced by liver macrophages, they are responsible of HDV-induced liver damage. Furthermore, in the absence of RIPK1, HDV-induced severe liver damage is counteracted by liver macrophages supporting the potential use of monocytes to prevent acute liver injury.

Image/Table:



Disclosure of Interest: None Declared

P013

VIROLOGICAL DIAGNOSIS OF HEPATITIS DELTA VIRUS INFECTION IN FRANCE: RESULTS OF 10 YEARS-EXPERIENCE OF THE FRENCH NATIONAL QUALITY CONTROL

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Abstract Content: Virological diagnosis of Hepatitis Delta virus (HDV) infection in France, relies upon total HDV antibodies (t-Ab) detection and on plasmatic HDV-RNA viral load (HDV-VL) using a real-time quantitative RT-PCR assay. Detection of t-Abs means the patient is or has been infected with HDV, while HDV-RNA positivity confirms a replicative HDV infection. As previously shown, the high HDV diversity greatly impacts the performances of the molecular assays (Le Gal et al., 2016). In this study, we aimed to review the results of 10 years-experience of the annual French national quality control (FNQC) for the diagnosis of HDV infection in serology and molecular biology. Between 2012 and 2021, 4 panels of 4 serum samples with various antibody titers and 8 panels of 4 to 12 plasma samples of various VL and genotypes (HDV-1 and -5 to -8) were sent to all French laboratories for antibody detection (t-Abs and IgM-Abs) and HDV-VL quantification, respectively. Serological results of a laboratory were considered as "non-compliant" when one sample of the panel was not properly characterized. Similarly, when HDV-VL value for one sample differed by more than two standard-deviations from the mean value obtained by all laboratories, results were declared "to be monitored", and "non-compliant" for more than one sample. Twenty-three laboratories participated to the serological FNQC (14 for IgM-Ab). They all used the commercial ELISA kit ETI-AB-DELTAK-2 assay, and since 2018 the new LIAISON® XL MUREX anti-HDV of Diasorin. Six laboratories, then 13 participated to the molecular FNQC, using most of them used the Eurobioplex HDV kit. Serological results were concordant for >80% of the participants. For IgM-Ab, concordance ranged from 43% to 100%. HDV-VL results were consistent with those expected for 80% of the centers, and "to be monitored" and "non-compliant" in 10% of cases, each. Globally, the concordance rate varied between 45 and 100% with, however a significant improvement in results over the last 3 years (>=90%).

In conclusion, results of the serological FNCQ were largely satisfactory for all French laboratories, except for IgM antibody screening, which is no longer performed in practice. Growing satisfactory results are also obtained for plasmatic HDV-VL due to availability of a validated commercia kit. In addition, the use of a newly developed WHO HDV standard allows expression of the results in international units per milliliter. However, complete standardization is still needed, including nucleic acid extraction methods, test samples and elution volumes, packaging and storage of the standard range and its storage, real time RT-PCR devices.

Disclosure of Interest: None Declared

P014

HBV INFECTION IMPOSES A RESHAPING OF HOST CHROMATIN IMPACTING ON CELLULAR CHOLINE AND IRON METABOLISM

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Background and Aims: HBV remains a major health problem worldwide with 250 million people chronically infected and at risk to develop liver cirrhosis and hepatocellular carcinoma (HCC). A complex host-virus interaction is responsible for both HBV-specific T and B cells dysfunction and the persistence of the viral cccDNA mini-chromosome, the two key challenges for HBV cure. The extent of HBV impact on the liver transcriptome remains controversial. Transcriptional activation in eukaryotic cells has been tightly linked with disruption of nucleosome organization at accessible genomic sites of remodeled chromatin. We used ATAC-seq (Assay for Transposase Accessible Chromatin followed by high throughput sequencing) to probe open chromatin and detect early changes in chromatin accessibility in HBV-infected Primary Human Hepatocytes (PHHs).

Methods: HBV-infected PHHs (2h/72h) from 2 donors were used for ATAC-seq and analysis. The libraries were sequenced (75x2 cycles) on a NextSeq 500 Illumina.

Results: ATAC-seq analysis revealed an average of 2000 and 3500 cellular differentially accessible regions (DARs) at 2h and 72h post infection (p.i.) respectively, indicating that after HBV infection an increasing number of genomic sites (including promoters, intragenic and distal intergenic regions) change their chromatin accessibility over time. Overall, the regions with different chromatin accessibility were enriched in genes involved in metabolism (KEGG) and GSEA analysis revealed an important role of the chromatin regulating complex PRC2 complex at 72h p.i.Interestingly, the 1804 DARs, that are equally impacted by HBV infection in both the donors, enriched the pathway of choline metabolism in cancer, which affects PRC2 function. The integration of the ATAC-seq and RNA-seq data allowed us to identify 614 genes that had significant changes in both the analysis at 72h p.i.These targets confirmed the impact of HBV infection on liver metabolism, and revealed a strong involvement of the iron metabolism in the cellular response to HBV infection. We validated the expression of iron-related genes and we found that HBV infection significantly upregulated the iron uptake in the cells. Finally, using the iron chelator, Ferrostain-1, we showed that lowering the available iron levels, results in a drastic inhibition of viral replication.

Conclusion: Altogether these results challenge the commonly accepted concept of HBV as a "stealth" virus and show that HBV infection impacts on host cell chromatin landscape and specific transcriptional programs. In particular, HBV imposes a reshaping of key cell metabolic pathways (e.g., choline and iron metabolism). Finally, we showed that available iron levels impact on HBV replication.

Disclosure of Interest: None Declared

P015

THE IDENTIFICATION OF NOVEL HOST FACTORS REGULATING THE EARLY STAGE OF HEPATITIS B VIRUS LIFE CYCLE AS POTENTIAL ANTI-HBV THERAPEUTIC TARGETS

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Abstract Content: Hepatitis B virus (HBV) is a DNA virus, belonging to the Hepadnaviridae family. HBV is a partially double-stranded DNA virus with a small viral genome (3.2 kb). Chronic HBV infection remains a global health problem. If left untreated, chronic HBV infection can lead to end-stage liver disease complications, such as liver cirrhosis and hepatocellular carcinoma (HCC). Until now, there is no curative drug for HBV, this is a result of the persistence of the relatively stable covalently closed circular HBV-DNA mini chromosome in the nucleus. To identify host factors affecting the early phases of HBV life cycle, which can be targeted by novel anti-viral drugs, we previously performed functional screening by siRNA library transfection and screening for the effect of more than 2000 host genes on HBV infection. From this screening, we previously reported MafF and KIF4 as key regulators of HBV life cycle. Other host factors which significantly affected HBV life cycle and its mechanism will be presented in this meeting.

Disclosure of Interest: None Declared

P016

HUMAN PEG-INTERFERON SUBSTANTIALLY SUPPRESSED HBSAG EXPRESSION IN A TYPE I INTERFERON RECEPTOR-HUMANISED MOUSE MODEL

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Background & Aims: The underlying mechanism of chronic Hepatitis B virus (HBV) functional cure by interferon (IFN), especially in patients with low HBsAg or/and young ages, is still unresolved for lacking surrogate models. We aim to generate a type I interferon receptor humanised mouse and explore the possibility of viral HBsAg suppression by human IFN.

Methods: Through a CRISPR/Cas9-based knock-in strategy, we generated a type I IFN receptor-humanised mouse model (huIFNAR mouse) that expresses both human IFNAR1 and IFNAR2. Then, the tissue gene expression profile against human IFNa2 stimulation was analysed by next-generation sequencing. Finally, using the AAV-HBV model, we test the efficacy of PEG-IFNa2 in reducing viral HBsAg, HBeAg, and viral DNA both in the serum and liver and analyzed the immune profile alternations using flowcytometry and single-cell sequencing.

Results: First, human IFN stimulated a similar gene expression profile of huIFNAR peripheral blood mononuclear cells (PBMC) to what in human PBMCs, supporting the representativeness of the novel mouse model in functionally analysing human IFN in vivo. Second, we revealed a markedly tissue-specific gene expression atlas against human IFN treatment in the brain, blood, liver, lung, heart, spleen, kidney, muscle and intestine, which has been less appreciated in healthy humans in vivo. Third, fifteen-week human PEG-IFNa2 treatment significantly reduced HBsAg and HBeAg and even achieved HBsAg seroconversion. Finally, activation of intrahepatic Ly6C+ monocytes and effector memory CD8 T cells by human interferon might be critical for HBsAg suppression.

Conclusions: The novel huIFNAR mouse can authentically respond to human Interferon stimulation, providing a novel platform to study interferon function in vivo. The PEG-IFNa2 treatment successfully suppresses intrahepatic HBV replication and achieved HBsAg seroconversion in some mice.

Disclosure of Interest: None Declared

P017

HEPATITIS B VIRUS AND BEHAVIOURAL RISK AMONG BLOOD DONORS

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Background: In resource- limited setting, co-infection between HIV and Hepatitis B virus (HBV) poses important public health considerations. This cross-sectional study was undertaken with the aim of determining HBV seroprevalence patterns in urban blood banks.

Methods: A cross-sectional study was conducted at an urban blood bank setting. A total of 1610 blood donors were enrolled, and 283 consecutive plasma samples with unknown HBsAg status were selected for risks factors. HBV seroprevalence was based on the Chemiluminescence method (Cobas® e601, Roche). Potential risk factors associated with overt HBV infection were assessed by calculating the crude and adjusted odds ratio, 95% confidence intervalley (95% CI) and p values.

Results: Of 1610 participants, overall rate seroprevalence of HBsAg was 5.5% (95% CI: 4.36%–6.58%) ranging from 0.06% (95% CI: 0-0.18) (HCV) to 0.12% (95% CI: 0-0.30) (Syphilis). Seroprevalence of infection increased in older age groups (20-39 years) but men had a statistically significant higher prevalence of overt HBV infection than women (*P=0.0001*). The multivariate model showed the following to be predictors of HBV infection: male gender (OR=2.5 (95% CI 1.14-5.58), *P= 0.02*), first-time donor status (OR = 11.06, (95% CI 5.34-22.9), *P= 0.01*) and residence outside of Libreville (OR = 2.52, 95% CI 1.09-5.83), *P=0.03*).

Conclusion: HB and co-infection are n o t common in Gabon. Intermediate seroprevalence was associated with male gender, first-time donor status and residence outside of Libreville. HCV and HBV infection among the younger age groups are becoming an alarming issue. Prevention and control of HBV infection are needed to reduce HBV transmission.

Disclosure of Interest: None Declared

P018

HEPATITIS B SURFACE ANTIGEN LOSS IN CHRONIC HEPATITIS B VIRUS AND HIV CO-INFECTIONS IN INDIVIDUALS ON ANTIRETROVIRAL THERAPY IN BOTSWANA

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Background: Hepatitis b virus (HBV) is a global health issue with approximately 296 million people infected with chronic Hepatitis b (chb). Human immunodeficiency virus (hiv) and HBV co-infection is associated with worse clinical outcomes such as rapid progression to end stage liver disease. Antiretroviral therapy with anti-HBV properties may occasionally result in Hepatitis b surface antigen (hbsag) loss and supress HBV viral load among chb infected patients. There is currently no cure for HBV hence hbsag loss is the ideal endpoint of treatment due to improved clinical outcome. However, there is sparse data on hbsag loss among chb infected patients due to art in botswana. Therefore we sought to determine hbsag loss due to art and predictors of hbsag loss among chb infected people with hiv (pwh) in botswana.

Methods: This was a retrospective longitudinal study utilizing hbsag positive archived plasma samples from pwh at baseline and 2 time points from the botswana combination prevention project (bcpp).serology screening was done on baseline samples for immunoglobulin m for HBV core antibody (anti-hbc igm) and, HBV e-antigen (hbeag). Hbsag was screened 2 consequent time points. Participants with the hbsag loss were compared to those without using the wilcoxon rank-sum test and fisher's exact test where appropriate and p values <0.05 were significant. Logistic regression was used to determine predictors of seroclearance.

Results: Of the 141 hbsag positive participants with follow-up samples, (6/141) had acute HBV while 95.0% (134/141) [95 % ci, 90.1-97.6] participants had chb infection. However, only 42.6% (60/141) participants were screened for hbeag at baseline resulting in 10% (6/60) [95% ci, 4.7-20.2] participants testing positive for hbeag. Hbsag loss 7.1% (10/141) [95% ci, 3.9-12.6] was recorded among hbeag negative chb participants at year 1 with no further hbsag loss at year 2. Hbsag loss due to art was reported in 5.7% (8/141) participants, four of whom were on tenofovir, one on lamivudine containing art while the art regimen was not specified in three participants. We also report spontaneous hbsag loss of 1.4% (2/141) [95%ci, 0.4-5.0] in two participants. Hbsag loss was found to be independent of all clinical variables.

Conclusion: We report 5.7% hbsag loss due to art among chb infected participants who were hbeag negative. Hbsag loss was found to be independent of all clinical variables assessed. Monitoring of chb infected patients is recommended and future studies can be conducted on hbsag loss in mono-infected patients. Studies can also focus on the possible correlation between hbeag status and hbsag loss since all participants that lost the hbsag were hbeag negative.

Disclosure of Interest: None Declared

P019

DISTRIBUTION AND PREVALENCE OF HEPATITIS B VIRUS GENOTYPES IN HEPATITIS B INFECTED PATIENTS AND THEIR ROLE IN DISEASE SEVERITY – A RETROSPECTIVE STUDY FROM A TERTIARY CARE INSTITUTE IN INDIA

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Background: Hepatitis B virus (HBV) genotypes have significant association with progression of liver disease, risk of cirrhosis, viral load, HBsAg clearance and response to treatment which enables the physician to individualize the treatment and to identify potential sequelae after chronic HBV infection.

Purpose: The present study was undertaken to study the prevalence of different HBV genotypes and their correlation with clinical and virological markers.

Methods: In this retrospective study from 1st March 2012 to 31st August 2022, records of 846 HBV infected patients where a genotyping request was received in the Department were obtained from the hospital information system.

Results: Out of 846 samples, in 445 (52.6%) genotyping could be done where the DNA load was > 2000 IU/ml. Mean age was 42.45 +15 yrs., male: female ratio was 4.05. Median viral load was 2.13 x 10^4 (IQR: 4.9 x 10^3 - 3.38 x 10^6) IU/ml. Out of these 23 (5.16%) were cirrhotic. Most predominant genotype was D (n= 357, 80.22%), than genotype A (n=75, 16.86%), genotype C (n= 11, 2.48%), genotype B (n=1, 0.22%), genotype I (n=1, 0.22%).

On comparing genotype D with genotypeA : median viral load in genotype D was 2.84 x10^4 (IQR: 4.98 X 10^3 - 4.35 x 10^6) IU/ml where as in genotype A median viral load was 8.69 x10^3 (IQR: 3.9 X 10^3 - 2.62 x 10^5) IU/ml, (p =0.07). HBsAg levels in genotype D were 8835 (0.02-125000) IU/ml, where as in genotype A were 13503 (145-125000) IU/ml, (p = 0.06). HBe antigen positivity in genotype D was 27.45% (n=98), and in genotype A it was 29.33% (n=22), p = 0.8. Median Serum ALT levels in genotype D were 50 (0.4-2664) IU/L and in genotype A were 50.5 (10-1021) IU/L, p =0.97. Median Serum bilirubin levels in genotype D were 0.91 (0.1-37.4) mg/dl and in genotype A were 0.8 (0.3-12.5) mg/dl, p =0.08. Cirrhosis was seen in 17 (4.76%) cases of genotype D and in 5 (6.66%) cases of genotype A. Median Ishak HAI (Histological activity index) in genotype D was 3 (1-11) and in genotype A it was 4 (2-9), p=0.89. Median Fibrosis score in genotype D was 1 (0-6) and in genotype A it was 1 (1-6), p=0.57.

Conclusion: In this study, D was the predominant genotype. On comparing genotype D with genotype A both caused similar disease in terms of virological markers and clinical presentation.

Disclosure of Interest: None Declared

P020

B CELL INVOLVEMENT IN HBSAG (HEPATITIS B VIRUS SURFACE ANTIGEN) SEROCLEARANCE IN PATIENTS WITH CHRONIC HEPATITIS B (CHB).

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Background and Aims: Hepatitis B Surface antigen (HBsAg) seroclearance, the development of antibodies against HBsAg, is associated with a better outcome for Chronic Hepatitis B (CHB) patients. The aim of the study was to characterize the B cells phenotype and associated-inflammatory cytokines profile and Toll-like Receptor 9 (TLR-9) expression in peripheral blood mononuclear cells (PBMCs) and plasma from patients with CHB who lost HBsAg (HBsAg-) as compared to patients with HBsAg and healthy controls.

Method: Patients who lost HBsAg, treated and untreated CHB patients were recruited in Beaujon Hospital along with controls, cured HCV patients. Peripheral blood mononuclear cell (PBMC) and plasma were isolated from the whole patient's blood. TNFα, IL-10 and IFNγ cytokines' levels was analyzed in the plasma of those patients using ELISA. B cell phenotype was identified using flow cytometry and TLR9 protein expression was studied using western blot.

Results: 14 HBsAg- patients were recruited and 51 HBsAg+ patients (40 untreated and 11 nucleoside analogues-treated) and 15 healthy controls. HBsAg- patients had a significant increase and restoration in the percentage of plasma B cells (CD19+, CD27+, CD38hi) compared to those with CHB was observed (0.502$\pm$0.12 and 0.83$\pm$ 0.107, p<.0001). On the other hand, a significant decrease in the percentage of atypical MBC (CD19+ CD10+ CD27- CD21-) in HBsAg-patients was found (5.9$\pm$2.06 and 2.8$\pm$0.91, p<.0001). Also, a significant decrease in the levels of TNFα (15.99$\pm$2.83 pg/ml and 12.07 $\pm$ 1.46 pg/ml, p<0.05) and IL-10 (10.8 $\pm$ 2.9 pg/ml and 8.05 $\pm$ 1.67 pg/ml, p<0.05) in HBsAg- patients compared to patients with CHB. A similar tendency in the case of IFNγ was seen, however it wasn't significant (37.65 $\pm$ 5.88 pg/ml and 33.15 $\pm$ 2.52 pg/ml, p>0.05). Interestingly, TNFα and IFNγ levels were decreased in treated patients compared to those untreated (15.99 $\pm$2.83 pg/ml and 11.14 $\pm$ 1.4 pg/ml, p<0.0001 and 37.6$\pm$5.8 pg/ml and 27.5$\pm$9.4 pg/ml, p<0.05 respectively). Finally, TLR9 expression was restored at the protein levels in HBsAg- patients in total PBMC extracts compared to CHB patients (0.7077$\pm$0.23 and 0.87 $\pm$0.2, p<.05).

Conclusion: A restored cytokine environment in HBsAg- patients characterized by a decrease in TNFα and IL-10 plasma levels was observed. A remodeling in B cells subsets was characterized by an increase in plasma B cell percentages and a decrease in atypical MBC that are usually high in CHB patients. Finally, TLR9 expression was restored upon HBsAg loss. A study of B cell functionality in HBsAg (-) patients will be subsequently conducted to better characterize B cell response when HBsAg is lost.

Disclosure of Interest: None Declared

P021

SITE DIRECTED MUTAGENESIS FOR AMINO ACID SUBSTITUTION IN HEPATITIS B VIRUS REVERSE TRANSCRIPTASE TO EVALUATE GAIN IN FUNCTION AND ITS POSSIBLE ROLE IN VIRUS BREAKTHROUGH

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Background: Chronic Hepatitis B (CHB) patients require long-term antiviral therapy to prevent disease progression to cirrhosis, liver failure, hepatocellular carcinoma and death. Current drug tenofovir and entecavir are highly potent to drug resistance and virus breakthrough during therapy. Before availability of these two drugs, patients were treated with lamivudine/adefovir/telbividune. We have characterized HBV RT region of previously treated compliant patients switched to tenofovir therapy. The functional gain of novel mutations detected by sanger sequencing was evaluated by site directed mutagenesis and reverse transcriptase activity.

Methods: The RT region of HBV DNA was PCR amplified from 12 patients experiencing virological breakthrough to tenofovir therapy. The PCR amplified product was sanger sequenced, genotyped. The deduce amino sequence was aligned for detection of novel mutation. The RT region was cloned in pcDNA vector and mutations were incorporated. Functional activity of mutant and wild type evaluated using EnzCheck Reverse transcriptase activity.HBV RT was model using PDB structure of MMLV RT for topological position of novel mutation.

Results: We did not observe primary drug resistance mutations (rtA181, rtM204 and rtN236), for Tenofovir therapy. We observe novel mutations (rtS256C and HBV rtW257Y) at domain E of HBV RT. To study functional significance, pcDNA HBV RT with seven mutations (YMDD deletion, N236T, A181T, N248H, L91I, Y257W, C256S) was generated. The HBV RT transfected cell lysate have shown gain in RT functions in fluorescence assay. Topological position of two amino acid are external whereas rest are in the internal to palm motif which may have functional relevance.

Conclusion: HBV breakthrough to Tenofovir therapy was seen in patients without primary drug resistance mutations. However secondary mutations may increase in RT activity with possible role to confer drug resistance.

Disclosure of Interest: None Declared

P022

ESTIMATION OF THE TIME TO THE MOST RECENT COMMON ANCESTOR: TRACING THE EVOLUTIONARY HISTORY OF HEPATITIS B VIRUS GENOTYPE H ENDEMIC TO MEXICO

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Background: Hepatitis B virus (HBV) continues to spread efficiently among all human populations worldwide. Currently, HBV is classified into 10 genotypes (A to J) that have their own geographic distribution and clinical features. In Mexico, HBV genotype H is the main cause of Hepatitis B and has been detected in indigenous populations, suggesting that HBV genotype H may be native to Mexico. However, little is known about the evolutionary history of HBV genotype H.

Objetive: This study aimed to determine the age of HBV genotype H in Mexico using a molecular dating technique.

Material and Methods: A total of 92 HBV reverse transcriptase domain of polymerase sequences (~1251 pb) were analyzed, from them, 48 were genotype H, 42 were genotype F, and the oldest HBV sequence from America was included as root. All sequences were aligned, and the time of the most recent common ancestor (tMRCA) was calculated using the Bayesian Skyline Evolutionary Analysis.

Results: Our results estimate a tMRCA for the genotype H in Mexico of 2175.0 (899.0-6089.5) years before the present (YBP). We identified that genotype H has experienced four major diversification events, named H1, H2, H3, and H4. H1 diverged from the rest about 1496.7(690.7-4171.6) YBP, followed by H2 (1450.2(734.9-3852.4)) YBP, H3 (1221.3 (507.4-3641.0)) YBP, and H4 (1208.3(559.6-1877.4)) YBP. We estimated that HBV genotype H diverged from its brother genotype F around 5674.4 (2730.3-15267.5) YBP.

Conclusions: This study found that HBV genotype H in Mexico has an estimated age of 2175 (899.0-6089.5) YBP and has experienced at least four major diversification events since then.

Disclosure of Interest: None Declared

P023

DEVELOPMENT AND CHARACTERIZATION OF AN RNA MOLECULAR STANDARD FOR THE CALIBRATION OF CIRCULATING HBV RNA ASSAYS IN CHB PATIENTS

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Background: The quantification of serum HBV RNA (mostly, but not exclusively, 3.5 kb RNAs) is increasingly recognized as a biomarker to evaluate HBV treatments activity and predict patient outcomes. In untreated patients, serum HBV RNA reflects cccDNA transcriptional activity. In addition to several homemade assays, 2 PCR-based research use only (RUO) investigational assays (IA) have been developed. These assays used either the WHO HBV-DNA standard or a synthetic armored RNA (arRNA) for calibration. We have generated a stable clonal cell line producing large quantities of secreted viral RNAs amenable to be used as an RNA standard to calibrate PCR-based circulating HBV RNA quantification assays.

Methods: HBV RNA producing Huh7-derived stable cell lines were generated by transfecting pTriEX plasmids containing 1.1 length HBV DNA genomes carrying mutations that are expected to strongly reduce / abolish HBV rc-DNA synthesis (YMAA in the Pol catalytic site, in the the polymerase TP-domain, A1G in the pgRNA ε-loop).

Results: The clonal cell line Huh7-3D29, carrying the double YMAA/Y63F mutation, displayed the desired RNA secretory phenotype with a stable high RNA/DNA ratio in cell supernatants and minimal residual DNA (~5 $\log_{10}$). Supernatants of Huh7-3D29 and the control Huh7-WT18 cell lines were analyzed by iodixanol/sucrose density gradient ultracentrifugation followed by HBsAg quantification by ELISA, HBV DNA and total HBV RNA quantification by ddPCR, HBc and CD9 detection by Western blot in each fraction. In Huh7-3D29 cells, the HBV RNA was found in RNA particles, in naked capsids and to a lower extent in exosomes, whereas the residual HBV DNA peak was found in virions. Notably, as compared to the Huh7-WT18 cell, a larger proportion of HBV RNA was found in naked capsids. The analysis of the RNA species secreted by the control Huh7-WT18 and mutant Huh7-3D29 clones by single molecule long reads Nanopore sequencing showed that the majority of HBV RNAs detected are full-length transcripts and pgRNA-derived spliced RNAs, whereas only a minority of PreS/S RNAs and HBx RNAs were detected. Huh7-3D29 SNs were then tested as a calibrator for Roche HBV RNA investigational assays (doi: 10.1016/j.jcv.2022.105150). Serial dilution experiments indicate that Huh7-3D29 SN performs as the synthetic arRNA. Finally, Huh7-3D29 cells showed a high, constant, and easily up-scalable yield of secreted HBV RNAs (1,300 standard curves in 9 days from one 175 cm2 flask).

Conclusion: We generated and characterized a clonal cell line that secretes high amounts of HBV RNAs with very low quantities of HBV DNAs, representing a stable source of RNA standard for the calibration of all the HBV RNA assays.

Disclosure of Interest: None Declared

P024

PREVALENCE AND MOLECULAR CHARACTERISATION OF HEPATITIS B VIRUS IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF HIV POSITIVE ADULTS IN BOTSWANA: HBV LYMPHOTROPISM

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Background: Hepatitis B virus (HBV) is a hepatotropic virus but has been reported to be lymphotropic. HBV genomes and proteins have been found in extrahepatic sites such as peripheral blood mononuclear cells (PBMC). It has been reported that the prevalence of HBV in PBMC is 32.6%. HBV in PBMCs plays a role in vertical transmissions, re-infection of liver transplant recipients and occult HBV infection (OBI) where HBV deoxyribonucleic acid (DNA) is detected in serum/liver of HBV surface antigen (HBsAg)-negative patients and can remain detectable at low levels resulting in OBI persistence. HBV lymphotropism is an understudied area including in Botswana. We therefore sought to investigate the prevalence of HBV in PBMCs of HBV/ human immunodeficiency virus (HIV) co-infected individuals in Botswana.

Methods: The study utilized a total of 29 pre-screened achieved HBV positive entry visit participant samples of PWH from a previous study, Bomolemo, initiating a Truvada based regimen in Botswana between 2009 and 2012 (28 HBsAg positive and 72 OBI positive). HBV DNA from PBMC's were extracted using Qiagen DNA extraction kit and Real-time polymerase chain reaction (qPCR) was used to detect the HBV surface gene. The HBV VL was obtained from plasma samples of the same participant. Fishers exact test was used to compare categorical variables between participants that showed HBV lymphotropism versus those who did not while Wilcoxon rank-sum test was used for continuous variables. STATA v14.1 was used for statistical analysis and p-values less than 0.05 were considered statistically significant.

Results: There were 75.9% females (n=22) and 24.1% males (n=7) with the median CD4+ T cell count of 71 [86-233] (cells/mm^3), and log HIV viral load (logVL) of 5.01 [4.68-5.40] (copies/mL). About 13.8% (n=4) participants had plasma HBV DNA below detection threshold (TND), 75.9% (n=22) had VL <20,000, while 10.3% (n=3) had VL>20,000 (copies/mL). Out of 29 participants, 5 (17.2%) [95% CI: 5.8 – 35.8] showed HBV lymphotropism of which 2 out of 5 where OBI and 3 were HBsAg positive. There was no statistically significant difference between HBV lymphotropic participants vs non-HBV lymphotropic participants in gender, age, HBV VL, CD4+ T cell count, HIV VL, alanine aminotransferase (ALT), aspartate aminotransferase (AST), platelet ratio index (APRI) and fibros-4 (FIB4).

Conclusion: This study reports for the first time, the presence of HBV within PBMCs in Botswana in both HBsAg and OBI positive participants. Further studies in implications of HBV lymphotropism especially in immunocompromised individuals in Botswana are warranted.

Key words: Hepatitis B virus, prevalence, lymphotropism, peripheral blood mononuclear cells, Botswana.

Disclosure of Interest: None Declared

P025

OCCULT HEPATITIS B INFECTIONS AMONG PEOPLE LIVING WITH HIV IN RURAL AND PERI-URBAN COMMUNITIES IN BOTSWANA

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Background: Occult Hepatitis B virus (HBV) infections (OBI), characterised by the detection of replication competent HBV deoxyribonucleic acid (DNA) in the serum or liver of HBV surface antigen (HBsAg) negative individuals often go unreported in national HBV reports. OBI have clinical relevance such as vertical transmission, HBV reactivations particularly in immunocompromised individuals, drug resistance and hepatocellular carcinoma. We aimed to determine the prevalence of OBI among people living with HIV (PLWH) from rural and peri-urban communities in Botswana.

Methods: Archived Hepatitis B surface antigen (HBsAg) negative plasma samples of PLWH from 30 geographically dispersed villages in Botswana from a previous study, Botswana Combination Prevention Project (BCPP) were used. The samples were collected between 2013-2018 and were from participants aged 16-64 years of age. HBV DNA was quantified using the COBAS® AmpliPrep COBAS® Taqman®, HBV Test v.2.0 following the manufacturer's instructions with a lower limit of detection of 20 IU/mL and higher limit of detection of 170000000IU/mL. Participants demographics and HBV serological markers were retrieved from the parent study databases. Chi-square test and Wilcoxon rank-sum test were used to compare categorical and continuous variables, respectively, between OBI infected and uninfected participants. P-values less than 0.05 were considered statistically significant.

Results: A total of 381 HBsAg negative participant samples were screened for HBV DNA, and 126 [33.1% (95% CI: 28.5–37.9)] had detectable were OBI positive. DNA. Of those with detectable HBV DNA, 85/126 (67.5%) had HBV DNA levels <20IU/mL while the rest had HBV DNA levels ≥20IU/mL. One participant had a viral load of 7,874,196IU/mL. The participant was an antiretroviral therapy (ART)-naïve female aged 53 years with an HIV viral load of 1,505,646cps/mL. A total of 118 participants with OBI had HBV core antibodies (anti-HBc) results and 67/118 (56.8%) were positive for the anti-HBc while the remaining 43.2% were negative for anti-HBc. There was no statistically significant difference between OBI infected and OBI-uninfected participants in gender, age, nadir CD4+ T-cell count, log HIV viral load, ART status, ART type and duration on ART.

Conclusions: We note a high OBI prevalence of 33% among PLWH in understudied regions in Botswana, a first report in most of these communities. This is among the highest OBI prevalence rates in the region. OBI remains a source of transmission in the populations as high viral load OBI cases are present. Therefore, efforts towards identification and reporting of OBI are needed to contribute towards elimination of viral Hepatitis.

Disclosure of Interest: None Declared

P026

KINETICS OF VIROLOGICAL MARKERS AND LIVER ENZYMES OF CHRONIC HEPATITIS B VIRUS INFECTION DURING PREGNANCY AND POSTPARTUM

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Background and Purpose: Immunological changes occurring during pregnancy and postpartum may affect the natural history of chronic Hepatitis B (HBV) infection. The new HBV virological markers provide an unique opportunity to study in detail viral kinetics; however data during pregnancy is scarce. The aim of our study was to analyze the impact of pregnancy on infection control by analyzing changes in liver tests and viral markers longitudinally during pregnancy and in the postpartum.

Methods: Pregnant women with chronic Hepatitis B prospectively followed in our outpatient clinic between 2018 to 2021 were included. A control group of pregnant patients without HBV infection and matched by age was included. Monitoring was performed during the second and third trimester of pregnancy and at 6 and 48 weeks after delivery. Liver tests and viral markers including HBV-DNA, qHBsAg and HBcrAg, were analyzed at the different time points.

Results: Twenty-two patients and nine non-HBV controls were included. The median age was 34(30-39) years old and 45% were from Asia. Regarding the HBV disease phase, 86% were HBeAg-negative chronic infection, 9% HBeAg-positive chronic infection and 5% were HBeAg-negative chronic Hepatitis. Three pregnant women (14%) required antiviral therapy in order to prevent vertical transmission. In those not accomplishing treatment criteria during pregnancy, qHbsAg levels increased 6 weeks after delivery compared with the third trimester in 80% (median 2900 IU/mL vs 4820 IU/mL; p<0,01). The latter was not associated with a concomitant significant increase in DNA-HBV levels. HBcrAg values were positive in 54% patients (median 4log/mL) and remained stable during pregnancy and postpartum. In the three treated patients, a significant decrease in HBV-DNA was observed but no changes in qHBsAg and HBcrAg occurred. At 6 weeks after delivery, 4 patients (18%) presented an ALT flare (increase 2 times baseline value) compared to no patient in the control group. It is important to remark that two patients (9%) in the HBeAg-negative chronic infection phase for more than 5 years, achieved functional cure at 4 and 18 months after delivery,. All newborns received anti-Hepatitis B vaccine and immunoglobulin, and no cases of vertical transmission were detected.

Conclusions: Our data suggests a lower HBV viral control after delivery (increase in qHBsAg levels), which could be explained by an immune tolerance state associated during pregnancy and early postpartum. Afterwards, once immune reconstitution has occurred, there might be a higher chance of achieving functional cure. Changes in the virus-specific immune response in this cohort are currently under analysis.

Disclosure of Interest: None Declared

P027

QUANTITATIVE HBV/HDV MARKERS HELP TO DISTINGUISH DIFFERENT CLINIC/VIROLOGIC PHASES OF CHRONIC HEPATITIS DELTA

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Introduction and Aim: New therapy options for Chronic Hepatitis delta (CHD) urge a better clinic/virologic stratification of patients (pts). We quantified HDV/HBV markers to investigate their correlation with disease activity/stage in untreated and Interferon(IFN)-treated pts.

Methods: 146 consecutive anti-HDV+ pts admitted at Pisa University Hospital were classified in 4 groups based on biochemical/histological/imaging data: 1.Pts. without liver disease (no-CHD) [persistent ALT<40U/L, LS<6kPa]; 2.CHD w/o cirrhosis;3.CHD with cirrhosis;4.CHD with advanced cirrhosis (varices/decompensation/HCC). Quantitative(qt) HDV-RNA (RoboGene Kit 2.0; Bio-Rad Laboratories), anti-HDV (LiaisonXL Murex anti-HDV, DiaSorin) and HBV markers (HBVDNA/HBsAg/HBcrAg/IgG anti-HBc) were tested at baseline(BL); 31/146(21.2%) received IFN-treatment during follow-up(FU). Virologic response was defined by qualitative (ql) HDV-RNA (in-house-PCR) at end-of-therapy(EOT), 6-months after EOT (6mFU) and at end-of-FU (EOF). HBV/HDV markers were quantified at the same timepoints.

Results: Table 1 shows the main characteristics of 146 anti-HDV+pts at BL:11(7.6%)pts were no-CHD, all of them had positive qtHDV-RNA, with serum levels (sl)<1000 IU/mL in 10/11 (90.9%). Among 135 CHD pts, qtHDV-RNA was higher in pts with cirrhosis compared to those without and among cirrhotics declined in the advanced compared to early stage. All no-CHD subjects had anti-HDV titer≤1:100, while 132/135 CHD pts(97.8%) had anti-HDV≥1:1000. At multivariate, HDV-RNA [OR=1.816, P=0.007],anti-HDV [OR=4.429, P=0.012] and IgG anti-HBc [OR=3.260, P=0.041] were associated with higher disease activity(ALT>100 U/L); Age[OR=1.059, P=0.032] and HDV-RNA [OR=1.643, P=0.006] with cirrhosis. Of 31 IFN-treated-pts [median duration 12.4 (2.0/91.7)months],15(48.4%) were non-responders, 13(41.9%) had undetectable qualitative HDV-RNA at 6mFU (9/13 with qtHDV-RNA <6IU/mL), 3 relapsed (9.7%). After a median FU of 4.6(1.3-18) years,14 pts had undetectable qualitative HDV-RNA and normal ALT: all of them had detectable qtHDV-RNA<1000 IU/mL [median HDV-RNA 1.70 (0.85/2.34)LogIU/mL] and 12/14 (85.7%)anti-HDV≤1:100. The remaining CHD pts at EOF had HDV-RNA>1000 IU/mL and anti-HDV≥1:1000 in 92.3% and 100% of cases, respectively.

Conclusions: In CHD pts HDV-RNAsl independently correlate with biochemical activity and stage of liver disease. HDV infection can persist without active liver damage in a status, either spontaneously-acquired or IFN-induced, characterized by low levels of viral replication (HDV-RNA<1000 IU/mL) and anti-HDV titer (≤1:100). The quantitative analysis of HDV/HBV markers qualifies as a useful tool for clinic-virological classification and treatment monitoring of CHD pts.

Image/Table:

Table 1:

	A	B	C	D	*P values*		
	no-CHD n=11	**CHD without cirrhosis n=24**	**CHD with cirrhosis n=73**	**CHD with Advanced Cirrhosis n=38**	*A vs B+C+D*	*B vs C+D*	*C vs D*
Age (yrs)	34.7 (22.2/70.3)	39.7 (17.9/54.4)	42.3 (19.1/69.1)	51.8 (25.0/71.7)	0.906	*0.062*	**0.005**
LS (kPa)	5.2 (3.4/6.0)	7.0 (4.3/12.0)	16.0 (7.0/69.0)	23.5 (11.1/66.4)	**<0.001**	**<0.001**	**<0.001**
ALT (UI/L)	17 (10/40)	75 (12/194)	73 (5/500)	62 (26/206)	**<0.001**	0.364	*0.087*
HDV-RNA (Log IU/mL)	2.28 (0.82/4.14)	4.39 (0.70/6.75)	5.55 (0.70/7.73)	4.81 (0.70/6.48)	**<0.001**	**0.002**	**0.008**
Anti-HDV (< / ≥ 1:1000)	11 (100) -	- 24 (100)	3 (4.1) 70 (95.9)	- 38 (100)	**<0.001**	0.959	0.516
HBsAg (Log IU/mL)	2.88 (-1.40/3.53)	3.90 (1.59/4.59)	3.90 (-1.40/4.57)	3.90 (-1.40/4.50)	**<0.001**	0.993	0.234
HBV-DNA (Log IU/mL)	1.00 (0.70/3.87)	1.28 (0.70/7.61)	1.24 (0.70/5.94)	1.53 (0.70/5.34)	0.912	0.363	0.447
HBcrAg (Log IU/mL)	2.00 (2.00/3.00)	3.47 (2.00/6.97)	3.60 (2.00/7.19)	3.69 (2.0/6.17)	**<0.001**	0.930	0.859
Anti-HBc IgG (Log COI)	278.6 (23.0/2314.0)	265.8 (29.2/2355)	158.9 (7.7/2679)	152.9 (7.0/841.0)	0.333	*0.065*	0.265

Disclosure of Interest: None Declared

P028

CONSTRUCTION OF A CIRCRNA-MIRNA-MRNA REGULATORY NETWORK REVEALS POTENTIAL MECHANISM AND TREATMENT OPTIONS FOR HEPATITIS B VIRUS (HBV) SUBGENOTYPES C2

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Background: Hepatitis B virus (HBV) is one of the major public health problems worldwide and a major pathogenic factor of hepatocellular carcinoma (HCC). HBV has at least 10 genotypes (A to J) and 40 subgenotypes with different geographical distributions, HBV/C2 is presently the major sub-genotype in China. Recently, Circular RNAs (circRNAs) have received increasing attention for their involvement in tumorigenesis and metastasis of HCC. However, the role of circRNAs in HBV/C2-related HCC remains unclear.

Purpos:e The purpose of this study is to uncover circRNAs and their molecular mechanism in HBV/C2-infected Huh7 cell, and to explore some potential biomarkers for HBV-reated HCC.

Metho:d Huh7 cell stably transfected with pcDNA3.1(+)/HBV-C2 were performed RNA-seq. After data preprocessing, differentially expressed (DE) circRNAs (DECs), miRNAs (DEMs) and genes (DEGs) between Huh7-HBV/C2 and Huh7 were obtained using DESeq2 package,Q value$\leq$ 0.05 and the absolute value of Log2 Fold change (2FC) $\geq$ 1 as the default threshold to judge the significance of expression difference. CircRNA-miRNA interactions and miRNA-mRNA interactions were determined by Circular RNA Interactome (CircInteractome) database and microRNA Data Integration Portal (mirDIP) database, respectively. Cytoscape 3.8.2 software was used to visualize the established ceRNA regulatory network. Function enrichment analysis of miRNA and mRNA was performed by DIANA-miRPath v3.0 and Metascape database, respectively. mRNAs with significant prognostic value were identified based on Kaplan-Meier Plotter HCC database.

Results: Significantly DECs, DEMs and DEGs between Huh7-HBV/C2 and Huh7 were identified. Among them, the top 10 DECs were selected to further analysis. Then, 25 pairs of circRNA-miRNA interactions and 514 pairs of miRNA-mRNA interactions were identified, function enrichment analysis indicated that these miRNAs and mRNAs in the network were involved in the process of viruses and tumorigenesis response. A ceRNA network of hsa_circ_0003812-hsa-miRNA -29c-3p-DLG2 was constructed. Overall survival analysis showed that poorer survival rate for liver cancer patients was with low DLG2 mRNA.

Conclusio:n In conclusion, the identified ceRNA interaction axis may be crucial targets for the treatment of HBV/C2-related HCC and might assist in the development of diagnostic and/or therapeutic targets for HCC.

Disclosure of Interest: None Declared

P029

IDENTIFICATION OF SHUTTLE PROTEIN HNRNPA1 AS A MODULATING FACTOR OF CIRCULATING HEPATITIS B VIRUS RNAS RELEASE IN CHRONIC HEPATITIS B PATIENTS

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Abstract Content: Circulating HBV RNA (CirB-RNA) reflects the transcriptional activity of the intrahepatic cccDNA, thus representing a promising non-invasive serum biomarker for the reduction or inactivation of cccDNA pool. Although several studies have pointed out the significance of cellular releasing mechanisms to determine the composition of these RNAs, the specific regulators of the shuttle machinery involved remain largely unknown.

Expression of candidate CirB-RNA shuttle proteins were analyzed by Western Blotting and RT-qPCR in cell lysate and supernatant from HBV-infected HepG2-NTCP cells and Primary human hepatocytes (PHHs). Shuttle protein interaction with CirB-RNAs was investigated by RNP-IP(Ribonucleoprotein-Immunoprecipitation) and Biotin pull down assay. Adapted Iodixanol/Sucrose density ultracentrifugation allowed to isolate exosome-enriched fractions from sera of 5 untreated [2 HBeAg(+) and 3 HBeAg(-)], 2 HBeAg(-) chronic infection and 2 NUC-treated chronic Hepatitis B (CHB) patients.

Among the RNA-binding proteins analyzed, heterogeneous nuclear ribonucleoprotein A1 (hnRNPA1) expression was increased in both cell lysates and supernatants of HepG2-NTCP cells and PHHs upon HBV infection, via a HBx-dependent mechanism. hnRNPA1 was detected in the serum of CHB patients and, after density ultracentrifugation of serum samples, hnRNPA1 was mostly detected in the exosome-enriched fractions. Loss-of-function studies in HepG2-NTCP cells indicated that hnRNPA1 downregulation was associated to reduce secretion of CirB-RNA in exosome fractions. Anti-CD9 and anti-CD81 IP confirmed the association between hnRNPA1 and exosomes. RNP-IP experiments revealed that hnRNPA1 was able to bind to 5' region of 3.5Kb RNA and to the 3' region common to all HBV transcripts. Specific binding sites for hnRNPA1 on HBV RNAs were mapped by Biotin pull-down assays.

Altogether, our data suggest that hnRNPA1 directly binds to HBV RNAs and can function as a novel direct and indirect contributor to CirB-RNA shuttling mechanisms in chronically infected patients.

Disclosure of Interest: None Declared

P030

GENETIC DIVERSITY OF HEPATITIS B VIRUS QUASISPECIES IN DIFFERENT BIOLOGICAL COMPARTMENTS REVEALS DISTINCT GENOTYPES

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Background: The selection pressure imposed by the host immune system impacts Hepatitis B virus (HBV) quasispecies variability. Previous studies have demonstrated the applicability of dried blood spot (DBS) and oral fluid samples as convenient alternatives for HBV detection. They are less invasive, easier to collect, require minimal training, and may be useful for accessing HBV diversity in settings where blood collection is difficult. However, little is known about HBV diversity in these different fluids in the same host.

Purpose: This study aims to evaluate HBV genetic diversity in different biological fluids to understand the compartmentalization of virus in the host.

Methods: Twenty paired serum, oral fluid, and DBS samples from chronic HBV carriers who had complex viral molecular profiles (more than 2 nonsynonymous mutations) in previous studies were collected. HBV DNA was extracted from different samples using commercial assays based on silica column. For HBV amplification, optimized PCR was performed using oligonucleotides for the overlapping S/polymerase gene (~900 base pairs). After amplification, samples were submitted to both Sanger and next generation sequencing (NGS). Viral load was measured using commercial Taqman assay.

Results: Mean HBV viral load in serum was 5.19 $\pm$ 4.3 log IU/mL. Genotype distribution was: HBV/A1 55% (11/20), A2 15% (3/20), D3 10% (2/20), F2 15% (3/20), and F4 5% (1/20). Genotype agreement between serum and oral fluid was 100% (genetic distances: 0.0-0.006), while that between serum and DBS was 80% (genetic distances 0.0-0.115). Two individuals presented discordant genotypes in serum and DBS. Minor population analysis revealed a mixed population. All samples displayed mutations in polymerase and/or surface genes. Major population analysis of the polymerase pointed to positions H122 and M129 as the most polymorphic ($\geq$75% variability), followed by V163 (55%) and I253 (50%). Neither Sanger nor NGS detected any antiviral primary resistance mutations (major population). Minor population analysis, however, demonstrated the rtM204I resistance mutation in all individuals, ranging from 2.8 to 7.5% in serum, 2.5 to 6.3% in oral fluid, and 3.6 to 7.2% in DBS.

Conclusions: This study demonstrated that different fluids can be used to assess HBV diversity, nonetheless, genotypic differences according to biological compartments can be observed.

Disclosure of Interest: None Declared

P031

HEPATOMA CELL LINE ALLOWING EFFICIENT REPLICATION OF HEPATITIS B/C/D/E VIRUSES CAN BE A RELEVANT MODEL FOR DRUG SCREENING

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Abstract Content: The liver can be infected by several viruses such as Hepatitis B (HBV), Hepatitis D (HDV), Hepatitis C (HCV), Hepatitis E (HEV) viruses, leading to end-stage liver diseases. Cases of multiple infections have been reported especially in low-income countries. Currently, only HCV infection can be cured with antivirals. Although, the 4 viruses replicate into the same cell type (the hepatocyte), few data are available about their replicative interplay in case of multi-infections. We therefore engineered an HuH7.5-NTCP cell line, that can be partially re-differentiated into hepatocyte with particular cell culture conditions, and showed it can replicate the 4 viruses for at least 3 weeks. To determine if this cell line can be used to screen for novel broad antivirals, we tested several known antivirals in mono-infections conditions. We observed a strong antiviral effect of IFN-α on HCV, HDV and HEV, but not on HBV in this model. We confirmed the antiviral effect of RG7834 (an inhibitor of PAPD5/7, involved in the A/G-mixed tailing of RNAs) on HBV and showed that it additionally decreased HCV and HEV RNA levels, while increasing that of HDV. Interestingly, whereas we confirmed the antiviral effect of an FXR-agonist (GW4064) on HBV and HDV (that we initially identified in primary human hepatocytes), we found here that GW4064 also strongly inhibited HEV replication, while increasing that of HCV. Altogether, these data illustrate that a molecule inhibiting one virus may actually boost another one. To conclude, we set-up a new *in vitro* model allowing multi-infections with Hepatitis viruses that can be used for drug screening.

Disclosure of Interest: None Declared

P032

REAL-WORLD DATA OF TENOFOVIR ALAFENAMIDE VERSUS TENOFOVIR DISOPROXIL FUMARATE FOR THE TREATMENT OF PATIENTS WITH CHRONIC HEPATITIS B

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Background/Aims: The goal of this study was to compare the efficacy and safety of these drugs in patients with chronic Hepatitis B (CHB) in clinical practice for 2 years.

Methods: We retrospectively reviewed the medical records of patients with CHB receiving tenofovir alafenamide (TAF) (*n*=75) and tenofovir disoproxil fumarate (TDF) (*n*=650) in two hospitals. We used a 1:1 propensity score matching analysis to pair 75 patients in the TAF group with 75 patients in the TDF group.

Results: There was no significant difference between Hepatitis B e antigen (HBeAg)-positive patients (*n*=418) in the TAF and TDF groups in terms of the 2-year cumulative rate of virological (70.8% vs. 76.8%, *p*=0.365, respectively) and biochemical (77.1% vs. 78.4%, *p*=0.838) responses. Similar results were observed among HBeAg-negative patients (*n*=307) with regard to virological (100% vs. 92.1%, *p*=0.237) and biochemical (81.5% vs. 76.8%, *p*=0.579) responses. Further, these responses of the propensity score matching cohort were consistent with those of the entire cohort. Mean changes in estimated glomerular filtration rate and serum phosphorus level did not reveal a significant difference between the groups; however, total cholesterol was significantly lower in the TDF group than in the TAF group after the 2-year treatment in the propensity score matching cohort (-14 mg/dL *vs.* -2.4 mg/dL *p*=0.032, respectively).

Conclusions: In patients with CHB, the efficacy and safety of TAF were similar to those of TDF at 2 years, regardless of the HBeAg status. A significant decline in total cholesterol levels was observed in patients who received TDF.

Disclosure of Interest: None Declared

P033

COMBINATION OF HBV CAPSID/CORE ASSEMBLY MODULATORS (CAMS) LEADS TO A LONG-LASTING ANTIVIRAL EFFECT IN VITRO

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Abstract Content: Current treatments of Hepatitis B virus (HBV) chronic infections, based mainly on nucleoside analogues (NAs), are not sufficient to cure HBV infections mainly because there are inefficient on the circular covalently closed DNA (cccDNA), which is responsible for long-term persistence. To get an *HBV cure*, cccDNA should be either targeted physically (*i.e.* degradation) or functionally (*i.e.* repression of transcription). Capsid/core assembly modulators are currently being developed to complement NAs and foster a fastest loss of cccDNA in patients. It is expected that CAMs could replace NAs if potent, and safe enough ones are discovered; potency being instrumental to achieve the three modes of actions that have been so far described for CAMs (*Lahlali et al. AAC 2018*). Here, we describe a fourth MoA of CAMs that can be obtained in particular with a CAM-Ab (which induces aberrant capsid structures) and concerns HBV RNA biogenesis when the concentration/potency is high. Using Run-On experiments, we indeed show that nascent RNA synthesis is impaired, as a result of cccDNA transcription inhibition, and lead to reduced HBV RNA accumulation as well as downstream viral entities (HBsAg, viremia...). Interestingly we also demonstrate that combination of CAM-Ab with CAM-N (which makes empty capsids with normal structures) further amplifies this inhibitory phenotype, allowing a prolonged antiviral effect after treatment cessation (no or weak rebound), which is not obtained in respective monotherapies. This long-lasting inhibitory phenotype is due to a strong and long-lasting repression of cccDNA activity, which is being epigenetically/epitranscriptomically characterized. This opens new perspectives for antiviral HBV treatment.

Disclosure of Interest: None Declared

P034

THERAPEUTIC VACCINATION OF HBV INFECTED PATIENTS WITH LOW-LEVEL OF HBSAG USING A COMBINATION OF A THIRD GENERATION PRES/S VACCINE (SCI-B-VACTM) AND NUCS

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Background: Treatment regimens for chronic Hepatitis B virus (HBV) infection are efficient in suppressing viral load and improving hepatocellular injury and its complications. However, current anti-viral agents such as NUCs or IFN alpha are inefficient to reconstitute immunologic control of persistent HBV infection or clearance of HBVcccDNA. It was hypothesized that high levels of circulating HBV surface antigens (HBsAg) lead to immune tolerance against HBV and contribute to persistence of chronic HBV infection. Hence, low-level HBsAg in some patients may create a window for the reconstitution of an HBV-specific immune response and control of infection. Previous studies in non-responders to classical HBV vaccines with a third generation PreS/S vaccine (Sci-B-Vac™), lead to 95% anti-HBs seroconversion at high protective levels. The present report describes an attempt to evaluate the potential role of Sci B Vac™, the preS/S HBV vaccine in a therapeutic maneuver to clear persistent HBV.

Results: Three low-level HBsAg carriers (448, 20.2 and 19.2 IU/L, respectively), were vaccinated 5 to 7 times with 20 µg Sci-B-Vac™. All three vaccinated patients seroconverted to anti-HBs. Two years after completion of the vaccination series, anti-HBs titers were 100, 260 and 623 IU/L, respectively. One year after stopping NUC treatment, one patient was still HBsAg and HBV DNA negative and anti-HBs positive at >1000 IU/L.

Summary: This PreS/S vaccine against HBV has recently been approved by the FDA and EMEA for prevention of HBV. Based on our preliminary observation, there is a rational to further evaluate a potential role of this vaccine as a therapeutic agent, possibly in combination with one or more of new antiviral agents against HBV.

Disclosure of Interest: None Declared

P035

IMPACT OF USING ORAL SEMAGLUTIDE IN PATIENTS WITH TYPE 2 DIABETES AND NON-ALCOHOLIC FATTY LIVER DISEASE

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Background and Aim: Non-alcoholic fatty liver disease (NAFLD) is common in patients with type 2 diabetes (T2DM). Regarding treatment options for NAFLD, it is well known that are limited. Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist approved for the treatment of T2DM with an important role in weight management. Also, may represent a new therapeutic option for the treatment of NAFLD in T2DM patients. The aim of this study is to assess the impact of treatment with semaglutide on liver steatosis and fibrosis in patients with T2DM by using Vibration-Controlled Transient Elastography (VCTE) with Controlled Attenuation Parameter (CAP).

Material and methods: Thirty consecutive patients with T2DM and NAFLD being treated with oral semaglutide were enrolled and evaluated using VCTE with CAP from June 2022 to December 2022. Clinical and laboratory data were recorded in all patients. Oral semaglutide was initiated according to the indications of the diabetologist, a dose of 3 mg once daily, and the dose was sequentially increased to 7 mg at 4weeks and 14mg at 8weeks.

Results: According to VCTE measurements, 22 (66.66 %) diabetic patients had improved values of CAP significantly from baseline to 24weeks. An improvement in hepatic fibrosis occurred only in 9 (30%) diabetic patients. Regarding body mass index (BMI), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), have improved significantly compared to the baseline (mean BMI 29.12$\pm$5.64 kg/m^2 to 25.35 $\pm$6.24 kg/m^2, mean AST 55.87 $\pm$ 12.33 IU/L to 30.97 $\pm$ 10.8 IU/L, mean ALT 60.44 $\pm$ 9.43 IU/L to 36.1 $\pm$ 17.6 IU/L). Hemoglobin A1c (HbA1c) values significantly decreased from baseline to 24weeks (mean HbA1c 8.6% to 7.2%). Changes in CAP values were significantly associated with fasting plasma glucose (Δ=0.243, p=0.024), AST (Δ=0.169, p=0.051), and BMI (Δ=0.320, p=0.005). The most common adverse effects that occurred were represented by nausea and fatigue.

Conclusion: Patients with T2DM and NAFLD treated with oral semaglutide have improved glycemic status, liver enzymes, body weight, and liver steatosis. Hence, further research regarding liver fibrosis is necessary since these findings raise the possibility that semaglutide may be useful in the management of NAFLD patients.

Disclosure of Interest: None Declared

P036

USE OF A SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITOR IMPROVES LIVER STIFFNESS IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background: There are no medications that can cure NAFLD. A key link in the pathogenesis of NAFLD is a violation of the systemic energy balance, which is characterized by an excess of carbohydrates and fatty acids, which targets pharmacological studies on these metabolic pathways of NAFLD. Sodium-glucose cotransporter-2 inhibitors decrease glucose reabsorption in the proximal renal tubules. The results of recent studies have shown that the drugs have pleiotropic effects, cause lipid profile improvement, an increase in adiponectin secretion and reduction in the risk of cardiovascular death.

The aim: To evaluate the effect of sodium-glucose cotransporter-2 inhibitors on non-alcoholic fatty liver disease.

Materials and methods: The prospective study included 53 patients with NAFLD without diabetes mellitus (28 women (52.8%) and 25 men (47.2%) aged 21 to 64 years (45.9±10.9 years)). The diagnosis of NAFLD/NASH was made according to the criteria of the EASL 2016 clinical guidelines. The liver stiffness was assessed in kPa on the METAVIR scale, the steatosis in db/m by a Fibroscan 502 CAP (Echosens, France). The patients were divided into two groups: in treatment group (n=26) patients used dapagliflozin 10 mg per day; the control group (n=27) – without therapy. Patients of both groups were comparable in the course of the disease and the main clinical, laboratory and instrumental indicators. The duration of follow-up was 48 weeks (95% CI = 48.2, 49.3).

Results: In the treatment group (n=26) was found a statistically significant decrease of BMI (p=0.001), waist circumference (p=0.01), steatosis degree (p<0.0001), liver stiffness (p<0.0001), NOMA -IR index (p<0.0001), ALT (p=0.001), cholesterol (p=0.008), LDL (p=0.04), TG (p=0.001), uric acid (p=0.001). In the control group (n=27) was a statistically significant increase in BMI (0.006), degree of steatosis (p=0.008), liver stiffness (p=0.001). In a one-dimensional comparative analysis of dynamic indicators, a decrease in BMI (p=0.003), the NOMA-IR index (p=0.006), ALT level (p=0.02), TG (p=0.002), uric acid (p=0.04) were statistically significant for reducing the degree of steatosis. On multiple regression BMI decrease was statistically significant in reducing of steatosis degree (OR = 4.9; 95% CI 3.463-8.317; p = 0.0001). Steatosis degree decrease (OR = 4.6; 95% CI 0.006-0.017; p = 0.0001), NOMA–IR index decrease (OR=2.1, 95% CI -0.396- -0.008; p = 0.04) were statistically significant in liver stiffness reducing.

Conclusion: The use of a sodium-glucose cotransporter-2 inhibitor (dapagliflozin 10 mg per day) positively affected the main metabolic components, including liver steatosis and liver stiffness in patients with non-alcoholic fatty liver disease.

Disclosure of Interest: None Declared

P037

AKKERMANSIA MUCINIPHILA-DERIVED ACETATE ACTIVATES HEPATIC AMPK-SIRT1-PGC1A TO REDUCE LIPID PEROXIDATION IN METABOLIC-ASSOCIATED FATTY LIVER DISEASE

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Background: Ferroptosis is an iron-dependent regulated cell death type, and emerging evidence have verified its participation in the progression of the metabolic-associated fatty liver disease (MAFLD), thus inhibiting ferroptosis is a promising target for MAFLD. The gut commensal bacterium *Akkermansia muciniphila* (*A. muc*) exhibits great potential to ameliorate metabolic disorders in MAFLD. Latest studies have demonstrated the anti-oxidative effect of *A. muc*, however, the its anti-ferriototic effect remains unclear.

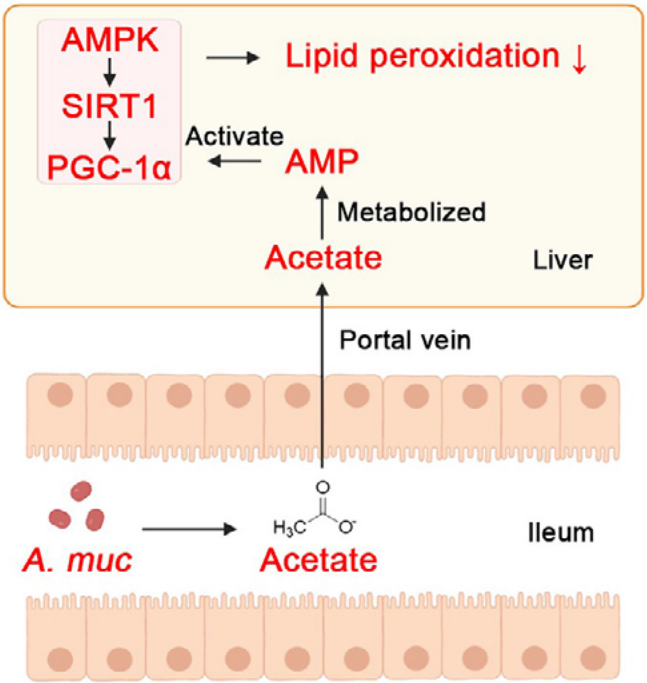
Purpose: The current study investigated the effect of *A. muc* on MAFLD-related ferroptosis.

Method: We investigated the protective effect of *A. muc* on MAFLD using a murine MAFLD model induced by long-term high fat high fructose diet (HFHFD) feeding. 16s rRNA sequencing and untargeted metabolomics were conducted to identify key microbes and metabolites. Fecal microbiota transplantation (FMT) and germ-free mice were conducted to verify the role of microbiota in the progression.

Result: *A. muc* intervention efficiently reversed HFHFD-induced lipid peroxidation and oxidative damage in the liver. These beneficial impacts were mediated by activation of hepatic AMPK-SIRT1-PGC-1α axis, as evidenced by AMPK deficiency induced by adeno-associated virus (AAV)-shRNA or antagonist Compound C abrogated its amelioration in lipid peroxidation. Further, we observed elevations in the short chain fatty acids upon *A. muc* treatment and identified acetate as key activator of hepatic AMPK. Mechanically, microbiota-derived metabolite acetate is transported to the liver and metabolized to adenosine monophosphate (AMP) which triggers AMPK activation. Further, we confirmed *A. muc* mediates anti-ferroptotic effect by itself in the absence of the other microbes.

Conclusion: These data indicate that *A. muc* exerts anti-ferroptotic effect through producing acetate, which activates hepatic AMPK-SIRT1-PGC-1α axis to strengthen mitochondrial biosynthesis. *A. muc* could be a potential therapeutic approach targeting ferroptosis in MAFLD.

Image/Table:



Disclosure of Interest: None Declared

P038

ROLE OF THE MIXED LINEAGE KINASE DOMAIN LIKE IN THE DEVELOPMENT OF NONALCOHOLIC STEATOHEPATITIS-RELATED HEPATOCELLULAR CARCINOMA

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Abstract Content: Mixed Lineage Kinase domain Like (MLKL) is a pseudokinase that was first described as the main effector of cell death by necroptosis, a form of regulated necrosis, but it is also implicated in other functions such as gene induction or autophagy. It has also been reported that this protein may be involved in certain cancers, where it would play either an anti-or a pro-tumor role. To decipher the potential implication of MLKL in the development of hepatocellular carcinoma (HCC) in the context of non-alcoholic steatoHepatitis (NASH), male mice, with liver parenchymal cells expressing ($Mlkl^{fl/fl}$) or not ($Mlkl^{LPC\text{-}KO}$) the pseudokinase, were included in an experimental protocol that mimics the emergence of HCC in humans. Results showed that the lack of MLKL in liver parenchymal cells partly limits the emergence of HCC in the context of NASH, suggesting its pro-tumor role.

Disclosure of Interest: None Declared

P039

KNOCKDOWN OF ANTISENSE NONCODING MITOCHONDRIAL RNAS INDUCE CELL DEATH AND DOWNREGULATION OF HBX IN A HEPATOCELLULAR CARCINOMA MODEL

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Abstract Content: Hepatocellular carcinoma (HCC) is the most prevalent type of tumour and is the third cause of death by cancer worldwide. Hepatitis B Virus (HBV) is the main etiologic agent associated with developing HCC (HCC-HBV). Different reports have shown that HBx expression is regularly detected in a patient's tumours with HCC-HBV, considering HBx as the main determinant of the hepatocarcinogenesis process. One of the main limitations of both antitumour (HCC) and antiviral (HBV) treatments is their high refractory rate and low survival rate. Our group has reported that the knockdown of antisense noncoding mitochondrial RNA (ASncmtRNAs) used a phosphorothioate oligonucleotide (ASO) complementary at this transcript (ASO-AS), induces proliferative arrest, apoptosis, and invasiveness reduction in tumour but not normal cells. Interestingly, tumour cells such as HeLa or SiHa (transformed by HPV) show a high vulnerability to treatment, concomitant with a decrease of mRNA of E6/E7 levels. Normal keratinocytes treated with ASO-AS show only 10% cell death. When we evaluated the effect of ASO-AS in transformed murine hepatocytes and HCC tumour cell lines expressing HBx on tumour cell viability and HBx expression, we observed a high rate of cytotoxic effect by flow cytometry, trypan blue staining and MTT assay of ASO-AS on HepM-HBx, HepG2 and PLC/PRF/5 (HBV+) of cell death ($\geq$70%) concomitant with the downregulation of two anti-apoptotic proteins survivin and Bcl-xL by western blotting, while HepM only induced $\leq$10% cell death. This effect was characteristic of an apoptotic event because all tumour cells presented a high percentage of annexin V+ cells ($\geq$20%), TUNEL + cells ($\geq$30%) and activation of the intrinsic caspase pathway evaluated by flow cytometry, TUNEL assay and western blot. All these effects were accompanied by decreases in the tumorigenic capacity (decreased clonogenic capacity, matrix invasion and sphere formation). When we evaluate this effect in an intrahepatic xenograft model using a doxycycline induction model of HBx (HepG2-HBx tet-on), we observed after 6 doses of ASO-AS at 100ug decrease the tumour growth concomitant with downregulation of survivin protein, at the difference the animal controls (saline). Finally, to assess the effect of ASO-AS on the HBx expression in vitro and in vivo surprisingly we observed that at DNA and RNA levels a reduction of about 30-45% but at protein levels a reduction of 50-70% in all cells and animals treated. These results suggest that ASncmtRNA knockdown could be inducing a post-transcriptional or post-translational regulation on the HBx expression and that the mechanism involved in this process may be a new mitochondrial axis of HBx regulation.

Disclosure of Interest: None Declared

P040

HEPATOPROTECTIVE EFFECTS OF NATURAL FLAVONOIDS TRANS-CHALCONES IN THE SUPPRESSION OF HEPATOCELLULAR CARCINOMA BY THE REGULATION OF FERROPTOSIS

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Background: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death worldwide with an extremely poor prognosis and limited treatment options. Due to insufficient diagnosis and serious side effects, conventional therapies like chemotherapy, radiation, and surgical resection remain challenging and ineffective for the treatment of HCC. Therefore, the urge for more effective and less toxic chemoprevention agents is necessary to prevent hepatocarcinogenesis. Chalcones is a polyphenolic compound derived from a natural plant with potential antitumor effects in multiple tumor cells. Here, chalcone was demonstrated to trigger ferroptosis through the modulation of mitochondrial ROS. Ferroptosis is a novel way of non-apoptosis cell death resulting from the iron-dependent accumulation of lipid hydroperoxides, that shows a potential target for the treatment of cancer, especially in HCC.

Methods: Hep3B and Huh7 cell lines were treated with various concentrations of *trans*-chalcone (10, 20, 40, 60, and 80) μM in a time and dose-dependent manner. Cell viability, colony generation, and migration assay were performed by MTT, wound healing, transwell migration assay, and trypan blue colony formation assays. Expression of cell cycle-related markers and ferroptosis-related markers were evaluated by immunoblotting. Loss in mitochondrial membrane potential was determined using TMRE assay. Furthermore, HCC cells were treated together with *trans*-chalcone and ferroptosis inhibitor ferrostatin-1 (1.5 μM) to determine the effects of *trans*-chalcone in the modulation of ferroptosis.

Results: *Trans*-chalcone inhibits the proliferation of Hep3B and Huh7 cells as determined by reduced cell viability, decreased number of colonies formed, and loss in expression of cell cycle-related markers. Furthermore, *trans*-chalcone suppressed HCC cell growth by inducing loss of mitochondrial membrane potential and reducing the levels of ferroptosis-related proteins.

Conclusion: Together, these findings suggest chalcone as a lead anticancer compound it acts through modulation of ferroptosis providing a promising track for chalcone derivatives' anticancer mechanism.

Keywords: *trans*-chalcone, Ferroptosis, HCC, Ferostatin-1

Disclosure of Interest: None Declared

P041

EFFECT OF ETHANOLIC EXTRACT OF BALANITES AEGYPTIACA (L.) DELILE (BALANITACEAE) ROOT BARKS ON HUMAN HEPATOCARCINOMA CELL LINES HEP3B AND FIBROTIC LX-2

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Abstract Content: *Balanites aegyptiaca* (L.) Del (Balanitaceae) fait partie de ces plantes utilisées pour le traitement de diverses affections telles que la syphilis, l'épilepsie, la jaunisse et les affections hépatiques. En effet, ces écorces de racines sont utilisées pour le traitement des maladies du foie par les tradipraticiens au Burkina Faso. Dans le sens de la recherche de solutions médicamenteuses alternatives aux pathologies hépatiques, cette étude visait à évaluer l'effet de l'extrait sur les lignées cellulaires d'hépatocarcinome humain Hep3B et fibrotique LX-2.

L'effet préventif a été évalué en administrant l'extrait (25, 50 et 100 mg/kg pc) par voie orale à des rats wistar pendant 6 jours, puis au 7ème jour, l'hépatotoxicité a été induite avec du tétrachlorure de carbone (CCl 4) par injection intrapéritonéale. Les paramètres biochimiques et enzymatiques ont été mesurés. L'effet antifibrotique a été étudié en deux phases, *in vitro* dans des lignées cellulaires fibrotiques LX2 et *in vivo* chez des rats Wistar. *In vivo* , la fibrose a été induite par l'administration intrapéritonéale de CCl 4chez le rat pendant 4 semaines. Ensuite, des rats ont été traités par administration orale de l'extrait à des doses de 25, 50 et 100 mg/kg pc pendant 4 semaines. Les paramètres biochimiques et enzymatiques ont été mesurés et des coupes histologiques ont été réalisées. L'effet de l'extrait sur les cellules cancéreuses du foie a été étudié en utilisant les lignées cellulaires d'hépatocarcinome humain, Hep3B.

L'effet préventif de l'extrait était meilleur avec la dose de 50 mg/kg pc avec des paramètres biochimiques et enzymatiques proches de ceux des rats témoins. L'IC50 sur la lignée cellulaire fibreuse LX-2 était de 3,89 $\pm$ 0,76 ug/ml. L' activité antifibrotique *in vivo* de l'extrait à 100 mg/kg pc était meilleure avec des paramètres biochimiques, enzymatiques et histochimiques comparables à ceux des rats témoins. Avec les cellules cancéreuses, l'IC 50 de l'extrait était de 4,29 $\pm$ 0,83 µg/ml sur la lignée cellulaire Hep3B et était inférieure à celle du composé de référence (12,5 $\pm$ 0,13), Sorafenid.

Cette étude a mis en évidence les propriétés hépatoprotectrices et antifibrotiques de l'extrait éthanolique de *Balanites aegyptiaca in vitro* dans des lignées cellulaires fibrotiques LX2 et *in vivo* chez le rat. Elle a démontré l'efficacité de l'extrait sur les lignées cellulaires d'hépatocarcinome humain (Hep3B). Ces résultats fournissent une base scientifique pour son utilisation en médecine traditionnelle et une recherche de médicaments alternatifs pour les pathologies hépatiques.

Key words: *Balanites aegyptiaca*; Extract; Hepatroprotective activity, Antifibrotic activity.

