

ABSTRACT BOOK

Viral Hepatitis Elimination 2022

Towards a hepatitis-free world

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**POSTER
ABSTRACT
PRESENTATIONS**

Clinical and epidemiological characteristics of Chronic Viral Hepatitis in Kazakhstan: data from Unified Nationwide Electronic Healthcare System 2014-2019

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Background and Aims: Studies on epidemiology of viral hepatitis in Kazakhstan have been carried out mostly on single center analysis, yet the large-scale data is not available to date. The aim of the study was to investigate mortality in hepatitis patients using the centralized data from the Unified National Electronic Health System (UNEHS) for the period 2014-2019. UNEHS provides a good platform to overcome limitations and enables to perform survival analysis based on sex and ethnicity with adjustment for age of patients with Hepatitis B (HBV) and C (HCV).

Method: The UNEHS registries contained records of patients who had either been diagnosed with hepatitis or died while under outpatient care in 2014-2019. Out of 11,157,509 total outpatient records, and 9,653,402 inpatient records, the final cohort of 82,700 unique patients with HBV and/or HCV was derived. Mortality for HBV and HCV patients was calculated based on the recorded date of death, linked to patient's unique ID. Kaplan-Meier method was used to estimate and graphically depict the failure functions for HBV and HCV patients. Cox proportional hazards regression analysis was used to obtain crude and adjusted hazard ratios.

Results: In Kaplan Meier analysis in Figure-1 the estimates of probability of death were obtained. Males with HBV infection tend to have higher probability of death than females (Figure-1A), among male patients with HCV infection this gender-based trend is even stronger (Figure-1B). Russian ethnicity was found to be in higher risk of death in HBV patients compared to Kazakhs and Other ethnicities (Figure-1C), whereas in HCV patients Russian and Others are similar in risk for death, but higher compared to Kazakhs (Figure-1D). All differences are statistically significant based on log-rank test ($p < 0.001$). Male patients with hepatitis are at higher risk of death with unadjusted HR 1.86 (95% CI, 1.74-1.99), and 2 times higher after adjustment for age, hepatitis type, and ethnicity (HR 2.24; 95% CI, 2.10-2.40). Ethnicity of Russian had higher death risk with unadjusted HR 1.28 (95% CI 1.16-1.42), after adjustment for sex, age, and hepatitis type HR equaled 1.16 (95% CI 1.04 – 1.28). Similarly, Kazakh ethnicity had higher HR of 0.81 (95% CI 0.74-0.89), and after adjustment – HR 0.92 (95% CI 0.84-1.01) compared to the other ethnicities with hepatitis.

Conclusion: According to these data for the period of 2014-2019, male patients with either HBV or HCV have been found to have higher probability of death from all causes. Ethnicity has shown that in both types of hepatitis Russians tend to have higher probability of death than Kazakhs. In terms of other ethnicities, the scale of differences is small, thus needs to be evaluated in further studies for other confounding factors and associated comorbidities in this group.

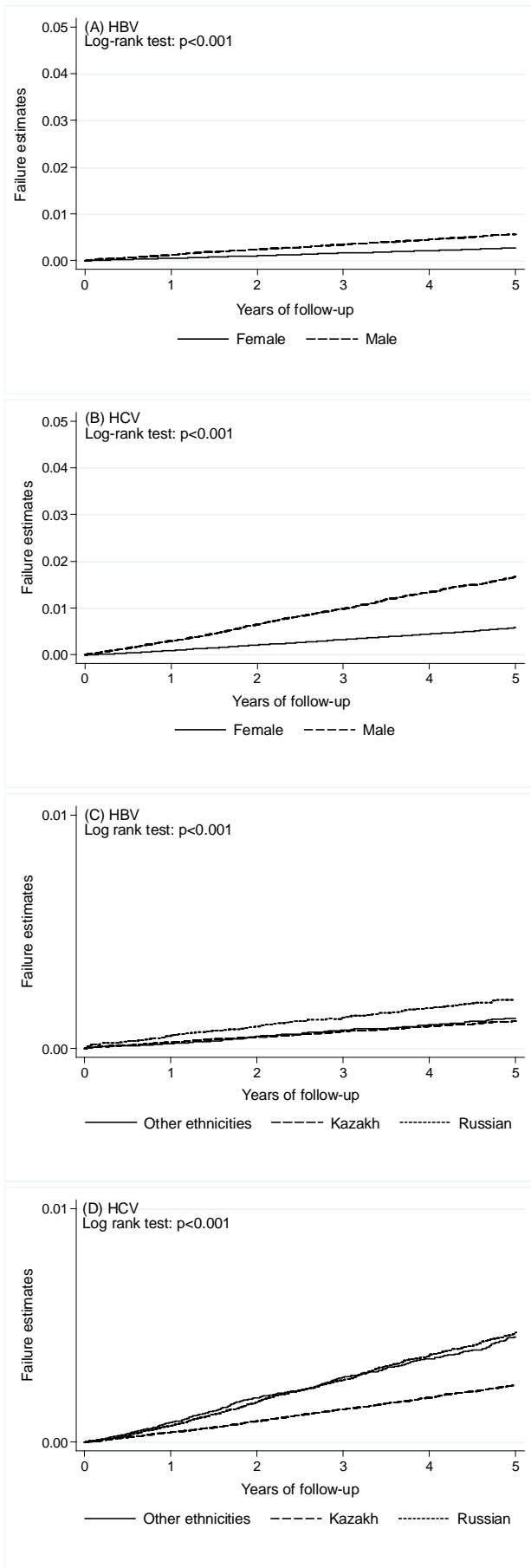


Figure 1. Failure estimates in HBV patients (A – based on sex, C – ethnicity), and in HCV patients (A – based on sex, C – ethnicity).

Are men who have sex with men (MSM) in Europe protected from Hepatitis A and B? Results from the European MSM internet survey (EMIS-2017)

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Background and Aims: Men who have sex with men (MSM) are at increased risk of hepatitis A virus (HAV) and hepatitis B virus (HBV) infections. Vaccination against these infections is widely recommended, but data on vaccination programmes are scarce. We collected information on vaccination recommendations and analysed vaccine uptake among MSM in 43 countries in the WHO European Region to guide prevention.

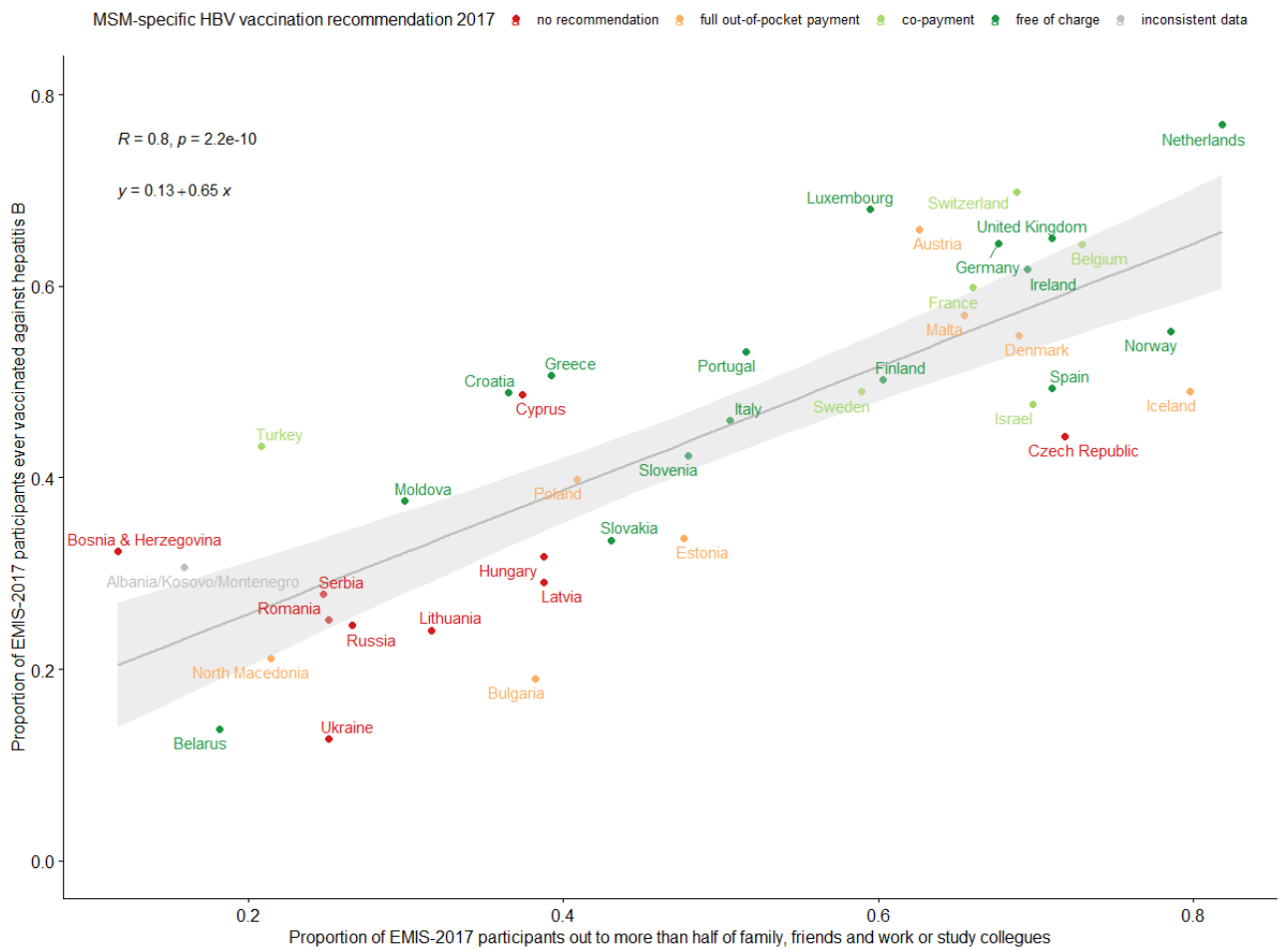
Method: From a large (N = 127,792) pan-European MSM internet survey (EMIS-2017), we analysed data on self-reported HAV and HBV vaccination status by age, educational level, financial coping, city size, and disclosure of same-sex sexual orientation ('outness', a proxy for societies' homopositivity). We excluded participants with a history of HAV or HBV infection. Additionally, we collected information on national vaccination recommendations for each country for these infections. In multilevel (participants, countries) logistic regression models, we calculated adjusted odds ratios (aOR) with 95% confidence intervals (CI).

Results: We analysed data of 113,884 MSM in 43 countries. Median age was 36 years (interquartile range: 27–47), 47% had a higher-level education as defined by over 6 years of full-time education since the age of 16, 49% lived comfortably on their income, 45% lived in cities with more than 500,000 inhabitants, and 59% were out to more than half of the people they knew. In 18 countries HBV and in 7 countries HAV vaccination was recommended for MSM and free of charge, corresponding to 60% and 49% of participants, respectively. Altogether, 53% reported ever being vaccinated against HBV and 48% against HAV.

In a multivariable model, the odds for ever being vaccinated against HBV increased with outness ('out to more than half': aOR = 1.6, 95% CI = 1.6–1.7 vs. 'out to less than half'), and were higher in countries, where HBV vaccination was recommended for MSM and free of charge (aOR = 2.4, 95% CI = 1.5–3.8 vs. 'no recommendation'). Results for HAV were of similar magnitude (outness: aOR = 1.6, 95% CI = 1.6–1.7; MSM-specific recommendation: aOR = 2.3, 95% CI = 1.3–3.8). Across countries, outness correlated highly positively with vaccination coverage (HBV: R = 0.8, p < 0.001, figure).

Conclusion: A large proportion of MSM in Europe remain vulnerable to HAV and HBV, despite available vaccination. Implementation of MSM-specific vaccination recommendations and greater effort to improve the societal climate for MSM are both needed to address gaps in vaccine coverage.

Figure:



HCV micro-elimination strategies for the PWUD population of the Balearic Islands

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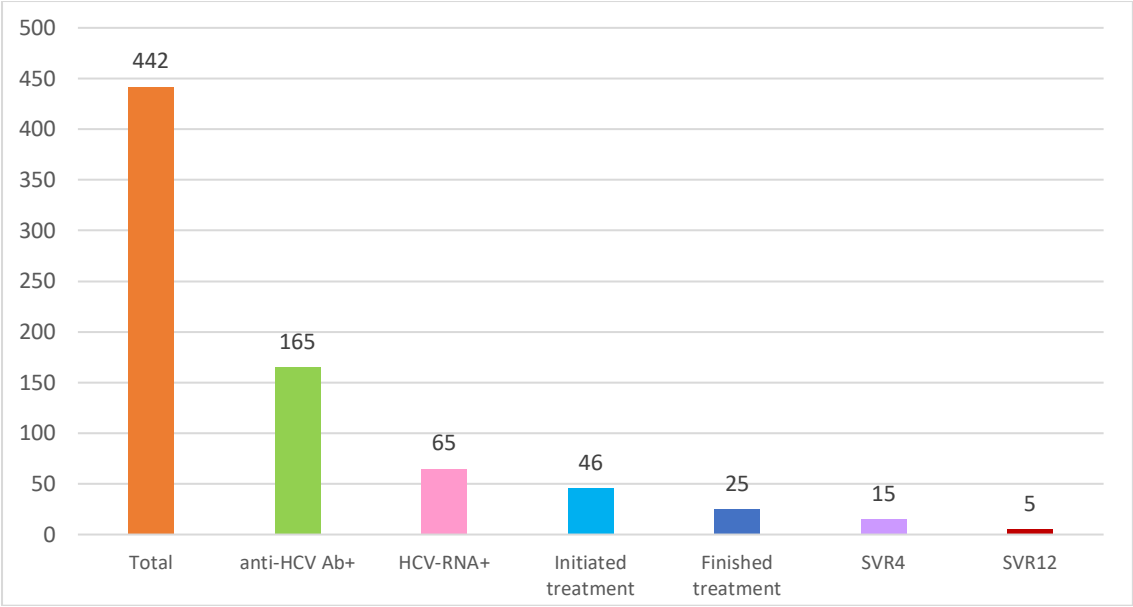
Background and Aims: To reach the 2030 hepatitis C virus (HCV) elimination goal set by the World Health Organization, it is necessary to implement strategies adapted to the population groups that are at higher risk of suffering from it, such as people who use drugs (PWUD). The *Hepatitis C Free Balears* project proposes a new model with simplified circuits adapted to PWUD from the Balearic Islands, Spain, attending addiction services centers.

Method: This project has been launched in 13 of the 17 addiction services centres in the Balearic Islands. The strategies used are: 1) onsite rapid diagnostic tests via anti-HCV antibody testing (Oraquick®) and the dried blood spot (DBS) sample collection method to confirm viremia (HCV-RNA) and facilitate screening and diagnosis; 2) treatment prescription via telemedicine and repackaging to facilitate its dispensing in the addiction services centres and to strengthen patients' adherence to treatment; 3) use of onsite DBS tests at sustained virological response (SVR) monitoring 4 and 12 weeks after treatment and for re-infection monitoring; and 4) new communication channels between professionals from the addiction services centres and hospitals to facilitate patients' linkage to care.

Results: Of the 442 recruited patients, 165 (37%) were anti-HCV+ and 65 (15%) of the total had an active HCV infection. The mean age of the HCV+ patients was 45.5 (SD: 8.54); 44 (68%) were men; 56 (86%) were Spanish-born; 55 (85%) reported a previous HCV diagnosis; 14 (22%) reported previous HCV treatment; and 10 (15%) had an HIV co-infection. Also, of the HCV+ patients, 46 (71%) have started treatment, 19 (29%) are pending and 25 (38%) have completed it. SVR4 and SVR12 monitoring tests were performed in 15 (60%) and 5 (20%) patients who completed treatment, respectively. Four (16%) SVR4 and 3 (12%) SVR12 tests were not performed due to patient absenteeism and 6 (24%) SVR4 tests and 17 (68%) SVR12 tests are pending, as the required period of time has not been reached yet. 93% (n=14) and 100% (n=5) of the SVR4 and SVR12 monitoring tests showed undetectable HCV-RNA, respectively. Four (1%) patients abandoned the project.

Conclusion: The strategies carried out in the *Hepatitis C Free Balears* project are improving the screening, diagnosis, treatment, follow-up and linkage to care of the PWUD attending addiction services centres in the Balearic Islands, thus helping to achieve HCV elimination in this vulnerable population.

Figure: Hepatitis C Free Balears project results.



Low hepatitis C virus-viremia prevalence yet continued barriers to direct-acting antiviral treatment in people living with HIV in the Netherlands

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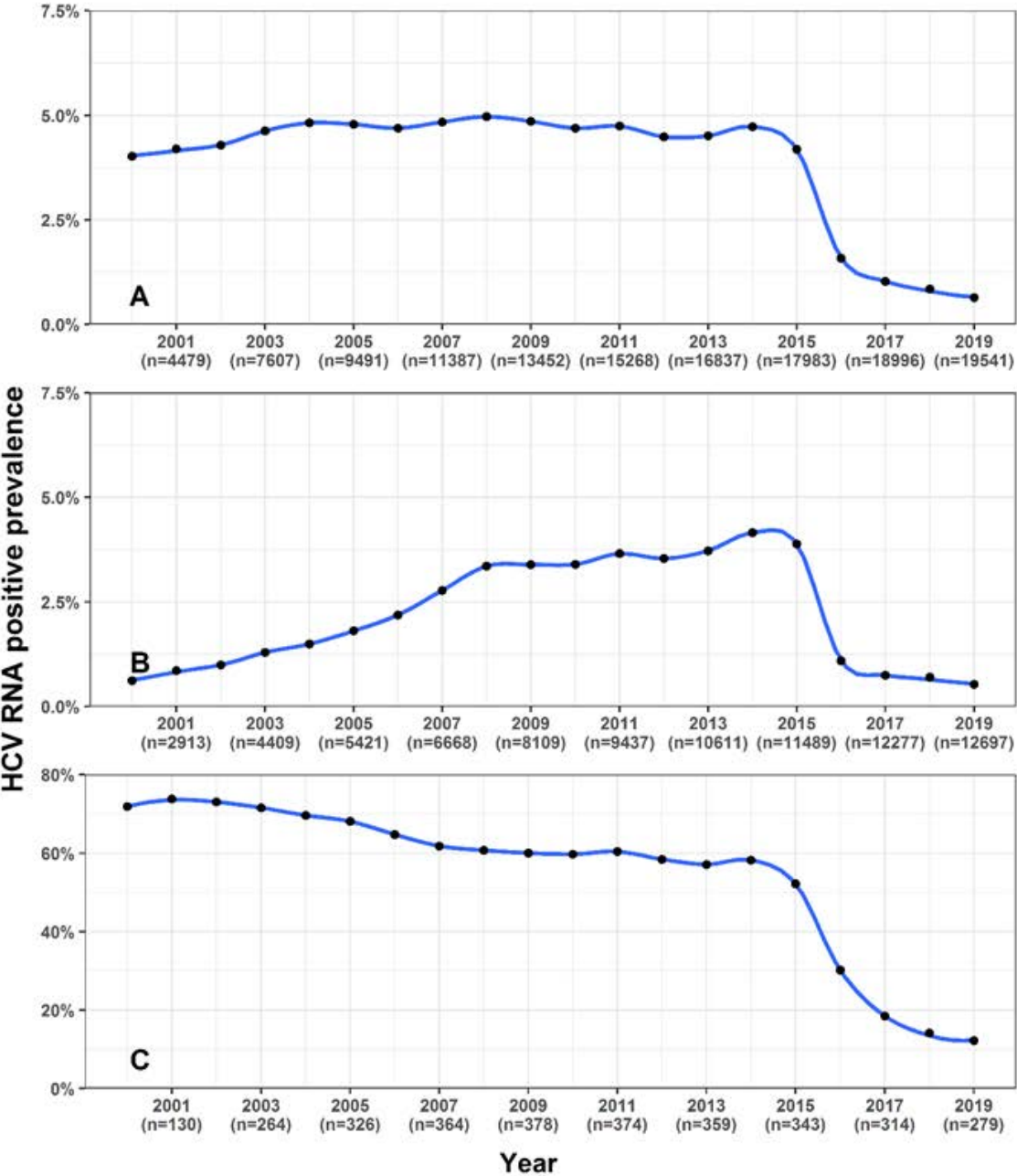
Background and Aims: The Netherlands has had universal access to direct-acting antivirals (DAA) for hepatitis C virus (HCV) treatment in people living with HIV (PLWH) since November 2015. Using data from a nationwide cohort of PLWH, we described HCV-viremia prevalence and barriers to treatment of the individuals remaining HCV-viremic in the DAA-era.

Method: We calculated yearly HCV-viremia prevalence as the proportion of HCV RNA-positive individuals ever tested for HCV. We then included HCV-viremic individuals with ≥ 1 visit during the era of universal DAA-access. Based on their last visit, individuals were grouped as DAA-treated or -untreated. Variables associated with lack of DAA-treatment were assessed using targeted maximum likelihood estimation. In November 2020, physicians of DAA-untreated individuals completed an in-depth questionnaire on barriers to DAA-uptake and risk of onward HCV-transmission.

Results: We included 25,196 PLWH. HCV-viremia decreased from 4-5% between 2000-2014 to 0.6% in 2019 (Figure 1: men who have sex with men (MSM), 0.5%; persons who inject(ed) drugs (PWID), 12%). Factors associated with being DAA-untreated were belonging to a key population other than MSM (OR = 4.8, 95% CI: 2.7 – 8.5), older age (OR = 1.9, 95% CI = 1.2 - 3.2), infrequent follow-up (OR = 9.7, 95% CI = 5.5 - 17.1), severe alcohol use (OR = 1.9, 95% CI = 1.2 - 3.0), detectable HIV RNA (OR = 2.3, 95% CI = 1.5 – 3.4) and HCV genotype 3 (OR = 1.7, 95% CI = 1.2 – 2.5). With universal DAA-access, 72/979 HCV-viremic individuals remained DAA-untreated at their last visit. Of these, 39 were no longer in care, 27 remained DAA-untreated in care, and six initiated DAA since database lock. Most common physician-reported barriers to DAA-uptake were patient refusal (20/72, 28%) and infrequent visit attendance (19/72, 26%). Only one DAA-untreated individual in care was engaging in activities associated with onward HCV-transmission.

Conclusion: Current prevalence of HCV-viremic PLWH in care is low in the Netherlands, coinciding with widespread DAA-uptake. However, HCV-viremia prevalence remains highest in PWID. Barriers to DAA-uptake appear mostly patient-related, while HCV-transmission seems unlikely from the few DAA-untreated individuals in care.

Figure: HCV RNA-positive prevalence among HIV-positive individuals tested for HCV in the Netherlands from 2000 to 2019



Legend: Prevalence of HCV RNA-positive persons with HIV included in the ATHENA cohort overall (A), and stratified by men who have sex with men (B) and people who inject drugs (C). Numbers in parenthesis represent the number of individuals with a known HCV RNA status linked to care during that year. Abbreviations: HCV: hepatitis C virus. PLWH: people living with HIV.

The prevalence of Hepatitis B in the UK: a systematic review

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Background and Aims: Estimates suggest that 200,000-400,000 people are living with chronic hepatitis B virus (HBV) in the UK. More robust estimates are needed to monitor trends, focus interventions to prevent and control spread, and monitor the impact of interventions and progress towards WHO HBV elimination targets. We aimed to describe and synthesise the available data on HBV prevalence in key populations in the UK to inform statistical modelling of national HBV burden estimates.

Method: The review was undertaken in line with PRISMA guidelines. Articles published between 1 January 1995 and 31 October 2019 in the databases Embase, Medline, Cochrane and Trip were searched for terms relating to HBV, prevalence and the UK. In addition, HBV surveillance data was obtained from the following sources: Public Health England (PHE) Sentinel Surveillance of Blood Borne Virus Testing (SSBBVT), PHE Unlinked Anonymous Monitoring (UAM) Survey of PWID, and PHE and NHS Blood and Transplant (NHSBT) data on blood donor testing. After screening, data were extracted for key variables and prevalence of HBV markers (HBsAg, anti-HBc, anti-HBs). A narrative synthesis was conducted. Meta-analyses were conducted where there were 2 or more studies of the same population group. Heterogeneity of prevalence within each population group was evaluated using the I² statistic and Chi² test p value.

Results: Database searches found 1,483 records. After title and abstract screening, 150 records were selected for full text screening, of which 63 were selected for inclusion. In addition, 4 records found from reference list screening and 16 surveillance datasets were included. Considerable heterogeneity exists in the pooled HBsAg prevalence estimates (Figure). Pooled HBsAg prevalence estimates were lowest in blood donors and highest in people living with HIV.

Conclusion: HBV prevalence is not evenly distributed in the UK population. More data is needed on HBV prevalence in migrant sub-populations to inform burden modelling.

Figure: Pooled prevalence estimates by population group

Population group	Number of data sets	Sample size	Pooled prevalence estimate	Heterogeneity chi2 p	I2
Key high-risk populations					
Migrants	23	26079	2.9% (2.1%-3.9%)	<0.001	97.76%
People who inject drugs (PWID)	11	23407	0.6% (0.4%-0.9%)	<0.001	79.95%
MSM	6	2779	1.01% (0.53%-1.61%)	0.19	33.12%
Sexual health attendees	6	6599	0.3% (0.1-0.6)	0.08	52.23%
Other higher risk groups					
ED attendees	9	50200	0.9% (0.8%-1.0%)	0.31	14.41%
People living with HIV	6	29439	6.5% (5.7%-7.3%)	0.12	43.27%
TB patients	6	1965	2.1% (1.4%-2.8%)	0.35	10.87%
General or unknown risk groups					
Pregnant women	10	933643	0.4% (0.3%-0.6%)	<0.001	98.85%
General tested population	8	2057689	0.8% (0.6%-1.0%)	<0.0001	99.55%
Primary care	2	4680415	0.0% (0.0%-0.1%)	-	-
Fertility clinic attendees	2	4725	1.7% (1.4%-2.1%)	-	-
Low risk groups					
Blood donors	24	5889444	0.03% (0.03%-0.03%)	<0.001	51.60%

Mortality rates among individuals with laboratory diagnosed hepatitis B virus (HBV) infection: England, 1999-2018

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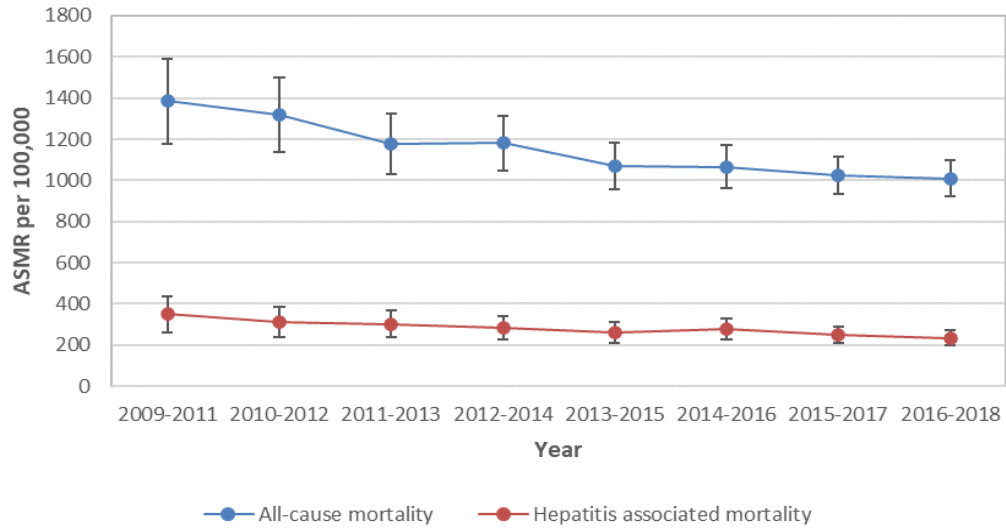
Background and Aims: Understanding hepatitis B (HBV)-associated mortality is important to monitor the care cascade and the impacts of efforts to diagnose and treat individuals with HBV infection and move towards the WHO target of reducing absolute mortality from HBV to $\leq 4/100,000$ per year. This study aimed to estimate mortality rates for individuals (aged ≥ 1 year) first reported with diagnosed HBV infection between 1999 and 2018 and describe trends.

Method: An observational virtual cohort study using record linkage. A cohort of all HBV-diagnosed patients identified from routine laboratory reports of HBV diagnosis to UKHSA was linked to all death certificates in England. We calculated median age at death and time from diagnosis to death for those who died in the follow up period. Age-sex standardized mortality rates (ASMR) were calculated for all-cause and hepatitis-associated (where liver cancer, end stage liver disease or hepatitis were recorded as one of the causes of death) mortality in individuals diagnosed with HBV 1999-2018 for all ages (≥ 1 year) and persons aged 30-69 years (premature mortality) and compared to the England general population. We examined trends by calculating 3-year annual average ASMR for 2009-2018.

