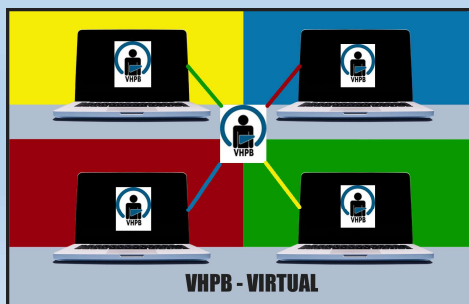# VHPB TECHNICAL MEETING

Treatment as Prevention (TAP) for Hepatitis C in Risk Groups

Background document

15 October 2020 – 17h tot 20h

VHPB - VIRTUAL

Prepared by Greet Hendrickx & Sara Valckx

VHPB Secretariat

Table of Content

MEETING OBJECTIVES

Treatment as prevention:

- Review scientific evidence of TAP to avoid hepatitis C infections in risk populations
- Discuss Real-life data of TAP project in different risk groups (PWID, MSM, people living with HIV)
- Lessons learnt from HIV

PARTICIPANTS (± 35)

Global scientists, opinion leaders, infectiologists, hepatologists, vaccinologists, paediatricians and public health representatives who are experts in the field of viral hepatitis prevention.

INTENDED IMPACT

- An evaluation of the contribution of TAP to reaching the elimination goals.

OUTLINE OF THE MEETING

Presentations on selected topics about Hepatitis C TAP in risk groups will be pre-recorded by the speakers and made available latest one week before the meeting. Both topics will be covered in separate 3h sessions, 1 week apart.

NOTE: This pre-meeting document contains general background information on the topic of the VHPB meeting. It contains a list of selected abstracts/references from a Pubmed MEDLINE search on different search terms depending on the topic discussed in a session of the meeting. The references are sorted by publication year (most recent first). This document should guide you in the preparation of the meeting, it should not be considered as complete literature review, but hopefully, it will give an overview of what has been published on the topics of the meeting. Because of the abundance of publications regarding "treatment as prevention for viral hepatitis", only publications of the last 10 years are shown and the abstracts are included for publications of the last 5 years.

GENERAL BACKGROUND INFORMATION

WHO Global Health Sector Strategy on Viral Hepatitis 2016-2021.

WHO Progress report on HIV, viral hepatitis and sexually transmitted infections 2019.

World Hepatitis Alliance: Prevention, diagnosis, treatment of hepatitis B and C.

Chen, S., et al. (**2020**). "Combating hepatitis B and C by 2030: achievements, gaps, and options for actions in China." BMJ Glob Health **5**(6).

> China has the highest number of hepatitis B and C cases globally. Despite remarkable achievements, China faces daunting challenges in achieving international targets for hepatitis elimination. As part of a large-scale project assessing China's progress in achieving health-related Sustainable Development Goals using quantitative, qualitative data and mathematical modelling, this paper summarises the achievements, gaps and challenges, and proposes options for actions for hepatitis B and C control. China has made substantial progress in controlling chronic viral hepatitis. The four most successful strategies have been: (1) hepatitis B virus childhood immunisation; (2) prevention of mother-to-child transmission; (3) full coverage of nucleic acid amplification testing in blood stations and (4) effective financing strategies to support treatment. However, the total number of deaths due to hepatitis B and C is estimated to increase from 434 724 in 2017 to 527 829 in 2030 if there is no implementation of tailored interventions. Many health system barriers, including a fragmented governance system, insufficient funding, inadequate service coverage, unstandardised treatment and flawed information systems, have compromised the effective control of hepatitis B and C in China. We suggest five strategic priority actions to help eliminate hepatitis B and C in China: (1) restructure the viral hepatitis control governance system; (2) optimise health resource allocation and improve funding efficiency; (3) improve access to and the quality of the health benefits package, especially for high-risk groups; (4) strengthen information systems to obtain high-quality hepatitis epidemiological data; (5) increase investment in viral hepatitis research and development.

A Heffernan, GS Cooke, S Nayagam, M Thursz, TB Hallett (**2019**) Scaling up prevention and treatment towards the elimination of hepatitis C: a global mathematical model. Lancet. 2019 Mar 30;393(10178):1319-1329. Epub 2019 Jan 29.

> Background: The revolution in hepatitis C virus (HCV) treatment through the development of direct-acting antivirals (DAAs) has generated international interest in the global elimination of the disease as a public health threat. In 2017, this led WHO to establish elimination targets for 2030. We evaluated the impact of public health interventions on the global HCV epidemic and investigated whether WHO's elimination targets could be met.
>
> Methods: We developed a dynamic transmission model of the global HCV epidemic, calibrated to 190 countries, which incorporates data on demography, people who inject drugs (PWID), current coverage of treatment and prevention programmes, natural history of the disease, HCV prevalence, and HCV-attributable mortality. We estimated the worldwide impact of scaling up interventions that reduce risk of transmission, improve access to treatment, and increase screening for HCV infection by considering six scenarios: no change made to existing levels of diagnosis or treatment; sequentially adding the following interventions: blood safety and infection control, PWID harm reduction, offering of DAAs at diagnosis, and outreach screening to increase the number diagnosed; and a scenario in which DAAs are not introduced (ie, treatment is only with pegylated interferon and oral ribavirin) to investigate the effect of DAA use. We explored the effect of varying the coverage or impact of these interventions in sensitivity analyses and also assessed the impact on the global epidemic of removing certain key countries from the package of interventions.
>
> Findings: By 2030, interventions that reduce risk of transmission in the non-PWID population by 80% and increase coverage of harm reduction services to 40% of PWID could avert 14·1 million (95% credible interval 13·0-15·2) new infections. Offering DAAs at time of diagnosis in all countries could prevent 640

000 deaths (620 000-670 000) from cirrhosis and liver cancer. A comprehensive package of prevention, screening, and treatment interventions could avert 15·1 million (13·8-16·1) new infections and 1·5 million (1·4-1·6) cirrhosis and liver cancer deaths, corresponding to an 81% (78-82) reduction in incidence and a 61% (60-62) reduction in mortality compared with 2015 baseline. This reaches the WHO HCV incidence reduction target of 80% but is just short of the mortality reduction target of 65%, which could be reached by 2032. Reducing global burden depends upon success of prevention interventions, implemention of outreach screening, and progress made in key high-burden countries including China, India, and Pakistan.

Interpretation: Further improvements in blood safety and infection control, expansion or creation of PWID harm reduction services, and extensive screening for HCV with concomitant treatment for all are necessary to reduce the burden of HCV. These findings should inform the ongoing global action to eliminate the HCV epidemic.

Funding: Wellcome Trust.

N Scott, DP Wilson, AJ Thompson, E Barnes, M El-Sayed, AS Benzaken, HE Drummer, ME Hellard (**2019**). "The case for a universal hepatitis C vaccine to achieve hepatitis C elimination." BMC Med **17**(1): 175.

BACKGROUND: The introduction of highly effective direct-acting antiviral (DAA) therapy for hepatitis C has led to calls to eliminate it as a public health threat through treatment-as-prevention. Recent studies suggest it is possible to develop a vaccine to prevent hepatitis C. Using a mathematical model, we examined the potential impact of a hepatitis C vaccine on the feasibility and cost of achieving the global WHO elimination target of an 80% reduction in incidence by 2030 in the era of DAA treatment. METHODS: The model was calibrated to 167 countries and included two population groups (people who inject drugs (PWID) and the general community), features of the care cascade, and the coverage of health systems to deliver services. Projections were made for 2018-2030. RESULTS: The optimal incidence reduction strategy was to implement test and treat programmes among PWID, and in settings with high levels of community transmission undertake screening and treatment of the general population. With a vaccine available, the optimal strategy was to include vaccination within test and treat programmes, in addition to vaccinating adolescents in settings with high levels of community transmission. Of the 167 countries modelled, between 0 and 48 could achieve an 80% reduction in incidence without a vaccine. This increased to 15-113 countries if a 75% efficacious vaccine with a 10-year duration of protection were available. If a vaccination course cost US$200, vaccine use reduced the cost of elimination for 66 countries (40%) by an aggregate of US$7.4 (US$6.6-8.2) billion. For a US$50 per course vaccine, this increased to a US$9.8 (US$8.7-10.8) billion cost reduction across 78 countries (47%). CONCLUSIONS: These findings strongly support the case for hepatitis C vaccine development as an urgent public health need, to ensure hepatitis C elimination is achievable and at substantially reduced costs for a majority of countries.

AF Luetkemeyer, DL Wyles (**2019**). "CROI 2019: highlights of viral hepatitis." Top Antivir Med **27**(1): 41-49.
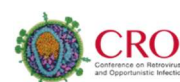
At the 2019 Conference on Retroviruses and Opportunistic Infections (CROI), there was a major focus on hepatitis C virus (HCV) elimination and improving each component of the hepatitis C care cascade. Many interventions showed promising improvements in diagnosis and linkage to care. Settings with robust access to direct-acting antivirals (DAAs) continue to demonstrate the role of HCV treatment as prevention. However, substantial barriers to accessing curative therapy remain. Reinfection after treatment presents an important barrier to elimination, particularly in some populations of men who have sex with men (MSM). MSM without HIV infection are at an elevated risk for sexual acquisition of HCV, and several studies reported HCV rates that were as high as those seen in MSM living with HIV. There was also a focus on HCV and HBV in pregnant women. Rates of HCV infection in women of child-bearing potential have increased, making prenatal diagnosis a priority. In the first study of HCV treatment during pregnancy, sofosbuvir/ledipasvir started at 28 weeks of gestation led to cure in 8 pregnant women. Hepatitis B virus (HBV)-active antiretrovirals are generally effective in suppressing HBV but have low rates of surface antigen loss despite long term treatment. Initial results from novel laboratory assessments of intrahepatic HBV viral infection events were presented, hopefully paving the way for more effective HBV treatment strategies to control and potentially cure HBV.

EJ Aspinall, SJ Hutchinson, DJ Goldberg, H Valerio, A Mozalevskis, T Noori, E Duffell, L Tavoschi (**2018**). Monitoring response to hepatitis B and C in EU/EEA: testing policies, availability of data on care cascade and chronic viral

hepatitis-related mortality - results from two surveys (2016). HIV Med. Feb;19 Suppl 1:11-15. doi: 10.1111/hiv.12599.

Objectives: The World Health Organization (WHO) developed a European Regional Action Plan (EAP) to fast-track action towards the goal of eliminating viral hepatitis. Robust monitoring is essential to assess national programme performance. The purpose of this study was to assess the availability of selected monitoring data sources in European Union/European Economic Area (EU/EEA) Member States (MS).

Methods: Availability of data sources at EU/EEA level was assessed using two surveys distributed to 31 EU/EEA MS in 2016. The two surveys covered (A) availability of policy documents on testing; testing practices and monitoring; monitoring of diagnosis and treatment initiation, and; (B) availability of data on mortality attributable to chronic viral hepatitis.

Results: Just over two-thirds of EU/EEA MS responded to the surveys. 86% (18/21) reported national testing guidance covering HBV, and 81% (17/21) covering HCV; while 33% (7/21) and 38% (8/21) of countries, respectively, monitored the number of tests performed. 71% (15/21) of countries monitored the number of chronic HBV cases diagnosed and 33% (7/21) the number of people treated. Corresponding figures for HCV were 48% (10/21) and 57% (12/21). 27% (6/22) of countries reported availability of data on mortality attributable to chronic viral hepatitis.
Conclusions: The results of this study suggest that sources of information in EU/EEA Member States to monitor the progress towards the EAP milestones and targets related to viral hepatitis diagnosis, cascade of care and attributable mortality are limited. Our analysis should raise awareness among EU/EEA policy makers and stimulate higher prioritisation of efforts to improve the monitoring of national viral hepatitis programmes.