Disclosure of Interest: None Declared

P042

ASPARTATE-B-HYDROXYLASE, A PROMISING BIOMARKER FOR THE DIAGNOSIS OF GLYPICAN-3-NEGATIVE HEPATOCELLULAR CARCINOMA

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Background: Glypican-3 (GPC3) is an emerging target for hepatocellular carcinoma (HCC) that has been evaluated in clinical trials and has high specificity and sensitivity for the diagnosis of HCC. However, strategies to improve the diagnostic rate of GPC3-negative HCC remain elusive. The aim of our study was to investigate the relationship between aspartyl-(asparaginyl)-Δ-hydroxylase (ASPH) and GPC3 expression in HCC and to further determine the significance of ASPH in the prognosis of HCC.

Methods : HCC tissue samples (n=190) obtained from patients who were ultimately confirmed the diagnosed as HCC by pathological analysis between 2009 and 2013 were analyzed in this study. Lymph node metastasis, tumour size, and distant metastasis were determined through imaging and pathological approaches. The expression levels of alpha-fetoprotein (AFP), Ki67, ASPH and GPC3 were tested via immunohistochemical staining. Protein-protein interaction (PPI) network was used to identify the possible regulatory genes.

Results: The 190 samples were categorized as two subtypes, namely, ASPH+HCC and ASPH–HCC. Among the GPC3-HCC samples, 80.70% were ASPH positive. No AFP-positive staining was detected in ASPH-negative tissues. The expression of ASPH was positively related to TNM staging and AFP levels in HCC ($P=0.001$; $P<0.001$). ASPH+HCC had a worse prognosis than ASPH-HCC ($P = 0.016$). Patched 1 (PTCH1) may be a key molecule involved in the connection between ASPH and GPC3 during the progression of HCC.

Conclusions: ASPH can increase the efficiency of GPC3-negative HCC diagnosis. ASPH is a potential prognostic biomarker for HCC and is closely related to the malignant behaviour of HCC. Compared to $ASPH^-$HCC, $ASPH^+$HCC may confer a more aggressive subtype.

Disclosure of Interest: None Declared

P043

SEQUENCE ANALYSIS SUGGEST A DIFFERENT HEPATITIS E VIRUS TRANSMISSION PATTERNS IN EUROPEAN AND ASIAN DEER SPECIES

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Background: Hepatitis E virus genotypes 3 and 4 (HEV-3 and HEV-4) cause zoonotic infection in humans, with domestic pigs and wild boars being the main reservoir of infection. Besides suids, HEV-3 and HEV-4 are found in ruminants, most frequently in deer species. However, it is still debatable, whether HEV infection in deer is a spillover, or indicate a stable virus circulation in these species.

Purpose: To explore the patterns of HEV-3 and HEV-4 transmission in deer using Bayesian analysis of HEV sequences available in GenBank.

Methods: Total 33 HEV sequences from different deer species were found in GenBank. Sequences from wild boars collected in the same territories, as well as sequences from other species that were most similar to deer sequences in blast search were added to dataset, comprising 617 in total. Due to partial genomic sequences, they were divided into 3 subsets (ORF1 fragment and two different fragments of ORF2) and analyzed separately. Bayesian analysis was performed using the BEAST v1.10.4 software using following parameters: HKY with Gamma, Strict clock and "Coalescent: Constant Size" as the Tree Prior. The initial clock rate 8.3*10-3 subs./site/year. The MCMC method was run for 50 million generations and sampled every 5000 steps in two repetitions for all data subsets.

Results: All deer ORF1 sequences belonged to HEV-3. Asian deer HEV-3 sequences formed a distinct cluster indicative of intraspecific transmission and originated from wild boar HEV-3 25 years ago (HPD 95%: 21-27). In Europe, two deer HEV-3 ORF1 sequences were identified, one in wild boar cluster, and the second one in domestic swine cluster that had human origin (node age 45 years, HPD 95%: 37-50).

Deer ORF2 sequences from Europe belonged to HEV-3 and resulted from multiple spillovers with domestic pigs as a source. In contrast, sequences from wild boars collected in the same territories formed separate clusters originated from domestic pigs, indicative of stable HEV circulation in wild suids. All deer HEV-4 ORF2 sequences had Asian origin and evolved about 22 years ago (HPD 95%: 17-24) from strain identified in domestic pigs with subsequent circulation among deer. However, single deer HEV-4 sequences were also observed in wild boar clusters, indicating spillover infections.

Conclusion: In Asia, both HEV-3 and HEV-4 circulate in deer species showing that these ruminants can be a true host for HEV. In contrast, in Europe HEV-3 in deer resulted from spillover from wild or domestic suids. Complete HEV genomic sequences from additional countries are crucial for further understanding of the HEV circulation patterns in wildlife.

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Disclosure of Interest: None Declared

P044

SEROPREVALENCE OF HEPATITIS E IN NORD SARDINIA: AN ANALYSIS OF SARS-COV-2 PATIENTS, HEALTCARE WORKERS AND HIV PATIENTS

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Abstract Content: Hepatitis E is a viral disease with a viral-oral transmission whose causative agents is the Hepatitis E virus belonging to the hepevirus genus of the hepeviridae family.

The general objective of this study is to evaluate the spread of HEV infection in Northern Sardinia and in particular to estimate the prevalence of Hepatitis E by geographical area, age and sex.

IgM and IgG were tested during a pilot project from June 2022. Risk factors were also evaluated. Samples were collected as follows:

1. Hospitalized patient: Upon admission(at baseline)
2. Outpatient non-hospitalized patients: at the time of the visit(at baseline)
3. Non-hospitalized patients healt workers: at the time of taking into service and according to the availability of the reference laboratory (at baseline).

Overall 85 patient were included from June 2022 to September 2022.

Of them, 23/85(%) tested positive to anti-HEV IgG antibodies. A serological investigation was not performed on all patients after the first sampling, while it was not possible to recover the serum of 1 parient at baseline who tested positive for anti-HEV IgM antibodies (doubtful result).

A more in-depth analysis revelated the following:

- At baseline, 15 male patients (65.2%) with a mean age of 79.9 years and respectively 8 female patients (34.8%) with a mean age 78.4 years were positive for IgG HEV only.
- At baseline, patients hospitalized for SARS CoV-2 infection were positive only for IgG HEV: 15 male patients (65.2%) and 7 female patients (30.4%).
- Only one healtcare provider tested positive for anti-HEV IgG antibodies (4.3%).

In conclusion, our data are confortant with available literature on HEV seroprevalence and transmission.

Advanced age or probably poor education (to be confirmed), are predictors of HEV infection highlighted in this study, indicating continuous exposure as well as the literature reports the fecal, oral transmission of the virus or food transmission.

There was no difference in the seroprevalence rates of anti-HEV IgG antibodies between study participants in terms of time (the study was based on a retrospective observational model for a limited time), or risk factors such as HIV infection or other viral infections or blood transfusions (44; 48). There was only one case, but subsequently unconfirmed, of the presence of anti-HEV IgM in an 84-year-old woman for whom it was not possible to identify the viral genome.

In Sardinia transmission in the population is likely to occur through slaughter and consuption of undercooked pork.

Disclosure of Interest: None Declared

P045

INVESTIGATION OF HEPATITIS C VIRUS AND HEPATITIS E VIRUS IN THE CEREBROSPINAL FLUID OF PATIENTS TESTED POSITIVE FOR HIV AND SARS-COV-2 IN DR. GEORGE MUKHARI ACADEMIC HOSPITAL, PRETORIA IN 2020-2021

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Introduction: Hepatitis C and Hepatitis E viruses are a global health problem. Enteric transmittable Hepatitis E is believed to be associated with a limited lack of good hygiene, which might lead to fecal-oral transmission. HCV is usually transmitted through infected blood. Both viruses, HCV and HEV, can cause hepatocellular inflammation, liver cirrhosis, and hepatocellular carcinoma (HCC) in more severe cases. Neurotropism by both HCV and HEV viruses has been reported in the cerebrospinal fluid (CSF). The aim of this study was to investigate the HCV and HEV prevalence and characterize the circulating strains from the CSF samples of patients suspected of having neurological disorders at the Dr. George Mukhari academic hospital.

Methods: This was a cross-sectional descriptive study, the study population consisted of 54 CSF samples that were positive for SARS-Cov-2 and collected between 2020 and 2021. Both HCV and HEV were tested by subjecting the CSF samples to RNA isolation, Reverse Transcriptase PCR (RT-PCR), and conventional PCR; the sanger sequence targeted ORF2/ORF3 for HEV and NS5B for HCV; the identity of the amplicons was determined by NCBI Blast and phylogenetic tree reconstruction.

Results: HEV prevalence in CSF was 40% (23/57), while HCV was not detected in any of the CSF samples tested 0% (0/57). The 13 HEV strains were characterized as genotype 3, subgroup 3a, and were closely related to HEV sequences found in humans and swine previously. Isolates HEV_SA2022_B895, HEV_SA2022_B17, HEV_SA2022_B897, cluster with HEV3 sequences from swine feces in Japan and human specimen from China (GenBank accession no. LC406611.1, KX574712.1, and FJ527832.2). HEV_SA2022_B5, HEV_SA2022_B4, HEV_SA2022_712, HEV_SA2022_32, HEV_SA2022_911, HEV_SA2022_101, HEV_SA2022_55 and HEV_SA2022_78 cluster with HEV3 from Japan previously isolated from both human and swine.

Conclusion: This is the first study to detect the presence of HEV genotype 3 in CSF samples in South Africa. This observation has public health and clinical implications for patients with neurological disorders and HIV. Our finding necessitates studies to further understand the diagnostic meaning of HEV RNA in the CSF of HIV-infected patients to better manage neurological disorders in these patients.

Keywords: Cerebrospinal fluid, Hepatitis E Virus, Hepatitis C Virus, SARS-Cov-2, HIV, Neurological disorder.

Disclosure of Interest: None Declared

P046

CHARACTERIZATION OF HEPATITIS E VIRUS GENOTYPE 3 IN PIGS AND IN WASTEWATER IN CAMEROON: AN ENVIRONMENTAL AND FOOD SAFETY PROBLEM

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Background: Hepatitis E occurs around the world both as outbreaks and as sporadic cases. It represents an important public health concern in many developing countries including Africa. This virus infects humans and certain animal species, mainly pigs. Transmission is mainly through contaminated water. Pigs and other animals shed large amounts of virus in their faeces, posing an environmental concern. Various epidemics have been reported in Africa and the etiology of some has still not been elucidated. In cameroon, a serological study carried out in 2013 declared the first outbreak of Hepatitis E in the north region. It was confirmed by molecular biology which showed that genotypes 1 and 3 were responsible for this epidemic.

Purpose: This study aimed to investigate the presence of hev reservoirs in cameroon and to verify the presence of this virus in the environment.

Methods: We conducted a prospective study from 2018 to 2020 by collecting 615 pig samples (blood and stool) in 4 regions (north, center, west and littoral) and 157 wastewater samples in all 10 regions of cameroon. Molecular and/or serological analyzes were carried out at centre pasteur of cameroon. Serological diagnostics for anti-hev antibodies detection in pigs were carried out using commercial elisa kits. Molecular biology for hev rna amplification in sewage samples and serology-positive pig samples was performed using the nested rt-pcr technique.

Results: In pigs, 32.52% (200/615) of pigs were positive for anti-hev igm and 21.3% (131/615) for anti-hev igg. Hev rna was amplified by nested rt-pcr in 5.9% (8/136) of anti-hev igm positive pigs. Phylogenetic analyzes had identified genotype 3 in the center region. For sewage samples, 2/157 were positive and phylogenetic analyzes had identified genotype 3 in the north region.

Conclusion: This study confirms that pigs are the main reservoirs of hve in cameroon and also demonstrates that hev is present in the environment, thus posing an environmental and food security problem.

Keywords: Hepatitis E virus, wastewater, pigs, Cameroon

Disclosure of Interest: None Declared

P047

RELEVANCE OF HEPATITIS E VIRUS IN EJACULATE OF CHRONICALLY INFECTED PATIENTS AND ITS INFECTIVITY IN VITRO

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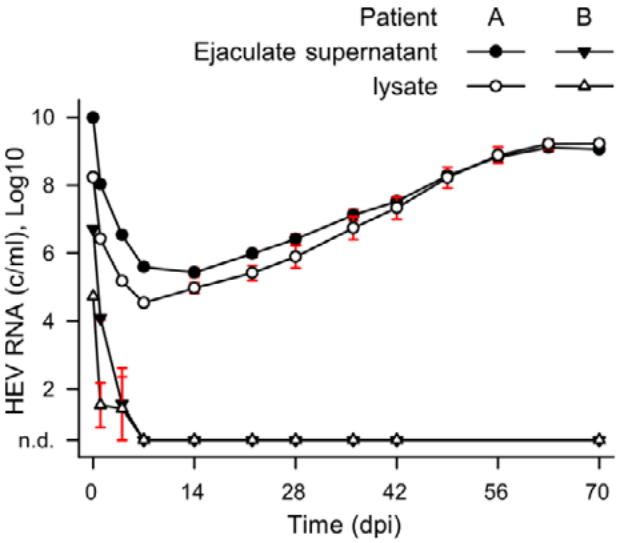
Background: Recently, Hepatitis E virus (HEV) particles have been detected in the ejaculate of 2 out of 3 chronically infected patients. HEV RNA in the ejaculate can be significantly higher than in serum or plasma. However, it was unclear whether these viral particles in the ejaculate are infectious, and how often HEV generally occurs in the ejaculate of chronically infected individuals.

Methods: After a previous cell culture model failed to demonstrate the infectivity of HEV particles from the ejaculate of two chronically infected patients (Horvatits et al. Journal of Hepatology 2021), we now used an alternative cell culture model based on overconfluent PLC/PRF/5 cells (Schemmerer et al. Viruses 2019) to study these particles for infectivity. Furthermore, we monitored HEV viral load in blood, urine, stool and ejaculate in 9 chronically HEV infected patients.

Results: For the first time, HEV particles from ejaculate were shown to be infectious in overconfluent PLC/PRF/5 cells (figure). HEV replicated to high viral loads of 10e9 HEV RNA copies per ml. Moreover, HEV was detected in the ejaculate of 7 out of 9 chronically infected patients (age 36-67 years, median 56 years). In 5 of the patients the viral loads were significantly higher (more than 2 log) compared to their serum, while in 2 patients, viral loads were lower than in their serum (more than 1 log).

Conclusions: In the context of chronic HEV infection, HEV particles can be detected in the ejaculate of 78% (7/9) of infected men, usually with significantly higher viral loads than in serum. In this regard, it should be noted that the gap between high viral load in ejaculate compared to viral load in blood may even be much higher than previously suspected. After the infectivity of HEV particles from ejaculate could not be demonstrated so far, it could now be shown that they are infectious in PLC/PRF/5 cells. While there is probably no danger from this ejaculate for immunocompetent sexual partners, safer sex practice should be followed if the sexual partners are immunocompromised.

Image/Table:



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P048

CELLULAR CROSS-TALK AND MODULATION OF THE HEPATIC PROFIBROTIC PROFILE IN THE CONTEXT OF HIV-HCV COINFECTION

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Background: Coinfection with the human immunodeficiency virus (HIV) in patients with chronic Hepatitis C virus (HCV) infection significantly accelerates liver damage, favoring the progression of fibrosis. After the injury, mediators secreted by damaged hepatocytes and from the microenvironment (eg, T lymphocytes -LT-), maintain an environment of chronic inflammation that promotes activation of hepatic stellate cells (HSC) capable of producing extracellular matrix and promoting liver fibrosis. The mechanism of the acceleration in the progression of liver fibrosis due to coinfection has not been defined.

Purpose: To evaluate the ability of HIV and HCV to modulate programmed cell death (PCD) and mitochondrial homeostasis of HSCs, giving them a profibrotic profile.

Methods: Using a fluorescent HIV (pNL43-GFP), the permissiveness of HSCs (LX2) to infection was assessed after challenging them for 5 hours with: (i) free virus (HIV-GFP+), and (ii) cell-cell infection (co-culture with LT-HIV+). After 72h in culture, the kinetics of HIV replication was evaluated by quantifying the HIV-p24 antigen in supernatants, and the infection efficiency by quantifying GFP+ cells by flow cytometry. The effect of HCV was assessed by exposing the LX2/LT-HIV co-cultures to a conditioned medium (hepatocyte-HCV+ supernatant or "SN-HCV") immediately after co-cultivation. Using flow cytometry on LX2, the level of PCD (Annexin-V/7AAD) and the generation of mitochondrial reactive oxygen species –mROS- were defined. Collagen production was determined by Sirius Red staining and subsequent spectrophotometric reading.

Results: LX2 were not susceptible or permissive to HIV infection by cell-free virus, and cell-cell contact, resulting in undetectable production of p24 or GFP expression in them. Exposure to HIV of LX2 did not affect PCD compared to control (6.1 vs. 8.6%, p>.05) nor did it affect after exposing them to SN-HCV (6.1 vs. 8.1%, p>.05). However, PCD in LX2 was significantly increased after simultaneous exposure to LT-HIV+ and SN-HCV (11.33%, p<.05). Besides, mROS production was significantly increased compared to control (1.18%) in these 3 conditions such that: LX2/LT-HIV+: (2.17%, p<.05), LX2/SN-HCV: (2.52% p <.05), LX2/LT-HIV+/SN-HCV: (7.9% p<.001). Under these conditions, collagen production by LX2 increased significantly such that: LX2/LT-HIV+: 1.6x (p<.001), LX2/SN-HCV: 1.9x (p<.001), LX2/LT-HIV+/SN-HCV: 1.9x (p<.001).

Conclusions: Despite the HSCs are not susceptible or permissive to HIV infection, the microenvironment of HIV/HCV coinfection affects their viability and metabolism, favoring the generation of a profibrotic profile.

Disclosure of Interest: None Declared

P049

BIFIDOBACTERIUM LONGUM R0175 PROTECTS MICE AGAINST APAP-INDUCED LIVER INJURY BY MODULATING THE NRF2 PATHWAY

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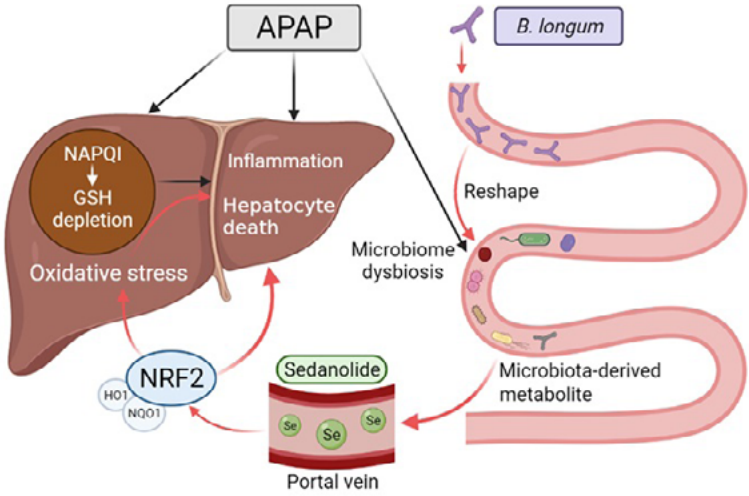
Background: Acetaminophen (APAP) overdose is the most common driver of drug-induced liver injury (DILI) worldwide, and the gut microbiome plays a crucial role in this process. Previous studies indicate that B. longum holds promise as a multifunctional probiotic against diseases, the role of B. longum R0175 in APAP-induced liver injury requires further exploration.

Purpose: In this study, we estimated the effect of Bifidobacterium longum R0175 on APAP-induced liver injury in mice and explored the underlying mechanisms. Method(s): C57BL/6J male mice were given normal saline or B. longum for 14 days followed with APAP administration. 16s rRNA sequencing and LC-MS were conducted to identify key microbes and metabolites. The Nrf2 pathway inhibitor ML385 was used to validate the effect of Nrf2 pathway and the sedanolide was used to validate the protective impacts in C57BL/6J male mice.

Result(s): We discovered that B. longum R0175 alleviated liver injury by diminishing inflammation, reducing oxidative stress levels, inhibiting hepatocyte death and improving APAP-induced microbiome dysbiosis. Further studies revealed that the antioxidative effects of B. longum R0175 were primarily due to activation of the Nrf2 pathway, which was supported by ML385 counteracting these ameliorative effects. B. longum R0175 modified intestinal metabolites, especially the key metabolite sedanolide, which could activate the Nrf2 pathway and contribute to the protective effects against APAP-induced liver injury. Moreover, we found that sedanolide exhibited close interrelationships with specific microbial taxa, indicating that this factor may be derived from gut microbes.

Conclusion(s): In conclusion, our work demonstrated that B. longum R0175 could reduce oxidative damage, inflammation and hepatocyte death by activating the Nrf2 pathway. Importantly, we identified the microbiota-derived metabolite sedanolide, which was first discovered in the mouse intestine, as a key agonist of the Nrf2 pathway and primary effector of B. longum R0175 in APAP challenge. These findings provide new perspectives for APAP overdose therapy and demonstrate the enormous potential of B. longum R0175 in alleviating acute liver injury.

Image/Table:



Disclosure of Interest: None Declared

P050

A COMPARISON OF LIVER INJURY AMONG ACUTE COVID-19, HIV, AND HIV/HCV INFECTIONS

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Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection causes multiple organ damage involving the liver. It has some similarities with human immunodeficiency virus (HIV) infection and chronic Hepatitis C (HCV), including the belonging to retroviruses, high prevalence worldwide and mortality, and the possibility to cause liver damage in different ways. A simultaneous course of HIV and HCV infections promotes faster progression of liver fibrosis than mono-infections.

Purpose: To compare the level of liver injury in acute COVID-19, HIV, and HIV/HCV using non-invasive markers of liver fibrosis and apoptosis.

Methods: The study included 53 patients with acute COVID-19, 58 patients with HIV/HCV, and 48 patients with HIV. The age of patients was similar (24-62 years). The mean interval between a confirmed HIV-1 infection and entry into the study was 6.0 $\pm$ 4.0 years. The blood analysis for acute COVID-19 patients was performed upon admission to the hospital.

Liver injury was assessed by hyaluronic acid (HA) and caspase-cleaved cytokeratin 18 fragment M-30 (CK18-M30), detected in serum by ELISA, and by FIB-4 index. Additionally, CD4 T lymphocytes were measured by flow cytometry. The Kruskal–Wallis test for independent groups was applied to compare groups of patients.

Results: Patients with COVID-19 had a higher level of HA (48.1 ng/ml, IQR [30.9; 82.7]) than HIV/HCV (29.8 ng/ml, IQR [16.3; 52.3]) and HIV (22.7 ng/ml, IQR [13.5;28.5]), $p<0.001$. The use of "cut-off" levels showed increased HA ($\geq$75 ng/ml) for 32% of acute COVID-19, 17% for HIV/HCV, and 0% for HIV patients. The level of CK18-M30 in COVID-19 (221 U/l, IQR [153; 301]) was similar to patients with HIV/HCV (181 U/l, IQR [125; 310]) and higher than in HIV (136 U/l, IQR [115; 169]), $p<0.01$. An increased CK18-M30 ($\geq$200 U/l) was detected in 57% of COVID-19 patients, 45% of HIV/HCV, and 20% of HIV patients. The index of advanced liver fibrosis (FIB-4$\geq$3.25) in patients with acute COVID-19 (1.99, IQR [0.86; 3.27]) was similar to HIV/HCV (1.32, IQR [0.84; 2.25] and higher than in HIV (0.97, IQR [0.68; 1.30]), $p<0.01$. FIB-4$\geq$3.25 was observed for 24% of COVID-19, 17% of HIV/HCV, and 0% of HIV patients. The median of CD4 T lymphocytes was lower in COVID-19 (535 cells/µl, [378; 729]) than in HIV/HCV (277 cells/µl, IQR [136; 489]) and HIV (417 cells/µl, IQR [249; 507]). The CD4<400 cells/µl was detected in 27% of COVID-19, 59% of HIV/HCV, and 49% of HIV patients.

Conclusion: The level of liver injury in acute COVID-19 was higher or similar to HIV and HIV/HCV, pointing to intensive liver involvement in inflammation and fibrogenesis during the acute COVID-19 phase, which might cause long-term liver-related consequences.

Disclosure of Interest: None Declared

P051

GUT MICROBIOTA DEPLETION AGGRAVATED DDC-INDUCED CHOLESTATIC LIVER FIBROSIS VIA INHIBITING THE FXR SIGNALING PATHWAY

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Abstract Content: Primary sclerosing cholangitis (PSC) is a cholestatic liver disease mainly characterized by excessive hepatic accumulation of bile acid. The resulted cholestasis caused toxic damage to hepatocytes and could progress to fibrosis, cirrhosis, or even hepatic cholangiocarcinoma. The etiology of PSC is still unidentified. Currently, there is no effective treatment for this disease. The gut microbiota played a crucial role in the development of cholestatic liver disease. Researchers have carried out much research on the microbiota in the pathogenesis of PSC, but these studies are controversial and fail to reach consistent conclusions. In this study, antibiotic cocktail-induced gut microbiota depletion was applied to a 0.1% DDC-fed mouse model was applied to improve the current understanding of the PSC-microbiota relationship.

Gut microbiota depletion caused exacerbation of DDC-induced cholangiopathy evidenced by significantly increased serological levels of ALT, AST, TBIL, DBIL, and TBA. The number and diameter of bile ducts, epithelial cell proliferation, intra-biliary cholestasis, or bile duct surrounding infiltration of inflammatory cells and fibroplastic proliferation all exhibited a more severe histological phenotype in antibiotic cocktail-treated mice. Microbial depletion caused a server fibroblast proliferation as indicated by a higher H-score of a-SMA, as well as a significantly upregulated level of hepatic Acta2. Additionally, the expression levels of hepatic fibrogenesis-associated genes, like Tgfb1, Timp1, Col1a1, Col3a1, all significantly increased after wiping off the commensal bacteria. Gut microbiota depletion aggravated DDC diet-induced hepatic inflammation by increasing hepatic accumulation of macrophage and neutrophils, as well as the mRNA levels of il1b, tnfa, and nlrp3. Microbiota depletion reshapes fecal bile acid metabolism. Abx treatment significantly decreased fecal levels of DCA, LCA, CA, and CDCA, and increased TaMCA, and TbMCA, and the hepatic levels of CA and DCA while the levels of CDCA and UDCA remain similar. Since TaMCA, TbMCA were considered FXR antagonists whereas CDCA, DCA, CA, and LCA were considered FXR agonists, this indicated the inhibition of both the ileum and hepatic FXR signaling pathway. Furthermore, the significantly decreased shp mRNA levels and fgf15 mRNA levels indicated a suppression of ileal fxr-fgf15 signaling pathway. Gut microbial depletion has also a decreased shp level and similar fxr level, and increased levels of BA synthesis enzyme (cyp7a1), suggesting an increased BA synthesis.

Thus, our results suggested microbial depletion could inhibit both hepatic fxr-shp and ileal fxr-fgf15 pathways and further activate the key BA synthesis enzyme cyp7a1, and consequently increase BA synthesis, aggravating BAs toxic liver injury.

This study helped to harness the therapeutic properties of the commensal microbiota for translation into potential therapies for PSC, as well as the potential of FXR agonist.

Disclosure of Interest: None Declared

P052

EARLY POSTOPERATIVE RENAL DYSFUNCTION IN THE LIVING DONOR LIVER TRANSPLANTATION

Submitted by Hosny Eleneen, Supervision of E. Hmad , K. El-Ella HBP Surgery Department., National Liver Institute, Menofiya University , Egypt. Correspondence to Hosny Aboeleneen

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Abstract: Living donor liver transplantation (LDLT) is a widely accepted treatment for end-stage liver diseases. Renal dysfunction is frequent complication after liver transplantation and has an favorable effect on prognosis.

The purpose of the present study: was to identify the incidence and risk factors of post transplantation. The study population consisted of adults and pediatrics who received LDLT from April 2003 to April 2012 in National liver institute (Menofia University). Data were collected from preoperative records, operative records, post-operative files (in ICU and ward) and from follow up records of all patients for one month after operation. According to the preoperative results, patients were classified into: patients with preoperative normal renal function and patients with preoperative RD. preoperative renal dysfunction were defined as serum creatinine levels greater than 1.5 mg/dl and GFR <60ml/min (estimated by renal radioisotope scan).The 173 patients (adult and pediatric) who were followed to one month after LDLT (Hospital stay time) were classified as group I (n = 144) 82.7%, creatinine < 1.5 mg/dl versus group II (n = 29), 17.3%, creatinine > 1.5 mg/dl.Each group was classified as subgroups into gp.I (125) 85.8% and gp.II (18) 14.4%in adults, gp. I (25) 77.3% and gp.II (4) 22.7% in pediatrics. The mean MELD score (within one week before liver transplantation), in adult group was 18.50+7.66 with p-value > 0.05. PELD score was 19.7576+19.8798 in ped. group with p-value >0.05. Hepatitis C (HCV) was the main underlying etiology of liver cirrhosis and indication for OLT studied patients (n=82)61.6%, while HCC was (n=45)19.2%. Only (n=3)2.1% of the studied patients Suffered from pre LDLT hypertension, (n=35) 24.3% and (n=6) 4.2% in both. Noted that all the studied patients received grafts with GRWR not less than 0.9. As regards the postoperative complications, primary graft non function and post-LT infection were statistically significant risk factors for ARD (P>0.05, P=0.05) respectively. Post-operative surgical interference, acute cellular rejection (ACR), CMV infection, and type of calcineurin inhibitor (CNI) based immunosuppression (whether cyclosporine |or tacrolimus) were significant factors associated with ARD (p>0.05

In conclusion: postoperative renal transplantation in adult's groups. In both groups, operative time/min, intraoperative plasma transfusion /unit, actual graft w.t SFS (GRWR < 0.8) are the most important risk factors for early postoperative renal transplantation. Considering the limitation of the uncontrolled retrospective nature of the present analysis, these observations may be useful to establish a treatment strategy for high risk liver transplant patients.

Disclosure of Interest: None Declared

P053

NOVEL PERSPECTIVES FOR EARLY DIAGNOSIS OF HEPATIC CIRRHOSIS AS A NEW APPROACH TO PREVENTING DISEASE

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Abstract Content: In cases of neglected persistent metabolic disorders of the liver, which are more often associated with toxic phenomena, eventually lead to liver cirrhosis. The biochemistry of liver failure is very complicated because the liver is involved in all metabolic processes in the body. The biochemical, physiological, and behavioral processes of diverse living organisms adapt to a variety of geophysical cycles, including the lunar cycle.

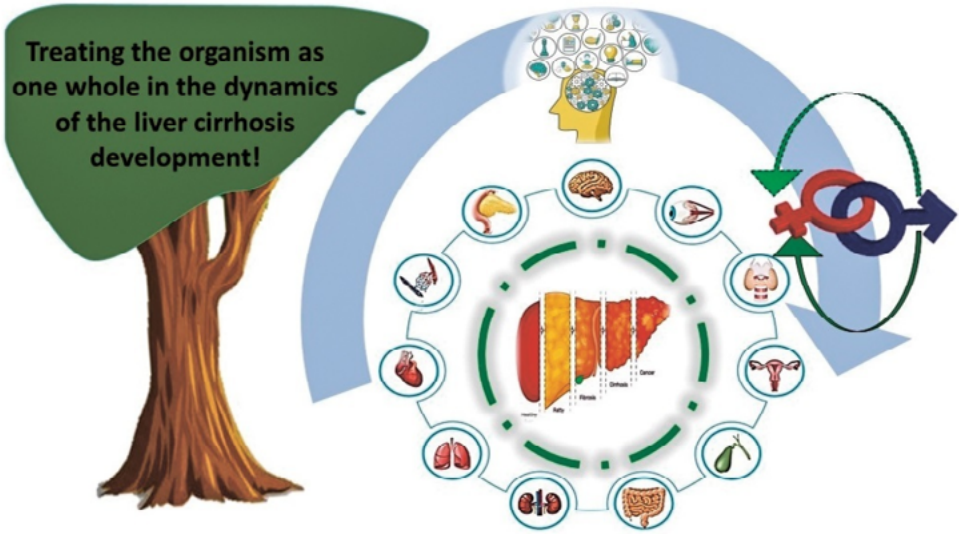
In this study, we set out to investigate the characteristics of gender-specificity, seasonality, and the lunar cycle in our model of pre-diagnosis of cirrhosis. Experimental designs of carbon tetrachloride-induced hepatic cirrhosis were used in the laboratory studies.

Research has documented that the manifestations of weight changes vary with the lunar calendar. In male animals, weight loss was predominantly observed during the full moon cycle. It may be related to hormonal features and emotional manifestations and is dependent on functional deviation from organic affiliation. Weight gain or loss can be attributed to the violation of the relationship between functional impairment of the liver and irritability. It's mixed during the full moon.

Estimation of hepatocyte nuclearity showed severe variations depending on gender. The total percentage of binuclear hepatocytes is higher in females compared to males, indicating more intensive regenerative processes. It turns out that during the preliminary diagnosis of cirrhosis, it is necessary to consider that in females there may be a delay in the development of cirrhosis because of the intensification of regenerative properties.

At first glance, the same anatomical modifications of the liver may be contradictory to the preliminary diagnosis of cirrhosis, unless taken seasonality and gender specificity into account right down to emotional manifestations. According to lunar rhythms, the approach of diagnosis and examination of cirrhosis should also be re-examined also according to gender.

Image/Table:



Disclosure of Interest: None Declared

P054

BIOINFORMATICS STUDY OF GENES E1 AND E2 FROM HEPATITIS C VIRUS (HCV) WITH GENOTYPES 1, 2, 3, AND 6 AS VACCINE CANDIDATES FOR VIRUS-LIKE PARTICLES (VLPS)

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Abstract Content: Hepatitis C is a liver infection caused by the Hepatitis C virus (HCV). Hepatitis C can be a short-term illness, but for most people, acute infection leads to chronic infection. Chronic Hepatitis C can cause serious health problems, including liver damage, cirrhosis (scarring of the liver), liver cancer, and even death. Chronic Hepatitis C can be a lifelong infection if left untreated. HCV vaccine is very necessary to prevent transmission of infection. The difficulty faced is the number of HCV genotypes in circulation. In Indonesia, there are genotypes 1, 2, 3, and 6. The HCV vaccine must be able to provide protection against infection with several genotypes. Therefore, the development of the HCV vaccine takes a long time. One vaccine approach is the Viral-like Particles (VLPs) vaccine. The E1-E2 protein found on the surface of the virus is a very good candidate to be used as a VLPs vaccine material because it has high immunogenicity. In this study, bioinformatics analysis was carried out on genes E1 and E2 from genotypes 1, 2, 3, and 6. The sequences of these genes were obtained through the GenBank and further analyzed using some software such as Bio Edit Sequence Alignment Editor, BLAST, and BLAST Primer. The results of this study were successful in obtaining consensus sequences of E1-E2 genes derived from genotypes 1, 2, 3, and 6 which have a length of 1672 bp. This sequence forms the basis for the primary pair design and the primers are obtained. Primary X sequence has been confirmed using BLAST and X primary sequence has a high homology rate (> 90%).

Disclosure of Interest: None Declared

P055

PREVALENCE OF HEPATITIS A VIRUS AND HEPATITIS E VIRUS INFECTION IN PATIENTS PRESENTING WITH ACUTE VIRAL HEPATITIS IN A TERTIARY CARE HOSPITAL IN NORTH INDIA

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Background: Despite being significantly different in genetic structure both Hepatitis A (HAV) and E (HEV) virus employ almost similar strategies to evade host immune system and environmental transmission. Millions of cases of acute viral Hepatitis Caused by Hepatitis A and Hepatitis E virus are being reported each year worldwide which causes significant risk to public health specially in resource limited settings.

Purpose: Present study was conducted to determine the epidemiology, prevalence and correlation with Serum Glutamic Pyruvic Transaminase (SGPT) levels in acute viral Hepatitis Cases due to Hepatitis A virus and Hepatitis E virus.

Methods: This retrospective observational study was conducted from January 2019 to November, 2022, which included 6517 participants presenting with clinical features of acute viral Hepatitis. Serum samples of these patients were tested for IgM anti HAV and IgM Anti HEV. SGPT levels of all the patients were also recorded.

Results: Of 6517 patients, 596 (9.14%) patients tested positive for IgM Anti HAV while 1195 (18.33%) tested positive for IgM anti HEV antibodies. A total of 49 patients showed positivity for both anti-HAV IgM and anti-HEV IgM antibodies indicating coinfection. Our study indicated that both Hepatitis A and Hepatitis E virus infection was present in higher frequency among males than females. SGPT levels were raised in 88.6% of HAV and 73.6% of HEV infection.

Conclusion: Our study revealed though HEV infection has high frequency than HAV infections but liver enzyme (SGPT) was more deranged in HAV infection. Though, we found high prevalence of HAV (9.14%) and HEV (18.33%) infection; cause of rest of the cases of acute Hepatitis (72.53%) was not HAV and HEV. We also did not find Hepatitis B and Hepatitis C infection as the only cause of acute Hepatitis in HAV and HEV negative cases though very few were found co-positive along with HAV and HEV.

Disclosure of Interest: None Declared

P056

RIFAMPICIN INDUCES HEPATOTOXICITY THROUGH PARAPTOSIS LIKE ALTERNATE PROGRAMMED CELL DEATH PATHWAY IN LIVER CELLS

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Background and Purpose: Drug-induced liver injury (DILI) poses a considerable threat to liver and overall therapeutic outcomes in the clinics. Rifampicin is an antibiotic drug frequently used to treat several types of bacterial infections including tuberculosis. Rifampicin is known to cause acute liver injuries that may become severe or sometimes fatal. However, the mechanism underlying rifampicin-induced DILI remains poorly understood. Here, we have investigated the mechanism underlying rifampicin-induced DILI.

Method: Rifampicin-induced liver toxicity was studied in human hepatocyte line17 cells (HHL-17) and male Wistar rats. HHL-17 cells were treated with rifampicin for 24h at different concentrations [100µM-1mM], and animal were treated with 150 mg/kg body weight/day for 14 days, to examine the toxicity. Various parameters e.g. cell viability (Alamar blue assay), reactive oxygen species (DCFDA) analysis, protein and mRNA expression of targets involved in cell death using Western blotting, RT-PCR respectively, histopathology and serum markers (ALT, AST and ALP) analysis were performed to understand the mechanism underlying rifampicin-induced liver injury.

Results: Rifampicin treatment induced a dose-dependent cell death in HHL-17 liver cells as evident with the viability assay and IC_{50} of rifampicin was noted at 600 µM in HHL-17 cells after 24 h of treatment. Histopathology analysis in rifampicin-treated rats also corroborated the rifampicin-induced liver injury. Further, rifampicin induced reactive oxygen species generation that accompanied with the peculiar morphological changes having as numerous vacuole formation within the cytoplasm in HHL-17 cells. Western blot analysis indicated the absence of catalytic cleavage of caspase 3 and PARP1 in rifampicin treated HHL-17 cells. Moreover, Rifampicin treatment resulted in the reduced expression of alix1 protein that suggested the involvement of paraptosis like alternate cell death pathway.

Conclusion: Rifampicin may exert hepatotoxicity by inducing paraptosis like alternate cell death pathway. Targeting of paraptosis pathway may help to reduce rifampicin-induced liver injury.

Disclosure of Interest: None Declared

P057

ANTI-HBV ACTIVITY OF TARGETED BIOLOGICAL NANOPARTICLES LOADED WITH CRISPR/CAS RIBONUCLEOPROTEIN COMPLEXES

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Abstract Content: Chronic Hepatitis B (CHB) is a global health issue, with over 250 million people infected around the world. CHB is caused by infection of hepatocytes by Hepatitis B virus (HBV), which forms a highly persistent covalently closed circular DNA (cccDNA) genome which cannot be purged out of infected cells using available antivirals. Several highly effective anti-HBV approaches able to directly target HBV cccDNA have been devised recently based on CRISPR/Cas systems. CRISPR/Cas systems are powerful tools for genome editing, correcting disease-associated mutations, regulating transcription of genes and, in general, manipulating the genome. Moreover, they are being studied as highly effective antivirals. Previously, CRISPR/Cas nucleases were shown to reduce HBV cccDNA and other viral parameters by >99%. However, the major issue in the practical use of CRISPR/Cas is the lack of effective systemic delivery tools. Many efforts were undertaken to develop CRISPR/Cas delivery tools using nanotechnologies, but with limited success. Here, we developed a novel approach for delivering CRISPR/Cas ribonucleoprotein complexes (RNPs) in biological nanoparticles (NPs). We developed a novel genetic technology, which we called «CRISPR-touch», that enables tunable, stimulus-inducible co-packaging of Cas proteins together with sgRNAs into several types of biological nanoparticles. Moreover, we combined it with novel technologies for programming the surface of NPs to ensure effective targeted delivery into hepatocytes using several hepatocyte-specific peptides.

«CRISPR-touch» technology was characterized for in vitro nucleolytic activity, loading efficiency of Cas protein and sgRNA, nucleolytic and anti-HBV activity. Produced NPs were characterized by DLS, cryoEM and western blotting. Loading of Cas protein and sgRNA was enhanced by CRISPR-touch technology over 10-1,000-fold compared to stochastic packaging. Functionalization of NPs increased NPs internalization by >10-times compared to non-functionalized NPs at an in vitro HepG2 model, and by 30-40% in mice in vivo. Treating HepG2 cells transfected with recombinant HBV cccDNA with a single dose of CRISPR/Cas-loaded NPs demonstrated remarkable antiviral and nucleolytic activity with >90-95% reduction in HBsAg, HBV DNA, cccDNA and pgRNA.

To conclude, we developed the first genetic technology for tunable co-packaging of CRISPR/Cas RNPs into biological NPs that demonstrated remarkable antiviral activity and efficient organ-specific delivery.

Funding: this study was supported by RSF grant No 20-15-00373.

Disclosure of Interest: None Declared

P058

SEROLOGIC AND MOLECULAR DETECTION (POOLYMERASE CHAIN REACTION) OF HEPATITIS B VIRUS IN LOW-VOLUME SAMPLES

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Background: Hepatitis b virus (HBV) is a global health issue with approximately 296 million people chronically infected. The detection of the Hepatitis b surface antigen (hbsag) is the cornerstone of HBV diagnosis. Most HBV testing protocols use plasma or serum however in certain instances such as in infants or retrospective studies, insufficient sample volumes is a limitation. Therefore we sought to optimize a protocol for serologic and molecular detection of HBV in low-volume samples.

Methods: archived plasma samples from people living with hiv (plwh) from the botswana combination prevention project (bcpp) were used. Twenty-four hbsag positive samples with known optical densities (ods) were used. The samples were divided into three categories: high positive, low positives and medium positives based on their ods as shown in table 1 below. Serial dilutions of 1:10, 1:100, 1:1000 and 1:10 0000 of sample: phosphate buffered saline (pbs) were performed. Hbsag was then screened in the samples with the various dilutions using the murex hbsag version3 following manufacturer's instructions.

For dna extraction, 2 samples were selected at random from each of the three categories and serial dilutions were done as described above. Polymerase chain reaction (pcr) was used to amplify the 415 base pair fragment of the surface gene.

Results: the results show that all high and medium positives remain positive from the1:10 to the 1:10 000 dilutions. The low positives were all positive at the 1:10 dilution, however (4/9) 44% of low positives lost hbsag at the 1:100 dilution and an additional (3/9) 33% lost the hbsag positivity by the 1:1000 dilution. These results show that regardless of the od, 10-1dilution remains positive.

There was a (3/4) 75% pcr success rate for the 1:10 dilutions from all three categories for the samples that had enough volume. A pcr success rate of (3/6) 50% in the 1:100 dilution, both high positives were amplified but none of the low positives were amplified while only one of the medium positives was amplified. The success rate from the 1:1000 dilution was (2/5) 40% of the samples amplified with low positive and medium positive being amplified.

Conclusions: we conclude that the 1:10 sample dilution retains hbsag positivity in high positives, low positives and mid-positives. We also found that regardless of od, 75% of the 1:10 diluted samples were amplified. Optimization of dilution protocols for other HBV markers is warranted.

Table 1: classification of samples based on od

Keywords: hbsag, pcr, dilutions, optical density

Disclosure of Interest: None Declared

P059

ROLE OF THERAPEUTIC PLASMA EXCHANGE (PLEX) IN VIRAL HEPATITIS WITH PROLONGED CHOLESTASIS - A RETROSPECTIVE STUDY

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Background : Hepatitis A is a common viral cause of Hepatitis but is usually self limited. In certain cases it has a prolonged cholestatic course which manifests as pruritis, malaise, malnutrition , rising bilirubin and risk of bilirubin cast nephropathy. Pruritis refractory to medical management causes severe discomfort impaired quality of life. Use of therapeutic plasma exchange (PLEX) for cholestatic liver disease has been reported in various case reports and series. Here we report a retrospective analysis of patients who underwent PLEX for viral Hepatitis with prolonged cholestatic phase.

Methods: Patients with viral Hepatitis with prolonged cholestatic phase (>2 weeks) who underwent therapeutic PLEX were included in this retrospective study. Indication of PLEX was refractory pruritis and High/rising serum bilirubin(>25 mg/dl). The primary outcome was to assess response to pruritis and improving quality of life. Secondary objectives were to observe change in serum bilirubin, ALP, INR, and to assess the adverse events related to PLEX.

Results: A total of 15 patients underwent PLEX. The mean age was 20 years. All 15 patients had viral Hepatitis A (IgM HAV positive) with refractory prolonged cholestasis. Three patients had history consumption of complementary alternative medicine (CAM) after the onset of jaundice. Each patient in both the groups underwent a median of 2 sessions of PLEX. Each PLEX was standard volume (Total plasma volume x 1 time). There was a significant decrease in serum bilirubin levels(-7.93+/-5.1, P=0.5) and prothrombin time post-PLEX. 13 patients had significant reduction in pruritus after PLEX which was analysed by pruritis visual analogue scale. This adequate response lasted for median duration of 10 days (+/- 3 days) with later mild pruritis which was adequately managed medically. The other 2 patients had a short lasting response (2 days) in reduction in pruritis after 2 sessions of PLEX. These were the patients who had intake of CAM along with viral Hepatitis. One patient developed volume overload features and was managed conservatively.

Conclusions: Plasma exchange efficacious in reduction of refractory pruritis, serum bilirubin and improving quality of life in prolonged cholestatic viral Hepatitis. Response was short lasting among those with additional aetiology like complementary alternative medication.

Image/Table:

Base line variables of patients

Variables	Total number (15)	P
Age	17.75±5	0.66
Gender	Males 11 , Females 4	
Pre-TB	32.07±5.1	0.7
Pres-AST	158.63±102	0.92
Pre -ALT	190+/-120	0.88
PT	15.5+/-10	0.39
INR	1.3+/-0.6	0.84
TLC	6800+/-3000	0.74
Na	137±3.74	0.1

Disclosure of Interest: None Declared

P060

EVALUATION OF A NOVEL NONINVASIVE TEST (FIB-6) SCORE IN ASSESSMENT OF LIVER FIBROSIS IN CHRONIC HEPATITIS B

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Background: Non-invasive alternatives to liver biopsy have been assessed with suboptimum accuracy in assessing liver fibrosis in patients with chronic Hepatitis B (CHB). We recently developed a simple novel index called fibrosis 6 (FIB-6) using machine learning data analysis. This index integrates routine clinical and laboratory parameters for predicting the stage of hepatic fibrosis and is both internally and externally validated in Chronic Hepatitis C.

Aims: To evaluate the performance of the FIB-6 index in the diagnosis liver fibrosis and cirrhosis in CHB.

Methods: This is a retrospective observational analysis of data obtained from seven sites (Egypt, KSA, Turkey, Greece, Oman, Qatar, and Jordan) of CHB patients. The inclusion criteria include receiving an adequate liver biopsy and a complete dataset (biochemical and hematological data). Diagnostic performance analysis of the FIB-6 index was conducted and compared with other non-invasive scores.

Results: In this study, 603 patients met the criteria, and their data were included for analysis; the AUROC for FIB-6 for the discrimination of patients with cirrhosis (F4), cACLD (F3 and F4), and significant fibrosis (F2–F4), from the lower stages, were 0.854, 0.812, and 0.745, respectively. Analysis using the optimal cut-offs of FIB-6 showed a sensitivity of 70.9% and specificity of 84.1%. PPV = 40.3% and NPV = 95.0% for diagnosis of cirrhosis. For diagnosis of cACLD, the results were 71.5%. 69.3%. 40.8% and 89.2% respectively, while for diagnosis of significant fibrosis, the results were 68.3%, 67.5%, 59.9% and 75.0%).

When compared with those of FIB-4, APRI, and AAR, the AUROC for the performance of FIB-6 was higher than those of FIB-4, APRI, and AAR in all fibrosis stages. FIB-6 gave the highest sensitivity and NPV (89.1% and 92.4%) in ruling out compensated advance liver disease (cACLD) and cirrhosis, as compared to FIB-4 (63.8% and 83.0%), APRI (53.9% and 86.6%), and AAR (47.5% and 82.3%) respectively using the rule out cut-off value.

Conclusions: The FIB-6 index is valuable for diagnosing fibrosis stages in CHB patients. It can be used in ruling out cACLD, fibrosis, and cirrhosis with good reliability.

Disclosure of Interest: None Declared

P061

DIFFICULT TO TREAT PATIENTS WITH GT1A HEPATITIS C IN LIMITED TREATMENT OPTIONS: REAL LIFE DATA FROM LATVIA

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Background: WHO has settled a goal – to eliminate HCV as a public health threat by 2030 According to previous epidemiological studies there is 1.7% prevalence of HCV-RNA in Latvian population. There is available an effective HCV treatment with 100% reimbursement, but with restrictions – 1st genotype has to be treated with grazoprevir/ elbasvir, which is highly effective in GT 1b, but less effective in GT 1a, and not suggested by EASL. There are 5% GT 1a HCV patients in Latvia.

Purpose: The aim of this study was to evaluate HCV treatment efficacy in GT1a patients with grazoprevir/ elbasvir.

Methods: We analyzed results in GT1a Hepatitis C patients who were treated with grazoprevir/ elbasvir in Latvian Center of Infectious Diseases during 2019 – 2022. In total 268 patients received treatment, but 83 (31%) persons were lost from follow up. 185 (69%) were tested for SVR (HCV-RNA undetectable 12 weeks after treatment), in this group further analysis was performed. 136 out of them were men and 49 women, at the age range 22 to 75. According to the *Metavir* fibrosis score 81 patient had F1, 63 – F2, 14 – F3 and 27 – F4 Fibrosis stage was detected by *Fibroscan*. Patients received 12 weeks treatment with grazoprevir/elbasvir 100/50 mg once-daily. The primary efficacy end point was a sustained virologic response (SVR) 12 weeks after the end of treatment.

Results: Overall 169 patients out of 185 included achieved SVR, for a rate of 91,3%. In patients with F4 the SVR rate was 92,6% (25 patients out of 27), in patients with F1-F3 SVR achieved 144 out of 158 patients, for a rate of 91,1%, the difference between these groups was not statistically significant (*p value* 0.8). In men SVR was achieved 89% of cases (121 patient out of 136), in women – 98% (48 out of 49), the difference was not statistically significant (*p value* 0.055).

Conclusions: Treatment with grazoprevir/ elbasvir is effective in patients with HCV GT 1a and can be used in settings where pangenotypic DAA regimens for all genotypes are not available or reimbursed.

Disclosure of Interest: None Declared

P062

COMORBIDITY ASSESSMENT IN THE VULNERABLE POPULATION DIAGNOSED WITH CHRONIC B/D AND C VIRAL INFECTION FROM THE NORTHEAST REGION OF ROMANIA – STAGE SCREENING RESULTS LIVE(RO) 2 – EAST

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Introduction: Chronic viral Hepatitis B/D and C can be complicated by comorbid conditions that may influence treatment eligibility and outcomes. The aim of this study was to evaluate the presence of the most common comorbidities in patients diagnosed with chronic viral B/D and C infection using rapid diagnostic tests (TDR).

Materials and methods: Between July 2021 and September 2022, we performed prospective screening for chronic viral B/D and C infection in people in vulnerable groups (poor, uninsured, rural people, people in foster care, people without shelter, Roma people, people with disabilities, people suffering from alcohol and drug addiction) from different areas of North-Eastern Romania, during the national program for the elimination of viral Hepatitis LIVE(RO) 2-EST using TDRs for Hepatitis B virus (Wama Immuno-Rapid HBV®) and Hepatitis C virus (Wama Immuno-Rapid HCV®). We also investigated the presence of comorbid conditions in patients tested positive and presented at the Institute of Gastroenterology and Hepatology in Iasi for the staging of liver disease and the establishment of antiviral treatment.

Results: Our study included 1176 patients who came to a tertiary center for the staging of liver disease, of which 422 men (35.8%) and 754 women (64.1%), aged 35 to 83 years, with an average age of 56.32 years. The predominant source of origin was rural (73.1%). Of the patients with positive TDR, 635 (53.9%) of patients were detected with HBsAg, 521 (44.3%) of patients with anti-HCV antibodies, and 20 (1.7%) of patients with anti-HVD antibodies. Of these, 646 patients (54.9%) had at least one comorbid condition. The most common comorbidities were cardiovascular disease (21.5%), psychiatric disorders (11.5%), type 2 diabetes (8.9%), metabolic disorders (6%), thyroid disorders (5%) and cancer (2%). In addition, the presence of comorbidities was higher among patients with HCV infection than in those with HBV infection (64.9% vs. 48.5%, p = 0.014), while psychiatric disorders were most common in patients with HBV/HVD coinfection (42.3%), most likely due to the Interferon regimen that has been administered in the past to 19 individuals.

Conclusions: Patients with chronic viral Hepatitis B/D and C had a high prevalence of multiple comorbidities. Effective strategies are needed to manage these comorbid conditions as well as interdisciplinary collaboration to allow greater access to antiviral treatment and to reduce the future burden of advanced liver disease and its manifestations.

Disclosure of Interest: None Declared

P063

FEASIBILITY AND OUTCOMES OF A COMMUNITY-PHARMACIST LED PROGRAM TO TREAT HEPATITIS C VIRUS AMONG PERSONS WHO INJECT DRUGS

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Aim: Persons who inject drugs (PWID) are a key population for treatment with direct-acting antiviral medications (DAAs) to reach Hepatitis C virus (HCV) elimination goals. We describe clinical outcomes of a pilot program utilizing a community pharmacist to offer active PWID DAAs for HCV, as well as medications for opioid overdose and HIV prevention.

Methods: We conducted a single-arm prospective study of PWID with HCV who were recruited from a Seattle syringe service program, opioid treatment program, or emergency housing. Persons were eligible if they were ≥18 years old, had injected drugs within the past 90 days, reported having HCV, and were willing to link to a pharmacist through a patient navigator. Participants completed baseline and 6-month follow-up surveys. Data were abstracted from electronic health records for up to 12 months following enrollment? for information on linkage to the pharmacist. Secondary outcomes included HCV treatment initiation, treatment completion, and cure (undetectable viral load 12 weeks after treatment completion, SVR-12).

Results: Between November 2020 and October 2021, 40 PWID were enrolled and referred to the pharmacist. Of those, 21/40 (53%) had not previously sought HCV treatment. Mean age was 43.6 years, and 16 (40%) were female, 19 (48%) were non-white and 12 (30%) were homeless. Thirty-eight (95%) were successfully linked to the pharmacist for initial evaluation. At 6 months, 22/38 (58%) had received a DAA prescription, and 17/22 (77%) completed treatment. Among those who received DAAs, 12/22 (55%) had SVR-12 data available; of those, 11/12 (92%) achieved cure.

Conclusion: This study demonstrated the feasibility of linking PWID (many who were homeless and from marginalized communities) to a community pharmacist-led program for HCV care. Most participants initiated DAAs leading to cure, suggesting a role for this model in addressing treatment disparities.

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Disclosure of Interest: None Declared

P064

START OF THERAPY HBEAG NEGATIVE CHRONIC HEPATITIS B PATIENTS HAVE HIGHER RATES OF VIROLOGICAL RELAPSE AFTER NUCLEOS(T)IDE ANALOGUE WITHDRAWAL COMPARED TO HBEAG POSITIVE PATIENTS (RETRACT-B STUDY)

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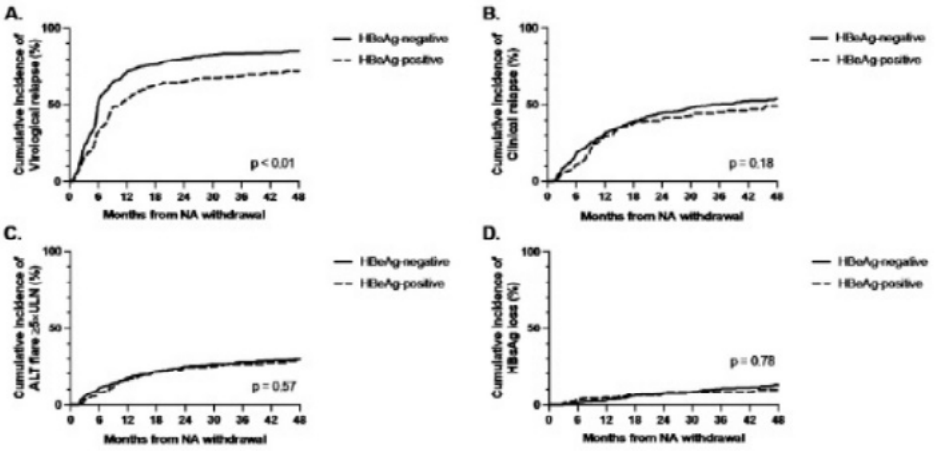
Background: The association between Hepatitis B e antigen (HBeAg) status at start of nucleos(t)ide analogue (NA) therapy, and off-therapy outcomes remains unclear. We aim to examine differences in off-therapy outcomes such as relapse, ALT flaresm and HBsAg loss by start of therapy HBeAg status among a large, international cohort of chronic Hepatitis B (CHB) patients who discontinued NA therapy.

Methods: Cohort study of CHB patients who stopped NA therapy from centres across North America, Europe, and Asia. All included patients were well suppressed, HBeAg negative, and non-cirrhotic at NA withdrawal. Race-stratified Cox regression (adjusted for age, sex, NA therapy duration, treatment history, and ALT and HBsAg levels at the end of therapy) was used to analyze rates of off-therapy relapse (virological: HBV DNA ≥2,000 IU/mL; clinical: HBV DNA ≥2,000 IU/mL and ALT ≥2xULN), ALT flares (≥5 or 10xULN), and HBsAg loss.

Results: Among 1,360 CHB patients, 1,142 were start of therapy HBeAg negative and 218 were HBeAg positive. The HBeAg negative group was older (54 vs 43 years), had a higher proportion of males (73% vs 65%), fewer patients previously treated with interferon (8% vs 14%), and lower HBsAg levels at NA withdrawal (2.6 vs 3.1 $\log_{10}$ IU/mL) ($p<0.05$ for all). Duration of NA therapy and racial composition were comparable between groups. The HBeAg negative group had relatively higher rates of virological relapse (adjusted hazard ratio [aHR] 1.9, $p<0.01$) but not clinical relapse (aHR 1.2, $p=0.14$). Other significant predictors of virological relapse included HBsAg levels at NA withdrawal ($\log_{10}$ IU/mL, aHR 1.7), tenofovir vs entecavir treatment (aHR 1.6), and prior use of other NAs (aHR 1.2) ($p<0.05$ for all). For clinical relapse, HBsAg ($\log_{10}$ IU/mL, aHR 1.9) and ALT (xULN, aHR 1.4) levels at NA withdrawal, tenofovir versus entecavir treatment (aHR 1.6), prior use of other NAs (aHR 1.5), and male sex (aHR 1.6) were significant factors ($p<0.01$ for all). There were no significant differences in rates of ALT flares (≥5 or 10xULN) or HBsAg loss.

Conclusion: Compared to start of therapy HBeAg positive patients, start of therapy HBeAg negative CHB patients experienced higher rates of virological relapse, despite having longer time spent in the HBeAg negative phase of infection. Off-therapy ALT elevations and HBsAg loss were not associated with HBeAg status at start of therapy.

Image/Table:



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P065

A REVIEW OF COMPUTATIONAL DRUG REPOSITIONING: STRATEGIES, APPROACHES, OPPORTUNITIES, CHALLENGES, AND DIRECTIONS

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Abstract Content: Drug repositioning is the process of identifying novel therapeutic potentials for existing drugs and discovering therapies for untreated diseases. Drug repositioning, therefore, plays an important role in optimizing the pre-clinical process of developing novel drugs by saving time and cost compared to the traditional de novo drug discovery processes. Since drug repositioning relies on data for existing drugs and diseases the enormous growth of publicly available large-scale biological, biomedical, and electronic health-related data along with the high-performance computing capabilities have accelerated the development of computational drug repositioning approaches. Multidisciplinary researchers and scientists have carried out numerous attempts, with different degrees of efficiency and success, to computationally study the potential of repositioning drugs to identify alternative drug indications.

Disclosure of Interest: None Declared

P066

THE ASSOCIATION OF HEPATITIS B VIRUS E ANTIGEN WITH HBV VIRAL LOAD IN BOTSWANA

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Background: Hepatitis B virus (HBV) is a major worldwide health concern affecting approximately 296 million people globally. HBV diagnosis and monitoring are based on HBV surface antigen (HBsAg), HBV e antigen (HBeAg), and nucleic acid (NAT) testing. However, HBeAg is employed to evaluate chronic HBV (CHB) patients treatment eligibility and prevent mother-to-child transmission (PMTCT) in resource limited countries, thus a need to study it further. The aim of this study was to evaluate the use of HBeAg as a proxy for HBV viral load to determine treatment eligibility for the first time in Botswana.

Methods: A total of 299 archived HBsAg positive plasma samples from people living with HIV (PLWH) were screened for HBeAg and HBV viral load was quantified using a commercial platform with a lower limit of detection of 20 IU/mL. HBV viral load of ≥ 20000 IU/mL was used to determine treatment eligibility while ≥200000IU/mL cut-off was used for qualification of HBV PMTCT using World Health Organisation (WHO) guidelines. Chi-square was used to determine association of HBV viral load categories and HBeAg status. R v.4.0.1 package was used for statistical analyses and p-values of ≤0.05 were considered statistically significant.

Results: From 299 participants, 191 (63.9%) were females with a median age of 41 (IQR: 35 – 50). Median HIV viral load was 1.60 IU/mL (IQR: 1.60 – 2.09). HBeAg prevalence was 17/191 (8.9%) amongst females and 13/108 (12%) amongst males with no difference between genders (p-value=0.386). Only 167/299 (55.9%) were screened for both HBV viral load and HBeAg. Using a cut-off point of 20 000 IU/mL, 17 (73.9 %) participants who were HBeAg positive qualified for treatment while 7 (4.9%) were HBeAg negative with HBV viral load >20000. With PMTCT guidelines, 14 (16.8%) individuals had viral loads > 200000IU/mL while 2 (1.4%) were HBeAg negative with qualifying viral load (Table 1). There was an association between HBeAg and HBV viral load (p<0.001) for both treatments of CHB patients and PMTCT qualification.

Conclusions: The study results support the use of HBeAg as proxy for HBV viral load to evaluate patients eligibility for treatment in resource-limited settings where HBV NAT is unavailable. However, there remains a percentage of individuals who would not be treated based on HBeAg status only hence posing the risk of transmission and disease progression. Further studies on HBeAg negative participants with high viral loads are warranted

Disclosure of Interest: None Declared

P067

PRZ18072, A BILE ACID-AMINO ACID CONJUGATE, PREVENTS HEPATITIS B VIRUS INFECTION BY INHIBITING PRES1-SODIUM TAUROCHOLATE CO-TRANSPORTING POLYPEPTIDE INTERACTION

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Abstract Content: Despite efficient suppression of Hepatitis B virus (HBV) replication by s nucleos(t)ide analogue reverse transcriptase inhibitors, current therapeutic options for chronic Hepatitis B cannot inhibit de novo infection and maintenance of cccDNA. Thus, several antiviral strategies, including capsid assembly inhibition or elimination of viral RNAs, have been actively studied. Among such antiviral strategies, blocking HBV entry combined with viral replication inhibitors has been suggested as a novel therapeutic strategy to achieve the functional cure for chronic Hepatitis B by inhibiting de novo infection of newly differentiated hepatocytes. Recently, a peptide-based entry blocker, Hepcludex, was approved for the treatment of HBV/HDV co-infection.

We developed a series of novel synthetic bile acid compounds that inhibit HBV entry via sodium taurocholate co-transporting polypeptide (NTCP), an entry receptor for HBV and HDV. By screening the focused synthetic bile acid library, PRX18072 was identified as an efficient HBV entry inhibitor.

Orally administered PRZ18072 markedly diminished the levels of HBsAg, HBeAg, HBV DNA and cccDNA in chimeric mice with humanized liver (PXB mice). Also, PRZ18072 did not show any significant adverse events in GLP toxicology studies. Due to its similarity to endogenous ligand, PRZ18072 displayed entero-hepatic circulation pattern pharmacokinetics and high liver-to-plasma ratio. Collectively, our results suggest that PRZ18072 is a potential candidate as an orally available anti-HBV/HDV drugs with minimal side effects.

Disclosure of Interest: None Declared

P068

ANTIVIRAL EFFECTS OF GLYCO-PEPTIDE NUCLEIC ACID (PNA) CONJUGATES ON HEPATITS B VIRUS IN HEPARG CELL LINE

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Introduction: Hepatitis B infection represents a major global health problem worldwide. Because the efficiency of current treatments remains limited, the alternative therapeutic approaches for chronic infection need to be developed. In this view, peptide nucleic acid (PNA) appear of particular interest as novel therapeutic agents. Because the major problem of PNA application is their poor intracellular uptake, in this study, we chose the neoglycoproteins as vehicle for improve their transport across cell membrane. Indeed, the neoglycoproteins are the ligands for asialoglycoproteins receptors (ASGP-R), present on hepatocytes membranes, that is why we used the human hepatoma cell lines; the HepaRG cells.

Objectives and Methods: Thus, the ability of Glyco-PNA conjugates targeting Hepatitis B surface protein (anti-S PNA) and his DR1 region (anti-DR1 PNA), to inhibit viral replication was analyzed in HepaRG cells.

Results: Our results showed that anti-S PNA coupled to lactose specifically inhibit viral replication since a 2-nt mismatched PNA conjugate to the same sugar showed no marked inhibitory effect on release of HBsAg. By contrast the same PNA coupled to Mannose, inhibited viral replication in a not sequence-specific manner. Moreover, PNA targeting DR1 HBV region and coupled to the same Mannose, led to a specific inhibition of viral replication.

Conclusion: Taken together, our results suggest that the choice of sugar used as a vehicle may play an essential role in ability of glyco-PNA conjugates to inhibit viral replication. Additionally, the nature of PNA can influence or minimize the effect of coupling on the specificity of their antiviral activity.

Key words: Hepatitis B Virus (HBV); Peptide Nucleic Acid (PNA); Hepatocytes; Neoglycoproteins; Asialoglycoproteins Receptors (ASGP-R); HepaRG cells

Disclosure of Interest: None Declared

P069

IMPROVEMENTS IN BIOCHEMICAL HEPATITIS ACTIVITY DURING BULEVIRTIDE TREATMENT FOR HEPATITIS D ARE INDEPENDENT FROM VIROLOGIC RESPONSE

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Introduction: Hepatitis D is the most debilitating form of viral Hepatitis leading to liver cirrhosis and hepatocellular carcinoma. In 2020, the entry inhibitor bulevirtide was approved for the treatment of compensated liver disease in patients with chronic Hepatitis D. The conditional approval was based on promising results regarding improvements in biochemical Hepatitis activity and reduction of HDV-RNA. Indeed, the FDA and EMA suggest combined endpoints of virologic and biochemical response for clinical trials. Real-world data on treatment response are critical, as patient collectives in a clinical routine setting differ from those in controlled trials.

Methods: In a joint effort we retrospectively collected anonymized real-world data from 16 German centers treating patients with bulevirtide for chronic Hepatitis D. A total of 114 baseline cases was collected. ALT levels were considered normal when < 35 IU/l in female and < 45 IU/l in male patients. Virologic response was assumed when HDV-RNA was either undetectable, below the lower limit of quantification or had decreased by $\geq$ 2 log.

Results: At baseline, elevated ALT levels were measured in 99/114 patients. The mean ALT level was 115 IU/l. Over a mean observation time of 38 weeks we covered 4,289 patient weeks of bulevirtide treatment. Virologic response was observed in 87/114 cases. At the time point of virologic response ALT had decreased by 67 IU/l.

In analogy to clinical trials we investigated two distinctive time points (week 12 and week 24) in more detail. A subset of 33 patients had available data points at week 0, 12 and 24. In this group elevated ALT levels were seen in 26/33 patients. At week 12 and 24, ALT had normalized in 9/26 and 11/26, respectively. Within the first 12 weeks of treatment a significant decline of ALT was noted (114 IU/l vs. 53 IU/l, $p < 0.001$). This decline was also seen in patients without virologic response (Figure 1). We will present updated data with additional follow-up weeks at the meeting.

Conclusion: In real-world setting ALT levels improved under bulevirtide treatment. Interestingly, this improvement was independent from the virologic response status when investigating distinctive follow-up time points. A mechanistic explanation for this observation has not been found so far. The NTCP-blockade by bulevirtide protects hepatocytes from bile salts which may have anti-inflammatory effects. At the same time, the rise in bile salts in the peripheral blood may affect immune cells. The observation of improvements in biochemical Hepatitis activity is important as such improvements should theoretically translate into better clinical outcomes.

Image/Table:

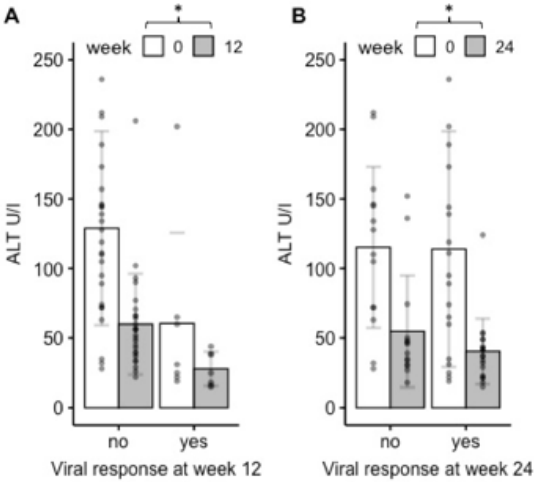

Figure 1. ALT levels at baseline and follow-up weeks grouped by viral response
Bars represent mean ALT levels at week 0 (white), week 12 (grey) and week 24 (dark grey). Error bars show the standard deviation. Individual data points are visualized by dots. Wilcoxon signed-rank tests were used for comparison of ALT at week 0 and 12 or 24; * $p < 0.05$

Disclosure of Interest: None Declared

P071

SUSTAINED VIROLOGICAL RESPONSE AFTER THE TREATMENT OF CHRONIC HEPATITIS C INFECTION AS A RISK FACTOR FOR OBESITY AND METABOLIC SYNDROME

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Aim: The cure of chronic Hepatitis C (HCV) is associated with decreased risk of liver-related complications in patients achieving virus clearance. Body weight gain is currently discussed as a negative consequence of the HCV cure. The aim of the study was to evaluate body weight gain and changes in serum lipid levels, the presence of diabetes mellitus, and hypertension in patients treated with direct-acting antiviral regimens (DAA).

Methods: We retrospectively evaluated data of 230 patients treated with DAAs who achieved sustained virological response (SVR), 127 males and 103 females, with an average age of 54 years. One hundred and seventy-nine (78%) were infected with HCV genotype 1, 45 (20%) with genotype 3, and 6 with other genotypes (2%). Sixty-eight patients (30%) had compensated liver cirrhosis before treatment. We recorded the body weight and clinical and laboratory data and assessed liver stiffness (LSM) and liver steatosis expressed as the Controlled Attenuation Parameter (CAP) by Fibroscan® before treatment and three years after the end of therapy.

Results: The mean patients' weight before treatment was 79.5 kg (46–130 kg). Three years after treatment, the mean body weight gain was 3 kg ($p < 0.0001$). Thirty-five patients (15%) gained more than 10% of their initial body weight. The weight gain did not differ between males and females and patients infected with HCV genotypes 1 and 3. The liver stiffness significantly decreased after the treatment, with a mean of 12.1 kPa (range 3.3–73.5 kPa) vs 8.1 kPa (range 1.9–75 kPa), $p < 0.0001$, but the CAP value did not change significantly (256 dB/m vs 261 dB/m, $p = 0.74$). Three years after the treatment, there was also an increased proportion of patients with hypertension (68 vs 93, $p < 0.03$) and hypercholesterolemia (21 vs 48, $p < 0.0006$), but not with diabetes (24 vs 31, $p = 0.39$). The patients with newly diagnosed hypertension or hypercholesterolemia did not have a higher weight gain than patients without the aforementioned ($p = 0.14$ and 0.14, respectively).