Results: Of 68,398 persons with laboratory reported HBV, 52.5% were males and the median age at diagnosis was 34 years (interquartile range (IQR): 28-44). Of the 2,234 (3.3%) persons who died in the follow up period the median time from diagnosis to death was 3.4 years (IQR 1.3-6.9 years), and median age at death was 63 (IQR 51-74). The all-cause ASMR was 1087 per 100,000 person years (PY), 1.2 times that for the general population (932 per 100,000 PY). In individuals aged 30-69 (premature mortality), all-cause ASMR was 673 per 100,000 PY, 1.7 times that for the general population (391 per 100,000 PY). All-cause ASMR decreased from 1,326 per 100,000 PY in 2009-2011 to 1010 per 100,000 PY in 2016-2018. Hepatitis-associated ASMR decreased from 351 per 100,000 PY in 2009-2011 to 233 per 100,000 PY in 2016-2018 (Fig 1). Cause-specific ASMRs were 81.4 times higher for viral hepatitis, 12.8 times higher for liver cancer, 4.5 times higher for non-alcoholic liver disease and 21.0 times higher for HIV-associated disease than the general population.

Conclusion: ASMR were higher in those with a diagnosed HBV infection than in the general population. Excess hepatitis-associated mortality decreased during the study period, which might reflect improved access and adherence to more effective HBV therapies. However, this slow decline is insufficient for England to meet the WHO mortality goal by 2030. Collective efforts to ramp up diagnosis and treatment, as is the strategy for HCV elimination, are needed to reduce avoidable and premature deaths from HBV in the UK.

Figure: ASMR by all-cause and hepatitis-associated mortality for HBV-diagnosed individuals aged ≥ 1 year in England, 2009-2011 to 2016-2018



A model for a pharmacist-led point-of-care hepatitis C treatment service in outreach settings

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Background and Aims: This project presents a novel pathway to provide directly acting antivirals (DAAs) for hepatitis C virus (HCV) in community settings for hard to reach populations such as homeless people and people who inject drugs (PWIDs). Funding was granted by the operational delivery network (ODN) for a pharmacist led treatment service, with the aim of offering immediate treatment start after a positive point of care (POC) PCR. Here we outline the processes involved in setting up a novel HCV rapid treatment service in an outreach setting, and the preliminary data.

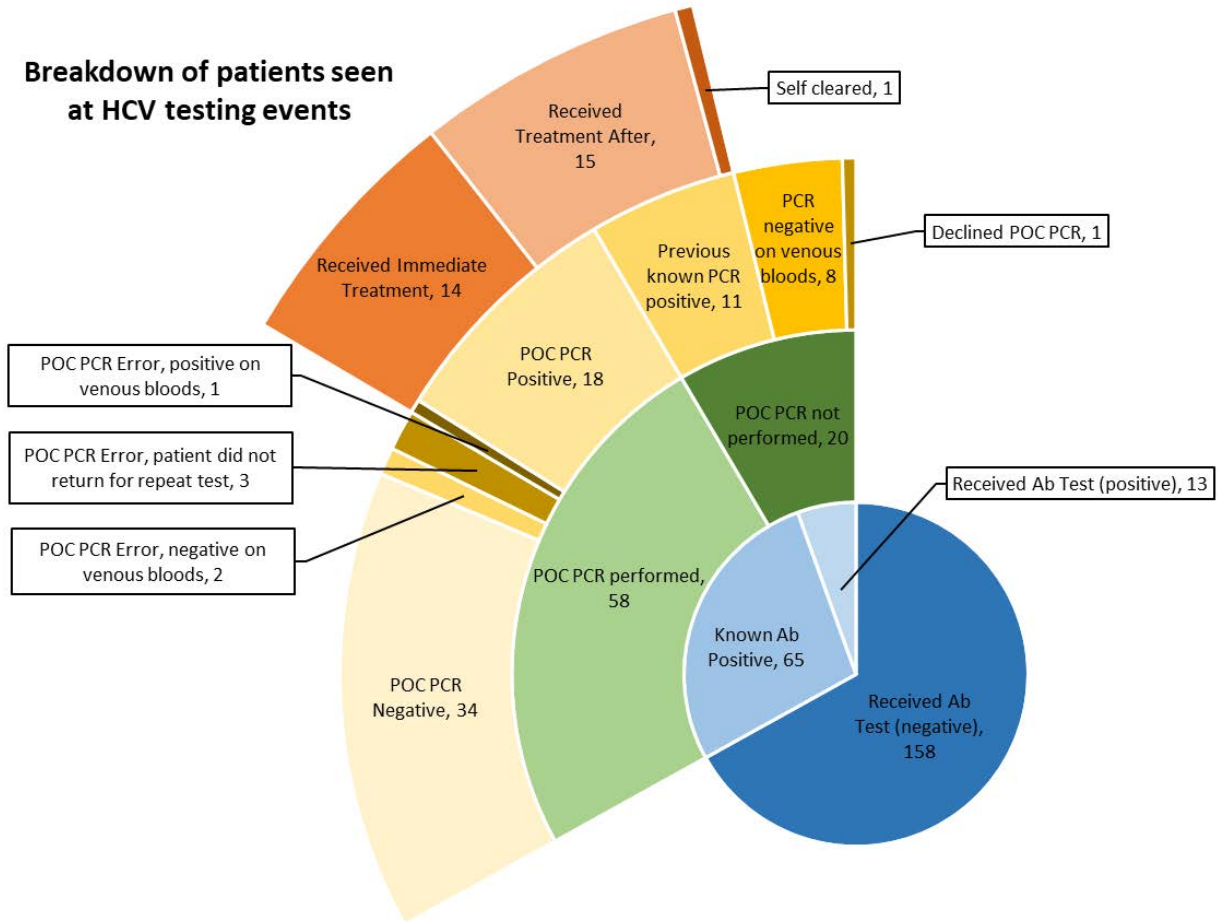
Method: To enable immediate treatment outside a conventional healthcare setting we issued over-labelled (OL) treatment packs of pan-genotypic HCV DAA sofosbuvir/velpatasvir, so that treatment could start without need for a genotype test. Over-labelling was done by our hospital pharmacy as there was no OL product commercially available. In the outreach setting patients were initially tested using POC HCV antibody (Ab) test. If Ab positive they were offered a rapid HCV PCR test via a Cepheid GeneXpert. Patients were incentivized with £5 vouchers if they waited the 1 hour for the test. If HCV PCR positive, the patient was informed, and an initial assessment done by a nurse or pharmacist. A virtual MDT was used to approve treatment, including a drug interaction check by the pharmacist. If appropriate for immediate treatment the patient was counselled by the pharmacist, who then prescribed and issued an OL pack. A follow up appointment was organized for 4 weeks time.

Results: In the 5 months since project launch, a total of 16 testing events at which POC PCR tests and immediate treatment were available have been held. These were in various settings including drug services, hostels and homeless centres. There were 236 separate user attendances at the events. 85.6 % (n = 202) had either a negative HCV Ab or PCR following the event. 30 patients were found to be PCR positive or were known to be recently PCR positive. 14 patients were commenced immediately on treatment with sofosbuvir/velpatasvir. One patient spontaneously cleared HCV. The remaining 15 all had treatment arranged after the event for reasons including: known genotype, error with or insufficient time for POC PCR, left before receiving result/treatment, needed resistance test or partner needed test (shared injecting equipment). Only 4 (1.7 %) patients were lost to follow up or declined further testing.

Conclusion: This project captured patients previously disengaged from services. So far, 29 patients have been started on treatment who would otherwise have remained untreated. We have demonstrated that availability of immediate treatment for HCV has been beneficial for patients who would otherwise be lost to follow up after testing. We have established a pharmacist led model that can be replicated and expanded to relieve the pressure on traditional hepatitis services.

Figure:

Breakdown of patients seen at HCV testing events



Immunity to hepatitis A and hepatitis B among men who have sex with men (MSM) attending sexual health clinics in London and the North of England, 2017-18

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Background and Aims: Although hepatitis A (HAV) and hepatitis B (HBV) immunisation for gay, bisexual and other men who have sex with men (MSM) is recommended in the UK, data on immunisation coverage are limited. We determined the seroprevalence of HAV and HBV immunity among a sample of MSM attending geographically dispersed sexual health services (SHS) in England.

Method: Residual serum samples taken for HIV/syphilis testing from adult MSM attending SHS (hereafter: 'sampled MSM') were obtained from laboratories providing testing for 8 SHS in London and 1 in the North of England. Data on individuals' characteristics were extracted from the GUMCAD STI Surveillance System, a depersonalised dataset of all attendances at SHS in England for the sampled and all non-sampled MSM attending the clinics during the study period. All samples were anonymised then tested for HAV IgG (past exposure to HAV infection or immunisation) and anti-HBs (immunisation, and less so, past exposure). Seroprevalence of HAV and HBV immunity was estimated, overall and stratified by individuals' characteristics. Using separate models for HAV and HBV, logistic regression was used to estimate crude and adjusted odds ratios (OR) between seropositivity and demographic and clinical characteristics.

Results: Of 2,577 samples tested for HAV IgG, 74.5% were positive. Of 2,551 samples tested for anti-HBs, 77.1% were positive. Median age of sampled MSM was 33 years (range 18-74) and 43.6% were non-UK born. Overall, 26.7% had a history of sexually transmitted infections (STI) in the past year, 13.5% were HIV positive, 14.9% and 28.0% respectively had received HAV or HBV vaccinations, and 21.5% and 24.1% respectively were coded as HAV or HBV immune. In adjusted analysis HAV IgG seroprevalence varied by clinic and WHO region of birth ($p < 0.01$), increased with older age (vs 18-25 age group; $p < 0.01$), was higher in those with an STI in the past year (OR 1.60, 95% CI 1.25-2.05) and those who were HIV positive (OR 1.68, 1.14-2.49). Anti-HBs seroprevalence varied by clinic ($p = 0.02$), increased with older age ($p < 0.01$) and was higher in those with a STI in the past year (OR 1.63, 1.26-2.10). For both infections seroprevalence was higher in those recorded as immune (OR 6.06, 3.91-9.41 for HAV, OR 4.93, 3.44-7.05 for HBV) but lower in those recorded as vaccinated (OR 0.42, 0.32-0.55 for HAV, OR 0.42, 0.34-0.53 for HBV).

Conclusion: Our analysis provides a baseline seroprevalence from which to monitor serial levels of immunity to HBV and HAV in MSM accessing SHS. Levels of immunity for both viruses are high at around 75%, noting samples were taken after recent widespread outbreaks and related vaccination campaigns. Older age, history of STI in past year and WHO region of birth were associated with HAV and HBV seropositivity. High vaccine coverage in all MSM should be maintained to prevent further outbreaks.

The "Mobile pathway", an opportunity in providing Hepatitis C services, during the challenging times of COVID-19

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Background and Aims: Hepatitis C virus (HCV) infection results in chronic liver disease, affecting approximately 71 million, worldwide. The World Health Organisation in 2016 proposed a strategy to eliminate HCV infection by 2030. Highly efficacious and well-tolerated drug therapy like direct-acting antiviral (DAA) could eliminate HCV effectively (American Association of the Study of Liver Diseases - Infectious disease society of America, 2020).

Lancashire and South Cumbria's HCV service covers a population of 1.8 million (Lancashire and South Cumbria Health and care partnership, 2021). During Covid-19, face-to-face clinics were cancelled, and a significant number of hepatology nurses were deployed into COVID-19 wards. Hence, a mobile outpatient clinic service consisting of a portable fibro scan, blood sampling and delivery of medication was introduced. Data collection from 01.06.2020 to 31.07.2021 has been reviewed on the number of clinics, attendees, HCV positive cases, treatment received, declined or lost follow up.

Method: Data has been collected from in-hospital records, primary care, prison probation services and Public Health England. Patients were contacted through telephones. The results collected were divided into three periods, "Period A" from June to September 2020, "Period B" from October 2020 to February 2021 and "Period C" from March to July 2021.

Results: The total number of mobile clinics performed were 17, 27 and 34 with attendees of 151, 130 and 163 during period A, B & C respectively. HCV positive cases were 49, 120 and 106 while the number that received treatment among positive patients were 24 in period A, 75 in B and 54 in C. The number lost follow up or declined therapy was 25, 44 and 34 respectively.

Data collected from mobile clinics services at Preston Prison, from June 2020 to July 2021 showed that among a total population of 700, 665 (95%) have been tested and the treatment has been offered to 55 out of 69 (92%) of HCV positive patients.

Conclusion: Although, the overall number of clinics have been considerably increased and micro-elimination was achieved among the Preston prison population, the interest in completion of the therapy among the patients who were diagnosed with HCV was significantly lower with a mean average of 54% over the total period.

Therefore, it is imperative to identify corrective measures needed in the services. Some of the proposed improvements are expanding the resources, establishment of an administrative department, providing telephonic clinics and introduction of incentive schemes for attendees such as supermarket vouchers.

Figure:

Hepatitis C Services, introduction of Mobile clinics in times of COVID 19

Period	Clinics number	Number of attendees	HCV-positive patients	Number received therapy	Number declined therapy or lost follow up
A	17	151	49 (32%)	24 (49%)	25 (51%)
B	27	130 (79%)	120 (92%)	75 (63%)	44 (37%)
C	34	163 (75%)	106 (65%)	54 (51%)	34 (32%)

Antenatal hepatitis C testing and care in maternity services in England, a national survey

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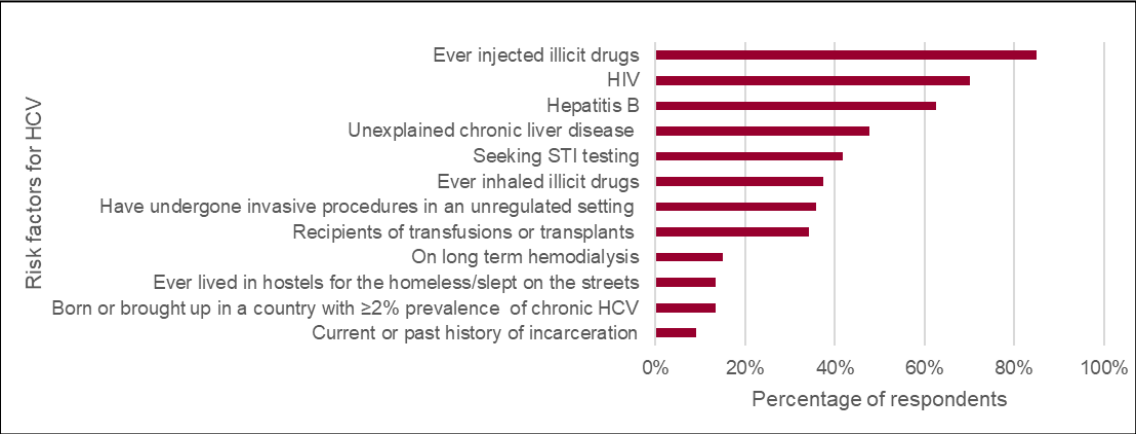
Background and Aims: Antenatal Hepatitis C (HCV) testing presents a unique opportunity to increase diagnosis among women. In England, the UK National Screening Committee (UKNSC) does not currently recommend a population-wide screening programme for HCV in pregnant women. The National Institute for Health and Care Excellence (NICE) recommend that maternity services identify and offer testing to women at high risk of HCV. We aimed to investigate HCV testing and management policy and practices during antenatal care.

Method: An online survey was circulated between November and December 2020 to maternity service providers via the National Infectious Diseases in Pregnancy Screening team. Questions covered topics including respondent characteristics, testing policy, training for healthcare staff, and management of pregnant women found to be HCV positive. Descriptive analyses were done on a per question basis with response rates for each question presented.

Results: Seventy-five questionnaires were returned with completion varying by question, representing 48% English maternity service providers. Most (87%) providers reported offering antenatal HCV risk-based testing. However, only 41% of respondents felt their hospital antenatal HCV testing policy would ensure that at-risk pregnant women would be identified. Risk factors used to identify pregnant women for testing varied (see figure), with less than 15% of respondents stating that the following groups are considered at high risk for HCV: women born or brought up in higher HCV prevalence areas; women that ever lived in hostels for the homeless or slept on the streets, and women with current or past history of incarceration. 87% of respondents indicated that they would access training to facilitate discussions around HCV testing if available. Public health actions to control transmission were infrequently reported, with 27% of respondents stating their trust notifies appropriate authorities and 83% stating contact tracing of the family was the responsibility of primary care.

Conclusion: Current HCV testing practices in maternity services are inadequate and HCV infection likely goes undiagnosed in pregnancy, especially among vulnerable population groups such as migrants and the homeless. Further work to improve knowledge of risk factors, testing and management among all maternity service staff is required. In addition, in the absence of national universal antenatal screening, re-framing HCV risk-based testing and management of HCV diagnosed pregnant women and their families as a quality improvement initiative, and developing HCV specific pathway guidance and resources for maternity units (as was done for hepatitis B in England) may strengthen uniform implementation of national recommendations with auditable outcomes.

Figure: Risk factors considered to identify pregnant woman for HCV testing in England*



**respondent dependent*

Primary care physician adoption of hepatitis C virus treatment in United States Medicaid programs

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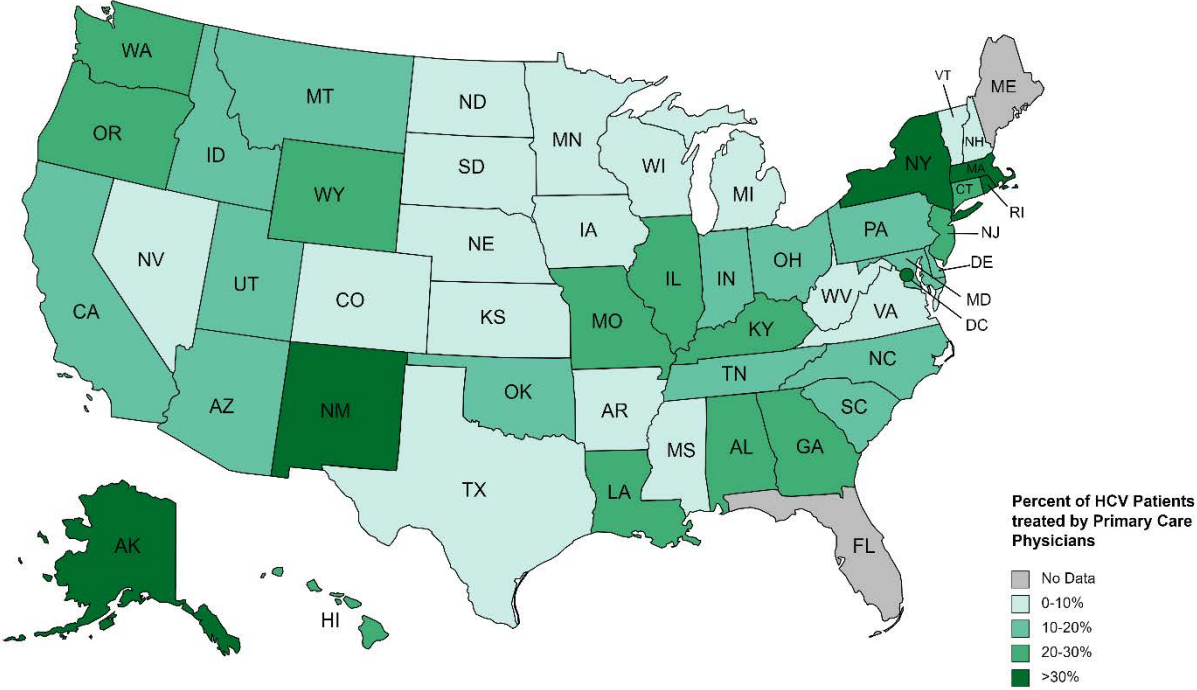
Background and Aims: To achieve hepatitis C (HCV) elimination goals in the United States (US), antiviral treatment needs to increase. One promising strategy is providing more HCV treatment through primary care physicians. Medicaid is a health insurance program jointly financed by federal and state governments that primarily serves low-income individuals and insures a large proportion of people with untreated HCV. We aimed to examine the extent to which primary care physicians provide HCV treatment in US Medicaid programs.

Method: We used the 2018 T-MSIS Analytic File, which contains health insurance claims for individuals enrolled in Medicaid programs administered by all US states. We identified prescriptions for HCV direct acting antiviral (DAA) medications, excluding prescriptions for children, the elderly (who are also eligible for federally-financed Medicare health insurance), and other individuals dually enrolled in Medicare and Medicaid. We excluded 2 states (Florida and Maine) that did not report prescriber identifier (ID). We used prescriber ID to identify medical specialty and categorize prescribers as 1) primary care physicians, 2) gastroenterology specialists, 3) infectious diseases specialists, 4) non-physicians (e.g., physician's assistants and nurse practitioners), and 5) other specialties or unknown. We report the proportion of patients treated by physicians of each specialty. We compare demographics of patients treated by primary care physicians compared to gastroenterologists and compare average patient volume between these specialties.

Results: In 2018, there were 56,342 patients prescribed DAA medications by 8,767 providers. Nationally 21% of patients were treated by primary care physicians, 31% by gastroenterologists, 27% by non-physicians, 11% by infectious diseases specialists, and 10% by other or unknown specialties. The proportion treated by primary care physicians varied substantially among states (Figure). Compared to those treated by gastroenterologists, patients treated by primary care physicians were more likely to be black (17% vs 13%, $p = <0.001$) and Hispanic (14% vs 10%, $p = <0.001$). Primary care physicians treated a similar number of patients per provider in 2018 as gastroenterologists [median (IQR) 2 (1-5) for both groups].

Conclusion: Primary care physicians make up about one-fifth of those prescribing HCV treatment to patients enrolled in US Medicaid programs, but this proportion varies substantially by state. To promote HCV elimination in the US, increasing involvement of primary care physicians in providing HCV medication treatment, especially in states with low involvement, is an opportunity for improvement. Future research should determine whether differences in states' Medicaid policies, HCV epidemiology, or healthcare resources might be associated with differences in primary care uptake of HCV treatment.

Figure:



Created with mapchart.net

FIB-5 and/or FIB-4 index for hepatic fibrosis assessment in chronic hepatitis B patients

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Background and Aims: Chronic hepatitis B virus (HBV) infection is one of the major health problems worldwide. Use of non-invasive tests for assessment of hepatic fibrosis such as the FIB-4 index could be used to avoid liver biopsy. Another promising noninvasive test, FIB-5, could also be used to detect a significant hepatic fibrosis. The aim of the study was to compare the use of FIB-5 and FIB-4 as noninvasive markers to assess chronic HBV-related hepatic fibrosis.

Method: This cross-sectional study was conducted on 176 chronic HBV patients who underwent liver biopsy. Grading and staging of liver fibrosis was done according to the METAVIR scoring system. FIB-5 and FIB-4 scores were calculated for all patients. Exclusion criteria of the study included patients co infected by hepatitis C virus (HCV), hepatitis D virus (HDV) or human immunodeficiency virus (HIV), patients with primary or secondary liver tumors, patients who received any previous antiviral or immunosuppressive medications, and also patients who refused liver biopsy or having any contraindication to undergo liver biopsy and patients with decompensated cirrhosis.

Results: There was a significant relationship between fibrosis stages and both serum indices. There was a significant increase in the level of FIB-4 as fibrosis progressed from non-significant (F0-1) to significant fibrosis (F2-4). A significant decrease in the level of FIB-5 ($p = 0.00001$) was observed with the progression of fibrosis stages from non-significant to significant fibrosis. As regards FIB-4 for differentiation between non-significant fibrosis (group I) and significant fibrosis (group II), at a cutoff level of 1.28 with positive predictive value (PPV) 41.4% and specificity 48% while at a cutoff level of 7.08 with PPV 98.8% and specificity 98% for FIB-5.

Conclusion: As regards both scores, the FIB-5 score was more specific than FIB-4 for diagnosing a significant from non-significant hepatic fibrosis in patients with chronic HBV infection.

Figure:

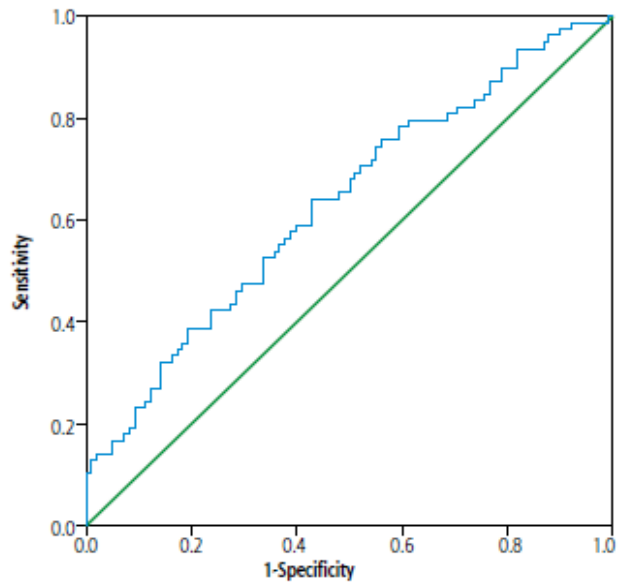


Fig. 1. Receiver-operating characteristic (ROC) curve generated by FIB-4 for differentiation between significant and non-significant fibrosis

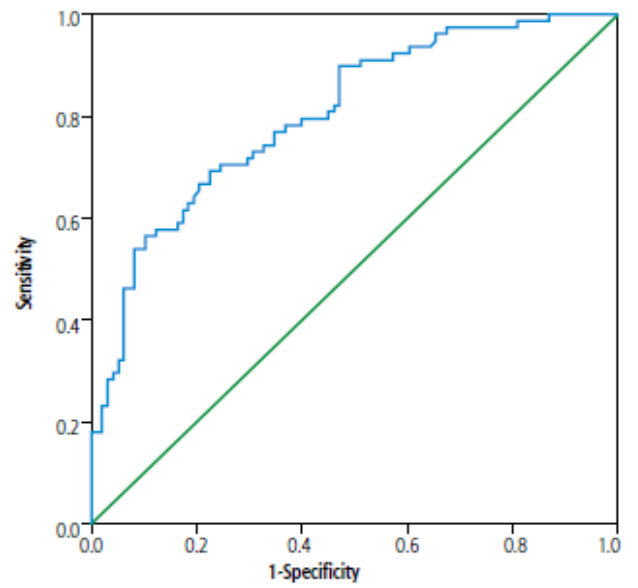


Fig. 2. Receiver-operating characteristic (ROC) curve generated by FIB-5 for differentiation between significant and non-significant fibrosis

Trends in hepatitis C treatment and chronic prevalence over the last decade among people who inject drugs

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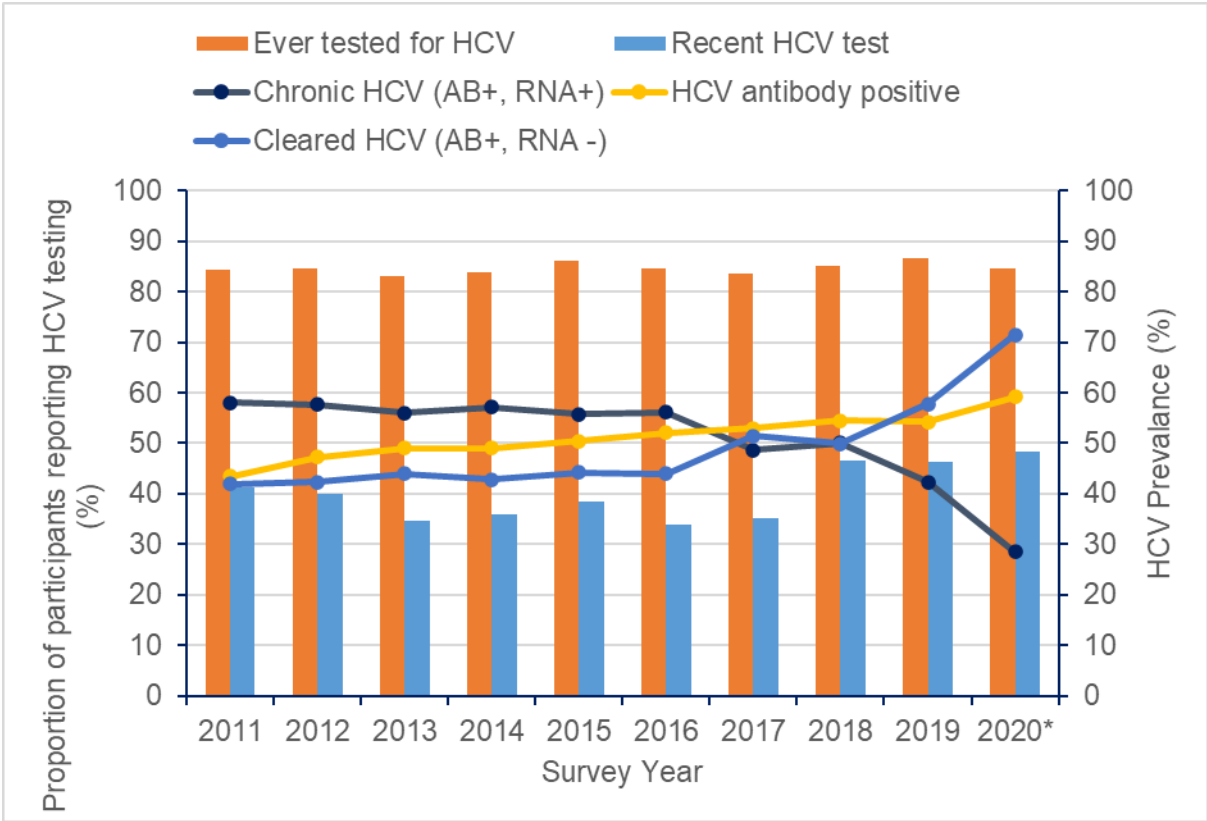
Background and Aims: People who inject drugs (PWID) are the group most affected by hepatitis C (HCV) in the UK. The introduction and scale up of direct acting antivirals (DAA) has transformed the landscape of HCV treatment. We aim to describe HCV infection, testing and treatment in this population over the last decade.