V Soriano, B Young, N Reau (**2018**). "Report from the International Conference on Viral Hepatitis - 2017." AIDS Rev **20**(1): 58-70.

The International Conference on Viral Hepatitis 2017 brought exciting news on the treatment of viral hepatitis. The most recent estimates of the burden for hepatitis B virus and hepatitis C virus (HCV) infections were presented. The current gaps and prospects for regional and global eradication of viral hepatitis were discussed on the light of the WHO roadmap until 2030. Debates focused on hepatitis C and expectations using the new approved HCV pan-genotypic, once daily, oral direct-acting antivirals (DAAs), glecaprevir-pibrentasvir, and sofosbuvir-velpatasvir-voxilaprevir. The management of difficult-to-cure HCV patients included individuals who had failed prior DAAs, people who inject drugs, patients with decompensated cirrhosis, or renal insufficiency. Special patient populations such as children, pregnant women, persons with acute hepatitis C, or HIV coinfection were addressed separately. The use of HCV treatment as prevention was subject to debate, balancing the benefits on halting transmission and the risk for HCV reinfections and high medication costs. Complementary efforts on behavioral interventions and harm reduction programs were highlighted. Data from both clinical trials and real-world experience (i.e., from the US Veterans) were compared. Further debates addressed hepatic conditions that may alter the management and outcome of viral hepatitis, such as hepatitis B reactivation, non-alcoholic fatty liver disease, liver transplantation, and hepatocellular carcinoma. Finally, the recent data on often neglected hepatitis D and E virus infections were reviewed.

MP Manns, M Buti, E Gane, J-M Pawlotsky, H Razavi, N Terrault, Z Younossi (**2017**). "Hepatitis C virus infection." Nat Rev Dis Primers **3**: 17006.

Hepatitis C virus (HCV) is a hepatotropic RNA virus that causes progressive liver damage, which might result in liver cirrhosis and hepatocellular carcinoma. Globally, between 64 and 103 million people are chronically infected. Major risk factors for this blood-borne virus infection are unsafe injection drug use and unsterile medical procedures (iatrogenic infections) in countries with high HCV prevalence. Diagnostic procedures include serum HCV antibody testing, HCV RNA measurement, viral genotype and subtype determination and, lately, assessment of resistance-associated substitutions. Various direct-acting antiviral agents (DAAs) have become available, which target three proteins involved in crucial steps of the HCV life cycle: the NS3/4A protease, the NS5A protein and the RNA-dependent RNA polymerase NS5B protein. Combination of two or three of these DAAs can cure (defined as a sustained virological response 12 weeks after treatment) HCV infection in >90% of patients, including populations that have been difficult to treat in the past. As long as a prophylactic vaccine is not available, the HCV pandemic has to be controlled by treatment-as-prevention strategies, effective screening programmes and global access to treatment.

V Soriano, B Young, N Terrault (**2016**). "Report from the International Conference on Viral Hepatitis (ICVH), San Francisco, March 2016." AIDS Rev **18**(2): 81-88.

> The International Conference on Viral Hepatitis 2016 brought exciting news on the treatment of viral hepatitis. The conference was mainly focused on the most recent estimates of burden for HBV and HCV; the current gaps and prospects for regional and global HCV eradication; the use of HCV treatment as prevention; and the management of difficult-to-cure hepatitis C patients, including individuals who fail on direct-acting antivirals, people who inject drugs, and those with decompensated cirrhosis or renal insufficiency. Special patient populations, such as children, pregnant women, HIV-coinfected and persons with acute hepatitis C, were addressed separately. Data from both clinical trials and real-world experience were discussed. Further debates focused on hepatic conditions that may alter the management and outcome of viral hepatitis, such as fatty liver disease, liver transplantation, and hepatocellular carcinoma.

B Hajarizadeh, J Grebely, M Martinello, GV Matthews, AR Lloyd, GJ Dore (**2016**). "Hepatitis C treatment as prevention: evidence, feasibility, and challenges." Lancet Gastroenterol Hepatol **1**(4): 317-327.

> The advent of interferon-free direct-acting antiviral therapy for hepatitis C virus (HCV) infection has heightened discussion of treatment as prevention. Rapid scale-up in many settings, and the prospect of further treatment simplification have extended therapeutic optimism towards HCV elimination. However, questions remain regarding the feasibility of HCV treatment as prevention, including real world efficacy of direct-acting antiviral therapy, particularly among people who inject drugs, and whether expanded treatment access will be sufficient to reduce HCV transmission. HCV re-infection among both people who inject drugs and HIV-infected men who have sex with men might also compromise the benefits of HCV treatment as prevention. Empirical studies of HCV treatment as prevention are ongoing, including among community-based people who inject drugs, prisoners, and HIV-infected individuals. Some national HCV elimination programmes have also been established. Key requirements to optimise benefits of HCV treatment as prevention will include enhanced HCV diagnosis and linkage to care, high-coverage harm reduction, drug price reform, and removal of liver disease and drug use-based restrictions to treatment access.

NK Martin, P Vickerman, GJ Dore, M Hickman (**2015**) The hepatitis C virus epidemics in key populations (including people who inject drugs, prisoners and MSM): the use of direct-acting antivirals as treatment for prevention. Curr Opin HIV AIDS. 2015 Sep;10(5):374-80.

> Purpose of review: The burden of hepatitis C virus (HCV) is high among people who inject drugs (PWID) and prisoners, and increasing among HIV-infected MSM, who are key populations for HCV transmission in high-income countries and may also play a role in many in low- and middle-income countries. There is an increasing interest in the use of HCV antiviral treatment for prevention in these populations.
> Recent findings: Numerous theoretical modelling studies have explored the potential impact of HCV treatment for prevention among PWID in a range of global settings, generally finding that modest and achievable levels of HCV treatment, especially with interferon-free direct-acting antiviral therapy (IFN-free DAAs), could substantially reduce HCV chronic prevalence among PWID within the next 10-20 years. In addition, modelling studies have shown HCV testing and treatment in prison (including prevention benefits) could be cost-effective if continuity of care is ensured, or HCV treatments are shortened with DAAs. Modelling work among HIV-infected MSM has shown that further HCV treatment scale-up is likely required despite high treatment rates in this population. However, no empirical studies have explored whether HCV treatment can reduce HCV prevalence and prevent onwards transmission among those at risk of transmission.
> Summary: HCV treatment for key populations such as PWID, prisoners and MSM could become an important HCV prevention intervention, especially in the IFN-free DAA era. However, there is an urgent need to test these hypotheses through empirical studies.

LM Hagan, PR Wolpe, RF Schinazi (**2013**). "Treatment as prevention and cure towards global eradication of hepatitis C virus." Trends Microbiol **21**(12): 625-633.

EJ Aspinall, G Hawkins, A Fraser, S J Hutchinson, D Goldberg (**2011**). Hepatitis B prevention, diagnosis, treatment and care: a review. Occup Med (Lond). Dec;61(8):531-40. doi: 10.1093/occmed/kqr136.

1. Modelling the elimination of hepatitis C: country examples

a) Modelling HCV TAP

T Rhodes, K Lancaster (**2020**). How to think with models and targets: Hepatitis C elimination as a numbering performance. Int J Drug Policy. Mar 31;102694. Online ahead of print.

> The field of public health is replete with mathematical models and numerical targets. In the case of disease eliminations, modelled projections and targets play a key role in evidencing elimination futures and in shaping actions in relation to these. Drawing on ideas within science and technology studies, we take hepatitis C elimination as a case for reflecting on how to think with mathematical models and numerical targets as 'performative actors' in evidence-making. We focus specifically on the emergence of 'treatment-as-prevention' as a means to trace the social and material effects that models and targets make, including beyond science. We also focus on how enumerations are made locally in their methods and events of production. We trace the work that models and targets do in relation to three analytical themes: governing; affecting; and enacting. This allows us to situate models and targets as technologies of governance in the constitution of health, which affect and are affected by their material relations, including in relation to matters-of-concern which extend beyond calculus. By emphasising models and targets as enactments, we draw attention to how these devices give life to new enumerated entities, which detach from their calculative origins and take flight in new ways. We make this analysis for two reasons: first, as a call to bring the social and enumeration sciences closer together to speculate on how we might think with models and targets differently and more carefully; and second, to encourage an approach to science which treats evidencing-making interventions, such as models and targets, as performative and political.

A Trickey, H Fraser, AG Lim, JG Walker, A Peacock, S Colledge, J Leung, J Grebely, S Larney, NK Martin, L Degenhardt, M Hickman, MT May, P Vickerman (**2019**) Modelling the potential prevention benefits of a treat-all hepatitis C treatment strategy at global, regional and country levels: A modelling study. J Viral Hepat. 2019 Dec;26(12):1388-1403. doi: 10.1111/jvh.13187. Epub 2019 Aug 30.

> The World Health Organization (WHO) recently produced guidelines advising a treat-all policy for HCV to encourage widespread treatment scale-up for achieving HCV elimination. We modelled the prevention impact achieved (HCV infections averted [IA]) from initiating this policy compared with treating different subgroups at country, regional and global levels. We assessed what country-level factors affect impact. A dynamic, deterministic HCV transmission model was calibrated to data from global systematic reviews and UN data sets to simulate country-level HCV epidemics with ongoing levels of treatment. For each country, the model projected the prevention impact (in HCV IA per treatment undertaken) of initiating four treatment strategies; either selected randomly (treat-all) or targeted among people who inject drugs (PWID), people aged ≥35, or those with cirrhosis. The IA was assessed over 20 years. Linear regression was used to identify associations between IA per treatment and demographic factors. Eighty-eight countries (85% of the global population) were modelled. Globally, the model estimated 0.35 (95% credibility interval [95%CrI]: 0.16-0.61) IA over 20 years for every randomly allocated treatment, 0.30 (95%CrI: 0.12-0.53) from treating those aged ≥35 and 0.28 (95%CrI: 0.12-0.49) for those with cirrhosis. Globally, treating PWID achieved 1.27 (95%CrI: 0.68-2.04) IA per treatment. The IA per randomly allocated treatment was positively associated with a country's population growth rate and negatively associated with higher HCV prevalence among PWID. In conclusion, appreciable prevention benefits could be achieved from WHO's treat-all strategy, although greater benefits per treatment can be achieved through targeting PWID. Higher impact will be achieved in countries with high population growth.

LE Cipriano, JD Goldhaber-Fiebert (**2018**). "Population Health and Cost-Effectiveness Implications of a "Treat All" Recommendation for HCV: A Review of the Model-Based Evidence." MDM Policy Pract **3**(1): 2381468318776634.