Conclusion: A significant weight gain seems common in patients who achieve DAAs-induced HCV clearance. The patients should be warned of the possible weight gain and the need for early dietary intervention after the end of antiviral treatment.

Disclosure of Interest: None Declared

P072

PREVALENCE AND RISK FACTORS OF NON-ALCOHOLIC STEATOHEPATITIS IN PATIENTS UNDERGOING CHOLECYSTECTOMY FOR GALLSTONE DISEASE WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Background: Gallstone disease (GSD) and non-alcoholic fatty liver disease (NAFLD) share common risk factors. Non-alcoholic steatoHepatitis (NASH) is a more progressive form of NAFLD and is among the most frequent causes of cirrhosis. There is a scarcity of prospective studies utilizing liver biopsy during laparoscopic cholecystectomy in patients with gallstones and NAFLD for assessing the prevalence of NASH and the factors associated with it. This study aimed to assess the role of liver biopsy in diagnosing NASH in patients with gallstones and NAFLD who underwent laparoscopic cholecystectomy.

Methodology: This was a prospective observational study done on 136 patients with ultrasound-diagnosed NAFLD out of 550 patients with symptomatic GSD. These patients underwent liver biopsy during laparoscopic cholecystectomy between March 2021 and June 2022. NASH was analyzed using the NAS score on hematoxylin and eosin-stained specimens of all patients. Fibrosis was analyzed on Mason's trichrome stained specimen of 82 patients.

Ordinal logistic regression analysis, adjusted for confounding variables, was performed to identify independent predictors of NASH in the entire study population. From this, the odds ratio and p-value were calculated.

Results: NASH was found in 21 (15.67%) patients [i.e., NAS score more than or equal to 5]. Fifty (37.31%) patients had probable NASH (i.e., NAS score of 3 and 4), and 63 (47.01%) had non-NASH scores (i.e., NAS score less than or equal to 2). In our study on univariate analysis, AST (aspartate aminotransferase) and ALT (alanine transaminase) levels were significantly different between the NASH and non-NASH groups (Table 1). The mean AST in patients with non-NASH was 28.95 $\pm$ 12.66 IU/L, with probable NASH was 33.12 $\pm$ 14.75 IU/L and in patients with NASH was 41.19 $\pm$ 20.53 IU/L (p-value = 0.028). On multivariate analysis, AST was found to be statistically significant with a p-value = 0.041 (Table 2). The mean CAP (Controlled Attenuation Parameter) in patients with non-NASH was 219.40 $\pm$ 60.44 dB/m, with probable NASH was 243.64 $\pm$ 59.70 dB/m and in patients with NASH was 265.48 $\pm$ 63.47 dB/m (p value = 0.006). Fibrosis was present in 33 of the 83 slides, with 17 patients having grade 2 and 2 with grade 3 fibrosis.

Conclusions: The high prevalence of NASH in patients of GSD with NAFLD may justify the need for routine liver biopsy during laparoscopic cholecystectomy in these patients to stage the disease and make necessary lifestyle changes to prevent complications.

Image/Table:

Table 1

Characteristics of patients with gallstones according to diagnosis on liver histology

Risk factors		Liver Biopsy			P-value
		Non-NASH (n = 63) (47.01%)	Probable NASH (n = 50) (37.31%)	NASH (n = 21) (15.67%)	
Age (in years)		41.2 5± 12.26	44.08 ± 10.31	46.76 ± 11.11	0.142
Sex	Male	18(40.9%)	22(50%)	4(9.1%)	0.076
	Female	45(50%)	28(31.1%)	17(18.9%)	
BMI(kg/m2)		25.86 ± 4.11	27.34 ± 3.69	26.65 ± 4.35	0.160
BMI Category	Normal	14(23.7)	3(6.5%)	3(18.8%)	0.158
	Overweight	24(33.6%)	23(50%)	5(31.3%)	
	Obese	21(42.9%)	20(43.5%)	8(50%)	
Presence of comorbidity	Absent	39(54.9%)	22(31%)	10(14.1%)	0.206
	Present	21(40.4%)	24(46.2%)	7(13.5%)	
Metabolic Syndrome	Absent	21(42.9%)	17(37%)	2(13.3%)	0.114
	Present	28(57.1%)	29(63%)	13(86.7%)	
Bilirubin (mg/dL)		0.72±0.54	0.67±0.42	0.63±0.39	0.652
AST (IU/L)		28.95 ± 12.66	33.12 ± 14.75	41.19 ± 20.53	0.028
ALT (IU/L)		28.26 ± 17.88	39.78 ± 27.45	44.71 ± 27.92	0.008
ALP (IU/L)		92.18 ± 44.44	98.25 ± 46.44	88.76 ± 25.20	0.633
Albumin (g/dL)		4.00 ± 0.40	4.03 ± 0.39	3.90 ± 0.57	0.492
INR		0.99 ± 0.13	0.94 ± 0.08	0.93 ± 0.10	0.073
Cholesterol (mg/dL)		160.0 ± 29.9	172.2 ± 44.2	172.4 ± 50.3	0.832
HDL (mg/dL)		50.45 ± 40.35	42.85 ± 10.46	38.20 ± 10.19	0.512
VLDL (mg/dL)		32.56 ± 13.30	29.99 ± 15.49	34.05 ± 9.96	0.480
LDL (mg/dL)		93.50 ± 29.38	99.30 ± 36.40	93.10 ± 42.66	0.651
Triglycerides (mg/dL)		161.77 ± 62.7	149.38 ± 76.7	219.97 ± 251.3	0.097
FBS (mg/dL)		104.50 ± 25.5	105.50 ± 27.4	106.32 ± 16.5	0.958
HbA1c (%)		5.72 ± 0.83	5.72 ± 1.41	5.66 ± 0.50	0.974
TSH (mIU/L)		3.82 ± 2.42	3.42 ± 3.39	5.33 ± 10.15	0.319
CAP (dB/m)		219.49 ± 60.4	243.64 ± 59.7	265.48 ± 63.47	0.006

Disclosure of Interest: U. Anand Conflict with: None, A. John Conflict with: None, R. Kumar Conflict with: None, T. Kumar Conflict with: None

P073

LOW-DOSE OBETICHOLIC ACID (OCA) IS SAFE AND EFFECTIVE FOR FIBROSIS REGRESSION IN NON-ALCOHOLIC STEATOHEPATITIS (NASH)

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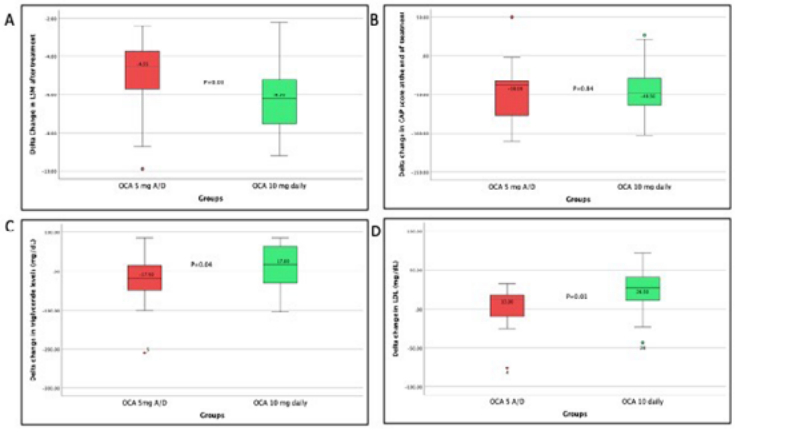
Background: Obeticholic acid (OCA) is a well-known anti-fibrotic drug. It has been used for the treatment of non-alcoholic steatoHepatitis (NASH). However, the adverse events associated with high-dose OCA are major concerns. We previously reported that 10 mg of OCA is sufficient for fibrosis regression in NASH. In this study, we aimed to compare the effect of low-dose (5mg) alternate-day OCA with 10 mg of OCA in patients with NASH.

Methods: In this retrospective study, patients with NASH treated with alternate-day OCA 5 mg (Gr.A), and daily 10 mg (Gr.B) were included. The primary objective was to compare the effect of OCA on fibrosis, and the secondary was to evaluate the effect on transaminases, lipid profile, and incidence of adverse events. Fibrosis was assessed using transient elastography.

Results: 42 non-lean patients (Gr.A-22 and Gr.B-20) with NASH were included over 2 years. Baseline characteristics were similar among both groups. Four in Gr. A and five in Gr. B had concomitant inactive HBV infection. Nine percent in Gr. A and 20% in Gr. B were females. The baseline mean controlled attenuation parameter (CAP) was 330.18 $\pm$ 37.66 dB/m in Gr. A and 348.25 $\pm$ 37.96 dB/m in Gr. B (P=0.13). Similarly, the baseline liver stiffness measurement (LSM) was comparable among both groups (Gr. A=12.6 $\pm$ 2.91 kPa vs. 11.84 $\pm$ 2.24 kPa; P=0.35). The median duration of treatment in Gr. A was 3 (range,2-6) months, and Gr. B was 3 (range,3-6) months (P=0.44). The mean reduction in LSM was -4.85 $\pm$ 1.86 kPa in Gr. A vs. -6.16 $\pm$ 1.93 (P=0.03) (Fig.A). The LSM remained the same even after a median follow-up of 8 months after treatment. The mean change in CAP score was -46.81 $\pm$ 36.26 dB/m in Gr. A vs. -44.55$\pm$36.92 dB/m in Gr. B. (P=0.84) (Fig.B). At the end of therapy, there was a comparable decrease in alanine transaminase levels (-36.6 $\pm$ 46.8 U/L vs. -47.85 $\pm$ 68 U/L; P=0.53) in both groups. There was a significant increase in triglyceride levels and LDL levels in Gr. B than in Gr. A (Fig.C and D). However, there was no significant difference in other lipid parameters, including total cholesterol, very low- and high-density lipoprotein levels, between the two groups. The incidence of adverse events was similar in both groups (9% vs. 20%; P=0.31).

Conclusions: Low-dose OCA is safe and effective in NASH. 10 mg OCA is more effective than alternate day 5 mg in fibrosis regression; however, 10 mg can alter the lipid profile significantly.

Image/Table:



Values presented here are median

Disclosure of Interest: None Declared

P074

ACUTE HEPATITIS B AND COVID-19 CO-INFECTION – A CASE SERIES AND SINGLE CENTER EXPERIENCE IN NORTHERN SERBIA

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Background: It is well documented that liver injury makes a negative prognostic factor in SARS-CoV-2 infection. Studies so far have examined the connection between chronic forms of viral Hepatitis and COVID-19, however, it is still unclear whether acute viral Hepatitis infection could make patients more susceptible to COVID-19 or if COVID-19 leads to worse outcomes in acute viral Hepatitis and COVID-19 co-infected patients.

Purpose: The aim of this case study is to analyze an uncommon co-infection of acute HBV and COVID-19, and present a series of patients and their treatment and outcomes.

Materials and Methods: This study was designed as a case series all of four patients presenting with acute Hepatitis B and COVID-19 co-infection to Clinical center of Vojvodina (Serbia), Infectious disease clinic during the COVID pandemic. We reviewed medical records of the patients, included and extracted demographic information, epidemiologic data, clinical features, diagnostic and treatment data, and outcome of acute HBV and COVID-19 infections.

Results: Since the beginning of the COVID pandemic declared in March 2020, there have been a total of four patients in our institution with confirmed acute Hepatitis B and SARS-CoV-2 co-infection. Two of the patients have been admitted to the hospital with a clinical presentation of severe, acute Hepatitis B and were tested within the epidemiological surveillance of COVID-19 in their 4th week of hospitalisation. In these patients, there were no clinical manifestations of COVID infection and the course of acute HBV infection was uncomplicated. One of the patients had developed fever in her 4th week of hospitalisation and a mild form of COVID-19 was confirmed which had no effects on acute HBV. The fourth patient was admitted with symptoms of acute Hepatitis B and high fever, and was found to be COVID positive. The patient was diagnosed with pneumonia and treated with Dexamethasone, as per the COVID protocols. Also, the patient had a rise in aminotransferase levels and a prolongation of prothrombin time. This patient was started on Tenofovir as therapy and later had a favourable hospitalisation course. The patient was discharged and later achieved anti-HBs Ab seroconversion.

Conclusions: The patients in this study patients have had mild symptoms of COVID and a benign disease course. Only one of the patients had developed pneumonia and required corticosteroid treatment and he was also the only patient in our study that has been co-infected with COVID possibly before his first doctors visit. In other patients, COVID came as an intrahospital infection. There patients were already started on antiviral treatment when they were tested positive for COVID and remained asymptomatic.

Image/Table:

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4
Age	35 years	41 years	39 years	44 years
Sex	Male	Female	Male	Male
Clinical presentation				
Jaundice	Yes	Yes	Yes	Yes
Fever	No	No	No	Yes
Abdominal pain	Yes	Yes	No	Yes
Nausea and vomiting	No	Yes	Yes	No
Laboratory tests (on admission/at the time of COVID diagnosis/at discharge)				
WBC	5.6/4.0/3.3	6,6/5.1/5.7	5.0/4.6/3.7	9.2/6.6/10.2
Limf	29%/53%/39%	26%/26%/31%	18%/30%/25%	21%/42%/38
PLT	210/220/161	203/268/295	334/410/319	230/201/274
CRP	3.8/1.3/1.8	4.0/5.2/1	8.9/7.2/2.3	4.3/6.2/2.0
ALT	3428/583/204	921/283/148	2092/368/168	1756/2306/694
AST	1622/178/71	577/207/54	820/223/65	604/1022/115
Tbil	142.5/74.5/20	246.4/96.5/70	319.5/118/90.1	68.6/145.5/44
PT	1.06/0.94/0.92	1.30/1.06/0.99	1.16/0.98/0.98	1.06/1.47/0.97
Chest radiograph	Normal	Normal	Normal	Pneumonia
USG of the abdomen	Perihepatic free fluid, periportal edema, cholecystitis	Focal changes in the liver parenchime, follow up is	Normal	Normal

Disclosure of Interest: None Declared

P075

INCREASED FIBROSIS LEVEL AFTER COVID-19 IN LIVER DISEASE PATIENTS: MULTICENTER BRAZILIAN LONGITUDINAL STUDY

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Introduction: Liver injury was described as common in patients with severe COVID-19 compared to mild cases of infection. Also, COVID-19 mortality has been observed in 32% and 8% of cirrhotic and non-cirrhotic patients, respectively. Evaluation of liver parameters is essential for investigating conditions associated with COVID-19. However, there is a lack of information about COVID-19 impact for patients with liver injury.

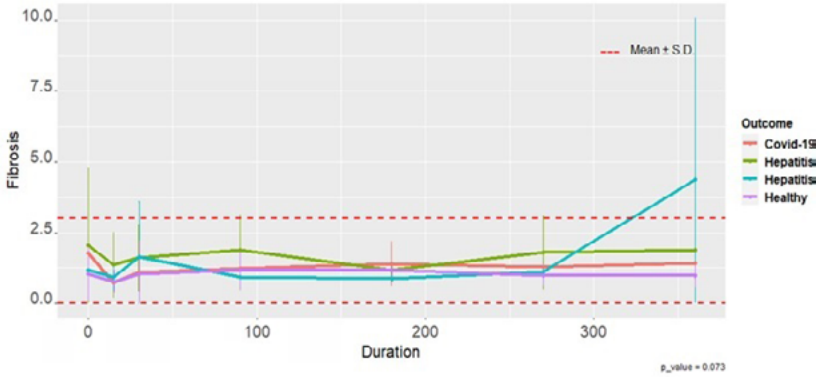
Purpose: The aim of this study was to evaluate the impact of SARS-CoV-2 infection in patients with prior liver injury in order to identify possible biomarkers of coinfection severity.

Methods: This is a longitudinal observational study conducted in two centers from Brazil where volunteers were accompanied during one year after inclusion in the study. A total of 230 individuals gave blood and respiratory samples during 2020 to 2021. Hematological and biochemical analysis was conducted. Nasal and oropharyngeal swab collections were performed using real time PCR for SARS-CoV-2. Fibrosis level was evaluated by the FIB-4 method.

Results: Mean age was 48 years (± 17.09; 11-90), 50% were women (115/230). Among the study participants, 40% (90/230) had Hepatitis, of this group, 14% (13/90) had covid-19. In the group of Hepatitis patients, HBsAg positivity was 34.4% (31/90), anti-HBc was 51% (46/90) and anti-HBs was found in 37.7% (34/90) and anti-HCV was found in 36.6% (33/90) of individuals. In the group without Hepatitis, anti-HBc rate was 5.7% (8/140) and anti-HBs was47% (66/140). Compared to the group without Hepatitis (n=140), 27% (39/140) had only covid-19 and high fibrosis grade (FIB-4) presented as a risk factor for this group. At the end of longitudinal follow-up, it was observed high degree of liver fibrosis (F3 and F4) in participants with Hepatitis and COVID-19. Figure 1 demonstrated fibrosis level of different groups accompanied during one year of study.

Conclusion: There are alterations caused by covid-19 in patients with a history of liver damage, an increased level of fibrosis was noticed as a post-covid condition in this group, which may represent an impact of SARS-CoV-2 infection in patients with a history of liver injury. This situation could lead to aggravation of liver disease and impact in the management of these patients.

Image/Table:



Disclosure of Interest: None Declared

P076

EFFICACY AND SAFETY OF 8- VERSUS 12-WEEK TREATMENT WITH SOFOSBUVIR/ RAVIDASVIR FOR HEPATITIS C: INTERIM ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL IN MALAYSIA

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Background: Sofosbuvir/ ravidasvir is a new pan-genotypic direct-acting antiviral (DAA) combination shown to be highly effective against Hepatitis C virus (HCV) infection.

Purpose: To report preliminary findings from an interim analysis of a clinical trial on the efficacy and safety of 8- and 12-week treatment with sofosbuvir/ ravidasvir in people living with HCV.

Methods: This was a randomized, open-label, controlled trial conducted in 9 hospitals and 18 primary healthcare centers across Malaysia. Individuals who had an HCV ribonucleic acid (RNA) load $\geq 10^4$ IU/mL, no cirrhosis and no history of receiving DAA-based treatment were included. They were randomized (1:1) to receive sofosbuvir (400 mg/day) and ravidasvir (200 mg/day) for either 8 or 12 weeks. The primary efficacy endpoint was the proportion of participants achieving a sustained virologic response 12 weeks after treatment completion (SVR12). Safety of treatment was assessed based on the number of adverse events (AEs) and serious AEs (SAEs). The interim analysis included half of the targeted number of participants (79 in each group) who had taken at least one dose of study drugs and undergone SVR12 testing. They were recruited between 20th March 2021 and 22nd June 2022. The findings reported were based on a per-protocol analysis, including only the participants who did not prematurely discontinue treatment and were compliant (taking ≥90% of study drugs).

Results: The mean age of the participants was 44.7 ± 10.1 years. Most of them were male (92.4%) and of Malay ethnicity (79.1%). Six of them were excluded from the interim analysis due to the absence of SVR test result (n=3) and non-compliance (n=3). The SVR12 rates of the 8- and 12-week groups were, respectively, 90.9% [95% confidence interval (CI): 84.3%, 97.5%] and 92.0% (95% CI: 85.7%, 98.3%). Less AEs were reported in the 8-week group (55 cases) than in the 12-week group (75 cases). However, the number of SAEs was comparable between the 8- and 12-week groups (4 versus 3 cases). One death case was reported in the 8-week group but was determined to be not related to the study drugs.

Conclusion: The interim analysis suggests that 8-week treatment with sofosbuvir/ ravidasvir is likely to be not inferior to 12-week treatment and is generally well tolerated in people living with HCV in the absence of cirrhosis.

Disclosure of Interest: None Declared

P077

EARLY POSTOPERATIVE RENAL DYSFUNCTION IN THE LIVING DONOR LIVER TRANSPLANTATION

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Background/Aims: To analyze the incidence and risk factors of outcomes and management of post-transplant renal dysfunction in LDLT recipient in National Liver Institute, Menofiya University ,Egypt.

Methods: This is a retrospective study was conducted on 173 patients which were classified in two groups, pediatrics (n= 29) 17.3% and adults (n=144) 82.7% who underwent LDLT in National Liver Institute, Menofiya University from April, 2003 until April, 2012. Cox multivariate proportional hazards model was used to determine the potential risk factors predicting the outcomes.

Results: A total of the patients in both groups,173 patients which were classified in two groups, pediatrics (n= 29) 17.3% and adults (n=144) 82.7% who underwent LDLT.Most of the patients were adult males in both groups, pediatrics (n=29)17.3% and adults (n=144) 82.7% and the mean age was 5.62±5.74 years in ped. and 46.97± 7.62 years in adults .Most of the patients were child class C ped.(n=14) 48.3% and adults (n= 93) 64.6%. Class B in ped. (n=11) 37.9%and adults (n=43) 29.9%. Class A in ped. (n= 4)13.8% and adults (n=8)5.6 %.The mean MELD score (within one week before liver transplantation),in adult group was 18.50±7.66 with p-value > 0.05. PELD score was 19.7576±19.8798 in ped. group with p-value > 0.05.Hepatitis C (HCV) was the main underlying etiology of liver cirrhosis. In the early postoperative period,two groups (adults and pediatrics) were followed up for one month after LDLT (Hospital stay time) and were classified as subgroups, gp.I (126) 86.2% and gp.II (18)12.5% in adults. gp.I (25) 87.5% and gp.II(4)13.8% in pediatrics. Subgroups I, serum creatinine ≤1.5 and subgroup II serum creatinine >1.5.HCC was (n=45)19.2%. Only (n=3)2.1% of the studied patients Suffered from pre-LDLT hypertension, (n=35) 24.3% and (n=6) 4.2% in both. Other indication for LDLT pediatrics (n=29)17.3% and adults (n=144) 82.7%. Among (22) 26.3% postoperative RD of total 173 patients (adults & pediatrics) who underwent LDLT,subgroup II (4) 13.8% in pediatrics group and (18) 12.5%, in adults group. (9)11.7% cases were died in both groups, (2) 3.7% cases in ped. While in adult (7) 8.0% were died.2 cases after RRT,1st case after VVHDF from HAT, 2nd case after conventional HD from fungal infection. (13)14.6% were recovered from early renal dysfunction,(2) 3.7%cases in ped.gp.and (11)10.9% cases in adult gp,(one case after 6 session dialysis Conventional HD).

Conclusion: This study is a good indicator of the post-LTprognosis in National Liver Institute and suggests a significant burden of post-LT complications for high risk patient's liver transplant.

Keywords: Incidence; Liver transplantation; Renal insufficiency; Risk factors.

Disclosure of Interest: H. aboeleneen Employee of: Grants are received from in National Liver Institute, Menofiya University for the conduct of this study. Authors declare that they have no other conflicts of interest regarding the content of this manuscript., K. Aboella Grant / Research support from: Grants are received from in National Liver Institute, Menofiya University for the conduct of this study. Authors declare that they have no other conflicts of interest regarding the content of this manuscript , E. Hamad Grant / Research support from: Grant / Research support from: Grants are received from in National Liver Institute, Menofiya University for the conduct of this study. Authors declare that they have no other conflicts of interest regarding

the content of this manuscript, H. Abdel Daym Grant / Research support from: Grant / Research support from: Grants are received from in National Liver Institute, Menofiya University for the conduct of this study. Authors declare that they have no other conflicts of interest regarding the content of this manuscript, E. Gawesh Grant / Research support from: Grant / Research support from: Grants are received from in National Liver Institute, Menofiya University for the conduct of this study. Authors declare that they have no other conflicts of interest regarding the content of this manuscript, O. Abdel salam Grant / Research support from: Grant / Research support from: Grants are received from in National Liver Institute, Menofiya University for the conduct of this study. Authors declare that they have no other conflicts of interest regarding the content of this manuscript

P078

DISTINCT FREQUENCIES OF SOMATIC TERT PROMOTER MUTATIONS IN HEPATOCELLULAR CARCINOMA, CIRRHOTIC AND NON-CIRRHOTIC TISSUE IN BRAZILIAN PATIENTS

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Abstract Content: Hepatocellular carcinoma (HCC) is the predominant form of liver cancer and the third leading cause of cancer mortality worldwide. Currently, prognosis for patients with HCC is dismal, with lower survival rates among patients at the advanced stage. HCC typically develops on a background of cirrhosis, with chronic Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections, alcohol abuse and nonalcoholic fatty liver disease being the major etiologies. The molecular mechanisms involved in the malignant transformation of hepatocytes are extremely complex and comprise the progressive accumulation of a variety of genetic alterations overtime. Somatic mutations in the telomerase reverse transcriptase (*TERT*) gene promoter have been reported as the earliest and most frequent genetic event in the multistep process of hepatocarcinogenesis. However, the pattern of somatic mutations in HCC varies in different geographic regions likely depending on the liver disease etiology, environmental factors, and host genetic diversity. Moreover, analyses of *TERT* promoter mutations in HCC samples have not been performed in the Brazilian population. The aim of this study is to determine whether *TERT* promoter mutations C228T and C250T are associated with HCC development in Brazilian patients. This study included 85 liver tissue samples; among these there were 26 matching tumor/surrounding tissue pairs (surrounding tissues included 12 cirrhotic and 14 non-cirrhotic samples), and 16 HCC, 9 cirrhotic and 8 non-cirrhotic unpaired samples. DNA was extracted from cryopreserved or formalin-fixed paraffin-embedded liver tissues and mutation analysis was performed by Sanger sequencing of PCR fragments. C250T was observed in 1/42 (2.4%) HCC tissue, and in none of the cirrhotic and non-cirrhotic tissues. On the other hand, C228T was more commonly detected in HCC (19/42, 45.2%) and cirrhotic (4/21, 19%) than non-cirrhotic (0/22, 0%) tissues, demonstrating a gradual increase according to the progression of liver disease. The differences in C228T frequencies were significant for HCC vs. non-cirrhotic (P=0.0001) and cirrhotic vs. non-cirrhotic (P=0.0485), but not for HCC vs. cirrhotic (P=0.0542) samples. In particular, 12/26 (46.2%) paired HCC and surrounding tissues showed C228T only in the tumor tissue, while none of the pairs had this mutation only in the adjacent non-malignant tissue (P=0.0001). Although C228T was more common in HCCs related to HCV infection (8/12, 66.7%) than in those of other etiologies, the differences were not statistically significant. Our collective findings support the utility of the *TERT* promoter mutation C228T as a useful biomarker for early diagnosis of HCC in Brazilian patients.

Disclosure of Interest: None Declared

P079

FREQUENCY OF MUTATIONS IN THE ABCB1 (1236C>T, 2677G>T AND 3435C>T) AND ABCB11 (1331T>C) GENES IN PATIENTS WITH CHRONIC HEPATITIS C

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Abstract Content: Keywords: Hepatitis C;ABCB1;ABCB11;drug resistance;genetic factors.

Viral and host factors are associated with susceptibility to Hepatitis C virus (HCV) infection and progression of liver disease to cirrhosis and hepatocellular carcinoma. The mutations 1236C>T (p.G412G), 2677G>T (p.A893S) and 3435C>T (p.I1145I) in ABCB1 gene that synthesize the drug export pump (P-glycoprotein) are associated with drug efficacy and hepatotoxicity. The 1331T>C (p.V444A) mutation in the ABCB11 gene that encodes the bile salt export pump is associated with cholestasis. The presence of SNPs 3435T, 2677T and 1236T can influence the plasmatic concentration and efficacy of several drugs used in the treatment of HCV, including telaprevir, sofosbuvir and ribavirin. And SNP 1331CC (ABCB11) is associated with significant changes in total bilirubin levels after antiviral therapy. These mutations can be an aggravating factor for liver tissue damage and may lead to a worse prognosis. In Brazil, there are no studies evaluating the frequency of these mutations in chronic HCV patients. This study aimed to investigate the frequency of genetic polymorphisms C1236T, G2677T and C3435T in ABCB1 and T1331C in ABCB11 in a cohort of patients chronically infected with HCV. Biological samples from 241 patients with chronic Hepatitis C (subtypes 1a and 1b) referred to the Liver Disease Outpatient Clinic of the Gaffrée and Guinle University Hospital (Rio de Janeiro, Brazil) were analysis by qPCR using TaqMan SNPs Genotyping Assays. Most of individuals (56.6%) were female and total mean age was 61.4 +- 9.8 years. More than half (59.5%) had cirrhosis (F4), and other comorbidities such as diabetes (28.5%) and hepatic steatosis (46.3%). In the ABCB1 gene, the most frequent mutation was C3435T in 14.9% (TT), in this group 40.7% were wild-type (CC) and 44.3% were heterozygous (CT). The frequency for C1236T wild type (CC) was 48.6%, heterozygotes (CT) 40.7% and mutants (TT) 10.8%. For G2677T, 8.7% of patients were mutants (TT), 55.6% were wild-type (GG) and 35.7% were heterozygotes (GT). As for T1331C in the ABCB11 gene, most individuals were heterozygous - TC (53.5%), followed by mutants - CC (32.0%) and wild type - CC (14.5%). Elevated serum levels of GGT were observed in individuals carrying wild genotypes for the ABCB1 (2677GG, 3435CC and 1236CC) and heterozygous (TC) for the T1331C mutation in ABCB11 compared to those carrying other genotypes, but there was no statistically significant difference. We observed a greater presence of heterozygous genes than the other genotypes in the population studied, which may be a characteristic of a mixed population such as the Brazilian. It is important to establish the risks associated with these mutations in patients with chronic HCV to understand their influence on the clinical picture and evolution of these individuals, mainly due to their association with cholestatic damage and efficacy and safety of antiviral drugs.

Support: CAPES, CNPq and FAPERJ.

Disclosure of Interest: None Declared

P080

THE LINK BETWEEN SPLANCHNIC VEIN THROMBOSIS AND PHILADELPHIA-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS.

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Abstract Content: Myeloproliferative neoplasms (MPN) are a group of rare hematological malignancies defined by somatic mutations in hematopoietic stem cells with secondary uncontrolled production of mature blood cells. These conditions include primary myelofibrosis (PMF), polycythemia vera (PV) and essential thrombocythemia (ET), and are characterized by some dominant driver mutations in three genes, respectively *JAK2*, *CALR* and *MPL*. Venous thrombosis in unusual sites, such as splanchnic veins, and progressive evolution towards myelofibrosis or acute leukemia are common complications of these diseases. Prior to the identification of mutations in patients with MPN, at least one-third of splanchnic vein thrombosis (SVT) cases were classified as idiopathic SVT. Currently, almost all of these cases are associated with chronic MPN and, rarely, with paroxysmal nocturnal hemoglobinuria. The risk factors for vascular events in patients with MPN are mutational profile, age, prior history of thrombosis, or number of blood cells. The mutational profile has major effects on MPN phenotype and on the risk of thrombotic events. The *JAK2* V617F mutation causes the greatest increase in the risk of thrombosis. Other mutations identified in both MPN and SVT patients are *MPL* W515L mutation in the thrombopoietin receptor gene and *JAK2* exon 12 mutations. A pathogenic role in promoting thrombotic events in patients with MPN is also played by local endothelial cells, circulating endothelial colony forming cells (ECFC) and intensification of neoangiogenesis processes. The development of thrombosis in the splanchnic territory has a negative effect on the morbidity and mortality of these patients. To improve the prognosis, in certain categories of patients with thrombotic events without an apparent cause, molecular investigations are recommended, to identify a possible MPN.

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Disclosure of Interest: None Declared

P081

CORRELATION OF SERUM PROCALCITONIN LEVEL AND NEUTROPHIL LYMPHOCITE RATIO WITH SURVIVAL IN SEPTIC SHOCK PATIENTS

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Background: Serum procalcitonin (PCT) is produced mainly by the liver and severe liver dysfunction can influence its levels. It is unclear whether there is a correlation between PCT and the survival of cirrhosis patients with sepsis. Neutrophil and lymphocyte ratio (NLR) is a sensitive marker of infection. PCT alone or in combination with NLR has not been investigated in septic cirrhosis patients.

Methods: We have conducted a retrospective study of 1422 patients who were admitted to ICU at the Institute of Liver and Biliary Sciences. Their baseline PCT was noted at the time of admission to ICU, along with other parameters. The final outcomes such as death ("Group 1") or discharged ("Group 2") were analyzed.

Results: Total of 1422 cases with mean age of 48.22 ± 13.742 years with 80.7 % male and 72% alcoholic were analysed. MELD Na in Group 1 was significantly elevated. In Model 1, Individual biochemical parameters were analysed and in Model 2, baseline PCT, NLR (neutrophil and lymphocyte ratio) and MELD Na were analysed.

In univariate analysis, baseline PCT was significantly elevated in Group 1 and predicted in-hospital mortality. As inclusion, biochemical parameters are found significant in Group 1 as shown in below table

Parameters	Group 1	Group 2	P-Value
Baseline PCT	5.41 ± 14.32	3.67 ± 10.61	0.02
Hb	8.96 ± 1.96	9.38 ± 2.27	<0.01
NLR	13.48 ± 13.90	10.25 ± 11.92	<0.01
TLC	13.59 ± 9.05	11.53 ± 8.31	<0.01
Platelets	100.49 ± 78.18	113.90 ± 95.19	<0.01
INR	2.87 ± 1.49	2.11 ± 0.97	<0.01
Total Bilirubin	14.11 ± 11.09	8.60 ± 9.68	<0.01
Urea	85.74 ± 59.19	66.73 ± 51.64	<0.01
Creatinine	1.93 ± 1.55	1.60 ± 1.58	<0.01
Bicarbonate	19.50 ± 5.19	20.26 ± 4.95	<0.01

In multivariate analysis, baseline PCT (OR >1; 95% CI (0.34 – 3.15)) was significantly elevated in Group 1, thus correlating well with in-hospital mortality. In Model 2, where baseline PCT along with NLR and MELD Na was compared in both the groups, it was found that NLR (OR = 1.01; 95% CI (1.00-1.04)) and MELD Na (OR = 1.06; 95% CI (1.05 – 1.07)) was significant.

Key Outputs:

Key Outputs	Baseline PCT	NLR	Baseline PCT + NLR
Sensitivity	56.2%	73.0%	88.6%
Specificity	70.8%	40.5%	32.0%
Positive Predictive Value	76.4	67.3	68.6
Negative Predictive Value	49.1	47.1	62.5
Youden's Index	27	13.5	20.6
Cut off value	1.7	8.17	-
AUC	72.3	59.6	-

The sensitivity of baseline PCT for bacterial infection is 56.2% and sensitivity of NLR is 73%. On combining both baseline PCT and NLR, the sensitivity increases significantly to 88.6% with specificity of 32% and Youden's index of 20.6.

Conclusion: This study concludes that baseline PCT is an independent predictor of in-hospital mortality. In Model 1, baseline PCT along with TLC, platelet counts, NLR, INR, total bilirubin, urea, creatinine, and bicarbonate are significantly related to mortality. While in Model 2, baseline PCT, NLR, and MELD Na are the best predictors of mortality. The sensitivity has been increased to 88.6 % on combining baseline PCT and NLR.

Disclosure of Interest: None Declared

P082

DIAGNOSTIC EFFICACY OF SERUM ASIALO A1-ACID GLYCOPROTEIN LEVELS FOR LIVER FIBROSIS AND CIRRHOSIS IN PATIENTS WITH CHB: A PROSPECTIVE STUDY

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Background Serum asialo α1-aid gycoprotein (AsAGP) has been suggested as a novel biomarker specific to liver fibrosis.

Aim: To evaluate the diagnostic efficacy of serum AsAGP levels in classifying the severity of liver fibrosis and differentiating liver cirrhosis (LC) in patients with chronic Hepatitis B (CHB) from healthy controls.

Methods: Overall, 206 subjects were prospectively enrolled. LC was diagnosed based on liver stiffness levels (>11 kPa) measured using transient elastography. Serum AsAGP levels were measured using an antibody-lectin sandwich immunoassay. We investigated the diagnostic performance by comparing serum AsAGP levels among healthy control, CHB, and CHB with LC groups. Sensitivity, specificity, and optimal AsAGP cut-off values were also calculated.

Results: Serum AsAGP levels were significantly different between healthy controls, CHB patients, and CHB patients with LC (1.04 $\pm$ 0.31 μg/ml, 1.12 $\pm$ 0.34 μg/ml, 1.51 $\pm$ 0.43 μg/ml respectively; $p<0.001$). Serum AsAGP levels positively correlated with liver stiffness ($r = 0.46$, $p < 0.001$). AUROC of healthy control versus CHB with LC was 0.821 ($p < 0.001$, optimal cut-off 1.036 μg/ml). AUROC of healthy control versus CHB was 0.624 ($p = 0.049$, optimal cut-off level 0.934 μg/ml). AUROC of CHB versus CHB with LC was 0.765, ($p < 0.001$, optimal cut-off 1.260 μg/ml). In multivriate comparison with healthy controls and CHB patients with LC, AsAGP levels (odds ratio 1.51, $p < 0.001$) were significant predictors of CHB with LC. In the comparison of CHB and CHB with LC groups, AsAGP levels (odds ratio 142.33, $p < 0.001$) were also independent predictors of CHB with LC.

Conclusions: Serum AsAGP levels in CHB patients with LC were significantly higher than those in healthy controls and CHB patients. AsAGP levels showed good diagnostic performance in predicting liver fibrosis and cirrhosis, which suggests a potential role as a biomarker for predicting the progression of liver disease in CHB.

Image/Table:

Table. Diagnostic performance of serum AsAGP levels through the mutual comparison of healthy controls, CHB patients, and CHB patients with LC.

	CHB patients versus healthy controls	CHB patients with LC versus healthy controls	CHB patients versus CHB patients with LC
AUC (95% CI)	0.624 (0.528-0.720)	0.821 (0.751-0.890)	0.765 (0.682-0.848)
Optimal cut-off (μg/ml)	0.933	1.036	1.260
Sensitivity	75.7%	83.8%	81.4%
Specificity	55.9%	67.6%	67.5%

Disclosure of Interest: None Declared

P083

TP53 AND B-CATENIN GENE DRIVER MUTATION FREQUENCIES IN THE CIRCULATING TUMOR DNA OF HEPATITIS B VIRUS-INDUCED HEPATOCELLULAR CARCINOMA AND ITS UTILITY AS LIQUID BIOPSY MARKER USING DROPLET DIGITAL PCR

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Background: Hepatitis B virus (HBV) is a partially double-stranded DNA virus and the 3.2 kb circular genome having four partially overlapping genes encode surface (S), core (C), polymerase, and X proteins. HBV is a major cause of hepatocellular carcinoma (HCC) and induces hepatocarcinogenesis through viral genome integration, chromosomal aberrations, and modulation of host signaling pathways through viral proteins (HBx, HBs). During this process of hepatocarcinogenesis, molecular alteration of cancer hallmark genes takes place. The signatures of these driver mutations may be released into the circulation and can be detected in circulating tumor DNA (ctDNA). Detection of these mutations in ctDNA may serve as liquid biopsy markers of cancer diagnosis, prognosis, and response to therapy for which this study was undertaken.

Purpose: To detect the novel driver mutation frequencies in the ct-DNA of CHB and CHB-HCC and to evaluate as a liquid Biopsy marker.

Methods: Consecutive CHB patients (n=35), CHB-induced HCC patients (CHB-HCC, n=80), and healthy (n=15) controls were recruited. Informed consent was taken for blood sample collection. The ctDNA was isolated from serum using a ctDNA extraction kit (Qiagen). Conventional PCR for amplification of TP53 exon 7 and β-catenin exon 3 was carried out using primers as per IARC recommendations. Sanger sequencing confirmed p.R249M mutation rather p.R249S which is highly prevalent in CHB patients. The droplet digital PCR (ddPCR) assays were performed for TP53 (p.R249M & p.R249S) and β-catenin (p.S45P) driver mutations for all enrolled patients including control subjects. All the data were analyzed by Graph pad Prism version 9.0.

Results: Thirty-two HCC patient samples were Sanger sequenced for β-catenin exon 3 and TP53 exon 7. Eight HCC patients were found mutated for TP53 c.746 G>T (p.R249M). The ddPCR data shows that 46 HCC patients (57.5%) show at least one driver mutation in the ctDNA. 12.5%HCC subjects showed any two driver mutations. 31.4% of chronic Hepatitis B patients showed any one-driver mutation while 11.4% of chronic Hepatitis B patients showed any two-driver mutations. The mutant allele frequency was 0.02%- 50% in HCC patients while in chronic Hepatitis B patients mutant allele frequency was 0.1%- 2.47%. Mutant allele copy number and frequency were observed highest in HCC patients followed by chronic liver patients with cirrhosis. No mutations were observed in healthy subjects.

Conclusion: Mutations in the ctDNA can be readily detected in HCC and advanced chronic liver disease patients. The driver mutation can be detected early in the circulation before the manifestation of clinical HCC.

Disclosure of Interest: None Declared

P084

IDENTIFICATION AND CHARACTERIZATION OF POTENTIAL ONCOGENIC MICRORNA AS A BIOMARKER FOR HEPATITIS B VIRUS INDUCED HEPATOCARCINOGENESIS

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Background: Hepatitis B virus (HBV) infection leads to chronic liver disease which further progress to cirrhosis and Hepatocellular Carcinoma (HCC). These chronic Hepatitis B (CHB) patients require long-term nucleos(t)ide analogues therapy to prevent disease progression to HCC, hepatic failure and death. There is no cure for HBV and drugs are only effective in reducing HBV load and have no effect on episomal HBV which is archived in the liver. Therefore, CHB patients need to be screened periodically for both HBV DNA load and HCC. Screening of HCC is done by radiological imaging which is costly and not suitable for routine screening like laboratory based tests. Simultaneous nucleic acid based test for HBV DNA and other novel markers like oncomiR is the need of the hour now for CHB patients. For this, we have identified potentially oncogenic microRNA (miRNA) by microarray and studied its mechanisms in cell culture and utility in patients.

Purpose: Identification of novel oncomiR in HBV induced hepatocarcinogenesis, functional characterization and utility as a biomarker for early detection of HCC

Methods: Serum profiling of healthy control (n=10), treatment naïve CHB (n=10), cirrhotic HBV (n=10), and treatment naïve HBV-HCC (n=10) patients were carried out by miRNA PCR array. We have selected nine microRNAs that are sequentially upregulated during disease progression from CHB to HCC. To evaluate its oncogenic potential, the expression of these miRNAs was further confirmed in hepatoma cell lines. The potential of these miRNAs as a biomarker for early hepatocarcinogenesis was evaluated in CHB and CHB-induced HCC patients.

Results: The results identified nine upregulated miRNAs in HCC with a fold change of 1.12 to 19.08 as compared to CHB and cirrhotic patients after normalization with healthy serum miRNA. Expression of all the selected nine miRNAs reconfirmed in hepatoma cell lines (HepG2/C3A, Huh7 and HepG2/2.2.15) after endogenous normalization. A significantly higher expression was shown by miR-19b-3p and miR-25-3p which are previously known to be overexpressed in HCC patients. Other miRNAs, miR-17-5p and miR-222-3p had also shown significant expression in hepatoma cell lines. The discrimination potential of these miRNAs for CHB-induced HCC from only CHB was carried out using the receiver operating characteristic curve. The targets of the dysregulated miRNAs were evaluated by using bioinformatic tools and its validation is under evaluation.

Conclusion: The potential oncomiRs were identified which are progressively upregulated during different stages of carcinogenesis. These were validated in the hepatoma cell line and their role as a potential biomarker is under evaluation.

Disclosure of Interest: None Declared

P085

ASSESSMENT OF LIVER FIBROSIS IN INDIVIDUALS WITH METABOLIC SYNDROME OR TYPE 2 DIABETES MELLITUS USING NON-INVASIVE TESTS

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Introduction: Individuals with metabolic syndrome (MS) or type 2 diabetes mellitus (T2DM) are at high risk for developing non-alcoholic fatty liver disease and advanced liver fibrosis. Although, there are currently no recommendations for screening patients with MS or T2DM. This study aimed to assess the diagnostic accuracy of non-invasive tests in predicting advanced liver fibrosis (≥F3) in patients with MS or T2DM using the novel non-invasive score namely the Agile 3+ score, which is done by combining straightforward clinical parameters with common laboratory biomarkers and liver stiffness measurements by vibration-controlled transient elastography.

Materials and Methods: We prospectively enrolled patients with MS or T2DM which have been evaluated using non-invasive tests such as aspartate aminotransferase to platelet ratio index (APRI) score, fibrosis-4 (FIB-4) index, NAFLD fibrosis score (NFS), and Agile 3+ score in the Gastroenterology and Hepatology Institute Iasi, between August to October 2022. We calculated the area under the receiver operating curve (AUROC), specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) for each of these biomarkers in the detection of advanced liver fibrosis (≥F3) compared with the Agile 3+ score. In addition, we used the Controlled Attenuation Parameter (CAP) with a cut-off $\geq$ 274 dB/m for diagnosed non-alcoholic fatty liver disease (NAFLD).

Results: Among 96 patients with T2DM and MS enrolled with a mean BMI of 26.98 ±4.73 kg/m2, 58 (60.4%) were females. According to Agile 3+ score, 28 (29.2%) individuals had at least advanced fibrosis (≥F3) using a cut-off ≥ 0.679. Moreover, 73 (76%) of the patients included in our study had NAFLD, according to a CAP $\geq$ 274 dB/m. A significant correlation was found between Agile 3+ score and FIB-4 index (r=0.578), NFS (r=0.591), and APRI score (r=0.644) (p <0.001). The FIB-4 index had the highest NPV (90.12%) followed by the NFS score (86.61%). In comparison with Agile3+ score, all the biomarkers had relatively low specificity (<80%) and PPV (<75 %). Although, the major finding of our analysis was that all these biomarkers had relatively high NPV (>85%) and accuracy (>83%) for predicting advanced liver fibrosis.

Conclusion: A novel non-invasive score, namely Agile 3+ score appears to improve the identification of advanced fibrosis and cirrhosis, among MS and T2DM patients, who are at high risk of developing NAFLD and at least advanced fibrosis (≥F3). Furthermore, it is possible to increase the PPV and reduce the number of cases with indeterminate results for identifying cirrhosis and advanced fibrosis in patients with NAFLD, which would minimize the need for liver biopsy.

Disclosure of Interest: None Declared

P086

DNA INTEGRITY INDEX, A LIQUID BIOPSY MARKER OF CIRCULATING-FREE DNA INTEGRITY AND FRAGMENTATION TO DIFFERENTIATE HEPATOCELLULAR CARCINOMA FROM CHRONIC LIVER DISEASE

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Background: Chronic Hepatitis B and C virus infection and Hepatitis due to non-viral etiologies have a spectrum chronic liver disease (CLD) that progresses to fibrosis, cirrhosis and hepatocellular carcinoma (HCC). Majority of Hepatitis patients requires future screening for early HCC diagnosis for which liquid biopsy holds great promise. Cell-free DNA (cfDNA) as a liquid biopsy marker can be easily detected by a real-time quantitative PCR (RT-qPCR) assay for a change in its concentration, integrity, and fragmentation. The cell free DNA integrity index (cfDII) studied earlier in different methods had reported both increased and decreased DII creating problem for its use cancer. We have studied differential potential of both cfDII-Fragmentation and cfDII-integrity

Methods: We have recruited both HCC (n = 100) and CLD (n = 100) patients following ethical approval to evaluate differential potential of cfDNA-integrity and fragmentation index for cancer. Healthy (n = 30) controls cfDNA and Huh7 cell genomic DNA served as normalization control. Real-time quantitative PCR (RT-qPCR) of four genes elements (ALU, LINE1, B-Actin and GAPDH) was carried out for large(>205 bp) and small (110 bp) fragments of same genes. Total cfDNA concentrations and DNA integrity index (DII) were determined. The cfDII by absolute quantitation method renamed as cfDII-integrity (L/S ratio) and by relative quantitation method renamed as cfDII-fragmentation.

Results: We have observed significant increase in cfDNA concentrations in HCC patients (244 ng/ml) than both CLD patients (33 ng/ml) and healthy controls(16.88 ng/ml). HCC patients have also shown both decreased cfDNA integrity and increased cfDNA fragmentation as compare to CLD patients and healthy controls. The GAPDH and ALU genes cfDII-integrity significantly differentiate HCC from CLD at AUROC 0.72 and 0.67, respectively. The cfDII-fragmentation following normalization with cfDNA of healthy control has shown significant differential capabilities of HCC from CLD at AUROC 0.67 using GAPDH gene and 0.68 using the ALU element.

Conclusions: The cfDII measuring both DNA integrity (L/S ratio) and fragmentation of the Alu and GAPDH genes can differentiate HCC patients from CLD and healthy individuals.

Disclosure of Interest: None Declared

P087

DNA INTEGRITY INDEX, A LIQUID BIOPSY MARKER OF CIRCULATING-FREE DNA INTEGRITY AND FRAGMENTATION CAN DIFFERENTIATE HEPATOCELLULAR CARCINOMA FROM CHRONIC LIVER DISEASE

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Background: Chronic liver disease (CLD) in patients due to Hepatitis B and C infection, alcohol and fatty liver further progresses to cirrhosis and hepatocellular carcinoma (HCC). These patients require radiological screening for HCC due to lack of biomarker. Liquid biopsy due to ease of detection and being a non-invasive technique holds great promise for early detection, prognosis, and assessment of response to cancer therapy. The cell-free DNAs (cfDNA) are originated both from tumor and extra-tumoral normal cells. These cfDNAs are more fragmented with higher levels are detected in cancer patients of various aetiologies. The cfDNA integrity index (cfDII) can assess both fragmentation and integrity of DNA. There are contradictory report of DII level (high or low) in cancer depending upon the methodology. In this study, we have evaluated cfDII of house-keeping genes and repetitive elements to evaluate its potential differentiating HCC from CLD.

Purpose: To evaluate the potential of cfDII-Fragmentation and cfDII-integrity to differentiate HCC from CLD

Methods: We have recruited both HCC (n = 100) and CLD (n = 100) patients following ethical approval to evaluate differential potential of cfDNA-integrity and fragmentation index for cancer. Healthy (n = 30) controls cfDNA and cellular (Huh7) genomic DNA used as normalization control. Real-time quantitative PCR (RT-qPCR) of four genes (ALU, LINE1, B-Actin and GAPDH) was carried out for large(>205 bp) and small (110 bp) fragments. Total cfDNA concentrations and DNA integrity index (DII) were determined. The cfDII by absolute quantitation method renamed as cfDII-integrity (L/S ratio) and by relative quantitation method renamed as cfDII-fragmentation.

Results: Increased cfDNA concentrations was found significant in HCC (244 ng/ml) than CLD (33 ng/ml) and healthy (16.88 ng/ml) subjects. Decreased cfDII-integrity and increased cfDII-fragmentation was found significant in HCC patients for ALU and GAPDH genes. The GAPDH and ALU genes cfDII-integrity significantly differentiate HCC from CLD at AUROC 0.72 and 0.67, respectively. The cfDII-fragmentation following normalization with cfDNA of healthy control has shown significant differential capabilities of HCC from CLD at AUROC 0.67 using GAPDH gene and 0.68 using the ALU element.

Conclusion: The cfDII measuring both integrity and fragmentation of cfDNA for Alu and GAPDH genes can differentiate HCC patients from CLD and healthy individuals.

Disclosure of Interest: None Declared

P088

AGE, BILIRUBIN, AND ALBUMIN (ABA) INDEX: A NEW NON-INVASIVE MARKER FOR THE PREDICTION OF FIBROSIS DURING CHRONIC VIRAL HEPATITIS C

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Introduction: The emergence of non-invasive methods for assessing fibrosis has marked the world of hepatology. Transient elastography (Fibroscan) and serum markers are among these methods. Age, bilirubin, and albumin (ABA) index is a serum marker that has recently been reported by some studies.

Aim: The purpose of our study was to see how well the ABA index predicted fibrosis in chronic viral Hepatitis C patients (VHC).

Methods: To achieve this goal, we conducted a retrospective single-center study on VHC patients treated in our program between September 1, 2016 and December 30, 2020. The patient was diagnosed with advanced chronic liver disease when the elasticity of the liver, as measured by fibroscan, was equal to or greater than 10 kPa. The ABA index was calculated at the time of diagnosis as follows: 1.5 + (0.065×age) + (1.85×bilirubin) - (1.65×albumin).Receiver operating characteristic (ROC) curves were used to assess ABA's diagnostic performance.

Results: We included 148 patients (47 men and 101 women) with an average age of 58 years old [19-85 years-old]. In 84.5% of cases, genotype 1b was the predominant genotype. Cirrhosis and advanced chronic liver disease were noted in 30.4% and 14.9% of patients, respectively. The ABA index had a significant statistical correlation with hepatic elasticity (p = 0.03). According to the analysis of the ROC curves, the ABA index had an area under the ROC curve of 0.635 [range of 95% confidence interval (CI), 0.502–0.768] for advanced chronic liver disease and 0.725 (95% CI, 0.602-0.849) for cirrhosis.

Conclusion: According to our study, the ABA index was a good serum marker for the prediction of fibrosis and especially cirrhosis during chronic viral Hepatitis C.

Disclosure of Interest: None Declared

P089

RELEVANCE OF BLOOD AUTOTAXIN QUANTIFICATION FOR THE PREDICTION OF ADVANCED FIBROSIS IN CHRONIC LIVER DISEASES

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Background: Liver fibrosis exposes patients to progression to cirrhosis and hepatocellular carcinoma (hcc). The "gold standard" for fibrosis assessment is the histological examination of the liver biopsy (lb). Markers or combinations of markers, such as fibrotest® (ft), or elastometry (fibroscan®, fs) are less invasive alternatives for identifying patients at risk of severe fibrosis.

Purpose: To evaluate a new biomarker of liver fibrosis, autotaxin (atx), discovered in the context of metastatic skin cancer, and then described in chronic fibrotic and inflammatory pathologies.

Methods: Patients with liver disease recruited from the hepatology department, hôpital de la croix-rousse, lyon, france, and for whom an ft was performed, had an atx assay on an aia360 (tosoh) analyzer. Fibrosis was assessed by the association of an ft and an fs. Only patients with a concordant equivalent metavir score with the 2 methods were retained in the study. A uni- and multivariable logistic regression analysis was conducted to identify the factors associated with the presence of advanced fibrosis (f3/f4). The prediction of the different models was studied using roc curves and their auc. A subgroup analysis of nash patients in whom lb had been performed (n=30) was also conducted.

Results: A total of 171 patients were analyzed. 37% were chronic HBV carriers, 12% chronically infected by hcv, 27% had nash, and 24% had another etiology. The median age was 50 years [iqr 39-60] and 11% of them had advanced fibrosis. The auc for prediction of severe fibrosis for atx alone was 0.840. The model combining atx+sex gave an auc of 0.921, that combining atx+sex+age an auc of 0.958, and finally that combining atx+sex+age+platelets an auc of 0.989. This combination of 4 parameters is even slightly more predictive than fib4 (auc=0.980) or apri scores (auc=0.944). Aucs using atx were of the same magnitude in the subgroups of patients carrying HBV or hcv. When fibrosis was assessed by lb (nash patients, n=30), the aucs of these different models based on atx were 0.724, 0.742, 0.769, and 0.829, respectively. In this subgroup of nash patients the auc of fib4 alone was 0.626 and that of fib4+atx 0.771.

Conclusions: Atx is a powerful marker of advanced fibrosis, more particularly in association with age, sex and platelet count. In patients at risk of fibrosis (viral infection, metabolic syndrome with fib-4 > 1.3), the atx result could lead to an early referral to the hepatologist and prompt more specialized investigations such as elastometry or lb.

Disclosure of Interest: None Declared

P090

IMPACT OF FIBROSCAN® ON MANAGEMENT DECISION OF CHRONIC HEPATITIS B IN CLINICAL PRACTICE, A LIBYAN EXPERIENCE

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Background and Aim: Until few years back liver biopsy was the gall standard in the decision of treatment of chronic Hepatitis B, later non-invasive methods for evaluation of liver fibrosis have emerged including Fibroscan®. In Libya Fibrotest/actitest, and other simple scores have replaced liver biopsy in evaluating liver fibrosis. Recently Fibroscan® become available, we aimed to evaluate its results in the guidance for treatment decision of chronic Hepatitis B.

Methods: We included subsequent Hepatitis B patients who were evaluated with Fibroscan® compact 530 for degree of fibrosis and steatosis at Attasami private clinic, from January 2021 to March 2022

Results: A total of 119 patients were transferred from different clinics for evaluation of fibrosis for the decision of starting treatment, mean age was 45 years, 84(70.5%) were males. Fibrosis stage F0-F1 was found in 71patients (60%), of these patients, duration of Hepatitis B was not known in 25(35%), 22(31%) were newly diagnosed, 7(9%) were less than 10 years of disease duration, and 17(24%) were diagnosed more than 10 years, fibrosis stage of F1-F2 was found in 11 patients (9%), fibrosis stage F2-F3 in 15 patients (13%), ≥ F3 in 22 patients (18%). Steatosis was absent in 69(58%) patients, and 50(42%) patients have steatosis at different stages; stage 1 in 13(26%), stage 2 in 16(32%), stage 3 in 21(42%). Steatosis was associated with fibrosis score of F0-F1 in 27/50 patients (54%). Alanine transferase (ALT) was elevated in 12 patients (10%), 5 were started treatment of Hepatitis B, 1 diagnosed as acute Hepatitis B, 3 steatoHepatitis, 2 autoimmune liver diseases, and 1 diagnosed as hepatocellular carcinoma

Conclusion: The quantification of liver fibrosis is a key factor for Hepatitis B treatment decision, the presence of high liver function with absence of fibrosis may indicate steatoHepatitis or other liver diseases.

Disclosure of Interest: None Declared

P091

INTRAHEPATIC CHOLESTASIS: ETIOLOGICAL, DEMOGRAPHIC, CLINICAL, DIAGNOSTIC AND OUTCOME IN AN EGYPTIAN COHORT

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Background: Intrahepatic cholestasis (IHC) is one of the most challenging diagnostic dilemma in hepatology.

Aim: Define the most frequent IHC causes, clinical, laboratory, and imaging features in an Egyptian cohort.

Patients and methods: A prospective hospital-based study conducted on 200 consecutive Egyptian patients with IHC from National Liver Institute Hospital, Menoufia University. All demographic, clinical, laboratory, imaging, histopathological if feasible, etiological, outcomes and mortality data were collected.

Results: The mean age of cases was 50.15 years, with female predominance (51%). Half cases presenting with itching, 45% jaundice, 31% abdominal pain, 27.5% fever and 25% fatigue. Etiologically, 13.5% of cases were due to drug induced liver injury (DILI) (mainly amoxycillin clavulanic acid), 11% primary sclerosing cholangitis, 9% referred to post-liver transplantation problems, 10% primary biliary cholangitis, 8% Nonalcoholic fatty liver disease, 5% sepsis and metastatic tumors, and ≤4.5% overlap syndrome, lymphoma, total parenteral nutrition, congestive hepatopathy, sarcoidosis, IHC of pregnancy, post-operative jaundice, IGg 4 cholangiopathy, hepatocellular carcinoma, secondary sclerosing cholangitis, viral Hepatitis, vanishing bile duct syndrome, amyloidosis and Alcoholic liver disease, Wilson disease, Brucellosis, benign recurrent IHC, and progressive familial IHC. In about 24% of cases either magnetic retrograde pancreatography or liver biopsy was the decisive diagnostic measure. The average hospital stay was 18.5 days with 16% mortality mainly due hyperbilirubinemia, anemia, and infections.

Conclusion: DILI should be primarily considered in any case with IHC. Imaging is the main diagnostic stay for IHC, while the invasive endoscopic or liver biopsy is only needed in about 25% for each.

Disclosure of Interest: None Declared

P092

CLINICAL FEATURES OF LIVER FUNCTIONAL ABNORMALITY IN PATIENTS INFECTED WITH THE NOVEL CORONAVIRUS SARS-COV-2

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Background: The new Coronavirus SARS-CoV-2 has been responsible for a major pandemic since its emergence in 2019. The COVID-19 disease often manifests itself by respiratory symptoms, nevertheless digestive manifestations, particularly liver damage, have been reported. Few data exist in Tunisia on the abnormal liver function related to SARS-CoV-2. The aim of this study was to determine the prevalence and features of COVID-19-related liver damage.

Methods: We conducted a retrospective, descriptive study including all patients hospitalized for management of SARS-CoV-2 infection at the COVID-19 unit of the Hepato-Gastro-Enterology Department of Habib Thameur Hospital between October 2020 and February 2022. Patients who did not have liver chemistries during the hospitalization were not included. Clinical, biological, microbiological and radiological data were collected from medical records. Abnormal liver function was defined as increased levels of alanine and aspartate aminotransferase (AST and ALT), gamma glutamyltransferase (GGT), alkaline phosphatase (ALP), and total bilirubin.

Results: A total of 120 patients were included, mean age 59.46±15.35 years with a sex ratio (M/F) of 0.9. Abnormal liver function tests was observed in 50.8% of the patients. AST and ALT levels were increased in 35% and 28.3% of cases, respectively. GGT and ALP were increased in 36.7% and 8.3% of patients respectively. Hyperbilirubinemia was present in 7.5% of patients. In univariate analysis, the factors associated with the occurrence of abnormal liver function tests related to COVID-19 were: BMI ($p=0.039$), ferritinemia ($p<0.001$), lipasemia ($p=0.017$), severe to critical radiological damage and ($p=0.008$). On the other hand, ALT elevation was significantly associated with male gender ($p=0.049$) and type two diabetes ($p=0.001$). Furthermore, liver abnormalities were predominant in the 60-69 age group (65.1%). In multivariate analysis, the factor independently associated with abnormal liver function was: the radiological involvement of severe to critical COVID-19 pneumonia (extension >50%) ($p=0.006$; OR 3.28; CI [1.41-7.63]).

Conclusion: Our study has shown that liver abnormal function during COVID-19 is frequent, affecting half of the patients. Therefore, the clinician must be aware of this type of manifestation and systematically perform liver chemistries check-up during COVID-19 in order to limit the diagnostic delay and to better assess the prognosis.

Disclosure of Interest: None Declared

P093

EMERGENCY DEPARTMENT LENGTH OF STAY AND ITS ASSOCIATION WITH 14-DAY READMISSION AND MORTALITY IN PATIENTS WITH CIRRHOSIS

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Background: Cirrhosis and chronic liver diseases remain prevalent in Taiwan. The emergency department (ED) has increasingly become patients' point of entry into the healthcare system, including those with cirrhosis presenting disease-related complications. ED length of stay (ED-LOS) is considered a key factor of bottlenecks and overcrowding. Since many patients are hospitalized after leaving the ED, early hospital readmissions are often used an important proxy for quality of care and an indicator for patient prognosis.

Purpose: The aim of this study is to examine the relationship between ED-LOS and 14-day readmission and mortality in patients with cirrhosis of various etiologies.

Methods: Retrospective data are collected from medical records of a tertiary hospital in Taiwan between 2012 and 2021. Patients with cirrhosis and history of ED visit before 2018 are first identified (n=3,137). After excluding individuals with cancer (n=1,675), under age of 20 (n=48), and without known etiology (n=352), a total of 1,062 cirrhosis patients who presented at the ED are included in the study. Outcomes of interest are 14-day readmission and mortality. Main predictor variable is ED-LOS in hours. Other covariates are sex, etiology (Hepatitis B, Hepatitis C, alcoholic cirrhosis, and nonalcoholic steatoHepatitis), decompensation, and Charlson comorbidity index. Multivariate logistic regression is performed to test the association between ED-LOS and the two outcome measures.

Results: Of the 1,062 cirrhosis patients presented at the ED, more than 70% are male (70.17-79.05%) with a mean age of 57.4 years. More than half of the subjects have alcoholic cirrhosis as their etiology. After stratifying ED-LOS into 5 groups (<6, 6-12, 12-24, 24-48, and >48 hours), we find that the proportion of 14-day readmission is highest in patients with ED-LOS of 6 to 12 hours (12.16%, 18 of 148) and lowest in patients with less than 6 hours of ED-LOS (4.39%, 5 of 114). Mortality is also highest in the 6-to-12-hour group (24.48%), but lowest in the 24-to-48-hour group (12.15%). In the adjusted logistic regression model, an ED-LOS stay of 6 to 12 hours for cirrhosis patient is associated with a significantly higher odds of hospital readmission within 14 days (odds ratio (OR): 3.051, 95% confidence interval (CI): 1.162, 9.548). Other ED-LOS groups do not exhibit statistical significance with the same outcome measure. For mortality, ED-LOS does not seem to have an association with patients' risk of death following admission.

Conclusions: Our results show that ED-LOS may exert impact on cirrhosis patient's risk of 14-day readmission. Thus, it is important for clinicians to consider ED capacity as well as patient safety in real practice.

Disclosure of Interest: None Declared

P094

CLINICAL SPECTRUM AND OUTCOMES OF PATIENTS WITH SEVERE SPONTANEOUS HEPATITIS B FLARES AND REACTIVATION

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Background: Reactivation of Hepatitis B presenting as acute hepatic flare can have variable outcomes; acute hepatic insult (serum bilirubin >5 mg/dl and INR >1.5) alone or with development of new ascites or hepatic encephalopathy (HE) within 4 weeks (ACLF-B), which connotes high mortality. The clinical outcome of Hepatitis B flare in patients with decompensated cirrhosis is largely unknown.

Methods: Patients with acute hepatic insult alone (Gr. A), those developing ACLF-B (Gr. B) and Hepatitis B flares in decompensated cirrhotics (DC flare) (Gr. C) were compared for clinical, biochemical and virological parameters. Patients with Hepatitis B related acute liver failures (ALF-B) were excluded. All patients received potent antivirals (Tenofovir/Entecavir) and standard medical therapy; none underwent liver transplantation.

Results: 827 consecutive patients (Mean age – 47.1 $\pm$ 16 years; Male: Female – 4:1) with acute hepatic insult presented as Group A, B or C: 23.9%, 53.3% and 22.7% respectively. Almost 15% patients with ACLF-B had superimposed alcoholic Hepatitis (n=23), drug-induced liver injury (n=31) and Hepatitis E superinfection (n=14). Baseline mean HBV DNA (Log 4.9 vs. 4.1 vs. 4.6 IU/ml; p-0.7), HBsAg levels and positive HBeAg rates (52% vs. 48.8% vs. 43%; p-0.6) were comparable among the groups and did not independently predict mortality. Patients in Group A as compared to Group B had higher baseline ALT (median - 850 IU/L vs. 140 IU/L; p-0.01), higher rates of HBeAg (34.6% vs. 7.7%; p-0.01) and HBsAg seroconversion (11.6% vs. 1.1%, p <0.05). In comparison to Gr. C, patients in Gr. B had higher baseline HVPG (19.4 $\pm$ 2.6 vs. 15.2 $\pm$ 2.4 mmHg; p-0.007), more liver related complications including HE (42.4% vs. 18.1%, p<0.01), acute kidney injury (32.9% vs. 18.6%, p<0.01) and sepsis (51.2% vs. 22.9%, p<0.01) but less frequent hepatocellular carcinoma (HCC) (5% vs. 21.9%, p<0.001). Mortality at 3-months was highest in ACLF-B group (45.1%) than in DC flare (18.6%) and acute hepatic insult alone group (1%), p <0.05. Presence of sepsis (HR-6.4) and HE (HR-2.7) were independent predictors of mortality.

Conclusions: More than one-half of symptomatic Hepatitis B flares have ACLF. Hepatitis B DNA or HBeAg at baseline or follow-up do not predict clinical outcomes. Development of ACLF-B leads to more complications and warrants careful monitoring and need for early liver transplantation. New-onset HE and sepsis are independently associated with high mortality.

Image/Table:

	Acute HBV/ Reactivation, no ACLF (N=198)	ACLF-B (N=441)	dCLD-B with flare (N=188)
HBV DNA (IU/ml)	4.9 (3.5-6)	4.1 (2.6-5.5)	4.6 (3.1-6.1)
HBeAg +ve	52%	48.8%	43.3%
ALT (IU/L)	850 (321-1535)	218 (149-444)	175 (112-353)
HBeAg Seroconversion	34.6%	7.7%	
HBsAg loss	11.6%	1.1%	
HVPG (mm Hg)		19.4 + 2.6	15.2 + 2.4
HE		42.4%	18.1%
AKI		32.9%	18.6%
Sepsis		51.2%	22.9%
HCC		2.5%	11.9%
3-m Mortality	1%	45.1%	18.6%

Disclosure of Interest: None Declared

P095

PATIENTS WITH DENGUE-INDUCED HEPATITIS PROGRESSING TO HYPERACUTE LIVER FAILURE: A TROPICAL MAYHEM AND A RARE CASE SERIES

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Background: The progression from acute viral Hepatitis to acute liver failure (ALF) is an uncommon phenomenon (usually <1%). Dengue is an important arboviral disease in tropical countries in which a range of hepatic involvement has been described, ranging from mild Hepatitis to ALF. The published data on ALF in dengue is extremely limited. Therefore, we present here clinical characteristics and outcome 8 patients of dengue Hepatitis progressing to ALF.

Methods: Consecutive patients with dengue with evidence of Hepatitis were evaluated for the presence of ALF. The diagnosis of dengue was made on the basis positive NS1 antigen and/or positive IgM antibody against dengue virus. ALF was defined by occurrence of encephalopathy within 4 weeks of symptoms in absence of preexisting liver disease. ALF was considered hyper-acute when icterus-encephalopathy interval was 7 days or less.

Results: The rate of progression to ALF among patients with dengue Hepatitis was 3.3% (08/246). The median interval from onset of fever to liver failure was 5 (4-6) days. All ALF patients had icterus-encephalopathy interval of less than a week, suggesting a uniform hyperacute presentation. All patients progressing to liver failure had severe dengue as per the WHO criteria. Five patients had advanced hepatic encephalopathy at presentation. The median age (range) was 36 years and 75% of patients were male. Each patient had massive elevation of serum transaminases levels at presentation, with median aspartate aminitransferase (AST) and alanine aminotransferase (ALT) levels being 15328 IU/L and 3241 IU/L, respectively. The levels of AST were greater than ALT in all patients. Four of 6 (75%) dengue ALF patients died. Patients who survived had a lesser degree of transaminase elevation.

Conclusion: Dengue Hepatitis Can rarely progress to hyperacute liver failure. These patients have massive elevation of serum transaminases levels, with AST greater than ALT, and a high mortality rate. A higher elevation of AST over ALT suggests extrahepatic release of AST in dengue Hepatitis.

Image/Table:

Table 1: Baseline characteristics, laboratory parameters and outcome of dengue ALF patients

Patients' characteristics	Total N=08	Non-survivors N=06	Survivors N=02
Median age, median (range) (years)	36	44	31
Male	75%	83%	50%
Hepatic encephalopathy grade>2	05	04	01
Icterus-encephalopathy interval (<7 days)	08	06	02
Bilirubin, median, mg/dl	3.5	4.8	3.1
Aspartate transaminase (AST), median (range) IU/L	15328	22642	4321
Alanine transaminase (ALT), median (range) IU/L	3241	5263	964
Albumin, mean, g/dl	3.1 ± 0.2	3.0 ± 0.5	3.2
Serum creatinine, median (mg/dl)	1.8	2.1	1.1
Hb, mean, gm/dl	12.8 ± 1.1	11.8 ± 1.6	12.9
PCV mean	40.7	41.2	40
TLC, median (range) /mm^3	9250	15671	9800
Platelet count, median, /mm^3	35000	22000	35000
INR, median (range)	3.1	4.2	2.3
Outcome, n (%)			
Died	06 (75%)		
Survived	02 (25%)		

Disclosure of Interest: None Declared

P096

FACTORS ASSOCIATED WITH SPONTANEOUS CLEARANCE OF RECENTLY ACQUIRED HEPATITIS C VIRUS AMONG HIV-POSITIVE MEN IN BRAZIL

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Introduction: The objective of the present study was to describe the clinical and epidemiological aspects of recently acquired HCV infection and the frequency of its spontaneous clearance in a PLWH cohort.