Method: We analysed data from the Unlinked Anonymous Monitoring (UAM) Survey of PWID, a cross-sectional survey monitoring blood-borne virus (HIV, hepatitis B and HCV) prevalence and behaviours in England, Wales and Northern Ireland. We examined trends in ever infection (HCV antibody positive), chronic infection (HCV antibody and RNA positive) and cleared infection (HCV antibody positive and RNA negative), uptake of HCV testing and treatment between 2011-2020. Data for 2020 are preliminary given the small sample size and differences in the geographic distribution, demographic and risk profile of participants compared to previous years.

Results: Over the last decade, ever infection with HCV increased from 43% to 59% (2011-2020, $p = 0.001$) (Fig). The proportion with chronic HCV remained stable around 57% between 2011-2016, decreasing to 49% in 2017 ($p = 0.002$) and 29% in 2020 ($p < 0.001$) (Fig). The proportion with cleared HCV infection was stable around 43% from 2011-2016 and increased from 51% in 2017 to 71% in 2020 ($p < 0.001$). In 2011-2016, among those with treatment status available, around 20% of those anti-HCV positive had seen a HCV specialist and had accepted treatment; this increased to 30% in 2017 ($p < 0.001$) and 63% in 2020 ($p < 0.001$). The proportion reporting ever testing for HCV has remained consistent at around 85% over the past decade (Fig). Among those tested for HCV, the proportion reporting a test in the current or previous year increased slightly over the last decade from 57% (2011-2017) to 65% (2018-2020) ($p < 0.001$).

Conclusion: The past decade has seen an increase in the proportion of PWID ever infected with HCV, with a proportional increase in cleared HCV and decrease in chronic HCV from 2017. This is consistent with the scale-up of DAAs and increase in the self-reported uptake of treatment in the UK. These results suggest increased access to treatment may be impacting levels of chronic HCV infection in PWID. Monitoring trends in HCV prevalence and treatment uptake is critical to assess progress against WHO HCV elimination targets by 2030.

Figure: HCV testing and prevalence: England, Wales and Northern Ireland, 2011-2020



*2020 data are preliminary

FOCUS Project: preliminary results toward Hepatitis C Virus screening and elimination in Almería, Spain

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Background and Aims: Hepatitis C virus (HCV) elimination is a global challenge, and Spain may be one of the first countries to achieve the World Health Organization's goal of eliminating viral hepatitis by 2030. A 2017-2018 Ministry of Health serosurvey estimated 0.22% active HCV infection among the general Spanish population, 29.4% without prior infection records.

Increasing HCV screening is key, particularly among vulnerable populations with high prevalence. 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.

Therefore, we aimed to evaluate HCV screening efficacy in the ED of Torrecárdenas University Hospital, in Almería, Andalusia, Spain.

Method: We implemented opportunistic HCV screening in the ED, using existing infrastructure and staff, aided by electronic health record system modifications to identify eligibility for the test and request serologies automatically. Patients were eligible for testing upon verbal consent if they were between 18 and 69, and had no known diagnosis or test performed in the previous year, and required blood tests in the current visit to the ED.

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 (i.e., reflex or single-step testing). Appropriate follow-up or discharge was given, regardless of test results. We contacted positive patients to ensure and monitor linkage to specialist medical care.

Results: We screened 1,131 patients for HCV from August to October 2021, finding 28 (2.47%) anti-HCV positive patients (with an average age of 55, 71% males), and 5 (0.44%) HCV RNA positive patients (80% males), 80% of whom had no prior records or knowledge of their infection.

Conclusion: Undocumented HCV infection among our ED population is higher than estimated in the general population, with twice the active infection rate and nearly two times undiagnosed infection. Thus, opportunistic HCV screening in EDs is feasible, non-disruptive, and effective in increasing diagnosis.

Screening for hepatitis C virus reinfection using a behaviour-based risk score among HIV-positive men who have sex with men

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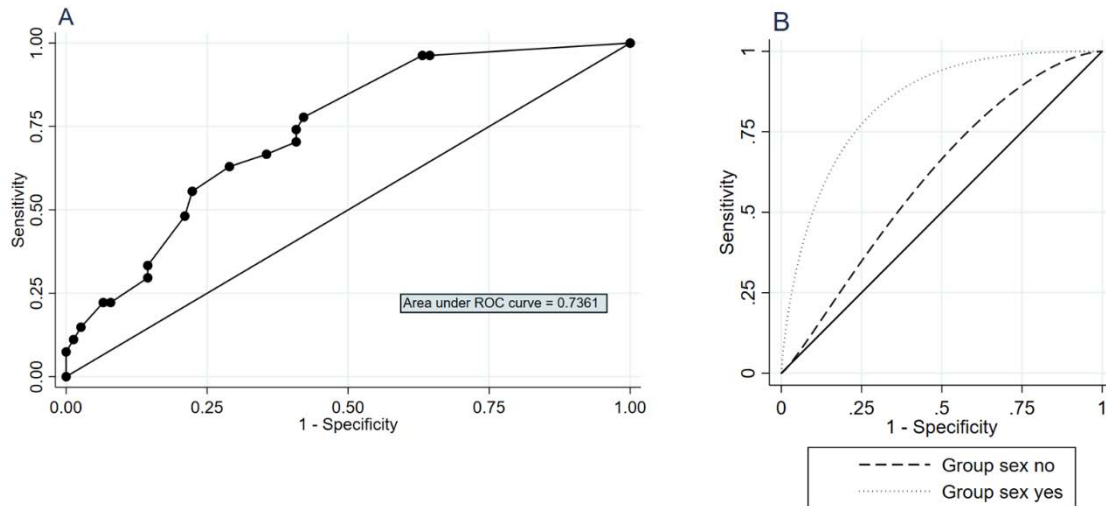
Background and Aims: After successful treatment or spontaneous clearance of hepatitis C virus (HCV) infection, HCV reinfection occurs frequently in HIV-positive men who have sex with men (MSM). The HCV-MOSAIC risk score has been originally developed and validated to identify HIV-positive MSM at high-risk for early primary infection. We aimed to assess the predictive capacity of the risk score as a screening tool for HCV reinfection in HIV-positive MSM.

Method: HCV-MOSAIC scores were calculated by summing coefficients specific to six self-reported, HCV-associated, sexual and drug-using behaviours. The overall predictive capacity of the score was assessed using the Area Under the Receiver Operating Characteristic (AUROC) curve. Effects of covariates on the Receiver Operating Characteristic (ROC) curve were assessed using parametric ROC regression. The score cut-off validated for primary early infection (≥ 2.0) was used, and the sensitivity (Se) and specificity (Sp) for HCV reinfection was calculated. To determine whether the cut-off needed to be re-calibrated for HCV reinfection, we conducted post hoc analysis in which an optimal cut-off was chosen at or above the score yielding the highest $(Se+Sp)/2$.

Results: 103 HIV-positive MSM who had been previously infected with HCV were included ($n = 27$ cases, $n = 76$ controls). The median age was 46.7 years (interquartile range (IQR) = 41.8 – 51.5) and 80.6% were of Dutch ethnic origin. Median HCV-MOSAIC risk score was 2.5 (IQR = 1.2 – 3.4) for cases and 1.1 (IQR = 0.0 – 2.3) for controls ($p < 0.001$). AUROC was 0.74 (95% confidence interval (CI) = 0.63 - 0.84). Group sex significantly affected the ROC curve, increasing predictive capacity. Using the validated cut-off, Se was 70.4% (95%CI = 49.8 - 86.2%) and Sp 59.2% (95%CI = 47.3 - 70.4%). In post hoc analysis, an optimal cut-off ≥ 1.2 was observed for this study population, at which Se was 77.8% (95%CI = 57.7 - 91.4) and Sp 57.9% (95%CI = 46.0 - 69.1).

Conclusion: The HCV-MOSAIC risk score may be useful for identifying individuals at risk of HCV reinfection and to find HCV RNA positive MSM in particular. In sexual health or HIV-care settings, this score may help guide HCV RNA testing in MSM with a prior HCV infection. Additionally, the risk score may also be used to identify those who would benefit most from behavioural interventions aimed at preventing HCV reinfection.

Figure:



Non-

parametric receiver operating characteristics (ROC) curve of the HCV-MOSAIC risk score for reinfection (A) and parametric ROC curves for the HCV-MOSAIC risk score according to engaging in group sex (B).

Abbreviations: HCV, hepatitis C virus; MOSAIC, MSM (men who have sex with men) Observational Study of Acute Infection with hepatitis C; ROC, receiver operating characteristic

Combined COVID-19 vaccination and hepatitis C virus and HIV screening intervention for high-risk populations at a mobile testing unit in Madrid, Spain

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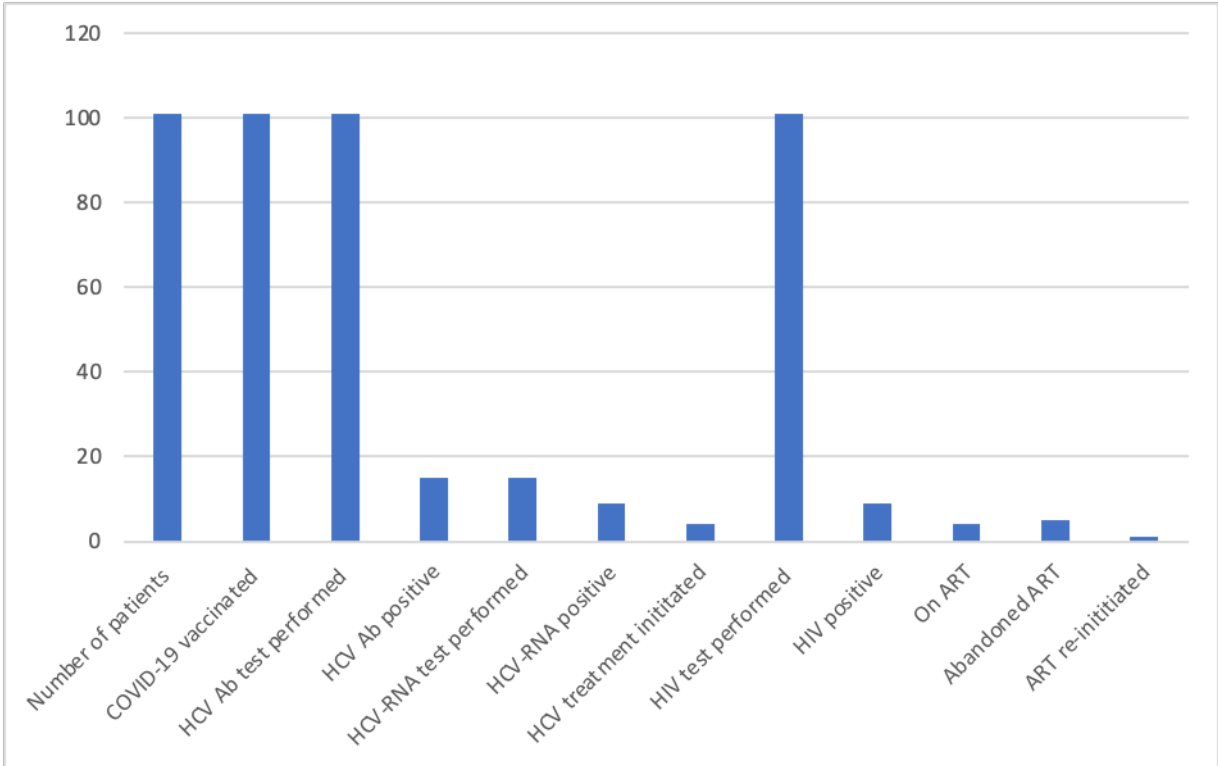
Background and Aims: The COVID-19 pandemic has hindered efforts to address hepatitis C virus (HCV) and HIV by reducing testing, particularly in marginalised groups, who have some of the highest rates of HCV and HIV and lowest rates of COVID-19 vaccination. This study aimed to explore the acceptability of combining HCV/HIV point-of-care testing (PoCT) with COVID-19 vaccination in a mobile testing unit (MTU) in Madrid, Spain.

Method: From 9/28/2021 to 10/26/2021, 101 individuals from high-risk populations (e.g., homeless people, those with substance use and/or mental disorders, sex workers, refugees, undocumented migrants) were invited to get the COVID-19 vaccine at the MTU. If HCV antibody (Ab) positive, they were offered HCV-RNA PoCT. HCV-RNA and HIV-positive patients not on antiretroviral therapy (ART) were offered linkage to care.

Results: All 101 participants accepted the combined intervention of which 69.3% were male, 30.7% of Spanish origin, most reported a precarious living situation or being homeless (59.4%) and being unemployed (70.3%), and 28.7% an incarceration history. The mean age was 35.6 (SD: 11.9). Of everyone, 11.9% reported a previous COVID-19 diagnosis, none had been vaccinated for COVID-19 and all received the Janssen vaccine without any identified adverse events (Figure). Everybody was tested for HCV Ab and HIV and 14.9% (n=15) and 8.9% (n=9) were positive, respectively. Of those HCV Ab positive, all were tested for HCV-RNA and 60.0% (n=9) were positive, of which most (55.6%, n=5) reported that the most likely route of transmission was injecting drug use, 44.4% (n=4) were probable reinfection cases and 33.3% (n=3) were HIV co-infected. Of those HIV positive, none were new diagnoses and most (55.6%, n=5) had abandoned ART. To date, 44.4% (n=4) have started treatment for HCV and 1 person (20.0%) has re-started ART. The duration between positive HIV diagnosis and ART re-initiation for the latter was 25 days. The average duration between positive HCV-RNA diagnosis and treatment initiation was 36 days (minimum: 22; maximum: 47) and of the MTU intervention was 20 minutes (minimum: 7; maximum: 60).

Conclusion: Combining HCV/HIV PoCT with COVID-19 vaccination in high-risk individuals at the MTU was effective, with an acceptability rate of 100%, and safe since no adverse events were reported. The process was also efficient, maximising the use of time that participants would have spent waiting for HCV/HIV test results or post-vaccine administration and linking those in need to care in about 1 month, to date. This intervention can serve as an example of a novel model of care to increase HCV/HIV screening and linkage to care as well as COVID-19 vaccination in high-risk populations.

Figure: Analysis of the combined COVID-19 vaccination and HCV and HIV screening intervention at the mobile testing unit in Madrid



Abbreviations: Ab, antibody; ART; antiretroviral therapy; HCV, hepatitis C virus.

Demonstrating control of perinatal transmission of hepatitis B in the UK: a low prevalence country with universal antenatal screening and selective neonatal immunisation programmes

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Background and Aims: Prevention of vertical or maternal to child transmission (MTCT) of hepatitis B virus (HBV) through infant immunisation starting with a birth dose is a cornerstone of global HBV elimination efforts. WHO Europe validates control of HBV in a country if it can demonstrate high (> 90%) vaccine coverage of hepatitis B birth dose (HepB BD) and 3 doses by 12 months (HepB3), < 2% rate of MTCT and < 0.1% HBV prevalence in < 5years birth cohort for at least 3 years. In the UK combined universal antenatal screening and selective neonatal immunisation with a HepB BD aims to reduce MTCT. In August 2017, the UK introduced universal infant immunisation (without a HepB BD). We analysed monitoring and evaluation data from the UK screening and immunisation programmes to review progress against WHO HBV control targets.

Method: English data on antenatal screening uptake and prevalence of HBV in pregnant women were obtained from the NHS Infectious Diseases in Pregnancy Screening programme. English data on HepB3 coverage as part of a 6 -in-1 vaccine (DTaP/IPV/HiB/HepB), and HepB BD were obtained from the Cover of Vaccination Evaluated Rapidly (COVER) system which extracts vaccine coverage data from primary care systems. English data on serostatus at 12 months of infants born to HBV infected mothers was obtained from the National Dried Blood Spot (DBS) testing service. Scotland, Northern Ireland (NI) and Wales provided equivalent data from their monitoring systems. Data from 2014 – 2019, where available, were used.

Results: Around 700,000 pregnant women give birth each year in the UK. Annual antenatal screening uptake is consistently > 95% with HBV prevalence in pregnant women < 0.5% for all UK countries. In 2018/19 HepB3 dose uptake was 92.1%, 94.5%, 95.9% and 95.4% in England, NI, Scotland and Wales, respectively. HepB3 data are not available for earlier years; however, coverage for DTP3 was > 90% for the UK in the 4 years prior. In 2018/19 timely birth dose (HepB BD) among babies born to HBV infected women was 98.9%, 100%, 92.3% and 100% for England, NI, Scotland and Wales, respectively, and remained > 90% for the preceding 3 years. Between 2015-2018, among these infants at risk of MTCT who were tested at 12 months old, < 0.5% were HBV infected, and hence the HBV prevalence in the full birth cohort was < 0.1%.

Conclusion: Monitoring and evaluation data from screening and immunisation programmes indicate that the UK is successful in preventing MTCT of HBV without a universal birth dose. DBS in England facilitates testing infants in primary care. Combined HBV universal antenatal screening and selective neonatal immunisation programmes may be a feasible approach for European countries with low HBV prevalence.

Community values and preferences regarding decentralisation and task-shifting of HCV services - results from an international online survey

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Background and Aims: To reach global targets of viral elimination, strategies such as decentralisation of HCV testing and treatment services to primary care clinics or community-based settings and task-sharing to non-specialists will be key. We undertook a global survey to understand the values and preferences for decentralisation of services and task-sharing among people living with or affected by HCV (PLHCV), including persons who inject drugs (PWID), to inform updated WHO guidance on simplified service delivery.

Method: An anonymous, self-administered international online survey was developed by non-governmental organisations World Hepatitis Alliance and Coalition PLUS, and the World Health Organization and distributed through social media, mailing lists and direct contacts, targeting persons living with or affected by HCV. The survey comprised 42 multi-choice questions that addressed preferences for simplifying HCV care, where to test and treat, and who to provide treatment for hepatitis C infection.

Results: 210 people from 49 countries participated in the survey. 56.2 % (n=113) of participants were male and median age was 42 [IQR:57]. 23.3% of participants identified as PLHCV, 20.8% as former PWID, 17.8% as current PWID. The majority of respondents (n=150, 71.8%) had been tested previously for HCV and 41.7% (n=60) were positive, and 91.1% of 56 respondents had been treated. Regardless of HCV testing history, participants indicated a preference for testing in a community-based center (39.7%) or "at a place of my choice using a self-test" (33.2%) compared to a hospital (32.6%) or primary care clinic (31.5%). Similarly, the main preference for treatment was at community sites (50.3%), followed by hospital (38.9%) or general practitioner's cabinet (28.6%). The most important reasons for choice of where to test or be treated were : Location of services (close to home or office) (53.2% and 56.0%), direct costs (37.6% and 40.0%), and having non-judgmental/non-stigmatising approach (36.6% and 39.4%). The majority (91.9%) of participants also expressed a strong preference for having testing and treatment in the same place for reasons of "convenience" (33.5%) and "continued follow up from testing to treatment" (32.3%). Almost half (47.6%) expressed a preference to see a specialist doctor to discuss their health care needs, followed by "community-friendly medical personnel" (22.9%).

Conclusion: The survey results showed a strong preference for testing and treatment in a community-based settings outside of traditional healthcare settings such as hospitals or primary care clinics. However, there was also a preference for seeing specialists when discussing health needs. A non-judgemental/non-stigmatizing approach among health care workers was identified as a key consideration for choice of testing and treatment location and should be addressed in decentralisation efforts.

Demographic characteristics and viral diversity in hepatitis B infected pregnant women in England: implications for control of maternal to child transmission

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Background and Aims: In April 2021, UK Health Security Agency launched a national enhanced maternal and infant hepatitis B surveillance programme. The first six months of data were analysed to characterise the hepatitis B virus (HBV) infected antenatal population in England, investigate the distribution of infectivity risk markers, HBV genotype and prevalence of potential vaccine escape mutations in these women.

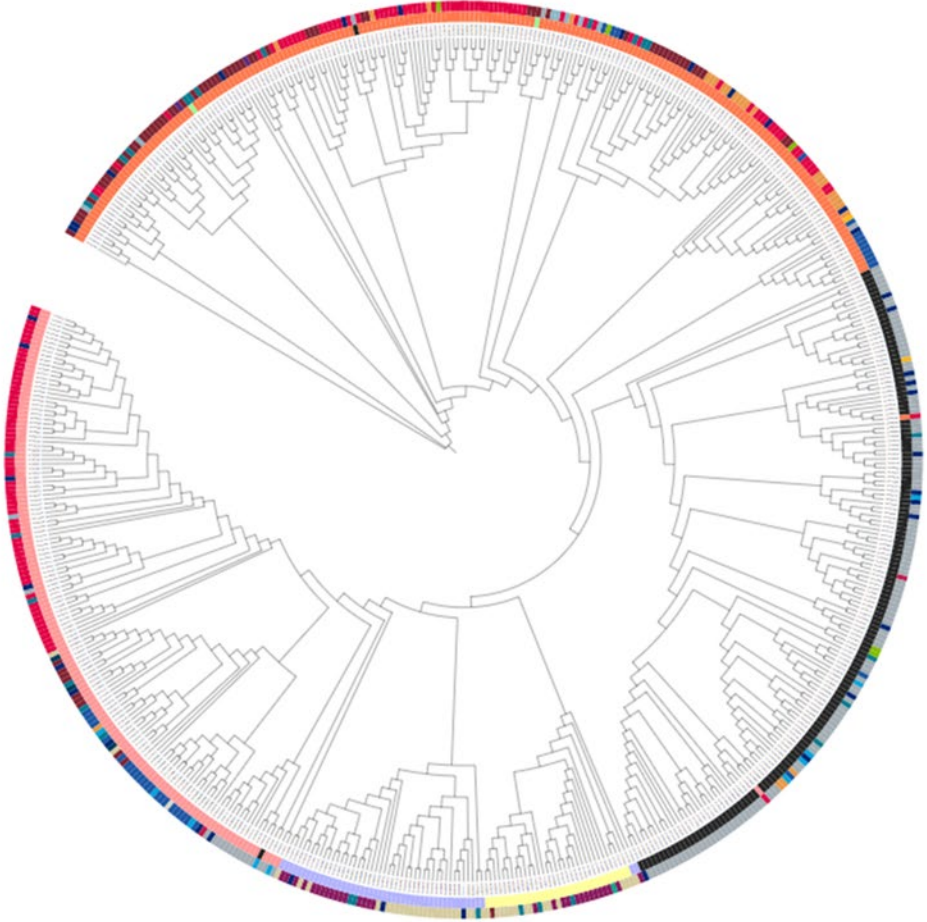
Method: Antenatal blood samples are requested from all women screening positive for HBV during pregnancy in England and sent to UKHSA Virus Reference Department. Demographic information is collected with each sample. All HBV surface antigen (HBsAg) positive samples received between April and October 2021 were tested for markers to the HBe protein (HBeAg and anti-HBe), DNA level and were sequenced.

Results: 85% of antenatal units across the UK submitted samples. Of the 859 samples received, 72 (8.4% 95% CI 6.5%-10.2%) were classified as higher infectivity risk according to national guidance. Most mothers were born in Eastern Europe (23.5%) or Western Africa (19.3%). The largest proportion of higher infectivity mothers were born in South East Asia (22.8% 95%CI 11.9%-33.7% p<0.001). Ethnicity was variably recorded, although fewer than 1% of women identified as White British. Mean HBV DNA levels were 6.2 log IU/ml (95% CI 5.39 -7.02) in those HBeAg positive and anti-HBe negative compared to 2.7 log IU/ml (95% CI 2.65-2.80) in those HBeAg negative and anti-HBe positive. All five major HBV genotypes were identified and correlated with country of birth. Mutations in HBsAg were detected in the major antigenic region in 28% of women.

Conclusion: This first look at new national data on HBV infected pregnant women suggests that over 99% were non UK born and likely acquired their infection in their country of birth. The distribution of HBV DNA levels correlated broadly with HBe status but also indicated the early use of antiviral treatment in the management of the woman. The evidence of potentially clinically significant mutations, which could reduce vaccine effectiveness, raises the importance of lowering the viral load in pregnancy to minimise transmission risk and timely immunisation of babies at birth to maximise effectiveness.

Figure: Phylogenetic tree of 581 sequences encompassing the entire HBsAg region. Inner circle; HBV genotype. Outer circle UN region of birth.

Genotype	Region of birth
A	Caribbean
B	Central Asia
C	East Africa
C/D	East Asia
D	Eastern Europe
E	Melanesia
	Middle Africa
	Northern Africa
	Northern Europe
	South America
	South East Asia
	Southern Africa
	Southern Asia
	Southern Europe
	Western Africa
	Western Asia
	Western Europe
	Information not provided



Enhancing Universal Hepatitis B and C Screening via the Electronic Medical Record: A Case Study

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Background and Aims: The United States CDC recommends one-time hepatitis C virus (HCV) screening for nearly all adults. In contrast, due its low (0.3%) prevalence nationwide, hepatitis B virus (HBV) screening is risk-factor based and is not universally recommended. In NYC, however, HBV prevalence is 2.9%, which is higher than the 2% threshold for universal screening recommended by the USPSTF, CDC, and AASLD. We aimed to demonstrate the need for universal HBV screening in our large, multi-site hospital system, which serves metropolitan NYC, and to facilitate testing by embedding automatic prompts in the electronic medical record (EMR). This case study outlines the process of implementing EMR modifications to enhance viral hepatitis screening from conception and planning to securing buy-in from stakeholders through rollout.


Method: Our viral hepatitis elimination team used local epidemiological data, government recommendations, WHO goals, and cost-benefit analyses to demonstrate the need to modify our health system's EMR automatic prompts to better support screening. We met with our hospital's population health and ambulatory care groups, EMR specialists, and laboratory team to ensure buy-in, and designed the implementation to ensure that the changes would not create an unnecessary burden for providers.

Results: Our request for HCV screening prompts was quickly granted, as it was supported by the clarity and consistency of the CDC, USPSTF and AASLD guidelines, which recommend nearly universal HCV screening (Fig. 1). The hospital was initially reluctant to implement a prompt for universal HBV screening because of the lack of a governmental guideline for the U.S. as a whole; however, when we provided local prevalence data and supporting information including cost-benefit analyses, the hospital agreed to add prompts for one-time universal HBV screening and for HBV vaccination for adults 18-59, as recommended by the CDC. Direct outreach to primary care providers is being done to ensure providers will understand and utilize the prompts. We also worked with our laboratory director to develop a pathway for the reflex testing by PCR of all samples testing positive for hepatitis delta antibody, as is done for HCV antibody positive samples; reflex testing raised HCV PCR RNA testing rates from 67.5% to 100%.

Conclusion: Automatic prompts in the EMR can help healthcare systems implement viral hepatitis screening and vaccination guidelines system-wide at low cost and can streamline ordering of the correct tests. These prompts support comprehensive viral hepatitis elimination strategies. Where government policies supporting universal screening and vaccination are lacking, garnering the necessary buy-in can be challenging. Presenting local epidemiological data to highlight unmet needs and potential benefits to patients and the hospital system can be a powerful tool to effect change.

Figure:

Hepatitis C Screening is Due

 [2020 CDC Hepatitis C Screening Guidelines](#)
The CDC recommends Hepatitis C screening for all adults (>=18yo) at least once. To satisfy this alert please open the Hepatitis C SmartSet below. If the patient has already satisfied screening, you may override this alert. Alternatively, you may postpone this alert.

Last HCVAB, collected/resulted: DD/MM/YYYY = Result value
Hepatitis C Screening last satisfied: DD/MM/YYYY

Open Order Set	Do Not Open	HEPATITIS C SCREENING ORDER SMARTSET Preview
Override	Do Not Override	Hepatitis C Screening Edit details
Postpone	Do Not Postpone	Hepatitis C Screening Edit details

- [Address Hepatitis C Screening HM Topic](#)
- [HM Activity \(Add patient reported, Postpone, Override\)](#)
- [Add relevant diagnosis to History](#)

[Accept](#) [Dismiss](#)

Outcome of Hepatitis C Virus co-infection treatment among Human Immunodeficiency Virus-infected people who inject drugs: an Egyptian real-life experience.

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Background and Aims: People who inject drugs (PWID) have an estimated prevalence of 55% for hepatitis C virus (HCV) and the highest prevalence of human immunodeficiency virus (HIV) (6.7 - 7.7%) in Egypt. To achieve the World Health Organization (WHO) HCV elimination targets, treating populations at risk of ongoing HCV transmission, such as PWID and HIV-infected patients is a priority. Our study aimed to evaluate the safety and efficacy of generic sofosbuvir (SOF) and daclatasvir (DCV) for HCV treatment in HIV-infected PWID in the real-life setting.