The World Health Organization HCV Guideline Development Group is considering a "treat all" recommendation for persons infected with hepatitis C virus (HCV). We reviewed the model-based evidence of cost-effectiveness and population health impacts comparing expanded treatment policies to more limited treatment access policies, focusing primarily on evaluations of all-oral directly acting antivirals published after 2012. Searching PubMed, we identified 2,917 unique titles. Sequentially reviewing titles and abstracts identified 226 potentially relevant articles for full-text review. Sixty-nine articles met all inclusion criteria-42 cost-effectiveness analyses and 30 models of population-health impacts, with 3 articles presenting both types of analysis. Cost-effectiveness studies for many countries concluded that expanding treatment to people with mild liver fibrosis, who inject drugs (PWID), or who are incarcerated is generally cost-effective compared to more restrictive treatment access policies at country-specific prices. For certain patient subpopulations in some countries-for example, elderly individuals without fibrosis-treatment is only cost-effective at lower prices. A frequent limitation is the omission of benefits and consequences of HCV transmission (i.e., treatment as prevention; risks of reinfection), which may underestimate or overestimate the cost-effectiveness of a "treat all" policy. Epidemiologic modeling studies project that through a combination of prevention, aggressive screening and diagnosis, and prompt treatment for all fibrosis stages, it may be possible to virtually eliminate HCV in many countries. Studies show that if resources are not available to diagnose and treat all HCV-infected individuals, treatment prioritization may be needed, with alternative prioritization strategies resulting in tradeoffs between reducing mortality or reducing incidence. Notably, because most new HCV infections are among PWID in many settings, HCV elimination requires unrestricted treatment access combined with injection transmission disruption strategies. The model-based evidence suggests that a properly constructed strategy that substantially expands HCV treatment could achieve cost-effective improvements in population health in many countries.

NK Martin, B Skaathun, P Vickerman, D Stuart (**2017**). "Modeling Combination HCV Prevention among HIV-infected Men Who Have Sex With Men and People Who Inject Drugs." AIDS Rev **19**(2): 97-104.

People who inject drugs (PWID) and HIV-infected men who have sex with men (MSM) are key risk groups for HCV transmission. Mathematical modeling studies can help elucidate what level and combination of prevention intervention scale-up is required to control or eliminate epidemics among these key populations. We discuss the evidence surrounding HCV prevention interventions and provide an overview of the mathematical modeling literature projecting the impact of scaled-up HCV prevention among PWID and HIV-infected MSM. Harm reduction interventions, such as opiate substitution therapy and needle and syringe programs, are effective in reducing HCV incidence among PWID. Modeling and limited empirical data indicate that HCV treatment could additionally be used for prevention. No studies have evaluated the effectiveness of behavior change interventions to reduce HCV incidence among MSM, but existing interventions to reduce HIV risk could be effective. Mathematical modeling and empirical data indicate that scale-up of harm reduction could reduce HCV transmission, but in isolation is unlikely to eliminate HCV among PWID. By contrast, elimination is possibly achievable through combination scale-up of harm reduction and HCV treatment. Similarly, among HIV-infected MSM, eliminating the emerging epidemics will likely require HCV treatment scale-up in combination with additional interventions to reduce HCV-related risk behaviors. In summary, elimination of HCV will likely require combination prevention efforts among both PWID and HIV-infected MSM populations. Further empirical research is required to validate HCV treatment as prevention among these populations, and to identify effective behavioral interventions to reduce HCV incidence among MSM.

L MacGregor, NK Martin, C Mukandavire, F Hickson, P Weatherburn, M Hickman, P Vickerman (**2017**). "Behavioural, not biological, factors drive the HCV epidemic among HIV-positive MSM: HCV and HIV modelling analysis including HCV treatment-as-prevention impact." Int J Epidemiol **46**(5): 1582-1592.

Background: Uncertainty surrounds why hepatitis C virus (HCV) is concentrated among HIV-positive men who have sex with men (MSM). We used mathematical modelling to explore reasons for these infection patterns, and implications for HCV treatment-as-prevention. Methods: Using a joint MSM HIV/HCV transmission model parameterized with UK behavioural data, we considered how biological (heightened HCV infectivity and reduced spontaneous clearance among HIV-positive MSM) and/or behavioural

factors (preferential sexual mixing by HIV status and risk heterogeneity) could concentrate HCV infection in HIV-positive MSM as commonly observed (5-20 times the HCV prevalence in HIV-negative MSM; defined as the HCV ratio). We explored how HCV treatment-as-prevention impact varies under differing HCV ratios. Results: Biological factors produced low HCV ratios (< 3), not explaining the skewed epidemic. However, combining preferential mixing by HIV status with sexual risk behaviour heterogeneity produced high HCV ratios (> 10) that were highly sensitive to both factors. Irrespective of the HCV ratio or behavioural/biological factors, HCV treatment of HIV-diagnosed MSM markedly reduced the HCV prevalence among HIV-positive MSM, but less impact was achieved among all MSM for lower HCV ratios. Conclusions: Sexual behaviour patterns likely drive observed HCV infection patterns among HIV-positive MSM. Changes in these patterns could disseminate HCV amongst HIV-negative MSM, limiting the impact of targeting HCV treatment to HIV-diagnosed MSM.

NK Martin, B Skaathun, P Vickerman, D Stuart (**2017**). "Modeling Combination HCV Prevention among HIV-infected Men Who Have Sex With Men and People Who Inject Drugs." AIDS Rev **19**(2): 97-104.

People who inject drugs (PWID) and HIV-infected men who have sex with men (MSM) are key risk groups for HCV transmission. Mathematical modeling studies can help elucidate what level and combination of prevention intervention scale-up is required to control or eliminate epidemics among these key populations. We discuss the evidence surrounding HCV prevention interventions and provide an overview of the mathematical modeling literature projecting the impact of scaled-up HCV prevention among PWID and HIV-infected MSM. Harm reduction interventions, such as opiate substitution therapy and needle and syringe programs, are effective in reducing HCV incidence among PWID. Modeling and limited empirical data indicate that HCV treatment could additionally be used for prevention. No studies have evaluated the effectiveness of behavior change interventions to reduce HCV incidence among MSM, but existing interventions to reduce HIV risk could be effective. Mathematical modeling and empirical data indicate that scale-up of harm reduction could reduce HCV transmission, but in isolation is unlikely to eliminate HCV among PWID. By contrast, elimination is possibly achievable through combination scale-up of harm reduction and HCV treatment. Similarly, among HIV-infected MSM, eliminating the emerging epidemics will likely require HCV treatment scale-up in combination with additional interventions to reduce HCV-related risk behaviors. In summary, elimination of HCV will likely require combination prevention efforts among both PWID and HIV-infected MSM populations. Further empirical research is required to validate HCV treatment as prevention among these populations, and to identify effective behavioral interventions to reduce HCV incidence among MSM.

N Durier, C Nguyen, LJ White (**2012**) Treatment of hepatitis C as prevention: a modeling case study in Vietnam. PLoS One. 2012;7(4):e34548. doi: 10.1371/journal.pone.0034548. Epub 2012 Apr 12.

P Vickerman, N Martin, M Hickman (**2011**) Can Hepatitis C virus treatment be used as a prevention strategy? Additional model projections for Australia and elsewhere. Drug Alcohol Depend. 15;113(2-3):83-5; discussion 86-7.

b) Country examples of HCV TAP

Pakistan - Ayoub, H. H. and L. J. Abu-Raddad (**2019**). "Treatment as prevention for hepatitis C virus in Pakistan: mathematical modelling projections." BMJ Open **9**(5): e026600.

OBJECTIVE: Direct-acting antivirals have opened an opportunity for controlling hepatitis C virus (HCV) infection in Pakistan, where 10% of the global infection burden is found. We aimed to evaluate the implications of five treatment programme scenarios for HCV treatment as prevention (HCV-TasP) in Pakistan. DESIGN: An age-structured mathematical model was used to evaluate programme impact using epidemiological and programme indicators. SETTING: Total Pakistan population. PARTICIPANTS: Total Pakistan HCV-infected population. INTERVENTIONS: HCV treatment programme scenarios from 2018 up to 2030. RESULTS: By 2030 across the five HCV-TasP scenarios, 0.6-7.3 million treatments were

administered, treatment coverage reached between 3.7% and 98.7%, prevalence of chronic infection reached 2.4%-0.03%, incidence reduction ranged between 41% and 99%, program-attributed reduction in incidence rate ranged between 7.2% and 98.5% and number of averted infections ranged between 126 221 and 750 547. Annual incidence rate reduction in the first decade of the programme was around 6%-18%. Number of treatments needed to prevent one new infection ranged between 4.7-9.8, at a drug cost of about US$900. Cost of the programme by 2030, in the most ambitious elimination scenario, reached US$708 million. Stipulated WHO target for 2030 cannot be accomplished without scaling up treatment to 490 000 per year, and maintaining it for a decade. CONCLUSION: HCV-TasP is a highly impactful and potent approach to control Pakistan's HCV epidemic and achieve elimination by 2030.

The Netherlands - A Boerekamps, A De Weggheleire, GE van den Berk, FN Lauw, MAA Claassen, D Posthouwer, WF Bierman, SJ Hullegie, S Popping, DACM van de Vijver, ASM Dofferhoff, GJ Kootstra, EM Leyten, J den Hollander, ME van Kasteren, R Soetekouw, HSM Ammerlaan, J Schinkel, E Florence, JE Arends, BJA Rijnders (**2019**). "Treatment of acute hepatitis C genotypes 1 and 4 with 8 weeks of grazoprevir plus elbasvir (DAHHS2): an open-label, multicentre, single-arm, phase 3b trial." Lancet Gastroenterol Hepatol **4**(4): 269-277.

BACKGROUND: Direct-acting antivirals effectively treat chronic hepatitis C virus (HCV) infection but there is a paucity of data on their efficacy for acute HCV, when immediate treatment could prevent onward transmission. We assessed the efficacy of grazoprevir plus elbasvir treatment in acute HCV infection and investigated whether treatment can be shortened during the acute phase of HCV infection. METHODS: The Dutch Acute HCV in HIV study number 2 (DAHHS2) study was a single-arm, open-label, multicentre, phase 3b trial. Adult patients (>/=18 years) with acute HCV genotype 1 or 4 infection (duration of infection 26 weeks or less, according to presumed day of infection) were recruited at 15 HIV outpatient clinics in the Netherlands and Belgium. All patients were treated with 8 weeks of grazoprevir 100 mg plus elbasvir 50 mg administered as one oral fixed drug combination tablet once daily. The primary efficacy endpoint was sustained virological response at 12 weeks after the end of treatment (SVR12; HCV RNA <15 IU/mL) in all patients who started treatment. Reinfection with a different HCV virus was not considered treatment failure in the primary analysis. This trial is registered with ClinicalTrials.gov, number NCT02600325. FINDINGS: Between Feb 15, 2016, and March 2, 2018, we assessed 146 patients with a recently acquired HCV infection for eligibility, of whom 86 were enrolled and 80 initiated therapy, all within 6 months after infection. All patients who initiated treatment completed treatment and no patients were lost to follow-up. 79 (99%, 95% CI 93-100) of 80 patients achieved SVR12. All 14 patients who were infected with a virus carrying a clinically significant polymorphism in NS5A were cured. If reinfections were considered treatment failures, 75 (94%, 86-98) of 80 patients achieved SVR12. Two serious adverse events not considered related to the treatment were reported (traumatic rectal bleeding and low back surgery). The most common adverse event was a new sexually transmitted infection (19 [24%] of 80 patients). The most common reported possibly drug-related adverse events were fatigue (11 [14%] patients), headache (seven [9%] patients), insomnia (seven [9%] patients), mood changes (five [6%] patients), dyspepsia (five [6%] patients), concentration impairment (four [5%] patients), and dizziness (4 [5%] patients), all of which were regarded as mild by the treating physician. No adverse events led to study drug discontinuation. INTERPRETATION: 8 weeks of grazoprevir plus elbasvir was highly effective for the treatment of acute HCV genotype 1 or 4 infection. The ability to treat acute HCV immediately after diagnosis might help physicians to reach the WHO goal of HCV elimination by 2030. FUNDING: Merck Sharp and Dohme and Health-Holland.