Methods- We reviewed the medical records from all PLWH at the HIV outpatient reference clinic affiliated with the University of São Paulo, Brazil and identified HCV- infected individuals who seroconverted between January 2015 and December 2017. The factors associated with subsequent spontaneous clearance of the infection in this group were identified and analyzed.

Results- Among 3,143 PLWH individuals, 362 (11.5%) were infected with HCV. Forty-eight (13.2 %) of these subjects first became HCV-positive between January 2015 and December 2017. Spontaneous HCV clearance was documented in 23 individuals (47.9%). The majority of this latter group were male (83.3%) and the median age was 31 years (23-39). The main risk group for HCV acquisition was men who had sex with men (MSM) (89.5%). In multivariate analysis, only an elevated CD4+ lymphocyte count at the time of seroconversion was associated with subsequent HCV clearance ($p = 0.025$).

Conclusions- In HIV infected individuals in Sao Paulo, Brazil, sexual transmission has replaced IDU as the most frequent mode of HCV acquisition. In PLWH, particularly in MSM, the individual's CD4+ count is a determinant in whether an acquired HCV infection will be prolonged or spontaneously clear.

Disclosure of Interest: None Declared

P097

SEVEN YEARS OF EXPERIENCE WITH HEPATITIS C VIRUS (HCV) DIRECT ACTING ANTIVIRALS (DAA) TREATMENT: WHO ARE THE NEW PATIENTS?

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Introduction: Chronic infection with the Hepatitis C virus (HCV) continues to be a global Public Health problem. The definition of effective strategies aiming the elimination of Hepatitis C depends on the knowledge of the epidemiological evolution of the infected population.

Since the availability of Direct Acting Antivirals (DAA) in Portugal, between 2015 and September 2022, 31.760 treatments have been performed and a sustained global virological response (SVR) rate of 96.5% has been obtained.

Objectives: Evaluation of demographic and epidemiological trends of the HCV-infected population over the last seven years.

Evaluation of sustained virological response rate obtained, response to retreatment (due to relapses or reinfection) and rate of associated complications development over the study period (deaths, hepatocellular carcinoma and liver transplantation).

Patients and Methods: Demographic, epidemiological, clinical and therapeutic response characterization of HCV infected patients, with or without HIV co-infection, that are followed at the Infectious Diseases Service, of a central hospital in Lisbon, in the period between 2015 and 2022.

Results: Between January 2015 and September 2022, 824 DAA treatments were initiated.

The demography of the treated population revealed a predominance of males (76.2%), mean age of 49.7 years, 85.6% of Portuguese nationality, with an increase in the migrant population, mainly born in Brazil (1.3% between 2015- 2018 to 8.8% between 2019-2022).

About half (54.7%) of the patients had HIV co-infection. The most frequent route of transmission was associated with parenteral use of illicit substances (63.3%). Sexual transmission constituted 13.1% of all cases (58.3% in the group of men who have sex with men). Sexual transmission rate among MSM increased from 1.8%, between 2015-2018, to 8.1%, between 2019-2022. Since 2020, there have been an increase in diagnosis of acute HCV infection, all associated with sexual contact between MSM.

At the time of this analysis, 91.5% (n=784) completed treatment for 12 or more weeks, recording an overall SVR of 96.7%. 31 patients (4%) underwent retreatment, 21 due to recurrence and 10 due to reinfection, acheiving 100% SVR.

Over the study period, the overall lost to follow up rate was 2.1%, there were 16 (1.9%) deaths, 7 (0.9%) patients developed hepatocellular carcinoma and 2 (0.2%) were undergoing liver transplantation.

Conclusion: In this population, overall SVR rate was 96,7%, with no significant impact related to the presence of HIV coinfection.

During the study period, there was a trend towards an increase in the migrant population, especially those from Brazil, and an increase in sexual transmission, predominantly among MSM.

Disclosure of Interest: None Declared

P098

VENOUS THROMBOSIS, SEGMENTAL HYPOPERFUSION AND ISCHEMIC HEPATITIS IN AMOEBIC LIVER ABSCESS: COMPUTED TOMOGRAPHIC DEMONSTRATION AND ITS IMPLICATIONS

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Purpose: To report venous thrombosis and associated perfusion defect indicating segmental ischemic Hepatitis in amoebic liver abscess (ALA) using multidetector computed tomography (MDCT).

Method: MDCT images of 62 patients with ALA were reviewed for venous thrombosis and associated perfusion abnormalities.

Result: The study found 43 (69%) patients with venous thrombosis: portal vein thrombosis (PVT) occurred in 39, hepatic vein thrombosis (HVT) in 37 and inferior vena cava (IVC) thrombosis in 4. Combined PVT and HVT occurred in 33 (77%) patients. The portal vein thrombi remained localized in subsegmental branches in 25 patients and extended to segmental branches in 14. The hepatic vein thrombi were confined to peripheral branches in 18 patients; they progressed to the main trunk in 19 and to the IVC in 4. A wedge-shaped hypoattenuating zone suggesting ischemia was identified in 33 (77%) patients in portal phase: 31 had combined PVT and HVT, 2 had HVT alone, but none had PVT alone. It occurred significantly more often with combined PVT and HVT than HVT alone ($p = 0.05$). Arterial phase enhancement occurred in 2 of 13 patients with multiphasic CT.

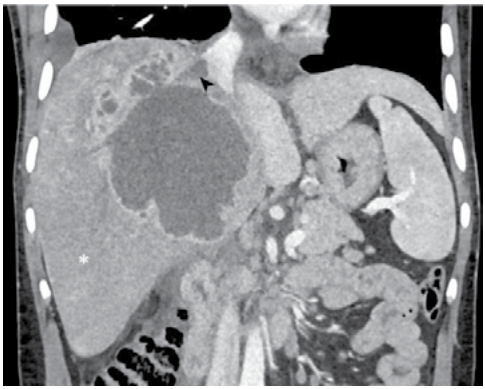
Laboratory data revealed marked leukocytosis (average total leukocyte counts 29,882 $\pm$ 9,243 /μL in all patients. The average level of alanine aminotransferase was 206.3 $\pm$ 133.6 U/L, of aspartate aminotransferase was 233.6 $\pm$ 122.4, of alkaline phosphatase was 408.1 $\pm$ 188.1 U/L, and of total bilirubin was 2.9 $\pm$ 2.1 mg/dL.

All patients were symptomatic despite medical therapy and therefore required percutaneous drainage. About half of the patients were identified with ruptured abscesses. Segmental atrophy was observed in seven of nine patients who underwent follow-up CT.

Conclusion: Combined PVT and HVT commonly occur with ALA and often manifests as segmental hypoperfusion in portal venous phase, indicating segmental ischemia. The detection of such events by CT may be indicative of severe disease that requires aggressive management involving percutaneous drainage

Figure legend: Coronal CT image of a 32-year-old man shows an amoebic abscess in the right lobe of liver with thrombus in the right hepatic vein trunk (arrowhead). There is presence of a large wedge-shaped hypoattenuating zone (asterisk) surrounding the abscess indicating segmental hypoperfusion (ischemic Hepatitis).

Image/Table:



Disclosure of Interest: None Declared

P099

STANDARD VOLUME PLASMA EXCHANGE IS SAFE AND EFFECTIVE FOR PATIENTS WITH ACUTE LIVER FAILURE DUE TO VIRAL ETIOLOGY

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Background: Plasma exchange (PLEX) is an effective bridging therapy for patients with acute liver failure (ALF). There are no studies comparing the efficacy of standard volume (SV) vs. high volume (HV) PLEX. Therefore, we aimed to compare the safety and efficacy of SV PLEX with HV PLEX.

Methods: Patients with ALF due to viral etiology who underwent PLEX were included in this retrospective study. The primary outcome was to compare the transplant-free survival among SV (total plasma volume x 1) and HV (total plasma volume x 1.5) PLEX groups at 30-days. Secondary objectives were to compare the effect of SV and HV PLEX on total bilirubin, INR, ammonia levels, SOFA, and MELD Na scores, and lastly, to assess the adverse events related to PLEX.

Results: A total of 17 patients underwent PLEX: SV-7 and HV-8.Cause of acute viral liver failure were Hepatitis E (10),Hepatitis A (4) and Hepatitis B (1). The mean age and severity scores (SOFA-4.13 $\pm$1.72 in SV group vs. 4.89$\pm$1.7 in HV group; P=0.37) were similar among both the groups. Fifty percent in SV and 34% in HV group satisfied King's College Criteria for liver transplantation (P=0.41). Each patient in both the groups underwent a median of 2 sessions of PLEX. There was a significant decrease in serum bilirubin levels and prothrombin time in both the groups post-PLEX. Post-PLEX, the change in total bilirubin, INR, ammonia, SOFA, and MELD Na score was comparable (Fig. A). Mortality at seven days was similar among both groups (SV-12.5% vs. 33.3% in HV; P=0.57). Mortality at day 30 was 25% in SV compared to 67% in the HV group (P=0.1). On Kaplan Meier analysis, transplant-free survival at day 30 was similar in both the groups (P=0.26) (Fig. B). Two patients in the HV group developed volume overload features and were managed conservatively compared to none in the single volume group.

Conclusions: Standard volume plasma exchange has similar efficacy as high volume plasma exchange on severity scores. Standard volume plasma exchange is safe and effective for patients with acute liver failure due to viral etiology.

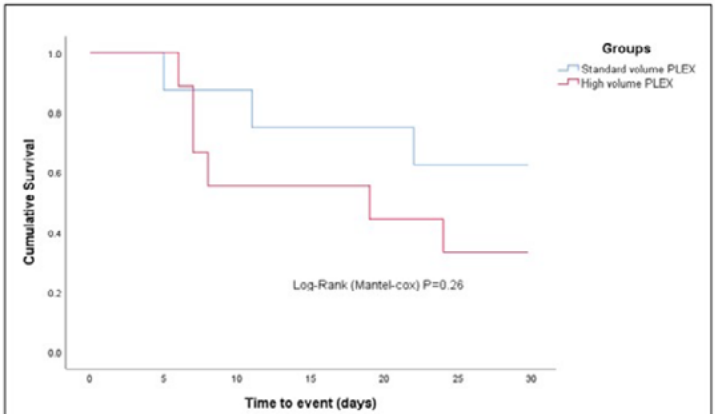
Image/Table:

A. Change in laboratory variables and severity scores after PLEX in each group

Variables	Standard volume	High-volume	P-value
Total bilirubin	-6.53±5.45	-9.8±6.86	0.3
PT	-34.9±30.21	-26.52±17.16	0.48
INR	-2.35±1.48	-2.32±1.46	0.96
SOFA	-0.62±0.74	-0.12±1.16	0.3
MELD NA	-10.12±4.94	-10.55±7.8	0.89
Ammonia	-11.33±29.6	-39.37±28.21	0.09

PLEX, plasma exchange; PT, prothrombin time;
INR, international normalized ratio;
SOFA, sequential organ failure assessment score,
MELD NA, model for end-stage liver disease

B. Kaplan-Meier Transplant-Free Survival analysis



Disclosure of Interest: None Declared

P099B

DEVELOPMENT AND VALIDATION OF A NOVEL ICP-MS METHOD TO QUANTIFY DIFFERENT COPPER SPECIES IN HUMAN PLASMA FROM PATIENTS WITH WILSON DISEASE

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Background and Aims: Wilson disease (WD) is a rare autosomal recessive genetic disorder. Functional mutation of ATP7B causes inadequate loading of copper (Cu) into ceruloplasmin (CP) and defective Cu excretion into bile, resulting in Cu accumulation in liver and other organs. Currently, WD treatment monitoring lacks reliable and fully validated bioanalytical methods. The calculated non-CP Cu (NCC) method assumes a CP-Cu:Cp ratio of 6:1 and can yield negative NCC values, which are biologically implausible. A direct assay is needed to monitor NCC, especially for patients treated with an investigational Cu-binding agent, ALXN1840 (bis-choline tetrathiomolybdate), which mobilizes tissue Cu, contributing to a non-bioavailable pool of circulating Cu.

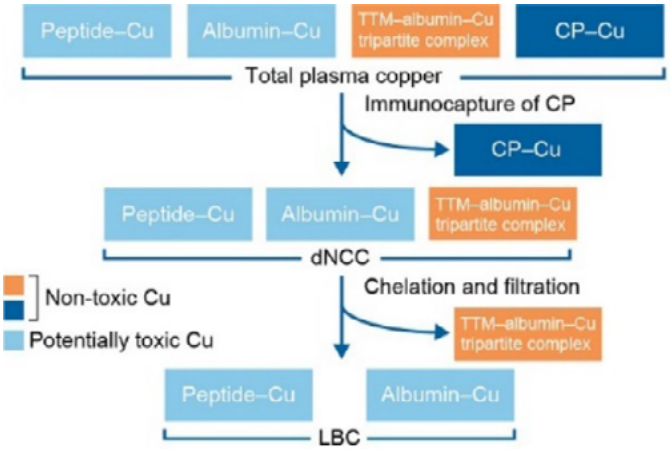
Method: A novel method utilizing immunocapture of CP, followed by chelation and filtration to isolate different Cu fractions subject to ICP-MS analysis (Figure) was developed to fractionate and directly quantify multiple Cu species from human plasma. It permits measurement of CP-protein via LC-MS method and Cu species including CP bound Cu (CP-Cu), direct NCC, and labile bound Cu (LBC) via one workflow. Methods were validated for precision, accuracy, selectivity and stability following the FDA guidance for Bioanalytical Method Validation. A monoclonal anti-CP antibody was screened and selected for long-term assay use. Samples from healthy volunteers and from patients with WD were assessed for the Cu concentration in the CP fraction and the CP-Cu:Cp ratio.

Results: Full validations were successfully performed for each Cu fraction as well as CP-protein and showed a linear range from 5-1000 ng/mL (0.08 – 15.75 µM) for CP-Cu, direct NCC, LBC, and 5.00 - 800 µg/mL (0.03 – 5.97 µM) for CP-protein. The mean [95% confidence interval] for the CP-Cu:CP ratio was 4.68 [4.35, 5.00] in healthy volunteers and 4.09 [3.36, 4.82] in patients with WD, both being below the assumed ratio of 6.

Conclusion: Conventional calculated NCC is inaccurate and cannot be used for therapeutic guidance for WD. A novel method was developed that utilizes an immunocapture step and subsequent quantification of various fractions, including CP-Cu, direct NCC, LBC, and CP-protein. Validation data met defined acceptance criteria in terms of precision, accuracy, selectivity and stability. The assay is precise and reproducible and is valuable for accurate quantification of CP-Cu:CP-protein ratio, direct NCC and LBC, which may benefit WD therapy development.

Previously presented at EASL 2022.

Image/Table:



Disclosure of Interest: A. P. O. B. O. A. Ala Grant / Research support from: Alexion & Orphalan – Contracts for study to organization, Conflict with: Honoria payments and travel expenses from Alexion and Honoria from Orphalan, T. Liang Employee of: Alexion Pharmaceuticals, Inc. at the time the research wad carried out., H. Zhang Employee of: Frontage Laboratories, L. Zhang Employee of: Alexion Pharmaceuticals, Inc., S. Moseley Employee of: Alexion Pharmaceuticals, Inc., P. Guo Employee of: Frontage Laboratories, M. Chen Employee of: Alexion Pharmaceuticals, Inc., T. Hall Employee of: Alexion Pharmaceuticals, Inc. at the time the research wad carried out., L. Ming Employee of: Alexion Pharmaceuticals, Inc., E. Swenson Employee of: Alexion Pharmaceuticals, Inc., W.-J. Pan Employee of: Alexion Pharmaceuticals, Inc., B. Meltzer Employee of: Alexion Pharmaceuticals, Inc., R. Pelto Employee of: Alexion Pharmaceuticals, Inc., M. Ma Employee of: Alexion Pharmaceuticals, Inc. at the time the research wad carried out.

P100

BURDEN OF HEPATITIS C VIRUS INFECTION IN PUNJAB PROVINCE OF PAKISTAN: THE PUNJAB HEPATITIS SURVEY 2018

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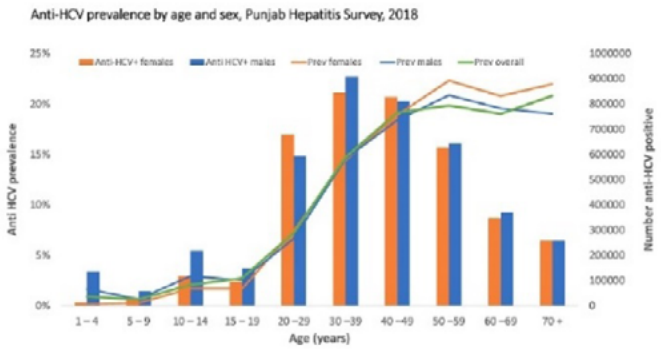
Background: Pakistan has one of the highest burden of Hepatitis C virus (HCV) infection in the world. However, recent population level data to inform HCV elimination efforts are not available. We conducted a population based survey in the Punjab province of Pakistan (population >110 million people) to estimate the prevalence, risk factors, engagement with care and treatment for HCV. This abstract describes prevalence estimates and risk factors for HCV.

Methods: We conducted a multi-stage stratified cluster survey of population in the Punjab province in 2018. Clusters were selected through stratified random design from the enumerated list of all clusters stratified into urban and rural areas. 20 houses per cluster were selected using systematic sampling with random start. All household members of selected houses were interviewed for household characteristics, HCV risk factors and engagement with HCV care and blood was collected was anti-HCV, and RNA testing. We computed the prevalence of anti-HCV and RNA positive population while accounting for the survey design. We identified factors associated with anti-HCV positivity by logistic regression.

Results: Of 21,668 participants, questionnaire and laboratory results were available for 14,305 participants. Overall prevalence of anti-HCV was 9.0%, translating into 7.96 million people, slightly higher among females than males(9.2% vs 8.8%). The anti-HCV prevalence increased with age in both females and males (females:1-4 yrs: 0.2%, 15-19yrs:1.7%, 20-29yrs:7.5%, 30-39y:14.4% to >40yrs: 19-22%; males: 1-4 yrs:1.6%, 15-19yrs:2.6%, 20-29yrs:6.7%, 30-39y:14.6% to >40yrs: 18-21%). Of anti-HCV positive, 56% were positive for RNA. The prevalence of active infection was 5.0%, translating into 4.5 million infections. Majority of infections were genotype 3 (90%). In a multivariable model, age, education, number of injections during the past 3 months, history of blood transfusion, dental care during the past 10 years and tattoos were significantly associated with higher risk. Among females, transfusion receipt was significant, while gravidity as well as dental treatment were not significant risk factors. Among males ever receiving a cut from barber was significantly associated with higher infection odds while transfusion was not a significant risk factor.

Conclusion: This population based survey in the largest province of Pakistan shows a very high disease burden requiring immediate and concerted efforts to scale up testing and treatment. Risk factor analysis highlights concurrent need for prevention efforts with specific focus on infection control in the healthcare sector and community services.

Image/Table:



Disclosure of Interest: N. Janjua Conflict with: AbbVie, Speakers bureau of: AbbVie, Gilead, A. Naveed : None Declared, H. Velásquez García: None Declared, S. Ul Huda: None Declared, S. Rasul: None Declared, A. Ahmad: None Declared, Z. Sarwar: None Declared, S. Akhter: None Declared

P101

DEVASTATING RISE OF HEPATITIS-C CASES IN RURAL SINDH, PAKISTAN - IDENTIFICATION AND TREATMENT OF A PUBLIC HEALTH THREAT

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Background: As of december 2022, pakistan has the highest global burden of Hepatitis C virus (hcv) infection, with 10 million infected individuals. According to the us centre for disease analysis, from 2015-2021 approximately half a million new cases were reported in pakistan. Sindh province has the second highest prevalence in pakistan at 6%. Most infected individuals in pakistan do not know their Hepatitis status while who states that, 95% of people infected with hcv can be cured within 2–3 months with highly effective direct-acting antiviral drugs.

Purpose: The aim of this study was to identify and treat patients of Hepatitis-C in sindh, pakistan. Secondarily, the study aimed to assess the most common risk factor leading to the potential transmission of Hepatitis-C in the region.

Method: Informed consent was obtained from all participants. Adults above 18 years visiting a primary care centres in gharo, sindh were randomly selected for health screening. HCV rapid antibody test was used to screen for Hepatitis-C. Individuals that showed a reactive result were further asked about the potential risk factors before a confirmatory pcr test was performed. Once identified, daclatasvir and sofosbuvir were dispensed for 03 months with monthly follow up where baseline blood work up was taken to monitor overall patient condition.

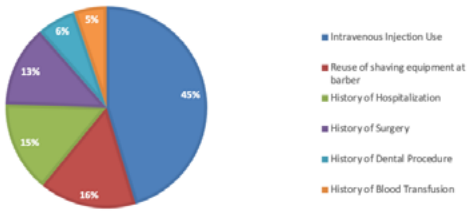
Results: During a 21-month period a total of 3476 screening tests were conducted from march 2021 till november 2022. The mean age of the participants was 37 years and the majority of the individuals screened were female (62.7%). A total of 498 individuals (14.3%) tested positive on the screening test and the confirmatory pcr diagnosed 247 individuals (figure 1) suffering from Hepatitis-C. When asked about the potential risk factors the main cause identified was intravenous medication at clinics with a reused needle. Other causes are shown in figure 2. Complete treatment leading to a disease-free state was seen in 53 individuals while the remaining are still under care. Two cases reported a positive pcr after 3 months of treatment and were referred to specialist care.

Conclusion: Considering the devastating rise in Hepatitis-C cases, emergency protocol should be implemented to curb the disease burden in the region. Screening of the disease should be conducted at a community level via home visits and preventive interventions should be encouraged, especially, health education methods and education content creation in the regional language of the area. Resistant cases to treatment should be reported to the health authorities and patients should be supervised to ensure routine medication intake. If no action is taken Hepatitis-C cases will lead to a breakdown in the healthcare system of pakistan.

Image/Table:

FIGURE 1: PCR POSITIVITY RATE PER MONTH

FIGURE 2: RISK FACTORS OF HEPATITIS-C IN RURAL SINDH



Disclosure of Interest: None Declared

P102

PREVALENCE, CLINICAL FEATURES AND OUTCOMES OF HEPATITIS B AND HEPATITIS C CO-INFECTIONS AMONG HIV-POSITIVE ADULTS IN A TERTIARY HOSPITAL IN MANILA, PHILIPPINES

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Introduction: The Philippines is one of the countries with the fastest-rising HIV rate in Asia. HIV, Hepatitis B (HBV) and Hepatitis C (HCV) have similar transmission routes; hence, People Living with HIV (PLHIV) are also at risk of acquiring HBV and HCV. Despite the high prevalence of HBV and HCV in the Philippines, there is limited information regarding HBV and HCV co-infections in PLHIV in the Philippines. This study aims to provide local data on Hepatitis B and C co-infections among HIV-positive adults.

Objectives: To identify the prevalence, clinical features, and outcomes of HBV and HCV co-infections among PLHIV enrolled in a treatment hub in Manila, Philippines.

Methods: A retrospective study was conducted on PLHIV enrolled at San Lazaro Hospital treatment hub between 2015 and 2019. Demographic data, pre-treatment laboratory results, including Hepatitis B surface antigen (HBsAg) and HCV antibody (anti-HCV), and outcomes were retrieved from the medical records and the National Reference Laboratory - STD AIDS Cooperative Central Laboratory (NRL-SACCL) database.

Results: Among 1,658 HIV-positive patients, the prevalence of HIV/HBV co-infection was 12%, and the prevalence of HIV/HCV co-infections was 0.4%. There were no triple co-infections of HIV/HBV/HCV. Most patients with Hepatitis Co-infections were male (99.4%), and the most common mode of HIV transmission was homosexual contact (68%). HIV/HBV and HIV/HCV patients exhibited mild elevations of serum transaminases. Based on the non-invasive fibrosis scores of HIV/HBV patients, 17.3% have fibrosis, and 11.3% have cirrhosis. The mortality rate for HIV/HBV co-infection was 28.4%, while the mortality rate for HIV/HCV co-infection was 16.7%.

Conclusion: Our findings show that the prevalence of HBV among HIV patients was lower than that of the reported prevalence of HBV among the general population in the Philippines. Also, our results showed a higher prevalence of HIV/HBV co-infection as compared to the median HIV/HBV co-infection rate of Sub-Saharan Africa. Furthermore, the prevalence of HIV/HCV co-infection in our setting is very low, which can be attributable to this population›s uncommon injection drug use. The findings of this study highlight the importance of HBV and HCV screening, Hepatitis B vaccination and early anti-retroviral therapy in all PLHIV.

Image/Table:

Table 1. Prevalence of HIV/HBV and HIV/HCV co-infections in the H4 Department of San Lazaro Hospital from January 2015 to December 2019.

	anti-HCV result	HBsAg result
Non-Reactive		
n	1619	1194
%	99.6	87.6
Reactive		
n	6	169
%	**0.4**	**12.1**
Total	1625	1363

Disclosure of Interest: None Declared

P103

HIGH PREVALENCE OF LIVER FIBROSIS IN THE INFECTION BY THE HEPATITIS B AND C VIRUS IN A COUNTRY OF LIMITED RESOURCES IN CENTRAL AMERICA

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Introduction: It is known that patients with chronic Hepatitis C virus (HCV) and Hepatitis B virus (HBV) infection develop early fibrosis in the first 5 years of infection. The evaluation of liver fibrosis is currently reliable by noninvasive methods such as transient vibration-controlled elastography (VCTE), the Fibrosis Index 4 (FIB-4) and the Aspartate Aminotransferase-Platelet Ratio Index (APRI). In Guatemala in 2015, HCV was the main cause of chronic Hepatitis, cirrhosis and liver cancer. Despite this, there are few studies of the prevalence of fibrosis in these patients, especially in countries with limited resources like Guatemala.

Aims: To determine the prevalence of liver fibrosis by non-invasive methods in patients with chronic HBV and chronic HCV infection.

Methods: Retrospective descriptive study including patients registered in the Unit for HIV and Chronic Infections of the Hospital Roosevelt in Guatemala during the period from January 2015 to December 2020. Patients between 18 and 80 years of age were included. The non-invasive methods used were the FIB-4 index, APRI and VCTE.

Results: 429 patients were included, 275 with HCV infection and 154 with HBV, 50.6% were male with an average age of 56 years. 54.2% of the patients identified with fibrosis was made by the VCTE method and 45.8% by the APRI and FIB-4 method. 48.4% of the patients with fibrosis were F4, the most frequent grade of fibrosis was F4, followed by F3 in HCV and F1 in HBV. Most of the patients with fibrosis (55%) were 6 months to 2 years after diagnosis of the infection. The most frequent clinical manifestation was esophageal varices (15.5%), ascites (5.0%) and upper gastrointestinal bleeding (2.9%)

Conclusion: There is a high prevalence of liver fibrosis and advanced fibrosis in patients with chronic infection by Hepatitis B and C viruses in Guatemala, mainly in the first two years of diagnosis. This study shows that chronic Hepatitis b and c infections are still diagnosed late in developing countries.

Disclosure of Interest: None Declared

P104

PREVALENCE DE L'INFECTION PAR LE VIRUS DE L'HEPATITE B CHEZ LA FEMME ENCEINTE AU CENTRE HOSPITALIER UNIVERSITAIRE MÈRE-ENFANT FONDATION JEANNE EBORI DE LIBREVILLE

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Introduction: Les infections par le Virus de l'Hépatite B (HBV) représentent un problème majeur de santé publique. En effet, on compte près de 2 milliards de personnes actuellement infectées par le HBV dans le monde, soit 240 millions de porteurs chroniques. Ces porteurs chroniques en l'absence de traitement, sont exposés à un risque accru de développer des lésions hépatiques graves telles que la cirrhose et le carcinome hépatocellulaire. Aussi, le Gabon étant une zone endémique, la surveillance de la femme enceinte est primordiale, car la transmission mère-enfant du HBV représente la principale cause de nouvelles infections.

Objectif : Dans cette optique, nous nous sommes intéressés à l'étude de la prévalence de l'infection à HBV, chez la femme enceinte au Centre Hospitalier Universitaire Mère-Enfant Fondation Jeanne-Ebori (CHUME-FJE).

Materiel et Methodes : Pour ce faire, des femmes enceintes reçues au laboratoire, au service des urgences gynécologiques, et en maternité du CHUME-FJE ont été enrôlées et inclues dans cette étude.

Resultats : Un total de 182 femmes enceintes ont été testées et les résultats obtenus montrent que parmi ces patientes, 7 sont infectées par le HBV, soit une prévalence de 3,8 %. La tranche d'âge la plus touchée par l'infection à HBV est celle des femmes ayant un âge compris entre 24 et 35 ans. Ces femmes infectées par le virus de l'hépatite B vivent majoritairement dans des quartiers de classe moyenne et possèdent toutes une activité professionnelle.

Conclusion : L'ensemble de ces résultats montre que l'infection par le HBV chez la femme enceinte, touche principalement les tranches d'âge de 20 à 25 ans et de 30 à 35 ans avec une prévalence de 3,8%.

Mots-clés : Hépatite B, prévalence, femme enceinte

Disclosure of Interest: None Declared

P105

HIGH INCIDENCE AND PERSISTENCE OF OCCULT HEPATITIS B VIRUS INFECTION AMONG PEOPLE WITH HIV IN BOTSWANA

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Background: About 2.73 million people with human immunodeficiency virus (PWH) worldwide are coinfected with Hepatitis B virus (HBV), with 71% being from sub–Saharan Africa. HBV/HIV coinfection results in worse disease outcomes than either infection alone. Routine HBV screening is through the detection of Hepatitis B surface antigen (HBsAg), however, occult HBV infection (OBI) is missed by this algorithm. OBI, described as detectable HBV deoxyribonucleic acid (DNA) in the absence of detectable HBsAg is transmissible, can cause liver disease including hepatocellular carcinoma and is common among PWH. In Botswana, we found a high OBI prevalence of 24% among PWH initiating antiretroviral therapy (ART) and 6.6% in pregnant women. There is limited data on the natural progression of OBI owing to the few longitudinal studies on OBI.

Purpose: We aimed to determine the incidence and clearance of OBI in PWH in Botswana.

Materials and Methods: Archived plasma samples from a longitudinal HIV natural disease progression study which followed up participants for at least 24 months (2004 –2009) were used. Participants with available follow-up plasma samples were selected for this study. HBsAg screening was done by enzyme-linked immunosorbent assay (ELISA) and all HBsAg negative samples were screened for OBI using an in-house real-time polymerase chain reaction (qPCR) assay at yearly intervals.

Results: Demographic data were available for 126 participants with 32/126 being male (25.4%). The median age of participants was 34 years (IQR: 29 – 42). Median CD4+ T-cell count was 423 cells/uL (IQR 312 – 543) while $\log_{10}$(HIV viral load) was 4.10cps/mL (IQR: 3.59 – 4.75). We report a HBsAg prevalence of 9/126 [7.1% (95% CI: 3.8 – 13.0) at baseline and an OBI prevalence of 21/95 [22.1% (14.9 – 31.4). Two of the 9 HBsAg-positive participants lost the HBsAg at year 1. Out of the 21 OBI-positive participants, 20 were screened for OBI at the year 1 time-point and 9 of those had persistent OBI (45.0%). Sixty-five OBI-negative participants were screened for DNA at year 1 and 17 OBI incident cases were observed, [26.2% (17.0 – 38.0). Of the 17 incident cases, 5 were screened at year 2 and 2/5 (40.0%) persisted. Twenty-seven of the OBI-negative participants from year 1 were screened for DNA at year 2 and 12 OBI incident cases were observed, [44.4% (27.6 – 62.7). Total OBI incident cases over a 2-year period were 29 and one of the OBI incident cases was a participant who lost HBsAg.

Conclusions: There was a high incidence and persistence of OBI in this study with minimal association with prior HBsAg positivity. OBI screening in PWH should be considered. Further studies on factors associated with OBI persistence are warranted.

Disclosure of Interest: None Declared

P106

HBV CIRCULATION AND IMMUNE-ESCAPE VARIANT PREVALENCE IN THE RUSSIAN FEDERATION TWENTY YEARS AFTER THE START OF MASS VACCINATION

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Background: Neonatal vaccination against Hepatitis B virus (HBV) infection has been initiated in Russia twenty years ago along with catch-up immunization of adolescents and adults under the age of 60 launched in 2006.

Purpose: To assess HBV infection prevalence and immunity to it among general population of Russia following twenty years of nationwide vaccination campaign and to evaluate the role of virus immune escape variants in maintenance of HBV circulation.

Methods: Total 36,149 healthy volunteers from nine regions spanning the Russian Federation from west to east were tested for HBsAg, anti-HBc and anti-HBs antibodies using commercially available ELISA kits. HBV sequences from 481 chronic Hepatitis B patients collected in 2018-2022 were analyzed for HBsAg immune escape variants in comparison with 205 sequences obtained at the same territories before 2010. The population dynamics (effective number of infection and reproduction number) was analyzed separately for wild-type and immune-escape variant sequences using methods of Bayesian analysis.

Results: The national average HBsAg prevalence was 0.8%, and the only study region where HBsAg prevalence significantly exceeded this level was Dagestan Republic (2.4%, $p<0.0001$). In generation vaccinated at birth, average HBsAg prevalence was below 0.3%, ranging from 0% to 0.7% depending on region. Anti-HBc prevalence in subjects under 20 years was 7.4%, indicating ongoing HBV circulation. The overall proportion of participants under 20 years with vaccine-induced HBV immunity (anti-HBs positive, anti-HBc negative), was 41.7%, but below 10% in Tuva Republic and below 25% in Sverdlovsk Region and Kaliningrad Region. The overall prevalence of immune escape HBsAg variants was 25.2% in sequences obtained in 2018-2022, similar to prevalence of 25.8% in sequences collected before 2010 ($p>0.05$). The population dynamics of immune escape variants predicted by Bayesian analysis remained stable over the last twenty years, indicating the absence of vaccine-driven positive selection. In contrast, wild-type HBV population size showed the rapid decrease since mid-1990s, following the introduction of mass immunization, but started to restore afterwards, reaching the pre-vaccination levels by 2020.

Conclusion: Vaccination gaps, but not the virus evolution may be responsible for the maintenance of virus circulation despite twenty years of mass vaccination. To address this issue, vaccination quality control program should be implemented, as well as the booster immunization for young adults in populations where neonatal HBV vaccination uptake was suboptimal.

Funding: This research was funded by grant of the Russian Science Foundation (ID-20-15-00148).

Disclosure of Interest: None Declared

P107

PREVALENCE AND VIRAL LOAD QUANTIFICATION OF HEPATITIS DELTA VIRUS AMONG PEOPLE LIVING WITH HIV IN BOTSWANA

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Abstract Content: Approximately 15-20 million people worldwide are Hepatitis delta virus (HDV) infected, which is approximately 5% of people with chronic Hepatitis B virus (HBV). Sub-Saharan Africa has high HDV prevalence, reaching 25% among HIV/HBV co-infected people in Guinea Bissau. HIV/HBV/HDV multi-infection is associated with worse clinical outcomes. There are limited data on HDV prevalence among people living with HIV (PLWH) who are HBV infected and uninfected in Botswana. We here aimed to determine HDV prevalence among Hepatitis B surface antigen (HBsAg) positive and negative PLWH in Botswana.

This was a retrospective cross-sectional study utilising archived plasma samples from the Botswana Combination Prevention Project (BCPP) (2013-2018). Samples with results for HBV markers such as HBsAg, anti-HBc IgM and Hepatitis B e antigen (HBeAg) were categorized according to their HBV status, and screened for anti-HDV using the General Biologicals HDV Ab kit according to the manufacturer's instructions. Total nucleic acid was extracted from samples with a single positive anti-HDV result using DaAn Gene nucleic acid extraction kit and HDV viral loads were quantified using the Altona Diagnostic RealStar® HDV RT-PCR Kit as per the manufacturer's instructions. Statistical analysis was performed using R version 4.2.1 where p-values <0.05 were considered statistically significant.

The study cohort (n=478) included HBsAg positive (44%) and HBsAg negative (56%) participants. The mean age of these participants was 42 [95% CI: 41 – 43], with majority (70.0%) being females. Anti-HDV prevalence of (15/211) [7.1%, 95% CI: 4.4-11.4] was recorded among HBsAg positive participants, all of whom were anti-HBc IgM negative. HDV viral load was detected in 11/12 anti-HDV positive participants, ten of whom also had detectable HBV viral load despite receiving antiretroviral therapy (ART) with anti-HBV activity. There was no statistically significant difference in HIV and HBV viral loads between HDV positive and negative participants (p>0.05). No HDV prevalence was recorded among participants who were HBsAg negative, therefore the overall HDV prevalence was (15/478) [3.1%, 95% CI: 1.9-5.1].

We report relatively high HDV prevalence among HIV/HBsAg positive participants in Botswana, compared to previous WHO reports. Most of these participants had active HDV infection due to HDV viral load detection, therefore HDV screening in HBV/HIV infected individuals is recommended.

Disclosure of Interest: None Declared

P108

CHALLENGES IN IDENTIFYING HEPATITIS D IN BRAZIL: A DESCRIPTION OF REPORTED CASES IN THE MEDICINE CONTROL SYSTEM

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Introduction: Hepatitis D Virus (HDV) has been detected more often in the northern region of brazil, which in a historical series between 2000-2021 concentrates 74% of notified cases. Its epidemiological impact is justified by greater severity and rate of progression to cirrhosis, which increases risk of hepatocellular carcinoma and mortality when compared to Hepatitis b virus (HBV) monoinfection. In 2020, the medicine control system (siclom) was implemented in brazil, allowing to report variables with clinical information.

Objective: To describe the cases of HDV infection registered in siclom.

Methods: Epidemiological and clinical analysis of the national HBV database cases with a result "reagent" in the variable "exam of anti-hdv igg", between 2020-2022. Anonymized data was used.

Results: 37,231 cases of HBV were identified, which 518 (1.4%) were reagent for anti-hdv igg. Among the cases, 271 (58%) were male, 172 (37%) were between 40 and 49 years old, 184 (40%) had from 8 to 11 years of study. No foreign population, homeless or deprived of liberty were found. About liver disease, 349 (67%) did not have cirrhosis, 132 (26%) had child b or c cirrhosis and 44 (9%) progressed to liver failure. The northern region concentrated more than 80% of cases.

Conclusion: Due to historical predominance of hdv in the northern region, the flow of investigation is better established in this territory, and data is probably closer to the real prevalence. However, case reports in other regions may indicate underreporting. A study of hdv seroprevalence in brazil would be of utmost importance to determinate the real frequency of the virus in the country.

Keywords: HDV, Viral Hepatitis, prevalence, information system

Disclosure of Interest: None Declared

P109

EPIDEMIOLOGY OF OCCULT HEPATITIS B VIRUS INFECTION IN AFRICA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Occult Hepatitis B virus (HBV) infection (OBI) is described as the identification of HBV DNA in the liver (with detectable or undetectable HBV DNA in serum) of individuals testing negative for Hepatitis B surface antigen by currently available diagnostic methods. Although there is substantial data on OBI in Africa, no relevant meta-analysis has been conducted.

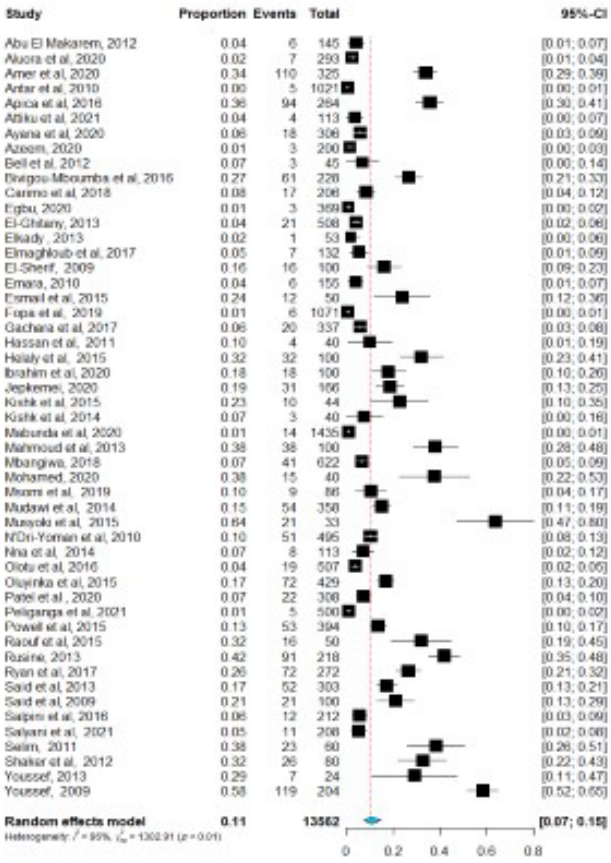
Objectives: This study was conducted to assess the pooled prevalence of occult Hepatitis B virus infection OBI in Africa.

Method: We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Relevant published studies were searched in the MEDLINE/PubMed, Google Scholar, Cochrane Library, African Medical Journals, and ScienceDirect databases. The quality of the retrieved studies was assessed using the Modified Newcastle-Ottawa Scale.

Results: Fifty-one studies involving 13,562 patients were included in this systematic review and meta-analysis. The pooled prevalence of OBI was 11% (95% confidence interval: 7–15%). Due to high heterogeneity, a random-effects model was used. Subgroup analysis revealed a slightly higher pooled prevalence of OBI (11.0%) in human immunodeficiency virus patients and in studies conducted in Egypt (14.0%). Meta-regression analysis showed that only the sample size was associated with the prevalence of OBI (estimate: −0.003, standard error = 0.0006, 95% CI: −0.004 to −0.002; $P < 0.001$). Publication bias was detected and funnel plot asymmetry was corrected by adding 16 new studies according to trim and fill methods.

Conclusion: This meta-analysis provides evidence with a moderate certainty level of a high prevalence of OBI in Africa. There is a need for re-evaluation of current preventative measures, adequately screening at-risk populations as well as blood and organ donors and improving, ensuring and extending Hepatitis B vaccination coverage.

Image/Table:



Disclosure of Interest: None Declared

P110

PREVALENCE AND RISK FACTORS OF HEPATITIS B VIRAL INFECTION IN HIV INFECTED PATIENTS ATTENDING SECONDARY HEALTHCARE FACILITIES

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Introduction: Human Immunodeficiency Virus (HIV) and Hepatitis B virus (HBV) are most common chronic viral infections of public health importance worldwide. HBV infections cause acute and chronic liver infection with the potential for liver cirrhosis and hepatocellular carcinoma (HCC). This study was carried out to determine the prevalence of and risk factors for Hepatitis B viral infections among HIV infected volunteer patients.

Method: A total of Four hundred (400) samples were collected from HIV patients and screened for HBsAg using the Micro point test kit .Thereafter, Nested Multiplex PCR assay was carried out for the HBV DNA amplification using the universal primers (P1) and (S1-2) for the outer primers. The tests and results interpretation were carried out according to manufacturer's instructions, while observing universal precautions.

Result: Overall prevalence of 7.8% (31/400) of the subjects were positive for HBsAg, with regards to gender, Male subjects screened recorded a prevalence of 10(8.1%) compared to the females with a positivity of 21(7.6%) positivity: [P value of 0.845}:P>0.05].The HBsAg positivity among the study participants with regards to age showed that subjects aged 21 – 30 years recorded the highest Sero-positivity of 10.1% (6/400) compared to those aged 41 – 50 with a recorded prevalence of 10.1 % (12/400), further more subjects aged 31 -40 had a prevalence of 7.4% (9/400) conversely, subjects within the age bracket of 8 – 20years recorded a prevalence of 9.8% (39/400);[P value of 0.407}:P>0.05]. With regards to HBV DNA status, association of HBsAg status of the study participants that were seropositive, showed 22 (70.9%) DNA positive compared to 9 (29.1%) DNA Negative for HBV DNA,[P value of 0.001}:P<0.05].There was no significant association with the identifiable risk factors and the HBV status among the subjects screened. **Conclusion**: This study has been able to establish the prevalence of Hepatitis B virus infection among HIV positive individuals at our study location. This underscores the need for immune boosting measures among the study subjects, while the need for early diagnosis of HBV among HIV positive individuals is stronglyand promptly advocated.

Key words: HBsAg, HBV-DNA, HIV, Patients, Infection,

Disclosure of Interest: J. A. Ndako Employee of: Authors declare that there is no conflict of interest whatsoever.

P111

EVOLUTION OF HEPATITIS B VIRUS (HBV) SEROLOGICAL MARKERS DURING 2014 TO 2022 ON A FRENCH CARIBBEAN ISLAND (MARTINIQUE)

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Abstract Content: The epidemiology of HBV infection has been directly impacted by preventive measures through compulsory vaccination against Hepatitis B included in the vaccination schedule on French territory.

In this context, we retrospectively analyzed the serological markers of HBV carried out at the university hospital of Martinique from March 2014 to September 2022.

A total of 49,516 HBV serologies (HBsAg/HBsAc/HBc IgG Ac) were also analyzed. The sex ratio F/M is 0.98. The distribution by age group is represented by 8.5%, 64.8% and 26.7% of patients aged between 0-20, 21-60 and 61-100 years respectively.

43.4% of the population studied do not present serological markers of HBV with a higher proportion (64.9%) for patients aged between 61-100 years. Conversely, the presence of anti-HBs antibodies indicating effective vaccination is predominant among 0-20 year olds with 60.54%. The overall prevalence of vaccinated population is 44.06%. The evolution over time, however, shows an increase in the rate of vaccinated patients between 2014 (39.82%) and 2022 (47.19%) with a slight acceleration after 2018 linked to the vaccination obligation.

The prevalence of chronic active Hepatitis B in the studied population is estimated at 0.94%. It is higher than the prevalence estimated in 2016 on a population aged between 18 and 75 years in France (0.30%). The most affected age group is that between 21 and 60 years (1.08%) followed by that between 61 and 100 years (0.95%). The prevalence among young people between 0 and 20 years old is very low at 0.07%.

Unsurprisingly, the population with an old Hepatitis B profile corresponds to the age group 61 - 100 years (21.42%) which is associated with an isolated HBc antibody rate of 3.37%. The prevalence of old Hepatitis B decreases with patient age (6.64% among 21-60 year olds and 1.13% among 0-20 year olds respectively).

In conclusion, Hepatitis B virus infection remains an important subject in the prevention of infectious diseases. The increase in the number of vaccinated patients is an important indicator in monitoring the implementation of vaccination recommendations, particularly for the pediatric population.

Disclosure of Interest: None Declared

P112

HEPATITIS D ANTIBODY DETECTION IN LOW VIRAEMIC CHRONIC HEPATITIS B PATIENTS WITH ELEVATED ALANINE AMINOTRANSEFERASE"

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Aim: To detect HDV- antibody (Ab) in low viraemic chronic Hepatitis B patients with persitently elevated alanine aminotranseferase (ALT).

Methods: This cross sectional study was carried out on 100 consecutive adult patients, attending Benha University hospitals with persistently positive HBsAg and elevated ALT serum levels for more than 6 months, after getting ethical approval. Real-time polymerase chain reaction (PCR) testing was done to determine the Hepatitis B viral load. All selected patients had HBV-DNA levels below 2000 IU/ml. All samples were negative for HIV- and HCV- Ab. An anti-HDV test was performed using human HDV- Ab (IgG) kit of CUSABIO Technology LLC, applying the enzyme linked immunosorbent assay (ELISA).

Results: The mean age of the studied patients was 54.04 $\pm$ 15.66 Ys and males represented 62%. The mean HBV DNA was 1014.82 IU/ml (range from 301 to 1987 IU/ml). The mean of ALT was 94.74 U/L (range from 56 to 287); mean of AST was 97.12 with range 31 to 371. All the studied patients showed negative HDV- Ab.

Conclusion: HDV infection seems to be very rare in Egypt.

Keywords: Hepatitis D, Hepatitis D, Low viremia, Aminotransferase

Disclosure of Interest: None Declared

P113

LACK OF HEPATITIS B VACCINATION AMONG HIGH-RISK POPULATIONS: A SINGLE-CENTER STUDY IN AN ADDICTION TREATMENT CENTER

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Background and Aims: Viral Hepatitis infections are a major transmissible infection among drug users. Vaccination against Hepatitis B Virus (HBV) is recommended to reduce the risk of HBV transmission. The aim of our study was to estimate vaccination coverage in this population and to investigate the reasons for non-vaccination.

Method: HBV screening tests are routinely proposed to all patients during their first consultation at the Addiction Care and Prevention Center of the Hospital Nord of Hospices Civils de Lyon. We retrospectively analyzed the results of all screening tests performed between January 2014 and December 2019. In addition, a prospective ancillary study based on anonymous patient questionnaires was performed to determine patient's reasons for non-vaccination.

Results: A total of 307 patients were screened for HBV with 15.4% of new patients screened per year. Of the patients screened, 138 (45.0%) had been vaccinated for HBV, 48 (15.6%) had markers of resolved HBV infection, 5 (1.6%) were positive for HBsAg and 116 (37.8%) were not vaccinated against HBV. Men (41.6%) were less often vaccinated than woman (53.4%). The most vaccinated age group was 30-49 years with 51.24% of people vaccinated. Half of the 136 respondents to the questionnaire did not want to be vaccinated, 47.6% did not feel concerned by vaccination, 28.6% mentioned a lack of information and 21.4% were anxious of side effects.

Conclusion: In this patient population at high risk of HBV transmission, HBV vaccination coverage remains low at around 45%. Information and vaccination strategies are essential to increase coverage in this high-risk population.

Disclosure of Interest: None Declared

P114

ASSESSMENT OF VIRAL AND CLINICAL CHARACTERISTICS OF PATIENTS WITH CHRONIC HEPATITIS B VIRUS INFECTION IN GEORGIA

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Background: Hepatitis B virus infection (HBV) is one of the major healthcare problems in Georgia. To achieve the WHO viral Hepatitis elimination targets, gaps in diagnosis and management of chronic HBV infection need to be addressed. The aim of our study was to collect data on the clinical and viral characteristics of patients with chronic HBV infection, assess the clinical phases of HBV infection and estimate the proportion of patients who may need antiviral treatment.

Methods: All relevant de-identified data about demographic, clinical, and viral characteristics were extracted from patients' medical records, who where recently diagnosed with chronic HBV infection and were at a primary visit in the clinic from December 2018, until december 2020. Descriptive statistical analyses were done for univariate assessment of demographic, virologic, and clinical characteristics.

Results: 96% (124/129) of patients with chronic HBV infection are HBeAg-negative. 84% (145/173) had no or mild fibrosis and 3% (6/162) had advanced liver fibrosis/cirrhosis by transient elastography (liver stiffness >10 kPa). 67 out of 126 (53%) patients were classified as HBeAg positive or negative chronic HBV infection (without Hepatitis); 11 (9%) as chronic Hepatitis B; 48 (38%) had not classified in any of the known HBV phases, while 30 of them (24% out of total) had high viral load and normal ALT. Statistically significant association was seen between high HBV-DNA and HBeAg-positivity (p=.043). High ALT level was also associated with liver fibrosis (p=.015). Significant positive correlation between age and the presence of moderate or advanced liver fibrosis was observed (p=.002).

Conclusion: This is the first study about the clinical and viral characteristics of patients with chronic HBV infection in Georgia. The vast majority were HBeAg negative, only 3% had advanced liver diseases; about half of patients had inactive diseases. However, one out of four patients had a high viral load but normal ALT. By the evaluation of HBV phases, we estimated that 9-36% of patients with chronic HBV mono-infection require antiviral treatment.

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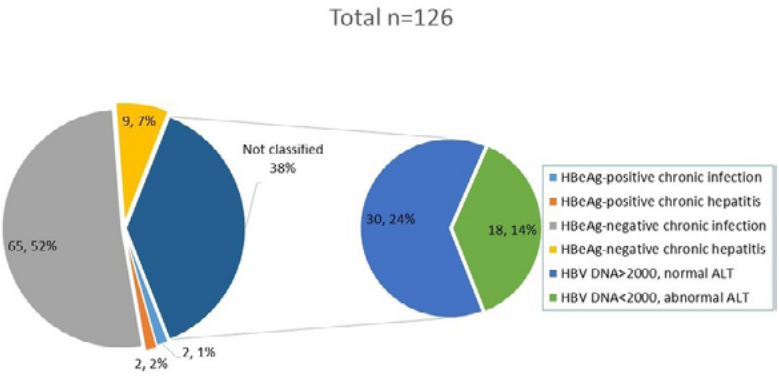

Disclosure of Interest: None Declared

P115

EFFICACY OF VIRTUAL SCREENING & TREATMENT FOR HEPATITIS C OF PATIENTS ENROLLED IN A COMMUNITY BASED OPIOID AGONIST MANAGEMENT PROGRAM

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Abstract Content: Hepatitis C is responsible for more life years lost than any other infectious disease in Canada, and people who use drugs (PWUD) are disproportionately affected because of barriers to accessing care. What started as a pilot project is now a full-time program comprised of; PATHOntario (Prevention, Assessment and Treatment of Hepatitis C in Ontario), TrueNorth Medical which provides Opioid Agonist Therapy (OAT) to individuals living with Substance Use Disorder (SUD), 68 affiliate sites, Care Coordinators, an RN, the Ontario Telehealth Network (OTN) and TEEMAP. TrueNorth has developed TEEMAP which stands for Telemedicine Enhanced Expanded Medical Access Partnership.TEEMAP consists of a group of coordinators who monitor live chats 7 days/week in order to connect patients with a of the clinical team.

Purpose: Our unique approach to the micro-elimination of Hepatitis C is an innovative and integrative framework that utilizes an entirely virtual-based model of care that focuses on meeting patients across Ontario at any of our 100+ OAT sites. Patients can opt to self-test with HCV Point of Care Test (POCT), Dried Blood Spot Test (DBS) as well as discuss treatment options and, check-in regarding treatment progress.

Method: The PATH team retrospectively reviews charts and sorts patients into 2 groups: Those with HCV RNA on file, untreated; and those not tested/due to be retested. Each PATH site has HCV testing kits which include all supplies needed for POCT and DBS testing. When TEEMAP checks in a patient for OAT, they also connect the identified patient to the RN. If patients request or require HCV or DBS testing, they receive a supply envelope and the RN guides the patient step-by-step through the testing process. Positive DBS results are followed up by consultations with the RN or HCV MD. Patients have now been merged into the HCV cascade of care.

Results: This entirely virtual model has ensured that patients do not fall through the cracks and has substantially increased how many patients are engaged in care. Alerts on patient charts have more than tripled the average number of patients screened, and doubled the number on treatment. Several measures allow for patients to connect to the RN in a variety ways - esepcially the underhoused, or those without phones.

Conclusions: Despite the complexity of having patients test themselves, we have had zero errors or returned DBS samples. Patients are empowered by self-testing and are much more easily enrolled into, managed and maintained in the cascade of care thus setting themselves up for HVC treatment success. Our aim is to expand to Northern Ontario and Canada, increase uptake, testing and screening to areas with far less accessibility due to their remote locations.

Disclosure of Interest: None Declared

P116

ASSESSMENT OF HCV SCREENING AND LINKAGE TO CARE MODALITIES WITHIN THE GEORGIA'S NATIONAL HEPATITIS C ELIMINATION PROGRAM AND DESIGNING THE MOST OPTIMAL MODELS FOR REACHING THE ELIMINATION TARGETS

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Background: Once a patient is diagnosed with HCV infection, it is essential to assure the continuum of care. Georgia launched the national Hepatitis C elimination program in April 2015. Within this program almost 80 000 persons initiated treatment. Patient enrollment in treatment has been slowing down, most likely because of deficiencies in HCV testing and linkage to care. Developing the most optimal model for linkage to care is paramount importance for the program.

Methods: We evaluated effectiveness of various modalities in terms of engagement in HCV care including linkage to care and treatment initiation and define the most optimal screening and linkage modalities. HCV screening and care cascades for centralized and decentralized hospital sector screening models, primary healthcare, harm reduction, HCV provider site and integrated HCV/HIV/TB screening models were quantified in the period of March 2018 – September 2022. We defined linkage to care as: 1) confirmatory HCV RNA or core-antigen test after screening HCV antibody test found a positive result; and 2) follow-up appointment for treatment was established with a specialist.

Results: Cohort included 44,625 persons with positive anti-HCV test result. The highest percentage of positive anti-HCV persons tested for viremia was seen in HCV provider site screening model, followed by harm reduction, hospital sector decenteralized, integrated HCV/HIV/TB, hospital sector centralized and primary healthcare screening models (92.6%, 88.7%, 79.9%, 78.5%, 78.0% and 68.1%, respectively). Engagement in HCV treatment was high in HCV provider site, integrated HCV/HIV/TB, harm reduction and primary healthcare screening models (88.3%, 81.9%, 78.8% and 74.5%, respectively).

Rates of HCV viremia testing and engagement in care were significantly higher in HCV provider site screening model compared to hospital sector centralized, hospital sector decentralized, primary healthcare, harm reduction and integrated HCV/HIV/TB screening models (92.6% vs. 78.0%, $p<0.0001$ and 88.3% vs. 53.8%, $p<0.0001$; 92.6% vs.79.9%, $p<0.0001$ and 88.3% vs. 65.3%, $p<0.0001$; 92.6% vs. 68.1%, $p<0.0001$ and 88.3% vs. 74.5%, $p<0.0001$; 92.6% vs. 88.7%, $p<0.0001$ and 88.3% vs. 78.8%, $p<0.0001$; 92.6% vs. 78.5%, $p<0.0001$ and 88.3% vs. 81.9%, $p<0.0001$, respectively).

Conclusion: HCV provider site screening model was most successful in linking persons to care. Best rates for treatment initiation were achieved in primary healthcare and harm reduction HCV screening models. Factors affecting linkage to care and engagement in cascade for each model should be further studied. Barriers to accessing HCV care at primary healthcare and harm reduction centers remain to be eliminated to achieve program targets.

Disclosure of Interest: None Declared

P117

ADDRESSING THE COST BARRIER IN ACCESS FOR VIRAL HEPATITIS C TREATMENTS COMMODITIES THROUGH JOINT STAKEHOLDER COLLABORATIONS

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Background: Despite global advancements in Hepatitis C (HCV) testing and treatment, minimal progress has been recorded in Africa .Access to the Sofosbuvir/Daclatasvir, HCV pan-genotypic curative treatments remain a crucial barrier stemming from the absence of donor financing and patients paying out of pocket. The 1st Global Health Sector Strategy on Viral Hepatitis in 2016 highlights the WHO 2030 elimination goal for viral Hepatitis, Clinton Health Access Initiative (CHAI) supported the Govt of Nigeria to develop the necessary policy framework which was subsequently domesticated in Nasarawa which is estimated to have an HCV seroprevalence of 14%,[2] significantly higher than the national average of 1.1%.[3] With patients paying out-of-pocket, treatment uptake remained low necessitating the Nasarawa State Govt to commit to a 5-year HCV Elimination plan in 2020.

Purpose : This abstract aims to describe the outcomes of the collaborative strategic market-shaping approaches employed by the State Government, CHAI, World Hepatitis Alliance (WHA) – civil society, and Pharmaceuticals – private sector to reduce the Direct Acting Antivirals and accelerate the uptake of services.

Approach/Methods:A systematic stepwise approach was employed. In phase 1, retrospective data of adult outpatient facility visits from 2016 to 2017 across 13 Secondary Health facilities were collected and using the state seropositivity and vireamic rates, calculated the yearly forecast of patient treatment numbers. CHAI with the SMOH initiated routine pooled procurement discussions with Pharmaceuticals to secure pricing decline in 2018, 2019, and 2020. The 2nd phase stemmed from the Government's Elimination commitments which saw an initial investment of $13,000 procure treatments for 70 patients. With a focus on the PLHIV cohort, the commodity requirement was determined from the treatment forecast. CHAI leveraged the existing relationships between the civil society (WHA) and Viatris Pharmaceuticals in collaboration with state actors to secure additional pricing reductions.

Results: Outcomes of the phase 1 approach led to 20%, 36%, and 20% decline in pricing for a 3-month treatment in 2018, 2019, and 2020 respectively, and increased treatment numbers from 189(2017) to 443(2020).Outcomes of strategic engagement of civil society led engagements led to a drastic 67% reduction in pricing ($180 to $60 /3months) with allocation procuring additional 76 treatments implying cost savings of 52%.

Conclusion: Government commitment and the engagement of the relevant stakeholders especially the civil society, who are the patient's advocate, is crucial to eliminating barriers to access of testing and treatment services, hence achieving cost-effectiveness.

Disclosure of Interest: None Declared

P118

CAN ANTI HCV SCREENING BE USED TO CATCH NEW PATIENTS TO BE TREATED?

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Introduction: It is estimated that 71 million people worldwide are infected with HCV. 14 million person (20%) can be diagnosed and 7.4% of them (1.1 million) have access to treatment. Therefore, it is important to know that HCV is a treatable disease and to screen larger populations. In our study, we aimed to identify the patients who were found to be positive for anti- HCV and HCV RNA in the tests requested in our hospital.

Material and Methods: Anti-HCV results in Kocaeli University Hospital between 31.07.2016-31.07.2019 and 1.01.2022- 31.10.22 in a total of 4 years were reviewed retrospectively using the hospital data system. The screened patient groups were patients who were routinely screened before surgery or dialysis, patients screened before immunosuppressant / chemotherapeutic drug therapy, and patients in the risk group for HCV transmission. The awareness of those with positive results was questioned and those who needed treatment were called to our polyclinic.

Results : Anti-HCV testing was applied to 43,133 patients. Anti-HCV test was positive in 534 patients (1.2%), 314 of them were HCV RNA negative, 53 were HCV RNA positive, and HCV RNA was not tested in 167 patients. Of the patients with positive HCV RNA results, 26 received treatment and their current HCV RNA values were negative. 20 patients who did not receive treatment were called for treatment. 167 patients whose HCV RNA was not tested were called and warned to undergo further examination. 31% of the patients were not referred for further examination. Even if HCV RNA was positive, 37.7% of the patients were not referred for treatment.

Discussion: Chronic HCV is usually asymptomatic and many people do not know they have an infection. In our study, anti-HCV positivity was found in 1.2% of patients, similar to the prevalence of HCV throughout the country. It is important to raise awareness of patients and physicians about treatment, since nearly 100% permanent viral response can be achieved with direct-acting antivirals. We think it's important to expand the groups to be screened for complete eradication, which is the target of World Health Organization.

Disclosure of Interest: None Declared

P119

EPIDEMIOLOGY OF CHRONIC VIRAL HEPATITIS B/D AND C IN THE VULNERABLE POPULATION IN THE NORTH-EAST AND SOUTH-EAST REGIONS OF ROMANIA – INTERMEDIATE STAGE RESULTS IN THE LIVE(RO)2 - EAST SCREENING

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Introduction: In order to meet the requirements of the WHO, namely - the eradication of viral Hepatitis by 2030, UMF "Gr. T. Popa" from Iasi together the Hospital "St. Spiridon" from Iasi, carries out since 2020 the project "LIVE(RO) 2 - Integrated regional program for prevention, early detection (*screening*), diagnosis and targeting treatment of patients with chronic liver disease secondary to viral infections with liver viruses B/D and C in the North-East and South-East regions". This study aimed to assess the epidemiological characteristics of the vulnerable population in the eastern part of the country diagnosed with chronic B/D and C viral infection.

Materials and methods: Between July 2021 and September 2022, we performed a prospective screening of chronic viral Hepatitis B/D and C in vulnerable people, within the national program LIVE(RO) 2 - EST. Rapid diagnostic tests were used to detect HBs antigen (HBsAg) and anti-HCV antibodies (HCVA): HBV (Wama Immuno-Rapid HBV®) and HCV (Wama Immuno-Rapid HCV®). Rapid test-positive patients were tested for HBV DNA and HCV RNA and those eligible under the national protocol were treated with antivirals.

Results: The study included 55593 individuals tested rapidly, of which 2160 (3.8%) patients were tested positive (1120 women, 1040 men, mean age 55.86 $\pm$ 6.023 years, predominantly rural background - 76.19%). Of these, 1077 (49.8%) were HBsAg positive, 918 (42.5%) with HCV positive needle, 37 (1.7%) HBV/HCV coinfection and 128 (5.9%) HBV/VHD coinfection. HBV-DNA was performed in 724 (67.3%) individuals, of which 452 (62.5%) subjects > 2,000 children/ml. Also, 518 (54.3%) patients with HCV-positive Ac had detectable HCV RNA, of which 375 (72.3%) received antiviral treatment. Depending on the ethnicity, the prevalence of viral infection was 4.29% in Roma people and 3.23% in Romanian people. Among the vulnerable groups determined by work, inactive people (27.7%), uninsured people (11.2%), unskilled people (1.87%), unemployed people (0.6%) and people working in agriculture (0.59%) were predominantly tested. Among the special vulnerable groups, people with disabilities (3.99%), people addicted to alcohol (2.43%) and people with a minimum income (1.21%) were predominantly tested.

Conclusions: The high prevalence of B/D and C viral infection in the vulnerable population tested in the North-East and South-East Region of Romania compared to the rest of the population, indicates the significant viral spread of the infection in these people, a condition that requires further testing and the need for policies public health in vulnerable groups to promote access to existing health services and early initiation of optimal antiviral treatment.

Disclosure of Interest: None Declared

P120

TREATMENT AS PREVENTION FOR HEPATITIS C VIRUS IN THE MIDDLE EAST AND NORTH AFRICA: A MODELING STUDY

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Background: Direct-acting antivirals opened an opportunity for eliminating Hepatitis C virus (HCV) infection in the Middle East and North Africa (MENA), the region most affected by HCV. Impact of HCV treatment as prevention (HCV-TasP) was investigated in 19 MENA countries: Afghanistan, Algeria, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates, and Yemen.

Methods: An age-structured mathematical model was used to assess program impact using epidemiologic and programming measures. The model was fitted to a database of systematically gathered HCV antibody prevalence data. Two scenarios were investigated for the treatment roll-out to achieve i) 80% reduction in HCV incidence by 2030 (World Health Organization global target) and ii) HCV elimination by 2030 (≤1 infection per 100,000 person-year).

Results: In the target 80% incidence reduction scenario, number of treatments administrated between 2023 and 2030 ranged from 1,524 in Lebanon to 132,359 in Sudan. Treatment coverage ranged between 38.4% and 81.6% by 2030. Prevalence of chronic infection ranged between 0.0% and 0.3% by 2030, and incidence rate, per 100,000 person-year, ranged between 0.7 and 16.1 by 2030. Program attributed reduction in incidence rate ranged between 45.4% and 86.8%, and number of averted infections ranged between 197 and 53,037. Proportion of infections averted was lowest in Saudi Arabia and highest in Somalia. Number of treatments needed to prevent one new infection ranged from 1.9 in Oman to 20.3 in Tunisia.

In the elimination scenario, number of treatments administrated between 2023 and 2030 ranged from 1,524 in Lebanon to 173,792 in Sudan. Treatment coverage ranged between 41.6% and 95.4% by 2030. Prevalence of chronic infection ranged between 0.0% and 0.1% by 2030, and incidence rate reached less than 1 per 100,000 person-year, per definition of this scenario.

Program attributed reduction in incidence rate ranged between 47.8% and 96.8%, and number of averted infections ranged between 197 and 79,509. Proportion of infections averted was lowest in Lebanon and highest in United Arab Emirates. Number of treatments needed to prevent one new infection ranged from 1.5 in Oman to 19.6 in Palestine.

Conclusion: HCV-TasP is a potent and effective prevention approach to control MENA's HCV epidemic and achieve elimination by 2030.

Disclosure of Interest: None Declared

P121

CASCADE OF CARE FOR HCV AND PROFILE OF PATIENTS WITH A POSITIVE VIRAL LOAD IN THE SECOND-LARGEST FRENCH PSYCHIATRIC HOSPITAL [2019-2021]: A CASE-CONTROL STUDY

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Introduction: eliminating Hepatitis C virus (HCV) will require to screen and treat the most affected populations, including people who inject drug, people in prison, and men who have sex with men. Moreover, people with severe mental disorders (PSMDs) constitute a less prevalent but larger population of individuals that may be of high risk of chronic HCV infection. In PSMDs, the prevalence of HCV has been found to reach approximately ten times that found in the general population, that is, approximately 5% in European. However, few studies have explored the profile of patient with active HCV among PSMDs.

Methods: the Vinatier hospital is the second largest psychiatric hospital in France, with more than 5,000 stays every year. The study explored the retrospective healthcare data for the years 2019, 2020, and 2021. All prescriptions of HCV serologies and their results, as well as all prescriptions of viral load counts and their results, were identified using global data from the electronic medical records. Moreover, the following parameters were extracted: sex (male, female), age (in years), previous history of illicit drug use except cannabis (yes or no), previous history of incarceration (yes or no), and the main psychiatric code according to the ICD-10. Among individuals with a positive serology and a documented viral load count, a retrospective bivariable case-control comparison was conducted, with the result of viral load count (i.e., positive vs. negative) as the dependent variable, and other individual features as the independent variables.

Results: the global cascade of care for HCV within the hospital is displayed in **Figure** 1. In total, 2,540 (19.1%) of all inpatients received at least one HCV serology, which was found positive among 55 (2.16%) of them. Among these individuals, 48 (87.3%) were prescribed a viral load count, which was found positive in 15 (31.3%) of them. Thus, a positive viral load was found in 0.6% of all inpatients who were initially prescribed an HCV serology. Overall, a previous history of illicit drug use ($p<0.01$) and a previous history of incarceration ($p<0.05$) were negatively associated with having a positive viral load, while a positive statistical trend for association ($p=0.12$) was found with a diagnosis of psychotic disorder.

Conclusion: PWMDs remain a substantial reservoir of chronic HCV infection. Patients in which an active infection was found seemed to differ from the most identified at-risk populations (i.e., people who use drugs, or people that have been incarcerated), and were more people with severe and chronic mental disorders.

Disclosure of Interest: None Declared

P122

CANTABRIA ON THE WAY TO HCV ELIMINATION. DIFFERENTIAL PREVALENCE OF HEPATITIS C IN CANTABRIA: @COHORTECANTABRIA VS ETHON COHORT

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Introduction: The overall prevalence of anti-HCV in the ETOHN cohort (EC; general population of Cantabria) in 2016 was 1.1%, with a prevalence of viremia of 0.34%. It is likely that the universal treatment of patients with HCV Hepatitis in recent years has brought us closer to its elimination in our region. Aims: 1) To determine the prevalence of seropositivity and chronic HCV infection and to analyze the associated factors in the Cantabria Cohort (CC, *@CohorteCantabria*) in the year 2022. 2) To determine the incidence of new cases of Hepatitis C and analyze the associated factors. 3) To compare these results with those obtained in the EC (year 2016).

Material and Methods: 1) CC: Cross-sectional study in the general population participating in the CC project, which includes volunteers and random sampling of the entire population of Cantabria between 40 and 70 years old. In the blood sample at baseline, HCV antibody (anti-HCV) detection was carried out and, in positive cases, automatic viraemia quantification was performed. The volunteers included in this cohort between March 2021 and March 2022 were analyzed. 2) EC: Population-based cross-sectional epidemiological study, carried out during the years 2015-2016, exclusively including the population of the Santander node. 3) Analysis of the set of all viremic subjects in Cantabria in the same period.

Results: CC: 11,094 subjects were included (4,355 from 40-49 years; 3,823 from 50-59 years and 2,916 from 60-69 years), 38% male. Anti-HCV was detected in 102 cases (0.9% prevalence). Excluding 10 cases pending definitive study, positive HCV-RNA was detected only in 7 cases (0.06% prevalence). The remaining anti-HCV positive subjects are divided into 18 cases with spontaneous clearance and 77 cases with SVR. The total incidence of viremic patients of the entire population of Cantabria (585,000 subjects) in this period was calculated (112 cases, 19 cases/100,000 inhabitants/year), of which 65 (58%) were previously known, accordingly the incidence rate of new cases was 10 cases/100,000 inhabitants/year. When we compare these results with those obtained in the EC (previously published, doi: 10.1111/jvh.13238) we observed a lower prevalence (1.1% vs 0.9%, $p<0.001$) and a great decrease in the viraemia rate among seropositives in CC (34% vs 6%, $p<0.0001$). The CC showed 11.8% (1310) of volunteers with elevated transaminases levels, compared to 17.8% of the population analyzed in the EC.