Method: This prospective cohort study was conducted in the period between March 2019 and March 2020. From a cohort of HIV/HCV coinfecting patients attending the main HIV/HCV coinfection multidisciplinary clinic placed in Imbaba Fever Hospital, Cairo, Egypt, 300 PWID were offered generic SOF (400 mg) and an adjusted dose of DCV (60 or 90 mg) according to the antiretroviral therapy (ART) for 12 weeks. All patients were HCV treatment naïve, had CD4 count \geq 100 cells/mm³ and were eligible for HCV treatment according to the national guidelines. They were followed up till 12 weeks post-treatment to assess the sustained viral response (SVR-12) defined as an undetectable HCV RNA at this time point. Independent predictors for SVR-12 were identified by multivariable logistic regression.

Results: The mean patients age was 34.72 ± 9.59 years, 277 were males (92.3%), 82.3% reported smoking, 41.3% reported current IV drug use, 85.7% had CD4 count \geq 200 cells/mm³ and 19% had significant liver fibrosis (\geq F2). Among 180 (60%) on ART and virally suppressed, 87.2% were on efavirenz based ART. From 272 (90.7%) patients completed treatment and 12 weeks of follow up, 261 (96%) achieved SVR-12 (87% as per intention to treat). SVR-12 rates were comparable whether the patients' CD4 count \geq or $<$ 200 cells/mm³, whether they had significant liver fibrosis (\geq F2) or not and whether they were active IV drug users or not (All $p > 0.1$). Patients on ART with suppressed viral load (regardless of its type) were more likely to achieve SVR-12 compared to those not on ART (92.2% vs 79.2%, $p = 0.001$).

Covariate associated with achievement of SVR-12 was being on ART with suppressed viral load (OR = 8.8; 95% CI 1.02 to 76.6) otherwise there was no association between baseline variables and SVR-12. There were no serious adverse events or consequent discontinuation of treatment.

Conclusion: SOF/DCV achieved a high SVR-12 and was well-tolerated in HIV/HCV-coinfecting PWID patients. Integrated HIV/HCV care among co-infected PWID ensuring their intake of ART and linkage to care is a promising strategy to improve HCV treatment outcome among such population and achieve HCV micro-elimination goals.

Approaches for a Hepatitis C-free city: preliminary results

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Background and Aims: We aimed to develop a Hepatitis C elimination program to make Seville a Hepatitis C free city. The main concern was the capability to reach marginal and vulnerable populations. To overcome this drawback, collaboration between different organizations is needed.

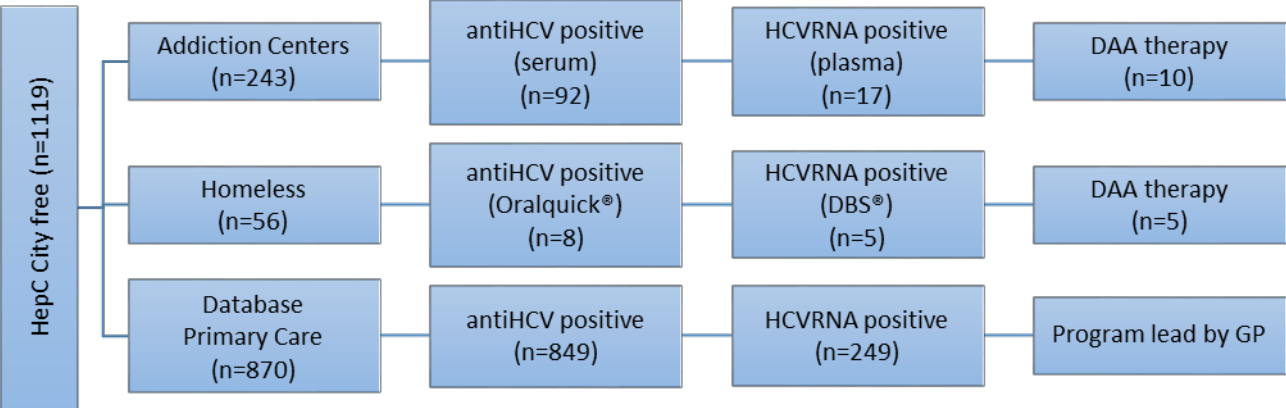
Method: Three groups were addressed: a) patients from primary care health centers database were classified according to anti-HCV status and viral load (HCVRNA); b) patients attended at addiction treatment centers; and c) homeless attended by non-profit organizations like Médicos del Mundo and Fundación Atenea, and social services from City Council in Seville. Anti-VHC was offered by Oralquick® test in saliva or blood test and, if positive, by dry blood spot (DBS) tests or serum samples to detect HCVRNA. Positive patients got an appointment in clinical hepatology or if not possible, a phone visit can be arranged to allow patient evaluation and remote drug dispensation.

Results: anti-HCV and HCVRNA tested positive in n=92/243 (38%) and 17 (6.9%) [10 treated with AAD] from addiction centers and n=8/56 (14%) and 5 (8.9%) [all 5 treated with AAD] in homeless population. In primary care centers n=849/870 tested antiHCV positive and 249 HCVRNA positive. We have identified 271 patients with a positive HCV viral load which may benefit from this Hepatitis C-free city program.

Conclusion: Collaborations between health, social and non-profit organizations is key for Hepatitis C elimination. In this sense, enabling HCV detection assays to be performed outside the hospital enhances the chances of identifying positive patients. Moreover, the short-cut for setting up the appointment allows faster access to treatment (presential or remote antiviral dispensation) at hepatology unit. At the same time, the possibility of doing phone visits and remote antiviral dispensation in patients refusing to be attended at the hospital increases treatment success rate. Coordinating these actions together can lead to a Hepatitis C-free city.

Acknowledgement: AEEH and Gilead Science for research grant and SAPD and Abbvie for providing Oralquick® and DBS®.

Figure:



Direct acting antiviral treatment for chronic hepatitis C are successful in Egyptian patients with chronic hepatitis C virus infection after a geographically focused, community-based HCV screening

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Background and Aims: Chronic hepatitis C virus (HCV) infection increases the risk for hepatic fibrosis, cirrhosis and hepatocellular carcinoma (HCC). This is the leading cause of liver transplantation in Egypt. The effect of interferon-free direct-acting antiviral(s) (DAAs) in the treatment of HCV is very high. We evaluated the outcome of screening and treatment with interferon-free DAAs that are required to control HCV incidence and complications.

Method: The prevalence of anti-HCV was determined on a mobile medical unit on 8 sessions in a cross-sectional survey in Kafr Ramaah village at Menoufia governorate. Three thousand participants were recruited for testing through door-to-door and street outreach and at community events and were educated about HCV prevention. Both HCV antibodies and hepatitis B virus surface antigen were measured using a commercially available third-generation quantitative enzyme-linked immunosorbent assay (ELISA) methods. Among patients with reactive tests, chronic infection was confirmed by quantitative HCV RNA real-time polymerase chain reaction (PCR). They underwent history taking, thorough clinical examination, abdominal ultrasonography, and liver stiffness measurement (LSM) by fibroscan. Laboratory investigations were done. Patients were assigned treatment with oral DAAs, as defined by the European association study of the liver (EASL) clinical guidelines.

Results: Prevalence of chronic HCV patients was 11.1 % in totally screened 3000 persons in the village (N = 333) with mean age 47.02 ± 13.26 years old. Among them, 99 patients showed spontaneous clearance at baseline while 234 patients who were confirmed by positive PCR received a once-daily oral combination of daclatasvir (DCV) and sofosbuvir (SOF) with or without ribavirin (RBV) (DCV + SOF \pm RBV). Sustained virological response (SVR) was 99.1 %.

Conclusion: Patients who were treated with interferon-free DAAs achieved marked reduction in HCV-associated morbidity and mortality. Aggressive expansion in HCV screening and treatment, particularly among rural areas was the cornerstone in the policy to eliminate HCV in Egypt.

Hepatitis C virus micro-elimination approach in vulnerable population in the South of Spain

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Background and aims: Since the introduction of direct-acting antivirals (DAA) thousands of chronic hepatitis C (CHC) patients have been successfully treated in Spain. However, vulnerable populations have high prevalence of hepatitis C virus (HCV) infection but important barriers to access to the treatment. We aimed to carry out an CHC microelimination program focused on vulnerable population in Malaga.

Method: A prospective study including adult patients in drug addiction treatment centers and in homeless shelter in Malaga was carried out between October 2020 and October 2021. Dry drop test were used as screening tool to identify HCV infection. Patients with active infection were scheduled for blood analysis, ultrasonography and elastography and prescription of DAA. Twelve weeks after end of treatment, sustained viral response (SVR) was analyzed.

Results: 270 dry drop tests were performed, 28 (10%) were positive for active infection (Table 1). Mean age of patients with active VHC was 54 years, 77% were male, 74% had HCV genotype 1a and one patient had HIV coinfection. Eight patients were active drug users (29%) while 20 were past drug users (71%). 10 patients were active alcohol drinkers (36%), eleven patients were on methadone treatment (39%), and 9 patients were on antipsychotic treatment (31%). 20% had advance fibrosis stage and one patient had hepatocarcinoma (4.8%). Eighteen patients finished treatment, 13 had sustained viral response, 4 were pending confirmation, 4 were on treatment and 1 refused to post-treatment control. 6 patients lost follow up before starting treatment.

Conclusion: Prevalence of HCV infection in vulnerable drug users population in Spain is still high (10%). Microelimination programs, along with diagnosis and treatment simplification in these difficult to treat patients are key for achieving the goal of the World Health Organization of eradicating hepatitis C by 2030.

Table 1. Results of drop tests in 270 patients from drug addiction treatment centers and in homeless shelter in the city of Malaga

Screening Centers	Screening Test n= 270	Positive Anti- HCV N= 30 (11%)	Positive HCV- RNA N = 28 (10%)	SVR N= 13/18 (72%)
<i>Adiction Treatment Center</i>	54	11	11 (20%)	6
<i>Reception center "Cruz Roja"</i>	87	12	12 (14%)	4
<i>Homeless refuge "Pozos Dulces" Home</i>	96	4	4 (4%)	3
<i>Alcoholic patients recovery center "AREA"</i>	30	3	1 (3%)	0
	3	0	0	0

Abbreviations: HCV: Hepatitis C virus; SVR: sustained viral response

Funding: In collaboration with the Gilead Sciences Scholarship Program

Screening for hepatitis C virus in high risk categories of Romanian population and updated prevalence data

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Background and Aims: Romania was considered over the last 15 years, the European country with the highest prevalence rate of HCV infection based on our previous reported HCV prevalence from the single nationwide cross-sectional study. The POLARIS group used these data to create a model about the changing prevalence of HCV due to ageing, treatment-cure and mortality. 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 positive subjects, as well as to refresh the HCV prevalence in this high-risk population. The screening project will be conducted till November 2023 in 24 out of the 41 counties of Romania, covering the North-Est and Southern part of the country.

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 rapid diagnosis tests in their office. Linkage-to-care and therapy will be further provided for all HCV-positive subjects. The project started on 28th of July 2021 (World Hepatitis Day) in the first 4 out of the 24 counties and engaged 321 FPs.

Results: Between 28th of July and 10th of November 2021, 39,674 subjects have been screened. The overall prevalence of anti-HCV Ab was 1.21%, with a higher prevalence among urban population (1.38% in urban vs. 1.17% in rural areas; $p=0.12$). The HCV prevalence was higher among females (1.39% vs 0.88%, $p=0.0001$) and increased with age. The highest HCV-Ab prevalence was in the North-Est region 1.37%. A significantly higher HCV prevalence was encountered in patients with a family contact of HBV/HCV or a sexual contact with positive HBV/HCV, persons with previous blood transfusions or surgical interventions, as well as in subjects previously diagnosed with sexually transmitted diseases. According to our results, a higher risk of being anti-HCV positive is associated with age >60 years, female gender, Roma ethnicity, inactive/retired, without or with low education level.

Conclusion: The burden of HCV infections is lower than previous estimates even in this vulnerable high risk category of screened persons, probably due to ageing population with increased mortality due to both liver and non-liver related causes. 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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Microelimination of Hepatitis C in patients with substance use disorders

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Background: The prevalence of chronic hepatitis C (CHC) is high in patients with substance use disorders (SUD), related to their high risk of contracting bloodborne infections. Due to a lower interaction with health care services, CHC may remain undiagnosed. The aim of this study was to implement universal CHC screening of patients in a SUD-dedicated psychiatric unit and to develop a strategy for microelimination of CHC.

Method: This prospective study, performed by a team of infectious diseases clinicians and psychiatrists, aimed to find the prevalence of CHC in the patients followed in the Dual Pathology Outpatient and Inpatient Unit - Psychiatry Department, Coimbra Hospital and University Center for 9 months and to promote access to CHC treatment. Additional information was obtained about demographic features, previous CHC status and substance use.

Results: 119 patients were enrolled. Of these, 78,2% were males, 9,2% had less than 30 years and 48,7% more than 50 years. 37,8% of patients reported previous use of more than one substance, with alcohol being the most used among all (85,7%), followed by cannabis (30,3%), cocaine (15,1%) and heroin (13,4%). A diagnosis of other mental illnesses was reported in 67,2% of patients, including recurrent depressive disorder (28,8%), dissocial personality disorder (20,0%) and bipolar affective disorder (13,8%), according to the International Classification of Diseases (ICD-10). Psychotropic agents were used in 99,2% of patients, specifically antipsychotics (89,9%), anxiolytics (86,6%) and antidepressants (64,7%). 12,9% of patients had positive HCV antibodies (76,9% of these had previous knowledge of this). The main factor associated with this was previous heroin use (relative risk 5.327, 95%CI 2.095-8.541). Of the patients with positive HCV antibodies, 30,8% reported a previous CHC treatment and were found to have no detectable HCV RNA, 38,5% reported a previous CHC treatment but had detectable HCV RNA and 7,7% had detectable HCV RNA with no previous treatments. CHC was confirmed in 5,9% of all patients.

Conclusion: There was a high prevalence of positive HCV antibodies (12,9%) and confirmed CHC (5,9%) in patients with SUD, specifically previous heroin use. As DAA therapy is available and has high rates of success, this project aimed to improve access to treatment to this group, with microelimination of CHC in mind. Psychiatrists can play an instrumental role in the screening for CHC and linkage to care of patients with SUD

Screening for hepatitis B virus in high risk categories of Romanian population and updated prevalence data

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Background and Aims: The 2016 Polaris Observatory study reported a global HBV prevalence of 3.9% (292 million persons) based on a country- and region-level modelling study of 120 countries; the collaborators furthermore estimated that only 10% (29 million) of infected persons were diagnosed. Romania, with a reported prevalence rate of 4.4 for HBs antigen (Ag), based on the nationwide cross-sectional survey conducted during 2006-2008, represents a high figure within the European Union. Aim: To screen socio-economic vulnerable population in order to provide high-quality medical services for the prevention, diagnosis, and referral to treatment for HBsAg positive subjects, as well as to refresh the HBV prevalence in this high-risk population. The screening project will be conducted till November 2023 in 24 out of the 41 counties of Romania, covering the North-Est and Southern part of the country.

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 HBsAg rapid diagnosis tests in their office. Linkage-to-care and therapy will be further provided for all HBV-positive subjects. The project started on 28th of July 2021 (World Hepatitis Day) in the first 4 out of the 24 counties and engaged 321 FPs.

Results: Between 28th of July and 10th of November 2021, 39,674 subjects have been screened. The overall prevalence of HBsAg was 1.75%, with a higher prevalence among urban population (1.95% in urban vs. 1.70% in rural areas; $p=0.14$). The HBV prevalence was higher among males (1.90% vs 1.66%, $p=0.07$). The highest HBsAg prevalence was encountered in subjects living in the South-Est part of Romania - 2.18%. A significantly higher HBV prevalence was encountered in patients with a family contact of HBV/HCV or a sexual contact with positive HBV/HCV, persons with previous blood transfusions or surgical interventions, with haemodialysis, with previous dental interventions, as well as with unprotected sexual contact with one or multiple partners. Patients with the highest risk of being HBV chronically infected are patients aged between 30 and 39 years, Roma ethnicity, unemployed, divorced and showing low education level.

Conclusion: The study demonstrated that the prevalence and profile (younger, urban residence) of HBV infection dramatically changed as compared to previous data. The understanding of the true burden of viral hepatitis in vulnerable Romanian population is necessary to develop targeted prevention and screening strategies aiming at achieving the 2030 WHO objectives of viral hepatitis elimination.

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No reinfections: elimination is feasible in drug addiction users

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Background and Aims: To eliminate Hepatitis C virus infection (HCV) in users of the centers for addiction treatment (CAT) we designed a Fast Track protocol based on screening, capture and supervision of treatment in the CAT, hospital diagnosis and dispensing of treatment in a single day. The main objective is to evaluate the reinfection rate after one year in cured patients. Secondary objectives: prevalence of HCV, results of treatment and description of the population.

Method: All users of Opioid Substitution Therapy (OST) of Santa Cruz San Miguel Addictions CAT (CATSC) who underwent HCV screening using dry blood spot (DBS) since March 2019 to October 2021 were included. Demographic, clinical variables and vulnerability factors were recorded from the positives. Patients cured more than a year ago were included for screening of reinfection using the DBS. For the analysis we used descriptive statistical methods and hypothesis testing with non-parametric tests (Chi Square), determining statistical significance when $p < 0.05$.

Results: There are 251 users at CATSC. Up to now 180 (71.71%) have been screened with DBS with a HCV prevalence of 39.44% (71). An additional 11% of patients were not screened because a recent negative HCV result in their clinical record; not being included in this study.

Of those who were positive, 6 were excluded from the study due to transfer to another center or control in an HIV unit. 98.46% (64) started treatment (mean age 50 years, 90.5% men); a patient rejected it. 37% had advanced fibrosis or cirrhosis. 42% reported active use of drugs intravenously or inhaled, 8% suffered from homelessness. In addition to drug use, 39% had another psychiatric illness and 55% used psychotropic drugs.

Of the 64 who started treatment, we confirmed cure in 90.62% (58), in 3 follow-up was lost after treatment, 1 dropped out and another died due to an unrelated cause, 1 was still in treatment at the time of the study. There were no virological failure.

Of the 56 cured for more than a year, it was possible to screen for reinfection in 71.43%. No patient was reinfected. Differences between the screened and non-screened groups were analyzed and it was observed that those subjected to screening consumed more drugs actively (52 vs 12%, $p 0.006$) and more psychotropic drugs (60 vs 25%, $p 0.018$). Although the associated psychiatric pathology was more frequent in the screened group, this difference did not reach statistical significance (45 vs 25%, $p 0.1$).

Conclusion: Elimination of HCV is maintained for one year after cure in patients attended by CATSC professionals despite active drug use and other associated vulnerability factors. Reinfection has not been a problem limiting efficacy in this population.

Modeling hepatitis C micro-elimination among people who inject drugs with direct-acting antivirals in metropolitan Chicago

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Background and Aims: Hepatitis C virus (HCV) infection is a leading cause of chronic liver disease and mortality worldwide. Propelled by the opioid epidemic, HCV incidence is rising in the United States, with a 63% increase from 2015-2019. Access to and uptake of highly efficacious direct-acting antivirals (DAAs) for U.S. PWID remains low despite evidence supporting PWID can be successfully treated for HCV with sustained virologic response (SVR) similar to non-PWID. However, persons who inject drugs (PWID) are at risk for reinfection after cure and may require multiple DAA treatments to reach the World Health Organization's (WHO) goal of HCV elimination by 2030. A micro-elimination approach [16], which entails pursuing eliminations goals in discrete populations at high risk for transmitting HCV such as PWID, has been suggested as a less daunting approach that could build momentum by generating small victories towards achieving WHO' global HCV elimination goal.

Method: We extended our previous work on simulating the PWID population in metropolitan Chicago, Illinois, U.S.A, including the social interactions that result in HCV infection, to develop an empirical-data driven agent-based model (ABM). Using our ABM, which accounts for the complex interplay of demographic factors, risk behaviours, social networks, and geographic location for HCV transmission among PWID, we examined the combination(s) of DAA enrolment (2.5%, 5%, 7.5%, 10%), adherence (60%, 70%, 80%, 90%) and frequency of DAA treatment courses needed to achieve the WHO's goal of reducing incident chronic infections by 90% by 2030 among a large population of PWID from Chicago, IL and surrounding suburbs. We also estimated the economic DAA costs associated with each scenario.

Results: Our results indicate that a DAA treatment rate of >7.5% per year with 90% adherence results in 75% of enrolled PWID requiring only a single DAA course; however 19% would require 2 courses, 5%, 3 courses and <2%, 4 courses), with an overall DAA cost of \$325 million to achieve the WHO goal in metropolitan Chicago. We estimate a 28% increase in the overall DAA cost under low adherence (70%) compared to high adherence (90%).

Conclusion: Our modelling results have important public health implications for HCV elimination among U.S. PWID. Using a range of feasible treatment enrolment and adherence rates, we report robust findings supporting the need to address re-exposure and reinfection among PWID to reduce HCV incidence.

Safety and efficacy of crushed sofosbuvir/velpatasvir in hepatitis C infected patients - a case series

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Background and Aims: Hepatitis C virus (HCV)-related liver disease is a cause of significant morbidity and mortality if left untreated. There is limited safety and efficacy data using crushed Sofosbuvir/Velpatasvir (SOF/VEL) to treat HCV. There are multiple instances where a patient is unable to swallow a tablet and the only option is to take the medication crushed. The aims of this case series are to evaluate the safety and efficacy of crushed sofosbuvir/velpatasvir tablet given orally or via a feeding tube.

Method: This case series includes patients from 13 US-based medical centers where providers reported deidentified data on patients who received crushed (SOF/VEL). Standardized case report forms were collected and the data is summarized. The data collected include specific medications, specific past medical and surgical history, HCV genotype, HCV viral load (HCV RNA measurement), liver fibrosis score, adverse events and sustained virologic response (undetectable HCV RNA 12 or more weeks after stopping treatment; SVR). An updated database is used for this report.

Results: A total of 20 cases were collected. Gender: 8 Male and 12 Female. Race: 11 white, 5 Hispanic, 3 black, 1 other. Baseline median HCV RNA was 830,400 IU/mL (\log_{10} 5.92), 16/16 patients (100%) who had end of treatment (EOT) viral load, were viral negative; 4 did not have EOT viral load. 19/20 patients (95%) had SVR12. Twelve patients had genotype 1 and 8 had genotype 3. Baseline Fibrosis score was available for 16 patients, 2 had fibrosis Stage F0, 3 F0-F1, 2 F1-F2, 2 F2, 1 F2-F3, 1 F3, 1 advanced fibrosis, 1 no advanced fibrosis, and 3 had F4 (cirrhosis). No patient had provider-reported on-treatment adverse events, none discontinued therapy. Three patients had dose interruptions, of whom 2 completed 84 days of therapy and one completed 73 days; 17 patients received 84 consecutive days of therapy. Six patients were on PPI during therapy, 1 on H2 blocker and 1 on antiviral Darunavir/Ritonavir. Three patients had small bowel resection, 1 had gastric band, 4 had organ transplant and 3 had other surgical procedures. 9 patients received crushed oral SOF/VEL (1 dissolved in soda, 6 dissolved in other and 2 none), 3 patients received crushed SOF/VEL via NG tube (1 in juice and 2 in water). 7 patients received dosing via PEG-tube (1 mixed in soda, 2 in water, and 4 in other). 1 received dosing via J tube mixed in water.

Conclusion: This case series demonstrates high hepatitis C cure rates and safety in patients receiving crushed SOF/VEL, despite historically considered negative predictors of failure, such as genotype 3, certain medications, prior surgical procedures and dose interruptions. There were no on-treatment adverse events or treatment discontinuation.

Going, going, gone? Routine Emergency Department hepatitis C testing can drive and monitor elimination

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Background and Aims: Emergency departments (EDs) are common access points for healthcare in England with over 23.8million ED attendances in 2017-18. People who visit EDs may not engage with other healthcare services, and are more likely to live in deprived areas or be of diverse ethnicities which overlap with target populations for hepatitis C (HCV) case-finding. Directly acting antivirals (DAAs) have revolutionised the treatment of HCV in England since their roll-out in 2016. We aimed to evaluate the impact of networked provision of directly-acting antiviral treatment for HCV by comparing the hepatitis C antibody and RNA positivity rates from routine blood borne virus testing programmes carried out at the ED of a teaching hospital in the area from 2014 until 2021.

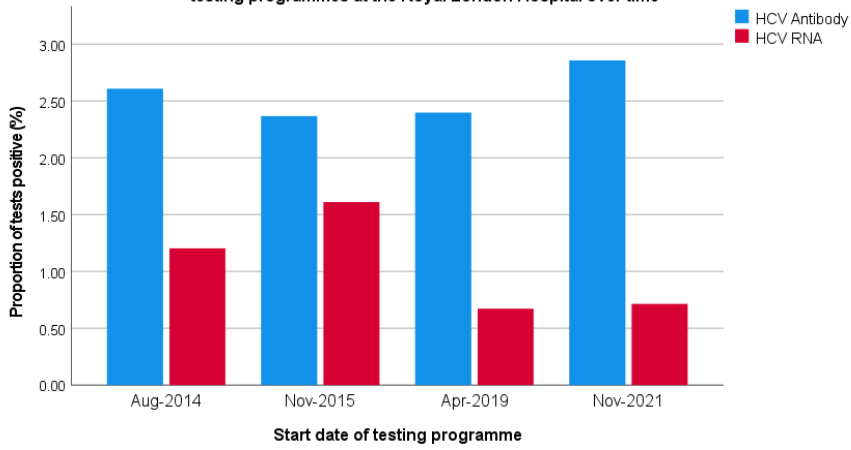
Method: HCV testing programmes carried out at a London Hospital ED were identified through discussion with local clinicians. Studies were included if they reported data from non-selected testing for hepatitis C where automatic, or reflex, HCV RNA tests were carried out on all HCV antibody positive samples. Programme methodology and results were extracted from reports. HCV antibody and RNA positivity rates with 95% confidence intervals (CIs) were calculated using Microsoft Excel 2016 and IBM SPSS Statistics V28. Programmes were either approved by the local ethics committee, or were part of service improvement initiative

Results: There were four routine hepatitis C testing programmes at the Royal London Hospital: In 2014 an anonymous seroprevalence study tested all biochemistry samples taken from the ED during one week. *Going Viral* programmes in 2015, 2019 and 2021 involved opt-out testing for hepatitis C and HIV by collecting an additional venous blood sample at the time of other blood tests. The clinical teams were automatically informed of positive results, permitting patient notification and linkage to care. The 2021 programme is ongoing. The number of HCV antibody tests carried out in each programme ranges from 140 in the 2021 programme, to 12,346 in the 2019 cohort. As shown in the figure, hepatitis C antibody positivity rates varied from 2.37% (95% CI 2.01% to 2.77%) in 2015 to 2.86% (95% CI 0.97% to 6.65%) in 2021. Hepatitis C RNA positivity rates decreased significantly over time from 1.61% (95% CI 1.32% to 1.95%) in 2015 to 0.67% (95% CI 0.54% to 0.83%) in 2019.

Conclusion: Routine hepatitis C testing programmes from a single urban emergency department have shown that while HCV antibody rates are similar, HCV RNA positivity rates have declined significantly from 2014 to 2019. Routine ED testing both identifies people with current hepatitis C infections in need of DAA treatment and, by monitoring changing viraemia rates, can evidence progress in reducing disease burden in local populations.

Figure:

Hepatitis C antibody and RNA positivity rates from routine Emergency Department testing programmes at the Royal London Hospital over time



Estimated prevalence of chronic hepatitis B in Denmark

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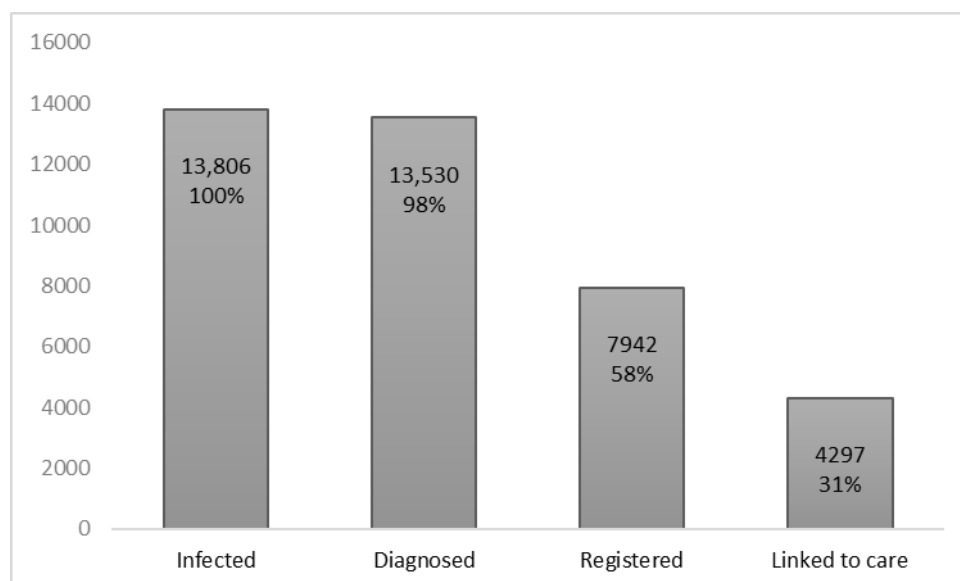
Background and Aims: The prevalence of chronic hepatitis B in Denmark has not been estimated since 2007 (0.245). To guide future efforts to achieve elimination, and to give a setpoint to measure the effect of these interventions we aimed to update the estimated prevalence of both diagnosed and undiagnosed chronic hepatitis B in Denmark. Moreover, we aimed to determine the fraction attending specialized care, and the fraction reported to the national register of communicable diseases.