The Netherlands - A Boerekamps, AM Newsum, C Smit, JE Arends, C Richter, P Reiss, BJA Rijnders, K Brinkman, M van der Valk, NVHB-SHM Hepatitis Working Group and the Netherlands ATHENA HIV Observational Cohort (**2018**). "High Treatment Uptake in Human Immunodeficiency Virus/Hepatitis C Virus-Coinfected Patients After Unrestricted Access to Direct-Acting Antivirals in the Netherlands." Clin Infect Dis **66**(9): 1352-1359.

Background: The Netherlands has provided unrestricted access to direct-acting antivirals (DAAs) since November 2015. We analyzed the nationwide hepatitis C virus (HCV) treatment uptake among patients coinfected with human immunodeficiency virus (HIV) and HCV. Methods: Data were obtained from the

ATHENA HIV observational cohort in which >98% of HIV-infected patients ever registered since 1998 are included. Patients were included if they ever had 1 positive HCV RNA result, did not have spontaneous clearance, and were known to still be in care. Treatment uptake and outcome were assessed. When patients were treated more than once, data were included from only the most recent treatment episode. Data were updated until February 2017. In addition, each treatment center was queried in April 2017 for a data update on DAA treatment and achieved sustained virological response. Results: Of 23574 HIV-infected patients ever linked to care, 1471 HCV-coinfected patients (69% men who have sex with men, 15% persons who [formerly] injected drugs, and 15% with another HIV transmission route) fulfilled the inclusion criteria. Of these, 87% (1284 of 1471) had ever initiated HCV treatment between 2000 and 2017, 76% (1124 of 1471) had their HCV infection cured; DAA treatment results were pending in 6% (92 of 1471). Among men who have sex with men, 83% (844 of 1022) had their HCV infection cured, and DAA treatment results were pending in 6% (66 of 1022). Overall, 187 patients had never initiated treatment, DAAs had failed in 14, and a pegylated interferon-alfa-based regimen had failed in 54. Conclusions: Fifteen months after unrestricted DAA availability the majority of HIV/HCV-coinfected patients in the Netherlands have their HCV infection cured (76%) or are awaiting DAA treatment results (6%). This rapid treatment scale-up may contribute to future HCV elimination among these patients.

Iceland - S Olafsson, T Tyrfingsson, V Runarsdottir, O M Bergmann, I Hansdottir, E S Björnsson, B Johannsson, B Sigurdardottir, R H Fridriksdottir, A Löve, M Hellard, T J Löve, T Gudnason, M Heimisdottir, M Gottfredsson (**2018**). "Treatment as Prevention for Hepatitis C (TraP Hep C) - a nationwide elimination programme in Iceland using direct-acting antiviral agents." J Intern Med **283**(5): 500-507.

A nationwide programme for the treatment of all patients infected with hepatitis C virus (HCV) was launched in Iceland in January 2016. By providing universal access to direct-acting antiviral agents to the entire patient population, the two key aims of the project were to (i) offer a cure to patients and thus reduce the long-term sequelae of chronic hepatitis C, and (ii) to reduce domestic incidence of HCV in the population by 80% prior to the WHO goal of HCV elimination by the year 2030. An important part of the programme is that vast majority of cases will be treated within 36 months from the launch of the project, during 2016-2018. Emphasis is placed on early case finding and treatment of patients at high risk for transmitting HCV, that is people who inject drugs (PWID), as well as patients with advanced liver disease. In addition to treatment scale-up, the project also entails intensification of harm reduction efforts, improved access to diagnostic tests, as well as educational campaigns to curtail spread, facilitate early detection and improve linkage to care. With these efforts, Iceland is anticipated to achieve the WHO hepatitis C elimination goals well before 2030. This article describes the background and organization of this project. Clinical trial number: NCT02647879.

Iceland - N Scott, S Ólafsson, M Gottfreðsson, T Tyrfingsson, V Rúnarsdóttir, I Hansdottir, UB Hernandez, G Sigmundsdóttir, M Hellard (**2018**). "Modelling the elimination of hepatitis C as a public health threat in Iceland: A goal attainable by 2020." J Hepatol **68**(5): 932-939.

BACKGROUND & AIMS: In Iceland a nationwide program has been launched offering direct-acting antiviral (DAA) treatment for everyone living with hepatitis C virus (HCV). We estimate (i) the time and treatment scale-up required to achieve the World Health Organization's HCV elimination target of an 80% reduction in incidence; and (ii) the ongoing frequency of HCV testing and harm reduction coverage among people who inject drugs (PWID) required to minimize the likelihood of future HCV outbreaks occurring. METHODS: We used a dynamic compartmental model of HCV transmission, liver disease progression and the HCV cascade of care, calibrated to reproduce the epidemic of HCV in Iceland. The model was stratified according to injecting drug use status, age and stage of engagement. Four scenarios were considered for the projections. RESULTS: The model estimated that an 80% reduction in domestic HCV incidence was achievable by 2030, 2025 or 2020 if a minimum of 55/1,000, 75/1,000 and 188/1,000 PWID were treated per year, respectively (a total of 22, 30 and 75 of the estimated 400 PWID in Iceland per year, respectively). Regardless of time frame, this required an increased number of PWID to be diagnosed to generate enough treatment demand, or a 20% scale-up of harm reduction services to complement treatment-as-prevention incidence reductions. When DAA scale-up was combined with annual antibody testing of PWID, the incidence reduction target was reached by 2024. Treatment scale-

up with no other changes to current testing and harm reduction services reduced the basic reproduction number of HCV from 1.08 to 0.59, indicating that future outbreaks would be unlikely. CONCLUSION: HCV elimination in Iceland is achievable by 2020 with some additional screening of PWID. Maintaining current monitoring and harm reduction services while providing ongoing access to DAA therapy for people diagnosed with HCV would ensure that outbreaks are unlikely to occur once elimination targets have been reached. LAY SUMMARY: In Iceland, a nationwide program has been launched offering treatment for the entire population living with hepatitis C virus (HCV). A mathematical model was used to estimate the additional health system requirements to achieve the HCV elimination targets of the World Health Organization (WHO), as well as the year that this could occur. With some additional screening of people who inject drugs, Iceland could reach the WHO targets by 2020, becoming one of the first countries to achieve HCV elimination. The model estimated that once elimination targets were reached, maintaining current monitoring and harm reduction services while providing ongoing access to DAA therapy for people diagnosed with HCV would ensure that future HCV outbreaks are unlikely to occur.

Iceland – B Sigurethardottir (**2015**). "[Treatment as prevention for hepatitis C in Iceland: challenges despite optimism[Editorial]]." Laeknabladid **101**(11): 507.

Scotland - AL McNaughton, I Dugald Cameron, EB Wignall-Fleming, R Biek, J McLauchlan, RN Gunson, K Templeton, H Mei-Lin Tan, EC McWilliam Leitch (**2015**). "Spatiotemporal Reconstruction of the Introduction of Hepatitis C Virus into Scotland and Its Subsequent Regional Transmission." J Virol **89**(22): 11223-11232.

UNLABELLED: A more comprehensive understanding of hepatitis C virus (HCV) transmission dynamics could facilitate public health initiatives to reduce the prevalence of HCV in people who inject drugs. We aimed to determine how HCV sequences entered and spread throughout Scotland and to identify transmission hot spots. A Scottish data set with embedded demographic data was created by sequencing the NS5B of 125 genotype 1a (Gt1a) samples and 166 Gt3a samples and analyzed alongside sequences from public databases. Applying Bayesian inference methods, we reconstructed the global origin and local spatiotemporal dissemination of HCV in Scotland. Scottish sequences mainly formed discrete clusters interspersed between sequences from the rest of the world; the most recent common ancestors of these clusters dated to 1942 to 1952 (Gt1a) and 1926 to 1942 (Gt3a), coincident with global diversification and distribution. Extant Scottish sequences originated in Edinburgh (Gt1a) and Glasgow (Gt3a) in the 1970s, but both genotypes spread from Glasgow to other regions. The dominant Gt1a strain differed between Edinburgh (cluster 2 [C2]), Glasgow (C3), and Aberdeen (C4), whereas significant Gt3a strain specificity occurred only in Aberdeen. Specific clusters initially formed separate transmission zones in Glasgow that subsequently overlapped, occasioning city-wide cocirculation. Transmission hot spots were detected with 45% of samples from patients residing in just 9 of Glasgow's 57 postcode districts. HCV was introduced into Scotland in the 1940s, concomitant with its worldwide dispersal likely arising from global-scale historical events. Cluster-specific transmission hubs were identified in Glasgow, the key Scottish city implicated in HCV dissemination. This fine-scale spatiotemporal reconstruction improves understanding of HCV transmission dynamics in Scotland. IMPORTANCE: HCV is a major health burden and the leading cause of hepatocellular carcinoma. Public health needle exchange and "treatment as prevention" strategies targeting HCV are designed to reduce prevalence of the virus in people who inject drugs (PWID), potentially mitigating the future burden of HCV-associated liver disease. Understanding HCV transmission dynamics could increase the effectiveness of such public health initiatives by identifying and targeting regions playing a central role in virus dispersal. In this study, we examined HCV transmission in Scotland by analyzing the genetic relatedness of strains from PWID alongside data inferring the year individuals became infected and residential information at a geographically finer-scale resolution than in previous studies. Clusters of Scotland-specific strains were identified with regional specificity, and mapping the spread of HCV allowed the identification of key areas central to HCV transmission in Scotland. This research provides a basis for identifying HCV transmission hot spots.

USA - Coffin, P. O. and A. Reynolds (**2014**). "Ending hepatitis C in the United States: the role of screening." Hepat Med **6**: 79-87.

2. HCV Treatment as prevention in PWID

PO Coffin, GM Santos, E Behar, J Hern, J Walker, T Matheson, EN Kinnard, J Silvis, E Vittinghoff, R Fox, K Page (**2019**) [Randomized feasibility trial of directly observed versus unobserved hepatitis C treatment with ledipasvir-sofosbuvir among people who inject drugs](#). PLoS One. 2019 Jun 3;14(6):e0217471.

Aims: The advent of direct-acting antivirals for hepatitis C virus (HCV) and limited effectiveness of prevention have generated interest in "Treatment as Prevention" (TasP), in which those most likely to transmit HCV (i.e. people who inject drugs [PWID]) are treated to reduced secondary transmission. However, there are scant data regarding the feasibility of treating PWID at high risk for secondary transmission or the optimal approach to treatment delivery.

Methods: We conducted a 2:1 randomized trial of modified directly-observed (mDOT) versus unobserved HCV treatment with ledipasvir-sofosbuvir daily for 8 weeks among PWID with 36 weeks of follow-up in San Francisco from 2015-2017. We evaluated recruitment-enrollment, treatment completion, end-of-treatment and 12-week response, and reinfection rate.

Results: Of 83 individuals eligible for screening, 72 (87.6%) attended the screening visit, 33 were eligible, and 31 enrolled; mean age was 42 years, 81% were male, 74% white. All but one participant (in the mDOT arm) completed treatment and 89.4% of mDOT and 96.6% of unobserved arm visits were attended. HCV was undetectable for 96.8% (30/31) at end of treatment and 89.7% (26/29) 12 weeks later (1 relapse, 1 reinfection), with no differences by arm. Two additional reinfections were subsequently identified, for a reinfection rate of 16.3 (95% CI 5.3-50.5) per 100 person-years of observation.

Conclusions: It was feasible to recruit active PWID for HCV treatment and achieve high retention, viral response, and satisfaction with either mDOT or unobserved protocols, supporting treatment of PWID at risk of transmitting HCV to others. The reinfection rate suggests we successfully reached a high-risk population and that successful HCV TasP initiatives may aim to be sufficient in scope to significantly lower prevalence in the community.