Conclusions: The current prevalence (2022) of anti-HCV was slightly lower than that reported previously (2016) in the same population; In addition, and as the most outstanding fact of the study, the prevalence of viraemia was less than 10% of the seropositives. This fact, associated with an incidence of 10 new-cases/100,000 inhab./year, places Cantabria close to the goals set by the WHO for the definition of HCV elimination in a certain geographical region.

Disclosure of Interest: None Declared

P123

ANALYZING IMMUNOGENICITY OF HEPATITIS B VACCINE DELIVERED BY MICRONEEDLE PATCH IN MICE AND RHESUS MACAQUES

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Background: A timely Hepatitis B birth dose vaccine (HepB-BD), administered within 24 hours of birth, is essential to prevent mother-to-child transmission and can be a critical tool to achieve the HBV elimination goals. However, timely HepB-BD coverage in Africa was only 17% in 2021.

Purpose: Vaccination against Hepatitis B using a dissolving microneedle patch (dMNP) could increase access and coverage with HepB-BD by reducing refrigerated storage and expertise needed for vaccine administration and providing safer disposal of biohazardous sharps waste. To achieve these goals, we developed a dMNP to administer Hepatitis B surface antigen (HBsAg) adjuvant-free monovalent vaccine (AFV).

Methods: dMNPs were prepared at doses of 5 µg, 10 µg, and 20 µg, and compared its immunogenicity to vaccination with 10 µg of standard monovalent HBsAg delivered by intramuscular (IM) injection either in an AFV or as aluminum-adjuvanted vaccine (AAV). Vaccination was performed on a three-dose schedule of 0, 3, and 9 weeks in mice and 0, 4, and 24 weeks in rhesus macaques. Immunogenicity of HBsAg administered by dMNP was analyzed to determine the cellular and humoral immune responses in vaccinated mice (n=24) and rhesus macaques (n=20). In addition, the host gene expression profiles of vaccine reactogenicity in each vaccination group (dMNP and IM injection) were identified.

Results: dMNP vaccination induced protective anti-HBs antibody responses (anti-HBs) ($\geq$ 10 mIU/ml) in mice and rhesus macaques at all three HBsAg doses. dMNP HBsAg delivery generated 1.5 to 1.9-fold higher levels of anti-HBs responses than the 10 µg IM AFV in mice. In rhesus macaques (n=4/group), two animals with 5 µg dMNP, all four animals with 10 µg dMNP, two animals with 20 µg dMNP, one animal with IM AFV, and all four animals with IM AAV had protective levels of anti-HBs responses. HBsAg-specific CD4+ and CD8+ T cell responses were detected in all vaccine groups. Differential gene expression profiles related to each vaccine delivery group found that tissue stress, T cell receptor signaling, and NFkB signaling pathways were activated in all groups. These results indicate that HBsAg delivered by dMNP, IM AFV, and IM AAV have similar signaling pathways to induce innate and adaptive immune responses. In addition, dMNP was stable at room temperature (20°C- 25°C) for 6 months, maintaining 67% HBsAg potency.

Conclusion: This study provides evidence that dMNP delivery of 10 µg AFV induced protective levels of antibody responses in mice and rhesus macaques. The dMNPs developed in this study could be used to improve HepB-BD vaccination coverage levels in resource-limited countries to advance Hepatitis B elimination.

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P124

INFORMATION SYSTEM FOR THE MEDICATION CONTROL OF VIRAL HEPATITIS B AND C: IMPLEMENTATION ANALYSIS IN BRAZIL

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Introduction: Brazil, as a signatory to the world health organization (who) proposal to eliminate viral Hepatitis as a public health issue by 2030, is developing strategies to expand diagnosis and treatment of viral Hepatitis (vh) by the unified health system (sus). Among these (strategies), one stands out: the formulation of the new medication control and logistics system (siclom) for viral Hepatitis, in order to register and analyze patients who have received treatment for HBV and hcv. Thus, this study aims at describing the process of development and implementation of the siclom in all health services responsible for dispensing drugs against viral Hepatitis in brazil.

Methods: Descriptive study of the development process and steps to implement the new information system in the public health services responsible for dispensing the medicines.

Results: Gradually, the development of the siclom started in 2019, being completed the implementation in april 2022, across the country, through an agreement between different levels of management, considering the components: system, training and pharmaceutical network. It encompasses information based on the brazilian guidelines, with proper critiques addressed for optimizing and qualifying the pharmaceutical care provided to patients, monitoring the stock of medicines in the services and providing national data to analyze the proposed targets for the viral Hepatitis elimination. Currently, the siclom is used by circa 1,340 services throughout the country and, like the hcv, commenced with 49 dispensations registered in 2020 up to 7,052 in 2022, recording the clinical data of all patients, defining the appropriate treatment regimen for each case.

Conclusion: Siclom contributed with the correct application of guidelines, with the registration of information in a single system, and the follow-up of the patient undergoing treatment. The implementation was possible due to the commitment and accession of the new system, by the managers of health services of states and municipalities.

Keywords: medication, viral Hepatitis, treatment, information system

Disclosure of Interest: None Declared

P125

#HEPCITYFREE/SPANISH ALLIANCE FOR VIRAL HEPATITIS ELIMINATION: THE COMMITMENT OF SPANISH CITIES FOR HEPATITIS C ELIMINATION

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Background & aims. #HepCityFree is an action launched by the Spanish Alliance for Viral Hepatitis Elimination (AEHVE) to promote the commitment of cities on the elimination of Hepatitis C. The goal of the study is to evaluate the response of the Spanish cities to #HepCityFree since its launch in 2020.

Methods: Compilation of the processes of adherence to #HepCityFree initiated or completed by Spanish cities and the population they cover. Both the constitution and activities developed by the local committees (LC), as well as other awareness results obtained through #HepCityFree were analysed.

Results: Until November 28, 2022, there are 17 cities adhered to #HepCityFree by agreement of the Government bodies of their Town Halls (Plenary or Governing Boards), which add up to a population of about 7.5 million people. The cities are: Sevilla, Valencia, Santander, Gijón, Granada, Alcoy, Vigo, Madrid, Santiago de Compostela, Ferrol, Pontevedra, León, Córdoba, Salamanca, Écija, Málaga and A Coruña. Moreover, there are another 10 cities completing the process of accession, that add up to another 1.7 million people and 21 LC coordinators (hepatologists and microbiologists) who participate in meetings with council governments for accession and/or starting actions. #HepCityFree has got the support of the Public Health Commission of the Spanish Federation of Municipalities and Provinces (FEMP), which will promote it among their cities from 2023. AEHVE is also involved in the elimination plans of two regional Spanish governments, published in 2022, and incorporated their strategic lines for local entities in accordance with the objectives of #HepCityFree, which has also received the recognition from the Health Commission of the Spanish Parlament. Seven cities (Sevilla, Madrid, Écija, Santander, Ferrol, Vigo and Alcoy) have already designed and/or started their respective roadmaps that include, among others, micro-elimination actions in centers attending vulnerable persons under local jurisdiction (immigrants, homeless, IDUs), review of medical records, telemedicine, training and awareness. All of these have allowed the screening of more than 3,800 patients.

Conclusions: The commitment of cities with the elimination of Hepatitis C is feasible and viable despite the fact that health service responsabilities depend on the Regional Governments rather than councils. In addition, there is a high predisposition of the councils with this AEHVE action, as demonstrated by the high number of cities involved to #HepCityFree. Specific roadmaps are currently being defined for each council, through direct actions in local centers that attend vulnerable groups.

Disclosure of Interest: None Declared

P126

HOW CAN WE ACHIEVE WHO HEPATITIS C ELIMINATION TARGETS?

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Background: In 2016, WHO's *Global health sector strategy on viral Hepatitis* outlined targeted an 80% reduction in chronic Hepatitis C infections by 2030 from 2015 levels [1]. In 2015, there were 71.1 million people with Hepatitis C [2]. Currently, there are 58 million, representing a reduction of 18% [3]. Only 11 countries are on track to achieve elimination by 2030 [4]. Generic Hepatitis C drugs are available for very low cost in India: $37 for SOF/DAC and $84 for SOF/VEL.

Purpose: We considered the increases in global testing and treatment that would be required to achieve WHO targets by 2030.

Methods: We analysed data on the global Hepatitis C epidemic in 110 countries from the Polaris database [5]. Modelling the epidemic size between 2022 and 2030, we assumed that rates of new infections, deaths and the number of people treated annually could vary by up to 10%.

Results: In 2020, there were 1.5 million new infections, 267,000 HCV-related deaths, 870,000 non-HCV related deaths and 750,000 people treated. If treatment coverage remained at this level, there would be 54.8 million living with Hepatitis C in 2030 – a reduction of 23% from 2015. Globally, we need to treat 5.7 million people annually to achieve an 80% reduction in chronic cases from 2015 levels by 2030 (See Figure 1).

Conclusions: To achieve WHO Hepatitis C elimination targets by 2030, 5.7 million people need to be treated each year from now onwards. In 2020, only 750,000 were treated, and for every person treated and cured, two new people were infected. A co-ordinated test-and-treat strategy, with drugs sold at close to cost price, is required to achieve elimination. There is a risk of "diagnostic burnout", where not enough people are diagnosed to keep up with treatment rates. Investment in novel testing strategies such as same-day test-and-treat models is critical [6].

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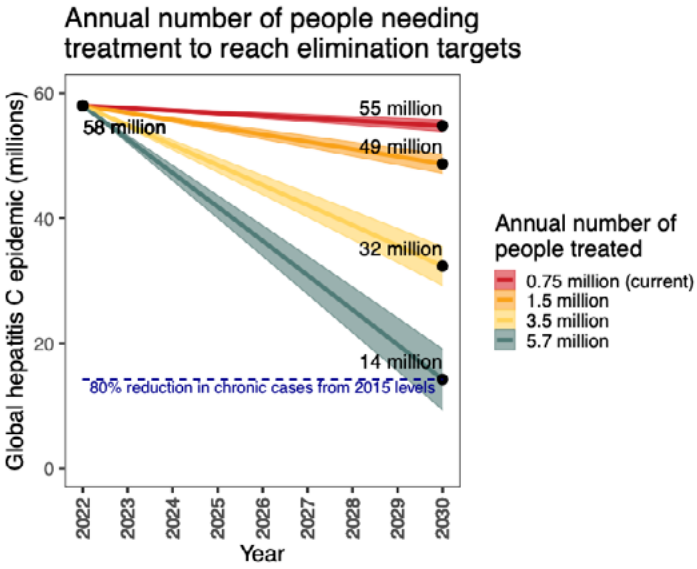
Image/Table:



Disclosure of Interest: None Declared

P127

EMBEDDING VIRAL HEPATITIS MANAGEMENT INTO PRIMARY HEALTH CARE: READINESS ASSESSMENT OF VIET NAM AND THE PHILIPPINES

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Abstract Content: Chronic viral Hepatitis remains a major public health threat in the Western Pacific, including in Viet Nam and the Philippines. To accelerate progress toward meeting the 2030 elimination goals, the World Health Organization (WHO) encourages countries to adopt a 'people-centered' health sector responses to Hepatitis, grounded in Primary Health Care (PHC). A review of the academic and grey literature was conducted to describe the health system context and response to Hepatitis B and C in Viet Nam and the Philippines to date. The responses were compared and analyzed against the levers of the Operational Framework for PHC to identify challenges and opportunities. The findings suggest that Viet Nam is in a stronger position at a strategic level, but both countries share many operational challenges and opportunities for learning and improvement. Our application of the Operational Framework for PHC could be used to nationally benchmark progress toward the 2030 goals, and feasibly applied to other disease areas to support government policies to achieve Universal Health Coverage (UHC).

Disclosure of Interest: None Declared

P128

HBV AND HCV PREVALENCE AND INCIDENCE AMONG HIV-POSITIVE INDIVIDUALS IN GERMANY, 1996-2019 – KEEPING TRACK OF THE WHO ELIMINATION GOALS FOR VIRAL HEPATITIS

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Background: Individuals co-infected with viral Hepatitis and HIV face a double burden due to accelerated progression of liver disease and AIDS. In order to assess the magnitude of Hepatitis B and C (HBV, HCV) co-infections and potential changes over time we analyzed the prevalence and incidence of HBV and HCV infection among HIV-positive individuals for the years 1996-2019. This will help target prevention strategies and support efforts to reach the WHO goals to eliminate HIV/AIDS, viral Hepatitis and sexually transmitted infections as a public health threat by 2030.

Methods: This analysis includes blood sample and questionnaire results from HIV-positive individuals participating in the nationwide, multicenter observational, prospective HIV-1 seroconverter cohort study. HBV and HCV prevalence and incidence as well as HBV vaccination coverage were determined for the years 1996-2019.

Results: About 87% (3,018/3,477) of the study participants were reported having MSM-contacts as their likely risk of HIV transmission. Acute/chronic and resolved HBV infections decreased from 4.1% and 45% in 1996-1999 to 1.3% and 16% in 2019, respectively. Simultaneously, the proportion of participants being HBV vaccinated (anti-HBs positive) continuously increased from 25% in 1996-1999 to 69% in 2019. However, 38% had received their first HBV vaccination after their HIV-seroconversion. Prevalence of acute/chronic and resolved HCV infections increased from 4.4% and 1.0% in 2004 to 7.3% and 4.2% in 2014, respectively. Since then prevalence of acute/chronic HCV infections decreased to 3.3% in 2019 while resolved infections increased to 10% in 2019. The incidence rate for HBV decreased from 6.8 per 100 person years in 2004-2007 to 0.45 per 100 person years in 2015. HCV incidence did not significantly change over the years, despite the highest rate of 2.2 per 100 person years in 2010 and the lowest rate of 0.4 per 100 person years in 2017.

Conclusion: The increasing HBV vaccination coverage likely prevented numerous infections and contributed to the declining HBV prevalence and incidence over time. While the HBV prevalence decreased almost to the prevalence level reported for the general population in Germany (< 1% HBsAg prevalence), the incidence rate still exceeds the 2030 WHO target for HBV incidence of 0.002 per 100 person years. The decreased prevalence of acute/chronic HCV infection is likely the result of directly-acting antiviral agents for HCV treatment that were widely introduced in 2014. Nevertheless, prevalence and incidence of HCV among these HIV-1-positive study participants remained high compared to the general population. These results emphasize the need for continued HBV and HCV prevention efforts through HBV vaccination and regular risk-adapted screening among HIV-positive individuals and persons at risk for HBV and HCV infection in order to achieve the WHO elimination goals by 2030.

Disclosure of Interest: None Declared

P129

IMMUNOLOGICAL AND EPIDEMIOLOGICAL EFFECTIVENESS OF SINGLE-DOSE VACCINATION AGAINST HEPATITIS A IN ENDEMIC REGION (TYVA REPUBLIC, RUSSIAN FEDERATION) NINE YEARS FOLLOWING ITS IMPLEMENTATION

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Background: Since August 2012, universal single-dose vaccination in children aged at least three years has been implemented in the Republic of Tuva. Following the introduction of vaccination, Hepatitis A incidence rapidly decline in the region. Since 2006, no Hepatitis A cases are registered in Tuva.

Purpose: To assess long-term immunogenicity and epidemiological effectiveness of single-dose vaccination against Hepatitis A nine years after its implementation.

Methods: Serum anti-HAV antibodies were quantified in 504 healthy children aged 10 to 17 years who were vaccinated against Hepatitis A by single-dose schedule. Samples were collected in 2020, nine years after vaccination. Total anti-HAV antibodies were measured using quantitative immunoassay Elecsys® Anti-HAV (Roche, Mannheim, Germany). To monitor HAV circulation, total 187 sewage samples and samples from different water bodies across Tuva Republic were collected in 2021-2022, concentrated using commercially available Virosorb-M reagent kit (Bioservice Biotechnology Co Ltd., Russia) and tested for HAV RNA using RT-PCR with primers to VP1/2A junction region. Identified HAV sequences were subjected to phylogenetic analysis using the maximum likelihood (ML) method in the MEGA 7.0.18.

Results: Protective anti-HAV antibody concentrations (≥20 mIU/ml) were detected in 99.4% (95% CI: 98.2-99.9% [501/504]) of children tested nine years after single-dose immunization. Among 501 seropositive samples, 440 samples contained anti-HAV antibodies in concentrations in the range 20 to 6000 mIU/ml (minimum – 30 mIU/m, maximum – 1632 mIU/ml). Meanwhile, 12.2% (61/501) of reactive samples contained anti-HAV antibodies in concentration above 6000 mIU/ml, indicating the possible vaccination after the infection or vice versa, the boosted antibody response following the exposure. HAV RNA was detected in two out of 187 sewage and water samples: in water from the lake near the recreational area in 2021, and in sewage sample from Tuva capital, Kyzyl city, in 2022. Phylogenetic analysis indicated that HAV sequences detected in environment samples in 2021-2022 are belong to a local epidemic strain that has been prevalent in Tuva in 2008, prior the start of vaccination, suggesting the ongoing HAV circulation in the region despite the absence of reported clinical cases.

Conclusion: Protective anti-HAV antibody concentrations persist for at least nine years following single-dose vaccination. The ongoing HAV circulation suggest the presence of a sufficient proportion of susceptible individuals and indicate the need to maintain a high level of herd immunity to preserve the sustainability of the vaccination effect.

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Disclosure of Interest: None Declared

P130

PATHOLOGIES DISCOVERED INCIDENTALLY IN PATIENTS WITH CHRONIC VIRAL INFECTION B / D AND C DIAGNOSED IN THE SCREENING PROGRAM LIVE (RO)2 – EAST

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Introduction: The overall burden of B / D and C viral Hepatitis remains substantial, despite the major advances in the prevention and treatment of patients in recent years, due to comorbidities and complications associated with liver disease. In this context, the national screening program LIVE (RO) 2 aims to further assess all patients identified as positive for one of the Hepatitis B / D / C viruses.

Objectives: The study aimed to identify fortuitous pathologies discovered in patients with chronic viral B / D / C infection diagnosed in the LIVE (RO) screening program 2.

Materials and methods: We conducted a prospective study that included people from vulnerable groups in different areas of North-Eastern Romania, between July 2021 - September 2022, during the national screening program LIVE (RO) 2-EAST. We also investigated the presence of newly discovered conditions in patients who tested positive and directed to the Institute of Gastroenterology and Hepatology in Iasi for the staging of liver disease and the establishment of antiviral treatment.

Results: The study group included 1176 patients, of which 422 men (35.8%) and 754 women (64.1%), aged between 35 and 83 years, with a mean age of 56.32 years. The predominant source of origin was rural (73.1%). Of the patients with positive RDTs, 635 (53.9%) patients were detected with HBsAg, 521 (44.3%) patients with anti-HCV antibodies, and 20 (1.7%) patients with anti-HVD antibodies. Of these, 215 patients (18.2%) were diagnosed with a new pathology associated with B / D / C viral infection. The most common pathologies discovered incidentally were liver cirrhosis (94, 43.7%), liver cysts (35, 16.2%), liver hemangiomas (29, 13.4%), gallstones (24, 11.1%), type II diabetes mellitus (T2DM) (15, 6.9%), uterine fibroids (9, 4.1%), hepatocellular carcinoma (7, 3.2%), choledochal lithiasis (2, 0.9%). In addition, the presence of fortuitous pathologies was higher among patients with HBV infection than in those with HCV infection (65.3% vs. 42.1%, p = 0.012). Among the risk factors associated with hepatocellular carcinoma (HCC) are chronic alcohol consumption (43%, compared to 19% in the group of patients without HCC), and the association of T2DM in 3 patients (31%, compared to 10% in the group of patients with HCC).

Conclusions: Patients with chronic B / D / C viral infection had a high prevalence of incidentally detected comorbidities, which necessitates the need for public health policies in vulnerable groups to promote access to existing health services to reduce the future burden of chronic diseases but also secondary complications of chronic liver disease.

Disclosure of Interest: None Declared

P131

PREPARING FOR THE FINAL PHASE OF ELIMINATION: A MODELLING AND IMPLEMENTATION TRIAL OF TEST-AND-TREAT APPROACH TO MICRO-ELIMINATE HEPATITIS C IN CAIRNS

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Background: Cairns, a regional city in Far North Queensland, Australia, with a population of ~150,000, was one of the first locations to lead a Hepatitis C micro-elimination response in Australia. Between 2016-2020, >1,368 people received treatment and HCV RNA prevalence in a community sample of people who inject drugs declined from 26% to 4%. However, in 2019 an outbreak in the local prison seeded a resurgence of new infections in the community, particularly among Aboriginal and Torres Strait Islander populations.

Purpose: As Cairns gets closer to micro-elimination there is increased risk of ongoing outbreaks, requiring a continued effort to case-find new infections in a timely manner. We utilised local health service, surveillance, treatment data and modelling to help identify priority interventions to ensure the successful elimination of HCV at a local geographical area.

Methods: The 'Final Phase Of Elimination' program includes a same-day test & treat trial, which delivers rapid point-of-care (POC) RNA testing (GeneXpert®) and simplified same-day dispensing of treatment to reduce time to cure using a nurse-led approach, incentives, and peer-support.

Results: During the 5 months to December 2022, 94 participants completed POC testing. Median age was 43 years, majority male (54%), unemployed (78%), 13% were experiencing homelessness. Over a quarter were Aboriginal (27%), Torres Strait Islander (4%) or Aboriginal and Torres Strait Islander (8%). Majority had injected drugs in the past month (91%), mostly methamphetamine (77%), and had a history of incarceration (52%). Of the 95 tested, 8 were RNA positive (8.4%) and 100% received treatment (median time to script was 7 days, range 0-45 days). Incentives were used to engage 95% of participants, peer workers were involved in recruiting 37% of participants and 63% were new clients.

Conclusions: For micro-elimination programs in Cairns and other regions, in Australia and elsewhere, ensuring momentum is maintained is critical for achieving the final phase of elimination. We are finding success in delivering a package of interventions involving POC testing, incentives, peer support and nurse-led models.

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P132

JOINING FORCES TO ADVOCATE FOR THE RIGHT TO PROVIDE EASY ACCESS, COMMUNITY-BASED SCREENING IN QUEBEC, CANADA

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Abstract Content: In Canada, an estimated 44% people living with HCV are not aware of their status. In 2016, Canada signed on to the World Health Organization's (WHO) Global Hepatitis Strategy aiming to achieve Hepatitis elimination by 2030. Considering that public health is a shared responsibility between the provincial and federal governments, access to HCV screening is uneven in Canada. In Quebec, HCV testing is an act reserved to doctors and nurses even if community-based screening has been proven to be efficient and safe many times and in multiple contexts. This creates barriers limiting the diversification of the HCV screening offer. This includes at point-of-care services which can be accessed by more people, especially those who are more isolated.

To reach WHO strategy's targets, an increased outreach is necessary. Access to STBBI screening in Québec, including HCV, was inadequate before COVID pandemic; now it is even lower. As the WHO' new strategy calls for decentralisation and simplification of the services delivery, community organizations request Quebec government the right to offer HCV antibodies quick tests.

The Communities most at-risk of contracting HCV in Canada are people who inject and use drugs, immigrants and newcomers from countries where HCV is endemic, Indigenous people, people with experience in the prison system, gay, bisexual, and other men who have sex with men, and people born between 1945-1975. A coalition of 31 community organisations based in Quebec who work with these communities have collaborated to build an argumentative and documented plea to request the right for community workers to offer HCV rapid tests. Based on the coalition's knowledge of the realities faced by key populations reality and the limitations that they face within healthcare system (delays, understaffed teams, stigmatisation and discrimination), the coalition argues that being able to offer point-of-care HCV rapid testing would greatly increase access to treatment and the share of people living with HCV who know their status. Organizations already have a strong trust-based relationship with their participants. They also have experience providing linkage to care and support to people with a Hepatitis C diagnosis and have developed connections with healthcare professionals experienced in HCV treatment and the stigmatization faced by key populations.

With the plea being submitted to Quebec's government, organizations will be waiting for answers and the possibility to get Quebec on the track toward HCV elimination by 2030.

In 2022, Quebec is still facing major organisational barriers to the implementation of a more diverse offer of services, A shift in Quebec's political actions would allow community organizations to be valuable partners in HCV elimination process by granting access to screening to thousands of people.

Disclosure of Interest: None Declared

P133

PREVALENCE AND OUTCOME OF VACCINE-PREVENTABLE (HEPATITIS A AND HEPATITIS B) CAUSES OF PEDIATRIC ACUTE LIVER FAILURE

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Background and Objectives: While drug-induced liver injury and metabolic liver diseases are the commonest causes of pediatric acute liver failure (PALF) in the west, viral Hepatitis are the commonest cause of PALF in Asia and parts of south America. Hepatitis A and Hepatitis B are 2 preventable diseases responsible for a major chunk of PALF in the Indian subcontinent. This study aims to identify the burden of vaccine-preventable causes (Hepatitis A and B) of PALF.

Methods: Data of all cases of PALF presented between January 2011 and September 2022 were retrieved from the hospital information system after obtaining institutional ethical committee approval. PALF was defined as per the PALF study group definition: (i) biochemical evidence of acute liver injury, (ii) uncorrectable coagulopathy (INR > 1.5 with HE OR INR > 2 without HE), and (iii) no evidence of chronic liver disease. Acute Hepatitis A was defined on the basis of IgM HAV positivity. Acute Hepatitis B was defined as the presence of high titres of IgM anti-HBc, low viral DNA load, and absence of signs of chronicity. The outcome was defined as survival with the native liver at 28 days since admission.

Results: A total of 351 cases of PALF presented during the study period. Vaccine-preventable diseases accounted for 166 (47.3%) of these cases. Of these 163 were Hepatitis A-induced PALF and only 3 cases were Hepatitis B-related PALF. Among Hepatitis A related PALF, 93 (57%) survived with their native liver, 54 (33.1%) died and 16 (9.8%) received liver transplantation. Among Hepatitis B-related PALF, all 3 patients survived with their native liver.

Conclusion: As many as 47.3% of PALF in the Indian subcontinent are caused by vaccine-preventable viruses and these cases have high mortality rates. This provides us a window of opportunity to ramp up our immunization program and improve sanitation to reduce the mortality due to PALF.

Disclosure of Interest: None Declared

P134

IMPACT OF DIRECTLY ACTING ANTIVIRAL THERAPY ON REDUCING THE DIVERSITY OF CIRCULATING HEPATITIS C GENOTYPE 3A VIRUSES

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Introduction: Australia offers free directly acting antiviral (DAA) treatment for Hepatitis C virus (HCV) infected eligible patients since 2016. Epidemiological surveillance data indicates that HCV infected patients have declined since then, but these estimates may not capture hidden infected populations. This study uses a phylogenetics based model to see if the epidemiological predictions of a decline in HCV case numbers in New South Wales (NSW), Australia can be reproduced.

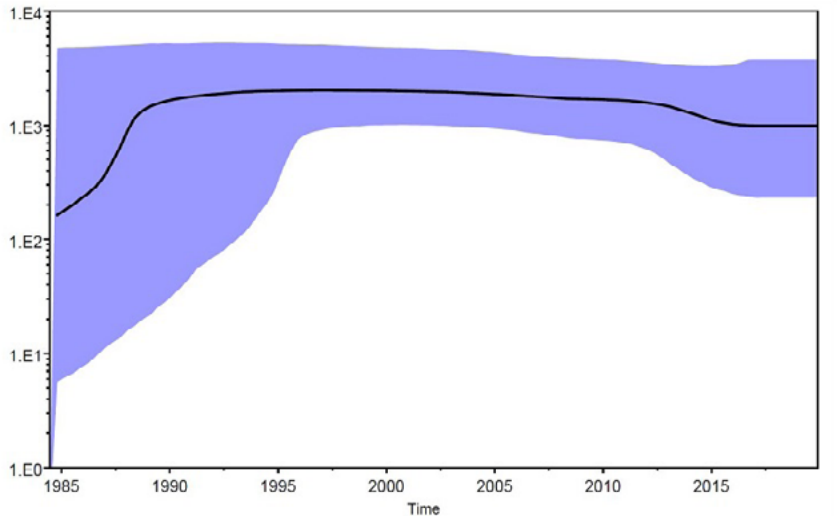
Method: Near-full-length HCV consensus sequences were generated from 63 genotype 3a infected people recruited from two prison-based cohort studies in NSW between 2004 – 2019. All samples were collected within 6 months since the estimated date of infection. Changes in effective population sizes (a modeled population based on phylogenetic diversity of circulating viral sequences) of infected people were explored with BEAST software suite (v1.10) using coalescent Bayesian skyline model.

Results: The projected infected median effective population size showed a 12-fold increase between 1984 – 1996 to reach a peak in 1996. Between 1996 and 2012 (16 years) there was a 22% gradual decline in the median infected population size. Since then, between 2012- 2019 there has been a more precipitous reduction in numbers by a further 37% compared to 2012 (when DAAs entered the market). Much of this drop was observed between 2012 – 2017, with the numbers stabilizing between 2017-2019.

Conclusions: The decline in the diversity of the circulating HCV genotype 3a viruses in the community agrees with the current epidemiological projections which suggests that the upscale of DAA treatment has led to a decline in the number of infections.

Figure 1. Changes in effective population size (a modelled population living with HCV infection) in NSW, Australia from pre-DAA to post-DAA era (2012 - 2019). The X axis shows calenday year while the y axis shows the effective population size on a log scale. The solid line is the median effective population size while the shaded area is the 95% high posterior density (the equivalent of confidence intervals in Bayesian statistics).

Image/Table:



Disclosure of Interest: None Declared

P135

DIAGNOSTIC PERFORMANCE OF THE SD BIOLINE®HBEAG RAPID TEST USED ROUTINELY IN BURKINA FASO FOR THE MANAGEMENT OF HBV-INFECTED INDIVIDUALS

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Abstract Content: The HBeAg is a marker of replication of the wild Hepatitis B virus. Its detection is fundamental for the clinical classification of chronic Hepatitis B. In addition, WHO recommends its use in combination with ALT to assess eligibility for antiviral treatment in the context of inaccessibility to molecular tests for the quantification of Hepatitis B virus (HBV) DNA. In resource-limited countries where access to enzyme-linked immunosorbent assays also remains a challenge, RDTs are a good alternative and are therefore widely used.

The objective of this work was to determine the diagnostic performance of the SD Bioline®HBeAg test used in routine for the detection of HBeAg.

It was an evaluation study of a diagnostic tool that focused on the samples of HBsAg positive patients received at the laboratory of the "Assault-Hepatitis" Center for the detection of HBeAg with SD Bioline®HBeAg. The samples were then tested for the detection of HBeAg with the Vidas HBeAg.Anti-HBe Kit (Gold standard) and for the quantification of HBV DNA by real-time PCR. Performance was calculated using statistical analyses with R software.

The sensitivity (Se) and specificity (Sp) of the Bioline HBeAg SD were 33.3% and 97.9%, respectively. An increase in the sensitivity of the test was observed as a function of the viral load. Thus, for a viral load < 2000 IU/mL, the Se and Sp were 8.8% and 98.3%, and increased to 35.5% and 98.4% for a DNA amount > 200,0000 IU/mL.

The results show a low Se of the SD Bioline®HBeAg test. This implies that a therapeutic decision based on this RDT could exclude most of the persons eligible for treatment.

Disclosure of Interest: None Declared

P136

CURRENT ACHIEVEMENTS AND CHALLENGES IN VIRAL HEPATITIS B AND C ELIMINATION PROGRAM IN THE REPUBLIC OF ARMENIA

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Background: In November 2018, Center for Disease Analysis (CDA) Foundation in collaboration with the WHO European Region and the Ministry of Health of the Republic of Armenia (MOH RA), analyzed the main results of the burden of viral Hepatitis C and B. Rely on published studies and field expert consensus, it was estimated that 4.0% of the adult population of RA were anti-HCV seropositive, viremic 2.8%, HBsAg+ 1.6%.

Purpose: Using CDA modeling the MOH RA for achievement of two main Viral Hepatitis elimination by 2030 develops programs for HCV-infection treatment with directly acting antiviral agents (DAAs) and MTCT triple elimination, including HBV-infection.

Methods: Despite the heavy burden of fighting with COVID-19, since 2020 Armenia has successfully implemented a state program for the treatment of viral Hepatitis C with DAAs. MOH RA choose more realistic stepwise scenario aims to gradually improve diagnosis and treatment reaching a maximum of 3,000 patients in 2026 and beyond. At the first stage it was planned to treat 1000 patients in the framework of the state procurement with the combination of Sofosbuvir plus Daclatasvir. In order to select the first thousand patients, a model was based on patients with grade 4, 3 fibrosis, extrahepatic manifestations (vasculitis, lymphoproliferative diseases etc.) and patients with concomitant diseases (diabetes mellitus, fatty liver disease etc.) that contribute to the progress of the disease. After one year it was decided to provide the DAAs despite stage of fibrosis and co-morbidities. In August of 2022 regimen was change on Sofosbuvir/Velpatasvir with simplified approaches for screening and diagnosis of HCV-infection.

Result: From the beginning of the program gradually more valuable groups of patients involved starting with HIV-HCV-coinfected patients (200), MDR- and XDR-TB (26), then in 2022 HCV-infected patients in prisons (210), psychiatric clinics (28) and finally special program for PWID (250). During mentioned period 2020-2022 have been organized different screening program: among migrants in PCS, include regions with rapid testing, IBBS and checking among patients hospitalized in surgical divisions. Currently MOH RA develops MTCT triple elimination strategy, National Register Viral Hepatitis and National Plan for 2023-2026.

Conclusion: The state program for HCV-infection treatment with DAAs has been successfully launched in the Republic Armenia in August 2020, despite difficulties associated with COVID-19 pandemic. For achievements Viral Hepatitis elimination by 2030 enlargement of screening programs for HBV and HCV, implementation of National Register, triple elimination strategy and health care workers educational programs are crucial.

Disclosure of Interest: None Declared

P137

IMPACT OF ON SITE-TESTING AND LINKAGE TO CARE ON HEPATITIS C INFECTION IN INTRAVENOUS DRUG USERS IN LUXEMBOURG

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Background : Intravenous drug users (IDU) represent the majority of new cases of HCV infection in Luxembourg. Outreach interventions are recommended to achieve HCV micro-elimination in this high risk and vulnerable population.

Purpose : We established an interventional program in four different harm reduction centers to improve screening and medical care of IDU infected with HCV.

Methods: The study was conducted at the national drug consumption facility and in 3 drug substitution treatment sites by the National Service of Infectious Diseases. Participants were offered a blood drawing for HCV, HIV, HBV and syphillis serologies, viral loads if positif for serology, HCV genotyping, liver biomarkers and a fibroscan. Interviews were conducted using a standardized questionnaire including demographic and social characteristics, drug use patterns, risk and harm reduction behaviours.

Results: 480 participants (72% male) were recruited between October 2015 and December 2019, and followed untill December 2021 for Direct Acting Antiviral treatment (DAA)'s outcome. Among them, 73% were unemployed, 48% had no income, and 70% reported to live in unstable housing or were homeless. 58% of the participants were under Opioid Substitution Therapy, 53% were injecting drugs every day, 58% had heavy alcohol consumption, 45% had been incarcerated at least once, and 27% of women were sex worker. Among the 473 participants tested for HCV serological markers, 71% (336) were anti-HCV positive, 64% of those (216) were HCV RNA positive. Four genotypes were identified (56% G1, 0.5% G2, 38% G3, 5.5% G4) in 203 HCV sequences. Fibroscan testing indicated that 66% of IDU were graded as F0-F1, 21% as F2-F3, and 13% as above F3. 11% were HIV positive, and 1.5% were HBs Ag positive. 72 drug users (33% of HCV RNA positive cases) initiated a DAA treatment at enrolment : 85% achieved Sustained Virological Response 3 weeks after the end of the treatment (SVR3), and 74% SVR12 when retained in care. Reinfections were recorded in 9.7% of the cases at the end of 2021 or 2.5 reinfections/1000 patient-years of follow-up. Increased treatment uptake tend to decrease HCV positive serology to 54 % in 2018 and the percentage of HCV RNA positive persons to 40% in 2019 at enrolment in this cohort. Phylogenetic analyses revealed 18 clusters with more than 5 sequences and a large G1a cluster of 40 sequences. These clusters included HCV sequences obtained before 2015 indicating frequent transmissions across long timer periods, and highlighted missed treatment opportunities to prevent further HCV transmission.

Conclusions: The study demonstrated the feasibility of effective screening and HCV care among high risk drug users in harm reduction sites. Screening, provision of DAA and virologic monitoring are now being implemented using HCV-RNA testing on site to accelerate HCV micro-elimination in this key group.

Disclosure of Interest: None Declared

P138

VIRAL HEPATITIS ELIMINATION EFFORTS IN EASTERN EUROPE AND CENTRAL ASIA (EECA) – RESULTS FROM A JOINT EVALUATION WORKSHOP

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Background: The World Health Organization (WHO) has defined ambitious targets for eliminating viral Hepatitis (VH) as a public health threat by 2030. COVIMPACT Hepatitis (2021-2023) set out to assess the impact of COVID-19 on VH elimination in Eastern Europe and Central Asia (EECA). At the end of the project, a workshop brought together all country partners to exchange lessons learned and ideas on how to scale-up elimination efforts in countries of EECA.

Purpose: The aim of the workshop was to discuss and evaluate ways to scale-up the efforts needed to reach VH elimination targets in the context of the challenges posed by the COVID-19 pandemic.

Methods: The workshop took place in Berlin, Germany, from 17 to 21 October 2022. The participants were divided into three groups and discussed in four exercises which targets are most important, most difficult, and most realistic to achieve and ranked them using the online tools "Mentimeter" and "Miro". Groups also identified most important interventions that are needed to reach these targets.

Results: Stakeholders from Georgia, Kyrgyzstan, Ukraine and Uzbekistan took part. The targets identified as most important were VH diagnosis and Hepatitis B vaccination. Provision of harm reduction services was listed as least important (Table 1). Hepatitis B vaccination was considered the easiest to reach target. Participants considered reduction of mortality as both the most difficult and least realistic target to reach. The two most realistic targets were Hepatitis B vaccination and blood safety. Most important interventions needed to reach the targets were improved testing coverage, better linkage to care and free of cost treatment, awareness-raising and capacity building.

Conclusions: With less than 10 years to go to reach the WHO targets, gathering partners for discussions and exchange of lessons learned is pivotal. The workshop facilitated an increased understanding of why there is less progress on some targets and which efforts can help to close gaps towards elimination by 2030.

Image/Table:

Table 1: Ranking of WHO elimination targets (average for the three groups)

	WHO 2030 target	How important (1: most, 9: least)	How difficult (1: easiest, 9: most difficult)	How realistic (1: most, 9: least)
Impact				
Incidence: New cases of chronic hepatitis B and C infections	90% reduction	3	7	8
Mortality: hepatitis B and C deaths	65% reduction	7	9	9
Service coverage				
Hepatitis B vaccination: childhood vaccine coverage	90%	2	1	1
Prevention of hepatitis B mother-to-child transmission	90%	8	4	3
Blood safety: % of donations screened in a quality- assured manner	100%	6	5	2
Safe injections: percentage of injections administered with safety-engineered devices in & out of health facilities	90%	5	2	5
Harm reduction: number of sterile needles & syringes provided per person who injects drugs per year	300	9	3	7
Hepatitis B & C diagnosis	90%	1	6	4
Hepatitis B & C treatment	80%	4	8	6

Disclosure of Interest: None Declared

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PROGRESS TOWARDS ACHIEVING HEPATITIS C ELIMINATION IN THE COUNTRY OF GEORGIA, APRIL 2015 – SEPTEMBER 2022

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Background and Aims: Georgia launched the world's first national Hepatitis C elimination program in April 2015. Key strategies include nationwide screening, active case finding, linkage to care, decentralized care, and provision of treatment for all persons with Hepatitis C virus (HCV) infection, along with effective prevention interventions. The elimination program aims to achieve the following targets: a) diagnose 90% of HCV-infected persons, b) treat 95% of those diagnosed, and c) cure 95% of those treated. We report progress towards elimination targets of the elimination program.

Method: The estimated number of persons living with HCV infection was based on a 2015 population-based national seroprevalence survey, which showed that 5.4% of the adult general population had chronic HCV infection (approximately 150,000 persons). We analyzed data in the national HCV screening and treatment databases during April 2015-September 2022.

Results: As of September 30, 2022, 146,804 adult persons screened positive for HCV antibodies. Of them 126,334 (86.1%) underwent HCV viremia testing. A total of 99,401 (78.7%) persons tested had active HCV infection, and 79,932 (80.4%) of them initiated treatment. Of 56,337 patients who were evaluated for sustained virologic response (SVR), 55,750 (99.0%) tested negative for HCV by PCR. Based on the 90-95-95 program goal, Georgia has diagnosed 66.3% of the estimated 150,000 adults living with chronic HCV, treated 62.3% of the target 128,250, and cured 45.8% of the target 121,837.

Treatment effectiveness was comparable among persons with advanced fibrosis (F3 and F4) with 98.3% achieving SVR, and among patients with mild or no liver fibrosis (≤ F2), SVR= 99.2%, $p<0.0001$.

Conclusion: Georgia has made substantial progress towards eliminating Hepatitis C. Over 65% of persons with chronic HCV infection have been diagnosed, and most have initiated treatment with high cure rates regardless of fibrosis status. Challenges remain in identifying and linking to care persons living with HCV in Georgia. The Nationwide integrated, decentralized model of HCV treatment, which is already implemented in many locations, will be critical to improve linkage to care and close gaps in the HCV cascade of care.

Disclosure of Interest: None Declared

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INTERFERON ANTIBODIES THAT DIMINISH RESPONSE TO PEGINTERFERON-BASED THERAPY FOR CHRONIC HBV INFECTION ARE MORE COMMON IN CHILDREN AND IMMUNOTOLERANT DISEASE

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Background: Development of interferon (IFN) antibodies in patients treated with peginterferon and entecavir during the immunotolerant (IT) phase of chronic Hepatitis B virus (HBV) infection are associated with diminished response to treatment. Whether antibodies develop and their impact during peginterferon treatment in patients in other phases of chronic HBV are unknown.

Aim: To evaluate the presence of neutralizing (nAb) and non-neutralizing (non-nAb) antibodies to interferon (IFN) in patients treated with tenofovir and peginterferon for 24 weeks followed by 3.5 years of tenofovir monotherapy in the Immune Active (IA) trial of the Hepatitis B Research Network (HBRN).

Methods: Pre-, on- and post-treatment serum from combination tenofovir and pegIFNa therapy from IA trial participants were pre-incubated with +/- recombinant IFNa (rIFN) (100 U/mL) and added to Huh7 cells to measure interferon stimulated gene (ISG) induction by qPCR. Abs to IFNa were measured by ELISA. Correlations between serum induced ISG inhibition, the presence of anti-IFNa Abs and quantitative HBsAg (qHBsAg) decline during treatment, were evaluated and compared to results from patients in the IT trial treated with entecavir and peginterferon.

Results: Of 98 participants in the IA trial, no Ab were present at baseline but Ab to IFN developed after treatment initiation in 36 (36.7%). Pre-incubation of on-treatment serum from 5 (5.1%) Ab-positive patients with rIFNa markedly blunted ISG induction in Huh7 cells by rIFNa, whereas the samples from the other Ab-positive patients and those without detectable Ab did not inhibit ISG induction ($p<0.0001$). The mean decline in qHBsAg during IFN treatment was 0.48+/-0.73 log IU/mL in those with non-nAb or no Ab, compared to -0.012+/-0.15 in those with nAb ($p=0.025$). nAb developed in 26 (42.6%) of the 61 participants in the IT trial, of whom 21 (80.7%) were children. Among adults, nAb developed in 20% of IT participants compared to 5.1% of IA participants ($p=0.015$). Among adults, age, sex and ethnicity were not associated with development of nAb. Ab persisted after treatment until the end of study follow-up. Ab did not inhibit ISG induction by rIFN-beta or rIFN-lambda in Huh7 cells.

Conclusions: Neutralizing Abs to IFN develop during peginterferon treatment for chronic HBV and diminish antiviral responses to therapy. Abs develop more frequently in children and during the IT phase of HBV. Understanding how and why IFNa Abs develop may allow for improved patient selection and optimization of IFN-based therapy, which is of particular importance given its use in HBV cure strategies.

Disclosure of Interest: None Declared

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EXPANDED ACCESS TO THE PREVENTION, DIAGNOSIS AND TREATMENT OF PEOPLE WITH VIRAL HEPATITIS AND THE NURSE'S ROLE

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Abstract Content: Brazil has been developing, through the Ministry of Health, guidelines to enhance the shared care and the role of nurses in the management of care for people with viral Hepatitis. Objective: to develop a strategy to expand access to prevention, diagnosis and treatment of people with viral Hepatitis, highlighting the role of nursing. This is an experience report about the process of elaborating interventional actions in health, built through the assumptions of research-action. The participants were health professionals and managers of the reference municipality of the health regional, composed by 28 municipalities, in Bahia/Brazil. Techniques such as the "World Café" dynamics were used to discuss the themes: management; prevention; epidemiological surveillance and assistance; diagnosis and treatment, and the "Interactive Panel" to work on the viral Hepatitis issues. After the thematic survey and discussions, the strategies to be implemented were defined. 35 health professionals and managers participated in this activity. The defined strategies were: the continuous care of people with viral Hepatitis and the work plan that will be implemented in health services by nurses. For continuous care, the following services were considered: maternity; urgency and emergency; private health services; testing and counseling centre; Primary Healthcare (APS) and blood bank. For the shared care of people with viral Hepatitis diagnosed in these services, it was defined the referral to the Specialized Assistance Service (SAE) of the reference municipality. The work plan presents the actions considering the themes: Management: establishing continuous care for people with viral Hepatitis within the scope of APS and SAE, carrying out prevention and diagnosis actions; sending people with a confirmed diagnosis for treatment at the SAE. These actions will be led by the nurses. Prevention: warning the population about viral Hepatitis; ensuring the complete vaccination schedule for Hepatitis A and B; encouraging condom use. Assistance: ensuring rapid tests; decreasing the waiting time for the results of laboratory tests; strengthening shared care with APS; training professionals for diagnosis and treatment in the APS; monitoring children exposed to viral Hepatitis. Epidemiological surveillance: qualifying the cases' notification process of viral Hepatitis; strengthening dialogue between health care and surveillance services; expanding vaccination coverage for Hepatitis A and B; improving information systems. The implementation of continuous care for people with viral Hepatitis and the development of a working plan will support municipalities, as well as contribute to the process of eliminating viral Hepatitis.

Disclosure of Interest: None Declared

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HEPATITIS DELTA VIRUS SCREENING STRATEGIES IN FRENCH UNIVERSITY HOSPITAL LABORATORIES: ADVOCACY FOR REFLEX TESTING IMPLEMENTATION

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Background: Chronic infection with Hepatitis delta virus (HDV) is the most severe form of chronic viral Hepatitis, with an increased risk of cirrhosis, hepatic decompensation and hepatocellular carcinoma than with Hepatitis B virus (HBV) mono-infection. International liver societies recommend systematic HDV screening for all HBsAg positive patients. However, screening rates are often scarce. Therefore, laboratories have implemented an "HDV reflex testing" protocol, consisting of a systematic detection of anti-HDV antibodies in all Hepatitis B surface antigen (HBsAg)-positive samples for the first time.

Purpose: The aim of this study was to analyse the different strategies implemented in seven French university hospital laboratories and to compare their efficiency for HDV antibody and HDV RNA testing in HBsAg+ samples.

Method: In this multicentre retrospective survey, the virological databases from seven University hospital laboratories were searched for all HDV tests performed in HBsAg+ patients for the first time from January 2018 to October 2022. Duplicates were excluded based on name, sex and date of birth. Total or IgG HDV antibodies (HDV-Ab) were assayed with automated serological tests, and HDV RNA levels were assayed with in-house or commercial molecular tests.

Results: Depending on the hospital, between 10,000 to 26,000 patients per year were screened for HBsAg in each laboratory, with a mean±SD HBsAg positivity of 1.70±0.78% (range 0.68-3.11%, mean age of 39.9 years, 67% males). Annual HDV-Ab screening rate ranged from 47% to 99%. Lowest rates were observed in centres performing only on-prescription analyses whereas the highest rates were observed in centres performing reflex testing. Addition was manual (i.e. biologist-driven) in 3 centres whereas automatically set in the local information system in 2 centres. Mean±SD HDV-Ab positivity was 6.3±2.5% (mean age of 40.9 years, 70% males). At least one HDV RNA measurement was available for 77.8% of the HDV-Ab+ patients and 59% of patients had a replicative HDV infection.

Conclusion: Even in this university hospital context, HDV was underdiagnosed with a prescription-based strategy alone. Both manual and automatic reflex testing were highly effective. Early identification of HBV-HDV infected patients allowed a faster referral to a specialized medical consultation for adequate management, especially in the era of new HDV treatments. The prevalence of HDV coinfection in HBsAg+ patients in French university hospitals was twice higher than that reported in HBsAg+ blood donors. Active HDV replication was present in 59% of coinfected patients. This work strongly argues for changing public health policies and allowing laboratory-driven HDV reflex testing.

Disclosure of Interest: None Declared

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SURVEY TO EVALUATE THE IMPLEMENTATION OF THE RECOMMENDATIONS ON THE COMPREHENSIVE DIAGNOSIS OF VIRAL HEPATITIS IN A SINGLE EXTRACTION: WHERE ARE WE?

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Introduction: The SEPD (Spanish Association for Digestive Diseases), AEEH (Spanish Association for the Study of the Liver), SEIMC (Spanish Society of Infectious Diseases and Clinical Microbiology), SEIMC-GEHEP (Work-group for Viral Hepatitis) and AEHVE (Spanish Viral Hepatitis Elimination Alliance) agreed on a document at the beginning of 2022 to carry out a comprehensive diagnosis of viral Hepatitis (B, C and D): a positive result in serology to detect viral Hepatitis (HBV, HCV and HDV), as well as HIV, would trigger the analysis of the rest of the virus, including the viral load when necessary, from the same blood sample. This process would increase the diagnosis rate and it would reduce the time to be evaluated.

Aim: To evaluate the situation in Spain regarding the comprehensive diagnosis of viral Hepatitis in a single blood draw.

Methods: A panel of experts prepared a structured survey disseminated through the Google Forms platform to all Spanish hospitals, public or private with teaching accreditation, with 200 beds or more. The survey was sent on 20th Oct 2022 and the reception of the results closed on 1st Dec. 2022.

Results: Of the 130 hospitals with inclusion criteria, 48 responded (37% response rate, 34 centers >500 beds). All centers have tools for the determination of HBV surface antigen, anti-HCV and HIV serology. 92% have a PCR technique for HBV/HCV. Only 67% of the centers have capacity for the determination of anti-HDV, and this drops to 31% for the detection of HDV-RNA; 88%, who do not have this technique, outsource it. The availability of Point-of-Care (POC) tests is low (21% of centers), GenXpert HCV (38%) and dry blood spot (38%) being the most frequent. Most of the POCs (90%) are supervised by Microbiologists and are always included in the clinical records. Reflex-test diagnosis is performed simultaneously in 88% of centers for HCV, 62% for HBV, 50% for HDV, and only 41% for HBV-HDV. Although 90% of centers believe that HBV and HCV serology should be performed on HIV-positive patients in the same sample, it is only done on 18% of HBsAg-positive and/or anti-HCV-positive subjects. When there is an active infection, any communication strategy is used in 38/48 (79%) of the hospitals (38 hospitals for HCV, 18 for HBV and 10 for HDV). The automated appointment arrangement is only available in 19% of the centers. Only 44.2% of the respondents believe that the determinations to reach a definitive diagnosis must be made with a single blood sample.

Conclusions: Although most hospitals have the procedures to carry out a comprehensive diagnosis of viral Hepatitis in a single analytical sample, this is used in less than 50% of cases for HBV/HDV. Alerts to maintain continuity of care are widely available for Hepatitis C, but they need to be increased for HBV and HDV. Likewise, it is necessary to implement the devices for decentralized diagnosis.

Disclosure of Interest: None Declared

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THE EVALUATION OF PEOPLE SUSPECTED OF SEXUALLY TRANSMITTED DISEASES REQUIRES TOOLS FOR THE COMPREHENSIVE DIAGNOSIS OF VIRAL HEPATITIS AND HIV

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Introduction: The prevalence of viral Hepatitis is higher in patients with a sexually transmitted disease (STD). The World Health Organization recommends ruling out the existence of a secondary STD and/or concomitant viral Hepatitis in all people with a suspected STD. Objective: To evaluate the simultaneous diagnosis of viral Hepatitis in subjects suspected of having an STD.

Methods: Review of STD studies (syphilis, *Trichomonas vaginalis, Chlamydia trachomatis, Mycoplasma genitalum*, and *Neisseria gonorrhoeae*) to assess the performance of diagnostic tests for Hepatitis B, Hepatitis C, and HIV in the three months before or after the index sample for STD diagnosis. The results available between April 2019 and September 2022 from the Microbiology Department of our center were evaluated.

Results: We found 157,185 serology determinations against syphilis and/or exudates against STD. Of the 49,664 serologies for the study of syphilis, anti-HCV serology was determined in 62.2% of the cases; in 1092 subjects with syphilis, an anti-HCV prevalence of 2.3% was detected; 3 viremic, 12 with sustained viral response and 8 spontaneous clearance. HBsAg was requested in 82.4%, detecting 20 positive cases (0.8% prevalence in patients with anti-treponemal antibodies). Finally, the presence of anti-HIV was evaluated in 89.3% of the requests for syphilis, being positive in 150 cases (prevalence = 5.8%; 72 new cases and 78 already known). The determination of HBsAg and anti-HCV and anti-HIV antibodies in subjects with other STD were respectively: 1) *Trichomonas vaginalis* (27,924 samples): 1.6% of the cases had a study for HBsAg, detecting 2 positives; 1% study for HCV (1 positive) and 1.6% study for HIV (2 positive). 2) *Chlamydia trachomatis* (6,018 samples): 2.2%, 2.3% and 2.7% had an HBV, HCV and HIV study, respectively; detecting 2 anti-HCV positive subjects and 4 anti-HIV positive subjects. 3) *Mycoplasma genitalum* (4,879 samples): 1.9%, 2.1% and 2.5% had an HBV, HCV and HIV study respectively, detecting 2 positive anti-HCV and 4 positive anti-HIV. 4) *Neisseria gonorrhoeae* (5,978): 2.2%, 2.3% and 2.7% had an HBV, HCV and HIV study respectively, detecting 3 anti-HCV positive subjects and 4 anti-HIV positive subjects.

Conclusions: In subjects with suspected syphilis there is an underdiagnosis of viral Hepatitis, higher for HCV than for HBV (60% vs 80%). The reflex diagnosis of HIV, although not optimal, is clearly better (90%). The absence of a diagnostic study aimed at ruling out a concomitant infection by viral Hepatitis is the rule in the rest of the STD. These results highlight the need to implement tools for the complete and comprehensive diagnosis of viral Hepatitis in subjects with suspected sexually transmitted diseases.

Disclosure of Interest: None Declared

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INSUFFICIENT KNOWLEDGE OF HEPATITIS B AND C VIRUS REACTIVATION AMONG SPECIALIST PHYSICIANS IN DUTCH-SPEAKING BELGIUM: THE CHOICE TRIAL (CHRONIC HEPATITIS B/C SCREENING IN PATIENTS ON IMMUNOSUPPRESSIVE THERAPY AND CHEMOTHERAPY)

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Background: Hepatitis B and C virus (HBV/HCV) reactivations in chronically infected patients are an emerging problem because of the increasing use of cytotoxic and immunosuppressive therapy regimens. Even though several scientific societies propose universal HBV screening before initiating therapy, HBV reactivation still occurs in daily practice. No recent surveys have been performed/published assessing HBV/HCV knowledge in specialists prescribing these medications.

Purpose: This study aims to assess knowledge and awareness regarding HBV/HCV reactivation among oncologists, gastroenterologists, rheumatologists, and dermatologists in Belgium.

Methods: A short questionnaire (Q) was designed in duplicate [i.e., Q1 for an oncologic and Q2 for a non-oncologic setting] assessing descriptive variables and nine content questions (four background and five clinically oriented questions). Of these five clinical questions, three were discipline-specific (specific for Q1 and Q2).

The survey was disseminated by e-mail between 10/01/22 and 20/05/22 to 11 hospitals in Belgium (three university, eight non-university). Statistical analysis was done using SPSS version 28.

Results: Table 1 provides an overview of survey participant characteristics. Out of 116 survey responses, 104 were complete. Less than 30% of participants obtained a score above 50%. Mean overall scores (total, Q1, and Q2) were 36.2%, 33.7%, and 40.2% respectively. Mean scores for clinical questions (total, Q1, and Q2) were 48.6%, 44.4%, and 55.6% respectively. Mean overall scores for background and non-discipline-specific questions were 20.2% and 36.0% respectively. Scores were not influenced by years of experience, nor working in a university hospital.

HBV/HCV prevalence in Belgium, clinical course of HCV reactivation, and timing of HBV/HCV prophylaxis were better known by gastroenterologists. They scored significantly better on non-discipline-specific questions ($p=0.009$). Moreover, oncologists that have already witnessed a Hepatitis B reactivation in their own practice, are better aware of Hepatitis B screening guidelines prior to administration of chemotherapy ($p=0.005$) and immunosuppression ($p=0.033$).

Conclusion: Knowledge of HBV/HCV reactivation is at present insufficient among specialist physicians, with differences according to specialty. Gastroenterologists scored better on non-

discipline-specific questions. Oncologists are better aware of HBV screening guidelines, especially if they have witnessed an HBV reactivation themselves, showing that creating awareness is feasible. National hepatology and oncology organizations can play an important role in providing clear guidance and raising awareness among all physicians of the involved specialties.

Image/Table:

Table 1: Characteristics of survey participants		n	%
Specialty	Oncology	64	55.2%
	Gastroenterology	21	18.1%
	Rheumatology	16	13.8%
	Dermatology	15	12.9%
Oncology subdiscipline	Solid tumors	33	52.4%
	Hematological malignancies	21	33.3%
	Gastrointestinal tumors	9	14.3%
Years of experience	<5 years	39	33.6%
	5 - 10 years	24	20.7%
	>10 years	53	45.7%
Working in an academic center	Yes	43	37.1%
	No	72	62.1%
Having witnessed an HBV reactivation in their own practice	Yes	33	28.4%
	No	83	71.6%

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P146

ELIMINATING HEPATITIS C IN AUSTRALIA: SAME-DAY TESTING AND TREATMENT OF PEOPLE WHO INJECT DRUGS

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Background: Despite universal access to government funded Direct Acting Antivirals (DAAs) in 2016, the rate of treatment uptake in Australia has declined over time. People who inject drugs are a key population driving Hepatitis C transmission in Australia and reducing the disease burden in this population is critical for achieving Hepatitis C elimination targets. The requirements for venous pathology samples before dispensing are a barrier to treatment uptake in this population.

Purpose: Rapid point-of-care testing can provide antibody results (OraSure®) in 20 minutes and RNA results in 60 minutes (GeneXpert®). We are considering the effects of rapid testing and same-day dispensing on treatment retention and cure.

Methods: The QuickStart study is a crossover cluster randomised controlled trial with three intervention arms and a control arm (NCT05016609, clinicaltrials.gov). Arm A provides rapid antibody testing; Arm B provides antibody and rapid RNA testing; Arm C provides rapid antibody testing and same-day treatment initiation; the Control Arm provides standard of care.

Results: Rapid testing does not require venepuncture, which is a notable barrier to testing for people who inject drugs. The QuickStart study is measuring the proportion of people (a) receiving a complete diagnosis, (b) receiving treatment and (c) achieving cure a sustained virological response to consider whether rapid testing results in higher proportions tested, treated and cured. Challenges in site recruitment have included the perception – true or false – that all people with Hepatitis C in the community serviced by a clinic have already received treatment. The COVID-19 pandemic also presented challenges to site recruitment due to closure of some face-to-face services.

Conclusions: Individuals who were aware and willing to receive DAAs were treated in the initial stages DAA availability in Australia. Hepatitis C treatment in Australia now faces new challenges in engaging individuals who may be doubtful, uncertain, or unaware of their serostatus. To engage these populations, we must invest in appropriate testing strategies that facilitate capability and opportunity to access treatment.

QuickStart is funded by an NHMRC clinical trials grant with support from an investigator initiated research grant from Gilead.

Disclosure of Interest: None Declared

P147

PHARMA-C: A KNOWLEDGE TRANSFER APPROACH TO IMPLEMENT HEPATITIS C SCREENING IN COMMUNITY PHARMACIES IN QUEBEC

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Abstract Content: Increasing accessibility to Hepatitis C virus (HCV) screening is essential to eliminate HCV. Approaches to improve accessibility include point-of-care testing (POCT). Some studies have demonstrated that community pharmacists are key players in the decentralization of access to HCV testing with the judicious use of HCV antibody tests.

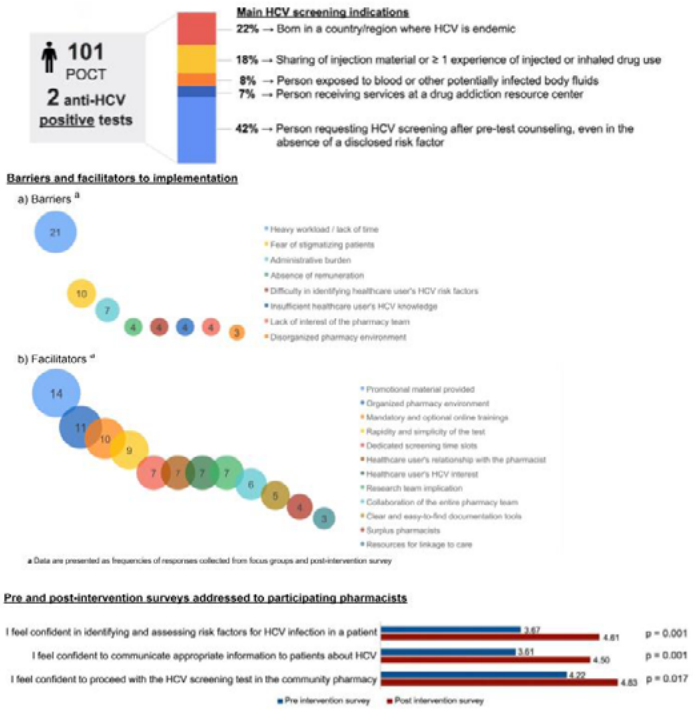
This study evaluated knowledge transfer (KT) and the feasibility of HCV POCT in community pharmacies in Quebec (Canada).

During this 6-month prospective KT pilot study (February to September 2022), all community pharmacists in Quebec were invited to participate. Eligible participating pharmacists (PPs) first completed a webinar. They recruited healthcare users (HUs) based on their risk factors and offered HCV antibody POCT (OraQuick®HCV). PPs were included if they worked at least 8 hours per week for at least 3 months. Advisory committees, PPs' focus groups and collected barriers and facilitators provided guidance and feedback to improve the implementation program. To assess feasibility and knowledge acquisition, pre and post-intervention surveys were completed by PPs and results were compared with Student's T-test. HUs were invited to fill out a satisfaction survey following screening.

Sixteen PPs performed 101 tests in 11 pharmacies. More than 75% of PPs in the pre and post-surveys deemed the implementation of HCV screening feasible. The PPs intervention (excluding the time waiting for the test result) lasted on average 22 minutes. All users with positive results were linked to care (n = 2). Post-intervention surveys showed that PPs felt more confident in identifying HCV risk factors ($p = 0.001$), communicating information ($p = 0.001$) and performing the screening test ($p = 0.017$) when compared to the beginning of the study. PPs reached various populations, particularly individuals born in endemic regions for HCV (22%). The 77 HUs who answered the satisfaction survey described a positive experience of POCT in pharmacy (mean score of 4.94 out of 5.00). Promotional material and additional training offered were facilitators to implementation, while work overload and fear of stigmatizing patients were the main barriers. To address these issues, pamphlets on HCV risk factors and training on harm reduction and communication with high-risk populations were created following the KT approach.

HCV screening by community pharmacists is feasible in Quebec. Any motivated pharmacist can screen HCV with adequate training. These first-line healthcare professionals can contribute to the decentralization of HCV screening and participate in the efforts of HCV elimination. Initiatives to expand the role of pharmacists in HCV testing, treatment and follow-up in the province are encouraged.

Image/Table:



Disclosure of Interest: É. Roy-St-Pierre Grant / Research support from: The test material was provided free of charge by Gilead Sciences Inc program. An educational AbbVie grant was obtained for the preparation and delivery of continuing education sessions for pharmacists. *, R. Prévost Grant / Research support from: *, K. Idir Grant / Research support from: *, A. Khodamoradi Grant / Research support from: *, F. Provost Grant / Research support from: *, D. Martel Grant / Research support from: *, N. Sheehan Grant / Research support from: *, V. Martel-Laferrière Grant / Research support from: * - Dre Valérie Martel-Laferrière is supported by the program Clinical Research Scholars - Junior 2 of FRSQ., R. Therrien Grant / Research support from: *

P148

USE OF DRIED BLOOD SPOT TEST FOR HCV SCREENING AND DIAGNOSIS AMONG PEOPLE WHO USE DRUGS IN THE BALEARIC ISLANDS, SPAIN

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Background: One of the key at-risk populations for Hepatitis C virus infection (HCV) are people who use drugs (PWUD) given that they are a vulnerable population due to the stigma, discrimination and socioeconomic inequalities. They often have difficulties in accessing healthcare and are therefore at increased risk of infection, access treatment less often, and are more often lost to follow-up. The *Hepatitis C Free Balears* project employs a micro-elimination strategy to facilitate the screening, treatment, and monitoring of this population.

Purpose: To investigate if the use of the dried blood spot (DBS) test to increase HCV screening among PWUD is effective.

Methods: This project is being implemented in 21 addiction service centres of the Balearic Islands and includes 4phases: 1) recruitment and HCV screening onsite via a point-of-care anti-HCV antibody (Oraquick®) and DBS testing or blood analysis to confirm viremia (HCV-RNA) and screen for Hepatitis B surface antigen (HBsAg) and HIV antigen/antibody; 2) linkage to care; 3) treatment prescription via telemedicine; and 4) monitoring onsite of sustained virological response (SVR) at 12 weeks after treatment and for reinfection monitoring after a year. DBS samples are analysed with chemiluminescent technology for serological determinations and RT-PCR assay for HCV viral load quantification.

Results: Of the 1200 recruited patients, 387 (32%) were anti-HCV+ and DBS testing was chosen by 295 (76%) to examine viremia, rather than standard phlebotomy. Among the anti-HCV+ participants, 8 (2%) were positive for HBsAg, 68 (6%) were anti-HIV+ and 142 (12% of the total population) had active HCV infection.

Of those HCV-RNA+, 123 (87%) initiated treatment, 19 (13%) are pending treatment initiation and, of those who initiated, 104 (85%) have completed. SVR12 monitoring was performed in 75 (72%) of those patients who completed treatment, of which 60 (80%) were done by DBS testing. Of those who were monitored for SVR12 72 (96%) showed undetectable HCV-RNA. Of the patients screened a year ago and were anti-HCV+(n=180), 18 (10%) have been screened for reinfection, of which 89% were done by DBS and 3 reinfections have been detected.

Conclusions: DBS testing can be a useful strategy to determine HCV, HBV, and HIV prevalence among PWUD, as it can be carried out on-site and without patients having to travel. Findings also show that DBS testing is useful for continued monitoring, since it simplifies the pathway and reduces difficulties faced by PWUD in engaging with conventional health care services. To eliminate HCV an emphasis should be placed on HCV models of care that are person-centred and adapted to their unique needs.

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P149

PREVALENCE OF UNDIAGNOSED HCV INFECTION IN HOSPITALIZED PATIENTS FROM UNIVERSITY HOSPITAL OF NORTH SARDINIA

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Abstract Content: HCV infection is the main cause of cirrhosis, hepatocarcinoma (HCC), and liver failure. World Health Organization (WHO) estimated that, globally, around 71 million people live with Hepatitis C virus (HCV) infection, and they aimed to eliminate the Hepatitis C virus by 2030. Since the introduction of Direct-acting Antiviral Agents (DAAs), infection's clinical evolution changed significantly; now almost 95% of treated patients are cleared of the virus.

The two fundamental steps to achieve the WHO's goal are finding patients eligible for the treatment and prescribing them the appropriate drug.

In 2021 a protocol was approved in a North Sardinia Hospital to screen for HCV infection in all hospitalized patients. This hospital is a natural checkpoint for public health in the Sassari hinterland.

This protocol involves:
- Physicians who admit the patient and prescribe the screening test
- Physicians from the laboanalyzingalysing the test
- Physicians belonging to the hepatology service

The first step is screening for HCV. If positive, the admitting doctor prescribes the HCV RNA and genotype and is referred to hepatology services (HS). The HS receives a report every 15 days on screened patients who have tested positive and if necessary, schedules a visit in light of HCV RNA and genotype results. The report is sent by the laboratory and the visit is requested by the admitting doctor.

Most of the departments that joined the screening were already performing this test as part of their admission routine. HCV screening in our surgical wards is performed to stratify the biological risk of patients that needs surgical intervention.

Our hospital has two hepatology services, one from the Medical Clinic and the other from the Infectious Disease Department of the University.

The data observed are related to the patients to the latter: from November 2021 to September 2022, 157 positive patients were found. For 44 of 157 patients, the process proceeded with the physician's request for HCV RNA. Only 2.5% of patients completed the therapeutic diagnostic process.

Most of the patients in our surgical wards do not complete the diagnostic iter after a positive screening, mainly because the test is not meant for a diagnostic purpose but is done just to be aware of the biological risk that surgeons go thru when they perform the surgical intervention. Although HCV screening was a test performed in some departments long before the protocol was approved, HCV RNA is a test that is asked for in only 40.70% of cases

Our strategies to improve the protocol are:
- Weekly report instead of bimonthly report
- Insert note "it is advised to request HCV RNA and HCV genotype. It is also suggested to schedule evaluation at outpatient Hepatology clinic or Infectious Diseases clinics."

In conclusion, we need to improve colleagues' awareness of diagnostic processes and the effectiveness of treatment to have an early diagnosis, set effective treatment, and avoid progression to cirrhosis and or hepatocarcinoma.

Disclosure of Interest: None Declared

P150

PERFORMANCE EVALUATION OF THREE RAPID DETECTION TESTS FOR HEPATITIS B SURFACE ANTIGEN IN A RESOURCE-LIMITED SETTING

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Background: Rapid, easy-to-use and efficient diagnostic tests are an alternative to automated methods in accessing Hepatitis B virus screening in low-income settings. This study aimed to evaluate the diagnostic performance of the Determine™ HBsAg2, Standard Q™ HBsAg, and OnSite® HBsAg Combo Rapid tests in the detection of Hepatitis B virus antigen in Ouagadougou.

Material and Methods: This was a laboratory evaluation of the performance of the Determine™ HBsAg2, Standard Q™ HBsAg, and OnSite® HBsAg Combo Rapid tests using blood samples collected during the period of February to May 2021. A panel of 300 individual serum including 110 HBsAg positive and 190 HBsAg negative was selected from blood donors for the study. The presence or absence of HBsAg in the serum was confirmed by the "Alinity HBsAg Reagent" test on the "Abbott™ Alinity™ i System" (Abbott Laboratorie) used as the reference test. Index tests (Rapid Diagnostic Tests, RDTs) performance such as sensitivity, specificity were calculated using the free and open source epidemiological statistics software, OpenEpi (http://www.openepi.com,), with their 95% confidence intervals. Cohen's Kappa coefficient was used to assess the agreement of the index tests with the reference test. Interpretation of Kappa results was done according to the following criteria: kappa ≤ 0 indicating "no agreement" and 0.01- 0.20 as "very poor agreement," 0.21- 0.40 as "poor agreement," 0.41-0.60 as "moderate agreement," 0.61-0.80 as "strong agreement," and 0.81-1.00 as "near perfect agreement."