Method: Using four registers with national coverage, we identified all individuals registered with chronic hepatitis B, aged 16 years or older, and alive in Denmark on December 31, 2016. The diagnosed population was then estimated using capture-recapture analysis. Finally, the undiagnosed population was estimated using data from the pregnancy screening program in Denmark.

Results: We estimated a chronic hepatitis B prevalence of 13,806 persons corresponding to 0.29% of the Danish population of whom 13,530 (98%) were diagnosed and 7,942 (58%) were registered in one or more of the source registers. Only 32% of the diagnosed population had attended specialized care and only 24% were reported to the Danish communicable disease register.

Conclusion: The prevalence of chronic hepatitis B increased from 2007 to 2017. The majority in the diagnosed population did not receive care as recommended by national guidelines and were not reported to the national register. Future efforts should focus on linking persons diagnosed with chronic hepatitis B to specialized care and improve reporting of diagnosed cases.

Figure: Cascade of care for chronic hepatitis B in Denmark.



Framework for hepatitis C virus (HCV) Micro-Elimination in Ho Chi Minh City (HCMC), Vietnam: A Path to National HCV Elimination

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Background and Aims: Micro-elimination is to break down HCV elimination goals into smaller goals for specific populations or geographic areas, so interventions can be delivered using targeted methods. This study leveraged the micro-elimination concept to establish a framework comprising specific HCV epidemiological profiles and self-reported linkage to care in HCMC and Viet Nam.

Method: From 2018 to 2020, using Probability Proportionate to Size sampling method, we applied a multistage cluster survey to invite 17,600 adults (18+) representing an HCMC population of 9 million. Participants were screened for anti-HCV and confirmed with HCV RNA testing if anti-HCV was positive. The distributions of and associations with sociodemographics and known HCV infection risk factors were evaluated using bivariate analyses and multiple logistic regression with forward selection. Survey weights were applied to account for non-response and non-coverage. Based on self-reported HCV awareness, positive anti-HCV, and self-reported linkage to care, a cascade of care for HCV in HCMC (CoC) was constructed.

Results: 87.4% (15,395/17,600) of the invited responded and phlebotomy-based screening and questionnaire surveys. 95.3% (14,675/15,395) had complete data for analysis. The prevalence of anti-HCV and HCV RNA in HCMC was 1.3% (95%CI, 1.1%-1.6%) and 0.54% (95%CI, 0.36%-0.73%), respectively. District 1, an urban district, was the epicenter of HCV infection with the prevalence of 3.9% (95% CI, 1.9%-5.9%). Individuals born 1945-1964 represented 40.4% of all HCV cases. Key risk factors found in multivariate analysis were history of blood transfusion, tattoo, and IV drug use. In the CoC, 28.5% of persons with anti-HCV (+) were aware of their HCV status, with 70% (60/85) diagnosing HCV incidentally and 7.1% (6/85) experiencing jaundice. Of those, 82.7% initiated anti-HCV therapy, and 69.8% had HCV cures. The diagnosis rates in general population and high-risk subgroups remained below WHO's targets (90%) in 2030 (Table).

Conclusion: A framework for HCV micro-elimination was established in HCMC. There remains a considerable burden of HCV and significant gaps in diagnosis and access to care in HCMC community. Future interventions must have pragmatic targets; be tailored to the local needs; and emphasize screening.

Figure:

Population	Anti-HCV Prevalence	People diagnosed	Treatment initiation	HCV cure
	% (95% Confidence Interval) (n)	Unweighted % (n)	Unweighted % (n)	Unweighted % (n)
General population	1.3% (1.1-1.6%) (298)	28.5% (85)	82.7% (62)	69.8% (30)
1945-1964	3.6%(3.0-4.2%) (201)	28.9% (58)	72.4% (42)	47.6% (20)
Blood transfusion	3.5 (2.1- 4.9%) (45)	42.2% (19)	78.9% (15)	73.3% (11)
High-risk subgroups for micro-elimination				
Advanced liver disease	16.9 (1.6-32.3%) (11)	72.7% (8)	-	-
Drug abusers	6.0 (2.2-9.8%) (16)	31.3% (5)	-	-
Tattoo	2.2 (1.5-2.8%) (73)	30.1% (22)	72.2% (13)	-

Is it possible a real “Point-Of-Care”? – Feasibility evaluation of telemedicine project to overcome the last barriers to treatment in PWIDs.

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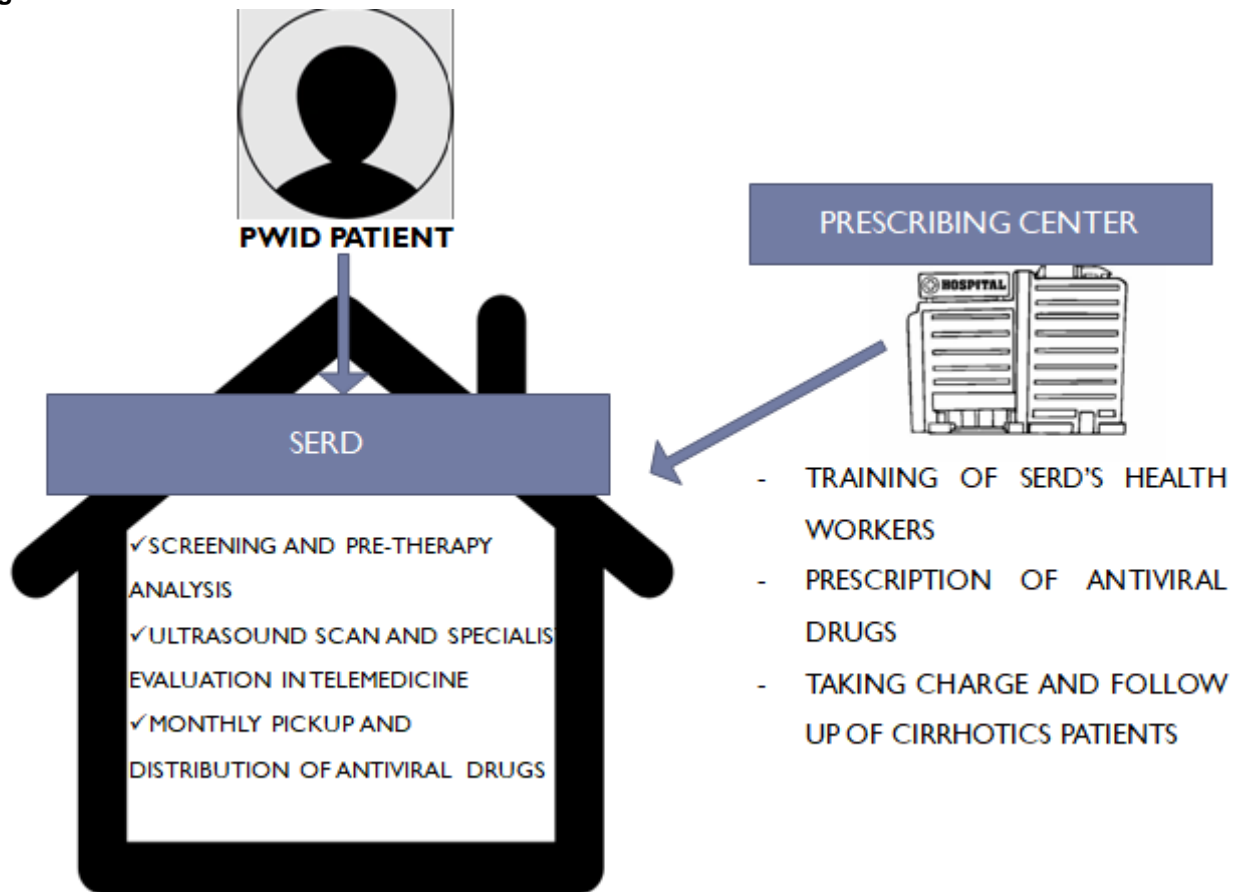
Background and Aims: In Italy management of PWID is performed in specialized outpatient centers named SerD, while DAAs prescription is reserved to few prescribing center to which those patients must be referred. There are many barriers in the referral process as difficulties in reaching public health services or in scheduling ultrasound scan and elastometry. ASL Roma 1 is a big health department of Rome. It includes five SerD with almost 3000 annual access of patients with various addiction problems. From unpublished data, it emerges that only 76.9% of their PWID patients with detected viremia were treated, even with a simplified referral procedure. The aim of this study is to fill that gap and reach the 100% of patient treated creating a real point-of-care with help of telemedicine, moving information, instead of patients.

Method: We aim to allow the complete pre-therapy assessment at SERD with the remote support of specialized center. Here patients will undergo blood chemistry test and FIB4 evaluation. Also the US scan will be executed in loco with a wireless US probe, sending a link to the expert gastroenterologist for remote real time visualization of the exam. Who perform the exam doesn't need to be an expert sonographer because he will be supervised by the gastroenterologist who will decide who can be treated at SERD and who must be necessarily referred. The prescribed therapy will be picked up and transported to the SERD monthly. To put all this into practice, the project will be divided into two phases: 1) Technical feasibility test and education of SerD health workers; 2) Real-life implementation. Here we discuss the first part.

Results: In November 2021, we organized a 5-days course to train the healthcare operator to the basic of ultrasound images and to the use of portable US scan. In technical feasibility test, we found acceptable concordance in measure of US parameter between the operators involved, with no differences between nurses and physicians (discrepancy < 10%). Quality of images was sufficient to identify those patients who need to be necessarily referred to the specialist. The system was found easy to use and the indications given by the specialist easy to follow, even in absence of familiarity with the ultrasound anatomy. However, the wireless probe was found to be slightly heavy and unwieldy for first-time users. Another limit can be the presence of a bad internet connection, resulting in a small time gap that make the examination more annoying for the patients.

Conclusion: The system proposed is easily applicable to every setting because the US scanners are affordable for most health institutions and the healthcare staff doesn't need an extremely specific training. The scan is intuitive to use and the remote guidance of an expert gastroenterologist it is sufficient to make a first classification to divide those patients who must necessarily be referred from those who can be treated at SerD.

Figure:



Characteristics of childhood hepatitis B diagnosed cases reported to the national enhanced surveillance system, England 2017-2021

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Background and Aims: Universal infant hepatitis B (HBV) immunisation via a 6 in 1 vaccine was introduced in England in August 2017. To monitor the impact of the vaccination programme as well as monitor risks and trends in children diagnosed with HBV, a national enhanced surveillance system of childhood HBV was established in 2017. This surveillance data analysis aims to characterise this population and evaluate the early impact of universal HBV infant immunisation in England.

Method: New diagnoses of HBV in children < 10 years are identified from the national laboratory reporting system for notifiable organisms and the national Virus Reference Department. General Practitioners (GPs) then complete a case questionnaire on demographics, clinical details, risk factors, likely transmission route and vaccine history.

Results: Between November 2017 and October 2021, 124 diagnoses were identified, an average of 37.7 children diagnosed per year. 50.8% (63/124) of cases were male and the median age at notification was 6 years. 73% of GPs responded to questionnaires; sufficient data were available for 97 cases. Key characteristics of cases are shown in Figure 1. For children born outside the UK (38/97, 39.2%) Romania was the most frequent country of birth (11/38, 29%). The most common ethnicity was White Other (17/97, 17.5%). Of all cases born in the UK, 67.3% (37/55) of children had ≥ 3 vaccine doses. Of these children (UK born and ≥ 3 vaccine doses), 87.9% (29/33) versus 100% (4/4) were born to a HBV positive mother before compared to after August 2017, respectively. Of all those born in the UK to HBV positive mothers, 81.6% (31/38) had a birth dose within 24 hours.

Conclusion: This surveillance provides a robust way to identify childhood HBV cases and monitor trends in England, which are influenced by immigration. The reduced number of new diagnoses in those born in the UK and the higher relative contribution of perinatal transmission after introduction of universal HBV immunisation are encouraging early indicators of a successful universal programme. Perinatal transmission events in UK born children should be further investigated to identify and address avoidable programme issues versus vaccine failure or in-utero transmission.

Figure: Table of case features

Feature	Born in UK (%) N = 55	Not born in UK (%) N = 38	Total (%) N = 97
Age (years) at notification			
1-4	20 (36.4)	8 (21.1)	28 (28.9)
5-9	35 (63.6)	30 (78.9)	69 (71.1)
Transmission Route			
<i>Perinatal (confirmed)</i>	26 (47.3)	0	26 (26.8)
<i>Perinatal (probable)</i>	12 (21.8)	32 (84.2)	45 (46.4)
<i>Household contact</i>	12 (21.8)	0	13 (13.4)
<i>Other/unknown</i>	5 (9.1)	6 (15.8)	13 (13.4)
Symptoms (multiple options can be selected)			
<i>Asymptomatic</i>	25 (45.4)	20 (52.6)	45 (46.4)
<i>Clinical features</i>	13 (23.6)	10 (26.3)	24 (24.7)
<i>Unknown</i>	21 (38.2)	12 (31.6)	36 (37.1)
≥ 3 vaccine doses			
<i>Born before 1/8/2017 N = 51</i>	33 (64.8)	<i>n/a</i>	33 (64.8)
<i>Born after 1/8/2017 N = 4</i>	4 (100)	<i>n/a</i>	4 (100)

n/a = not available

HCV elimination among People Who Use Drug in Rome outside the hospital setting is possible during the COVID19 pandemic.

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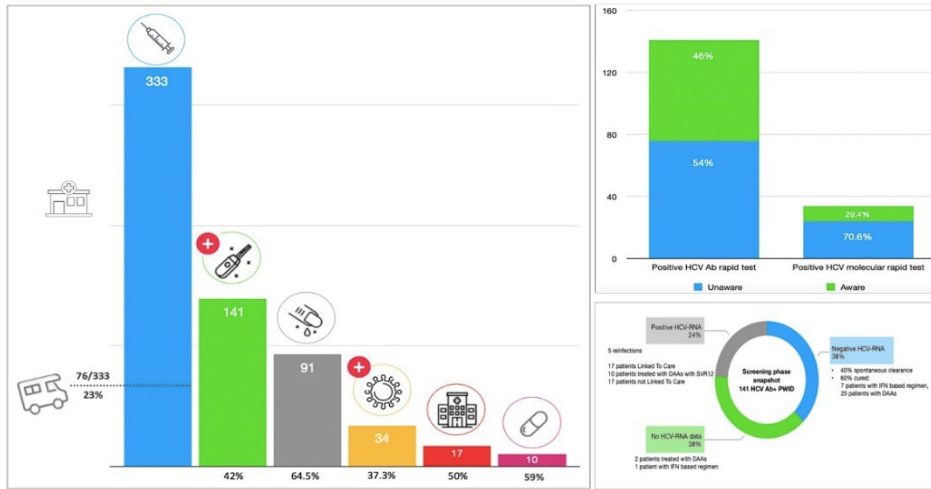
Background and Aims: We evaluated in the key population of People Who Use Drugs (PWUD) in the extra hospital setting of Villa Maraini Foundation: HCV seroprevalence, HCV active infections and re-infections, Linkage to Care (LtC) rates and the efficacy in terms of Sustained Virological Response (SVR).

Method: The diagnostic-therapeutic algorithm included: voluntary based execution of a rapid HCV serological test using OraQuick® Rapid HCV Antibody Test on whole blood obtained by finger stick, after informed consent and an operator-guided questionnaire to investigate the main risk factors for HCV; in case of positivity, execution of HCV-RNA molecular rapid test; in case of diagnosis of HCV active infection, promptly LtC to the Infectious Diseases Clinic of Tor Vergata Polyclinic.

Results: From May 2020 to January 2021, 333 PWUD (of which 23% intercepted at the street unit) performed HCV serological rapid test, and among these ones, 42% (141/331) was positive. All 141 subjects were promptly offered to perform the rapid HCV molecular test to confirm the presence of Hepatitis C and 64.5% (91/139) agreed it. Of these, 37.3% (34/91) were positive and therefore received confirmation of Hepatitis C. 50% of patients diagnosed in an out-of-hospital setting (17/34) actually went to hospital for access to treatment and 59% (10/17) received treatment with DAAs and obtained SVR12. 38% of PWUD with positive serology had negative HCV-RNA, of these 40% had spontaneously cleared the virus, while 60% had obtained SVR thanks to treatment (7 patients with IFN-based regimens, 25 patients with DAAs); of 38% of PWUD with positive serology we have no information about HCV-RNA as they did not want to perform the rapid molecular test; 24% of PWUD with positive serology had active replication of HCV detected by rapid molecular test and among these 5 reinfections were highlighted. 17/34 patients with chronic active hepatitis were LtC and of these 10/17 received treatment and obtained SVR12. It also emerged that PWUD were unaware of their serological and viraemic status respectively in 53% and 70.6%.

Conclusion: Rapid diagnostics (both serological and molecular) and the experience on the territory of Villa Maraini Foundation have been a winning formula in terms of diagnosis for out-of-care PWUD and which would never have approached the hospital system mostly despite the lockdown and restrictions due to COVID19. To date, the most delicate and weak part in the cascade of care is the LtC, therefore the process of access to care must be remodeled through the decentralization of care.

Figure: Villa Maraini and Univeristy Hospital of Tor Vergata HCV Care Cascade, HCV awareness among PWUD and Linkage To Care focus.



What can Europe learn from HCP knowledge and attitudes towards hepatitis A vaccination in the US?

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Background and Aims: An estimated >100 million new hepatitis A (HepA) infections occur annually worldwide. Centres for disease control and prevention reported 42936 HepA cases in the US since 2016, and 4475 outbreak-confirmed cases in Europe between 2016-2018. HepA outbreaks resulted mainly from person-to-person contact, especially among homeless, illegal drug users (IDU) and men who have sex with men (MSM). In 2020, we surveyed US health care providers (HCPs) to understand their knowledge and attitudes towards HepA vaccination in these populations at higher risk of infection and complications.

Method: This was a cross-sectional, web-based survey of 400 HCPs (primary care providers, nurse practitioners, gastroenterologists, internal medicine and infectious disease specialists [IDs], emergency room physicians [ERs]) who had recommended and/or administered HepA vaccines to ≥19-year-olds.

Results: 85% of 371 HCPs reported recommending HepA vaccine to homeless, 87% of 393 to IDU and 83% of 397 to MSM, although vaccination may not actually occur after recommendation. Results varied by specialty, 16% fewer ERs than IDs reported recommending the vaccine in these at-risk populations. Moreover, 64%, 75% and 71% of all (400) HCPs reported *extremely important* that homeless, IDU and MSM, respectively, get vaccinated for HepA, while 6%, 7% and 8% of all HCPs reported this as *slightly*, or *not important*. Reasons for not recommending HepA vaccine to homeless, IDU and MSM included uncertainty on guidelines (reported by 22/56, 24/50 and 29/66 HCPs, respectively) and low risk of infection (reported by 20/56, 30/50 and 27/66 HCPs, respectively).

Conclusion: Despite recent HepA outbreaks and strengthened recommendations for vaccination in at-risk populations, knowledge gaps persist among US HCPs. This survey may motivate European countries to reinforce national HepA vaccination recommendations and, in parallel, consider efforts to raise vaccination awareness.

Funding: GlaxoSmithKline Biologicals SA

Encore of EUPHA (2021) congress: O Herrera-Restrepo, P Ghaswalla, K Davis, C Sweeney, E Davenport, A Andani, PO Buck. What can Europe learn from HCP knowledge and attitudes towards hepatitis A vaccination in the US? Eur J Public Health. 2021;31(Suppl 3):ckab165.467

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Point of care screening tests for hepatitis B and commitment of a dedicated nurse lead to successful linkage to care of ethnic minorities

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Background and Aims: In low endemic countries, screening for hepatitis B surface antigen (HBsAg) in migrants is cost-effective to reduce the disease burden of hepatitis B virus (HBV) infections, but linkage to care (LTC) remains a challenge. We previously found outreach screenings for HBV using point of care tests (POCT) to result in a 2.5 times higher LTC compared to venepunctures in an Asian migrant population. In the current study we compared LTC between different ethnic groups screened for HBsAg with POCT in an outreach setting. A secondary objective, was to compare the estimated HBsAg seroprevalence for ethnic minorities to the established prevalence in the general population in order to guide future screening initiatives.

Method: Opportunistic outreach screenings using finger prick Vikia HBsAg tests were performed at municipal integration classes between 11/2017 and 03/2021. If tested positive, an appointment was given immediately at the outpatient hepatology clinic for follow-up and confirmation of HBsAg positivity in blood. A dedicated nurse contacted identified patients via phone, social media or home visits to motivate them for further linkage to care. The latter was defined as having received medical care from a hepatologist, a blood test and an abdominal ultrasound.

Results: A total of 521 persons with different ethnicities (Asia, Middle-East and Africa) were serologically screened using POCT tests. The seroprevalence for HBsAg was 3.45 % (18/521) and was significantly higher compared to that of the general population (i.e. 0.66 % in 2003 ($p < 0.0001$)). All HBsAg-positive patients were linked to care and assessed by a hepatologist. LTC for all ethnicities combined ($p < 0.0001$), for Sub-Saharan African patients ($p = 0.023$) and Middle-Eastern patients ($p < 0.0001$) was significantly higher compared to the previously observed rate of 34.38 % (11/32 patients) using venepunctures as a screening method, but without the commitment of dedicated nurse. Among the HBV infected patients, 22.22 % (4/18), 83.33 % (15/18) and 22.22 % (4/18) met criteria for treatment indication, intrafamilial transmission risk and HCC surveillance respectively. Despite COVID-19 pandemic, linkage to care remains high using POCT and through the commitment of a dedicated nurse. However, the time frame between screening and the first hospital visit is significantly higher ($p = 0.0049$) during the COVID-19 pandemic than in the pre-pandemic period.

Conclusion: HBsAg seroprevalence in ethnic minorities is higher than the general population and warrants targeted screening. Most of the identified patients meet the indication for treatment, counseling to prevent intrafamilial transmission or HCC surveillance. In addition, the use of POCT and commitment of a dedicated nurse can overcome previously identified barriers for linkage to care.

A model for detection and linkage to care of hepatitis C infected persons in prisons in Croatia

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Background and Aims: In the era when effective treatments for hepatitis C virus (HCV) are available, case finding has become the major obstacle for HCV elimination. In Croatia, around 20.000 people are estimated to be chronically infected with HCV (0.5% prevalence in the general population) and around 14% of these are people who actively inject drugs (PWID), who are responsible for most of new infections. Incarcerated people also have increased prevalence of HCV infection (8.3%-44% according to various reports) and have limited access to health care. There are no standard protocols for HCV testing and linkage to care in Croatian prisons. A pilot study investigating the possibility of HCV screening and linkage to care in prison setting was conducted using mobile medical teams in four different prison facilities in the northwestern part of Croatia.

Method: A point-of-care anti-HCV test was offered by a prison study coordinator to prisoners considered at high risk of HCV infection, most of whom belong to PWID. A mobile medical team consisting of a hepatologist and a nurse experienced in HCV treatment visited prisoners on one occasion in the period from September to November 2021. Medical history and physical examination were performed during the visit, together with transient elastography, urine toxicology screening, blood sampling for routine biochemical analysis, serology for HCV, hepatitis B and human immunodeficiency virus, HCV viral load and genotyping.

Results: Out of 201 subjects tested, a total of 46 (22.9%) anti-HCV positive persons were identified, with prevalence ranging from 11.9% to 35.2% among different prison facilities. 34 subjects (mean age 42 years, range 24-56, 33 male) consented and were available for medical workup. Of the results available, 18 of 30 patients (60%) were viremic, and 4 (13.3%) were previously treated and cured. The most common genotypes were 1a (61.1%) and 3a (27.8%) with mean viral load of 1.853.388 IU/ml (range 78-7.251.877). Mean liver stiffness was 11.1 kPa (range 3.2-75) with fibrosis stage (F) 0-1 in 63.6%, F 2-3 in 12.1% and F4 in 24.2%. Although all subjects were former PWID, several of them had multiple risks for acquiring HCV infection (tattooing, sexual transmission and 1 perinatal transmission). Patients' medical records are now being processed to obtain treatment approval from health authorities.

Conclusion: Detection of incarcerated HCV positive patients and their linkage to care is important for HCV elimination. This project is a proof of concept that detection and diagnostic work-up of HCV infection in prison setting in Croatia is feasible. The study offers a possibility of continued HCV care for incarcerated persons in the future. Treatment of HCV patients in prisons may offer many benefits to an individual and the community, and is necessary to achieve a goal of HCV elimination by 2030.

The Elimination of hepatitis C by the Cherokee Nation

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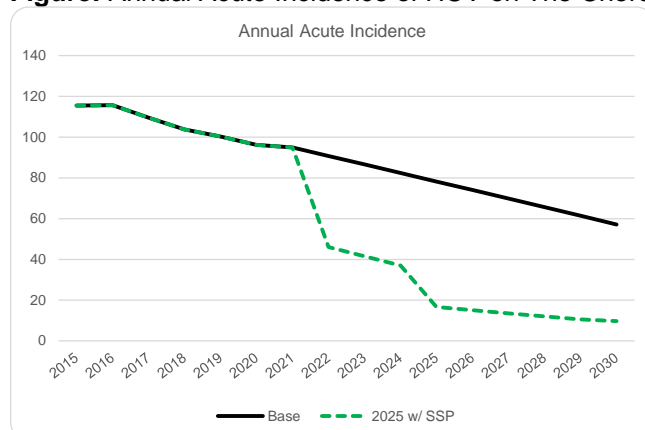
Background and Aims: In the United States, American Indians/Alaskan Natives have the highest rates of hepatitis C virus (HCV) incidence, liver cancer, and mortality compared to all other racial/ethnic groups. The Cherokee Nation (CN), a sovereign tribal nation, launched a (HCV) elimination program in 2015 with a 6-fold increase in treatment in 2016. The primary aim of this study is to utilize modeling to estimate when the CN will meet the World Health Organization's (WHO) 2030 HCV elimination targets. Recently, the CN approved syringe service programs (SSP). The secondary aim of this study was to estimate the potential impact of SSP and if elimination could be met by 2025.

Method: A dynamic Markov model was populated with Cherokee Nation specific input data. Two scenarios were considered. The Base scenario examined the impact of the current treatment and diagnosis levels remaining constant into the future. The second scenario, 2025 w/ SSP, examined the impact of widespread SSP in the CN and the accompanying treatment uptake necessary to meet the 2030 goals in 2025.

Results: We estimate that the CN will meet the 90% diagnosis and 80% treatment target prior to 2025 under the Base scenario. By 2030, there is estimated to be a 75% reduction in total viremic cases and an 84% reduction in mortality when compared to the 2015 baseline. Due to the levels of injection drug use and historical lack of access to needle and syringe programs, incidence was estimated to only be reduced by 50%. The 2025 w/ SSP scenario resulted in an 86% reduction in incidence and 65% reduction in mortality by 2025. This scenario required an increase of treatment to 255 individuals treated for three years, but only resulted in 70 additional individuals treated cumulatively.

Conclusion: The current elimination program of the CN is ambitious and would meet almost all of the WHO targets prior to 2030. However, in the absence of SSPs that provide access to all of those that need it, it is estimated that the incidence would not drop substantially enough by 2030. The recent approval of the SSP program provides the opportunity for the CN to meet all targets prior to 2030. This would require a comprehensive and broad SSP that should be rolled out as rapidly as possible, in combination with an incremental increase in treatment. The CN ambitious program has made large gains towards the elimination of HCV, and with harm reduction services will likely meet all elimination targets by 2025.