Trial registration: clinicaltrials.gov NCT02609893.

NH Latham, JS Doyle, AY Palmer, JW Vanhommerig, P Agius, S Goutzamanis, Z Li, A Pedrana, M Gottfredsson, J Bouscaillou, N Luhmann, A Mazhnaya, FL Altice, S Saeed, M Klein, OO Falade-Nwulia, E Aspinall, S Hutchinson, ME Hellard, R Sacks-Davis. (**2019**) [Staying hepatitis C negative: A systematic review and meta-analysis of cure and reinfection in people who inject drugs](#). Liver Int. Dec;39(12):2244-2260. doi: 10.1111/liv.14152. Epub 2019 Jun 10.

Background and aims: Direct-acting antivirals (DAAs) are highly effective in treating hepatitis C. However, there is concern that cure rates may be lower, and reinfection rates higher, among people who inject drugs. We conducted a systematic review of treatment outcomes achieved with DAAs in people who inject drugs (PWID).
Methods: A search strategy was used to identify studies that reported sustained viral response (SVR), treatment discontinuation, adherence or reinfection in recent PWID and/or opioid substitution therapy (OST) recipients. Study quality was assessed using the Newcastle-Ottawa Scale. Meta-analysis of proportions was used to estimate pooled SVR and treatment discontinuation rates. The pooled relative risk of achieving SVR and pooled reinfection rate were calculated using generalized mixed effects linear models.
Results: The search identified 8075 references; 26 were eligible for inclusion. The pooled SVR for recent PWID was 88% (95% CI, 83%-92%) and 91% (95% CI 88%-95%) for OST recipients. The relative risk of achieving SVR for recent PWID compared to non-recent PWID was 0.99 (95% CI, 0.94-1.06). The pooled treatment discontinuation was 2% (95% CI, 1%-4%) for both recent PWID and OST recipients. Amongst recent PWID, the pooled incidence of reinfection was 1.94 per 100 person years (95% CI, 0.87-4.32). In OST recipients, the incidence of reinfection was 0.55 per 100 person years (95% CI, 0.17-1.76).
Conclusions: Treatment outcomes were similar in recent PWID compared to non-PWID treated with DAAs. People who report recent injecting or OST recipients should not be excluded from hepatitis C treatment.

J Schulkind, B Stephens, F Ahmad, L Johnston, S Hutchinson, D Thain, Z Ward, P Vickerman, M Hickman, JF Dillon (**2019**). "High response and re-infection rates among people who inject drugs treated for hepatitis C in a community needle and syringe programme." J Viral Hepat **26**(5): 519-528.

To achieve WHO hepatitis C virus (HCV) elimination targets by 2030, mathematical models suggest there needs to be significant scale-up of treatment among people who inject drugs (PWID). We tested whether people who actively inject drugs can be recruited and treated successfully through a community needle and syringe programme (NSP), and assessed rates of re-infection. 105 HCV RNA positive participants were enrolled prospectively. Participants were recruited from the largest NSP in Dundee over 42 months. 94/105 individuals commenced treatment. Genotype 1 (G1) individuals (n = 37) were treated with peg-interferon+ribavirin+Simepravir/Telaprevir. Genotype 2/3 (G2/3) (n = 57) received peg-interferon+ribavirin. Weekly study visits took place within the NSP. Mean age of participants was 34.0 years (SD 6.9), 71.3% (61/94) were male. One in five (20/94) participants were homeless. 68.1% (64/94) were on OST (opiate substitution therapy) at enrolment; participants injected median 6.5 times/wk. In terms of clinical outcomes, >80% treatment adherence was 71.3% (67/94). There was no difference in SVR-12 rates by genotype: 81.0% (30/37) for G1 and 82.5% (47/55) for G2/3. At 18 months post-treatment, 15/77 participants were reinfected, followed up over 69.8 person-years, yielding a re-infection rate of 21.5/100 person-years (95% CI 13.00-35.65). This trial demonstrates that HCV treatment can be delivered successfully to the target population of treatment as prevention strategies. We report higher rates of re-infection than existing estimates among PWID. Scale-up of HCV treatment should be pursued alongside a comprehensive programme of harm reduction interventions to help minimize re-infection and reduce HCV transmission.

J Iversen, GJ Dore, B Catlett, P Cunningham, J Grebely, L Maher. (**2019**). "Association between rapid utilisation of direct hepatitis C antivirals and decline in the prevalence of viremia among people who inject drugs in Australia." J Hepatol **70**(1): 33-39.

BACKGROUND & AIMS: The World Health Organization (WHO) established targets to eliminate hepatitis C virus (HCV) infection as a public health threat by 2030. Evidence that HCV treatment can lower viraemic prevalence among people who inject drugs (PWID) is limited. Broad accessibility of direct-acting antiviral (DAA) therapy in Australia, since March 2016, provides an opportunity to assess the efficacy of these treatments at a population level in a real-world setting. METHODS: Data from Australia's annual bio-behavioural surveillance examined treatment uptake and estimated viraemic prevalence among PWID attending needle syringe programs nationally between 2015 and 2017. Multivariate logistic regression identified variables independently associated with HCV treatment among those considered eligible (anti-HCV positive excluding HCV RNA negative with no self-reported history of HCV treatment) in 2017. RESULTS: Annual samples ranged from 1,995-2,380 PWID. Anti-HCV prevalence declined from 57% (2015) to 49% (2017, chi(2)p trend <0.001), with 40-56% of anti-HCV positive respondents providing sufficient sample for HCV RNA testing. Between 2015 and 2017, treatment uptake among those eligible increased from 10% to 41% (chi(2)p trend <0.001) and viraemic prevalence among the overall sample declined from 43% to 25% (chi(2)p trend <0.001). In multivariable analysis, older age (>/=50years adjusted odds ratio [aOR] 1.82; 95% CI 1.09-3.06;p=0.023 and 44-49years aOR 1.75; 95% CI 1.03-3.00;p=0.038 vs. </=37years) and history of opioid substitution therapy (aOR 2.06; 95% CI 1.30-3.26; p=0.002) were independently associated with treatment. CONCLUSIONS: This study confirms PWID are willing to initiate treatment when HCV DAA therapy is available and provides population-level evidence of a decline in viraemic prevalence among people most at risk of ongoing HCV transmission. Scaled up surveillance and monitoring are required to evaluate progress toward WHO HCV elimination goals. LAY SUMMARY: The World Health Organization's goal to reduce hepatitis C virus incidence by 80% will be difficult to achieve without widespread scale up and a corresponding reduction in viraemic prevalence among those most at risk of onward transmission. Our results indicate that a population-level reduction in viraemic prevalence is achievable through high levels of treatment and cure among people who inject drugs.

M Hickman, JF Dillon, L Elliott, D De Angelis, P Vickerman, G Foster, P Donnan, A Eriksen, P Flowers, D Goldberg, W Hollingworth, S Ijaz, D Liddell, S Mandal, N Martin, LJZ Beer, K Drysdale, H Fraser, R Glass, L Graham, RN Gunson, E

Hamilton, H Harris, M Harris, R Harris, E Heinsbroek, V Hope, J Horwood, SK Inglis, H Innes, A Lane , J Meadows, A McAuley, C Metcalfe, S Migchelsen, A Murray, G Myring, NE Palmateer, A Presanis, A Radley, M Ramsay, P Samartsidis, R Simmons, K Sinka, G Vojt, Z Ward, D Whiteley, A Yeung, SJ Hutchinson (**2019**). "Evaluating the population impact of hepatitis C direct acting antiviral treatment as prevention for people who inject drugs (EPIToPe) - a natural experiment (protocol)." BMJ Open **9**(9): e029538.

INTRODUCTION: Hepatitis C virus (HCV) is the second largest contributor to liver disease in the UK, with injecting drug use as the main risk factor among the estimated 200 000 people currently infected. Despite effective prevention interventions, chronic HCV prevalence remains around 40% among people who inject drugs (PWID). New direct-acting antiviral (DAA) HCV therapies combine high cure rates (>90%) and short treatment duration (8 to 12 weeks). Theoretical mathematical modelling evidence suggests HCV treatment scale-up can prevent transmission and substantially reduce HCV prevalence/incidence among PWID. Our primary aim is to generate empirical evidence on the effectiveness of HCV 'Treatment as Prevention' (TasP) in PWID. METHODS AND ANALYSIS: We plan to establish a natural experiment with Tayside, Scotland, as a single intervention site where HCV care pathways are being expanded (including specialist drug treatment clinics, needle and syringe programmes (NSPs), pharmacies and prison) and HCV treatment for PWID is being rapidly scaled-up. Other sites in Scotland and England will act as potential controls. Over 2 years from 2017/2018, at least 500 PWID will be treated in Tayside, which simulation studies project will reduce chronic HCV prevalence among PWID by 62% (from 26% to 10%) and HCV incidence will fall by approximately 2/3 (from 4.2 per 100 person-years (p100py) to 1.4 p100py). Treatment response and re-infection rates will be monitored. We will conduct focus groups and interviews with service providers and patients that accept and decline treatment to identify barriers and facilitators in implementing TasP. We will conduct longitudinal interviews with up to 40 PWID to assess whether successful HCV treatment alters their perspectives on and engagement with drug treatment and recovery. Trained peer researchers will be involved in data collection and dissemination. The primary outcome - chronic HCV prevalence in PWID - is measured using information from the Needle Exchange Surveillance Initiative survey in Scotland and the Unlinked Anonymous Monitoring Programme in England, conducted at least four times before and three times during and after the intervention. We will adapt Bayesian synthetic control methods (specifically the Causal Impact Method) to generate the cumulative impact of the intervention on chronic HCV prevalence and incidence. We will use a dynamic HCV transmission and economic model to evaluate the cost-effectiveness of the HCV TasP intervention, and to estimate the contribution of the scale-up in HCV treatment to observe changes in HCV prevalence. Through the qualitative data we will systematically explore key mechanisms of TasP real world implementation from provider and patient perspectives to develop a manual for scaling up HCV treatment in other settings. We will compare qualitative accounts of drug treatment and recovery with a 'virtual cohort' of PWID linking information on HCV treatment with Scottish Drug treatment databases to test whether DAA treatment improves drug treatment outcomes. ETHICS AND DISSEMINATION: Extending HCV community care pathways is covered by ethics (ERADICATE C, ISRCTN27564683, Super DOT C Trial clinicaltrials.gov: NCT02706223). Ethical approval for extra data collection from patients including health utilities and qualitative interviews has been granted (REC ref: 18/ES/0128) and ISCRCTN registration has been completed (ISRCTN72038467). Our findings will have direct National Health Service and patient relevance; informing prioritisation given to early HCV treatment for PWID. We will present findings to practitioners and policymakers, and support design of an evaluation of HCV TasP in England.

PO Coffin, G-M Santos, E Behar, J Hern, J Walker, T Matheson, EN Kinnard, J Silvis, E Vittinghoff, R Fox, K Page (**2019**). "Randomized feasibility trial of directly observed versus unobserved hepatitis C treatment with ledipasvir-sofosbuvir among people who inject drugs." PLoS One **14**(6): e0217471.