Results: Sensitivity and specificity of Determine™ HBsAg 2 in this study were 100% (95%CI: 96.63-100) and 100% (95%CI: 98.2-100), respectively. For the Standard Q™ HBsAg and the Onsite® HBsAg Combo Rapid test the sensitivities were 95.45% and 96.63% respectively, with specificities of 100% and 98.95% respectively. The variations observed between these performances by RDT are not statistically significant with respect to the confidence intervals. The concordance of the HBs RDTs with the reference test is estimated to be 1 for Determine™ HBsAg 2, and 0.96 and 0.98 for Standard™ Q HBsAg and Onsite® HBsAg Combo Rapid test

Conclusion: All three rapid diagnostic tests evaluated perform well in the detection of HBsAg and had perfect agreement with the Alinity HBsAg automatised method. These RDTs could be an alternative for Hepatis B virus screening in a context of limited laboratory resources.

Key words: HBs antigen, Rapid detection, hepatis B, RDT, screening.

Disclosure of Interest: None Declared

P151

FEASIBILITY OF HCV SELF-TESTING IN THE PRIMARY CARE SYSTEM: A REAL-WORLD STUDY INCLUDING 688 INDIVIDUALS FROM THE GENERAL POPULATION IN RIO DE JANEIRO (BRAZIL)

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Background: Hepatitis C virus self-testing (HCVST) has been recommended as a strategy to increase the identification of HCV infection. However, data on the feasibility of HCVST in the general population followed in the Primary Health Care (PHC) System in Brazil remain scarce.

Purpose: To assess the acceptability, usability, and re-reading/re-testing agreement of oral fluid HCVST among general population in Rio de Janeiro (Brazil).

Methods: This cross-sectional study was conducted in a Basic Health Unit in Rio de Janeiro (July-September 2022). Oral fluid HCVST [OraQuick® HCV Test] was proposed for people testing by standard finger-prick HCV rapid-test (HCVRT) [SD BIOLINE® HCV Test]. Participants had access to written instructions and a step-by-step video to perform HCVST. The process of HCVST was observed by a trained healthcare provider (HCP). After HCVST, a second HCV test using the same oral fluid kit was performed by the HCP. People with anti-HCV test positive was linked-to-care. Usability of HCVST was assessed by observing errors and difficulties. A post-testing questionnaire assessed the acceptability of HCVST and agreements (re-reading of HCVST results and re-testing) were assessed by Cohen's Kappa (k).

Results: Of 888 subjects who had HCVRT during the study period, 688 participants [74% female; 52.4% with schooling ≤ 10 years] agreed to perform HCVST. Three participants were excluded due to eating or drinking 30 minutes before HCVST. Despite a significant lower age [52 (IQR,39-61) vs 55 (IQR,45-63) yrs, p=0.014], there were no other difference between those who agreed or not to HCVST. A total of 86.1% watched the video and 90.5% read the instructions before testing. The majority of participants correctly opened the kit package (95.6%), organized the material (94.6%), inserted the tube in the tube support (91.4%) and time keeping (93.0%). However, 67.2% (n=460/865) correctly collect oral-fluid sample and 35.6% (n=244/865) of participants needed assistance in any step of HCVST (**Figure 1**). Re-reading agreement of HCVST results was 95.3% (k=0.57). This agreement was higher in people with age < 60 years compared to those ≥ 60 years (k=0.59 vs 0.50). The agreement between HCVST results and oral fluid HCV rapid test performed by HCP was 99.8% (k=0.86,excluding invalid tests,n=657). Additionally, concordance between HCVRT and HCP-performed oral fluid HCV test was 99.4% (k=0.50). HCVST was very well accepted in the post-testing questionnaire. A total of 69.3% would prefer to perform HCVST in a health unit, and few people would prefer presential (29.2%) assistance for HCVST **(Figure 2**).

Conclusion: Oral fluid HCVST was feasible and well-accepted in general population from the PHC System in Brazil.

Image/Table:

Figure 1. Observer assessment of steps for HCV self-testing in participants from the general population recruited from the Primary Care System (n=685)

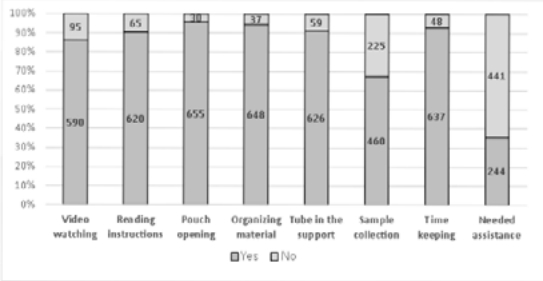
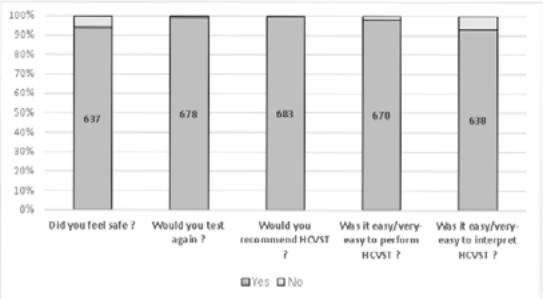


Figure 2. Post-test questionnaire after HCV self-testing in participants from the general population recruited from the Primary Care System (n=685)



Disclosure of Interest: None Declared

P152

HEPATITIS C SEROLOGICAL AND MOLECULAR POINT-OF-CARE (POC) TESTS TO INFORM ON TESTING ALGORITHMS IN A CLINICAL SETTLING, SOUTH AFRICA

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Background: We need to progress on viral Hepatitis testing and treatment, if we are to meet the 2030 goals for viral Hepatitis elimination. The use of venipuncture may deter patients and people at-risk from testing. To improve diagnostics and reduce patient loss to follow up, validated HCV point-of-care assays are required.

Purpose: We evaluated the performance of the two POC assays for serology on oral fluid and capillary blood and one POC VL on capillary blood in a clinical setting, by comparing these to laboratory reference methods on plasma.

Methods: Patients were invited to participate in the study at the gastroenterology clinic, in 2019-2020, at the Charlotte Maxeke Johannesburg Academic Hospital , regardless of anti-HCV positivity. The OraQuick® HCV Rapid Antibody test and HCV SD Bioline was performed at the clinical site using oral fluid or capillary blood, respectively. Capillary blood (100µl) was placed directly on the assay cassette in the GeneXpert. At the laboratory, plasma volumes of 70µl and 650µl was tested by the reference tests for serology and for VL, respectively. All viral load analyses were performed in $\log_{10}$ -transformed values IU/ml. Performance was measured by accuracy, sensitivity, specificity and agreement by a Bland-Altman analysis.

Results: A total of 77 individuals were enrolled in the study. Forty-three were tested on the antibody POC tests and 71 were tested on the HCV GX FS VL and the CAP/CTM HCV VL. Sensitivity and specificity of the Oraquick HCV antibody POC was 72% (95%CI 29.04%-96.33%) and 97% (85.08%-99.93%), respectively and of the SD Bioline HCV antibody POC was 63% (95%CI 24.49%-91.48%) and 100% (89.72%-100%), respectively.

Of the two samples that tested negative on the both the POC's but positive on the EIA, one showed a low serum/cut-off value of 2.37 on the laboratory reference EIA and was negative on the FS VL and the CAP/CTM VL assays. If we consider the samples to be negative on EIA, the sensitivity of the Oraquick and he SD Bioline HCV POC assays increases to 83% and 72%, respectively.

A total of 62 results on the HCV GX FS VL were compared to the CAP/CTM HCV VL. The diagnostic sensitivity of the assay was 89% (95%CI 65.3% - 98.6%) and the specificity was 100% (95%CI 91.6% - 100.0). The Bland-Altman plot showed a mean difference between the two platforms of 0.03 $\log_{10}$ IU/ml $\pm$ 0.45 with 95%CI [-0.21; 0.27 $\log_{10}$ IU/ml].

Conclusion: With sensitivities and specificities of greater than 70% for both the HCV antibody POCs, it is recommended to simplify the HCV testing algorithm at clinics to a POC using either oral fluid or capillary blood and a POC VL assay. Simplification of the HCV testing algorithm will keep patients in care and treatment programs.

Disclosure of Interest: None Declared

P153

A 'ONE-STOP-SHOP' INTERVENTION INTEGRATING POINT-OF-CARE HCV RNA TESTING TO ENHANCE HEPATITIS C TESTING AND TREATMENT UPTAKE AMONG NEW RECEPTIONS TO PRISON: THE PIVOT STUDY

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Background: Prisons are key venues for Hepatitis C (HCV) elimination, but complex clinical pathways and frequent prisoner movements remain barriers to efficient HCV care. This study evaluated the impact of an intervention integrating point-of-care (PoC) HCV RNA testing, Fibroscan®, nurse-led clinical assessment, and fast-tracked direct-acting antiviral (DAA) prescription (a 'one-stop-shop' intervention) on HCV testing and treatment uptake compared to standard of care among people recently incarcerated in Australia.

Methods: PIVOT was a prospective, non-concurrent, controlled study comparing HCV testing and treatment uptake during a 'one-stop-shop' intervention (n=301; June 2020–April 2021) compared to standard of care (n=239; November 2019–May 2020) at one reception prison in New South Wales, Australia. The primary endpoint was uptake of DAA treatment at 12 weeks from enrolment. Secondary outcomes included uptake of HCV testing at 12 weeks from enrolment and time from enrolment to DAA treatment initiation.

Results: 540 male participants were enrolled. Median age (29 vs. 28 years) and history of injecting drug use (48% vs. 42%) were similar between standard of care and intervention phases. The proportion of people receiving HCV antibody/RNA testing was higher among participants in the intervention phase compared to standard of care (99% vs. 26%, p<0.001). Among people diagnosed with current HCV infection (n=18/63 in the standard of care phase vs. n=30/298 in the intervention phase), the proportion initiating DAA treatment within 12 weeks from enrolment in the intervention phase was higher (93% [95% CI: 0·78-0·99] vs 22% [95% CI: 0·64-0·48]; p<0·001), and the median time to treatment initiation was shorter (6 days [IQR: 5-7] vs. 99 days [IQR: 57-127]; p<0·001) compared to standard of care.

Conclusion: A 'one-stop-shop' intervention integrating PoC HCV RNA testing, Fibroscan®, and fast-tracked DAA prescription enhanced testing and treatment uptake, and reduced time to treatment initiation, among people recently incarcerated in Australia, thereby overcoming key barriers to treatment scale-up in the prison sector.

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Image/Table:

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EVALUATION OF THE HEPATITIS C TREATMENT AND CARE MODEL IN THE PRIMARY HEALTHCARE IN THE COUNTRY OF GEORGIA

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Background and Aims: In April 2015, with a partnership with Gilead Sciences and technical assistance from U.S. CDC, Georgia launched the world's first Hepatitis C elimination program. By October 2022, about 80 thousand patients initiated treatment, achieving >99% cure rates. Broad access to direct acting antivirals (DAAs) resulted in rapid increase in treatment uptake in 2016, which has since declined due to barriers in diagnosis and linkage to care. To address this issue Georgia initiated service decentralization in 2018 by integrating Hepatitis C virus (HCV) screening and treatment in primary healthcare centers (PHCs). We report preliminary results of an integrated model of HCV care in PHCs.

Method: By September 30, 2022 a total of 10 PHCs were providing HCV care services throughout the country. The integrated model was based on "one stop shop" approach, where patients receive all HCV screening, treatment and care services in selected PHCs. PHCs provided care to HCV treatment-naïve patients with no or mild fibrosis (FIB-4 score<1.45) using simplified diagnostics and a treatment monitoring approach, while persons with advanced liver fibrosis/cirrhosis were referred to specialized clinics. Patients received Sofosbuvir/Ledipasvir and/or Sofosbuvir/Velpatasvir for 12 weeks. Sustained virological response (SVR) was defined as undetectable HCV RNA at 12-24 weeks after end of therapy. The Extension for Community Healthcare Outcomes (ECHO) telemedicine model was used to train and support primary healthcare providers. Regular teleECHO videoconferencing was conducted to provide primary care providers with advice and clinical mentoring.

Results: Among persons diagnosed with active HCV infection, 1,659 were evaluated for FIB-4 score. A total of 1,080 patients initiated treatment, and of them 1,000 (92.6%) completed treatment. Of 971 patients eligible for SVR testing, 780 had been tested at the time of analysis, and 766 (98.2%) achieved SVR.

Conclusion: Our study reported the feasibility and effectiveness of integrating a simplified HCV diagnostic and treatment model in PHCs. Countrywide expansion of this model is warranted to bridge the gaps in the HCV care continuum and ensure high rates of treatment uptake towards achieving elimination targets.

Disclosure of Interest: None Declared

P155

HEPATITIS B CORE-RELATED ANTIGEN RAPID TEST (HBCRAG-RDT) TO IDENTIFY HBV-INFECTED WOMEN AT HIGH RISK OF MOTHER-TO-CHILD TRANSMISSION IN CAMBODIA, CAMEROON, AND BURKINA FASO

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Background: Prevention of mother-to-child transmission (PMTCT) of Hepatitis B virus (HBV) is a key intervention to globally eliminate HBV as public health issue. WHO currently recommends universal infant Hepatitis B vaccination starting immediately after birth and peripartum antiviral prophylaxis to HBV-infected pregnant women having high HBV DNA levels (≥200,000 IU/mL). However, access to HBV DNA test is severely limited for pregnant women living in resource-limited countries. To enable decentralization of HBV PMTCT to antenatal care services at peripheral health facilities, we recently developed an immunochromatographic rapid test for Hepatitis B core-related antigen (HBcrAg). We evaluated its diagnostic performance to identify HBV-infected women with high viral loads (≥200,000 IU/mL) using real-time PCR as reference in three countries with high HBV prevalence: Cambodia, Cameroon, and Burkina Faso.

Methods: We evaluated the performance of HBcrAg-RDT: i) retrospectively using stored sera obtained from pregnant women positive for Hepatitis B surface antigen (HBsAg) who participated in two large cohorts in Cambodia (ANRS 12345 TA PROHM) and Cameroon (ANRS 12303); and ii) prospectively using capillary blood collected by finger prick from mothers of infants in Burkina Faso (NéoVac study).

Results: In Cambodia, a total of 1194 HBsAg-positive pregnant women were tested and 367 had HBV DNA levels ≥200,000 IU/mL. The sensitivity and specificity (95% CI) were 93.7% (90.7-96.0) and 95.2% (93.5-96.5), respectively. In Cameroon, of 502 HBsAg-positive pregnant women 88 had high viral load ≥200,000 IU/mL. The sensitivity and specificity were 89.8% (81.5-95.2) and 91.7% (88.6-94.2), respectively. In Burkina Faso, a total of 698 women participated, of whom 57 (8.2%) were positive for HBsAg and seven had high viral load ≥200,000 IU/mL. In HBsAg-positive women, the sensitivity was 85.7% (42.1-99.6) and the specificity was 94.3% (80.8-99.3). In 641 HBsAg-negative women, none were tested positive for HBcrAg-RDT.

Conclusion: HBcrAg-RDT may be useful alternative to identify pregnant women eligible for peripartum antiviral prophylaxis at decentralized settings in resource-limited context.

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EVALUATION OF THE PERFORMANCE OF THREE RAPID SCREENING TESTS BEING USED FOR SCREENING HEPATITIS C VIRUS ANTIBODIES

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Background: Pakistan has the second highest burden of Hepatitis C in the world. Most of the people living with Hepatitis C virus in Pakistan are undiagnosed. There is a dire need to diagnose the missing millions living with Hepatitis C virus in Pakistan. Large number of HCV rapid screening tests are available in the market and many of them have substandard results. There is a need to have highly effective rapid screening tests for the screening of HCV in a country like Pakistan with high burden of Hepatitis C virus.

Purpose: To evaluate the performance of three best Hepatitis C virus rapid test available in Pakistani market. The study was conducted at Rawalpindi and Islamabad, the capital twin cities of Pakistan.

Methods: We enrolled 300 subjects including 50 pregnant women, 50 blood donors and 200 HCV positive individuals. Blood samples from all the 300 participants were screened by using three rapid screening test for anti-HCV including Intec Products Advanced Quality Rapid Anti-HCV Test, SD Bioline One Step anti-HCV test, and CTK Biotech's OnSite HCV Ab Rapid Test. The performance of these three rapid tests was also compared with the Roche Anti-HCV II test performed on the cobas 601 platform based on the electrochemiluminescence immunoassay principle.

Results: In total, 300 samples were analyzed in this study, out of which 92 were negative for anti-HCV and 208 were found positive for anti-HCV. The sensitivity of Intec test, SD Bioline test and CTK Biotech test were 98.56%, 97.59%, and 95.67%, respectively. The specificity of CTK Biotech test and SD Bioline test were found 100% whereas the specificity of Intec test was found 98.91%. The positive predictive value (PPV) of CTK Biotech and SD Bioline was 100%, but Intec products showed 99.51% PPV. The negative predictive values of the Intec product, SD Bioline, and CTK Biotech were 96.80%, 94.84%, and 91.09%, respectively.

Conclusion: The rapid test evaluated in this study showed very good results and they can be used for Hepatitis screening of Hepatitis C virus on large scale.

Disclosure of Interest: None Declared

P157

SIMPLIFIED CRITERIA TO ASSESS LONG-TERM ANTIVIRAL TREATMENT INDICATION IN CHRONIC HBV INFECTED PREGNANT WOMEN IN CAMBODIA: A CALL FOR SIMPLIFICATION AND STANDARDIZATION

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Introduction: The American Association for the Study of Liver Diseases (AASLD) recommended that women identified as HBsAg positive during pregnancy should receive additional testing and determination of need for long-term antiviral treatment (LTT). This study aims to assess the eligibility to LTT among HBV-infected pregnant women in Cambodia using different international guidelines as a reference and to evaluate the performances of simplified criteria free from HBV DNA quantification and fibrosis evaluation to identify women eligible to LTT.

Methodology: A retrospective analysis of HBV-infected pregnant women enrolled in the phase 4 multicenter interventional prospective ANRS 12345 TA-PROHM study was conducted. Eligibility to LTT was evaluated at inclusion during pregnancy according to the AASLD and EASL's guidelines and at 6 months post-partum according to the AASLD, EASL and APASL's guidelines. The performances of four models of simplified criteria were evaluated: the algorithm used in the TA-PROHM study (positive HBeAg and/or ALT > 40 U/L), the TREAT-B score, the HBcrAg RDT alone and the HBcrAg / ALT based score. The area under the receiver operating characteristics (AUROC), the sensitivity and specificity were calculated.

Results: Overall, 651 HBsAg positive women were analyzed. Among them, 209 (31.71%) received an antiviral prophylactic treatment. At inclusion, 21% and 24% of women eligible to prophylactic treatment were also eligible to LTT, according to the AASLD and EASL guidelines respectively. Reversely, 2% and 5% of women ineligible to prophylactic treatment were eligible to LTT. With AASLD as a gold standard, the HBcrAg score (HBcrAg positivity & ALT level) had an AUROC at 0.90 (0.87-0.92), a sensibility at 87.50% and a specificity at 75.29%. The TREAT-B score (HBeAg & ALT level) had an AUROC at 0.88 (0.85-0.90), a sensibility at 80.36% and a specificity at 79.16%. The TA-PROHM algorithm (HBeAg positivity and/or ALT > 40 IU/L) had an AUROC at 0.76 (0.73-0.80), a sensibility at 82.14% and a specificity at 70.16%. At 6 months post-partum, 2.10% with APASL, 5.80% with EASL, and 6.08% with AASLD, of the women non-eligible to prophylactic treatment at inclusion were eligible to LTT.

Conclusion: Most women non-eligible to prophylactic treatment did not require LTT. Simplified scores using HBcrAg or HBeAg and ALT levels are reliable, simple to use and accessible and could be used as a triage option to delay assessment of those not eligible to LTT but must be completed by other exams as transient elastography for those eligible. The international guidelines are numerous and complex, and there is an urgent need of standardized guidelines simple and accessible for low and middle-income countries

Disclosure of Interest: None Declared

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IT'S YOUR RIGHT – A PEER-LED HEPATITIS C TESTING AND TREATMENT CAMPAIGN DESIGNED BY PEOPLE WHO INJECT DRUGS, FOR PEOPLE WHO INJECT DRUGS

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Background: The eliminate Hepatitis C australia (ec australia) partnership, led by the burnet institute, brings together public health researchers, community organisations, government and health services to focus on a multipronged approach to increase Hepatitis C testing and treatment. Health promotion is one of ec australia's key programs. An estimated 117,800 people in australia live with Hepatitis C, and despite the widespread availability of direct acting antiviral therapy, many barriers remain to Hepatitis C treatment. Without addressing these barriers, especially for people from at-risk populations, including people who inject drugs and aboriginal and torres strait islander people, people with Hepatitis C will miss out on curative treatments, and australia will not achieve the world health organisation 2030 Hepatitis C elimination targets.

Method: The it's your right campaign was the first australia-wide peer-led health promotion campaign to be codesigned and delivered by peer workers with lived and living experience of injecting drug use. Ec australia partnered with the australian injecting and illicit drug users league and co-chaired a national reference group to codesign it's your right. A separate codesign process was also conducted to develop specifc messaging and artwork to reach aboriginal people who inject. The campaign combined bold rights-based messages and engaging street advertising, with peer outreach and engagement strategies tailored to the needs of communities who may not use mainstream services. Localised engagement strategies included peer-referrals to trusted services, cash incentives, and point-of-care testing.

Results: It's your right was implemented across australia by eight peer-led services and seven needle and syringe programs between april and december 2022. The campaign was evaluated by analysing organisational service delivery data, surveys of people who inject drugs (n=140), and interviews (n=18) and focus groups (n=9) with people who designed and implemented the campaign. During the campaign, staff of participating services had more than 2000 conversations about Hepatitis C with clients, and more than 1000 people were rna tested for Hepatitis C.

Conclusions: It's your right provided opportunities to trial new peer-led Hepatitis C services to reach people who inject drugs who had not previously engaged with the service. Incentives and onsite testing facilitated testing uptake by people who inject drugs and the visibility of the campaign enabled peers to initiate conversations more easily and to also strengthen enhanced service delivery. Challenges included the implementation of new services on top of usual workloads and supporting clients to commence treatment.

Disclosure of Interest: None Declared

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STRATEGIC APPROACHES TO IMPLEMENTING HCV ELIMINATION IN LOW RESOURCE SETTINGS USING NASARAWA STATE NIGERIA: A CASE STUDY

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Background: Despite global advancements in Hepatitis C (HCV) testing and treatment, minimal progress to democratize treatment access has been recorded in Africa, where an estimated burden of 10M people live with HCV, with only 5% diagnosed as of 2019.[1] Substantial gaps remain in treatment volumes, in part due to minimal supply-side interventions and limited government commitment. In line with global guidance, Clinton Health Access Initiative (CHAI) supported the Government of Nigeria to develop the necessary policy framework to build HCV "test and treat" programs and further domesticated this framework in Nasarawa State. Nasarawa is estimated to have an HCV seroprevalence of 14%,[2]To address the high burden, in 2020, the Nasarawa State Government committed to a 5-year HCV Elimination plan aimed at screening not less than 2.4M persons and placing an estimated 141K chronically infected persons on treatment.

Purpose: This abstract aims to describe strategic approaches used in the Nasarawa HCV Elimination program to drive testing and treatment volumes to date.

Approach/Methods: Given the low resource setting in Nasarawa, a stepwise methodology was employed. The elimination framework was developed having a four-pronged approach: plan wisely, test smart, cure-all, and prevent new cases. The key focus of this approach was to identify high-yield opportunities to enhance program implementation.The rollout followed a two-pronged approach, prioritizing enrolled HIV patients across secondary healthcare centers for the initial screening and a regional strategy for linkage to diagnostic and treatment services for seropositive patients. Healthcare workers were trained and supported with the required reporting tools.

Results: Exploring a patient-centered approach, HCV services were integrated into HIV services across the cascade of care to drive screening, viral load testing, and treatment initiations. A total of 13 secondary health facilities currently provide HCV screening, with 6 facilities prioritized for diagnostic testing and treatment. Through this approach, as of June 2022, a total of 13,206 persons have been screened, 610 anti-HCV positive individuals accessed HCV viral load testing, and 334 individuals with chronic HCV initiated treatment. Currently, using WHO programmatic targets, micro-elimination has been achieved in 2 facilities through the diagnosis of $\geq$90% of enrolled PLHIVs and $\geq$80% placed on treatment.

Conclusions: In resource-limited settings with limited donor support, viral Hepatitis elimination is feasible with government commitment, effective planning, and the establishment of a data-driven micro-elimination strategy.

Disclosure of Interest: None Declared

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MOLECULAR CHARACTERIZATION OF HEPATITIS B VIRUS (HBV) IN A POPULATION OF FOREIGN IMMIGRANTS IN BRAZIL

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Abstract Content: Hepatitis B is one of the most prevalent viral infections in humans and a major global public health problem. Hepatitis B virus (HBV) is a highly variable DNA virus due to its unique life cycle, which involves an error-prone reverse transcriptase that generates numerous viral variants. Based on the genetic diversity of the complete genome, HBV is phylogenetically classified into ten genotypes, called A-J, and several subgenotypes. The frequencies of clinically relevant mutations vary significantly between HBV genotypes. In addition, viral genotypes and subgenotypes have a characteristic ethno-geographical distribution, which reflects historical patterns of human migrations. However, recent globalization trends and increased human mobility strongly contribute to changes in the geographical dispersion of HBV genotypes in the world, and the introduction of exotic strains in destination territories. Foreign immigrants under vulnerable conditions constitute a growing group in Brazil. So far, there are no data in the country that elucidate the molecular profile of HBV in this population. The present study aims to identify the circulating HBV genotypes/subgenotypes and clinically relevant mutations in a population of foreign immigrants residing in Goiás, Central-West Brazil. A total of 102 subjects (24 HBsAg-reactive, and 78 anti-HBs + anti-HBc or anti-HBc only) were included in this study. The countries of origin were Haiti (79.4%), Guinea Bissau (11.8%), Venezuela (7.8%), and Colombia (1%). Until now, 55 serum samples were subjected to DNA extraction and PCR amplification of the S and C regions. HBV DNA was detected in 14 samples: 12 of them were HBsAg-positive and two were HBsAg-negative, resulting in an occult Hepatitis B infection (OBI) prevalence of 3.6%. Immune escape mutations were not detected in any S gene sequence. HBV subgenotypes A1 (n=6, 42.9%), A5 (n=6, 42.9%), F2 (n=1, 7.1%), and F3 (n=1, 7.1%) were identified. HBV/A1-infected subjects were from Haiti (n=5) and Guinea Bissau (n=1), while those infected with HBV/A5, HBV/F2, and HBV/F3 were from Haiti (A5) and Venezuela (F2 and F3). To our knowledge, this is the first detection of HBV/A5 in Brazil. Remarkably, 2/4 (50%) HBV/A5 core sequences showed the A1762T/G1764A double mutation, which has been associated with liver cancer development. This study will contribute to public health policies for this population, as well as to the identification of HBV exotic strains in Brazil, which may impact the diagnosis, immunization, treatment, and prognosis of Hepatitis B in the country.

Disclosure of Interest: None Declared

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EXPLORING OPPORTUNITIES TO IMPROVE HEPATITIS C TREATMENT UPTAKE IN AUSTRALIA AMONG PEOPLE WHO INJECT DRUGS: A QUALITATIVE STUDY

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Background: Despite universal access to highly effective Hepatitis C treatments, uptake has declined in Australia. Most Hepatitis C virus (HCV) infections in Australia are among people who inject drugs (PWID), who often face barriers to accessing health services. Eliminating HCV in Australia requires a nuanced understanding of the barriers to HCV treatment experienced by PWID and new strategies to improve treatment pathways.

Purpose: This study aims to understand the reasons people avoid or delay HCV treatment and identify potential pathways that can increase uptake of HCV treatment from a health systems perspective.

Methods: Semi-structured interviews with 15 participants who were HCV positive and had a history of active or recent injecting drug use. Thematic and framework analysis based on Hoj's integrated framework were used to identify barriers and opportunities to HCV treatment.

Results: Findings were categorised as individual-level, socio-structural-level and system-level barriers and potential enablers to HCV treatment. At an individual-level, other competing priorities such as mental health conditions, family circumstances and ongoing drug use impeded treatment opportunities. Being engaged in opioid agonist therapy (OAT) improved treatment readiness. At the socio-structural level, unstable housing and stigma deterred engagement in HCV care whilst family and peer support could improve care pathways. At the system-level, misinformation, limited availability of OAT prescribers and gaps in care coordination especially within the prison system were identified as missed opportunities for treatment. In contrast, organisational support and respectful relationships with service providers were key to engagement with health services.

Conclusion: Multipronged strategies are needed to improve HCV treatment uptake in Australia. Person-centred care addressing the specific needs of PWID, such as housing, and drug and alcohol treatment should be enhanced, and HCV care embedded within these services. Strengthening care pathways especially within and between prisons and other primary care services is urgently needed.

Disclosure of Interest: None Declared

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HEPATITIS C TREATMENT INITIATION AMONG PEOPLE WHO INJECT DRUGS IN AUSTRALIA: TIME-TO-EVENT ANALYSIS OF A LONGITUDINAL COHORT

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Background: Despite the universal access to direct acting antivirals (DAAs) in Australia since 2016, the treatment uptake of DAAs remains low. To achieve WHO Hepatitis C elimination targets in Australia, transformation of the health system tailored to people who inject drugs are needed. Our study aimed to understand the social and drug use characteristics influencing treatment initiation, and the time-to-treatment-initiation to inform strategies to improve Hepatitis C care.

Methods: The data for our study was derived from the SuperMIX study, the longest-standing cohort of people who inject drugs in Australia, with routine data collection on the characteristics of participants and their health outcomes over more than a decade. Time-to-event analysis using Cox regression methods, was performed for the data collected between 2009 and 2021, among a selected cohort of Hepatitis C-positive participants.

Results: Among 230 participants who were tested positive for active Hepatitis C infection, 102 people (44.4%) reported treatment initiation while 128 people (55.7%) did not initiate treatment. The median time-to-treatment from the time of Hepatitis C positive result was 7.0 years. For those who were tested positive after 2016, the median time-to-treatment was 2.3 years.

Cox regression analysis showed treatment initiation was positively associated with opioid agonist therapy (HR 2.3, $p<0.000$), health service engagement (HR 2.8, $p<0.000$) and diagnosis after 2016 (HR 26.1, $p<0.000$). Treatment was less likely with longer periods of injecting drug use (HR 0.1, $p<0.000$).

Conclusion: There is considerable delay in treatment initiation of Hepatitis C despite the universal access to DAAs in Australia. Strategies to improve engagement with health services including incorporating drug and alcohol services into routine Hepatitis Care are needed.

Disclosure of Interest: None Declared

P163

NEXT STEPS IN MICRO-ELIMINATION: PEER POINT OF CARE HEPATITIS C TESTING IN VICTORIA, BRITISH COLUMBIA

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Background: Canada is currently on target to reach the 2030 WHO goal of HCV elimination. Continued high rates of treatment initiation are required to meet this goal. People who use drugs (PWUD), account for the majority of new HCV cases in BC and continue to have many barriers to accessing DAA therapies, despite demonstrated high SVR rates in clinical trials. Improved elimination efforts including innovative outreach testing and treatment with this population are essential. Novel models have a proven successful to engage PWUD in HCV therapy with a simplified, task-shifted cascade of care. Peer-based testing and support models have been piloted in other communities and may help connect to more marginalized populations. People with lived and living experience of HCV treatment and drug use (peers) are seen as trusted sources of knowledge who can vouch for the efficacy, few side effects and lowered barriers to eligibility that now exist in the current DAA era.

Purpose: The Peer HCV POC testing project seeks to determine whether a peer model of HCV POC testing in outreach sites in Victoria BC can be successful in finding populations who use drugs without regular access to primary care still living with HCV. This task shifting approach is the next phase of local micro-elimination efforts and has not been attempted previously.

Method: Six peers have been trained to provide hep C point of care antibody and dried blood spot RNA tests. Our goal is to pilot the program, learn from our experiences, specifically from the direct input of peers to develop effective and supportive testing and treatment strategies. Peers have worked with research staff in two-hour blocks and are paid $26/hr for these shifts to provide testing around local supportive housing, shelters, social service sites and special events. Each client tested is offered a $10 incentive to test. We are able to offer both point of care antibody testing and, for those who have been exposed to hep C (currently infected, treated or cleared), RNA testing by dried blood spot RNA or if available, bloodwork by nursing from our mobile outreach van.

Result(s): Within the first 4 months of the project peers and staff tested 304 people: 251 people with hep C point of care antibody tests (227 negative and 24 positive results), 41 people with hep C dried blood spot RNA tests and 28 with nurse RNA blood work. To date 12 people tested RNA+ (11 with previously unknown hep C active RNA that require treatment) and 7 people have been started on treatment.

Conclusion(s): This innovative and novel approach to HCV therapy in PWUD was able to successfully use a peer-based approach to find people with limited connection to primary health care to test and treat HCV. We still have much to learn from the valuable knowledge, established relationships and novel perspectives of peers in our efforts to reduce barriers and reach PWUD and others who remain untreated.

Disclosure of Interest: None Declared

P164

ADAPTING AND TRANSLATING THE "HEP B STORY" APP THE RIGHT WAY: A TRANSFERABLE TOOLKIT TO DEVELOP HEALTH RESOURCES WITH, AND FOR, ABORIGINAL PEOPLE

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Background and Aims: In 2014 the Menzies hep B team released the first Hepatitis B (HBV) educational app in an Aboriginal language, the "Hep B Story", addressing the need for HBV information in a patient's first language. In 2018 the "Hep B Story" was assessed and adapted prior to translation into a further 10 Aboriginal languages. Whilst initially thought the task to be simple, this was not so. The translation process developed iteratively along the way and evolved into a model that may be applied when creating any health resource in Aboriginal languages.

Methods: The adaptation and translation of the "Hep B story" process:

1. Focus groups with language speakers to assess cultural suitability of content.
2. Adaptation of content or images as required.
3. Forward and back translation of script using translators.
4. Translations checked for content accuracy, queries discussed and corrected with translators.
5. Voiceovers recorded.6. Revised versions of the app produced, reviewed, and finalised.

Results: The process of adaptation and translation appears straightforward, and in planning the project, we naively allowed 12 months to complete 10 language translations. Forming consultation groups, finding translators to write in language, and removing barriers to work, was not easy when dealing with the remoteness of the Northern Territory (NT) of Australia. The consultation process for each language group resulted in extensive HBV education community wide, with many participants sharing the story with their family and encouraging them to get a HBV check-up. Culturally, several issues were present across each language group and were rectified for the new version. The project become one owned by the entire community, with those involved feeling the importance of getting the HBV story out to "their people".

Conclusion: With more than 100 people involved in the project and thousands of kilometres travelled across the NT we produced not only an educational tool for many Aboriginal people in their preferred language, but developed a model for working with translators to develop health resources for different cultural and linguistic groups across the NT.

Disclosure of Interest: None Declared

P165

PREVALENCE OF HBV AND SARS-COV-2 AMONG RECYCLABLE WASTE COLLECTORS, HOMELESS PEOPLE, IMMIGRANTS AND REFUGEES, LGBTQIA+ PEOPLE, SEX WORKERS, PEOPLE USING ILLICIT DRUGS, AND PATIENTS WITH HIV IN GOIÂNIA, A LARGE CITY IN MIDWEST BRAZIL

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Background: HBV infection is another widely spread virus that chronically affects about 257 million individuals, and HBV is responsible for nearly 900,000 deaths each year, mostly as a result of complications of cirrhosis and hepatocellular carcinoma (hcc). The 2019 coronavirus disease (covid-19) caused by severe acute respiratory syndrome coronavirus 2 (sars-cov-2) has emerged as a major burden worldwide, resulting in serious public health challenges. It is still unclear whether HBV itself could make patients more vulnerable to covid-19 or if covid-19 leads to worse outcomes in patients with underlying HBV infection. Despite infectious diseases affecting mainly socially and economically vulnerable people. There is few data about the frequency of HBV and sars-cov-2 infections among them. Purpose: investigated the prevalence of HBV and sars-cov-2 among recyclable waste collectors, homeless people, immigrants and refugees, lgbtqia+ people, sex workers, people using illicit drugs, and patients with hiv in goiânia, a large city in midwest brazil. Method(s): therefore, between july and october 2020a total of 685 individuals were recruited. Participants underwent an interview and blood collection for the detection of HBV serological markers (hbsag, anti-hbs and total anti-hbc) and and samples of oropharynx and nasopharynx were collected for the detection of rna-sars-cov-2 was real-time quantitative polymerase chain reaction (rt-pcr) results: the median age was 33 years and 57.8% were male. The majority of individuals (79.2%) were non-white. The median number of years of formal education was 10 years. HBV exposure (anti-hbc+) was 13.7%; hbsag+ was 2.6%. Only 47.1% of the participants had HBV vaccination-like profile (anti-hbs+ alone). Most individuals were susceptible to HBV (83.6). Rna-sars-cov-2 was positive in 177/685 (17.1%) samples. Rna-sars-cov-2/hbsag co-infection (0.71%).

Conclusion: these findings highlight the need for continuous epidemiological surveillance of HBV and covid-19 in the invulnerable population, to better target prevention and control strategies for HBV and sars-cov-2 in this key and vulnerable population.

Disclosure of Interest: None Declared

P166

HEPATITIS B AND SARS-COV-2: PREVALENCE AND CO-INFECTION AMONG RECYCLABLE WASTE COLLECTORS, HOMELESS PEOPLE, IMMIGRANTS AND REFUGEES, LGBTQIA+ PEOPLE, AND PATIENTS WITH HIV IN CENTRAL BRAZIL

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Background: HBV infection is another widely spread virus that chronically affects about 257 million individuals, and HBV is responsible for nearly 900,000 deaths each year, mostly as a result of complications of cirrhosis and hepatocellular carcinoma (hcc). The 2019 coronavirus disease (covid-19) caused by severe acute respiratory syndrome coronavirus 2 (sars-cov-2) has emerged as a major burden worldwide, resulting in serious public health challenges. It is still unclear whether HBV itself could make patients more vulnerable to covid-19 or if covid-19 leads to worse outcomes in patients with underlying HBV infection. Despite infectious diseases affecting mainly socially and economically vulnerable people. There is few data about the frequency of HBV and sars-cov-2 infections among them.

Purpose: Investigated the prevalence of HBV and sars-cov-2 among recyclable waste collectors, homeless people, immigrants and refugees, lgbtqia+ people, and patients with hiv in goiânia, a large city in midwest brazil. Method(s): therefore, between july and october 2020. A total of 685 individuals were recruited. Participants underwent an interview and blood collection for the detection of HBV serological markers (hbsag, anti-hbs, and total anti-hbc) and samples of oropharynx and nasopharynx were collected for the detection of rna-sars-cov-2 were real-time quantitative polymerase chain reaction (rt-pcr) results: the median age was 33 years and 57.8% were male. The majority of individuals (79.2%) were non-white. The median number of years of formal education was 10 years. HBV exposure (anti-hbc+) was 13.7%%; hbsag+ was 2.6%. Only 47.1% of the participants had HBV vaccination-like profile (anti-hbs+ alone). Most individuals were susceptible to HBV (83.6). Rna-sars-cov-2 was positive in 177/685 (17.1%) samples. Rna-sars-cov-2/hbsag co-infection (0.71%).

Conclusion: These findings highlight the need for continuous epidemiological surveillance of HBV and covid-19 in the invulnerable population, to better target prevention and control strategies for HBV and sars-cov-2 in this key and vulnerable population.

Disclosure of Interest: None Declared

P167

GLOBAL ELIMINATION OF HEPATITIS C STRATEGIES MUST ADDRESS THE GENDER GAP IN TREATMENT AND CARE OF WOMEN WITH HCV

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Background: To achieve Global Elimination of HCV by 2030, the World Health Organization (WHO) set a target for 90% diagnosis and an 80% treatment rate. However, significant gender disparity exists in the cascade of care; women are under-diagnosed and under-treated. Providers and policy makers must increase gender equity, particularly for women at high risk of HCV infection and transmission.

Purpose: To critically evaluate published research and policy on screening, testing and outcomes for women infected with HCV, their experience during pregnancy/childcare, and double stigma faced with injection drug use (IDU) and substance use disorder (SUD).

Method: We evaluated recent studies focused on women with HCV during pregnancy/childcare, and studies that stratified results by gender in high risk populations.

Results:

Women and HCV: The WHO estimates that 29 million women worldwide have chronic Hepatitis C (2022). The US Centers for Disease Control (CDC) found a 250% increase in HCV infection rate in women (from 2004-2014).

Women of Child-Bearing Potential (WOCBP): The CDC reported an 89% increase in US maternal HCV prevalence (from 2009-2014). The Center for Disease Analysis estimated that 15 million women aged 15-49 had HCV globally (2019). HCV in women results in significantly higher gestational complications and maternal mortality compared to uninfected controls. HCV+ RNA correlates with increased pregnancy complications and >6 $\log_{10}$ IU/mL increases risk of mother to child transmission 4-fold. Concerns about vertical transmission may influence the decision to seek HCV treatment.

Women with HCV, SUD and IDU: HCV infection rates correlate with SUD and IDU. Women who inject drugs have higher risk for HCV compared to male counterparts due to overlapping sexual and injection risk factors. Women with IDU are more likely to have IDU sex partners, inject after male partners, be injected by others, and share syringes. They are less likely to participate in harm reduction services, receive guideline recommended HCV treatments, and have lower medication adherence. Medications for women must be specifically managed due to differential pharmacokinetic response and increased adverse event risk.

Conclusion: Disparities in HCV care for women highlight the immediate need for effective gender-based treatment. Research must focus on the lived experience of women and include gender-stratified analyses to correct existing disparities. The CDC, AASLD, ACOG and IDSA recommend screening or testing for all pregnant women; all practice guidelines must continually integrate new evidence on HCV in women. Replicating effective gender-inclusive care models must be part of our commitment to achieve viral Hepatitis elimination by 2030.

Disclosure of Interest: L. Chen Shareholder of: Gilead, Pfizer, Employee of: Gilead, S. Scherbakovsky Employee of: Gilead, J. Wolf Shareholder of: Gilead, Employee of: Gilead, C. Frenette Employee of: Gilead

P168

ELIMINATING CHRONIC HEPATITIS B IN THE NORTHERN TERRITORY OF AUSTRALIA THROUGH A HOLISTIC CARE PACKAGE DELIVERED IN PARTNERSHIP WITH THE COMMUNITY

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Background and Aims: Hep B PAST is a partnership project developed to eliminate chronic Hepatitis B (CHB) from the Aboriginal population of the Northern Territory (NT) in Australia. Preliminary results from the project demonstrate significant improvements in the cascade of care for those living with CHB. The project aims to:
1. Improve Hepatitis B related health literacy
2. Improve the cascade of care for people living with CHB

Method: **Aim 1:** Using a participatory action approach (PAR) the "Hep B Story" educational app was designed, translated (forward and back translation) launched in pilot language Yolŋu matha, and evaluated, with the process then repeated for the seven next most widely spoken NT Aboriginal languages.

Aim 2: Reviewing existing pathology and vaccination data from electronic health record systems, individuals in consenting health services were allocated to one of six Hepatitis B sero-status codes (Hep B: Fully vaccinated, Hep B: Immune by Exposure, Hep B: Infected ON Treatment, Hep B: Infected NOT ON Treatment, Hep B: Non-Immune, No data) triggering an appropriate follow-up response for all clients. To support primary care to manage recalls and follow ups as appropriate, we delivered Hepatitis B education to remote doctors, nurses, and Aboriginal Health Workers (AHWs). Using a PAR, a Hepatitis B management education course for AHWs was developed, delivered, and evaluated.

Results: The Hep B Story App is now available in English and eight Aboriginal languages spoken in the NT and roll out and evaluation is underway. All client files in participating health services have been reviewed, with approximately 30,000 Aboriginal clients allocated a Hepatitis B serocode and appropriate care pathway. Hepatitis B education has been delivered to over 150 general practitioners and nurses in the NT, and to approximately 100 AHWs. The cascade of care for those living with Hepatitis B in the NT has significantly improved, now exceeding National Hepatitis B Strategy Targets, with 90% allocated a serocode (national target = 80%), 61% engaged in care (national target = 50%), and 21% receiving antiviral treatment (national target = 20%)

Conclusion: This project is demonstrating the effectiveness of a partnership approach with communities, with AHWs at the centre of the care model, and creating a community led, culturally acceptable, in-language health promotion tool in improving client outcomes for CHB. The preliminary findings from the project demonstrate improvements in clinical care whilst preserving Aboriginal languages and empowering community through increased health literacy.

Disclosure of Interest: None Declared

P169

SCREENING FOR HEPATITIS B AND C VIRUS IN VULNERABLE CATEGORIES OF ROMANIAN POPULATION - UPDATED PREVALENCE DATA AND RISK FACTORS - PRELIMINARY RESULTS FROM LIVERO2-SUD PROJECT

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Background: Romania was considered over the last 15 years among the European country with the highest prevalence rates of HCV and HBV infection based on our previous reported HCV/HBV prevalence from the single nationwide cross-sectional study performed during 2006-2008.

Aim: To screen socio-economic vulnerable population in order to provide high-quality medical services for the prevention, diagnosis, and referral to treatment for HCV-Ab and HBsAg positive subjects, as well as to refresh the viral Hepatitis prevalence and risk factors in this high-risk population from the Southern and South-West part of Romania.

Method: Subjects from vulnerable categories as defined for the study purpose signed the informed consent and were consequently enrolled. Screening providers are family physicians (FPs) affiliated with the project that performed HCV-Ab and HBsAg rapid diagnosis tests in their office. Linkage-to-care and therapy will be further provided for all HCV and HBV-positive subjects. The project started on 28th of July 2021 (World Hepatitis Day) and will end-up in November 2023.

Results: Between 28th of July and 1st of October 2022, 102,915 subjects have been screened; 61.68% were females and 38.32% males with a median age of 54 years old and 79.4% of them living in rural areas. The overall prevalence of anti-HCV Ab was 0.91%, with a significantly higher prevalence among females (1.12%), over 60 years old (1.37%), from rural area (0.99%), unemployed (2.08%), Roma people (1.28%), widows (2.33%) and with only 1-4 classes of education (2.61%). The overall prevalence of HBsAg was 1.50%, with a significantly higher prevalence among males (1.85%), aged 30 to 39 years (3.37%), Roma people (2.44%), unemployed (7.14%), without any education or with 1 to 4 classes (5.78%, respectively 2.16%), divorced or single persons (2.09% , respectively 1.99%). The main transmission routes of HBV/HCV infections according to the risk factor questionnaire were interfamilial, imprisonment and beauty salons, as well as nosocomial infections through sanitary institutions (hospital, dental clinics or FPs praxis).

Conclusion: The burden of HCV/HBV infections is significantly lower compared to previous estimates even in this vulnerable high risk category of screened persons due to joint efforts of community (hepatology professionals, patient associations, civil society, media, and political will), good access to antiviral treatment, awareness campaigns, and increased screening including microelimination campaigns. Our results contribute to more objective data compared to modelling forecasting, as well as to development of national strategies to achieve the WHO elimination targets for 2030.

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Disclosure of Interest: None Declared

P170

REACH TO HARD-TO-REACH SILENT MAJORITIES - CHALLENGES, ISSUES AND APPROACHES WHEN WORKING WITH MIGRANTS IN RESOURCE RICH COUNTRY

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Background: Hepatitis B is a significant health issue among migrants in Australia. According to the Australian annual surveillance report on Hepatitis B 2021, of an estimated 222,559 people living with chronic Hepatitis B in Australia, 69.7% of them were born overseas.

Despite a good health system in Australia that can provide world-class Hepatitis B testing, care and treatment, the rates of diagnosis, care and treatment are still low as 73%, 23% and 11% respectively, due to the vast affected populations being migrants from non-English speaking backgrounds. Largely due to language and culture barriers that prevent them from accessing needed information and care.

Purpose: To raise awareness and increase testing, diagnoses, care and treatment for people living with chronic Hepatitis B in the migrant population.

Methods: We recruit and train bilingual community health workers (BCHW) to work with target migrant communities. BCHWs share the same langue, culture, and life experience and they are the best to deliver health information that can be well received and understood.

As the migrant population is complex with many different languages, cultures, education levels, visa statuses and English skills, and also our resources are limited, we prioritise target migrant communities based on several factors such as English proficiency, the number of people living with Hepatitis B, the size of the population so we can better use limited resources. A comprehensive approach is implemented to increase the reach of the interventions including face-to-face education, developing and distributing resources, promoting messages through social media and ethnic media, supporting people living with chronic Hepatitis B, and engaging and supporting health care providers who provide care to patients with Hepatitis B.

Results: We focus our efforts on areas with highly concentrated migrant populations that are most affected by Hepatitis B. After five years of effort, the rates of diagnosis, care and treatment have improved significantly based on the Hepatitis B Mapping Project Report that is conducted annually.

Conclusions: Our model is working to reach the migrant population from non-English speaking backgrounds using bilingual community health workers through a comprehensive approach.

Disclosure of Interest: None Declared

P171

HCV PREVALENCE AMONG PEOPLE WHO INJECT DRUGS IN GEORGIA (DATA FROM INTEGRATED BIO-BEHAVIORAL SURVEY, 2022)

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Background: Georgia has the high prevalence of injecting drug use. People who inject drugs (PWID) are at high risk for HCV transmission and represent the key population for HCV elimination program implemented since 2015 in the country.

Purpose: This study aimed to evaluate the prevalence of HCV infection and associated risk factors among PWID participating in Integrated Bio-Behavioral Surveillance Survey (IBSS) conducted in 2022.

Methods: The inclusion criteria were being ≥18 years and injecting illicit drugs during the last month. Respondent-driven sampling (RDS) was used to conduct a cross-sectional IBSS among PWID in seven cities of Georgia. Blood samples were collected to assess anti-HCV and HCV RNA prevalence. Socio-demographic data, history of drug use, drug use related risky behaviors, sexual practice, knowledge, attitude and practice regarding HCV, participating in preventive programs and social impact were studied using survey tool. Chi-square test was performed to find associations between HCV seroprevalence and associated risk factors. Binary logistic regression was performed to understand the independent predictors of HCV seropositivity.

Results: A total of 2005 PWID were surveyed and blood samples were collected. Majority of participants were male (98.6%) and >35 years old (78.3%). 58.7% were unemployed and 49.1% were married. More than half of respondents (58.1%, n=1164) were HCV seropositive. Anti-HCV (+) was higher among male (58.4% vs 35.7%; p<0.05) and older (68.4% vs 20.7%; p<0.001) PWID. Daily injection of opioids during the last 12 months was associated with anti-HCV prevalence (OR=1.72; 95% CI: 1.43-2.07). HCV seropositivity was 1.4 times higher among PWID having experience of using needles/syringes pre-used by others (75.9% vs 52.3%; OR=2.87; 95% CI: 2.28-3.61). HCV antibodies were found among 85.3% (n=198) of PWID who had injected drugs in prison versus 66.2% (n=229) of those who didn't have (OR=2.97; 95% CI: 1.94-4.55). By multivariate analysis age (>35), daily injection of drugs during the last 12 months, using pre-used syringes and injecting drugs in prison were independent predictors of anti-HCV positivity. Chronic HCV was documented among 32.1% of anti-HCV positive PWID.

Conclusions: HCV seroprevalence among PWID in Georgia is high. Despite the fact that Georgia is implementing HCV elimination program since 2015 one third of PWID are still HCV RNA positive. Using pre-used syringes and injecting drug use in prisons are the major risk factors of HCV infection.

Disclosure of Interest: None Declared

P172

DIRECT-ACTING ANTIVIRAL EXPOSURE IN PREGNANCY: INITIAL FINDINGS FROM THE "TIP-HEPC" CLINICAL CASE REGISTRY

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Abstract Content: Background: About 20% of HCV infections worldwide are in women of childbearing age. Increased antenatal screening in many countries will lead to greater numbers of pregnant persons diagnosed with HCV. However, guidance for HCV treatment for persons diagnosed during pregnancy is limited, and post-partum linkage to treatment is extremely poor. Currently, data assessing the safety of direct-acting antiviral (DAA) exposure during pregnancy are scarce. Pregnancy and infant outcomes after DAA exposure are not systematically reported, and only one phase II trial has been completed. The TiP-HepC registry was launched in June 2022 as the first global registry for DAA exposures in pregnancy.

Methods: Clinicians reported outcomes of maternal-infant pairs exposed to DAAs during pregnancy to the registry through a secure web-based portal. Patients exposed to interferon or ribavirin were excluded. Primary adverse pregnancy outcomes were preterm delivery (<37 weeks GA), stillbirth or fetal demise, and maternal death. Primary adverse birth outcomes were low birth weight (<2500g, LBW), small for gestational age (SGA), neonatal intensive care, and congenital anomalies. Descriptive analysis was conducted for cases through October 31, 2022.

Results: To date, 23 case reports were submitted, all from the USA. 20 (87%) were purposefully treated after the 1st trimester, of which all were previously published, and 9 were part of a clinical trial. Of these 20, 10 (50%) reported injection drug use in the past 12 months, and median gestational age at treatment initiation was 187 [158-270] days. 14 (70%) were treated with sofosbuvir/ledipasvir and 6 (30%) with sofosbuvir/velpatasvir (SOF/VEL). 16 (80%) completed treatment, and 13 (65%) had HCV cure. There were 14 (70%) full-term births, 4 (20%) pre-term births, and 2 (10%) unknown birth outcomes. Among 18 infants with data, 7 had NICU admission at birth (4 with neonatal abstinence syndrome), 1 LBW, and none had SGA or congenital anomalies.

Among the 3 cases with 1st trimester DAA exposure, 2 received glecaprevir/pibrentasvir and 1 SOF/VEL; all 3 completed treatment. Outcomes were available for 1 case, which was a live full-term birth with no adverse pregnancy or infant outcomes.

Conclusions: The TiP-HepC registry provides timely and valuable real-world data on pregnancy and birth outcomes following exposure to DAAs in pregnancy. For HCV elimination, data are needed to guide safe and reliable HCV treatment pathways to improve outcomes among maternal-child dyads. In complement to much needed phase III trials, further accrual of case reports to the TiP-HepC registry will better inform shared decision-making by patients and providers on the optimal approach to HCV in pregnancy.

Disclosure of Interest: None Declared

P173

GLOBAL, REGIONAL, AND COUNTRY-LEVEL COVERAGE OF TESTING AND TREATMENT FOR HIV AND HEPATITIS C INFECTION AMONG PEOPLE WHO INJECT DRUGS: A SYSTEMATIC REVIEW

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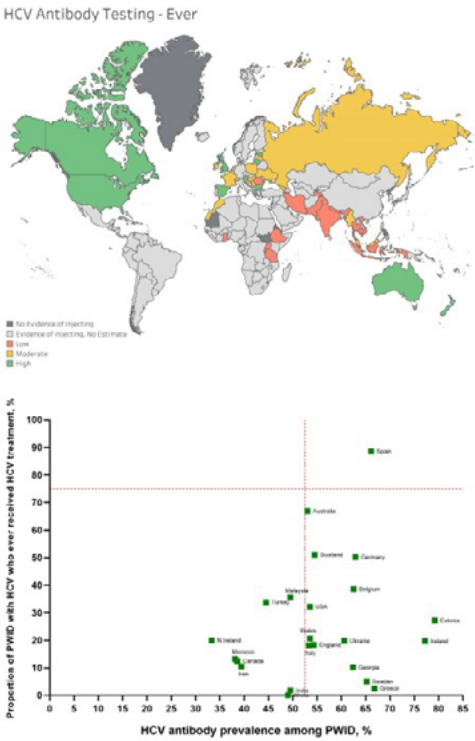
Background: People who inject drugs (PWID) are disproportionately affected by HIV and Hepatitis C virus (HCV) infections in most countries. Global data on HIV and HCV testing and treatment coverage among PWID are limited. We conducted a systematic review to evaluate country-level, regional, and global coverage of HIV and HCV testing and treatment among PWID.

Methods: We searched bibliographic databases (MEDLINE, Embase, PsycINFO) and grey literature for studies, published until April-2022, that evaluated the proportion of PWID who received testing or treatment for HIV or HCV. For each country, we estimated the proportion of PWID tested for HIV antibody in the past 12 months (recent), and those ever tested for HCV antibody and HCV-RNA. We also estimated the proportion of PWID with HIV currently receiving antiretroviral therapy, and those with HCV ever receiving HCV antiviral treatment. Regional and global estimates, weighted by PWID population size, were generated where sufficient data were available.

Findings: Data of recent HIV antibody testing and ever HCV antibody testing were available for 67 and 47 countries, respectively. Globally, we estimated that 53% of PWID were recently tested for HIV antibody [uncertainty interval (UI): 48-58%; range: <1-86%], and 46% had ever tested for HCV antibody (UI: 41-53%; range: <1-93%). HCV RNA testing data were available from three countries. Coverage of HIV antibody and HCV antibody testing was >75% in five and 14 countries, respectively. Estimated uptake of current HIV treatment (18 countries) ranged from 3% to 82% across countries. Estimated uptake of ever HCV treatment (23 countries) ranged from 2 to 89% across countries. Uptake of HIV and HCV treatment was >75% in two and one countries, respectively.

Conclusion: HIV and HCV testing and treatment uptake among PWID was highly variable, and sub-optimal in most countries. Strategies to improve access to HIV and HCV care among PWID and availability of public health surveillance are urgently required.

Image/Table:



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P174

EXPERIENCES OF RAPID POINT-OF-CARE HEPATITIS C TESTING IN A COMMUNITY SETTING

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Background: In Australia, venepuncture is required to diagnose and treat Hepatitis C. Venepuncture is a recognised barrier to diagnosing people who inject drugs because of the frequency of (a) challenging venous access and (b) prior experiences of discrimination. Rapid point-of-care tests use fingerprick samples to provide antibody results in 20 minutes (OraSure®) and RNA results in 60 minutes (GeneXpert®).

Purpose: We explore nurses' preliminary experiences implementing rapid testing in people who inject drugs, considering the feasibility and acceptability of a rapid testing approach in this population.

Methods: QuickStart is a randomised controlled trial of nurse-led care using point-of-care testing to improve Hepatitis C diagnosis and treatment rates among people who inject drugs in community settings (NCT05016609, clinicaltrials.gov). Qualitative experiences of nurses engaged in the study can provide crucial insights into point-of-care test administration, implementation and acceptability among people who inject drugs.

Results: First, nurses observed that participants were willing to wait on site for rapid antibody test results (20 minutes). However, participants typically declined to wait for rapid RNA results (60 minutes), which inhibited delivery of results at the "point-of-care". Second, the OraSure® rapid antibody test results provided a valuable visual engagement tool. This increased willingness to consent to venepuncture to confirm Hepatitis C status. Third, OraSure® rapid antibody tests require minimal specialised equipment and skills once training has been completed. The portability of OraSure® rapid tests also means that they have been easy for nurses to transport and store at study sites.

Conclusions: People who inject drugs are a key population driving Hepatitis C transmission in Australia. Engaging and retaining this population in care is paramount for realisation of Hepatitis C elimination targets. Nurses in the QuickStart study found rapid point-of-care results to be a valuable visual tool to aid participant engagement in testing and care.

QuickStart is funded by an NHMRC clinical trials grant with support from an investigator initiated research grant from Gilead.

Disclosure of Interest: None Declared

P175

DISTRIBUTION OF DRUG PARAPHERNALIA IN GERMANY IN 2021 AND CHANGES SINCE 2018 – SECOND ROUND OF A CROSS-SECTIONAL STUDY TO ASSESS THE CURRENT STATUS TOWARDS ACHIEVING THE WHO ELIMINATION TARGETS FOR VIRAL HEPATITIS

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Introduction: One of the World Health Organization (WHO) Hepatitis targets related to harm reduction recommends the distribution of 300 sterile needles and syringes per person who inject drugs (PWID) annually by 2030 to prevent the transmission of blood-borne infections. We aimed to measure this target and the type and quantity of distributed drug paraphernalia in Germany in 2021 and to assess changes to a previous cross-sectional study from 2018. This evidence will inform harm reduction programs in Germany.

Methods: This second cross-sectional survey among low-threshold drug centres in Germany was conducted from March to August 2022. We assessed the type and quantity of distributed drug paraphernalia, and the number of PWID who were served in 2021 via an online and paper-based questionnaire. The questionnaire was distributed to low-threshold services in a researched comprehensive database and via newsletters and the project homepage (snowballing). We conducted a descriptive statistical analysis of cross-sectional data from 2021 and estimated progress towards the WHO target for participating centres in 2018 and 2021.

Results: Of 1760 distributed questionnaires plus snowballing, 534 were returned (estimated response rate 30%) in 2021. This results in 204 drug centres from 15/16 federal states confirming drug paraphernalia distribution and covers 21% of Germany's rural and 48% of urban counties; 108 of these centres had also participated in 2018. The most commonly distributed paraphernalia for injecting drug use in 2021 were syringes (97%), needles (96%) and vitamin C (90%). Drug paraphernalia for inhalant use, such as pre-cut aluminium foil (79%) and pipes (28%), and for nasal use, e.g. sniff-tubes (43%), were distributed less frequently. We found a decrease in the median number of distributed syringes and needles per supplied PWID: centres participating both 2018 and 2021 distributed 159 needles and 102 syringes per PWID in 2018, compared to 100 needles and 73 syringes in 2021. Among the responding centres in 2021, on average 127 needles and 84 syringes per PWID were distributed. In 2021, 2/15 federal states reached the needle target and 1/15 reached the syringe target for 2030.

Conclusion: The current national estimates for drug paraphernalia distribution in both 2018 and 2021 seem far from meeting the WHO target. Reasons for this could be a change in drug consumption behaviour towards fewer people injecting drugs, and more inhalant/nasal use, or could be the effects of the COVID-19 pandemic (supply difficulties, social distancing, lockdowns, and reduced opening hours of centres). We observed pronounced regional differences in adequately supplied PWID. To address this deficit, Germany needs to expand drug paraphernalia distribution programs, and other harm reduction services, e.g., drug consumption rooms. Further investigation of determinants of adequate distribution is essential to reduce blood-borne infections in this key population.

Disclosure of Interest: None Declared

P176

HEPATITIS B VACCINATION STATUS AND ATTITUDE TOWARDS THE VACCINE AMONG PEOPLE WHO INJECT DRUGS, INTEGRATED BIO-BEHAVIORAL SURVEY 2022, GEORGIA

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Background: Hepatitis B is responsible for significant global disease burden and mortality despite the availability of safe and highly effective preventive vaccine. People who inject drugs (PWID) are at high risk of contracting and spreading HBV infection due to risky injection and sexual practices. Georgia is a country with intermediate to high burden of Hepatitis B. The country has one of the highest rates of injection drug use in the world (national prevalence estimates for injection drug use is 2.24% in 18-64 years old population). Since 2000, Georgia incorporated HBV vaccine into routine immunization schedule for infants. While progress has been made in HBV vaccination coverage rates in infants, this indicator is still low among adult population, especially in high-risk groups, including PWID.

Purpose: This study was conducted to determine Hepatitis B vaccination status and attitude among PWID in Georgia.

Methods: Integrated bio-behavioral surveillance survey was conducted among PWID in seven major cities of Georgia in 2022. Study design was cross-sectional, using Respondent Driven Sampling method. In total 2005 PWID were enrolled. Data were collected through individual, face-to-face interviews using a structured questionnaire.

Results: Only 7.5% of the respondents reported that they received vaccine against Hepatitis B, of which 63.6% were vaccinated at medical facility, 20.5% - in prison and 9.9% - abroad. Among unvaccinated PWID only 27.8% expressed their willingness to get HBV vaccine. Of those study participants treated for chronic Hepatitis C within the National HCV Elimination Program (which includes free Hepatitis B vaccination) only 10.6% were vaccinated against Hepatitis B. Statistically significant association was found between Hepatitis B vaccination status and age, as younger PWID (≤35 years) were less likely to be vaccinated compared to older ones (4.4% vs 8.4%; OR 0.5; 95%CI 0.3-0.8; p=0.005). Level of education was associated with the attitude towards HBV vaccination. Lower proportion of PWID with lower level of education (24.9%) were willing to get HBV vaccine compared to those with higher level of education (32.5%) (OR 0.7; 95%CI 0.5-0.9; p<0.005).

Conclusions: Vaccination coverage for Hepatitis B and willingness to get HBV vaccine is significantly low among PWID in Georgia. Educating PWID about importance of HBV vaccine and introduction of vaccination for Hepatitis B at harm reduction centers and opioid substitution therapy clinics will increase the coverage of HBV vaccination. In addition, HCV elimination program providers should be instructed/recommended to improve HBV vaccination rates among the program beneficiaries, especially among high-risk individuals such as PWID.

Disclosure of Interest: None Declared

P177

OPTIMIZING LINKAGE TO HEPATITIS C VIRUS (HCV) CARE FOR UNTREATED INDIVIDUALS RELEASED FROM CANADIAN PROVINCIAL PRISONS: INTERIM ANALYSIS OF THE BEYOND PRISON WALLS STUDY

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Background: More than half of the Canadian provincial prison population is sentenced for less than one month, meaning that many living with chronic Hepatitis C virus (HCV) are released into community untreated. Given numerous competing priorities following release, only 15% are linked to HCV care post-release from Quebec provincial prison, underscoring the need for new models of care to optimise linkage to care.

Purpose: We evaluated the impact of an evidence-informed prison-based multidisciplinary model of care in the largest provincial male prison in Quebec, l'Établissement de détention de Montréal, on linkage to HCV care following community re-entry.

Methods: We conducted a prospective, single arm study; men aged > 18 years and sentenced between 2-12 weeks were approached to participate. Participants underwent nurse-led point-of-care HCV-antibody (HCV-Ab) testing via the fingerprick OraQuick® test. HCV-Ab+ individuals immediately underwent confirmatory HCV RNA testing via venipuncture. HCV RNA+ individuals were assessed by a social worker, who performed a needs assessment and provided community referrals upon release, and a patient navigator, who scheduled a post-release HCV appointment, made reminder phone calls, and accompanied participants to their first appointment. The primary outcome was linkage to care, defined as the proportion of released individuals who presented for an HCV clinical assessment within 30 ("early linkage") or 90 days ("delayed linkage") from release. Secondary outcomes included the proportion of released individuals who (1) initiated direct-acting antivirals (DAAs); (2) completed DAAs; and (3) achieved sustained virologic response (SVR) (obtained through provincial electronic medical records).

Results: From January 7, 2020 to December 1, 2022, 2022 (interrupted by the COVID-19 pandemic), 423 incarcerated individuals were approached, of whom 313 (74%) agreed to participate. A total of 31 (10%) were HCV-Ab+, among whom, 13 (42%) were HCV RNA+. Median age of those with chronic HCV was 49 years; nine (69%) self-identified as White and six (46%) reported injection drug use in the week prior to incarceration. Four (31%) reported unstable housing and seven (54%) reported an annual income of less than $30,000 CAD. Five (38%) reported a history of a mental health disorder and four (31%) reported having a primary care physician. Of the 10 who were released from prison, six (60%) were linked to care, four within 30 days and two within 90 days of release. Of these, five (83%) initiated and completed DAAs and, among the two with available RNA testing 12 weeks post-DAA completion, 2 (100%) achieved SVR.

Conclusions: A multidisciplinary model of care, which includes patient navigation, increased linkage to HCV care by approximately five-fold among untreated individuals released from provincial prison. Public policy should support similar models of care to promote linkage to care and treatment uptake in this high-risk population.

Disclosure of Interest: None Declared

P178

EVOLUTION IN REAL-WORLD DATA (RWD) STUDIES DEMONSTRATE HIGH SOFOSBUVIR/VELPATASVIR (SOF/VEL) EFFECTIVENESS IN DIVERSE GLOBAL POPULATIONS OVER TIME

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Background: HCV is curable with currently available therapies. SOF/VEL was approved in 2017 with clinical trials demonstrating sustained virological response (SVR) rates >95% across all HCV genotypes with or without compensated cirrhosis. Real-world studies have confirmed similar effectiveness. Data generation has evolved to address changing HCV patient profiles (from end-stage liver disease to vulnerable populations with early disease) and global therapeutic objectives (from patient cure to HCV elimination).

Purpose: Evaluate how RWD studies of SOF/VEL are evolving to focus on emerging clinical questions, and demonstrate treatment effectiveness in specific populations to meet the needs of HCV patients over time.

Method: SOF/VEL effectiveness was evaluated in 3 waves of RWD studies that adapted to evolving patient profiles and global objectives: Wave 1 (Mangia et al. Liver Int 2020), Wave 2 (Rosati et al. Future Virol 2022; Conway et al. Future Virol 2022; Wedemeyer et al. Viruses 2022), Wave 3 (ongoing SVR study).

Results: Wave 1 involved 5,552 HCV patients (12 cohorts, 7 countries in Europe, Canada, USA). 98.9% achieved SVR at 12 or 24 weeks after treatment with once daily oral SOF/VEL without ribavirin. The findings reflected patients seen in routine clinical practice: 13% treatment-experienced, 21% compensated cirrhotic, various genotypes, 13% current/former IV drug use, 4% HIV coinfection. Analyses also included fibrosis status, treatment history, IV drug use, and use of proton-pump inhibitors.

Wave 2 focused on high-risk vulnerable populations, HCV patients who were incarcerated, unstably housed, and/or diagnosed with mental health disorders. This included 1,888 HCV patients in 9 countries (EU, Canada, USA, Australia). SOF/VEL SVR12 rates ranged from 97% to 100%; adherence rate was 99%. Treatment initiation (time from positive RNA to SOF/VEL initiation) in the first month ranged from 24% in patients with mental health disorders to 60% in unstably housed patients. Antipsychotic medication use ranged from 12% in incarcerated patients to 30% in patients with mental health disorders.

Wave 3 is represented by an ongoing RWD study aggregating data from >10,000 HCV patients. Geographic scope extends to Asia, Nordics, Latin America, and Middle East to close the gap in worldwide representation. Variables relevant to today's landscape include COVID-19 coinfection and medications, and HCV management using telehealth. Outcomes will be presented at the meeting.

Conclusion: RWD studies of SOF/VEL have adapted over time to show treatment value irrespective of changing HCV patient profiles. SOF/VEL's effectiveness in multiple real-world cohorts reassures us of generalizable benefit beyond clinical trials.

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P179

THE IMPACT OF A SPECIALIST OUTREACH SERVICE ON THE HEPATITIS B CARE CASCADE IN INCLUSION HEALTH POPULATIONS IN LONDON

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Background: Almost 300 million people are living with Hepatitis B virus(HBV) globally, resulting in 0.8 million annual deaths. Around 9% are diagnosed, and numbers linked-to and engaged-in care are unknown. Find & Treat(F&T) are a specialist community outreach service, pioneering a peer-led model of care to screen, vaccinate and link-to-care(LTC) people who experience multiple social exclusions and barriers to accessing health services, known as inclusion health(IH) populations.

Purpose: We evaluate F&T HBV screening service and share our vision of future IH HBV care.

Methods: F&T provide on-site infection screening across London, including hostels for people experiencing homelessness(PEH), Covid hotels(emergency accommodation for PEH) and initial assessment centres(IACs, temporary accommodation for people seeking asylum). A person positive for HBV surface antigen(HBsAg) is offered an on-site fibroscan and peer-supported specialist referral. We retrospectively review HBV LTC(engagement with specialist care) and loss to follow up(LTFU, no engagement for 1 year). Data were collected using electronic patient records and contacting specialists. Analysis was performed on GraphPad(Fisher's Exact Test). Written consent was given to share data for care and research.

Results: Between May20-January22, F&T screened 955 people in hostels, 809 in IACs, 359 in Hotels, 39 on home visits and 311 elsewhere. HBsAg prevalence was 1.7%(43/2473), highest in IACs(3.5%,28/809). 86%(37/43) were males and most common countries of birth were Sudan(30.2%,13/43) and Romania(11.6%,5/43). 25.6%(11/43) did not receive a HBV work-up. Variable numbers had further tests: 38.7(12/31) HBVDNA >2000 IU/ml, 50%(15/30) abnormal liver function tests, 18.5%(5/27) F3/4(severe fibrosis/cirrhosis) on transient elastography and no liver cancer on US(0/21). 72.1%(31/43) were LTC, but only 58.1%(25/43) within 3 months. 46.5%(20/43) were LTFU:45%(9/20) due to health-system factors, 40%(8/20) patient factors and 15%(3/20) unknown. 60%(12/20) of those LTFU did not achieve LTC. IAC groups had greater 3-month LTC (67.9%,19/28 vs 40%,6/15,p=0.11) and worse LTFU(53.6%,15/28 vs 46%,7/15,p=0.75) than non-IAC.