Figure: Annual Acute Incidence of HCV on The Cherokee Nation, 2015-2030



Implementing a simplified model of care for hepatitis c virus micro-elimination among people living with human immunodeficiency virus who inject drugs in Egypt

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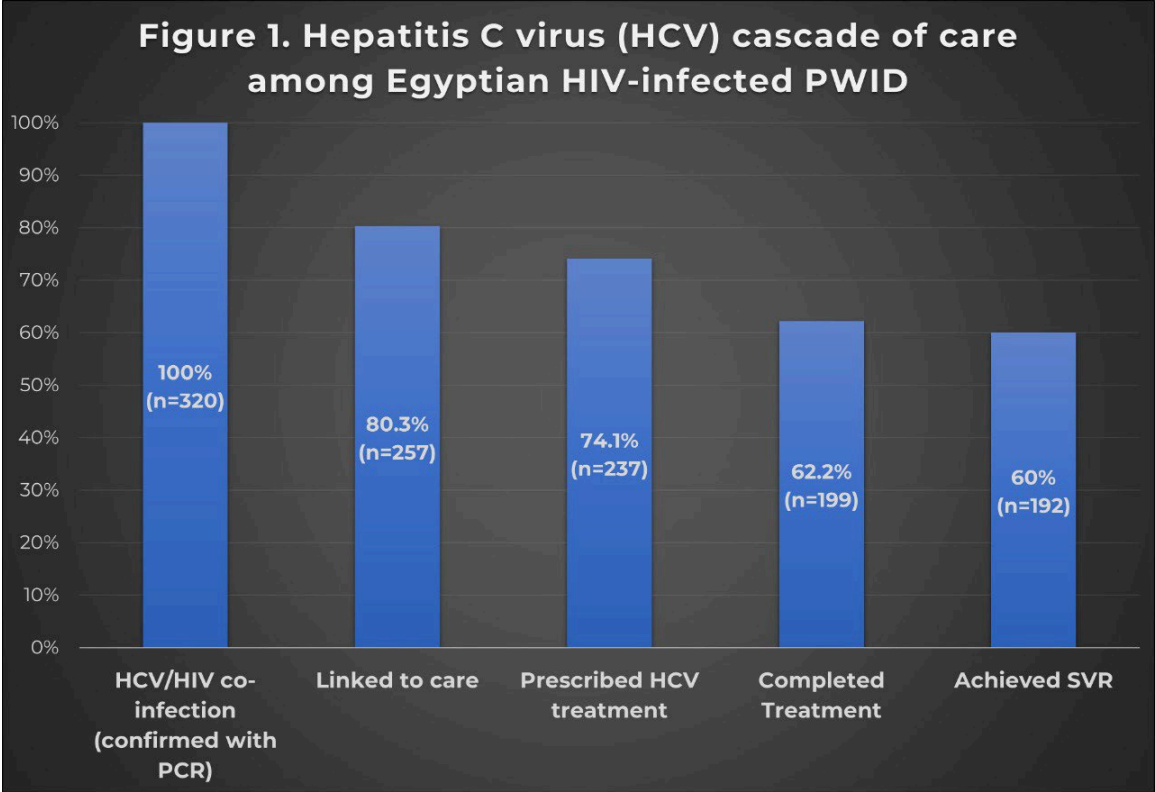
Background and Aims: In order to further advance the national progress towards the World Health Organization (WHO) elimination targets in Egypt, micro-elimination initiatives to scale up HCV diagnosis and treatment uptake among key at-risk groups as people living with HIV and people who inject drugs (PWID) are crucial. Our aim was to evaluate the outcome of implementation of a model of care includes establishing a colocated HCV clinic within an HIV clinic on the HCV treatment cascade, especially linkage to and initiation of treatment among HIV-infected PWID.

Method: Between December 2016 and March 2020, 828 HIV-infected PWID attending the HIV clinic at Imbaba Fever Hospital, Cairo, Egypt, were screened for HCV antibody (Ab) using enzyme-linked immunosorbent assay (ELISA) with confirmation of active infection with HCV RNA polymerase chain reaction (PCR) test. Patients were subsequently referred to a colocated multidisciplinary team for fast-track evaluation, HCV treatment initiation with direct-acting antiviral therapy and monitoring of sustained virological response 12 weeks after treatment (SVR12). A multivariate logistic regression was carried out to identify factors independently associated with HCV status and SVR12.

Results: Of 828 HIV-infected PWID, 319 (38.5%) had a positive HCV Ab result at initial screening. A total of 200 patients had an initial negative HCV Ab test result and at least 1 subsequent HCV Ab test result, contributing > 428 person-years. Of them 15 (7.5%) seroconverted, with an overall HCV incidence of 3.5 cases per 100 person-years (95% CI: 2.05 - 5.64). Among the 334 HIV-infected PWID diagnosed with prevalent or incident HCV, 85.3% were male, 47% in the age group (between 30-39 years), 66.2% were on antiretroviral therapy, 59.6% had undetectable HIV viral load, 29.6% had CD4 cell count \geq 500 cells/mm³, and 25.3% had significant liver fibrosis (\geq F2). Overall, 320 had positive HCV PCR result (95.8%), of them 257 (80.3%) were linked to care, 199 (62.2%) completed HCV treatment, and 192 (60%) achieved SVR12. Comparison between those with SVR12 and those unsuccessfully linked, or treated, showed that among those with SVR12, a higher proportion were younger (mean age 32.36 vs 34.45 years old, $p = 0.004$), female patients ($p = 0.003$), had higher educational level ($p < 0.001$) and liver fibrosis stage F0 - F1 ($p = 0.005$)

Conclusion: Co-localization of HIV and HCV care model was successful in facilitating linkage to care of 80.3% of coinfecting patients with overall SVR12 in 60% of patients (96.5% of treated patients). However, achieving the WHO targets requires interventions to address remaining barriers to linkage to care and treatment completion, besides enhanced screening, and combination of treatment strategies along with harm reduction services among both co-infected individuals and the broader PWID.

Figure:



PO-124

A single centre 2020 view of blood borne viruses and risk behaviour in male Irish prisoners

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Background and Aims: There is a high prevalence of blood borne viruses (BBVs) in the prison population. Knowledge of the prevalence of BBVs and risk factors guides future strategies and responses. A 2019 Irish prison- based study on BBV prevalence in a Dublin prison showed a 21% Hepatitis C (HCV) antibody (Ab) positive rate with a 57% HCV RNA positive rate. Our aim was to establish the prevalence and risk factors for BBV in the Midlands Prison, a medium security prison for adult males, and committal prison for six counties outside of Dublin.

Method: An observational single-centre study was conducted consisting of a risk-based questionnaire, peer- supported screening and serological testing for HCV and hepatitis B (HBV) was performed following prior consent. Posters and information leaflets on the proposed study were distributed to prisoners on the landings and to prison staff a number of weeks before the study start date.

Results: 320 prisoners participated, mean age 40.48 years. 4.6% were HCV Ab positive. There were no cases of HBV or cases of co-infection. 33% were HCV RNA positive. The seroprevalence of HCV was greatest among IDU and those with a history of tattoos done in prison at 31% and 15% respectively. This compares to a 3.35% seroprevalence of HCV in patients having a history of tattoos done outside of prison. 12.5% of inmates with a family history of hepatitis tested positive for HCV. Among prisoners having unprotected sex and dental surgery abroad the seroprevalences of HCV were respectively 4.89% and 3.85%.

Conclusion: The prevalence of HCV in our prison study at 4.6% is much lower than previously reported in other Irish studies. This is likely a reflection of the prison population, type of prisoner and geographic location. Positivity bias also may explain the low rates of HCV. The discrepancy in HCV seroprevalence between prisoners reporting a history of having tattoos done inside and outside of prison is interesting. Ultimately the main risk factor for HCV in our study is IDU mirroring previous studies. HCV was the most frequent infection isolated and therefore still needs treatment prioritisation. All patients have subsequently been treated.

Evidence of hepatitis B virus (HBV) horizontal transmission and a significant proportion of adults remaining at high risk of horizontal HBV transmission are barriers to HBV elimination in Ho Chi Minh City (HCMC), Vietnam

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Background and Aims: Little information is available on Vietnam's HBV serological and epidemiological profiles. We examined HBV serological and epidemiological characteristics, and HBV vaccine adults concerning elimination of HBV in HCMC.

Method: During 2018-2020, a multistage cluster coverage in survey with proportion to size selection was conducted to representatively invite 17,600 adults (18+) of 9 million HCMC residents for screening of HBsAg, anti-HBs, and anti-HBcT. Participants' HBV serologic profiles were grouped as HBV immunity to HBV vaccination [isolated anti-HBs (+) \geq 10IU/mL], susceptible to HBV infection [all anti-HBs (-), HBsAg (-), anti-HBcT (-)], active HBV infection [HBsAg (+)] or "HBV exposure" (anti-HBcT with or without anti-HBs(+)). Distributions and associations of HBV serologies of surveyed demographics, risk factors for HBV infection and HBV testing status were evaluated with bivariate analyses and multiple logistic regression with purposeful selection. Data analysis involved base weights and adjustment for non-coverage and non-response.

Results: 87.4% (15,395/17,600) of respondents were assessed and 95.3% (14,675/15,395) were included in the final analysis. 7.5% (95% CI 6.8-8.2%) were HBsAg(+), 36.1% (95% CI 34.4-37.8%) were positive for anti-HBcT, 18.7% (95% CI 17.3-20.0%) had evidence of HBV vaccination and 37.7% (95% CI, 35.6-39.8%) were susceptible to HBV infection. Within the "susceptible" group, there was a significantly larger proportion of individuals < 30 years old (55.1%, 95%CI 51.9-58.2%, vs. > 30 years old) and of ethnic minorities (67.4%, 95% 52.3 -82.6%, vs. Kinh/Chinese). In the model containing all the predictors of "susceptible", the odds of being susceptible to HBV infection were significantly higher in those with the age range 18-30 years, living in rural areas, ethnic minorities, without health insurance, having lower education levels, being infected with hepatitis C virus (HCV), living with family member who had no HBV or HCV infection, and having no history of HBV testing.

Conclusion: The significantly higher rate of HBV exposure in comparison to the HBsAg(+) rate in adults in HCMC may be explained by a significant contribution of horizontal HBV transmission, in addition to the well-known HBV vertical transmission in the country. This coupled with a large population of adults unprotected from HBV acquisition horizontally presents barriers to HBV elimination by 2030. Future studies are needed to quantify the role of horizontal HBV infection in Vietnam and whether risk-based or universal HBV vaccination is more cost-effective.

Hepatitis C virus in people who inject drugs at the Needle and Syringe Program in Uppsala, Sweden

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Background and Aims: The World Health Organization has set a goal to reach world elimination of hepatitis B virus (HBV) and hepatitis C virus (HCV) by 2030. Needle and syringe programs (NSP) for people who inject drugs (PWID) are crucial to achieve this goal. The NSP in Uppsala, Sweden, opened in 2016 and has since 2018 provided HCV treatment for PWID. The aim of this study was to investigate HCV prevalence, risk factors, sero-status awareness and HCV treatment outcome in participants at the NSP.

Method: Registration data from 446 PWID registered at the Uppsala NSP between November 1st 2016 and June 1st 2021 was collected from the national quality registry InfCare NSP. Further, a subsample of HCV treated was created from the national quality registry InfCare hepatitis. Descriptive and inferential analysis was performed. Ethical approval was obtained from the Ethical Review Board in Uppsala (dnr 2019/00215).

Results: The mean age was 34 years of which 75 % (334/446) were males and 25 % (112/446) females. The overall HCV prevalence was 44 % (162/370) with a declining trend from 50 % (44/87) in 2017 to 43 % (36/84) in 2020. The majority had HCV genotype 1 (49 % (43/87)), followed by genotype 3 (45 % (39/87)). Regarding pre-testing awareness, 90 % (104/115) of those with self-reported positive HCV sero-status, 50 % (22/55) of those who reported not knowing their HCV sero-status and 17 % (34/198) of those with self-reported negative HCV sero-status were HCV RNA positive. Factors associated with a higher risk of HCV RNA positivity were older age at NSP registration (OR 1.027, 95% CI 1.003 – 1.051) and self-reported co-infection with HBV (OR 3.739, 95% CI 1.186 – 16.840) whilst factors associated with a lower risk of HCV positivity were older age at debut of injection drug use (OR 0.950, 95% CI 0.913 – 0.989) and education level higher than or equal to upper secondary school (OR 0.587, 95% CI 0.359 – 0.959). The overall uptake of HCV treatment was 49 % (82/168). Among participants given HCV treatment 97.5 % (77/79) showed a sustained virologic response. Over the study period 8 participants had a HCV re-infection, of which 6 were treated, all were male with mean age of 36.

Conclusion: Older age at NSP registration, younger age at injection drug debut and self-reported co-infection with HBV was associated with positive HCV sero-status and these groups should be subjects for special attention. Encouragingly, we see a downward trend in HCV prevalence at registration among NSP participants. The data emphasize the importance of HCV sero-status awareness, repeat testing and most importantly improving HCV treatment uptake at the Uppsala NSP. Outreach HCV treatment programs for PWID should be implemented to facilitate higher treatment uptake and contribute to reduce HCV transmission to reach the HCV elimination goal.

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Phyloepidemiological analysis of antiviral resistance to NS5A inhibitors in subtype 1a in England post-rollout of direct acting antivirals

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Background and Aims: A minority of patients do not clinically respond to HCV DAA and may be at risk of developing and transmitting resistant virus. We aimed to assess the characteristics of HCV transmission clusters in England, including those with resistant virus.

Method: UKHSA provides a HCV whole genome sequencing clinical service receiving samples from across the UK National Health Service. We performed phylogenetic analyses for subtype 1a and linked results to clinical data in the national HCV Registry. Statistical analysis was with X^2 and Kruskal Wallis tests.

Results: Of 1750 individuals sampled from 2016-2020, 279 (15.9%) were in clusters; of these, 67 (24%) were in a cluster with ≥ 1 sequence containing NS5A RAS. Within clusters, the commonest RAS were M28V (27/44, 61.4%) and Q30R (11/44, 25%); one and three individuals had triple and double RAS, respectively.

Individuals in clusters were younger ($p < 0.0001$), more likely UK-born ($p = 0.0025$), treated outside England ($p < 0.001$), be current/recent PWIDs ($p = 0.0022$) or HIV-positive ($p = 0.0015$) and less likely matched to the Registry ($p < 0.0001$), vs non-clustering individuals (see Table). Across the cohort, individuals with NS5A RAS were more likely to be NS5A inhibitor experienced ($p < 0.0001$) and to have failed first line DAA ($p < 0.0001$).

Conclusion: Transmission clusters were observed including those with resistant HCV. Transmission prevention strategies should be focused on younger individuals, current/recent PWIDs or those who are HIV-positive. The lower likelihood of Registry matching suggests those in clusters may be less engaged with services and may represent a threat to HCV elimination.

Figure: Characteristics of clustering and non-clustering individuals with HCV

	Clustering sequences where ≥ 1 sequence has RAS	% / IQR	Clustering sequences without RAS	% / IQR	Non-clustering sequences with RAS	% / IQR	Non-clustering sequences without RAS	% / IQR	P value
Total*	67		201		278		1204		
Female	9	14.5	41	21	51	19	249	22.1	0.386
Median age, years	37.2	30.8-45.9	40.4	32.2 - 49.2	52.4	44.2-59.1	46.4	38.4-54.9	<0.0001
Region									
London	10	14.9	40	20.3	61	22.2	223	18.6	
Rest of England	43	64.1	100	50.8	178	64.7	549	68.1	
Other UK or Ireland	14	20.9	57	28.9	36	13.1	159	13.3	<0.001
NS5A inhibitor exposure	13	22.4	10	7.5	82	38	55	6	<0.0001
Matched to Registry	34	50.7	99	49.3	193	69.4	764	63.4	<0.0001
Ethnicity									
White	30	93.8	73	86.9	147	85	622	91	0.151
Birth country									
UK	28	90.3	74	94.9	111	69.8	536	85.9	0.0025
Route infection									
PWID	26	92.9	63	86.3	102	76.7	476	83.7	0.002
Current/recent PWID status	15	53.6	40	55.6	40	27.2	188	31.4	<0.0001
HIV positive	5	14.7	10	10.1	8	4.1	29	3.8	0.0015
First line DAA									
Elbasvir-grazoprevir	8	32	30	49.2	64	43.2	304	54.5	
Ledipasvir-sofosbuvir	9	36	14	23	47	31.8	123	22	
Other	8	32	17	27.9	37	25	29	6.4	0.062
Treatment outcome									
SVR12	18	58.1	56	72.7	69	40.8	453	68.7	
Failure	5	16.1	1	1.3	63	37.3	48	7.3	
Lost to follow up	8	25.8	20	26	37	21.9	158	24	<0.0001

*Totals may not add up to 100% due to missing data.

Combined telephone and home assessment and home treatment delivery improves drug service client access to hepatitis c care and treatment uptake during the COVID-19 pandemic

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Background and Aims: In the 12 months' preceding COVID-19, only 43 clients of a single drug-service initiated hepatitis C (HCV) treatment: 40 within the hospital outpatient clinic and 3 within the drug service. A further 60 known HCV RNA-positive clients, for whom access to and consistent engagement with either clinic had not been possible, remained untreated. In March 2020, at the onset of the COVID-19 pandemic and first UK national lockdown, the hospital and drug service discontinued face-to-face appointments. We aimed to design and pilot an alternative model of HCV care delivery to maintain and potentially improve uptake of HCV assessment and treatment amongst drug service clients, whilst minimizing COVID-19 transmission risk and conforming to national COVID-19 restrictions.

Method: Known HCV RNA-positive clients were contacted and completed initial telephone assessment. If available, historical venous blood results (within last 6 months) were used to confirm ongoing HCV RNA positivity and HCV genotype and to assess liver fibrosis using APRI and FIB-4. For clients without recent HCV RNA and/or genotype or recent AST, ALT and platelet assessment, a home visit was performed by two nurses using appropriate COVID-19 PPE and infection control precautions, to obtain up-to-date venous bloods, including INR in clients with elevated or equivocal APRI and/or FIB-4. HCV treatment was determined by videoconference MDT meeting, involving the responsible consultant physician. The full HCV treatment course was delivered to clients' homes. Further telephone consultations were conducted to verify treatment delivery, start and ongoing adherence. If indicated, transient elastography and/or liver ultrasound were deferred until after treatment initiation, pending easing of COVID-19 restrictions.

Results: From 1 April to 30 June 2020, 42 (70%) of 60 known HCV RNA-positive clients were successfully contacted and completed remote telephone assessment; 1 required home capillary blood sampling. 31 (51.7%) initiated HCV treatment, of whom: 25 (80.6%) achieved SVR12; 1 did not respond to treatment (likely non-adherence); 2 died before SVR12 assessment; and 3 were lost to follow up following treatment completion.

Conclusion: In spite of COVID-19 restrictions, HCV assessment and initiation was maintained by rapidly adopting new pragmatic methods of HCV care delivery, combining telephone and home assessment and home treatment delivery. This model facilitated HCV care engagement for clients historically unable to access hospital and drug service clinics and should be embedded alongside other models of HCV care to maximise HCV elimination potential.

Hepatitis B virus vaccination among people with human immunodeficiency virus in the Netherlands

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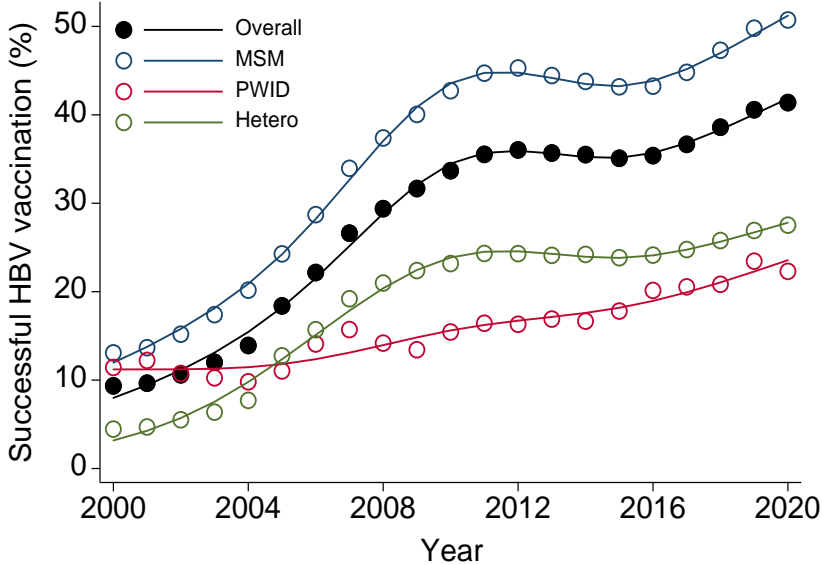
Background and Aims: The Netherlands recommends hepatitis B virus (HBV) vaccination for individuals who bear a high risk of acquiring HBV infection [e.g. men who have sex with men (MSM), people who inject drugs (PWID)]. Individuals with human immunodeficiency virus (HIV) more likely belong to these key populations susceptible to HBV. We estimated the percentage successfully vaccinated for HBV in the past two decades from a nationwide cohort of people with HIV.

Method: Prospectively-collected data from the ATHENA cohort of people with HIV aged ≥ 18 years attending any of the 24 HIV treatment centres in the Netherlands between 2000 and 2020 were assessed. We included individuals eligible for HBV vaccination, defined as those who did not have chronic HBV infection [hepatitis B surface antigen (HBsAg) positive] or past HBV infection [anti-hepatitis B core antibody (anti-HBcAb) positive]. We modelled the percent successfully vaccinated (anti-HBs antibody positive or documented in patient file) over calendar year using logistic regression with time as a smoothed spline function.

Results: Of the 28,223 people with HIV ever in care, 17,272 did not have HBsAg- or anti-HBcAb-positive serology and were thus eligible for HBV vaccination. 10,148 (58.8%) were MSM, 273 (1.6%) PWID, and 6,851 (39.6%) heterosexuals/other. The majority of individuals were using antiretroviral therapy (ART) to treat HIV (96.7%). The percentage of individuals with successful HBV vaccination increased from 9.3% (95%CI = 8.4-10.4) in 2000 to 41.4% (95%CI = 40.6-42.2) in 2020, with a more rapid increase in MSM compared to PWID or heterosexuals/other (Figure). In 2020, the percentage of vaccination was highest in MSM (50.7%, 95%CI = 49.7-51.8) compared to PWID (22.3%, 95%CI = 16.3-29.7) or heterosexuals/others (27.5%, 95%CI = 26.4-28.7). Of the 10,398 individuals who remained non-immunized at their last HBV serological battery, 8,281 (79.6%) were using tenofovir-containing ART, which confers protection against HBV infection, while this percentage was lower in PWID (117/217; 53.9%) compared to MSM (4,191/5,139; 81.6%) or heterosexuals/others (3,973/5,042; 78.8%).

Conclusion: The Netherlands has seen a substantial increase in HBV vaccination coverage in the last two decades, yet a considerable proportion is still in need of vaccination. Non-immunised individuals should be prioritized for vaccination, especially those without tenofovir or switching off tenofovir as part of their ART regimen.

Figure: Percentage of individuals with HIV in the Netherlands eligible for HBV vaccination who were successfully vaccinated, over calendar year



Update on hepatitis A in Europe – a systematic review on outbreaks and burden of disease in 11 countries, 2001–2021

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Background and Aims: Over 100 million new hepatitis A (HA) cases/year are estimated to occur worldwide, affecting individuals and communities via outbreaks. Older age is a risk factor resulting in more serious HA and complications. Global surveillance data grossly underestimate the actual HA incidence. Moreover, the implementation of national HA vaccination recommendations is untracked, in contrast to the tracked coverage rates for other vaccines. In Europe, HA is considered endemic, although endemicity is low. Historically, cases were associated mostly with overseas travel; this has evolved due to the globalised food trade and movement of people. Therefore, outbreaks in Europe have been due to factors like food and close person to person contact. Our systematic literature review summarised the data on HA epidemiology (focusing on outbreaks) and disease burden in 11 European countries. These data may provide further insight to inspire the launch of tracking the implementation of HA vaccination programmes and to evaluate the need to update recommendations on HA preventive strategies.

Method: We performed a systematic search in PubMed and Embase including articles published between 2001 and April 2021 in all languages, for Denmark, France, Germany, Greece, Hungary, Italy, the Netherlands, Spain, Sweden, Switzerland and the UK. Country selection was based on vaccination practices and recommendations, endemicity profile, population movement, surveillance and notification systems. Relevant data from ECDC, ProMED, ESCAIDE and national public health websites were also checked.

Results: Data were extracted from 134 articles and 85 reports. Peaks in notification rates (NRs) were observed in 2007–2009, 2013–2014 and 2016–2017 (although not in all countries). One HA outbreak, likely due to frozen berry consumption, occurred between January 2013 and August 2014, with most cases (1,438) in Italy. Before 2016, most outbreaks were foodborne, travel-related, or in day-care and school settings. The 2017 outbreak, which mainly affected men who have sex with men (>4,000 cases), was the largest multinational outbreak in Europe, with most cases in Spain (2,039) and Italy (976). Hospitalisation rates varied largely by country and year. 69% of fatal cases were in >60-year-olds. Study limitation: the total number of HA cases is underestimated as NRs are based on laboratory-confirmed HA cases (therefore asymptomatic or mild infections were likely underreported or not included).

Conclusion: HA virus is still circulating in Europe, leading to outbreaks and affecting various risk groups. We can reduce the disease burden in Europe by raising awareness on HA risks and prevention, strengthening implementation of current recommendations and broadening vaccination recommendations to cover all at-risk populations (all uninfected or unvaccinated persons).

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Covid-19 pandemic: a significant barrier for hepatitis c elimination for people who use drugs (PWUD) in Greece

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Background and Aims: PWUD remain the key population in the effort of Hepatitis C elimination. Coronavirus (Covid-19) infection has faced with several challenges in treatment of HCV infection. In Greece harm reduction programs reduced or stopped and linkage to care with liver units for HCV patients became difficult due to the regional lockdowns. Our aim was to determine whether Covid-19 affected linkage to care and treatment for PWUD and restrained HCV elimination programs

Method: We included 268 adult consecutive patients with HCV infection and a history or current drug use, who visited our outpatient liver clinic in order to start treatment from August 2018 until October 2021. Patients were divided in two equal period groups: Group A (pts from Aug. 2018 to Feb. 2020) and Group B (Pts from March 2020 to October 2021), based on the beginning of the pandemic and lockdown in Greece on March 2020.

Results: 203 patients consisted Group and 65 patients Group B. All patients had HCV RNA detectable and were eligible for antiviral treatment. 26 (18,4%) were with cirrhotic based on transient elastography (stiffness >11,5 kPa). However elastography was performed in 141/268 patients. Almost half of the patients in each of the two groups were attending substitution programs (methadone/buprenorphine). Application for treatment in the national HCV registry was performed in 203 patients in Group A. 181/203 patients (80% male, mean age 46,5 ±10 years, 55% Gn3 and 25,4% Gn1a) initiated HCV treatment. In contrast between March 2020 - October 2021 (Group B), 65 patients were registered for HCV treatment and 49 (69,3 % male, mean age 48±9,5 years, 67% Gn3 and 18% Gn1a) started treatment (p=0,01). In Group A 146 patients completed treatment and 108/146(59,6%) had HCV RNA testing for SVR vs 41 patients who completed treatment but only 10/41 patients (20%) were tested for HCV RNA testing (p<10⁻³). SVR rates were comparable between two groups (Group A vs Group B: 108/108 patients -100%- vs 9/10-90%- patients).

Conclusion: Our real world data postulated that all HCV–PWUD, regardless of attending substitution programs succeeded SVR in both periods; however there was a significant reduction (68%) in treatment initiation during the Covid-19 period. We also observed that pandemic affects HCV treatment at several steps of the care cascade. Implementation of new strategies is necessary in order to remain on HCV elimination track particularly for vulnerable populations.

Figure:

Patients (N=268)	HCV REGISTRIES	TX INITIATION	TX COMPLETION	SVR CHECK	SVR ACHIEVED
GROUP A	203	181	146	108	108
GROUP B	65	49	41	10	9

Estimating rates of hepatitis C virus reinfection among patients receiving antiviral treatment in England

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Background and Aims: In England, as treatment coverage of primary hepatitis C virus (HCV) infection expands, the proportion of new infections that are due to reinfection will increase potentially threatening England's ability to achieve the World Health Organisation's aim to eliminate viral hepatitis as a public health threat by 2030. Approaches to monitoring HCV reinfection vary depending on available data. We aimed to estimate the HCV reinfection rate among a cohort of patients receiving antiviral treatment using available surveillance data.

Method: HCV reinfection was defined using available linked surveillance data on treatment initiation and duration, sustained virologic response (SVR), and serial HCV RNA testing between 2015-2021. Patients who met one of the following criteria were defined as experiencing reinfection: (i) a positive HCV RNA test ≥ 213 days after treatment start date where SVR was recorded; (ii) a negative HCV RNA test ≥ 182 days after treatment start date followed by a positive HCV RNA test ≥ 30 days after their first negative test post treatment, or (iii) a subsequent treatment start date 168 days after the previous treatment where SVR was recorded. Multivariable logistic regression was used to compare sociodemographic variables between patients coded as experiencing HCV reinfection and a control group of patients with sufficient follow-up, who had received treatment, achieved an SVR and a negative HCV RNA test ≥ 182 days after their treatment start date with no known positive follow-up test.

Results: In total, 66,553 people received treatment. Of these, 16,505 achieved an SVR followed by a negative HCV RNA ≥ 182 days after treatment start; among this group, 1,336 (8%) met the criteria for reinfection. Among those with reinfection, 78% were men, median age at first treatment was 34 years, and median time between first treatment and reinfection was 19 months (range 5-67 months). In multivariable logistic regression, factors associated with higher odds of reinfection were first treatment in prison compared to other settings (18%, aOR 1.67, 95% confidence interval (1.41, 1.84)) and a history of injecting drug use (11%, aOR 1.61 (1.44, 1.95)). Being female (6%, aOR 0.80 (0.70, 0.93)) and of Asian ethnicity (4%, aOR 0.59 (0.44, 0.81)) were associated with lower odds of reinfection.

Conclusion: We estimated that HCV reinfection occurred in 8% of patients who had antiviral treatment and who had linked follow-up data. Whilst the requirement for follow-up data may select for a group at potentially higher risk for reinfection (e.g. people reporting injecting drug use and those in prison), our findings suggest that regular testing for HCV infection and structured harm reduction support efforts should be targeted to key population groups.