AIMS: The advent of direct-acting antivirals for hepatitis C virus (HCV) and limited effectiveness of prevention have generated interest in "Treatment as Prevention" (TasP), in which those most likely to transmit HCV (i.e. people who inject drugs [PWID]) are treated to reduced secondary transmission. However, there are scant data regarding the feasibility of treating PWID at high risk for secondary transmission or the optimal approach to treatment delivery. METHODS: We conducted a 2:1 randomized trial of modified directly-observed (mDOT) versus unobserved HCV treatment with ledipasvir-sofosbuvir

daily for 8 weeks among PWID with 36 weeks of follow-up in San Francisco from 2015-2017. We evaluated recruitment-enrollment, treatment completion, end-of-treatment and 12-week response, and reinfection rate. RESULTS: Of 83 individuals eligible for screening, 72 (87.6%) attended the screening visit, 33 were eligible, and 31 enrolled; mean age was 42 years, 81% were male, 74% white. All but one participant (in the mDOT arm) completed treatment and 89.4% of mDOT and 96.6% of unobserved arm visits were attended. HCV was undetectable for 96.8% (30/31) at end of treatment and 89.7% (26/29) 12 weeks later (1 relapse, 1 reinfection), with no differences by arm. Two additional reinfections were subsequently identified, for a reinfection rate of 16.3 (95% CI 5.3-50.5) per 100 person-years of observation. CONCLUSIONS: It was feasible to recruit active PWID for HCV treatment and achieve high retention, viral response, and satisfaction with either mDOT or unobserved protocols, supporting treatment of PWID at risk of transmitting HCV to others. The reinfection rate suggests we successfully reached a high-risk population and that successful HCV TasP initiatives may aim to be sufficient in scope to significantly lower prevalence in the community. TRIAL REGISTRATION: clinicaltrials.gov NCT02609893.

R Buchanan, R Meskarian, P van der Heijden, L Grellier, J Parkes, SI Khakoo (**2019**). "Prioritising Hepatitis C treatment in people with multiple injecting partners maximises prevention: a real-world network study." J Infect.

OBJECTIVE: To describe an injecting network of PWID living in an isolated community on the Isle of Wight (UK) and the results of a agent-based simulation, testing the effect of Hepatitis C (HCV) treatment on transmission. METHOD: People who inject drugs (PWID) were identified via respondent driven sampling and recruited to a network and bio-behavioural survey. The injecting network they described formed the baseline population and potential transmission pathways in an agent-based simulation of HCV transmission and the effects of treatment over 12 months. RESULTS: On average each PWID had 2.6 injecting partners (range 0-14) and 137 were connected into a single component. HCV in the network was associated with a higher proportion of positive injecting partners (p=0.003) and increasing age (p=0.011). The treatment of well-connected PWID led to significantly fewer new infections of HCV than treating at random (10 vs. 7, p<0.001). In all scenarios less than one individual was re-infected. CONCLUSION: In our model the preferential treatment of well-connected PWID maximised treatment as prevention. In the real-world setting, targeting treatment to actively injecting PWID, with multiple injecting partners may therefore represent the most efficient elimination strategy for HCV.

A Zelenev, J Li, A Mazhnaya, S Basu, FL Altice 5 (**2018**). "Hepatitis C virus treatment as prevention in an extended network of people who inject drugs in the USA: a modelling study." Lancet Infect Dis **18**(2): 215-224.

BACKGROUND: Chronic infections with hepatitis C virus (HCV) and HIV are highly prevalent in the USA and concentrated in people who inject drugs. Treatment as prevention with highly effective new direct-acting antivirals is a prospective HCV elimination strategy. We used network-based modelling to analyse the effect of this strategy in HCV-infected people who inject drugs in a US city. METHODS: Five graph models were fit using data from 1574 people who inject drugs in Hartford, CT, USA. We used a degree-corrected stochastic block model, based on goodness-of-fit, to model networks of injection drug users. We simulated transmission of HCV and HIV through this network with varying levels of HCV treatment coverage (0%, 3%, 6%, 12%, or 24%) and varying baseline HCV prevalence in people who inject drugs (30%, 60%, 75%, or 85%). We compared the effectiveness of seven treatment-as-prevention strategies on reducing HCV prevalence over 10 years and 20 years versus no treatment. The strategies consisted of treatment assigned to either a randomly chosen individual who injects drugs or to an individual with the highest number of injection partners. Additional strategies explored the effects of treating either none, half, or all of the injection partners of the selected individual, as well as a strategy based on respondent-driven recruitment into treatment. FINDINGS: Our model estimates show that at the highest baseline HCV prevalence in people who inject drugs (85%), expansion of treatment coverage does not substantially reduce HCV prevalence for any treatment-as-prevention strategy. However, when baseline HCV prevalence is 60% or lower, treating more than 120 (12%) individuals per 1000 people who inject drugs per year would probably eliminate HCV within 10 years. On average, assigning treatment randomly to individuals who inject drugs is better than targeting individuals with the most injection partners. Treatment-as-prevention strategies that treat additional network members are among the best performing strategies and can enhance less effective strategies that target the degree (ie, the highest

number of injection partners) within the network. INTERPRETATION: Successful HCV treatment as prevention should incorporate the baseline HCV prevalence and will achieve the greatest benefit when coverage is sufficiently expanded. FUNDING: National Institute on Drug Abuse.

PJ White, I Abubakar (**2018**). "Hepatitis C virus treatment as prevention in people who inject drugs." Lancet Infect Dis **18**(4): 379.

Alexei Zelenev and colleagues presented an elegant analysis of treatment-as-prevention (TasP) for hepatitis C virus (HCV) in people who inject drugs (PWID),[1] using a model capturing the dynamics of the injecting-partnership network, which is superior to the more-common approaches of compartmental modelling (omitting network structure) and static network modelling (omitting changes in partnerships over time).

Their findings regarding the importance of diversity in PWID populations and injecting-partnership networks reinforce a recent study[2] which used behavioural data from PWID in London, England, to parameterise and compare different dynamic network models, and a standard compartmental model, regarding the impact of TasP. In this population, where HCV prevalence is 43%, TasP can be highly effective but limited information on the detailed characteristics of the injecting-partnership network causes uncertainty in the coverage required.

Zelenev et al.[1] emphasise the need for "sufficient coverage" in settings where TasP could be effective. We highlight that an intense intervention with relatively high coverage will be cheaper and more effective than a less-intensive intervention that is nevertheless "sufficient".[2] This is because transmission is reduced more rapidly and therefore fewer courses of treatment are ultimately required to obtain the same reduction in prevalence (reducing costs) and fewer cases of illness occur (benefiting health).[2] We encourage funders to be bold and commit substantial resources initially, rather than providing 'incremental' funding and requiring evidence of impact before committing further funds. A similar approach to sexually-transmitted infections in England in the mid-2000s, informed by modelling,[3] which achieved success.[4]

Notably, direct comparison of dynamic injecting-partnership network modelling with compartmental modelling (which assumes that everyone is constantly connected equally to everyone else) found the latter is highly over-optimistic regarding TasP, greatly underestimating the coverage necessary for HCV control.[2]

Post-treatment reinfection risk is a key determinant of TasP's cost-effectiveness; it depends upon whether individual patients continue injecting drugs (and whether their injecting practices become safer if so), and HCV prevalence in their injecting partners,[2] which in turn depends upon the scale and targeting[1,2] of TasP and other interventions. Since "small-scale trials are suitable only for measuring the individual-level [behavioural] component [of reinfection risk]",[2] empirical study of the impact of TasP for HCV in PWID, and potential synergies[5] of combining with opiate substitution therapy and needle and syringe programmes, needs to be done at full scale.[6]

Finally, modelling would ideally use realistic dynamic networks, with local population parameters, including progression rates,[7] to inform appropriate intervention decisions.

1. Zelenev A, Li J, Mazhnaya A, Basu S, Altice FL. Hepatitis C virus treatment as prevention in an extended network of people who inject drugs in the USA: a modelling study. Lancet Infect Dis 2017; http://dx.doi.org/10.1016/S1473-3099(17)30676-X

2. Metzig C, Surey J, Francis M, Conneely J, Abubakar I, White PJ. Impact of Hepatitis C Treatment as Prevention for People Who Inject Drugs is sensitive to contact network structure. Sci Rep 2017; 7: 1833. http://dx.doi.org/10.1038/s41598-017-01862-6

3. White PJ, Ward H, Cassell JA, Mercer CH, Garnett GP. Vicious and virtuous circles in the dynamics of infectious disease and the provision of health care: gonorrhea in Britain as an example. J Infect Dis 2005; 192: 824–836. http://dx.doi.org/10.1086/432004

4. Mercer CH, Aicken CRH, Estcourt CS, Keane F, Brook G, Rait G, White PJ, Cassell JA. Building the bypass: implications of improved access to sexual healthcare: evidence from surveys of patients attending contrasting genitourinary medicine clinics across England in 2004/2005 and 2009. Sex Transm Infect 2012; 88: 9–15. http://dx.doi.org/10.1136/sextrans-2011-050257

5. Dodd PJ, White PJ, Garnett GP. Notions of synergy for combinations of interventions against infectious diseases in heterogeneously mixing populations. Math Biosci 2010; 227: 94–104. http://dx.doi.org/10.1016/j.mbs.2010.06.004

6. Hallett TB, White PJ, Garnett GP. The appropriate evaluation of HIV prevention interventions: from experiment to full scale implementation. Sex Transm Infect 2007; 83(Suppl I): i55–i60. http://dx.doi.org/10.1136/sti.2006.023663

7. Gubay F, Staunton R, Metzig C, Abubakar I, White PJ. Assessing uncertainty in the burden of Hepatitis C Virus: comparison of estimated disease burden and treatment costs in the UK. J Viral Hepatitis 2017; published online 23 Dec 2017. doi:10.1111/jvh.12847.

N Scott, R Sacks-Davis, A Pedrana, J Doyle, A Thompson, M Hellard (**2018**). "Eliminating hepatitis C: The importance of frequent testing of people who inject drugs in high-prevalence settings." J Viral Hepat **25**(12): 1472-1480.

Modelling suggests that more frequent screening of people who inject drugs (PWID) and an improved care cascade are required to achieve the WHO hepatitis C virus (HCV) elimination target of an 80% reduction in incidence by 2030. We determined the testing frequencies (2-yearly, annually, 6-monthly and 3-monthly) and retention in care required among PWID to achieve the HCV incidence reduction target through treatment as prevention in low (25%), medium (50%) and high (75%) chronic HCV prevalence settings. Mathematical modelling of HCV transmission among PWID, capturing testing, treatment and other features of the care cascade were employed. In low-prevalence settings, 2-yearly antibody testing of PWID was estimated to reach the elimination target by 2027-2030 depending on retention in care, with annual testing reducing the time by up to 3 years. In medium-prevalence settings, if close to 90% testing coverage were achieved, then annual antibody testing of PWID would be sufficient. If testing coverage were lower (80%), 6-monthly antibody testing with at least 70% retention in care or annual HCV RNA/cAg testing would be required. In high-prevalence settings, even 3-monthly HCV RNA/cAg testing of PWID was unable to achieve the incidence reduction target. Thus, for geographical areas or subpopulations with high prevalence, WHO incidence targets are unlikely to be met without 3-monthly RNA/cAg testing accompanied by other prevention measures. Novel testing strategies, such as rapid point-of-care antibody testing or replacing antibody testing with RNA/cAg tests as a screening tool, can provide additional population-level impacts to compensate for imperfect follow-up or testing coverage.

HT Duong, DD Jarlais, OHT Khuat, K Arasteh, J Feelemyer, PM Khue, HT Giang, D Laureillard, VV Hai, R Vallo, L Michel, JP Moles, N Nagot, Drive Study Group (**2018**). "Risk Behaviors for HIV and HCV Infection Among People Who Inject Drugs in Hai Phong, Viet Nam, 2014." AIDS Behav **22**(7): 2161-2171.