Conclusion: HBV is an important health concern for IH populations. Although small numbers, we highlight challenges of LTC and LTFU even in specialist services. LTFU is multifactorial, compounded by moving people in IACs long distances at short notice. Much LTFU occurred before LTC, therefore we suggest same-day evaluation, specialist referral pathways and peer support, especially for IAC groups facing unique challenges. Further research is needed to support innovations, such as point of care viral load and digital portable health records, to improve HBV care in IH.

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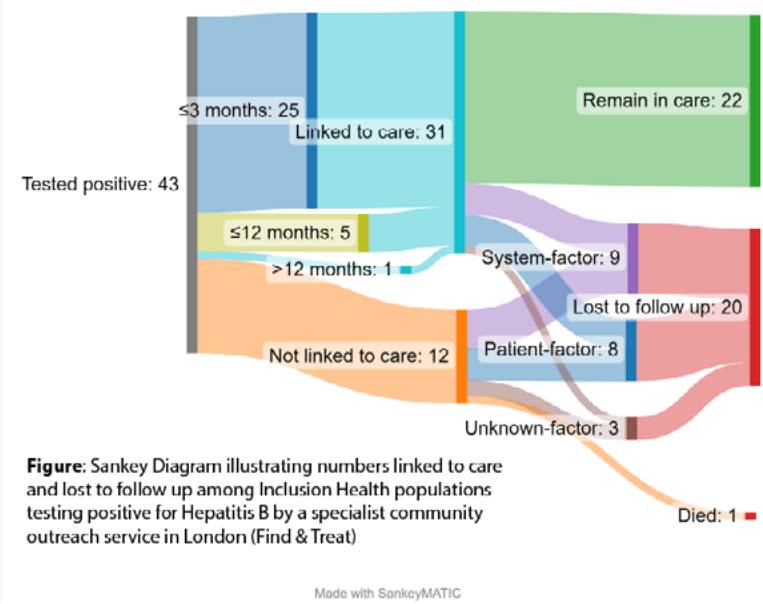

Figure: Sankey Diagram illustrating numbers linked to care and lost to follow up among Inclusion Health populations testing positive for Hepatitis B by a specialist community outreach service in London (Find & Treat)

Disclosure of Interest: None Declared

P180

HEALTH CARE WORKERS' REACTIONS TO THE NEWLY INTRODUCED HEPATITIS B VACCINE IN KALULUSHI, ZAMBIA: EXPLAINED USING THE 5A TAXONOMY

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Introduction: Hepatitis B virus (HBV) is a highly infectious and deadly disease transmitted through blood and body fluids. Healthcare workers (HCWs) have a high risk of contracting HBV in healthcare settings, the HBV vaccine one of the recommended prevention interventions/tools. However, the uptake of the vaccine among HCWs remains low in Sub-Saharan Africa. We aimed to explore the barriers and facilitators to uptake of the vaccine offered free of charge to HCWs and nursing students in Kalulushi district, Copperbelt Province of Zambia

Methods: A total of 29 in-depth interviews (IDIs), either in person or via telephone, with participants before and after they received the vaccines were used to collect the data. We analysed the barriers and facilitators to full or partial vaccination using Penchasky and Thomas's (1981) 5As (Access, Affordability, Awareness, Acceptance and Activation) taxonomy framework for vaccine hesitancy.

Results: All participants had access to the vaccine, and it was free of charge, making it affordable. Regarding awareness, all participants were aware of HBV infection as an occupational hazard, however, HCWs felt that more sensitization would be needed to increase awareness and knowledge of the vaccine. Acceptability of the vaccine was high among all completers and some non-completers as they felt it was safe and offered them protection. One non-completer felt coerced to accept the first dose due to supervisor expectations and would have preferred to have been given more time to decide. Most felt that vaccination should be compulsory for HCWs. Lastly, activation (vaccine uptake) among non-completers was hindered by late or no notification of appointments as the main reason for not completing the full vaccination schedule. HCWs advised that for countrywide roll-out, at least one week's notification would be necessary for HCWs to plan and be mentally prepared to be at their workstations when the vaccination is taking place.

Conclusions: The need to offer the vaccine free of charge locally to ensure easy access and affordability is essential to increase vaccine uptake. Vaccination policies and guidelines for health workers, ongoing training and knowledge sharing are required. Involving trained champions in the facility can also help encourage HCWs to get vaccinated.

Disclosure of Interest: None Declared

P181

HEPATITIS B AND C AMONG PEOPLE WITH DISABILITIES: A SEROPREVALENCE STUDY IN BURKINA FASO, A WEST AFRICAN COUNTRY

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Background: Several studies have indicated that people with disabilities are vulnerable to HIV/AIDS. HBV and HCV share the same routes of transmission as HIV, however, few studies have focused on the epidemiology of these infections among people with disabilities. This study aimed to estimate the prevalence of Hepatitis B and C viruses and associated factors among people with disabilities in Burkina Faso.

Materials and methods: We analyzed serum samples from people with disabilities recruited in a cross-sectional HIV seroprevalence study conducted from September to October 2017 in the Centre, Centre-West, Centre-East and Hauts-Bassins regions of Burkina Faso. People with disabilities were identified in households using the Washington Group Questionnaire, and consenting individuals were asked to complete a behavioral questionnaire, followed by a blood sampling. Archived serum samples were then tested in the laboratory for HBsAg and HCV antibody. Data were analyzed using Stata 15 software.

Results: A total of 864 serum samples from persons with disabilities were tested for HBsAg and anti-HCV antibody. HBsAg prevalence was 7.3% among disabled persons, and varied from 5.6% to 13.7% according to region. HCV antibody prevalence was 3.1% in the study population and ranged from 0.5% in the center to 7.8% in the center-west ($p<0.05$). Being female was associated with a reduced risk of being HBV positive, compared with being male among people with disabilities (OR=0.54, p=0.03). Compared to people with disabilities who were members of a disability advocacy organization, those without a disability advocacy organization were 4 times more likely to be HBV positive (OR=4.07, p=0.05). Unlike HBV, only region of residence was associated with HCV carriage among people with disabilities. People with disabilities from the Centre-West, Centre-East and Hauts-Bassins regions were more likely to be HCV carriers than those from the Centre region.

Conclusion: This study shows that beyond the high prevalences of HBV and HCV among people with disabilities in Burkina Faso, disparities are also found between regions for HCV, probably due to risky practices that further studies could confirm.

Key words: People with disabilities, HBsAg, HBV, HCV, seroprevalence.

Disclosure of Interest: None Declared

P182

PREVALENCE OF HEPATITIS B AND C, HIV, AND SYPHILIS AMONG PEOPLE WHO INJECT DRUGS RECRUITED VIA LOW-THRESHOLD DRUG AND OPIOID SUBSTITUTION SERVICES IN BERLIN AND BAVARIA, GERMANY

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Background: We piloted a future surveillance system among people who inject drugs (PWID) in two federal states of Germany (DRUCK2.0). Surveillance of prevalence and behavioural data for this key population is needed to provide regular up-to-date data that supports the viral Hepatitis/HIV/STI elimination process in Germany.

Methods: PWID aged 16+ years who injected drugs within the last 12 months were recruited by the staff of low threshold drug services and opioid substitution treatment (OST) practices during routine services in Berlin and Bavaria between 01/06/2021 and 28/02/2022. Participation included a questionnaire on sociodemographics, behaviour and access to care and testing for Hepatitis B and C (HBV, HCV), HIV and syphilis using capillary dried blood spots (DBS) or venous blood. All participants received a ten Euro incentive voucher. For evaluation group discussions were performed with staff and study participants, and an evaluation form was sent out to the recruiting facilities at the end of the study.

Results: In total, 596 PWID were included, median age was 39 years [range 17-66], 68% (404/595) were male, and 22% (131/596) born outside Germany, mostly in eastern Europe. Of all participants, 14% (66/487) reported recent use of unsafe needles/syringes and 77% (451/585) detention experience. Current OST was reported by 61% (357/582). Prevalence was 46% (272/588) for cured HCV, 27% (160/591) for active HCV, 17% (99/583) for cured HBV, 1.2% (7/584) for active HBV, 2.4% (14/590) for HIV and 1.7% (10/584) for previous Syphilis. Neither serological evidence of previous or active HBV infection nor isolated anti-HBs above detection threshold (>210IU/l for DBS and 10IU/l for venous blood) was found in 57% (331/579) of participants. HCV and HIV testing during the last 12 months was reported by 61% (354/581), respectively 55% (318/579). Of those with cured/active HCV infection, 84% (358/425) of participants knew about their infection and 56% (196/353) reported previous/current treatment. For HIV infection, 85% (11/13) knew about their infection and were treated. Motivation among participants to take part in the pilot study were the incentive vouchers as well as the testing opportunity. Staff reported the study questionnaire to support the health counselling of their clients. Of the facilities, 73% were willing to participate in a future surveillance system.

Conclusion: To decrease the heavy burden of infections among PWID in Germany, targeted measures regarding access to HCV treatment, HBV vaccination, and harm reduction (safer use measures, OST) need to be enhanced. The results of this pilot study showed that surveillance of infectious diseases via low threshold and OST services is feasible. We recommend a nationwide roll-out to guide the elimination progress of viral Hepatitis and HIV in Germany.

Disclosure of Interest: None Declared

P183

AN EXAMPLE OF HCV MICRO-ELIMINATION AMONG HIV/HCV CO-INFECTED PATIENTS IN ISFAHAN VCT CENTER, I.R.IRAN

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Background: The launch and advancement of antiretroviral therapy (ART) has significantly decreased the mortality rates among people living with HIV/AIDS (PLWHA) worldwide and transformed HIV/AIDS from a lethal disease to a chronic manageable condition. Since HIV and HCV have similar transmission routes, especially via IV drug using, coinfections are common in PLWHA and can lead to long-term morbidity and mortality; more than any single virus alone. HIV infection can accelerate the course of Hepatitis C, manifesting a faster progression to fibrosis and cirrhosis. Due to high prevalence of HCV infection among PLWH with history of drug use, this group are one of the most eligible patients for treating HCV.

Purpose: Because of access to PLWH in VCT centers, there is a chance of fully diagnosing and treating Hepatitis C, and can think about the elimination of Hepatitis C among them. We conducted diagnosis and treatment of HCV among identified PLWH in one of the main VCT centers of Iran, Isfahan, in order to eliminate HCV among the, an example of HCV micro-elimination in a high risk group.

Method: This study was done in Isfahan VCT center. HCV Ab ELISA test was done for all identified PLWH as a routine test and in the following qualitative HCVRNA nucleic acid test were done for HCV positive patients to diagnose viraemic infection. All PLWH who were eligible for HCV treatment, were under anti-retroviral therapy and two pan-genomic DAA regimen were considered including Sofosbovir + Dactalasvir and Sofosbovir + Velpatasvir for 3 to 6 months. Three months after completion of direct-acting antiviral (DAA), qualitative HCVRNA nucleic acid test was done for patients for evaluating treatment response.

Result: 134 out of 363 PLWH identified as HCV Ab positive in Isfahan VCT center that 119 of were actively linked to VCT centers. 82 PLWH needed treatment and rest of them were HCV PCR negative (31%). All treatted patients tolerated DAA without interruption. The response rate to treatment (three months after the end of treatment) was more than 94%. Three patients received second course of treatment and virally suppressed.

Conclusion: Hepatitis C treatment is very important among HIV/HCV co-infected individuals, and this group is one of the important populations that can be well treated due to access to the patients in the HIV care centers and possibility of follow-up. DAA are well tolerated and effective among PLWH. Even in small scale, HCV treatment can be considered for micro-elimination of HCV among high risk population.

Disclosure of Interest: None Declared

P184

HEPATITIS A VIRUS INFECTION AMONG TRANSGENDER WOMEN IN GOIÁS, CENTRAL BRAZIL: A CROSS-SECTIONAL STUDY

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Abstract Content: Hepatitis A virus (HAV) is transmitted predominantly by fecal-oral mode. Therefore oro-anal sex is a risk factor for HAV acquisition, and some LGBTIQA+ groups are at high risk for this infection, such as men who have sex with men (MSM) and transgender women (TGW). Brazil is considered a region of intermediate endemic for Hepatitis A virus (HAV). Therefore, cases of Hepatitis A occur more frequently among adults. We estimated the prevalence of Hepatitis A among transgender women (TGW) in Central Brazil. A Cross-sectional study was carried out among 440 TGW between 2018 and 2019 in three cities in Goiás (Goiânia, Itumbiara, and Jataí), Central Brazil. Respondent Driven Sampling recruited them. The Institutional Ethics Committee approved this study for Human Research of the Universidade Federal de Goiás (protocol number 77481417.5.0000.5083). All women were interviewed through a structured questionnaire and were tested for anti-HAV IgG and anti-HAV IgM by enzyme immunoassay (ELISA). RDS v. 7.1.76 was used to generate prevalence estimates with a 95% confidence interval. Pearson's chi-square test and Fisher's exact test were used to identify variables associated with anti-HAV IgG. Those associated with the outcome at < 0.20 were included in the multivariate logistic regression model (p-value < 0.05 were considered statistically significant). TGW were young (median age: 25 years; IQR: 9) and had low education (median time of education: 11 years; IQR: 2. Most self-declared black or brown (71.6%) and single (82.7%). The anti-HAV prevalence was 74.8% (95% CI: 68.5-80.8), ranging from 61.7% (95% CI: 48.2% – 73.3%) among TGW under 22 to 91.3% (95% CI: 83.9%-93.9%) among those aged between 26 and 30 (p <0.01). One woman aged 21 years was anti-HAV IgM positive. She reported the non-use of condoms during oral sex. TGW aged 26-30 were 14.3 times more likely to have had previous contact with the virus. Those with less than ten years of formal education were 11 times more likely to be positive for anti-HAV IgG. Despite not being statistically significant, some risky sexual deserve attention, such as the high frequency of active oroanal sex 42.7% (95% CI: 35.8%-50.2%), receptive oroanal sex (77.6%: CI 71.9%-83%), and non-use of condoms in the last sexual intercourse (37.3%; 95% CI: 30.3%-44.4%). Our findings show a window of opportunity to acquire HAV among TGW. About 40% of TGW aged under 22 years were HAV susceptible and most of them have sexual practices that put them at risk of Hepatitis A. It highlighted the importance of Hepatitis A vaccination among young TGW until the cohort of vaccinated children reaches adolescence.

Disclosure of Interest: None Declared

P185

HIV SERVICES ARE A MAJOR OPPORTUNITY TO ADDRESS VIRAL HEPATITIS: LEARNINGS FROM A DEMONSTRATION PROJECT IN VIETNAM

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Background: Vietnam estimates 8.8 million people living with Hepatitis B (HBV) and Hepatitis C (HCV); however, 80%-90% infected people remain undiagnosed and 95% of treatment-eligible people remain untreated. PATH and Vietnam's Ministry of Healthimplemented the HepLINK initiative funded by The Hepatitis Fund.

Purpose: HepLINK aimed to demonstrate an integrated model to address viral Hepatitis through HIV services targeting key populations (KPs), i.e., people who inject drugs (PWID) and use drugs (PWUD), men who have sex with men (MSM), female sex workers (FSW), and transgender women (TGW) in Vietnam.

Methods: We engaged 9 KP-led community-based organizations and 18 clinics providing community HIV testing, pre-exposure prophylaxis (PrEP), antiretroviral therapy (ART), and methadone maintenance treatment (MMT) in Hanoi and Ho Chi Minh City. These sites offered rapid HBV/HCV testing and linkage to confirmatory testing and treatment.

Results: From April 2021-July 2022, we reached 22,940 people, of whom 87.1% accepted HBsAg testing, yielding a 7.9% positivity rate. Of 1,572 HBsAg+ people, 47.8% were evaluated for treatment eligibility and 78.8% of those eligible enrolled on HBV treatment, ART and PrEP with tenofovir. HBV infection rate was highest in FSW (14.2%), followed by PWID (10.7%), PWUD (6.9%), MSM (5.2%), and TGW (3.6%). HBV-HIV co-infection rate was 7.8%. HBV positivity was significantly associated with age of clients at 25-49 years old (aOR = 1.50 [1.23-1.84]) and 50+ years old (aOR = 2.61 [2.01-3.39]); using community-based testing (aOR = 1.82 [1.57-2.11]); being PWID (aOR = 1.25 [1.02-1.54]), FSW (aOR = 2.19 [1.61-2.97]), MSM (aOR = 1.32 [1.07-1.63]), or PLHIV (aOR = 1.68 [1.14-2.46]); and not being HBV vaccinated (aOR = 3.26 [2.50-4.25]).

Among 22,940 people reached, 88.2% accepted anti-HCV testing, yielding a 12% positivity rate. Of 2,420 anti-HCV+ people, 53.0% received confirmatory testing, and 84.5% of those confirmed initiated HCV treatment. HCV infection rate was highest in PWID (13.3%), followed by PWUD (5.8%), FSW (3.8%), and MSM and TGW (1.4%). HCV-HIV co-infection rate was exceptionally high (27.4%). HCV sero-positivity was significantly associated with age of clients at 25-49 years old (aOR = 1.94 [1.48-2.54]) and 50+ years old (aOR = 2.23 [1.65-3.02]); using facility-based testing (aOR = 6.67 [5.56-7.69]); being a PWID (aOR = 7.08 [6.05-8.28]), PWUD (aOR = 2.91 [2.38-3.55]), FSW (aOR = 2.00 [1.27-3.15]), or PLHIV (aOR = 4.65 [3.71-5.82]); and using PrEP (aOR = 2.60 [1.73-3.94]) or MMT (aOR = 1.23 [1.05-1.45]).

Conclusions: Integrating viral Hepatitis and HIV services is a major opportunity to address gaps in KP access and uptake of HBV/HCV testing and treatment services.

Disclosure of Interest: None Declared

P186

HEPATITIS SCREENING IN PEOPLE LIVING IN POVERTY IN PAKISTAN: STEP TOWARDS FINDING THE MISSING MILLIONS

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Background: Viral Hepatitis Caused 1.1 million death annually. World Health Organization has developed a strategy to eliminate Hepatitis by 2030. Globally, 89% of people living with HBV or HCV are undiagnosed. World Hepatitis Alliance has started an initiative named "Find the Missing Millions" to trace the millions of undiagnosed Hepatitis Cases.

Purpose: To Find the Missing Millions in Pakistan by screening Hepatitis B and C in high risk populations living in poverty in Pakistan.

Methodology: We are doing Hepatitis awareness and screening in high risk populations groups in Pakistan including People who inject drugs, Transgender population, Refugees, Thalaseemia patients and street children.

Results: The prevalence of HCV was found 55.73% in thalassemia positive patients. All the patients above 20 years of age were found positive for HCV. While the prevalence of HBV was found 3.08%. We screened 11 Refugees camps in Muzaffarabad region for the presence of HBV & HCV. The prevalence of HBV and HCV was found 4.36% and 6.54% respectively. In Transgender population the prevalence of HBV, HCV and HIV was found 10.04%, 13.87% & 9.33% respectively. The prevalence of HCV was found 72% in people who inject drugs while HCV/HIV co-infection was found in 12% of PWIDs.

Conclusion: The prevalence of Hepatitis was found very high in high risk groups. There is dire need to speed up Hepatitis screening and find the missing millions living with Hepatitis in Pakistan.

Disclosure of Interest: None Declared

P187

SAFETY OF HEPATITIS E VACCINATION FOR PREGNANCY: A POST-HOC ANALYSIS OF A RANDOMIZED, DOUBLE-BLIND, CONTROLLED PHASE 3 CLINICAL TRIAL

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Background: Hepatitis E virus (HEV) infection is a non-negligible contributor to maternal mortality and abnormal fetal loss in areas with HEV epidemic. The world's first and only HE vaccine, Hecolin, was licensed in 2011 and 2020 in China and Pakistan, separately. Safety data of HE vaccination for pregnancy is scarce, however, close monitoring of pregnant women who received HE vaccine during or shortly before pregnancy is of great interest in guiding the usage of HE vaccine for pregnant women, especially during urgent HE outbreaks.

Objective: To assess whether administration of HE vaccination during or shortly before pregnancy is associated with increased risks of adverse pregnancy events.

Methods: This is a post-hoc analysis based on a phase 3 clinical trial of a human papillomavirus (HPV) bivalent vaccine (Cecolin) in China. Eligible healthy women aged 18-45 years were randomly assigned in a 1:1 ratio to receive three doses of Cecolin or Hecolin at months 0, 1 and 6 and were followed up for 66 months. All the pregnancy events throughout the study were followed up regularly. The occurrence of adverse events and pregnancy outcomes were analyzed based on the vaccine group and/or maternal age. The time interval between vaccination and the onset of pregnancy was categorized into distal and proximal exposure. The risks of abnormal fetal loss, neonatal anomalies and pregnancy complications between the two vaccine groups were analyzed under different types of exposure, and the risk of proximal exposure relative to distal exposure in the HE vaccine group was also specifically analyzed.

Results: During the whole study period, 1263 women in the HE vaccine group and 1260 in the HPV vaccine group reported having 1684 and 1660 pregnancy events, respectively. Women with pregnancy events of the two groups shared similar characteristics of maternal outcomes and neonatal profiles in either maternal age stratification. Among 140 women who were vaccinated inadvertently during pregnancy, the incidence of adverse reactions between the two groups showed no statistical difference (31.8% vs 35.1%, p=0.6782). The proximal exposure of HE vaccination was not associated with a significantly higher risk of abnormal fetal loss (OR 0.80, 95%CI 0.38-1.70), neonatal abnormality (OR 2.46, 95%CI 0.74-8.18) or pregnancy complications (OR 0.65, 95%CI 0.15-2.82) than that of HPV vaccination, as did distal exposure. In addition, within the HE vaccine group, the risk of proximal exposure was comparable to distal exposure.

Conclusion: HE vaccination during or shortly before pregnancy were not associated with increased risks for both pregnant women and pregnancy outcomes, more adequate and rigorous evidences should be continually explored.

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P188

HCC SURVEILLANCE FOR CHRONIC HEPATITIS B AND CIRRHOSIS PATIENTS IS COST-EFFECTIVE IN AUSTRALIA: EVIDENCE FROM A MICROSIMULATION STUDY

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Background and Aims: Globally, hepatocellular carcinoma (HCC) - the most common type of liver cancer - is one of the fastest increasing causes of cancer mortality. Recently published Australian Consensus Guidelines recommend HCC surveillance for high-risk groups living with chronic Hepatitis B (CHB) (i.e. Aboriginal and Torres Strait Islanders aged >50 years, Asian males >40 years, Asian females >50 years, people born in sub-Saharan Africa aged >20 years), and all patients with liver cirrhosis. The aim of this study was to assess the cost-effectiveness of these recommendations.

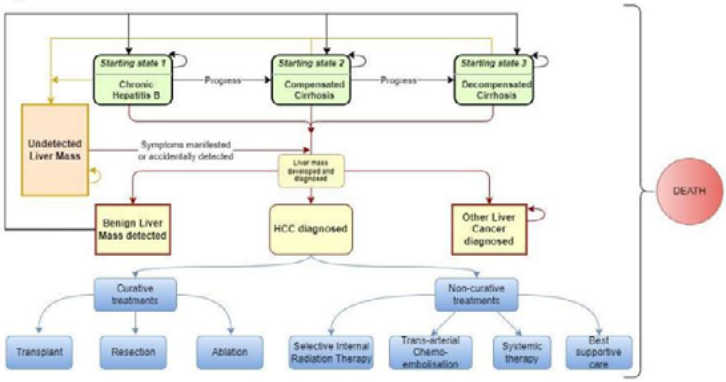
Method: A microsimulation model was developed. Three strategies were evaluated: biannual ultrasound scan (USS), biannual USS+ alpha-fetoprotein (AFP), and usual care (i.e. no formal surveillance). A hypothetical cohort aged 40-80 years with one of the conditions: non-cirrhotic CHB, compensated cirrhosis (CC) or decompensated cirrhosis (DC), was simulated. Face, internal and external validity were assessed. One-way, probabilistic sensitivity analyses were conducted. To account for uncertainties, scenario and threshold analyses were carried out. Scenarios included surveillance of each disease individually (CHB, CC, DC), reduced sensitivity of USS due to central adiposity and real-world adherence rates.

Results: The validation analyses indicated that the model is highly accurate in terms of reflecting observed real-world data. For a range of HCC surveillance scenarios for combined CHB, CC and DC patients, USS+AFP was the most cost-effective with an incremental cost-effectiveness ratios (ICER) compared to usual care less than the willingness-to-pay threshold of A$50,000 per quality-adjusted life year (QALY). Whilst USS alone was also cost-effective, it was dominated by USS+AFP. When evaluating cost-effectiveness by groups, surveillance was cost-effective in CC and DC groups (ICERs < $30,000), but not for CHB alone (ICERs > $100,000). Central adiposity decreased the performance of USS, however USS±AFP surveillance remained cost-effective.

Conclusions: HCC surveillance using USS±AFP for combined target populations is cost-effective. Surveillance limited to CC and DC groups is also cost-effective. Whilst surveillance for CHB patients alone was not cost-effective, this may be due to an important limitation of this model. As there is a lack of published data for model parameters on CHB and Indigenous status, region of birth, age and sex, our model was simplified and assumed that HCC risk was the same for all CHB patients. Our model will be updated with these data as they become available. Nonetheless, HCC surveillance based on Australian recommendations for all three groups is highly likely to be cost-effective in the Australian setting.

Image/Table:

Figure 1. Structure of the state-transition individual-level model



Disclosure of Interest: None Declared

P189

MACHINE LEARNING CLASSIFICATION OF HEPATOCELLULAR CARCINOMA BASED ON CT SCAN IMAGE USING PROBABILISTIC NEURAL NETWORK ALGORITHM

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Background/Aim: The most common type of liver cancer is Hepatocellular carcinoma (HCC), which begins in the main type of liver cell (hepatocyte). Hepatocellular carcinoma occurs most often in people with chronic liver diseases, such as cirrhosis caused by Hepatitis B or Hepatitis C infection. Examinations carried out to determine the presence of HCC are by measuring the level of Alpha-Fetoprotein in the blood, radiographic diagnoses such as ultrasound examination, CT-Scan, and MRI, as well as performing a liver biopsy. HCC is often not identified because the symptoms of HCC are masked by the underlying disease. So we need a method to make it easier to identify HCC disease through CT-Scan images. In this study, an alternative machine learning algorithm is used, namely the Probabilistic Neural Network that works to classify HCC.

Method: The method used in this study is a Probabilistic Neural Network to identify HCC disease. The steps taken to identify HCC disease are starting with pre-processing using Gaussian filtering to improve image quality by reducing noise in the image, then segmentation using thresholding, morphology operators, and finding contour which aims to get image segmentation in the heart, as well as to feature extraction using a gray level co-occurrence matrix to analyze the texture of the image as input for the identification process. The image data used in this study were obtained from The Cancer Imaging Archive (TCIA) and Radiopedia.org.

Result: The test results obtained indicate that the proposed method is able to identify HCC disease with an accuracy obtained of 94%. The use of the gray-level co-occurrence matrix method for the feature extraction process works well for recognizing objects so that they can identify HCC and normal categories.

Conclusion: The Probabilistic Neural Network method can identify HCC disease quite well based on the accuracy obtained exceeding 90%. However, further research and development are needed to improve the accuracy of the classification system.

Disclosure of Interest: None Declared

P190

PILOTING EHEALTH INITIATIVES: COMPUTER-BASED TRAINING AND TELEMENTORING FOR VIRAL HEPATITIS CARE IN THE PRIMARY CARE SETTING

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Background: Starting in 2020, the COVID-19 pandemic greatly affected the delivery of basic health services in the primary care setting in the Philippines. Different health programs were sidelined to divert financial, human and infrastructure resources to address the pandemic. One of the most affected was the recently piloted initiative for the management of Viral Hepatitis by the Department of Health. The restrictions and limitations of the movement of healthcare providers and patients hampered the delivery of services for viral Hepatitis and the sharing and transfer of knowledge among healthcare providers.

Purpose: To help address this concern, an eHealth Initiative was launched to provide a computer-based training and telementoring program for primary care workers involved in viral Hepatitis management.

Methodology: A computer-based training (CBT) platform for viral Hepatitis was developed in collaboration with the Department of Health (DOH), the World Health Organization (WHO)), the Hepatology Society of the Philippines (HSP), and the University of the Philippines Manila. These organizations provided the structure and content of the CBT following the interim national guidelines on viral Hepatitis management. To complement these learnings, a telementoring program was developed where hepatologists from the HSP become mentors to selected primary care physicians involved in the management of Hepatitis. This is the first time that these eHealth initiatives for viral Hepatitis will be done in the Philippines

Results: In the ongoing pilot eHealth initiatives, the CBT was conducted in two regions in the Philippines. a total of 236 health workers have enrolled in the CBT of whom 109 have already completed the course. For the telementoring program, on the other hand, we restricted the pilot to 13 physicians to participate in the scheduled sessions. To date, the feedback on the CBT has been very positive. The participants appreciated the effort wherein they are able to remotely learn about the latest on viral Hepatitis management even if they remain in their areas of responsibility in their respective regions and at their own pace. The telementoring program was likewise well received. They appreciated the scheduled synchronous sessions where they had the opportunity to engage and discuss their own viral Hepatitis Cases with hepatologists.

Conclusion: eHealth strategies are a novel way to address the training and continuing education of health workers. In the primary care setting, a pilot eHealth initiative is currently ongoing. Initial feedback has been very positive with the participants expressing their appreciation got the use of technology and for the capability to remotely increase their knowledge of Hepatitis management. Further assessment will be done at the end of the CBT and telementoring sessions.

Disclosure of Interest: None Declared

P191

APPLYING THE WORLD HEALTH ORGANIZATION SMART GUIDELINES TO THE PHILIPPINE NATIONAL VIRAL HEPATITIS INITIATIVE

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Background: Viral Hepatitis is a serious public health problem in the Philippines affecting nearly ten percent of the population. Its control will require close coordination of activities among clinical, public health, and non-health sectors. With many health facilities computerizing in preparation for the mandates of the Universal Health Care and Cancer Control laws, there will be an expected deluge of data from these different systems. Unfortunately, without clear health data standards and reporting framework , policymakers and planners will be unable to harness the power of these data and they will remain in silos. This paper describes the steps taken by a group of researchers to solve the problem of gathering data from disparate systems into a national viral Hepatitis data repository.

Methods: The viral Hepatitis project in the Philippines initially planned to follow a standard software development lifecycle (SDLC) approach. After identifying the relevant stakeholders from government and non-government sectors, the team then generated an interoperability solution based on the opportunities that presented.

Workshops were held with these stakeholders where consensus on the business process of viral Hepatitis Care were reached - from screening, diagnosis, and treatment. Further agreements on the data required in each of these steps. Finally, these agreements were converted into their computable representations using an international standard called Fast Healthcare Interoperability Resources (FHIR) from the Health Level 7 (HL7) Organization.

Conclusions: There are several lessons that can be learned from this project. First, creating a surveillance system for viral Hepatitis (or any disease of public health significance for that matter) is a complex exercise. It requires the collaboration and coordination of many stakeholders and the interoperability of separate non-standardized electronic systems.

Second, the standard software development lifecycle methodology is not sufficient for interoperability projects in healthcare where several applications need to exchange data. The SDLC's value is limited to standalone applications. It does not have enough features to enable the exchange of data across different systems.

Third, faced with multiple applications that need to exchange data, governance becomes a crucial requirement to ensure the coordination of efforts by different sectors. There should be a clear mandate coming from authority that the secure sharing of health data is required. Without this mandate, data will not be shared due to privacy concerns.

Fourth, once established, the governance can direct stakeholders to adopt the WHO SMART Guidelines as a framework for collaboration.

By adopting the SMART guidelines, countries can now systematically navigate the complex maze of public health surveillance systems for diseases like viral Hepatitis.

Disclosure of Interest: None Declared

P192

DEVELOPMENT AND VALIDATION OF A SIMPLE TREATMENT ELIGIBILITY SCORE FOR CHRONIC HBV INFECTION AT PERIPHERAL HEALTH FACILITIES IN SUB-SAHARAN AFRICA

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Background: To eliminate Hepatitis B virus (HBV) infection, it is essential to decentralize HBV care services in resource-limited settings to peripheral health facilities. However, at these facilities, access to diagnostic tools to assess eligibility for antiviral therapy (AVT), particularly quantitative HBV DNA tests and transient elastography, is severely limited. Through a multi-regional collaboration in sub-Saharan Africa (SSA), we developed and evaluated a simple scoring system, using tests available at peripheral health facilities, to identify HBV-infected individuals eligible for AVT.

Methods: Through HEPSANET (Hepatitis B in Africa Collaborative Network), we conducted a site survey to define the availability of biomarkers potentially useful for HBV management at different levels of health facilities. Then, using the HEPSANET dataset, the largest cross-sectional database of HBV-infected people living in SSA, we divided the sample into derivation and validation sets. We used data from those with a known HBV DNA levels, elastography score, and treatment eligibility status according to the EASL 2017 criteria, which was used as a reference. Using the derivation set, we identified a combination of variables available at peripheral health facilities that can best identify people eligible for AVT through a stepwise logistic regression. With the validation set, we estimated the sensitivity and specificity of the simplified score to identify people eligible for AVT.

Results: The survey of 11 sites found that on average, transaminases (AST, ALT) and platelet counts were available at the district hospital level, Hepatitis B e antigen (HBeAg) and point-of-care HBV DNA test (Xpert) at regional/provincial hospital level, and transient elastography and conventional quantititative HBV DNA tests were only available at national reference centers. Liver decompensation (jaundice, ascites, encephalopathy, etc) was diagnosed clinically at all levels. We proceeded to create a scoring tool for use at district level.

The analysis included 2928 treatment naïve HBV-mono infected individuals from seven SSA countries, of which 398 (13.6%) were eligible for AVT according to EASL guidelines. AST, ALT, and platelet count remained in the multivariable stepwise regression model and the following scoring system was developed: platelet counts (10^9/L), <100 (+2), 100-149 (+1), ≥150 (±0); AST (IU/L), <40 (±0), 40-79 (+1), ≥80 (+2); and ALT (IU/L), <40 (±0), 40-79 (+1), ≥80 (+2). Using a cut-off of ≥2, the score had a sensitivity of 79% and specificity of 87% to identify treatment-eligible individuals in the validation dataset.

Conclusions: We found that a combination of platelet counts, AST and ALT levels - tests available even at low level health facilities - can identify the majority of HBV-infected people in need of AVT. This suggests that even in the absence of upgrades in laboratory/radiology, decentralization of clinical staging for HBV-infected people may be realized in SSA.

Disclosure of Interest: None Declared

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CHALLENGES WITH THE STRATEGIC PHARMACEUTICAL CARE PROGRAM IN THE STATE OF RIO DE JANEIRO'S IMPLEMENTA ATION OF THE VIRAL HEPATITIS B AND C MEDICINES

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Abstract Content: Brazil is a signatory country to the World Health Organization (WHO) document for the elimination of viral Hepatitis by 2030. One of the strategies to eliminate viral Hepatitis is to increase the number of diagnoses and treatments. The migration of drugs for chronic viral Hepatitis B and C from the specialized component to the strategic component of pharmaceutical care was regulated by ordinance 1537 of the Ministry of Health of June 2020 and standardized by Technical Note 319 of 2020. A schedule was organized for this transition with the steps of the process and implementation of the logistics and dispensing system (SICLOM) in the states. SICLOM is a user registration system, drug dispensing, inventory control, evaluation of drug prescription criteria, in addition to issuing reports on the quantity of drugs dispensed. A fundamental step in the process was the agreement between the Municipal Dispensing Units (UDM) within the scope of the Regional Inter-management Commissions (CIR) and, later, in the Bipartite Inter-management Commission (CIB) to decide that these units would start the process as pharmacies that dispense Hepatitis drugs. B and C in the strategic component, using the SICLOM system, in the State of Rio de Janeiro. The objective of this work is to describe the process and evaluate the results related to the number of service points and quantitative of treatments dispensed from July/2021 to February/2022 in the State of Rio de Janeiro. The methodology included a literature review on the role of treatment as a strategy to eliminate viral Hepatitis, and the description of the activities planned and carried out in the timeline since the beginning of the process after the legal basis and the publication of norms, and the extraction of data and information on the number of treatments from SICLOM. The migration resulted in 1084 treatments from July to December 2021, corresponding to 56.4% of the total 1922 treatments dispensed by the Specialized Pharmaceutical Assistance Component (CEAF) throughout 2020. The migration was successful, increasing from 29 specialized dispensing centers to 61 DMUs, which are the pharmacies of the strategic component, making dispensing more agile than the previous wait. Despite the negative effects caused by the pandemic, it can be considered that there was a great advance in the public policy of assistance to viral Hepatitis.

Keywords: Viral Hepatitis. Pharmaceutical care. Strategic component. Health program evaluation. SUS.

Disclosure of Interest: None Declared

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IMPORTANCE OF PATIENT SUPPORT GROUP: A CROSS-SECTIONAL SURVEY OF HEPATITIS B AND C INFECTED PATIENTS OF WEST BENGAL IN INDIA.

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Background: A cross-sectional assessment of baseline knowledge among Hepatitis B & C infected patients of West Bengal was done to understand their knowledge about virus infection and consequences due to such. A knowledge gaps observed among HBV and HCV patients in the study suggesting a need for educational intervention and awareness dissemination through peer group advocacy. (Mukherjee et al. Hepatology, Medicine and Policy (2017) 2:6.

A Hepatitis patients' Forum (HPF) is a community based intervention, first patient support group of Hepatitis B & C infected patients in India was formed with the patients participated in the survey in 2014. After 8 years they were again participated in the same survey to understand their sustainability of empowered knowledge.

Purpose: To understand the knowledge empowerment and its sustainability amongst the same members of a Hepatitis patient group after 8 years using and also to measure the knowledge gap with the non-members of the HPF.

Method(s): A survey was conducted in 2022 among the participants of the same cohort of previous study in 2014 using the same questionnaire. In our previous study, patients who had tested positive for HBsAg or anti-HCV at government specialty clinics were invited to enrol in the study when they presented for follow-up laboratory testing. 158 members of the earlier cohort were participated in the survey. 36 new patients who had tested positive at government specialty clinics and had visited for the 1st time in the clinic of NVHCP in Kolkata, West Bengal for enrolment in November, 2022 were also included in the study. SPSS 16.0 software was used for data analysis. Descriptive statistical analysis was performed and the Wilcoxon- signed-rank test was done to check the level of significance in knowledge score.

Result: It was observed that mean knowledge score was significantly higher among the participants in September, 2022 to October, 2022 than the participants of the same cohort in February 2014 to January 2015 (5.59 vs. 4.76) ($p<0.05$). The mean knowledge score was found to be significantly lower (3.22) ($p<0.05$) among the new non-HPF member patient's than other two groups of participants of the same cohort. Half of the participants scored 6.0 points in this survey while it was 5.0 in the earlier study and the new group of patients was the least score 3.22 than the other two groups of HPF.

Conclusion(s): As testing, treatment are the major components of WHO's global Hepatitis strategy, patient support group can play important role in linkage with the national program. Education campaigns through peer advocacy can also reduce horizontal transmission among family members, friends and neighbours of support group.

Disclosure of Interest: P. Mukherjee Speakers bureau of: Nothing

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INCIDENCE RATES OF VIRAL HEPATITIS A, B, C, D AND E IN PATIENTS WITH CLINICAL CONDITIONS SUGGESTIVE OF ACUTE LIVER DISEASES ATTENDED IN PUBLIC BRAZILIAN HEALTH INSTITUTIONS THROUGOUT THE FIVE GEOGRAPHICAL REGIONS

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Introduction: Viral Hepatitis (VH) are notifiable infectious diseases and knowledge of the current patterns of incidence of the acute form in different regions of the country is fundamental for the elaboration of public policies for interrupting transmission chains.

Objective: To determine the incidence rates of VH A A, B, C, D and E in patients with clinical conditions suggestive of acute liver disease treated at some Brazilian health institutions participating in a PROADI project with the DCCI/SVS/MS.

Casuistry and Methods: Observational, prospective and multicenter study in 22 health institutions distributed in 14 Brazilian states, in the five regions of the country, in which only cases with suspected diagnosis of acute Hepatitis were included. Demographic, epidemiological and clinical data were collected, as well as blood samples for laboratory analysis to research serological and molecular markers for the detection of acute HV A, B, C, D and E.

Results: Between October 2019 and December 2022, 1360 suspected cases were studied and we had the following results: 1) anti-HAV IgM and/or HAVRNA: 57 – 4.2%; 2) IgM anti-HBc and (HBsAg and/or HBV DNA): 44 – 3.2%; 3) anti-HCV positive and viral load greater than 1,000 IU/mL: 91 – 6.7%; 4) positive anti-HEV IgM and/or detection of HEV RNA: 33 – 2.4%, only one of them positive for HEV RNA alone. 5) 12 patients from Western Amazon states were positive for anti-HDV and HDV RNA, but none were IgM anti-HBc positive. That is, in our series, all cases had a pattern of HDV/HBV superinfection and not coinfection.

Conclusion: These preliminary data confirm the presence of acute cases of VH A, B, C and E in different Brazilian states and cases of HV D in the Western Amazon, reinforcing the need to continue verifying the presence of acute cases when looking for elimination of Hepatitis as a public health problem.

Disclosure of Interest: None Declared

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UTILITY OF VIBRATION CONTROLLED TRANSIENT ELASTOGRAPHY IN SCREENING FOR SILENT CHRONIC LIVER DISEASES IN ASYMPTOMATIC APPARENTLY HEALTHY SUBJECTS

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Aim: to assess Vibration Controlled Transient Elastography (VCTE) and controlled Attenuation Parameter (CAP) for staging fibrosis and quantifying steatosis in asymptomatic apparently healthy subjects.

Methods: Prospectively, this study was carried out on 433 asymptomatic apparently healthy adults (225 males = 51.96% and 208 females = 48.04%) attending the outpatient clinics in 5 different Egyptian governorates (relatives of patients, nurses, etc), after getting the ethical approvals. All underwent full clinical evaluation (including BMI calculation) and FibroScan/CAP examination. Subjects with liver stiffness measurement (LSM) > 6 kilo pascal and/or CAP > 248 dB/m were further evaluated to assess the underlying CLD.

Results: According to the Fibroscan/CAP examination, subjects were classified into 4 subgroups: Normal (N=119) whose mean CAP score = 215.85$\pm$24.81 dB/m and mean fibrosis score = 4.47$\pm$0.81 kPa, subjects with steatosis only (N=133) with mean CAP score of 309.41$\pm$42.6 dB/m and mean fibrosis score of 4.74$\pm$0.82 kPa, subjects with both steatosis and fibrosis (N=95) with mean CAP score of 318.20$\pm$39.89 dB/m and mean fibrosis score of 7.92$\pm$2.58 kPa, and subjects with fibrosis only (N=86) with mean CAP score of 213.48$\pm$22.62 dB/m and mean fibrosis score of 6.96$\pm$1.11 kPa. According to the applied standard cutoffs, S0 was present in 205 (47.3%), S1 in 48 (10.2%), S2 in 16 (3.7%), and S3 in 168 (38.8%) of the studied subjects while F0-1 was present in 371 (85.7%), F2 in 44 ((10.16%), F3 in 16 (3.7%) subjects, and F4 in only one (0.23%) subject. Subjects with both steatosis and fibrosis showed significantly higher transaminases, triglycerides, and total cholesterol levels than the other subgroups.

Conclusion: LSM and CAP might represent one of the promising first line procedures for mass screening of liver disease in the general population.

Disclosure of Interest: None Declared

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OBLITERATING GASTRIC VARICES WITH GLUE INJECTION IN PATIENTS WITH PORTAL HYPERTENSION: EFFICACY, SAFETY AND REBLEEDING RISK FACTORS

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Background: Endoscopic management of acute gastric variceal (GV) bleeding has been premised on the injection of biological glue.

Purpose: The aim of this study was to assess the efficacy and safety of biological glue injection in the treatment of hemorrhagic GV and identify predictive risk factors of recurrent bleeding.

Methods: We conducted a retrospective study over a period of 13 years [2010 – 2022], including all patients with bleeding GV treated with biological glue injection. Demographic data and endoscopic findings were collected as well as treatment details and follow-up information.

Results: Thirty-eight patients were included with a mean age of 58.4 years. The portal hypertension syndrome was mostly caused by cirrhosis (81.6%). Seven patients (12.4%) were carriers of non-cirrhotic portal hypertension. Clinical presentation of GV rupture was gastrointestinal bleeding (92.1%) and deglobulisation in the rest of the cases. Bleeding GV were type 2 gastroesophageal varices (57%), type 1 gastroesophageal varices (39.5%), and type 1 isolated GV (15.8%). Glue injection was performed within a median time of 3 days after hospitalization. An average of 1.7 cc was inserted per patient without any incident. Primary hemostais was obtained in 100% of cases. Endoscopic treatment was complicated in 2 cases by pulmonary embolism secondary to glue migration in one case and severe sepsis in the other. Bleeding recurrence due to GV rupture was noted in nine patients (23.6%). The risk factors associated with a bleeding recurrence were Child-Pugh B or C score (p=0.04), as well as hypertensive gastropathy (p=0.03). In multivariate analysis, only hypertensive gastropathy is significantly associated to recurrence (p=0.048).

Conclusion: Glue injection is a key element in the management of gastrointestinal bleeding due to the rupture of GV. However, factors predisposing to rebleeding are deficiently studied and poorly defined. Yet, the identification of these factors would help select most-eligible patients of strict monitoring and closer follow-up.

Disclosure of Interest: None Declared

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FAMILIAL CLUSTERING OF HEPATITIS C VIRUS (HCV) AMONG PEOPLE LIVING IN SAME HOUSE IN PAKISTANI POPULATION

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Background: Pakistan has the second highest burden of Hepatitis C in the world. It is observed, If a member of family is infected with Hepatitis C virus, there are chances that the other member of the family may also get Hepatitis C infection. The country has joint family system and the number of people living in a house are very high. It is commonly observed that the family members are sharing many common things, like tooth paste, nail cutters etc while living in a house.

Purpose: The aim of the study was to investigate the familial clustering of HCV in Pakistani Population.

Methods: Study was conducted at Rawalpindi and Islamabad cities of Pakistan. A total of 683 individuals, who visited liver clinic during the study period, were screened for the presence of HCV infection. 534 individuals showed positive HCV infection were grouped in case group and 149 individuals with HCV negative status were grouped in control group. A detailed questionnaire was used to take demographic, clinical, HCV risk factor and familial clustering data.

Results: HCV familial clustering was found 23.5% in case group compared with 3.8% in control group. We also found 13.3% of patients had spouses who were also infected with HCV compared to 0.8% spouse infection in control group. Only 3% of patients had HCV positive mothers. We also found family history and sexual history as independent risk factors for transmission of Hepatitis C infection and mother's history has no significance as risk factor for transmission. The major risk factor for getting HCV infection are dental procedures, unsafe injections, surgery and blood transfusions.

Conclusion: Rates of HCV familial clustering was found high in Pakistani population. There is strong need to increase awareness about HCV transmission routes among positive patients to reduce the chances of HCV familial clustering.

Disclosure of Interest: None Declared

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A LARGE DATABASE REVEALS THE BENEFITS OF HEPATITIS B VIRUS (HBV) VACCINATION IN PATIENTS WITH CHRONIC LIVER DISEASE

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Background: Hepatitis B vaccine has proven highly successful in preventing Hepatitis B virus (HBV) infection and reducing consequential Hepatitis B-related disease burden in the countries where vaccination has been implemented. However, few studies have reported the impacts of the Hepatitis B vaccination particularly on patients with chronic liver disease (CLD) other than chronic Hepatitis B.

Methods: To investigate the efficacy of the Hepatitis B vaccine on patients with chronic liver disease, a large USA cohort of 57306 patients between 2000 and 2020 was obtained through the Observational Health Data Sciences and Informatics (OHDSI) consortium.

Results: 2.79% (1601/57306) of patients with chronic liver disease in the US were vaccinated. Generally, HBV-vaccinated patients with chronic liver disease had a significantly better survival (p=0.000). Patients with liver cirrhosis also showed a significantly improved survival (p=0.000). By investigating subgroups, particularly patients with chronic Hepatitis C (p=0.000), chronic non-alcoholic liver disease (p=0.000), or both alcoholic and non-alcoholic-induced cirrhosis (both p=0.000) all shared significant benefits from HBV vaccination (p=0.000). These benefits showed no gender difference.

Conclusion: Our results demonstrated that vaccinated patients with different kinds of chronic liver diseases generally had significantly better survival. As 97.21% (55706/57306) of the population were not vaccinated, appropriate vaccination status must be clarified for all patients with chronic liver disease.

Disclosure of Interest: None Declared

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ASSOCIATION OF COGNITIVE IMPAIRMENT WITH CHRONIC VIRAL HEPATITIS INFECTION AMONG OLDER ADULTS IN TAIWAN

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Background: Both Hepatitis virus infection and cognitive impairment are major public health threats worldwide. However, studies investigating their association remain disputable.

Purpose: To evaluate whether patients with chronic Hepatitis virus infection are at an increased risk of cognitive impairment.

Methods: In this population-based cross-sectional study, 912 and 22,874 participants over 60-year-old categorised as cases with cognitive impairment and as non-cognitive impairment controls were identified from the ongoing Taiwan Biobank Database in October 2022. The status of cognitive impairment was evaluated by mini-mental state examination (MMSE). Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infections were determined by serologic markers. Logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) associated with the risk of cognitive impairment in the HBV and HCV infection group and non-chronic viral Hepatitis group. The roles of *APOE* Δ4 polymorphisms per se and its interaction with HBV/HCV infection on the risk of cognitive impairment were also investigated.

Results: Our logistic regression model suggested that the adjusted odds ratio (aOR) of cognitive impairment was 1.40 (95% CI = 1.04-1.87, $P = 0.025$) and 1.15 (95% CI = 0.92–1.44, $P = 0.234$) in association with chronic HCV and HBV infections respectively. "Orientation" and "Attention and Calculation" were the two subcategories of the MMSE influenced most in association with HCV infection [HCV(+) vs HCV(-), $P < 0.05$]. For the subjects with variant Δ4-alleles in the *APOE* gene, HCV was more significantly associated with cognitive impairment risk (aOR = 2.23, 95% CI= 1.25–3.98, $P = 0.007$). The interaction effect of *APOE* genotype and HCV on the risk of cognitive impairment was borderline statistically significant (interaction test, $P = 0.083$).

Conclusions: Our findings suggested that patients with chronic HCV but not HBV infection are at an increased risk of developing cognitive impairment.

Image/Table:

Table 1. Association between HBV or HCV infection and risk of cognitive impairment

	Cognitive impairment					
	No		Yes			
	n	%	n	%	aOR (95% CI)[a]	*P* value[a]
HBV						
(–)	20985	91.74	822	90.13	1.00	
(+)	1889	8.26	90	9.87	1.15 (0.92–1.44)	0.234
HCV						
(–)	22415	96.81	858	94.08	1.00	
(+)	729	3.19	54	5.92	1.40 (1.04–1.87)	0.025
HBV/HCV						
(–)/(–)	20324	88.85	769	84.32	1.00	
(+)/(–)	1821	7.96	89	9.76	1.21 (0.97–1.53)	0.099
(–)/(+)	661	2.89	53	5.81	1.53 (1.14–2.07)	0.005
(+)/(+)	68	0.30	1	0.11	0.31 (0.04–2.22)	0.242

[a] Adjusted for age, sex, education level, income, alcohol drinking, exercise regularly, BMI, hypertension, stroke, and diabetes mellitus.

Disclosure of Interest: None Declared

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THE EVALUATION OF SEROPREVALENCE OF HEPATITIS E VIRUS INFECTION IN THE INHABITANTS OF THE POMERANIAN DISTRICT, POLAND

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Abstract Content: Hepatitis E is a growing health problem in Europe. It is suspected that infections are acquired during travel to countries of the hot zone and through the transmission of Hepatitis E virus associated with the consumption of animal products and professional contact with animals. In addition to the low awareness of the risks associated with infection with this virus, the disease may be mistakenly recognized as toxic or autoimmune Hepatitis and incorrectly treated. Acute HEV infection may be a serious clinical problem for people who are immunosuppressed as potential recipients of blood products. There have been reports of acute liver failure and chronic HEV replication in this group of patients. Detection of IgM and IgG antibodies against HEV by Elisa method is the first step in the diagnosis. The presence of antibodies is not a prove of infection but allows to confirm the contact of immune system with the virus. Detection of anti-HEV IgM and IgA strongly suggest acute Hepatitis E. In all patients with anti-HEV antibodies the evaluation of HEV antigen (less sensitive) and/or HEV-RNA (more sensitive) is recommended. Data regarding seroprevalence might however be affected by the different laboratory kits used in the analysis, which show significant variability in levels of sensitivity. The aim of the study was to assess the prevalence of anti-HEV IgG in the sera of 281 subjects observed in the University Center for Maritime and Tropical Medicine in Gdynia.

Disclosure of Interest: None Declared

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LB/P202

HEAVY BURDEN OF HIV AND HEPATITIS B VIRUS INFECTION AMONG COMMERCIAL SEX WORKERS IN NORTHERN ETHIOPIA: ASSESSMENT OF PREVALENCE AND RISK FACTORS

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Background: Sexually Transmitted Infections remain major public health problems among the most at risk population groups such as female commercial sex workers.

Objective: To assess the magnitude of Hepatitis B Virus and HIV/AIDS and identify the associated factors among female commercial sex workers.

Method: A Community Based Cross Sectional Study was conducted in Mekelle city. A total of 319 participants were selected using simple random sampling method. Data was entered and analyzed using SPSS version16.0. Bivariate and multivariate analysis were conducted to identify risk factors.

Result: Overall, the prevalence of HIV and HBV was 11.9% and 6%, respectively. The main factors associated with HIV include: age, educational status, having dependents, birth place, number of years in sex work, income, inconsistent condom use, history of condom breakage, having steady partner, sex during menses, history of genital ulcer, history of STI, alcohol consumption and sexual abuse ($P<0.05$). The major determinants of HBV were work place, inconsistent condom use, sex with male using drugs and use of drug by the sex workers ($P<0.05$).

Conclusion: The prevalence of HIV and HBV were moderately high. To reduce the prevalence of these diseases among FCSWs provision of condom, early treatment of genital ulcer, health education on condom utilization and not to have sex during menses, are recommended.

Disclosure of Interest: None Declared

LB/P203

THE EMERGING ROLE OF MYELOID DERIVED SUPPRESSOR CELLS (MDSCS) CELLS AND THE ROLE OF PLACENTAL TRANSFER OF MATERNAL IGG HBE ANTIBODIES IN IMMUNE SYSTEM RESPONSE IN HEPATITIS B AND B-DELTA COINFECTION IN NEONATES.

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Abstract Content: Many functions of the immune system are impaired in neonates, allowing vulnerability to chronic Hepatitis B and Hepatitis B-Delta co-infection which would otherwise not be chronic infections in healthy adults.

This vulnerability is exacerbated in neonates due to high frequency of myeloid derived suppressor cells (MDSCs), especially neonates exposed to Hepatitis B in the first week of life, are at increased risk of chronic Hepatitis B with highest values of quantitative Antigen HBs.

MDSCs differentially modulates B cell function in neonates exposed to Hepatitis B by selectively suppressing B cells through the absence of HBc IgM antibody production.

IgG HBe antibodies at the time of birth, are essential for controlling the initial disease, in case of simultaneous exposure to Hepatitis B virus in neonates.

Negative IgG HBe antibodies status at the time of birth in neonates lead to HBe antigen-positive chronicity when the infection is transmitted to the neonate from the HBe antigen-positive mother but also but also when neonates born from mothers with no history of Hepatitis B are exposed to Hepatitis B virus (IgG HBc antibodies negative).

Neonates exposed to Hepatitis B born from mothers with positive IgG HBc and HBe antibodies, have positive HBe antibodies at birth, as a result of acquired natural passive immunity by placental transfer of maternal IgG antibodies, leading to HBe antigen neutralization in the absence of HBc IgM antibodies.

In contrast, in young children and adults, and with a normal frequency of MDSCs, exposure to Hepatitis B leads to a distinct immunological function, HBc IgM are the first antibodies produced and regulate cellular immunity before seroconversion of HBe antigen to HBe antibodies. HBc IgM antibodies persist in acute Hepatitis after HBe seroconversion as long as quantitative HBs antigen values remain positive and continue to be present until HBs antigen seroconversion.

The immune response is also impaired in neonates in case of exposure to simultaneous Hepatitis B and Delta co-infection due to the presence of MDCSs because Hepatitis Delta is a defective virus that can infect only in the presence of HBs antigen and the primary immune response against co-infected cells is tolerant in the absence of HBc IgM antibodies.

In chronic Hepatitis B infection, subsequent exposure to Hepatitis Delta virus no longer correlates with age and immune immaturity, and the immune response is mediated in the acute phase by efficient B cells in recognizing new viral components and by T cells response, leading to incresed riscks of severe manifestation in the presence of Hepatitis B surface antigen.

Superinfection with Hepatitis Delta occurs at different levels of Antigen HBs quantitative in young children and adults, depending on the time of Hepatitis B exposure.

Disclosure of Interest: None Declared

LB/P204

COMPARTMENTALIZATION OF HEPATITIS E VIRUS (HEV) BETWEEN SERA AND FECES IN IMMUNOCOMPROMISED PATIENTS

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Background: Hepatitis E virus (HEV) is the main cause of acute Hepatitis. This zoonotic virus can lead to chronic Hepatitis E with persistent viremia and liver lesions in immunocompromised patients. Chronic Hepatitis E has been associated with neurological symptoms, extra-hepatic replication in brain cells and compartmentalization of HEV genomes in the cerebrospinal fluid. HEV is also able to replicate in human enterocytes. However, molecular mechanism associated with HEV compartmentalization in the digestive tract remains to be characterized.

Purpose: Characterize the HEV genetic changes in sera and feces during the course of HEV infection in immunocompromised patients.

Methods: Eight kidney transplant recipients with chronic HEV infection (≥12 weeks) were included in this retrospective clinical study. Paired sera and feces samples were collected at the same time during the acute (<12 weeks) or chronic phases (≥12 weeks) of HEV infection. The ORF1 and ORF2 regions of HEV genome were amplified and sequenced by NGS (MiSeq, Illumina). Positions with a sequencing depth of over 100X were analyzed in the Galaxy platform.

Results: Most HEV genetic changes selected during HEV infection were compartmentalized between plasma and feces (n=6/10 mutations) and were localized in predicted B, CD4+ or CD8+ T cell epitopes (n=9/10). Interestingly, position 749 of ORF1 was associated with a strict compartmentalization during the chronic phase of HEV infection, with the major mutation 749Q detected in 100% of read in feces and not detected in sera. Two positions were associated with selection of mutations during the **chronic phase** of HEV infection (ORF1 L828I and ORF2 H354Y). In contrast, mutations were selected at five positions of the ORF2 during the acute phase of infection but were no longer detected during the chronic phase of infection.

Conclusions: Our findings revealed a compartmentalization of HEV genomes between sera and feces. This could suggest an extrahepatic replication in the digestive tract or in another subpopulation of hepatocytes, which could contribute to re-infection, treatment failure or antiviral resistance. Also, the vast majority of HEV mutations were selected in relevant epitopes, suggesting that the adaptative immune response could be the major factor driving the evolution of intra-host HEV diversity.

Disclosure of Interest: None Declared

LB/P205

NATURAL POLYPHENOLS TRANS-CHALCONE AMELIORATES LPS-INDUCED LIVER INJURIES THROUGH THE INHIBITION OF ENDOPLASMIC RETICULUM STRESS, OXIDATIVE STRESS, AND INFLAMMATION

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Backgrounds: The liver is known as the primary organ important for drug and chemical substance metabolism. Liver injury may be induced by drug abuse, viral infection and heavy alcohol consumption, and is considered to be a common clinical disease. Chalcones, one of the main classes of flavonoids, are precursors of flavonoid and isoflavonoid biosynthesis. Natural and also synthetic chalcones exert various biological activities such as anti-inflammatory, antioxidant, anti-diabetic, and hepatoprotective activities. *trans*-chalcone is the precursor molecule to flavonoids and possesses antioxidant and anti-inflammatory properties. *trans*-chalcone, a semi-synthetic chalcone with a simple structure, is the core of chalcone compounds. In the past, *trans*-chalcone has also been shown to have anti-fibrotic and anti-inflammatory properties moreover, its protective effects on liver injury has not been clearly understood. In this study, we postulated the protective effects and molecular mechanisms of *tans*-chalcone on lipopolysaccharides (LPS) -induced toxicity in AML-12 cells.

Methods: Mouse hepatocytes (AML-12) were treated with *trans*-chalcone (10, 20, and 40 μM). ER stress, Oxidative stress and inflammatory proteins level were evaluated by western blot. LPS induced reactive oxygen species (ROS) level was determined by DiOxyQ (DCFH-DiOxyQ) assay.

Results: *trans*-chalcone treatment significantly reduced LPS-induced cytotoxicity of AML-12 cell in dose dependent order, reduced ER Stress, ROS levels, inhibits inflammation.

Conclusion: This results concluded that *trans*-chalcone possess a beneficial role in the prevention of hepatocyte injury by attenuating ER Stress, oxidative stress, apoptosis and inflammatory cytokines production through the regulation of ER stress pathway.

Keywords: *trans*-chalcone, LPS, ER Stress, inflammation, oxidative stress, apoptosis.

Disclosure of Interest: None Declared

LB/P206

CHANGES IN FATTY ACID PROFILE AND THE EXPRESSION OF GENES RELATED TO LIPID METABOLISM IN LIVER TISSUE OF PATIENTS WITH CIRRHOSIS.

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Background: The prevalence of chronic liver diseases associated with inflammation and fibrosis is increasing worldwide. Patients with liver cirrhosis are likely to develop end-stage liver dysfunction. The treatment of choice for those patients is an orthotopic liver transplant (OLT).

Fatty acids (FA) are a group of chemical compounds with different properties. Their metabolism takes place mostly in the hepatocytes and FA are components of many lipid structures, e.g. cell membranes. This makes a possible link between liver tissue damage and altered fatty acids profile. Alterations of FA profile in liver tissue may be also a potential target for therapy, e.g. by specific FA supplementation that may prevent liver disease development.

Purpose: The aim of this study was to compare fatty acids composition in cirrhotic and normal liver tissue and to analyze relative expression levels of genes responsible for FA metabolism.

Method(s): Intraoperative tissue samples were collected from patients undergoing OLT. Normal liver tissue was taken from the surgical margin of liver tumors resections. The samples were homogenized and total lipids were extracted with the Folch et al. method[1]. Subsequently, FA were derivatized into methyl esters and analyzed using gas chromatography coupled with mass spectrometry. Collected material was also used for RNA isolation. Analysis of gene expression was done by real time PCR.

Result(s): We have found increased amount of arachic acid (C20:0) (0.13±0.04% vs 0.10±0.03%, $p<0.05$) in the cirrhotic livers compared to the control group. Moreover, in cirrhotic livers we have found significantly lower FA with branched chain (BCFA) especially those with iso conformation (*iso* BCFA) (total BCFA 0.36±0.09 vs 0.42±0.06% p=0.049; *iso* BCFA 0.16±0.05% vs 0.19±0.024% p=0.023). Monounsaturated FA (MUFA) with 20 and 22 carbons in chain were significantly higher in OLTx samples (C20:1 – 0.27±0.10% vs 0.21±0.06% p=0.05; C22:1 – 0.048±0.02% vs 0.024±0.01% $p<0.001$).

Relative genes expression analysis has shown significantly lower expression of stearoyl-CoA desaturase (SCD1), fatty acids synthetase (FASN) and long chain fatty acid elongase 6 (ELOVL6) in cirrhotic samples compared to control subjects.

Conclusion(s): Patients with cirrhosis had increased levels of MUFA, which are associated with high cardio-metabolic risk. In turn, lowered BCFA, which have various beneficial properties, including anti-inflammatory, may be also a unfavorable change. Lower levels of the expression of all analyzed genes in liver with cirrhosis are probably a result of liver tissue degradation. Thus, the alterations in FA profile in cirrhotic liver can eventuate from changes in the expression of lipid metabolism genes that develop during the earlier stages of the disease.

References: 1. FOLCH, J.; LEES, M.; SLOANE STANLEY, G.H. A simple method for the isolation and purification of total lipides from animal tissues. J. Biol. Chem. 1957, 226, 497–509, doi:10.1016/s0021-9258(18)64849-5.

Disclosure of Interest: None Declared

LB/P207

SAFETY OF HERBAL MEDICINES FOCUSING ON LIVER AND KIDNEY FUNCTIONS : A SCOPING REVIEW OF CLINICAL STUDIES IN SOUTH KOREA

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Background: Approximately 27% of the individuals using Korean medicine (KM) services in South Korea have been prescribed herbal decoctions. In this context, the validity of the National Health Insurance coverage of herbal decoctions is discussed in South Korea. The safety of herbal decoctions has been highlighted as an important indicator.

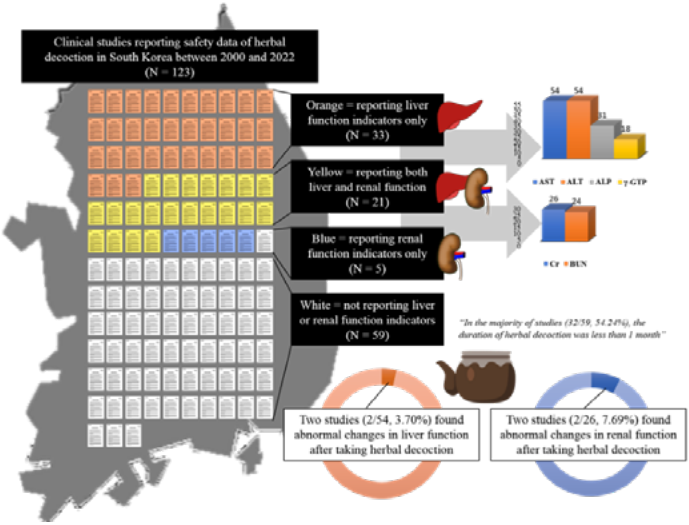
Aim of the study: The authors attempted to investigate the safety of herbal decoctions prescribed by KM doctors from the viewpoint of liver and kidney function tests by comprehensively analyzing Korean clinical studies using the methodology of a scoping review.

Methods: This scoping review was conducted by applying the Arksey and O'Malley framework and modified methods. A comprehensive search of seven electronic health databases was conducted, and relevant clinical studies published between 2000 and 2022 were collected. Only clinical studies reporting liver and/or renal function results of herbal decoctions prescribed by KM doctors were included in this review. The characteristics of the included clinical studies and the reported proportion of each liver and/or renal function indicator were analyzed. Moreover, meta-analyses of herbal decoction effects on liver and/or renal function in prospective cohort studies were conducted.

Results: In total, 59 clinical studies were included in this review. Although the number of clinical studies in this field changed little over time, the proportion of prospective cohort studies markedly decreased in the 2010s compared to the 2000s. In most of the included studies, the duration of herbal decoction prescriptions was less than 1 month. Abnormal changes in liver or renal function parameters were identified in a small number of studies (3.70% and 7.69%, respectively). In a meta-analysis of 15 prospective cohort studies, no statistically significant changes in four liver function indices and two renal function indices were found before and after the administration of herbal decoctions.

Conclusions: In this review, qualitative and quantitative analyses demonstrated favorable safety profiles related to herbal decoctions. This scoping review discusses the gaps found between clinical settings and research fields on this topic and suggests challenges for future research. These findings will be used as evidence for the introduction of National Health Insurance coverage of herbal decoctions in South Korea in the future.

Image/Table:



Disclosure of Interest: None Declared

LB/P208

SEROCONVERSION OF HEPATITIS C DURING DIALYSIS IN MAJOR CITIES OF PAKISTAN . AN EXPIERENCE FROM DEVELOPING COUNTRY

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Background: Hepatitis C is highly prevalent in Pakistan. Several studies worldwide have shown that patients undergoing hemodialysis are at a risk for developing Hepatitis C. So this study was carried out to determine the proportion of patients undergoing hemodialysis who seroconverted from HCV negative to HCV positive status in our hospitals,

Methods: This descriptive cross-sectional study was conducted at four tertiary care hospitals of Punjab from January 2016 to March 2016 on patients undergoing hemodialysis currently. With the help of WHO Sample Size Calculator, at confidence level 95%, absolute precision 5% and anticipated population proportion 14%, the minimally required sample size was calculated to be 186 patients but we included 190 patients in our study.

Our inclusion criterion was all those patients who were Hepatitis C negative (determined by HCV serology, based on the principle of immunochromatography) at the initiation of dialysis and remained negative for the subsequent six months after the initiation of hemodialysis.

Our exclusion criteria was all those patients who seroconverted to HCV positive with six months of initiation of hemodialysis (the period corresponding to the incubation period of Hepatitis C virus.) and those who were dialyzed on emergency basis

Results: Out of 190 patients who were HCV negative at the initiation of dialysis, 93 (i.e. 48.9%) patients converted to HCV positive status whereas 97 (i.e. 51.05%) patients remained HCV negative throughout the study. The mean time taken for seroconversion was 18.04 months (SD $\pm$ 15.43) months). The median was 12 months, with an inter quartile range of 14 months.

Conclusion: The proportion of HCV seroconversion in our hemodialysis units is very high.

Disclosure of Interest: None Declared

LB/P209

EVALUATION OF HEPATITIS C POSITIVE DONOR TO HEPATITIS C NEGATIVE RECIPIENT KIDNEY TRANSPLANT IN A HIGHLY SENSITIZED PATIENT POPULATION

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Purpose: This study assessed outcomes of Hepatitis C virus (HCV) donor positive to recipient negative (D+/R-) kidney transplants (KT) in high immunologic risk patients. Literature reports positive short-term outcomes in low immunologic risk patients, but limited data exists to support HCV D+/R- KT in high immunologic risk patients.

Methods: This retrospective cohort study included HCV antibody negative (-) recipients of a nucleic acid test (NAT) positive (+) KT who received HCV treatment with direct-acting antiviral therapy from 12/1/20 and 11/30/21. NAT+ KT recipients were matched 1:1 with NAT - KT recipients based on age, body mass index, and gender. All serologies were confirmed prior to study inclusion. The primary outcome was a composite of patient and graft survival 3 months post-KT. Secondary outcomes included percent of patients with sustained virologic response (SVR), time to HCV treatment initiation, incidence of cytomegalovirus (CMV) and BK viremia, presence of de novo donor specific antibody (DSA), rejection and HCV treatment related adverse drug reactions (ADRs). Descriptive statistics were used for baseline characteristics and a Log-Rank test was used for the primary outcome.

Results: Eighteen HCV NAT+ KT recipients were matched with 18 HCV NAT- KT recipients. Study population was similar between groups and had end stage renal disease due to diabetes and/or hypertension, mean class I PRA >14%, pre-transplant DSA in 16% of patients in each cohort, and all received induction with rabbit anti-thymocyte globulin (Table 1). There was no difference in patient (p=0.32) and graft survival (p=0.99) between groups at 3 months post-KT. One death due to COVID-19 occurred in the NAT- group. There was no difference in estimated glomerular filtration rate (eGFR) at 1 (p=0.39) and 3 months (p=0.28), incidence of delayed graft function (DGF) (p= 0.67) or CMV (p=0.1) and BK viremia (p=1) between groups. (Table 2). HCV transmission occurred in all NAT+ KT recipients, and all who completed therapy achieved SVR. Treatment was initiated on average 8.5 weeks post-KT (Table 3). Notably, 33% of patients required financial assistance to obtain HCV treatment.

Conclusions: Use of HCV D+/R- KT resulted in no difference in patient and graft survival at 3 months in this matched cohort. HCV NAT + KT patients should be connected with financial assistance programs early to promote timely treatment initiation.