Hepatitis C virus test positivity among pregnant women in England between 2016-2017

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Background and Aims: In England, there is no universal antenatal screening programme for hepatitis C virus (HCV). Testing is recommended for women with one or more risk factors for HCV (e.g. injecting drug use, coming from a country with a high HCV prevalence) and practice is variable. We aimed to investigate testing practice by exploring factors associated with anti-HCV test positivity among pregnant women in England.

Method: Data for pregnant women aged 12-49 who received an anti-HCV test in England between 2016-2017 were extracted from the sentinel blood-borne virus testing surveillance system. Multivariable logistic regression was used to investigate sociodemographic associations with anti-HCV test positivity.

Results: Of the 13,254 pregnant women tested for HCV (median age 32, 57% UK-born), 3% (380) were anti-HCV positive. In multivariable analyses, being 35 and over, Asian Pakistani ethnicity, born in Western/Southern Europe or Eastern Europe and being a person who injects drugs (PWID) were associated with increased odds of anti-HCV positivity. Black African ethnicity and residing in the least deprived quintile were associated with reduced odds of anti-HCV positivity. Among those anti-HCV positive, 47% (177/380) were new diagnoses (no known previous positive test).

Conclusion: The high HCV test positivity among pregnant women suggests targeted risk-based testing is occurring in antenatal services. This was corroborated by higher odds of being anti-HCV positive among PWID and women coming from endemic regions. Risk-based testing for HCV identified new infections but opt-out antenatal HCV screening may be an option in more demographically diverse areas, for new case-finding and re-engaging diagnosed women in care for treatment post-partum.

Figure:

	Total (N=13,254)	anti-HCV positive (N=380)	Row %	aOR(95% CI)
Age Group				
12-18	142	1	1	0.18 (0.03, 1.33)
19-24	1429	22	2	0.48 (0.31, 0.76)
25-34	6958	186	3	ref.
>=35	4725	171	4	1.53 (1.22, 1.91)
Ethnicity				
White British	7526	224	3	ref.
White Irish	279	10	4	1.28 (0.67, 2.47)
White Other	1717	64	4	0.96 (0.68, 1.36)
Asian Indian	380	5	1	0.49 (0.19, 1.21)
Asian Pakistani	695	41	6	1.70 (1.14, 2.55)
Asian Other	434	12	3	0.94 (0.50, 1.76)
Black Caribbean	20	1	5	2.82 (0.36, 21.83)
Black African	669	3	0.4	0.23 (0.07, 0.74)
Chinese	254	2	1	0.27 (0.06, 1.12)
Other	500	7	1	0.58 (0.27, 1.28)
Region of birth				
UK	7496	201	3	ref.
Western/Southern Europe	680	29	4	1.95 (1.27, 2.98)
Eastern Europe	864	54	6	2.82 (1.95, 4.07)
Africa	1180	11	1	0.50 (0.27, 0.96)
Asia	1649	48	3	1.18 (0.80, 1.74)
Central/Southern America	186	1	1	0.26 (0.04, 1.88)
North America	102	1	1	0.46 (0.06, 3.37)
Oceania	82	1	1	0.57 (0.08, 4.13)
Person who injects drugs				
No	13219	367	3	ref.
Yes	35	13	37	14.14 (6.84, 29.21)
Deprivation quintile				
1 (most deprived)	3121	122	4	1.17 (0.84, 1.63)
2	2224	59	3	ref.
3	1571	36	2	0.74 (0.48, 1.14)
4	1253	28	2	0.64 (0.40, 1.02)
5 (least deprived)	1135	14	1	0.34 (0.19, 0.62)

Seroprevalence of vaccine derived Hepatitis B antibodies in Germany: results from the German Health Survey for Children and Adolescents, 2014-2017

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Background and Aims: In Germany, 3 monovalent or 4 polyvalent doses of Hepatitis B virus (HBV) vaccinations were recommended for children until 2021, with 6 months between the 2 last doses. Since then, 3 polyvalent doses are recommended. A successful vaccination series is defined as having anti-HBs levels ≥ 100 IU/ml 4-6 weeks after vaccination. We aimed to estimate the proportion of vaccinated with an anti-HBs titer < 10 IU/ml, $10 < 100$ IU/ml and ≥ 100 IU/ml by vaccination status among children (3-17 years) in Germany, and assess if protective series are associated with an anti-HBs titre ≥ 10 IU/ml.

Method: We used data from a national population-based cross-sectional study (2014-2017) of children aged 3-17 years (KiGGS). Vaccination information was collected from vaccination cards. We excluded participants with unknown vaccination date, or with unreadable or incomplete vaccination cards and anti-HBc or HBsAg positive participants. A protective series was defined as having ≥ 3 vaccine doses with 6 months between the last 2 doses. We calculated weighted proportions with 95% CI.

Results: We included 2,489 participants. The estimated weighted proportion of vaccinated with anti-HBs levels < 10 IU/ml, ≥ 10 IU/ml and ≥ 100 IU/ml was 38.0% [95%CI 35.7-40.4%], 35.6% [95%CI 33.2-38.0%] and 26.4% [95%CI 24.5-28.4%], respectively. Protective series was not associated with anti-HBs titre ≥ 10 (Crude: OR 1.1 [95%CI 0.84-1.46], adjusted for time since last vaccination dose: OR 0.9 [95%CI 0.68-1.21]). This shift in the OR towards 0 suggests that the association between protective series and anti-HBs titre is explained by time since last vaccination dose.

Conclusion: Estimated proportion of participants with levels of anti-HBs ≥ 10 were similar among those with and without protective series. Protective series was not associated with anti-HBs titre ≥ 10 . More research is needed to understand factors influencing anti-HBs levels post childhood vaccination.

Figure:

Table 1: Anti-HBs level by vaccination status at time of examination (N=2,489)

	Total N	%	Anti-HBs titre <10 IU/ml		Anti-HBs titre 10 <100 IU/ml		Anti-HBs titre ≥100 IU/ml	
			N	% [95%CI]	N	% [95%CI]	N	% [95%CI]
Protective series								
Yes	2,130	100	818	37.6 [35.1-40.3]	764	35.5 [32.8-38.2]	548	26.9 [24.8-29.1]
No	359	100	141	40.1 [34.4-46.0]	136	36.0 [30.2-42.3]	82	24.0 [19.4-29.2]
Protective series with 3 doses	454	100	201	32.2 [27.5-37.3]	147	22.8 [19.0-27.1]	106	15.9 [12.7-19.8]
Protective series with 4 doses	1,644	66.1	610	22.5 [20.4-24.7]	610	23.3 [21.0-25.7]	424	17.2 [15.6-19.0]

Implementation of rapid point-of-care diagnostic systems to support HCV micro-elimination strategies in a tertiary hospital in Spain.

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Background and Aims: The implementation of rapid analysis techniques at point-of-care or hospital facilities allows the optimization of the HCV cascade of care. The aim of this work was to develop an integrated rapid diagnosis strategy that includes the identification of patients, samples testing, clinical diagnosis and communication to the Hepatology Unit for referral and treatment.

Method: We recruited patients from Comprehensive Care Centers for Drug Addicts (CAID) and Primary Care Centers (CAP) who met the inclusion criteria: A) risk populations without previous diagnosis of HCV infection, and B) untreated HCV positive patients. The diagnostic cascade consisted of: A) patient recruitment; B) taking samples in the CAID/CAP facilities; C) sample analysis; and D) communication of results to the hospital hepatologists. The HCV-RNA and genotype were analyzed with a rapid kit (HCV-kit, Epistem) and confirmed with the standard diagnostic techniques at the Hospital facilities.

Results: All patients referred to the hospital for HCV screening between 01/01/2019 and 03/10/2020 (moment at which the study was discontinued due to Covid-19 pandemics) were included. Sixty patients had a history of parenteral drug addiction. We identified 51 patients with detectable HCV-RNA [3 (6%) from CAIDs]. Five (4%), including 3 patients with active addiction practices, were aware of the HCV infection but they have not been previously treated. All HCV-RNA positive patients were infected with genotype 1. An exact correlation was confirmed between the results obtained with the point-of-care and hospital standard diagnostic systems. The gap time between the sample reception and the result communication to Hepatology Unit using the point-of-care strategy was in all cases less than 5 hours, allowing the results report in the same day. Antiviral therapy with DAAs was proposed to all patients and all except the 3 from the CAIDs agreed to be treated.

Conclusion: A) The point-of-care diagnostic systems were comparable, in terms of sensitivity and specificity, to the standard hospital techniques. B) The use of this strategy allows to the hospital hepatologist to have the necessary data for antiviral treatment prescription in the same day of patient recruitment. C) Re-uptake of patients from vulnerable populations with a previous diagnosis of HCV infection does not guarantee the treatment and this will require the development of additional management strategies of this kind of patients.

Clinical characteristics and survival of patients with cirrhosis and hepatocellular carcinoma in The Gambia

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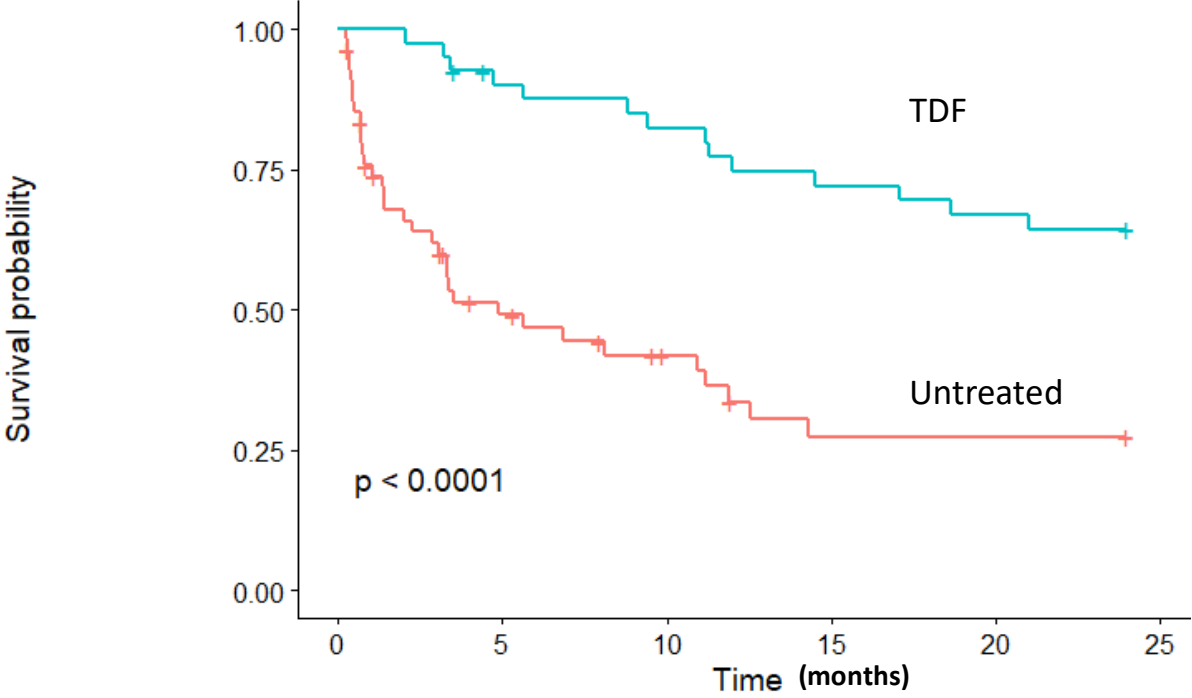
Background and Aims: Survival of patients with cirrhosis and hepatocellular carcinoma (HCC) has been inadequately documented in sub-Saharan Africa. We aimed to assess the clinical characteristics and outcomes of patients with advanced liver disease in The Gambia.

Method: Between January 2012 and December 2016, we enrolled consecutive patients (≥15 years) referred to the PROLIFICA clinic, the sole liver clinic in The Gambia by this time, for suspected advanced liver disease. Tenofovir Disoproxil Fumarate (TDF), not widely available, was only offered in cirrhotic patients without HCC. Survival data and verbal autopsy were collected until July 2019.

Results: Of 529 patients recruited, 405 patients were analysed, median age of 40 (IQR: 32-54) years, 78% (314/405) being males, with a poor performance status 53/100 (53%), median Fibroscan 59 KPa (32-86), ALT 48 U/L (30-88), and total bilirubin 23 mg/dL (12-54) at baseline. At first presentation, 153/405 (38%) had cirrhosis without HCC, mainly decompensated (66%), and 252/405 (62%) had HCC. HBV infection, including occult hepatitis B was the main cause of advanced liver disease in cirrhotic (83%) and HCC patients (68%) and delta co-infection was observed in 9%. Compared to non-HCC patients, HCC patients, were older (median age 45 vs 37 years, $p < 0.001$) but were similarly exposed to aflatoxin B1. Median tumor size was 7.5 cm (IQR: 5.4-10.8), median AFP was 1,986 ng/mL (IQR: 315-8000) and 64% had multifocal HCC. During the study period, 243/405 (60%) patients died, 194/208 (93%) due to liver-related cause and 14/208 (7%) due non-liver related cause. The overall survival was lower in HCC than in non-HCC patients: 13% vs 59% at 6 months and 3% vs 40% at 24 months, respectively ($P < 0.0001$). Among the HBV-related cirrhotic patients, the overall survival was significantly higher in TDF-treated patients (64%) than untreated patients (64 versus 27% at 24 months, $P < 0.0001$). The hazard ratio comparing those with TDF to untreated patients was 0.22 (95% confidence interval = 0.11 – 0.42, $P < 0.001$).

Conclusion: In The Gambia, HBV remains a major cause of cirrhosis and HCC, patients present at very advanced stages and have a poor survival. TDF was associated with a reduced mortality rate in cirrhotic patients without HCC. Efforts are urgently needed to implement early cirrhosis and HCC screening and regular surveillance system.

Figure: Kaplan–Meier Estimates of Time to Death during Treatment



How should reinfection rates be measured and presented? Pitfalls and practical lessons from the Trap HepC project

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Background and Aims: In most high-income countries, IDU accounts for majority of new and existing infections. Reinfections through IDU can hamper elimination efforts but analysis of reinfection rate (RIR) is highly dependent on various assumptions, including how to determine observation periods and how to account for low-risk individuals who are not retested following sustained virological response at 12 weeks or later (SVR12+).

Method: The Treatment as Prevention for Hepatitis C program started in 2016 in Iceland, offering treatment with direct-acting antivirals to hepatitis C virus (HCV)-infected individuals without restrictions. Clinical data were gathered prospectively. The study cohort consisted of HCV-cured patients with an estimated SVR12 between February 1st 2016 and November 20th 2018, with follow-up until November 20th 2019. For RIR calculations, the observation period was defined using two different approaches: 1) from end of treatment (EOT) to the most recent HCV RNA measurement; 2) from SVR12+ to the most recent HCV RNA measurement. In addition, we performed sensitivity analysis on RIR by including or excluding low risk cured individuals who were assumed to remain uninfected. The RIR was expressed as infections/100 person-years (PYs).

Results: The study included 640 HCV treatments with available EOT results in 614 patients. During 693.0 PYs of follow-up, 52 confirmed reinfections occurred in 50 patients. In the SVR12+ cohort there were a total of 617 treatments in 597 patients. During 484.8 PYs of follow-up, 44 confirmed reinfections occurred in 42 patients. In the EOT cohort, median observation time and time to reinfection were 329 days (IQR 229-679) and 230 days (IQR 91-706), respectively. The RIR was 7.5/100 PYs (95% CI 5.5-9.5). In the SVR12+ cohort, median observation time and time to reinfection were 595 days (IQR 298-824) and 252 days (IQR 139-596 days), respectively. The RIR was 9.1/100 PYs (95% CI 6.5-11.6). If all cured individuals within the cohort were assumed to have remained negative until the end of follow-up unless proven to be reinfected, the theoretical follow-up increased to 1699.6 PYs with a median observation time of 1022.5 days. Thus, the theoretical minimum RIR was 3.1/100 PYs (95% CI 2.2-3.9).

Conclusion: Calculations on RIR is highly dependent on definitions of observation time and which subpopulations are included, as estimates can vary up to three-fold. A uniform approach for these assessments is called for. Regular follow up is important among high-risk populations to diagnose reinfections early and reduce transmission.

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Effectiveness of non-nurse, non-doctor Community Liaison Officer programme in testing and treating hepatitis C in homeless populations

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Background and Aims: Some people living with hepatitis C do not engage with health well. This is a key population for elimination with significant ongoing infection. Our services in the North West of England appointed 2 health care workers (HCW) as part of the national (NHSE) elimination initiatives and supported by MSD. Our hospital employed a senior HCW to lead them.

Method: Social centres and hostels were identified, assessed, and run either regular drop ins or events depending on turnover. Testing was done using an antibody (Ab) point of care (POC) test (Matrix™). Those found positive had either a blood test or a dry blood spot (depending on location), Fibroscan™ was used if a private space was available. Otherwise treatment was offered without fibrosis assessment. Consultations were mostly performed by trained senior HCW with remote supervision by doctor of each case. A senior pharmacist reviewed all cases too.

Results: We reviewed the period from 1st April 2021 to 30th September 2021, when 65 different centres were visited. Clients were either street homeless or housed in temporary accommodation. A total of 361 clients were tested by POC (except 5 known Ab positive). 126 (35%) were found positive. Of those 62 were PCR positive (47% of those antibody positive, 17% of the total). 2 declined PCR and for 5 no result was available. Rest were negative. Of those positive, 53 (85%) started therapy. Seven patients were lost to follow up (LFU- 11%), one patient was considered too chaotic for therapy, 2 declined therapy. Of the 53 starting therapy, 9 took 1 month or less (1 achieved SVR and included in SVR results below rest not known).

Good concordance reported by 44. One patient took 4 days only but recently restarted with good concordance. SVR was obtained for 13 patients so far, 11 not detected and 2 positives (all with same EOT results), not due yet for 24 patients- 8 completed therapy but no end of therapy PCR (EOT) done, 9 still on therapy and 7 completed and PCR not detected at EOT. No SVR available for 8 patients (7 had a negative EOT and 1 not done). Overall 25 patients had a negative PCR at EOT or SVR. Only 2 patients had demonstrated failure (4%). Of the 25 patients with demonstrated good outcome, all acquired hep C through injecting, 11 were current users of heroin and/or crack (3 with alcohol excess), two were spice users, 2 alcohol excess, 2 cannabis and 7 reported no substance misuse. Half were on a methadone prescription.

Conclusion: A community liaison health care worker (without a nursing or medical degree) can run a successful test and treat programme and engage large numbers of clients without any adverse reported outcomes. A very high number of clients were started on therapy (85%) and most reported good concordance. Only 2 proven failures were identified. SVR tests are a challenge but a negative EOT could be a good surrogate.

National Hepatitis Elimination Profiles: Progress Towards HBV and HCV Elimination in the Americas

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Background and Aims: In 2016, WHO released a global strategy to eliminate hepatitis B and C as public health threats by 2030. In 2021, CGHE began development of National Hepatitis Elimination Profiles (NHEPs) to assess the country's progress towards elimination

Method: Countries within the WHO Americas region were examined for those with the highest hepatitis B and C burden. To develop the NHEPs, local partners in the Coalition including government officials, clinicians, and civil society stakeholders were convened. Country-level hepatitis data were collected from credible sources including academic publications, Ministry of Health reports, WHO, UNICEF, and the Institute for Health Metrics and Evaluation. Data covers key epidemiological, program monitoring, and policy indicators. NHEPs are dynamic and are revised as data become available.

Results: Progress towards elimination goals across a set of indicators was assessed for Argentina (AG), Brazil (BR), Canada (CA), Mexico (MX), Peru (PE), and the United States (US). Regarding national planning, all countries except PE have established HCV elimination goals. All countries have HCV national action plans. AG, CA, and the US have HBV elimination goals and together with PE have HBV national plans. Regarding elimination of mother to child transmission (EMTCT), all nations except MX have set EMTCT elimination goals for HBV. All nations except CA have policies for HepB birth dose vaccination with >50% coverage, the 2020 WHO interim target. AG, BR, and US have policies for routine HBV and HCV screening of pregnant women, while CA and PE only have policies for HBV, and MX only for HCV. Regarding hepatitis testing, all countries have risk-based screening policies for HCV. Except for CA and PE, countries have additional recommendations for general population or age-cohort HCV screening as well. AR, BR, CA and US have recommendations beyond HBV risk-based screening. Regarding HCV treatment, all countries have removed some or all restrictions and simplified care algorithms. MX adopted all national policies expanding access to HCV treatment. Regarding strategic information, only AG and BR have national public health systems to routinely track the number of persons tested and treated for HBV and HCV. BR is the only country on track to meet all WHO 2020 HBV and HCV interim elimination targets. All countries have achieved the WHO/SDG target of 1% HBsAg prevalence among under-5 children by 2020.

Conclusion: The NHEPs reveal the strengths and limitations of national HBV and HCV elimination programs in the Americas. Comparison of program attributes across countries promote sharing of lessons learned. Importantly, local coalitions can leverage the NHEPs to spur policy change that advance progress toward hepatitis elimination. Additional country profiles are in development.

Hepatitis C virus treatment uptake among marginalized people who inject drugs: a registry based study

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Background and Aims: Improving HCV treatment uptake among people who inject drugs (PWID) is crucial to achieve the WHO elimination targets. The aims were to assess HCV treatment uptake and associated factors, and to estimate HCV RNA prevalence in a large cohort of PWID in Norway.

Method: Registry-based observational study where all registered users of the City of Oslo's low-threshold social and health services for PWID between 2010-2016 (n=5330) were linked to HCV notifications (1990-2019) and prescriptions of HCV treatment, opioid agonist therapy (OAT) and benzodiazepines (2004-2019). Cases were weighted to account for spontaneous HCV clearance. HCV treatment rates were calculated using person-time of observation and factors associated with treatment uptake were analysed using logistic regression analysis. HCV RNA prevalence was estimated among users of the low-threshold services alive by the end of 2019.

Results: Among 2436 participants with chronic HCV infection (mean age 45.9 years, 30.7% female, 73.3% OAT), 1118 (45.9%) had received HCV treatment between 2010-2019. Treatment rates increased from 1.4/100 person years (PY) (95% CI 1.1-1.8) in the pre direct-acting antivirals (DAA) period (2010-2013) to 3.5/100 PY (95% CI 3.0-4.0) in the early DAA period (2014-2016; fibrosis restrictions) and 18.4/100 PY (95% CI 17.2-19.7) in the late DAA period (2017-2019; no restrictions), peaking at 24.1/100 PY (95% CI 21.7-26.7) in 2018. Treatment rates for 2018 and 2019 exceeded the previously modelled elimination threshold of 50/1000 PWID. Treatment uptake was less likely among women (aOR 0.74; 95% CI 0.62-0.89), those aged 40-49 years (aOR 0.74; 95% CI 0.56-0.97), and more likely among participants with current OAT (aOR 1.21; 95% CI 1.01-1.45). The estimated HCV RNA prevalence by the end of 2019 was 23.6% (95% CI 22.3-24.9).

Conclusion: Although HCV treatment uptake among PWID increased in the DAA era, strategies to enhance treatment among women and individuals not engaged in OAT should be addressed.

Figure:

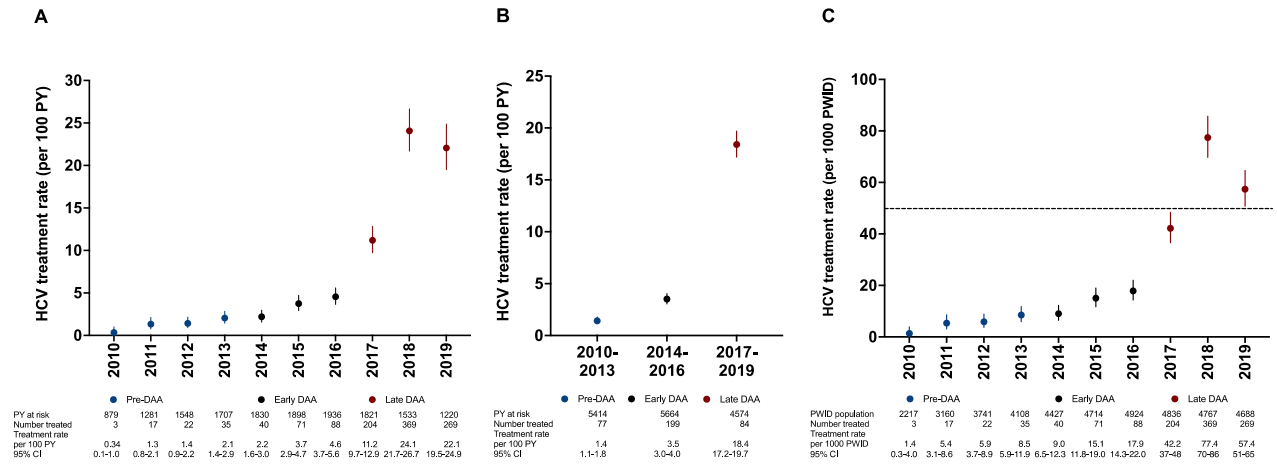


Figure 1. HCV treatment rates among users of low-threshold services for people who inject drugs in Oslo. (A) Annual rates per 100 PY between 2010 and 2019. (B) Rates per 100 PY according to time periods. (C) Annual rates per 1000 people who inject drugs between 2010 and 2019. Dots indicate point estimates and bars indicate 95% Poisson confidence intervals. The dotted line in (C) indicate a previously modelled elimination threshold.

A Canadian real-world 8 years' experience with DAA-based regimens in genotype 3: Preliminary data

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Background and Aims: Real-world data of direct acting antivirals (DAA) in genotype 3a hepatitis C virus (HCV) infection are still missing. Our study aimed to evaluate the effectiveness and safety of available DAA-based treatment regimens in patients chronically infected with HCV genotype 3a from a Canadian cohort in a “real-world” setting.

Method: All HCV genotype 3a infected patients from the *Centre Hospitalier de l'Université de Montréal* (CHUM), the referral center for hepatitis C treatment of Quebec, were included in the study between January 2014 to November 2021.

Results: One hundred thirty-seven chronically infected HCV genotype 3a patients were analyzed. Undetectable HCV RNA 12 weeks after the end of treatment (SVR12) rates according to regimen were as follows (table 1 and figure 1):

- All regimen including at least one DAA, overall 85.3% (116/136); without cirrhosis (F0-2) 90.7% (39/43); with cirrhosis (F3-4) 82.8% (77/93).

- Sofosbuvir/Velpatasvir for 12/24 weeks, overall 85.7% (24/28); without cirrhosis (F0-2) 88.9% (16/18); with cirrhosis (F3-4) 80.0% (8/10).

- Sofosbuvir/Velpatasvir/Ribavirin for 12 weeks, overall 100.0% (9/9); with cirrhosis (F3-4) 100.0% (9/9).

- Glecaprevir/Pibrentasvir for 8/12/24 weeks, overall 100.0% (11/11); without cirrhosis (F0-2) 100.0% (5/5); with cirrhosis (F3-4) 100.0% (6/6).

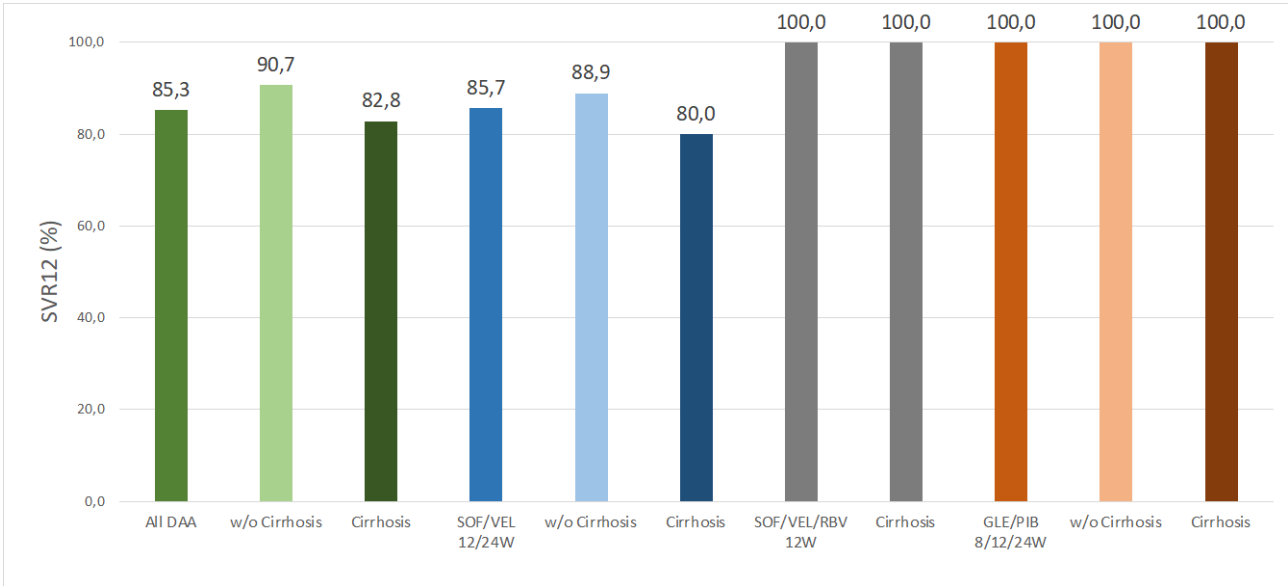
Sixteen patients had a relapse, 4 patients stopped treatment prematurely. Test for resistance associated substitutions (RAS), notably the Y93H, are ongoing.