We examined the potential for HIV and hepatitis C (HCV) transmission across persons who inject drugs (PWID), men-who-have-sex-with-men (MSM) and female commercial sex workers (CSW) PWID and the potential for sexual transmission of HIV from PWID to the general population in Hai Phong, Viet Nam. Using respondent driven and convenience sampling we recruited 603 participants in 2014. All participants used heroin; 24% used non-injected methamphetamine. HIV prevalence was 25%; HCV prevalence was 67%. HIV infection was associated with HCV prevalence and both infections were associated with length of injecting career. Reported injecting risk behaviors were low; unsafe sexual behavior was high among MSM-PWID and CSW-PWID. There is strong possibility of sexual transmission to primary partners facilitated by methamphetamine use. We would suggest future HIV prevention programs utilize multiple interventions including "treatment as prevention" to potential sexual transmission of HIV among MSM and CSW-PWID and from PWID to the general population.

DB Stephens, AM Young, JR Havens (**2017**). "Healthcare contact and treatment uptake following hepatitis C virus screening and counseling among rural Appalachian people who use drugs." Int J Drug Policy **47**: 86-94.

BACKGROUND: Hepatitis C virus (HCV) remains a major contributor to morbidity and mortality worldwide. Since 2009, Kentucky has led the United States in cases of acute HCV, driven largely by injection drug use in rural areas. Improved treatment regimens hold promise of mitigating the impact and transmission of HCV, but numerous barriers obstruct people who inject drugs (PWID) from receiving care, particularly in medically underserved settings. METHODS: 503 rural people who use drugs were recruited using respondent-driven sampling and received HCV screening and post-test counseling. Presence of HCV antibodies was assessed using enzyme immunoassay of dried blood samples. Sociodemographic and behavioral data were collected using computer-based questionnaires. Predictors of contacting a healthcare provider for follow-up following HCV-positive serotest and counseling were determined using discrete-time survival analysis. RESULTS: 150 (59%) of 254 participants reported contacting a healthcare provider within 18 months of positive serotest and counseling; the highest probability occurred within six months of serotesting. 35 participants (14%) reported they were seeking treatment, and 21 (8%) reported receiving treatment. In multivariate time-dependent modeling, health insurance, internet access, prior substance use treatment, meeting DSM-IV criteria for generalized anxiety disorder, and recent marijuana use increased the odds of making contact for follow-up. Participants meeting criteria for major depressive disorder and reporting prior methadone use, whether legal or illegal, were less likely to contact a provider. CONCLUSION: While only 8% received treatment after HCV-positive screening, contacting a healthcare provider was frequent in this sample of rural PWID, suggesting that the major barriers to care are likely further downstream. These findings offer insight into the determinants of engaging the cascade of medical treatment for HCV and ultimately, treatment-as-prevention. Further study and increased resources to support integrated interventions with effectiveness in other settings are recommended to mitigate the impact of HCV in this resource-deprived setting.

C Metzig, J Surey, M Francis, J Conneely, I Abubakar, PJ White (**2017**). "Impact of Hepatitis C Treatment as Prevention for People Who Inject Drugs is sensitive to contact network structure." Sci Rep **7**(1): 1833.

Treatment as Prevention (TasP) using directly-acting antivirals has been advocated for Hepatitis C Virus (HCV) in people who inject drugs (PWID), but treatment is expensive and TasP's effectiveness is uncertain. Previous modelling has assumed a homogeneously-mixed population or a static network lacking turnover in the population and injecting partnerships. We developed a transmission-dynamic model on a dynamic network of injecting partnerships using data from survey of injecting behaviour carried out in London, UK. We studied transmission on a novel exponential-clustered network, as well as on two simpler networks for comparison, an exponential unclustered and a random network, and found that TasP's effectiveness differs markedly. With respect to an exponential-clustered network, the random network (and homogeneously-mixed population) overestimate TasP's effectiveness, whereas the exponential-unclustered network underestimates it. For all network types TasP's effectiveness depends on whether treated patients change risk behaviour, and on treatment coverage: higher coverage requires fewer total treatments for the same health gain. Whilst TasP can greatly reduce HCV prevalence, incidence of infection, and incidence of reinfection in PWID, assessment of TasP's effectiveness needs to take account of the injecting-partnership network structure and post-treatment behaviour change, and further empirical study is required.

J Iversen, J Grebely, B Catlett, P Cunningham, GJ Dore, L Maher. (**2017**). "Estimating the cascade of hepatitis C testing, care and treatment among people who inject drugs in Australia." Int J Drug Policy **47**: 77-85.

BACKGROUND: Hepatitis C virus (HCV) infection is endemic among people who inject drugs (PWID) globally. Despite high prevalence, treatment uptake is low, with cumulative uptake <10% in most settings. This study aimed to populate the cascade of HCV testing, care and treatment among PWID using data collected in Australia prior to the introduction of broadly accessible interferon-free direct-acting antiviral (DAA) therapies in March 2016. METHODS: The Australian Needle and Syringe Program Survey is a cross-sectional surveillance system that recruits approximately 2300 PWID annually and collects behavioural data and dried blood samples (DBS). HCV antibody and ribonucleic acid (RNA) test results from DBS collected in 2015 were combined with data on HCV diagnostic testing, care and

treatment to populate the HCV cascade among Australian PWID. RESULTS: Among an estimated 93,000 PWID in Australia in 2015, the majority (89%) had a lifetime history of HCV antibody testing. More than half (57%) of PWID tested HCV antibody positive and of these, 79% had detectable HCV RNA consistent with active infection. Less than half (46%) of HCV antibody positive PWID had received confirmatory HCV RNA testing. Among the estimated 43,201 PWID with active infection or chronic infection that had been successfully treated, 31% had received specialist HCV assessment, 8% had received antiviral treatment and 3% were cured. CONCLUSION: This study provides baseline estimates of the cascade of HCV testing, care and treatment among PWID through enhancement of a well-established surveillance mechanism. Characterisation of the HCV cascade among PWID will be crucial to evaluating and monitoring the roll out of direct-acting antiviral therapies in Australia, including assessing potential HCV treatment as prevention benefits.

J Grebely, GJ Dore (**2017**). "Treatment of HCV in persons who inject drugs: Treatment as prevention." Clin Liver Dis (Hoboken) **9**(4): 77-80.

I Gountas, V Sypsa, O Anagnostou, N Martin, P Vickerman, E Kafetzopoulos, A Hatzakis (**2017**). "Treatment and primary prevention in people who inject drugs for chronic hepatitis C infection: is elimination possible in a high-prevalence setting?" Addiction **112**(7): 1290-1299.

> AIMS: To project the impact of scaling-up oral anti-viral therapy and harm reduction on chronic hepatitis C (CHC) prevalence and incidence among people who inject drugs (PWID) in Greece, to estimate the relationship between required treatment levels and expansion of harm reduction programmes to achieve specific targets and to examine whether hepatitis C virus (HCV) elimination among PWID is possible in this high-prevalence setting. DESIGN: A dynamic discrete time, stochastic individual-based model was developed to simulate HCV transmission among PWID incorporating the effect of HCV treatment and harm reduction strategies, and allowing for re-infection following treatment. SETTING/PARTICIPANTS: The population of 8300 PWID in Athens Metropolitan area. MEASUREMENTS: Reduction in HCV prevalence and incidence in 2030 compared with 2016. FINDINGS: Moderate expansion of HCV treatment (treating 4-8% of PWID/year), with a simultaneous increase of 2%/year in harm reduction coverage (from 44 to 72% coverage over 15 years), was projected to reduce CHC prevalence among PWID in Athens by 46.2-94.8% in 2030, compared with 2016. CHC prevalence would reduce to below 10% within the next 4-5 years if annual HCV treatment numbers were increased up to 16-20% PWID/year. The effect of harm reduction on incidence was more pronounced under lower treatment rates. CONCLUSIONS: Based on theoretical model projections, scaled-up hepatitis C virus treatment and harm reduction interventions could achieve major reductions in hepatitis C virus incidence and prevalence among people who inject drugs in Athens, Greece by 2030. Chronic hepatitis C could be eliminated in the next 4-5 years by increasing treatment to more than 16% of people who inject drugs per year combined with moderate increases in harm reduction coverage.

Dore, G. J. (**2017**). "Commentary on Gountas et al. (2017): Time to focus on empirical evidence for HCV treatment as prevention." Addiction **112**(7): 1300-1301.

A Cousien, P Leclerc, C Morissette, J Bruneau, É Roy, VC Tran, Y Yazdanpanah, J Cox (**2017**). "The need for treatment scale-up to impact HCV transmission in people who inject drugs in Montreal, Canada: a modelling study." BMC Infect Dis **17**(1): 162.

> BACKGROUND: HCV transmission remains high in people who inject drugs (PWID) in Montreal. New direct-acting antivirals (DAAs), highly effective and more tolerable than previous regimens, make a "Treatment as Prevention" (TasP) strategy more feasible. This study assesses how improvements in the cascade of care could impact hepatitis C burden among PWID in Montreal. METHODS: We used a dynamic model to simulate HCV incidence and prevalence after 10 years, and cirrhosis complications after 10 and 40 years. Eight scenarios of improved cascade of care were examined. RESULTS: Using a baseline incidence and prevalence of 22.1/100 person-years (PY) and 53.1%, implementing the current cascade of care using DAAs would lead to HCV incidence and prevalence estimates at 10 years of 9.4/100PY and 55.8%, respectively. Increasing the treatment initiation rate from 5%/year initially to 20%/year resulted in large decreases in incidence (6.4/100PY), prevalence (36.6%), and cirrhosis

complications (-18%/-37% after 10/40 years). When restricting treatment to fibrosis level >/= F2 instead of F0 (reference scenario), such decreases in HCV occurrence were unreachable. Improving the whole cascade of care led to the greatest effect by halving both the incidence and prevalence at 10 years, and the number of cirrhosis complications after 40 years. CONCLUSIONS: The current level of treatment access in Montreal is limiting a massive decrease in hepatitis C burden among PWID. A substantial treatment scale-up, regardless of fibrosis level, is necessary. While improving the rest of the cascade of care is necessary to optimize a TasP strategy and control the HCV epidemic, a treatment scale-up is first needed.

JD Leask, JF Dillon (**2016**). "Review article: treatment as prevention - targeting people who inject drugs as a pathway towards hepatitis C eradication." Aliment Pharmacol Ther **44**(2): 145-156.

BACKGROUND: Hepatitis C virus (HCV) is a leading cause of chronic liver disease worldwide. HCV predominates in people who inject drugs; a group in whom anti-viral therapy has previously been withheld on the basis of chaotic lifestyles and associated risks of reinfection. New research has emerged which suggests that by specifically targeting HCV-infected people who inject drugs for treatment, the pool of HCV would deplete, thus reducing overall transmission and eventually leading to HCV eradication. AIM: To outline the requirements for HCV eradication and review the evidence that this is achievable. METHODS: Expert review of the literature. RESULTS: The achievement of HCV eradication using 'treatment as prevention' is supported by numerous epidemiological modelling studies employing a variety of models in several contexts including people who inject drugs, men who have sex with men and prisoners. More recent studies also incorporate the newer, more efficacious direct-acting anti-viral drugs. These drugs have been shown to be safe and effective in people who inject drugs in clinical trials. There is no empirical evidence of the impact of treatment as prevention strategies on population prevalence. CONCLUSIONS: This review highlights the efforts to control HCV and evaluates the possibilities of achieving eradication of HCV. Currently, the technologies required to achieve HCV eradication exist, but the infrastructure to deliver them is not generally available or of insufficient scale outside of specific areas. Such areas are yet to demonstrate that elimination is possible, but results of studies in these areas are awaited. Such a demonstration would be proof of principle for eradication. Although we are aspiring towards HCV eradication, elimination is the more realistic prospect.