Image/Table:

Table 1: Baseline Demographics

	HCV NAT + (n:18)	HCV NAT – (n:18)	p-value
Recipient Information			
Male, n (%)	14 (77.78)	15 (83.33)	0.6737
Age, mean (SD)	58.44 (± 8.18)	58.94 (± 8.85)	0.8813
Indication for trans plant			
Hypertension, n (%)	16 (88.89)	10 (55.56)	0.0256
Diabetes, n (%)	8 (44.44)	11 (61.11)	0.3196
Focal segmental glomerulosclerosis, n (%)	1 (5.56)	0 (0)	1.000
Polycystic kidney disease, n (%)	0 (0)	1 (5.56)	1.000
Other, n (%)	1 (5.56)	4 (22.22)	0.1482
Race/Ethnicity			0.0670
Caucasian	0 (0)	5 (27.78)	
African American	12 (66.67)	8 (44.44)	
Hispanic	5 (27.78)	4 (22.22)	
Asian	0 (0)	1 (5.56)	
Pacific Islander	1 (5.56)	0 (0)	
Years on dialysis pre-transplant, median (IQR)	6 (5.0 to 7.0)	7 (4.25 to 9.5)	0.2750
Prior kidney transplant, n (%)	1 (5.56)	2 (11.11)	0.546
Estimated Post Transplant Score (EPTS), median (IQR)	90 (58 to 96)	75 (53.25 to 91.25)	0.9431
BMI, mean (SD)	34.79 (± 6.94)	33.08 (± 7.61)	0.4750
Panel reactive antibody (PRA), mean (SD)			
Peak Class I	14.94 (± 30.98)	21.44 (± 35.52)	0.5623
Peak Class II	7.06 (± 15.26)	17.67 (± 31.3)	0.2048
DSA at transplant, n (%)	1 (16.67)	3 (16.67)	0.1486
Thymoglobulin induction, n (%)	18 (100)	18 (100)	1
Maintenance therapy, n (%)			
Tacrolimus	18 (100)	18 (100)	1
Mycophenolic acid	18 (100)	18 (100)	1
Prednisone	1 (5.56)	3 (16.67)	0.2888
Donor Information			
Age, median (IQR)	40.5 (31 to 51)	53.5 (43 to 56)	0.0834
BMI, mean (SD)	31.90 (± 11.24)	29.88 (± 6.67)	0.4996
Male, n (%)	12 (66.7)	13 (72.2)	0.7175
Kidney Donor Profile Index (KDPI), median (IQR)	46 (45 to 87)	73.5 (38 to 86)	0.3864
Donation after cardiac death (DCD), n (%)	6 (33.33)	9 (50)	0.3105

Table 2: Results

	HCV NAT + (n=18)	HCV NAT – (n=18)	p-value
Patient survival at 3 months, n (%)	18 (100)	17 (100)	0.3179
Graft survival at 3 months, n (%)	16 (88.89)	16 (88.89)	0.9878
GFR at 1 month, mean (SD)*	40.38 (± 15.97)	46.82 (± 22.44)	0.3892
GFR at 3 months, mean (SD)*	53.25 (± 23.64)	46.06 (± 16.48)	0.2805
DGF, n (%)	4 (22.22)	3 (16.67)	0.674
CMV viremia, n (%)	0 (0)	3 (16.67)	0.1
BK viremia, n (%)	4 (22.22)	4 (22.22)	1
De-novo DSA formation, n (%)	5 (27.78)	5 (27.78)	1
Treatment for rejection, n (%)	2 (11.11)	2 (11.11)	1
Biopsy Proven, n (%) n=2	1 (50)	1 (50)	1

*Patients on dialysis excluded; n=16

Table 3: HCV NAT + ICT Cohort Results; n=18

Direct acting antiviral agent, n (%)	
Sofosbuvir 400 mg/vel lipitavir 100 mg x 12 weeks	16 (88.89)
Glecaprevir 100 mg/pibrentasvir 40 mg x 8 weeks	2 (11.11)
Mean time to positive HCV PCR post-KT, days (SD)	4.93 (± 3.73)
HCV Genotype, n (%)	
1a	14 (77.78)
2	2 (11.11)
3	2 (11.11)
Mean time to treatment initiation, weeks (SD) n=17	8.54 (± 3.3)
SVR, n (%) n=8	8 (100)
Patients requiring payment assistance for HCV treatment, n (%)	6 (33.33)
Dialysis during HCV treatment, n (%) n=8	2 (25)
Prior authorization required for DAA approval, n (%)	18 (100)
Appeal required for DAA approval, n (%)	0 (0)
Baseline AST before treatment, mean (SD)	16.44 (± 5.03)
Baseline ALT before treatment, mean (SD)	15.83 (± 8.78)
Peak AST, mean (SD)	32.71 (± 20.87)
Peak ALT, mean (SD)	41.25 (± 33.30)
AST at SVR n=8	15.37 (± 7.31)
AST at SVR n=8	15.62 (± 7.19)
ADEs associated with HCV treatment, n (%)	3 (16.67)
Headache	2
Fatigue	1

Disclosure of Interest: None Declared

LB/P210

KINETICS OF CIRCULATING HBV RNA AND HEPATITIS B CORE-RELATED ANTIGEN LEVELS IN PERSONS WITH HIV WITH AND WITHOUT FUNCTIONAL HBV CURE

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Background: The determinants of functional cure of Hepatitis B virus (HBV) infection during antiviral therapy are poorly understood. Hepatitis B core-related antigen (HBcrAg) and circulating HBV RNA correlate with intrahepatic covalently closed circular DNA (cccDNA) levels and cccDNA transcriptional activity. Both markers may help identify persons who eventually experience functional HBV cure on therapy.

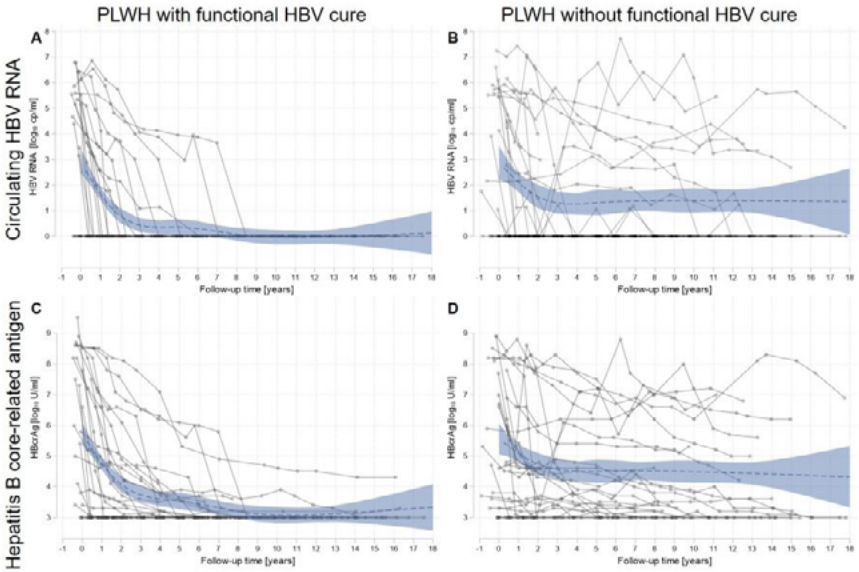
Purpose: We aimed to compare long-term kinetics of circulating HBV RNA and HBcrAg levels among persons with HIV and HBV treated with tenofovir in the Swiss HIV Cohort Study.

Methods: We matched 29 participants with to 29 participants without functional HBV cure based on age, sex, pre-treatment with lamivudine and $CD4^+$ T-cell count. We modeled HBV RNA and HBcrAg levels over time using generalized linear models, and compared HBV RNA and HBcrAg levels during tenofovir therapy in participants with and without functional HBV cure. We defined functional HBV cure as the first occurrence of a quantitative Hepatitis B surface antigen <0.05 IU/ml.

Results: Median follow-up time was 12 years (interquartile range [IQR] 8-14) with functional HBV cure occurring after a median of 4 years (range 0.5-14). At start of tenofovir, 23/58 (40%) participants had undetectable HBV RNA and 11/58 (19%) had HBcrAg below cut-off. Median levels of HBV RNA and HBcrAg at tenofovir start were similar in those with and without functional HBV cure (HBV RNA: 4.9 [IQR <1.0-5.7] vs. 3.9 $\log_{10}$ cp/ml [IQR <1.0 -5.7], p=0.64; HBcrAg: 6.9 [IQR 3.9-8.6] vs. 5.9 $\log_{10}$ U/ml [IQR 3.6-7.7], p=0.24). Among those with detectable HBV RNA at tenofovir start, 14/17 (82%) with functional HBV cure compared to 10/18 (56%) without cure had an HBV RNA decline of $\geq$1 $\log_{10}$ cp/ml after one year on tenofovir (p=0.15, Figure 1). In participants with HBcrAg above cut-off at tenofovir start, 14/22 (64%) with functional HBV cure compared to 8/25 (32%) without cure had an HBcrAg decline of $\geq$1 $\log_{10}$ U/ml (p=0.04) after one year. Five years after tenofovir start, HBV RNA was undetectable among 26/28 (93%) participants with functional HBV cure compared to 17/26 (65%) without cure (p=0.02), and 18/28 (64%) with cure had HBcrAg below cut-off compared to 6/26 (23%) without cure (p=0.003).

Conclusions: A decline in circulating HBV RNA and HBcrAg levels during tenofovir therapy is more likely in persons with HIV with functional HBV cure than in those without cure. HBV RNA and HBcrAg may be promising predictive markers of functional HBV cure.

Image/Table:



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LB/P212

A PUBLIC HEALTH APPROACH TO EXPANDING ACCESS TO CARE FOR PATIENTS LIVING WITH HEPATITIS C USING THE PROJECT ECHO MODEL

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Background: The Indiana Hepatitis C ECHO was established in 2018 to increase access to HCV screening, diagnosis, and treatment by leveraging the Project ECHO (Extension for Health Outcomes) model. Six years later, the program continues with the aim to mitigate many of the common challenges clinicians encounter when treating HCV. It is a virtual program that connects primary care providers (PCPs) across the state with leading hepatologists. During each session, learners enhance their skills to care for patients living with HCV and frequent co-occurring conditions like substance use disorder. Core to the ECHO model is case-based learning which allows participants to apply knowledge and skills in real time and receive recommendations for their patients' care.

Purpose: Utilizing technology to amplify and leverage scarce resources, the Hepatitis C ECHO connects primary care providers with specialists in the state to learn best practices on how to screen, diagnosis, and treat HCV. This free program allows participants to join according to their availability.

Method(s): Twice a month, rural and urban providers connect for 90-minutes for an opportunity to learn from their peers and gastroenterologists (GIs). ECHOs consists of an interprofessional cohort of learners including physicians, pharmacists, advanced practice nurses, social workers, case managers, and public health practitioners who provide a systemic perspective to patient care. Sessions begin with a timely didactic presented by a subject matter expert that covers content for both new and experienced clinicians treating HCV. Topics include ordering appropriate labs and analyzing findings, prescribing treatment, and scheduling follow-up care and testing. Every ECHO includes a case study in which learners present a de-identified patient they are currently caring for and receive feedback from the ECHO community, encouraging a comprehensive approach to patient-centered care.

Results: The Indiana HCV ECHO program has met for more than 120 sessions, welcomed 544 unique health providers, and discussed more than 203 patient cases. Until 2021, Indiana required prior authorizations and a GI consult for PCPs. At its onset, the ECHO worked with Indiana Medicaid to utilize ECHO as the GI consult so more PCPs could treat. The ECHO was used as supporting evidence that PCPs could expertly manage HCV care. Today, the program promotes linkage to care efforts, harm reduction, and dismantling stigmas.

Conclusion: Rather than moving patients, ECHO moves knowledge. The ECHO model amplifies the capacity of the healthcare and public health workforce and improves access to HCV services. It creates a sustainable community of health professionals who learn evidence-based skills for testing and treatment and best practices for addressing challenges for patients, often related to social determinants of health. The HCV ECHO is a simple, yet effective, program that trains leaders in ending the HCV epidemic.

Disclosure of Interest: None Declared

LB/P213

EVALUATION OF A PROGRAM PROVIDING OPERATOR TRAINING, QUALITY ASSURANCE, AND QUALITY CONTROL FOR POINT-OF-CARE TESTING FOR HEPATITIS C (HCV) INFECTION

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Background: The National Australian HCV Point-of-Care Testing Program has established point-of-care testing (antibody and RNA) at 57 of 90 planned health services in Australia. Training and quality frameworks are critical for point-of-care testing scale-up and management. This study evaluated Hepatitis C virus (HCV) point-of-care testing training outcomes and test error rates for operators during program scale-up.

Methods: Standardised training was delivered remotely for Xpert HCV Viral Load Fingerstick point-of-care testing operator training and quality management. In evaluation of training delivered, operators were enrolled in a longitudinal observational study and completed a self-assessed competency survey utilising a 5-point Likert scales to rank below average point-of-care competence (score ≤2 of 5) and >average point-of-care HCV test competence (score >3). Unsuccessful HCV tests (error/invalid/no result) were assessed.

Results: To date, 154 point-of-care operators have commenced training, with 142 (92%) completing all training aspects. The testing workforce consists of 55% nursing staff, 5% peer workers and 5% aboriginal health professionals. Overall, 23% of operators had previous GeneXpert experience. Standardised operator training increased self-assessed >average competence for processes of specimen collection (67% vs. 100%, P<0.001), quality control (58% vs. 100%, P<0.001), RNA testing (44% vs. 94%, P<0.001), and result interpretation (49% vs. 100%, P<0.01). The proportion with ≥average self-assessed competence significantly increased (P<0.001) following each step of training delivered. Between January 2022 and February 2023, 6,614 point-of-care HCV RNA tests were performed, with 5,936 (90%) demonstrating initial validity. Unsuccessful HCV tests (n=678) were categorised as "error" (sample quality related, n=568), "invalid" (cartridge related, n=78) and "no result" (instrument related, n=32), with the unsuccessful test rate lower among operators with prior GeneXpert experience (8% vs. 15%, P<0.001).

Conclusion: Standardised point-of-care operator training improved self-assessed GeneXpert competency and facilitated a high rate of valid HCV point-of-care results on first test attempt. The root cause of unsuccessful tests was predominantly related to collection of poor-quality capillary blood samples. These results demonstrate the importance of robust training, compliance with trained processes, and ongoing skill acquisition for the delivery of high-quality HCV point-of-care test results.

Disclosure of Interest: None Declared

LB/P214

ASSESSMENT OF KNOWLEDGE ,ATTITUDE AND PRACTICE TOWARD HEPATITIS B INFECTION AMONG HEALTHCARE WORKERS IN SIXTY PUBLIC AND PRIVATE HOSPITALS IN KHARTOUM STATE 2023

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Introduction: Hepatitis B is an endemic life threatening disease in Sudan. Its Sero-prevalence among population in Sudan varied from (47%) to (78%) (1).Risk of HBV infection is much higher in HCWs than other population.This study is directed to assess the level of KAP (Knowledge,attitude and practice) toward HBV among the HCWs in Khartoum state.

It is the first study to be accomplished in such a number of hospitals in Khartoum state from all the sixty hospitals of Khartoum state.

Aims and Objectives: The main aim of the study was to assess the level of (KAP) toward (HBV) among (HCWs) in 60 Public and Private hospitals in Khartoum state,Sudan.Specific objectives was to estimate the proportion of immunized HCWs,to estimate the proportion of needle stick injuries and their relationships with the endemic status of HBV in Khartoum.

Methodology: A Cross sectional descriptive study was conducted to assess the KAP of HCWs in sixty Public and Private hospitals in Khartoum State,Sudan.

Sample size calculation: Size of population:(21,576), P value:(0.58), q(1-0.58)= (0.42) , (95%) confidence level and (2%) error margin.

Here, n = required sample size, n = Z (α/2) 2 pp./d2, p = 0.58.

This resulted in the required sample size of 2111 HCWs.

Data collection method and analysis:

A self administered questionnaire was obtained from HCWs and

Analyzed by SPSS version 28.

Results: A sum of 2111 HCWs from different sixty public and private hospitals in Khartoum state participated in the study.

Participants in the study were from different positions including; surgeons , physicians , registrars, interns , nurses, midwives , imaging technicians and lab technicians.

Knowledge section: (84%) 1785 of HCWs they do not believe that HBV infection is transmitted by casual contact.

(69%) 1464 of HCWs they believe that HBV can cause (HCC) hepato-cellular carcinoma.

Attitude section: Analysis revealed that (83.4%) 1760 of the HCWs have positive attitude toward the disease. (22.1%) 466 HCWs stated that they do not wear protective hand gloves during medical/clean intervention with the patients for different causes.

Practice assessment: (19.8%) 418 HCWs have malpractice noticed toward the disease.

(3/5) of the HCWs 1276 (60.4%) confirmed they routinely do viral screening every three months.

(51.5%) 1089 of the HCWs have completed the three doses of the hep B vaccine.

(40.9%) 863 HCWs stated that they do have previous history with accidental needle stick injury. (84.5%) or 730 of 863 have reported their injury and did the protectice measures. While (15.4%) or 133 of 863 HCWs have completely neglected their injury.

Discussion: I suggest further implementation of protective guidelines for HCWs and vaccination campaign in developing countries.

Biliography: (1) Mudawi HM. Epidemiology of viral Hepatitis in Sudan. Clin Exp Gastroenterol. 2008;1:9-13. doi: 10.2147/ceg.s3887. Epub 2008 Dec 11. PMID: 21677820; PMCID: PMC3108625.

Disclosure of Interest: None Declared

LB/P215

TOWARD HEPATITIS C ELIMINATION IN CORRECTIONAL INSTITUTIONS: THE EXPERIENCE FROM THE NATION-WIDE OUTREACH PROGRAM IN TAIWAN

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Background: Prisoners are prioritized for Hepatitis C elimination due to the high prevalence. It is challenging to introduce screening, diagnosis and treatment for Hepatitis C virus (HCV) into the correctional institutions due to the special environment.

Purpose: To achieve the goal of eliminating Hepatitis C, a nation-wide outreach program for eliminating Hepatitis C in prisons was launched in Taiwan. This study aims at investigate the feasibility and performance of the program.

Methods: Among 46 correctional institutions, 37 institutions (including 21 out of 23 prisons, 7 out of 12 detention centers, 3 out of 3 open prisons, 3 out of 5 rehab institutions, and 3 out of 3 skill training institutions) has developed the Hepatitis C elimination team and the tailored eliminating program under the coordination of the Taiwan National Hepatitis C Program Office from the Ministry of Health and Welfare (MOHW), Agency of Corrections from the Ministry of Justice, and local health bureaus, and in collaboration with the contracted hospitals, the local branches of the National Health Insurance Administration, MOHW, and non-government organizations . To ensure that prisoners can receive health education, screening and treatment during the program, only those who still have more than 6 months in prison will be invited to attend the program. Anti-HCV testing and subsequent HCV RNA testing and DAA treatment would be provided to those who agree to enroll. The inclusion criteria, process, division of roles and responsibilities, timeline, etc. were depicted explicitly in each tailored elimination plan. In combination of WHO's diagnosis and treatment goals, namely ≧90% of chronic Hepatitis C (CHC) patients were diagnosed and ≧80% were treated, we set up the micro-elimination goal of more than 72% (=90%*80%) CHC patients were treated.

Results: The elimination programs were originally scheduled to start in May 2021 and be implemented by the end of the year. However, due to the huge Covid-19 outbreak in early May 2021, the implementation period was extended to the end of 2022. Among 43,512 prisoners, 31,579 fulfilled the inclusion criteria, 29,215 received health education and were invited. Among those invited, 17,073 (58%) agreed to attend the program and receive anti-HCV testing with 27.4% prevalence of anti-HCV positivity. Among those anti-HCV positive prisoners, 4,026 (86%) received HCV RNA testing with 69% viremic rate. Finally, 95.6% received DAA or peg-interferon

treatment. The SVR12 rate is 94.6%. Among those who fulfilled the inclusion criteria of the programs, 4 institutions has reached the micro-elimination goal.

Conclusions: All correctional institutions has established capacity for onsite screening, diagnosis, and DAA treatment through implementing the programs, which is the basis for micro-elimination in the near future. Moreover, it is necessary to develop elimination plan for those who have short term of penalty.

Image/Table:

Figure The correctional institutions in Taiwan

*Those marked in black have not yet jointed the program; those marked with a star have reached micro-elimination goal.

Disclosure of Interest: None Declared

LB/P216

IDENTIFYING THE UNDIAGNOSED HCV-POSITIVES: A MODEL-BASED APPROACH INFORMED BY HEALTH ADMINISTRATIVE DATA

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Background: Despite the availability of the highly effective direct-acting antiviral agents (DAA), Hepatitis C virus (HCV) infection continues to pose a major public health threat worldwide. The development of effective and tailored strategies to ensure equitable access to HCV care requires an understanding of trends in the geographic and demographic distribution of the disease burden in terms of the number of infections and, more importantly, the number of patients who remain undiagnosed, as the majority of infections remains asymptomatic until the onset of late-stage disease. Such evidence can guide strategic planning and allocation of the resources needed to implement programs for preventing disease transmission, improving screening, and improving treatment uptake.

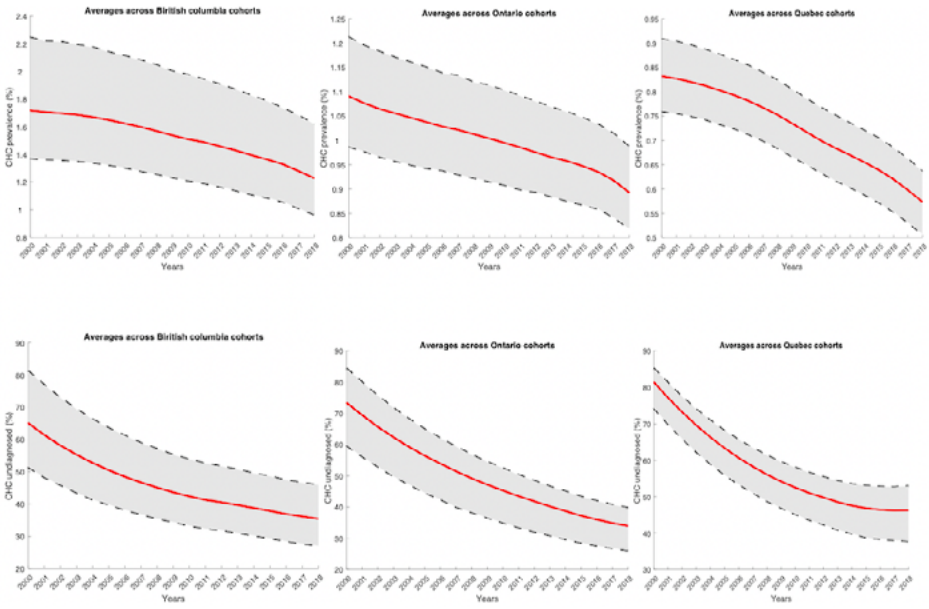
Purpose: Our objective is to estimate the chronic Hepatitis C (CHC) prevalence and undiagnosed proportion in Canada's three largest provinces, British Columbia (BC), Ontario and Quebec, using a back-calculation modeling approach informed by population-level health administrative data.

Methods: We conducted population-based retrospective analyses of health administrative data for the three provinces from 1999 to 2018 to generate the annual incidence of patients with newly diagnosed hepatocellular carcinoma (HCC), decompensated cirrhosis (DC) and CHC as well as patients treated for HCV for three birth cohorts: individuals born before 1945, born between 1945 and 1965, and born after 1965. We developed a back-calculation framework to estimate the historical prevalence of CHC for each cohort. We used a Bayesian Markov Chain Monte Carlo (MCMC) algorithm to back-calculate the historical CHC prevalence and the undiagnosed proportion through a calibration process. The algorithm constructs the probability distribution of the historical CHC prevalence and the undiagnosed proportion by comparing the model-generated predictions of the annual number of CHC health events against observed health administrative data such as the diagnosed HCC and diagnosed DC incidences generated in the retrospective analysis.

Results: Our results indicated a decreasing trend in the undiagnosed CHC proportion and CHC prevalence over time for all cohorts in the three provinces. The mean prevalence estimates for BC, Ontario and Quebec across all birth cohorts in 2018 were 1.2% (95%CI: 0.96%-1.6%), 0.91% (95%CI: 0.82%-1.04%), and 0.57% (95%CI: 0.51%-0.64%), respectively. The undiagnosed proportion estimates for BC, Ontario and Quebec across all birth cohorts were 35.4% (95%CI: 27.1%-45.8%), 34.28% (95%CI: 26.7%-41.6%), and 46.3% (95%CI: 37.9%-52.9%) in 2018, respectively.

Conclusion: This is the first study to estimate CHC prevalence and undiagnosed proportion in Canada after the introduction of new DAA treatment using provincial health administrative data. Our findings can provide evidence to guide decision-making on HCV screening strategies to reach undiagnosed individuals and help meeting the WHO elimination target.

Image/Table:



Disclosure of Interest: None Declared

LB/P217

PARTNERING WITH HARM REDUCTION AGENCIES TO ADDRESS HEALTH EQUITY IN HCV CARE: A PILOT STUDY IN THE SOUTHERN UNITED STATES

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Background: In 2020, the US Department of Health and Human Services published a report outlining a strategic plan for eliminating viral Hepatitis. People who inject drugs (PWIDs) were identified as a priority population. Modest increases in HCV treatment in PWIDs may significantly impact eradication; however, stigma and limited access to care continue to create barriers. To address these barriers, community-based prevention services such as syringe services programs can be leveraged to provide HCV screening and linkage to care.

Purpose: To describe a collaboration between the Mountain Area Health Education Center (MAHEC), which provides primary care in North Carolina, and a harm reduction (HR) agency to improve care for people with substance use disorder and HCV.

Method(s): Continuous quality improvement (CQI) cycles were performed to provide low-barrier access, optimize workflow, and improve patient experience. Key implementation strategies included:

- Flexible Lab Options – To promote screening and confirmatory testing, labs were performed at the HR agency or other places convenient for patients outside of traditional health care settings.
- Peer Support Services – The Linkage to Care Coordinator has a background in peer support and community health work, which allowed her to support PWIDs in a culturally and linguistically appropriate manner.
- Telehealth Utilization – All linkage to care and subsequent visits were done via telehealth, removing transportation and geographic barriers. Patients were able to use a private space and technology provided by the HR agency as needed.
- Registry Creation – Patient referrals were tracked in a registry using data reports provided by the EHR. Clinical staff tracked the flow of patients through screening, linkage to care, and treatment.
- Structured Communication – Initially, frequent meetings were scheduled for CQI efforts. For ongoing communication, both organizations identified key personnel to streamline referrals and provide ongoing patient updates.

A retrospective registry review was performed to generate aggregate, de-identified data for the pilot program. Screening data for the HR was compared to the general primary care population.

Result(s): Antibody positivity for the HR agency collaboration was 22% compared to 4% for the general primary care practice. RNA positivity was 68% and 51%, respectively.

From February 2022 to February 2023, 28 referrals were received from the HR agency. The median age was 42 years with the typical patient being non-Hispanic white (79%) and male (64%) with a diagnosed substance use disorder (96%). All patients attended their first appointment for linkage to care. The median time to linkage was 30 days (range 12-77).

Conclusion(s): Enhanced collaborations between HR agencies and the traditional health care system provide opportunities to increase HCV screening and linkage to care for PWIDs. Use of telehealth and peer support services reduce barriers faced by patients with limited access.

Disclosure of Interest: R. Grandy Grant / Research support from: FOCUS Program through Gilead Sciences, Inc. awarded to MAHEC , S. Shukla Grant / Research support from: FOCUS Program through Gilead Sciences, Inc. awarded to MAHEC , R. Barefoot Grant / Research support from: FOCUS Program through Gilead Sciences, Inc. awarded to MAHEC

LB/P218

HEPBCOMMUNITY.ORG: A GLOBAL ONLINE FORUM DEDICATED TO SUPPORTING PEOPLE WITH HEPATITIS B AND BRIDGING THE GAPS BETWEEN SCIENTIFIC, CLINICAL, AND AFFECTED COMMUNITIES

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Background/Approach: Hepatitis B is associated with stigma and discrimination. People with chronic Hepatitis B struggle to discuss their status openly and to form support networks. This isolation is a barrier to accessing accurate medical advice, exacerbates psychosocial impacts associated with the disease, and affects linkage to care. We established a forum (www.HepBCommunity.org) to foster an online community, connecting people living with Hepatitis B to health experts, scientists, and to one other.

Analysis/Argument: We expect that our forum will improve community engagement, reduce isolation, and improve health literacy and outcomes. The forum hosts real-time and interactive conversations that are more engaging than pamphlets, lectures, or other online content. The forum features anonymised posting, allowing users to discuss sensitive topics openly. Finally, since much of the information comes from verified experts or from peers, shared advice is likely to be seen as trustworthy.

Outcome/Results: After 2 years, the forum has registered >1400 users from around the world (including Australia, Russia, the US, Germany, Ghana, Sierra Leone, Slovenia, Bulgaria, India, Ireland, and Nigeria). Our user base is likely much broader: the forum has recorded >750,000 page views, suggesting unregistered users are visiting www.HepBCommunity.org for information. Registered users have posted >5000 posts, with topics including: seeking advice when newly diagnosed; when and how to disclose one's HBV status; considerations for starting antiviral treatment; and dietary and lifestyle changes to prevent progressive liver disease. Finally, we ran the first ever research showcase for the affected community, bridging the gap between the two often isolated communities (garnering >8000 views).

Conclusions/Applications: We expect that with greater awareness of this forum and active recruitment methods (e.g. point-of-care staff referring patients, social media, and partnerships with HBV advocacy organizations), we can provide a larger support network. The forum should not only to provide community and support for those with Hepatitis B, but also facilitate better community engagement for clinical studies and the development of a global grass-roots advocacy network for Hepatitis B.

Disclosure of Interest: None Declared

LB/P219

ROUTINE SCREENING, CONFIRMATORY TESTING, AND LINKAGE TO CARE FOR HCV AMONG PEOPLE WHO INJECT DRUGS IN APPALACHIA

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Abstract Content: Choice Health Network (CHN) is an HIV services organization based in Knoxville, Tennessee providing HIV treatment and prevention throughout the Appalachia region. CHN's harm reduction program includes syringe exchange and has integrated HCV screening, testing, and linkage to care for the past three years. CHN's harm reduction clients face a variety of obstacles including substance use, lack of housing access, food insecurity, rural isolation and transportation challenges, and HIV/HCV access to care. Since beginning screening for bloodborne viruses among syringe exchange participants in 2019, CHN has consistently found a ~30% HCV ab+ rate and a ~70% HCV RNA+ rate. By providing nonjudgmental care in a unique environment, harm reduction staff (including a nurse phlebotomist for RNA reflex and an alcohol & drug counselor) are able to build trust and rapport with clients who face discrimination in many other healthcare settings. CHN's harm reduction team is focused on bringing HCV services to the community's most vulnerable residents and provides outreach testing in encampments and rural surrounding counties in addition to the brick-and-mortar Knoxville location. Providing HCV rapid screening, confirmatory testing, and linkage to care through harm reduction services is a new and promising mechanism for improved HCV outcomes including elimination among critical populations.

Disclosure of Interest: None Declared

LB/P220

PHARMACY TECHNICIANS AS PATIENT NAVIGATORS IN HEPATITIS C LINKAGE-TO-CARE SERVICES AT A FEDERALLY QUALIFIED HEALTH CENTER

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Backgroun:d Per HepVU, it is estimated that as of 2016, 21,800 people were living with Hepatitis C Virus (HCV) in Arkansas (AR). Currently, AR is 1 of 2 states in the U.S. remaining with the most stringent restrictions for Medicaid Access for patients with HCV. ARcare is a Federally Qualified Health Center system of over fifty clinics across AR that utilizes a Clinical Pharmacy Services Team to perform comprehensive medication management. Through the FOCUS program, a public health initiative of Gilead Sciences, ARcare received support to develop innovative and replicable models for HCV screening and linkage to care to address the challenges associated with diagnosing individuals with HCV and overcoming personal and systemic barriers to accessing care. One movement for overcoming these barriers is employing patient navigators in linkage-to-care (LTC) services, who serve as a point of contact for both patients and clinic staff throughout the patient-centered care process.

Purpose: This project was designed for the advancement and professionalization of pharmacy technicians (PhT) assessing the utilization of a PhT to serve as a patient navigator in HCV LTC services.

Methods: A PhT was employed by ARcare in June 2022 to assist the clinic staff, including the clinical pharmacists, in caring for patients with HCV. Through a pharmacist-run LTC consult, the PhT's responsibilities included but were not limited to: identifying patients at high risk for HCV, completing medical background evaluations, scheduling follow-ups for patients, ensuring appropriate labs and procedures were completed, and assisting in external referrals. The PhT was trained in navigating the electronic health record, used a pharmacist-created intake form, and established communication with patients and staff throughout all clinics. In addition, the PhT aided in re-linking patients to care who may have been lost to follow-up. Patients defined as successfully LTC were those with positive HCV antibodies and confirmed HCV RNA viral load that returned for a follow-up with their provider or were referred externally to gastroenterology or hepatology. LTC progress was tracked and reported monthly.

Results: Out of 12,054 HCV antibody tests performed from January to May 2022, 5% of these tests were positive. Of the patients that had positive Hepatitis C antibodies, 47% had a detectable HCV RNA viral load, confirming an active HCV. From this population, 55% of patients were successfully LTC. Out of 7,097 HCV antibody tests performed from June 2022 to January 2023, 6% of these tests were positive. Of the patients that had positive HCV antibodies, 60% had a detectable HCV RNA viral load. From this patient population, 67% of patients were successfully LTC, showing a 12% increase in LTC after PhT implementation.

Conclusion: Although more studies are needed to further elucidate this role, utilizing a PhT was effective in HCV LTC services. It is important for the healthcare system to extend the role of PhTs.

Image/Table:

January 2022 – May 2022			June 2022 – January 2023		
Out of a total of 12,054 HCV Ab tests			Out of a total of 7,097 HCV Ab tests		
5% HCV Ab (+) tests	47% HCV RNA confirmed	55% patients linked to care	6% HCV Ab (+) tests	60% HCV RNA confirmed	66% patients linked to care

Disclosure of Interest: K. Carney Grant / Research support from: Support was received from Gilead Sciences, Inc., through their FOCUS Program (Frontlines of Communities in the United States). FOCUS is a public health initiative that enables partners to develop and share best practices in routine blood-borne virus (HIV, HCV, HBV) screening, diagnosis, and linkage to care in accordance with screening guidelines promulgated by the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Preventive Services Task Force (USPSTF), and state and local public health departments. FOCUS funding supports HIV, HCV, and HBV screening and linkage to the first medical appointment after diagnosis. FOCUS partners do not use FOCUS awards for activities beyond linkage to the first medical appointment., G. Douglass Grant / Research support from: Support was received from Gilead Sciences, Inc., through their FOCUS Program (Frontlines of Communities in the United States). FOCUS is a public health initiative that enables partners to develop and share best practices in routine blood-borne virus (HIV, HCV, HBV) screening, diagnosis, and linkage to care in accordance with screening guidelines promulgated by the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Preventive Services Task Force (USPSTF), and state and local public health departments. FOCUS funding supports HIV, HCV, and HBV screening and linkage to the first medical appointment after diagnosis. FOCUS partners do not use FOCUS awards for activities beyond linkage to the first medical appointment.

LB/P221

IDENTIFYING ACUTE HEPATITIS C VIRUS (HCV) IN PEOPLE WHO INJECT DRUGS (PWID): A EMERGENCY DEPARTMENT BASED SERIES OF CASES

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Background and Objectives: People with acute HCV disproportionately present to the ED during acute seroconversion. Revised CDC HCV screening guidelines recommend HCV Ab testing with caveat that in high pretest probability or recent exposure, consider HCV RNA PCR NAT (HCV PCR) if HCV Ab is non-reactive. This algorithm footnote does not well delineate or emphasize HCV PCR, leading to missed opportunities for identifying acute HCV. HCV PCR may identify and help link acute HCV infections to care and treatment, leading to decreased HCV transmission and WHO 2030 goals. In 2018, we increased HCV RNA PCR NAT in high-risk participants based on provider gestalt. In 2021, we formally implemented an RNA PCR model in PWID in the ED.

Methods: Retrospective chart review identified participants that underwent modified CDC HCV algorithm screening, May 2018 – June 2022. We identified Ab reactivity and labeled those with Ab+/RNA+ as chronic HCV. We identified/labeled those Ab+/RNA- with HCV remission. We identified those with Ab-/RNA- as negative HCV and those with Ab-/RNA+ as acute HCV. We considered whether current use of CDC guidelines would have routinely identified each group. We describe phenotypic characteristics of 3 ED PWID with acute HCV.

Results: 189 PWID underwent RNA PCR simultaneously with HCV Ab between 2018 and 2022 in an urban ED. 106 (56%) had reactive HCV Ab (56%). Of those, 51 (48%) also had detectable HCV RNA (chronic HCV). 55 (52%) were HCV Ab+/HCV RNA- (HCV remission). 83 (44%) did not have detectable Ab. Of those, 80 also had no HCV RNA (negative HCV). 3 participants had HCV Ab-/HCV RNA+ (acute HCV, not routinely identified).

Conclusion: This retrospective chart reviews examines the impact of a modified CDC HCV screening algorithm in the setting of high prevalence, high pretest probability PWID. While current use of CDC guidelines would have identified 186 participants, our modified algorithm identified 3 additional participants with acute HCV. Identification of HCV allows for immediate intervention for DAA linkage to care and status notification may decrease transmission to better meet 2020 WHO goals. In high pretest probability patients (PWID), a modified HCV algorithm should be considered

Disclosure of Interest: J. Wilson Grant / Research support from: Research and salary support through FOCUS, H. Henderson: None Declared, C. Reed Grant / Research support from: Research and Salary Support through FOCUS, M. Sarmento Grant / Research support from: Research and Salary Support through FOCUS, H. Hare: None Declared

LB/P222

HCV TESTING, LINKAGE AND TREATMENT IN MEDICATED ASSISTED THERAPY SITES COMPARED TO VULNERABLE POPULATIONS IN APPALACHIAN ALABAMA

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Background: CDC estimates Hepatitis C (HCV) at 1% in the general population and 7% for injection drug users. In Alabama, 45,100 are infected as estimated by the CDA Foundation. 30,200 are estimated to be diagnosed and 1400 treated. Alabama will not meet the 2030 elimination goal. Challenges during the pandemic especially with the rise of opioid use disorder (OUD) and deaths related to OUD has compounded this challenge.

Purpose: HCV testing has been a CDC recommendation since 2013 for baby boomers (born between 1945 to 1965). In 2020, it expanded to all adults (18-79 years old) but is not implemented in Alabama. According to the latest 2020 data available at CDC, Alabama ranks 2nd highest in newly reported cases of chronic HCV with an infection rate of 115.8 (per 100,000 population) in the US. Stigma challenges and cost barriers to implementing this guideline in Alabama prevail. For example, Alabama is one of 3 states in the USA rated with a grade of D+ by National Viral Hepatitis Roundtable. We implemented an EMR based routine birth cohort opt-out testing for HCV intervention as a standard of care in 2018 at community sites in clinical settings to address the above challenges.

Methods: Data are reported monthly with validation of linkage activities. Treatment data are collected beyond the scope of FOCUS funding with bias towards under-reporting. With a reach of 31 sites. 25 are in Appalachian counties. We partnered with 4 MAT sites also located in Appalachian counties.

Results: HCV testing from May 2018 to Oct 2022 resulted in a total of 39806 at all community sites with Appalachian sites comprising 69% (27,609/39806) of the overall testing volume. Sero-positivity at 12% were the same in and out Appalachia Alabama. For this same period, our MAT sites, tested an additional 2271 patients with a significantly higher seropositivity at 35.4% (805/2271) OR 4.0 CI 3.7 to 4.4) p = 0.0001. Linkage to care (LTC) was a 75% (1985/3648) for all our sites and at MAT sites, LTC was at 94.1% (510/542). The overwhelming majority of patients at our MAT sites linked to care were whites at 88.6% (452/510), 82.7% (422/510) were younger than baby boomers, and 91.6% (467/510) were uninsured.

Contrasted with our Appalachian population, 75.7% (1042/1377) were white, 60% (825/1377) and 66.4% (915/1377) were uninsured. 7.1% 36/510) of MAT patients LTC was treated. Conversely, at all our community clinic sites, 33.2% (662/1995) were treated compared to 31.6% (435/1377) treated at Appalachian sites.

Conclusion: We observed that HCV testing at MAT sites have significantly higher sero-conversion rates, and linkage rates are high. The key overwhelming challenges relating to the key demographic (financial and stigma) barriers such as being uninsured, younger and white indicate that patients at primary care settings are significantly more likely to be treated (OR 6.5, 95% CI 4.6 to 9.3, p = 0.0001).

Disclosure of Interest: None Declared

LB/P223

PREVALENCE AND SOCIODEMOGRAPHIC PROFILE OF HEPATITIS B AND HEPATITIS C IN PEOPLE LIVING WITH HIV (PLHIV): A MULTICENTER, RETROSPECTIVE STUDY

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Introduction: In the Asia Pacific region, the Philippines has been identified as the country with the fastest growing HIV epidemic. Among people living PLHIV, viral Hepatitis advances rapidly and results in more severe health problems. With the increasing incidence of HIV in the country, it is crucial to raise awareness about the co-infection of viral Hepatitis in PLHIV, as it poses a significant challenge due to its complexity.

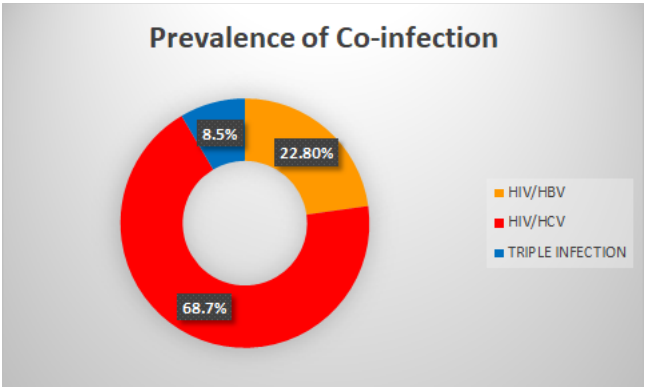
Methodology: This is a retrospective study which included cases of PLHIV enrolled in two key HIV treatment hubs in Cebu Philippines from January 2012 to June 2022.

Results: A total of 284 cases of PLHIV from the two centers were reviewed. Most of the cases of Hepatitis infection among PLHIV were mostly males (94.7%), single (83.1%), from Cebu City (77.1%) and unemployed (51.1%). The age group with the most cases belonged to the 31–40-year-old bracket. Among PLHIV with HBV, majority were College graduates (9.2%); those with HCV (25.7%) and those with triple infection (3.5%) were mostly High School undergraduates. Among the cases with HBV, the most prevalent risk profile was that of the MSM profile (17.3%). As for the HCV (59.9%) and triple infection (7.4%) categories, subjects were mostly persons who inject drugs (PWID). Of the 284 cases reviewed, HCV co-infection was more prevalent (68.7%) than HBV co-infection (22.9%).

Conclusion: Co-infection of HIV/HCV was more prevalent than HIV/HBV in this study. Notable cases of triple infection (HIV/HBV/HCV) were also observed. The data obtained can be used to pinpoint vulnerable populations and heavily affected areas to gain traction on a focused, assertive, and comprehensive information campaign. The psychosocial implications, economic burden and health consequences of these diseases individually and altogether, casts a heavy burden on the stricken, making this a public health concern worth revisiting.

Keywords: *Hepatitis B virus, Hepatitis C virus, HIV, co-infection, triple infection*

Image/Table:



Disclosure of Interest: None Declared

LB/P224

SUCCESSFUL HEPATITIS C SCREENING AND LINKAGE TO CARE AT A SOUTHERN UNITED STATES SAFETY NET HEALTH SYSTEM

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Background: HCV incidence is rising in the United States, and disproportionately affects underserved populations. Grady Health System (GHS) is a safety-net health system in Atlanta, GA, US that provides care for a largely Black, uninsured population. We implemented routine HCV screening at GHS in 2012 and uncovered a high prevalence of HCV infection (8%). We have expanded the screening program annually, adding additional sites and implementing innovations in testing and linkage to care.

Purpose: We describe the growth of our screening program in terms of sites served and innovations in screening practices. These include EHR-driven testing prompts, reflex RNA testing, navigator support for linkage and telehealth linkage options. Our HCV care cascade illustrates the success of these interventions.

Method: We started routine HCV screening of baby boomers in 2012 in GHS's Primary Care Center. We expanded the program in 2015, adding additional sites each year. Sites included ambulatory clinics, inpatient wards, Emergency Department (ED), and Walk-In Clinic. Key elements of the program include 1) Automation of screening: We built an EHR-based screening algorithm that identified patients for screening (born in target birth year and no prior HCV test or diagnosis) and prompted triage providers to order the test. On inpatient units, the HCV screening test was added to the admission lab order set. 2) We implemented reflex HCV RNA testing in 2018. 3) We utilized a patient navigator to provide HCV test results, counseling, and linkage to first visit appointments. We were nimble in strategies to deploy the navigator, pivoting from bedside navigator visits in the ED and inpatient units pre-COVID to telephone and in-clinic education sessions during the pandemic. 4) Prompted by the pandemic, we offered telehealth linkage to care visits at our onsite primary care-based Liver Clinic.

Result: From 2015-2022, we performed 102,423 anti-HCV tests and 7,024 were positive, revealing an anti-HCV prevalence of 7%. 6,255 HCV RNA tests were performed, 89% of all positive anti-HCV tests. Of those tested for HCV RNA, 3,120 were positive, revealing a chronic HCV prevalence of 50% (3% of all anti-HCV tested). 1,801 RNA positive patients (58%) were linked to care. When we adjusted linkage for those who were incarcerated, deceased, or already linked, we achieved a 62% linkage rate.

Conclusions: We implemented a successful routine HCV screening program in a safety-net health system in the Southeastern US that revealed a high prevalence of anti-HCV and chronic HCV infection. We were able to screen over 100,000 patients due to expansion of screening sites and EHR-based screening prompts. Innovations including reflex RNA testing and patient navigation resulted in high rates of confirmatory testing and linkage, even in a patient population with adverse social determinants of health. Large scale screening programs like this play a fundamental role in HCV microelimination.

Disclosure of Interest: L. Miller Grant / Research support from: Gilead Sciences, Conflict with: AbbVie, B. Park: None Declared, A. Palacio: None Declared

LB/P225

BUILDING A HUMAN BRIDGE TO HEPATITIS C CARE AMONG PERSONS WHO USE DRUGS IN THE SOUTHERN UNITED STATES

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Background: Georgia, United States (US) has experienced significant impact from the US Opioid Epidemic. Increases in injection drug use led to increases in Hepatitis C (HCV) cases. Imagine Hope is an organization that implements HCV testing and linkage in behavioral health clinics serving individuals with opioid use disorders in urban, suburban, and rural communities. In 2015, Imagine Hope began supporting HCV screening and linkage at 5 clinics. The screening program now includes 32 partners: 13 medication assisted treatment (MAT) clinics, 17 abstinence-based agencies, 2 drug courts, and 1 syringe services program. From 2015 - 2022, the initiative conducted 68,682 HCV antibody screens with 3,830 individuals found to be HCV RNA+. However, access to HCV treatment was limited, prompting us to seek a new model to meet our clients' needs.

Purpose: While there is a robust system of care for HIV in the US, a national system of care for uninsured HCV+ individuals does not exist. This is especially challenging in Georgia, a "non-Medicaid expansion" state. Most clients who need HCV treatment are uninsured. Appointments for uninsured clients are scarce, involve long wait times, pose transportation challenges and have sobriety requirements. To overcome barriers to HCV treatment, we needed to get creative. Here we describe implementation of an initiative to provide onsite HCV treatment at Imagine Hope partner clinics.

Methods: Clients with opioid use disorders served at MAT clinics traditionally keep appointments and are now routinely screened for HCV upon intake and annually. We implemented a program to deliver HCV treatment services in tandem with MAT services. We partnered with a local physician HCV treatment expert who led tailored educational sessions for MAT clinic medical staff to prepare them to provide onsite HCV treatment. Beginning with 1 MAT clinic in 2018, there are now 5 MAT clinics treating HCV onsite. Simultaneously, the Georgia Department of Public Health launched a viral Hepatitis ECHO project to support new HCV treaters. This online learning and support platform provides a vital resource for providers who are new to HCV care.

Results: From 2015 to 2022, 10,574 HCV Ab tests were conducted at the 5 agencies that launched onsite HCV treatment. 550 unique individuals were identified as HCV RNA+ (5.2%). Of those, a total of 154 initiated treatment and of these 127 achieved sustained virologic response (SVR). An additional 18 clients completed treatment but have not been tested for SVR. The vast majority (90/127 or 71%) of these cures were obtained in the last 5 years since onsite treatment became available.

Conclusion: HCV and MAT treatment can be delivered concurrently. This approach is client-focused and effectively removes barriers. Building capacity in additional clinics with the goal of making HCV treatment at MAT clinics the norm, bolstered by the support of Georgia's Project ECHO, promises to advance HCV elimination statewide.

Disclosure of Interest: M. Sutton: None Declared, L. Miller Grant / Research support from: Gilead Sciences, Conflict with: Consulting

LB/P226

REPEATED PEER-LED HEPATITIS C TESTING IN COMMUNITY PHARMACY: HIGH ACCEPTABILITY, HIGH TREATMENT ENGAGEMENT AND LOW (RE)INFECTION AFTER 18 MONTHS

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Background: Many people who inject drugs (PWID), including those on opiate substitution therapy (OST) and/or needle and syringe provision (NSP) have limited engagement with services and healthcare. Health inequalities facing this population are stark.

Pharmacy testing has been tried in many places to reach groups who face barriers accessing mainstream services. England national pharmacy programme has seen limited success; limited time and HCV knowledge in pharmacy teams have been identified as drivers of this. Leicester's HCV Peer and health service team worked with a local pharmacy to develop a new model, with Peers working in the pharmacy providing an in-reach, time-limited testing service from the pharmacy's clinical space.

Model: Identified and informed by lived experience, the Peer team initially delivered HCV awareness and engagement training for pharmacy staff. They then worked in the pharmacy for the duration of each project, engaging patients and providing testing.

All clients visiting the pharmacy for OST and/or NSP were offered testing. Testing was delivered under two projects 18 months apart.

Results: Project 1 was held over five sessions on five days in September 2021. 172 people accepted testing using a rapid point of care antibody test. 78 tests identified antibodies to HCV; 20 had been treated 3+ months previously but had not had a treatment outcome test (SVR12).

Of the 20 people who had HCV, 3 had previously been treated. All 20 people identified with HCV were offered treatment with peer support, and all subsequently completed treatment. 85% of these people have since had treatment success confirmed.

Project 2, returning to the same pharmacy 18 months later, was held over 5 days in February 2023. 102 people were tested of whom 35 had HCV antibodies. All of these people went on for further RNA testing, 33 RNA tests were negative (95%). One person who was RNA positive is known to, and has previously been treated by, the local HCV peer team. 1 result is still outstanding.

Many people tested at the pharmacy during project 1 were still in attendance during project 2. No reinfections were identified among patients diagnosed during project 1. Analysis of the full engagement and testing data, as well as surveys, will be available for the conference.

Conclusion and next steps: Providing pharmacy testing as a short-term, in-reach intervention has proven highly successful. People engaged well with testing delivered by peers, and progress to RNA testing and HCV treatment for those who needed it was excellent. Although most patients were at ongoing risk of HCV, they did not contract HCV (again) during the 18 months. This may be driven by lower rates of HCV within the community in Leicester as well as harm reduction and prevention information provided alongside testing. As well as scaling this project across the UK, we will conduct qualitative work with people tested to explore this.

Disclosure of Interest: None Declared

LB/P227

OUTREACHING HEPATITIS C: LEVERAGING A COMMUNITY-BASED TESTING MODEL TO INCREASE HCV LINKAGE-TO-CARE AMONG PERSONS WHO INJECT DRUGS

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Background: In 2019, Louisiana instituted a Hepatitis C treatment subscription model as part of a larger Hepatitis C virus (HCV) elimination plan with the intention of diagnosing 90% and treating 80% of Louisiana residents. This policy rapidly expanded access to no-cost HCV treatment among persons with Medicaid and prompted the development of a low-barrier, rapid entry HCV appointment type at CrescentCare, an FQHC offering comprehensive medical, prevention,and syringe services in New Orleans.

Purpose: Examine the addition of a community-based testing model to a menu of outreach modalities that leverage timely HCV treatment linkage among persons who inject drugs (PWID).

Methods: Outreach paired with a Counseling, Testing, and Referrals (CTR) program is the cornerstone of prevention at CrescentCare. When testing numbers declined due to COVID restrictions on in-person services, CrescentCare responded by developing a community-based testing model that was integrated into the existing CTR program. As restrictions lifted, this community-based testing model joined venue-based outreach, on-site general testing, and the testing component of NOSAP on the spectrum of outreach modalities employed to increase testing and linkage to HCV treatment. Our community-based testing model consists of going into New Orleans neighborhoods, conducting street intercepts, and providing testing while incorporating modern technology, such as a geolocator that broadcasts the team's location on the agency website. In addition, dedicated linkage navigators on the outreach team link persons to HCV treatment via point of care rapid testing administered during outreach or self-reported HCV status, as well as linkage to medical services such as HIV treatment, PrEP, STI care, syringe services, and primary care. Funding for non-treatment related activities was provided by Gilead Sciences through the Frontlines of Communities in the United States (FOCUS) program.

Results: Since implementation of the community-based testing model in early 2022, 812 participants have accessed rapid HCV testing. 51 self-identified as PWID. Additionally, 147 PWID self-reported as HCV positive, 138 of whom were identified during NOSAP and 9 were identified using the community-based testing model. Of those testing positive for HCV through any of prevention modalities, 30% were identified utilizing the community-based testing model, 36% were identified through testing at NOSAP, and 34% were identified using any other modality. In total, 177 persons living with HCV were referred to our rapid entry HCV program.

Conclusion: Our community-based testing model is an effective tool in finding persons at high risk for HCV. Self-disclosure of HCV status is another important pathway through which persons living with HCV can start treatment; infrastructure to support this linkage pathway is crucial to maximizing the benefits of a low barrier HCV treatment model.

Disclosure of Interest: None Declared

LB/P228

EVALUATION OF A COMMERCIAL REAL-TIME PCR ASSAY IN DRIED BLOOD SPOT SAMPLES FOR MONITORING HEPATITIS C TREATMENT OUTCOME AMONG PEOPLE WHO INJECT DRUGS IN A TEST-AND-TREAT PROGRAM

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Background:

Methods: This evaluation was performed within the context of an ongoing micro-elimination study targeting people who inject drugs (PWID) in the largest HRC in Barcelona. At baseline and at the time of SVR assessment, DBS samples were collected and shipped to the laboratory at room temperature. HCV-RNA was detected from DBS with the Abbott Real*Time* HCV assay (LLoD, 462 IU/mL) and results were compared with those obtained with the PoCT Xpert HCV VL Fingerstick assay from capillary blood (LLoD, 40 IU/mL) as the reference method. The Abbott assay is intended for use as an aid for the management of HCV infected patients undergoing antiviral therapy, and obtained CE regulatory approval for diagnostic use with DBS samples in 2020. HCV genotyping by NS5B amplification and sequencing was performed from DBS in order to differentiate between reinfection and treatment failure.

Results: From Oct 2021 to Jan 2023, 42 DBS samples from 38 patients corresponding to the SVR assessment were tested. The DBS-based assay showed 90% (95% CI, 69.9-97.2%) sensitivity (18/20), 100% (95% CI, 83.9-100%) specificity (22/22) and 95% diagnostic accuracy (22/24) for HCV-RNA detection. Two cases were not detected in DBS, with viral loads of 442 and 472 IU/mL. Sensitivity was therefore 100% (95% CI, 81.6-100%) for cases with viral loads >1000 IU/mL. The most frequent cause of recurrent viremia was reinfection (14/20, 70%), treatment failure was identified in three cases (15%) and HCV genotyping was not possible in the three cases (15%) with low viral loads (<1000 IU/mL).

Conclusion: Preliminary evidence shows the usefulness and a good clinical performance of DBS samples for assessing SVR after HCV antiviral treatment in the real world, facilitating decentralization of post-treatment follow up in PWID attending HRC in Catalonia. In agreement with previous results, few patients presented with low viral loads. While these cases might reflect acute infections that may be spontaneously cleared, repeat testing over time is recommended in this PWID population with high risk for reinfection.

Disclosure of Interest: None Declared

LB/P229

DEVELOPMENT OF A SIMPLE, AUTOMATION FREE, RAPID MOLECULAR TEST TO PREVENT MOTHER-TO-CHILD HBV TRANSMISSION

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Background: Perinatal transmission of Hepatitis B Virus (HBV) is a major public health concern, mainly in countries with limited ressources. Despite the existence of immunoprophylaxis against HBV to neonates, this preventive strategy is inefficient in presence of a high viral load in the pregnant woman. European and American hepatology societies recommend to identify these women with viral loads above 2×10^5 UI/ml.

Purpose: The aim of this project is to develop a simple molecular triage test to detect high viral loads in plasma to identify highly viremic pregnant women.

Methods: This approach includes a rapid genome extraction in a 5% chelex-100 (Biorad) resin and a isothermal recombinase polvmerase amplification at 39°C including an internal control. The visual detection is performed on a lateral flow assay. The analytical conditions were adjusted to obtain a positivity to the threshold of 2×10^5 UI/ml. In this proof of concept study assays were conducted on HBV-positive plasma samples from blood donors with various viral loads and genotypes. Typical results are shown in Fig 1.

Results: Eighty nine positive HBV plasma samples and 19 negative samples were analyzed. At the threshold of 2×10^5 UI/ml, a sensitivity and a specificity of 98.7% (95% CI:99.7-99.9%) and 88.2% (95% CI:73.4-95.3%) were obtained, respectively. An area value under the ROC curve of 0.99 (95% CI:0.99-1.00, $p<0.001$) was observed, attesting to the relevance of our assay.

Conclusion: This new simple and rapid approach (<1 hour), does not require any automate and opens new perspectives in the development of a «point of care» molecular test for improving the prevention of mother-to-child transmission of HBV.

Reference : Mayran C, Foulongne V, Van de Perre P, Fournier-Wirth C, Molès JP, Cantaloube JF. Rapid Diagnostic Test for Hepatitis B Virus Viral Load Based on Recombinase Polymerase Amplification Combined with a Lateral Flow Read-Out. Diagnostics (Basel). 2022 Mar 2;12(3):621. doi: 10.3390/diagnostics12030621. PMID: 35328174; PMCID: PMC8946908.

Image/Table:

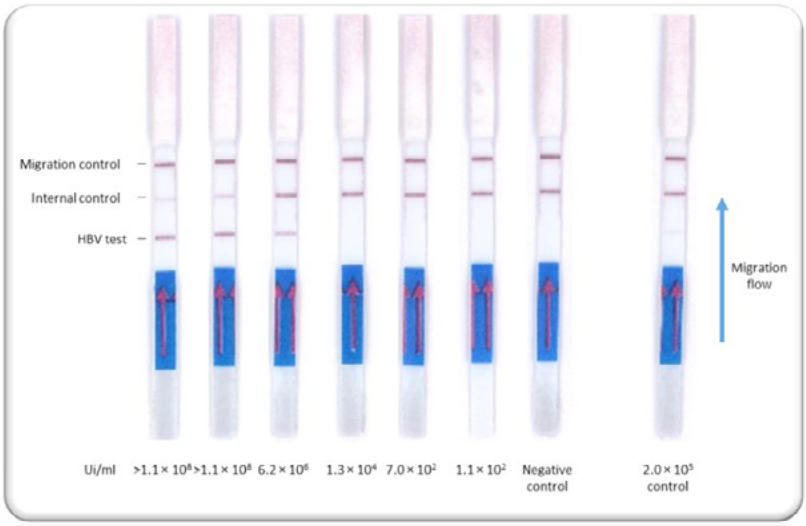

Fig 1. Visual detection of HBV (+) plasma samples

Disclosure of Interest: None Declared

LB/P230

HEPATITIS A EPIDEMIOLOGY IN EUROPE: A SYSTEMATIC LITERATURE REVIEW OF THE LAST 20 YEARS

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Background: Hepatitis A (HepA) global burden is estimated to be > 100 million new cases/year. HepA is vaccine-preventable, but outbreaks still occur in regions with low endemicity such as Europe. Guidelines for HepA vaccination in adult risk groups are available in European countries, but adherence to vaccination recommendations is not systematically documented. Here we review European data on HepA infection outcomes, we discuss the HepA risk in the population in order to assess the adequacy of HepA vaccination strategies.

Methods: A systematic search in PubMed and Embase was performed from January 2001 to April 2021. Relevant data from ECDC, ProMED, ESCAIDE and national public health websites was also reviewed. We included articles in all languages, covering all ages and data published on 11 countries (Denmark, France, Germany, Greece, Hungary, Italy, the Netherlands, Spain, Sweden, Switzerland and the United Kingdom [UK]). Studies on seroprevalence and risk factors for HepA virus (HAV) were excluded.

Results: Overall, 134 articles and 85 grey literature reports were included in our review. In Europe, in the last 20 years, HepA infections were reported in all ages. Hospitalization rates exceeded 50% in 8 of the surveyed countries during 2016–2019. HAV complications were reported by 30 publications (ps): 8 liver transplantation cases in 6 ps; liver failures in 0%–25% of HepA patients reported by 26 ps and hemorrhagic complications in 0%–51% of HepA patients reported by 8 ps. Fatality rates, reported by 12 ps for Italy, Hungary, Denmark, Germany and Spain were 0.05%–0.26%, mostly in adults/older adults.

Conclusion: In Europe, HepA infections are recorded in all ages despite not being consistently reported. Although the fatality rate is low, the hospitalization rates and the morbidity are high in adults/older adults. Considering the current epidemiological situation and HepA-related costs, authorities should raise awareness on HepA risk and adapt or improve compliance with the vaccination recommendations. Adherence to the existing recommendations should be monitored more closely. Universal HepA vaccination may be considered, similarly to the strategy adopted in the United States after widespread and ongoing HepA outbreaks.

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Disclosure of Interest: A. Andani Shareholder of: GSK, Employee of: GSK, K. Mellou: None Declared, E. Bunge Grant / Research support from: My institution received grants and payment for developing studies from GSK, Employee of: Was an employee of Pallas Health Research and Consultancy at the time of the study conduct, J. Eeuwijk Grant / Research support from: My institution received grants and payment for developing studies from GSK, Employee of: was an employee of Pallas Health Research and Consultancy at the time of the study conduct and is now an employee of P-95, G. Kassianos Conflict with: Receiving advisor/consulting fees from AstraZeneca, MSD, Novavax, Pfizer, Sanofi Vaccines, Seqirus and Valneva, Speakers bureau of:

President at the British Global and Travel Health Association and National Immunization Lead at Royal College of General Practitioners. European Scientific Working Group on Influenza and Northern European Conference on Travel Medicine, UK National Health Service and in chair at RAISE Pan-European Committee on Influenza, P. Van Damme: None Declared, R. Steffen Conflict with: Advisor/consultant fees and honoraria from GSK

LB/P231

KNOWLEDGE AND ATTITUDES OF EUROPEAN HCPS TOWARDS HEPATITIS A AND B VACCINATION OF ADULTS AT RISK

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Background: In Europe, despite low endemicity for both Hepatitis A (hepA) and B (hepB), hepA outbreaks were reported. Currently, no universal recommendations are in place for adult hepA/B vaccination in Europe. Limited data exist on the vaccination of populations at risk (e.g. travellers, men who have sex with men [MSM], patients with chronic liver disease, immunocompromised patients), although local recommendations exist. In 2021/2022, we surveyed health care professionals (HCPs) to understand their awareness of and adherence to hepA/B vaccination guidelines for adults at risk.

Methods: This was a cross-sectional, web-based survey of HCPs (general/family physicians and HCPs working in sexual health clinics [UK only]) from Germany/Spain/UK on recommending, prescribing and/or administering hepA/B vaccines to adults at risk.

Results: Of 698 HCPs included (Germany: 237, Spain: 230, UK: 231), 96% reported recommending, prescribing and/or administering hepA vaccine and 98% hepB vaccine. 91% of HCPs were aware of local guidelines and ≥73% used these for hepA/B/combined hepA+B vaccination decision-making always/most of the time. Most HCPs considered vaccination against hepA (72%–93%) and hepB (88%–92%) in adults at risk as moderately/extremely important. HCPs' recommendations on hepA/B vaccination to adults at risk ranged from 67% (adults with multiple sex partners) to 93% (travellers) for hepA and from 81% (travellers) to 92% (MSM) for hepB. The most common reasons for not recommending hepA/B vaccines were uncertainty on guidelines and perceived low risk in a given population, more frequent for hepA than hepB.

Conclusions: Despite high levels of awareness and recommendation of hepA/B vaccines, there is a disconnect between HCPs recommending and patients receiving the vaccine. Raising awareness on hepA/B diseases/prevention may increase vaccination coverage rates and is part of the WHO strategy for viral Hepatitis elimination by 2030.

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Disclosure of Interest: D. Shamarina Employee of: GSK and declares financial and non-financial relationships and activities, M. Sluga-O'Callaghan Employee of: RTI Health Solutions, V. Dave Employee of: RTI Health Solutions, E. Davenport Employee of: RTI Health Solutions, D. Curran Shareholder of: GSK, Employee of: GSK and declares financial and non-financial relationships and activities, P. Deeywadaa Employee of: GSK and declares financial and non-financial relationships and activities, A. Marijam Shareholder of: GSK, Employee of: GSK and declares financial and non-financial relationships and activities, A. Andani Shareholder of: GSK, Employee of: GSK and declares financial and non-financial relationships and activities

LB/P232

REPORTING ON PROGRESS TOWARDS HEPATITIS C ELIMINATION IN CANADA: SURVEILLANCE, POLICY AND PARTNERSHIPS

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Background: Canada has developed a pan-Canadian framework for action and a five-year action plan to help guide efforts towards reducing the health impacts of STBBIs, including Hepatitis C, by 2030. In 2016, Canada endorsed the global targets to eliminate viral Hepatitis as a public health concern by 2030.

Purpose: To provide an update on Canada's progress towards Hepatitis C elimination using key indicators including incidence, prevalence, undiagnosed proportion, and treatment.

Methods: A combination of back calculation modelling and workbook methods were used to estimate the incidence and prevalence of anti-HCV positive persons, the prevalence of chronic HCV infection and the undiagnosed proportion. The number of people treated for chronic HCV was estimated using administrative pharmaceutical data.

Results: An estimated 9,470 new infections occurred in 2019, a 2% decrease since 2015. The estimated anti-HCV prevalence in the Canadian population was 1.03% (plausible range: 0.83%–1.38%), and the estimated prevalence of chronic HCV was 0.54% (plausible range: 0.40%–0.79%). The overall proportion of anti-HCV positive persons who were undiagnosed was estimated at 24%, with individuals born between 1945 and 1975 being the population the most likely to be undiagnosed. An estimated 79,940 people with chronic HCV have been treated since 2012, meaning an estimated 30% of people with chronic Hepatitis C have been treated. The number of people treated for Hepatitis C has been decreasing since 2018, with a large decrease observed in 2020, thought related to COVID-19 as STBBI service providers reported decreased demand for, and ability to provide STBBI services, including treatment and harm reduction, especially among those living with Hepatitis C and HIV. Some examples of innovative projects funded by the Public Health Agency of Canada's Community Action Fund and Harm Reduction Fund will be presented.

Conclusions: New Hepatitis C infections have been decreasing since 2010, however the rate of reduction is insufficient to meet the 90% decrease expected by 2030. Although the burden of Hepatitis C on the overall population is relatively low, certain populations and communities remain disproportionately impacted. Progress has been slow on all targets, reaching our goal of elimination by 2030 will require targeted interventions to prevent new infections, increase testing and awareness, and increase treatment to reduce chronic HCV prevalence, especially among priority populations. By using these data to better understand who has not been reached, community and public health programs can be adjusted to improve their approaches and deliver the most effective programs tailored to the needs of people at greatest risk for infection in communities where Hepatitis C is most concentrated.

Disclosure of Interest: None Declared

LB/P233

HEPATITIS C SCREENING AND ELIMINATION STRATEGY: IMPLEMENTATION OF THE FOCUS PROGRAM IN ALMERÍA, SPAIN

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Abstract Content: Background and Aims: Spain may be one of the first countries to achieve the World Health Organization's goal of eliminating viral Hepatitis C by 2030. A serosurvey by the Ministry of Health 2017-2018 estimated a 0.22% Hepatitis C virus (HCV) active infection prevalence among the general Spanish population, with 29.4% unknown infections.

Increasing HCV screening is key. Emergency Departments (ED) often act as safety nets due to health equity issues for key populations affected by viral Hepatitis, as they often lack optimal links with their primary care providers.

We aimed to evaluate HCV screening efficacy in the ED of Torrecárdenas University Hospital, in Almería, Spain.

Methods: We implemented opportunistic HCV screening in the ED (FOCUS Program), using existing infrastructure and staff. Patients ages 18 to 69 were eligible for testing if they did not have a known diagnosis or test performed in the previous year and required blood tests at the current ED visit.

We used the LIAISON®X- Diasorin assay for HCV antibodies (anti-HCV) and the Roche Cobas® 6800 for viral RNA (HCV RNA) in the same specimen. Appropriate follow-up or discharge was given regardless of test results. We contacted positive patients to ensure linkage to care.

Results: We screened 10,641 patients from August 2021 to February 2023, finding 180 (1.70%) anti-HCV positive patients (average age of 56, 76% male) and 40 (0.38%) HCV RNA positive patients (80% males).

We identified risk exposures in 64% of viremic patients' records. Injected drug use (36%), HIV or HBV coinfection (36%), a history of incarceration (14%), and origin from countries with medium or high HCV prevalence (11%) were the top and only recorded risk exposures of the guidelines' 11 criteria. 93% of viremic patients had previously visited ED, and as of reporting, 16 patients have started antiviral treatment.

Conclusions: Undocumented HCV infection among our population is twice that estimated in the Spanish population. Hepatitis C screening in EDs is an effective strategy and should be considered in more hospitals.

Disclosure of Interest: None Declared

LB/P234

CAN ANTI-HCV SCREENING BE USED TO CATCH NEW CHRONIC HEPATITIS C PATIENTS?

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Introduction: It is estimated that 71 million people worldwide are infected with HCV. 14 million person (20%) can be diagnosed and 7.4% of them (1.1 million) have access to treatment. Therefore, it is important to know that HCV is a treatable disease and to screen larger populations. In our study, we aimed to identify the patients who were found to be positive for anti- HCV and HCV RNA in the tests requested in our hospital.

Material and Methods: Anti-HCV results in Kocaeli University Hospital between 31.07.2016-31.07.2019 and 1.01.2022- 31.10.22 in a total of 4 years were reviewed retrospectively using the hospital data system. The screened patient groups were patients who were routinely screened before surgery or dialysis, patients screened before immunosuppressant / chemotherapeutic drug therapy, and patients in the risk group for HCV transmission. The awareness of those with positive results was questioned and those who needed treatment were called to our polyclinic.

Results: Anti-HCV testing was applied to 43,133 patients. Anti-HCV test was positive in 534 patients (1.2%), 314 of them were HCV RNA negative, 53 were HCV RNA positive, and HCV RNA was not tested in 167 patients. Of the patients with positive HCV RNA results, 26 received treatment and their current HCV RNA values were negative. 20 patients who did not receive treatment were called for treatment. 167 patients whose HCV RNA was not tested were called and warned to undergo further examination. 31% of the patients were not referred for further examination. Even if HCV RNA was positive, 37.7% of the patients were not referred for treatment.

Discussion: Chronic HCV is usually asymptomatic and many people do not know they have an infection. In our study, anti-HCV positivity was found in 1.2% of patients, similar to the prevalence of HCV throughout the country. It is important to raise awareness of patients and physicians about treatment, since nearly 100% permanent viral response can be achieved with direct-acting antivirals. We think it's important to expand the groups to be screened for complete eradication, which is the target of World Health Organization.

Disclosure of Interest: None Declared

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