Conclusion: In conclusion, SVR12 in genotype 3a in real-world varies between 85 to 100%. Treatment strategies especially in patients with liver cirrhosis and DAA-experienced should be discussed in referral centers in order to avoid failures.

Table:

	n	SVR (%)	Relapse (%)	Stop treatment (%)
All DAA	136	85,3	11,8	2,9
w/o Cirrhosis	43	90,7	4,7	4,7
Cirrhosis	93	82,8	15,1	2,2
SOF/VEL 12/24W	28	85,7	7,1	7,1
w/o Cirrhosis	18	88,9	5,6	5,6
Cirrhosis	8	80,0	10,0	10,0
SOF/VEL/RBV 12W	9	100,0	100,0	0,0
Cirrhosis	9	100,0	0,0	0,0
GLE/PIB 8/12/24W	11	100,0	0,0	0,0
w/o Cirrhosis	5	100,0	0,0	0,0
Cirrhosis	6	100,0	0,0	0,0

Figure:



Hepatitis C screening in a psychiatric emergency department: 8-months results

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Background and Aims: The prevalence of HCV infection in the general population in Spain is 0.22%. There is a significant percentage of people unaware of their infection, especially among the vulnerable population with limited access to the health system. Based on this fact, a universal screening for HCV infection was carried out in the emergency department (ED) of our hospital, since this is the main point of contact with the healthcare system for vulnerable individuals. A preliminary analysis of the data has shown that a significant percentage of subjects with HCV infection had psychiatric pathology, which prompted us to implement HCV screening in a specific psychiatric emergency department. The aim of this study was to perform a HCV screening in psychiatric ED and link positive cases to care.

Method: Prospective, single-centre study carried out at a university hospital involving screening and linkage to care of hepatitis C cases detected in the psychiatric emergency department. Anti-HCV antibodies were performed in individuals >16 years who require phlebotomy for medical reasons. Reflex viral load was performed in all anti-HCV positive patients. Patient characteristics were analyzed in relation to HCV infection and linkage to care.

Results: A total of 302 patients were screened from May to December 2021. 15 (4.9%) individuals were anti-HCV positive and two individuals (0.66%) had detectable viral load. Median age of anti-HCV-positive subjects was 52 (± 11) years and 10/15 were male. Six individuals had HIV co-infection and 9 had a history of injecting drug use. The most prevalent psychiatric pathology was substance use disorder (SUD) in 10/15 patients and seven of them had dual pathology. 4/15 subjects had previous liver disease due to HCV infection. Six individuals had been previously treated for HCV and the two viremic patients were aware of their infected status, one of them started HCV therapy few months ago with poor adherence. Neither of the two viremic patients could be linked to care because of social problems.

Conclusion: Hepatitis C screening in a psychiatric ED showed a prevalence of active HCV infection of 0.66%, around three times higher than that reported in the general population. The implementation of hepatitis C screening in the psychiatric emergency department may be a useful tool for diagnosis but more efforts should be performed for improving linkage to care.

Testate C plus: an online self-sampling intervention for hepatitis C in gay, bisexual and other men who have sex with men and trans women in Spain

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Background and Aims: The objective of the study was to design, implement and evaluate the acceptability and effectiveness of an online self-sampling intervention for hepatitis C testing and online consultation of the results addressed to gay, bisexual and other men who have sex with men (GBMSM) and trans women in Spain

Method: The website www.testate.org was designed to offer the test, consult the results and collect sociodemographic and behavioral information. Participants were recruited through two different strategies: 1) Online: The website was advertised in: www.disfrutasin-c.org, dating apps, blogs addressed to chemsex users, Twitter, Telegram, Whatsapp and Instagram. 2) Outreach interventions in gay sex clubs, sexshops, cruising and sex work areas, CBVCTs, chemsex support services, harm reduction services, associations working with trans women sex workers, a union of sex workers and LGBTBI organizations. A snowball recruitment was implemented through key informants of the GBMSM and trans women communities in Spain. After signing the informed consent online, participants answer an online survey on sociodemographic variables, behavioral data and history of testing. Participants considered at risk (Mosaic algorithm) had the possibility to request the delivery of a dried-blood spot (DBS) self-sampling kit by mail and a postage-paid envelope to send the sample to the reference laboratory where a real time RT-PCR was performed to detect HCV RNA with a commercial assay for in vitro diagnostic use in DBS (Abbott Molecular), which has a lower detection limit of 462 IU/mL (2.66 Log(IU/mL))

Results: From July 2020 to November 2021, the project website had 85,255 visits, 669 individuals (0.78%) requested a self-sampling kit and 358 participants returned a sample to the reference lab (53.51% return rate). Less than half of participants (43.4%) had previously been tested for HCV, 58.3% had had an STI in the last 5 years and 17.8% were on PrEP. Out of the 358 received samples, 42 (11.73%) were considered not valid, 311 samples were negative and 5 (1.58% (5/316)) positive results were detected. Among the positive results, 3 were confirmed by conventional HCV-RNA testing. One of them was HIV-positive. The other 2 DBS-positive cases tested negative and were probably false-positive results (0.6% of the tested participants). The HCV viral loads in DBS were <3 Log(IU/mL) in 4 cases and 6.63 Log(IU/mL) in the remaining one. Taking into account the confirmed positive cases, the estimated prevalence of viremic HCV infection was: 0.96% (95% CI: 0% – 2,0%)

Conclusion: The intervention was well accepted by the target population. It allowed access to people at high risk of HCV infection. We found a 0.96% prevalence of viremic HCV infection. Scaling up this intervention at the national level could be useful to promote HCV early diagnosis elimination among GBMSM and trans women in Spain

To reconvene patients who were lost to follow-up is a useful strategy to eliminate hepatitis C virus. Results from the multicenter french study RECONVOCC.

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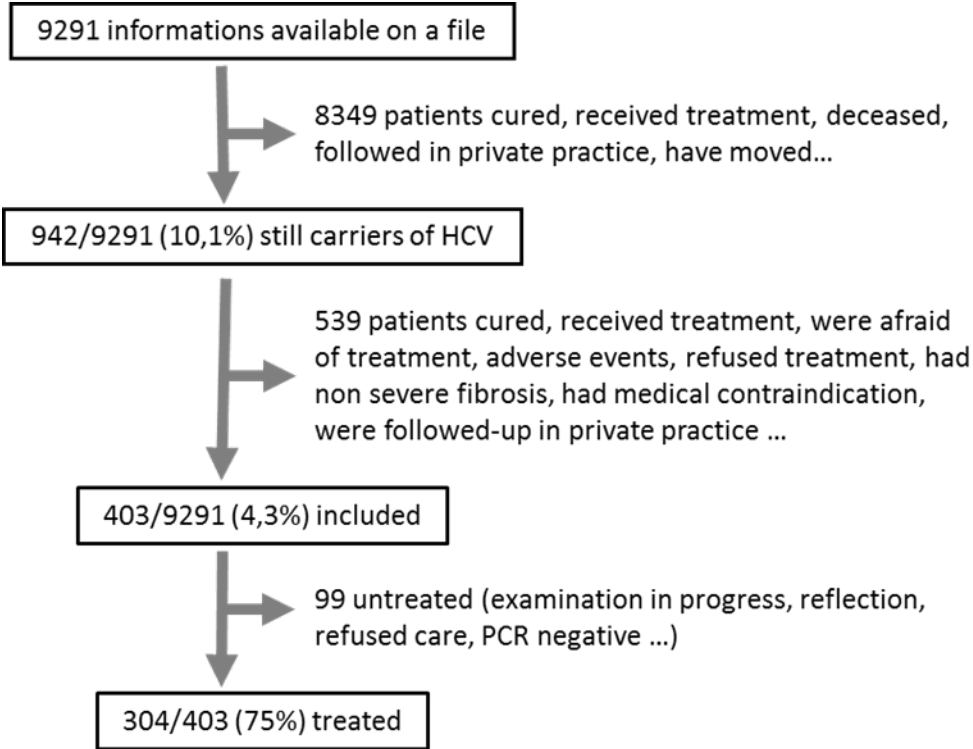
Background and Aims: The elimination of the Hepatitis C virus (HCV) by 2030, as set by the World Health Organization (WHO) requires that 90% of people with chronic hepatitis C are diagnosed and 80% treated. France is one of the countries engaged in this strategy. In this study we assessed the effectiveness of a recall strategy. This project was initiated by the "Federation des Pôles de Référence Hépatites" (FPRH). The aim of this project is to reconvene HCV+ patients who have been lost to follow-up (LTFU) by the clinical departments of hospitals mainly academics, and have not been treated and/or cured

Method: We included HCV positive patients seen from 2003 to 2018 who were not cured in 15 hospitals. The patients should be LTFU for over 18 months and be born after 1934. RECONVOCC takes place in 2 phases. In the first phase, we identified eligible patients including those tested in the virology department based on patient databases, medical records and followed by hepatologists and non hepatologists. To contact them and obtain information on their HCV status we used several methods. First, we have interrogated the national death register. If, the patient was alive we used the following tools: health insurance databases, social security card which contains the name of the general practitioner and is available on the data file of every hospital in France, contact of general practitioners or gastroenterologists. The second part corresponds to the inclusion in our database (REDCAP) of patients who may require treatment

Results: Out of 16 083 patients, 9291 could be contacted by phone. Up to now we identified 942 patients still carrying HCV and not treated (Table 1). Of the 403 patients included, 393 patients were analyzed. Fifty nine percent (233/393) were men and 88% were followed in the hepatology department. Mean age was 58+/-12 years. 301/393 (77%) were treatment naïve. 21% of patients (84/393) had clinically significant fibrosis (F3-F4). 42% (166/393) of patients were intravenous drug abusers and 25% (97/393) have been contaminated by transfusion. Genotype 1 (57%) was the most frequent. The most commonly cited reason for stopping hepatology monitoring were the absence of requests for consultation by general practitioners (38%) and the low severity of liver fibrosis (10%). The average duration of the follow-up break was 8 years. Until now 304 patients have already started treatment and 216/403 (54%) were cured. 55 patients were included but were not treated

Conclusion: This work shows that there is still a high number of patients infected with the HCV who have not yet benefited from treatment with direct antiviral agents in the hepatology departments. 4 to 10% of HCV patients LTFU were reconvened and 21% had severe fibrosis (F3-F4). To reconvene patients LTFU in the hepatology departments is a very useful strategy and contribute to the elimination of the HCV. The study is still underway

Figure: Flow chart of the patients



Hepatitis A and B infection and vaccination among MSM in Ireland: an analysis of the findings from the European MSM internet survey 2017 (EMIS-2017)

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Background and Aims: Viral hepatitis has led to a considerable burden of morbidity and mortality worldwide. Men who have sex with men (MSM) have a higher risk of acquiring hepatitis A and B viruses (HAV and HBV) when compared to the general population and are recommended for vaccination against both in Ireland. Using Irish data from the European MSM Internet Survey 2017 (EMIS-2017), this study seeks to measure the burden of HAV and HBV infection among MSM living in Ireland; it also aims to estimate their HAV/HBV vaccination coverage and explore factors associated with vaccination.

Method: EMIS-2017 was an anonymous, online, cross-sectional survey of MSM in 50 countries; the responses of the Irish-based participants were analysed. Self-reported responses on HAV/HBV infection and vaccination were used to calculate the prevalence of infection and vaccination. Multivariable logistic regression models were used to explore the sociodemographic, healthcare-related and behavioural factors independently associated with HAV and HBV vaccination among MSM. HIV-positive MSM were excluded from this study due to their high level of healthcare service engagement, which may have biased results.

Results: There were 2,083 respondents to EMIS-2017 in Ireland; 1,941 men (93.2%) were HIV-negative. The prevalence of previous HAV and HBV infection was 4.6% (n=89) and 4.4% (n=85), respectively. Fifty one percent (n=987) and 57.3% (n=1,112) of MSM received ≥ 1 vaccine dose for HAV and HBV, respectively. MSM had lower odds of HAV vaccination if they had lower levels of education (i.e. at most high school education) (adjusted OR (aOR) 0.65, 95% CI 0.45-0.92), lived outside the capital Dublin (aOR 0.61, 95% CI 0.48-0.78), were not tested for HIV in the last year (aOR 0.39, 95% CI 0.31-0.50) or had lower levels of healthcare service engagement. Similar associations were observed for HBV, but MSM who identified as bisexual also had lower odds of HBV vaccination (aOR 0.62, 95% CI 0.42-0.93).

Conclusion: The prevalence of HAV and HBV infection in Irish MSM is low compared with MSM in other high-income countries. Vaccination coverage is relatively high by international standards and is likely to have a protective effect against HAV/HBV infection, but it remains insufficient to protect the MSM community from future HAV/HBV outbreaks. MSM who live outside the capital and do not engage with healthcare services should be prioritized for vaccination campaigns.

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.

“Mind the Gap”: preliminary evaluation of the prevention of mother-to-child transmission of hepatitis B care cascade in rural western Uganda

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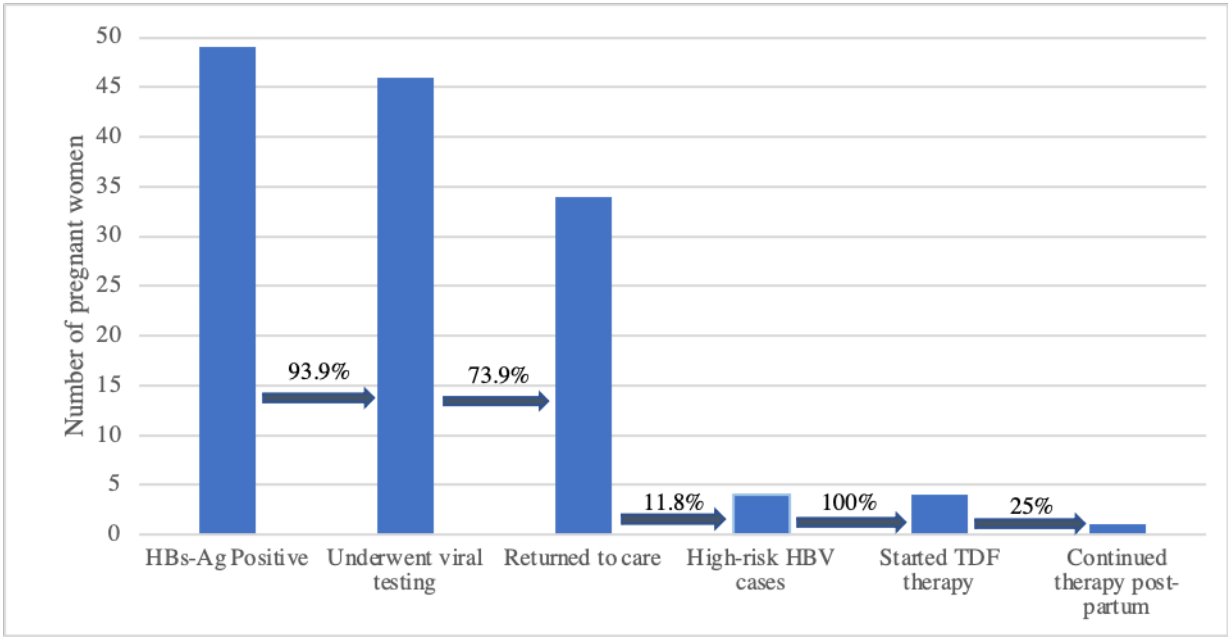
Background and Aims: Hepatitis B virus (HBV) is the most common cause of chronic hepatitis in the world with high, but likely under-recognized burden in sub-Saharan Africa (SSA). Children are at particularly high risk of exposure and development of chronic HBV infection, making the prevention of mother-to-child transmission (PMTCT) a key target to addressing the epidemic. Here, we assess the feasibility, acceptability, and effectiveness of a pilot HBV PMTCT program in rural western Uganda comprised of screening of pregnant women, identification of high-risk HBV cases (women with high viral load), and implementation of anti-HBV prophylactic therapy.

Methods: Between February 10, 2021 and January 21 2022, pregnant women presenting for their first visits at level II and III antenatal care facilities in western Uganda underwent screening with a Hepatitis B surface antigen (HBsAg) rapid diagnostic test. Women who were HBsAg-positive were notified and invited to return for serum HBV DNA testing (sent to Central Public Health Laboratory), baseline hemoglobin, and liver function testing. Patients with HBV DNA levels $\geq 200,000$ IU/mL were identified as having high-risk HBV and started on tenofovir disoproxil fumarate (TDF) prophylaxis at 28-32 weeks' gestation through 6 weeks post-partum. High-risk HBV positive women were monitored through the post-partum period for clinical symptoms and TDF adherence based on questioning at infant care visits and pill counts.

Results: As of January 2022, 1064 women seeking antenatal care in the Bugoye and surrounding regions underwent HBsAg testing. Upon enrollment, the women had a median age of 25 years (range: 16-47) and gestational age of 22 weeks (range: 8- 36). 95.0% of the participants completed at least primary- level education and 94.8% were married or in a domestic partnership. The seroprevalence of HBsAg was 4.6% (n= 49). Among those seropositive women who completed HBV viral DNA titer testing (n= 34), 11.8% were deemed high-risk HBV (n= 4). All high-risk HBV mothers were initiated on TDF by 28- weeks gestation, though only 25% continued therapy through the 6-week follow-up visit.

Conclusions: HBV seroprevalence among pregnant women in rural Uganda is high, but implementation of the PMTCT program was feasible and broadly accepted by patients. The prevalence of high-risk HBV (11.8%) was as expected based on reported literature of endemic areas of SSA, and all were successfully started on TDF therapy. Further work is required in supporting women through the care cascade- specifically in regard to facilitating follow-up clinic visits and adherence to TDF prophylaxis. Our team will continue screening women through June 2022 and will evaluate risk factors for HBV in this population as well as rate of vertical transmission via infant HBsAg testing.

Figure: HBV PMTCT care cascade of seropositive mothers in rural western Uganda



PO-204

Contact tracing in networks of people who inject drugs with hepatitis C is the most efficient testing strategy to maintain hepatitis C elimination post 2030

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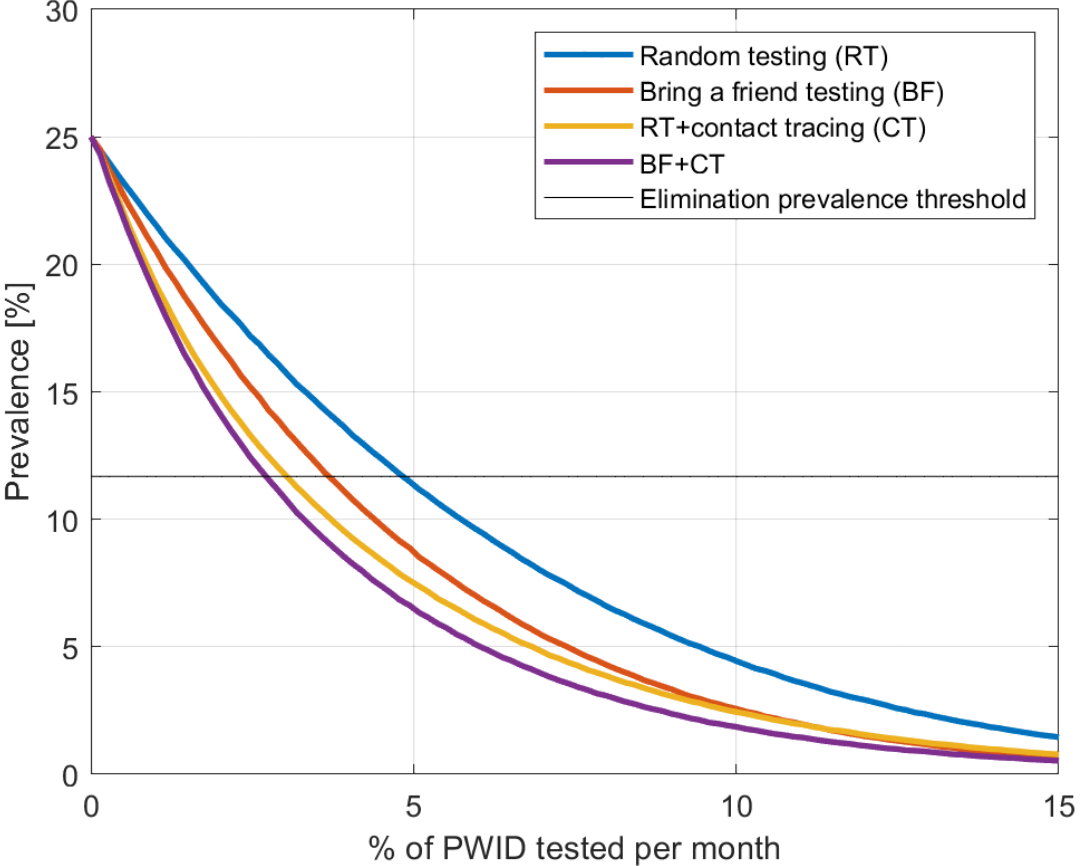
Background and Aims: The World Health Organisation has set a target for the global elimination of Hepatitis B (HBV) and C (HCV) by 2030. Few targeted testing interventions have utilised contact tracing to identify undiagnosed HCV. In this study we model the effect of contact tracing within an injecting network of people who inject drugs (PWID).

Method: We create a dynamic injecting network structure connecting 689 PWID based on empirical data. A burn-in period, where PWID are randomly treated according to empirical parameters until the elimination target is achieved, is followed by the 5-year simulation period. The primary outcome is the testing coverage required per month to maintain prevalence at the elimination threshold over 5 years. We compare four treatment strategies: random testing (RT) vs. RT+CT contact tracing and 'bring you friends' (BF) testing vs. BF+CT.

Results: To maintain elimination with RT, on average 4.92% (SD 0.84%) of the injecting network needs to be tested per month. However, with a BF strategy, 3.69% (SD 0.63%) of the network needs to be tested per month ($p < 0.001$). The addition of contact tracing reduced the required testing coverage to 3.13% in RT ($p < 0.001$) and to 2.80% in BF testing ($p < 0.001$). The superiority of the CT approaches were maintained in a sensitivity analysis that adjusted for changes in needle and syringe provision and the rate of engagement with treatment following a positive test.

Conclusion: The addition of contact tracing to establish HCV testing strategies in PWID reduces the testing coverage required to maintain HCV elimination by over 25%. The effectiveness of contact tracing interventions should be tested in this population.

Figure:



Targeted immunotherapy with heterologous prime-boost and adjuvanted hepatitis B core (HBc)/surface (HBs) proteins in adult chronic hepatitis B patients showed positive HBc- and HBs-specific CD8⁺ and CD4⁺ T cell responses in a phase I/II trial

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Background and Aims: GSK's chronic hepatitis B-targeted immunotherapy (CHB-TI) applies heterologous prime-boost administration of chimpanzee-derived adenovirus encoding the human invariant chain and hepatitis B virus (HBV) proteins (ChAd155-hli-HBV) and Modified Vaccinia Ankara virus encoding HBV proteins (MVA-HBV), and adjuvanted recombinant proteins (HBc-HBs/AS01_{B-4}). It was designed to induce HBV-specific functional T cell responses, humoral and innate responses to promote functional cure in CHB patients. We present initial results on T cell-mediated immunity (CMI) responses from an ongoing clinical trial.

Method: This first-time-in-human phase I/II randomised, single-blind, controlled dose-escalation trial (NCT03866187) conducted in adults with CHB well-controlled under nucleo(s)tide analogue therapy, follows a staggered design: low doses of CHB-TI components in Step A (ratio 1:1:1) and target doses in Step B (ratio 2:1:1). Patients received prime-boost regimen of ChAd155-hli-HBV at day (D) 1 and MVA-HBV at D57 (groups [gr] A1, B1) or 2 doses of HBc-HBs/AS01_{B-4} (gr A2, B2) or placebo (control gr A3, B3) at D1 and D57. CMI samples were collected at D1, D15, D57, D64, D71 and tested by intracellular cytokine staining to assess frequencies of HBc- and HBs-specific CD8⁺ and CD4⁺ T cells, CD8⁺ and CD4⁺ T cells responders. Polypositive CMI response is defined as T cells expressing ≥ 2 activation markers of CD40L, TNF α , IFN γ , IL2, CD137 (4-1BB), IL13 and IL17 including ≥ 1 cytokine (lower limit of quantification = 590 cells/million of CD8⁺ or CD4⁺ T cells). HBV-specific CMI responder is defined as post-/pre-treatment ratio in polypositive T cell frequencies above the maximum ratio observed in controls.

Results: The exposed set included all patients in Step A (13) and 50% in Step B (37): 13 and 28 patients respectively, had CMI samples. Polypositive CMI responses were observed (Figure) mainly HBc-specific CD8⁺ and CD4⁺ T cell responses in ChAd-MVA recipients (gr B1) and HBc- and HBs-specific CD4⁺ T cell responses in the HBc-HBs/AS01_{B-4} recipients (gr B2). Prime-boost effect was observed in group B1 for HBc-specific CD8⁺ T cell responses, a similar effect was observed for 1 patient in the same group for HBs-specific CD8⁺ T cell responses. No increases were observed in controls. Individual responses were most pronounced for HBc-specific CD8⁺ T cells (up to ≥ 6 -fold increase) in group B1 and for HBc-specific CD4⁺ T cells (up to ≥ 8 -fold increase) in group B2.

Conclusion: CMI responses up to 14 days post-dose 2 of CHB-TI observed in a subset of patients showed potent and polyfunctional HBc- and HBs-specific CD8⁺ and CD4⁺ T cells in CHB patients. This suggests that the full regimen of the CHB-TI consisting of ChAd-MVA and adjuvanted proteins is capable of inducing highly potent CMI responses. More immunogenicity and efficacy data from this and other regimens are planned.

Funding: GSK

Figure. Number and percentage of responders for HBV-specific CD8⁺ and CD4⁺ T cells (groups A1, A2 and groups B1, B2 compared to control groups A3, B3) and frequencies of HBc- and HBs-specific CD8⁺ and CD4⁺ T cells observed in the responders

Polypositive		HBc-specific								HBs-specific							
		CD8 ⁺ T cells				CD4 ⁺ T cells				CD8 ⁺ T cells				CD4 ⁺ T cells			
Timing		D15	D57	D64	D71	D15	D57	D64	D71	D15	D57	D64	D71	D15	D57	D64	D71
Group A1	N	4	3	4	3	3	3	4	3	4	3	4	3	3	3	4	3
	n	-	-	-	1	1	-	-	1	-	-	-	-	-	-	-	-
	%	-	-	-	33	33	-	-	33	-	-	-	-	-	-	-	-
	(Min, Max)*	-	-	-	1362	938	-	-	657	-	-	-	-	-	-	-	-
Group A2	N	3	2	3	3	3	2	3	3	3	2	3	3	3	2	3	3
	n	-	-	-	-	1	-	1	1	-	-	-	-	-	-	-	-
	%	-	-	-	-	33	-	33	33	-	-	-	-	-	-	-	-
	(Min, Max)*	-	-	-	-	796	-	687	861	-	-	-	-	-	-	-	-
Group B1	N	9	9	7	9	7	6	5	7	9	9	7	9	7	6	5	7
	n	1	1	3	4	1	-	-	1	-	-	1	1	-	-	-	-
	%	11	11	43	44	14	-	-	14	-	-	14	11	-	-	-	-
	(Min, Max)*	789	979	(1585, 2696)	(817, 3930)	633	-	-	711	-	-	751	1229	-	-	-	-
Group B2	N	7	7	7	7	8	7	7	8	6	6	6	6	7	6	6	7
	n	-	-	-	-	5	2	3	3	-	-	-	-	-	1	1	-
	%	-	-	-	-	63	29	43	38	-	-	-	-	-	17	17	-
	(Min, Max)*	-	-	-	-	(654, 5415)	(1168, 1884)	(749, 3168)	(1203, 2149)	-	-	-	-	-	1412	1166	-

HBc, hepatitis B core protein; **HBs**, hepatitis B surface protein; **D15**, 14 days post-dose 1; **D57**, vaccination 2; **D64**, 7 days post-dose 2; **D71**, 14 days post-dose 2; **N**, number of patients with CMI results available at pre-/post-treatment at each timepoint; **n**, number of responders; **Min**, minimum frequency in responders; **Max**, maximum frequency in responders (*at timepoints with only 1 polypositive CMI responder the maximum value is presented); **Group A1**: patients received ChAd155-hli-HBV (5x10⁹ virus particles [vp]) at D1 and MVA-HBV (2x10⁷ plaque forming unit [pfu]) at D57; **Group A2**: patients received 2 doses of HBc-HBs/AS01_{B-4} (20-20 µg) at D1 and D57; **Group B1**: patients received ChAd155-hli-HBV (5x10¹⁰ vp) at D1 and MVA-HBV (2x10⁸ pfu) at D57; **Group B2**: patients received 2 doses of HBc-HBs/AS01_{B-4} (80-80 µg) at D1 and D57. **AS01_B** is an Adjuvant System containing MPL, QS-21 and liposome (50 µg MPL and 50 µg QS-21).



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