A Cousien, VC Tran, S Deuffic-Burban, M Jauffret-Roustide, J-S Dhersin, Y Yazdanpanah (**2016**). "Hepatitis C treatment as prevention of viral transmission and liver-related morbidity in persons who inject drugs." Hepatology **63**(4): 1090-1101.

UNLABELLED: Hepatitis C virus (HCV) seroprevalence remains high in people who inject drug (PWID) populations, often above 60%. Highly effective direct-acting antiviral (DAA) regimens (90% efficacy) are becoming available for HCV treatment. This therapeutic revolution raises the possibility of eliminating HCV from this population. However, for this, an effective cascade of care is required. In the context of the available DAA therapies, we used a dynamic individual-based model including a model of the PWID social network to simulate the impact of improved testing, linkage to care, and adherence to treatment, and of modified treatment recommendation on the transmission and on the morbidity of HCV in PWID in France. Under the current incidence and cascade of care, with treatment initiated at fibrosis stage >/=F2, HCV prevalence decreased from 42.8% to 24.9% (95% confidence interval: 24.8-24.9) after 10 years. Changing treatment initiation criteria to treat from F0 was the only intervention leading to a substantial additional decrease in prevalence, which fell to 11.6% (95% CI: 11.6-11.7) at 10 years. Combining this change with improved testing, linkage to care, and adherence to treatment decreased HCV prevalence to 7.0% (95% CI: 7.0-7.1) at 10 years and avoided 15% (95% CI: 14-17) and 29% (95% CI: 28-30) of cirrhosis complications over 10 and 40 years, respectively. CONCLUSIONS: Major decreases in prevalent HCV infections occur only when treatment is initiated at early stages of fibrosis, suggesting that systematic treatment in PWID, where incidence remains high, would be beneficial. However, elimination within the 10 next years will be difficult to achieve using treatment alone, even with a highly improved cascade of care.

JS Doyle, EJ Aspinall, SJ Hutchinson, B Quinn, C Gore, SZ Wiktor, ME Hellard (**2015**) Global policy and access to new hepatitis C therapies for people who inject drugs. Int J Drug Policy. Nov;26(11):1064-71. doi: 10.1016/j.drugpo.2015.05.008. Epub 2015 Jun 2.

People who inject drugs (PWID) are disproportionately affected by hepatitis C virus (HCV). This review outlines policy recommendations made in the 2014 World Health Organisation (WHO) Guidelines on Screening, Care and Treatment of HCV and their relevance to PWID. It also canvasses issues that will affect translation of these global guidelines into practice. The first global HCV guidelines released by WHO have recently advocated targeted HCV testing for PWID, assessment of liver disease and support for alcohol reduction during care. They also strongly advocate treatment using currently licensed direct-acting antiviral agents for all individuals, in particular PWID as a key affected population. New HCV treatment regimens have the potential to cure more than 90% of treated individuals. Scaling-up treatment among PWID has the potential to improve individual and population health by reducing HCV transmission, improving quality of life and supporting behaviour modifications that lead to less risk-taking over time. PWID face several barriers to accessing HCV care and treatment that need to be overcome. Testing services need re-orientation toward PWID, individuals need to be informed of their results and provided with direct linkage to ongoing care. Health services need to provide care in the community using simpler, cheaper and more accessible modes of delivery. Healthcare costs and pharmaceutical costs need to be minimised so PWID, who are highly marginalised, can access HCV treatment. Sustained scale-up of treatment for PWID could simultaneously improve individual health and achieve the goal of eliminating HCV transmission among this high-risk and vulnerable group.

SJ Hutchinson, JF Dillon, R Fox, SA McDonald, HA Innes, A Weir, A McLeod, EJ Aspinall, NE Palmateer, A Taylor, A Munro, H Valerio, G Brown, DJ Goldberg (**2015**). Expansion of HCV treatment access to people who have injected drugs through effective translation of research into public health policy: Scotland's experience. Int J Drug Policy. Nov;26(11):1041-9. doi: 10.1016/j.drugpo.2015.05.019. Epub 2015 Jun 6.

Seven years have elapsed since the Scottish Government launched its Hepatitis C Action Plan - a Plan to improve services to prevent transmission of infection, particularly among people who inject drugs (PWID), identify those infected and ensure those infected receive optimal treatment. The Plan was underpinned by industrial scale funding (around £100 million, in addition to the general NHS funding, will have been invested by 2015), and a web of accountable national and local multi-disciplinary multi-agency networks responsible for the planning, development and delivery of services. Initiatives ranged from the introduction of testing in specialist drug services through finger-prick blood sampling by non-clinical staff, to the setting of government targets to ensure rapid scale-up of antiviral therapy. The Plan was informed by comprehensive national monitoring systems, indicating the extent of the problem not just in terms of numbers infected, diagnosed and treated but also the more penetrative data on the number advancing to end-stage liver disease and death, and also through compelling modelling work demonstrating the potential beneficial impact of scaling-up therapy and the mounting cost of not acting. Achievements include around 50% increase in the proportion of the infected population diagnosed (38% to 55%); a sustained near two-and-a-half fold increase in the annual number of people initiated onto therapy (470 to 1050) with more pronounced increases among PWID (300 to 840) and prisoners (20 to 140); and reversing of an upward trend in the overall number of people living with chronic infection. The Action Plan has demonstrated that a Government-backed, coordinated and invested approach can transform services and rapidly improve the lives of thousands. Cited as "an impressive example of a national strategy" by the Global Commission on Drug Policy, the Scottish Plan has also provided fundamental insights of international relevance into the management of HCV among PWID.

M Alavi, T Spelman, GV Matthews, PS Haber, C Day, I van Beek, N Walsh, B Yeung, J Bruneau, K Petoumenos, K Dolan, JM Kaldor, GJ Dore, M Hellard, J Grebely, ATAHC Study Group. Injecting Risk Behaviours Following Treatment for Hepatitis C Virus Infection Among People Who Inject Drugs: The Australian Trial in Acute Hepatitis C. Int J Drug Policy. **2015** Oct;26(10):976*-83

Background: A barrier to hepatitis C virus (HCV) treatment among people who inject drugs (PWID) has been a concern that interferon-based HCV treatment may increase injecting risk behaviours. This study

evaluated recent (past month) injecting risk behaviours during follow-up among PWID that did and did not receive HCV treatment.

Methods: The Australian Trial in Acute Hepatitis C (ATAHC) was a prospective study of natural history and treatment of recent HCV infection. Analyses were performed using generalized estimating equations.

Results: Among 124 participants with a history of injecting drug use (median age 32 years), 69% were male, and 68% were treated for HCV infection. HCV treatment was not associated with an increase in recent injecting drug use (adjusted odds ratio (aOR) 1.06, 95% CI 0.93, 1.21) or recent used needle and syringe borrowing during follow-up (aOR 0.99, 95% CI 0.89, 1.08). HCV treatment was associated with a decrease in recent ancillary injecting equipment sharing during follow-up (aOR 0.85, 95% CI 0.74, 0.99). Further, among treated participants who remained in follow-up (n=24), ancillary injecting equipment sharing significantly decreased from 54% at enrolment to 17% during follow-up (P=0.012).

Conclusions: HCV treatment was not associated with drug use or used needle and syringe borrowing during follow-up, but was associated with decreased ancillary injecting equipment sharing during follow-up. Programs to enhance HCV assessment and treatment among PWID should be expanded, given that HCV treatment does not lead to increases in injecting risk behaviours and has previously been demonstrated to be safe and effective among PWID.

Trial registration: ClinicalTrials.gov NCT00192569.

DC Perlman, AE Jordan, A Uuskula, DT Huong, CL Masson, BR Schackman, DC Des Jarlais (**2015**). "An international perspective on using opioid substitution treatment to improve hepatitis C prevention and care for people who inject drugs: Structural barriers and public health potential." Int J Drug Policy **26**(11): 1056-1063.

People who inject drugs (PWID) are central to the hepatitis C virus (HCV) epidemic. Opioid substitution treatment (OST) of opioid dependence has the potential to play a significant role in the public health response to HCV by serving as an HCV prevention intervention, by treating non-injection opioid dependent people who might otherwise transition to non-sterile drug injection, and by serving as a platform to engage HCV infected PWID in the HCV care continuum and link them to HCV treatment. This paper examines programmatic, structural and policy considerations for using OST as a platform to improve the HCV prevention and care continuum in 3 countries-the United States, Estonia and Viet Nam. In each country a range of interconnected factors affects the use OST as a component of HCV control. These factors include (1) that OST is not yet provided on the scale needed to adequately address illicit opioid dependence, (2) inconsistent use of OST as a platform for HCV services, (3) high costs of HCV treatment and health insurance policies that affect access to both OST and HCV treatment, and (4) the stigmatization of drug use. We see the following as important for controlling HCV transmission among PWID: (1) maintaining current HIV prevention efforts, (2) expanding efforts to reduce the stigmatization of drug use, (3) expanding use of OST as part of a coordinated public health approach to opioid dependence, HIV prevention, and HCV control efforts, (4) reductions in HCV treatment costs and expanded health system coverage to allow population level HCV treatment as prevention and OST as needed. The global expansion of OST and use of OST as a platform for HCV services should be feasible next steps in the public health response to the HCV epidemic, and is likely to be critical to efforts to eliminate or eradicate HCV.

RS Mwatelah, RM Lwembe, S Osman, BR Ogutu, R Aman, RC Kitawi, LN Wangai, FA Oloo, GO Kokwaro, W Ochieng (**2015**). "Co-Infection Burden of Hepatitis C Virus and Human Immunodeficiency Virus among Injecting Heroin Users at the Kenyan Coast." PLoS One **10**(7): e0132287.

BACKGROUND: Injection drug use is steadily rising in Kenya. We assessed the prevalence of both human immunodeficiency virus type 1 (HIV-1) and hepatitis C virus (HCV) infections among injecting heroin users (IHUs) at the Kenyan Coast. METHODS: A total of 186 IHUs (mean age, 33 years) from the Omari rehabilitation center program in Malindi were consented and screened for HIV-1 and HCV by serology and PCR and their CD4 T-cells enumerated by FACS. RESULTS: Prevalence of HIV-1 was 87.5%, that of HCV was 16.4%, co-infection was 17.9% and 18/152 (11.8%) were uninfected. Only 5.26% of the HIV-1 negative injectors were HCV positive. Co-infection was higher among injectors aged 30 to 40 years

(20.7%) and among males (22.1%) than comparable groups. About 35% of the injectors were receiving antiretroviral treatment (ART). Co-infection was highest among injectors receiving D4T (75%) compared to those receiving AZT (21.6%) or TDF (10.5%) or those not on ART (10.5%). Mean CD4 T-cells were 404 (95% CI, 365 - 443) cells/mm3 overall, significantly lower for co-infected (mean, 146; 95% CI 114 - 179 cells/mm3) than HIV mono infected (mean, 437, 95% CI 386 - 487 cells/mm3, p<0.001) or uninfected (mean, 618, 95% CI 549 - 687 cells/mm3, p<0.001) injectors and lower for HIV mono-infected than uninfected injectors (p=0.002). By treatment arm, CD4 T-cells were lower for injectors receiving D4T (mean, 78; 95% CI, 0.4 - 156 cells/mm3) than TDF (mean 607, 95% CI, 196 - 1018 cells/mm3, p=0.005) or AZT (mean 474, 95% CI -377 - 571 cells/mm3, p=0.004). CONCLUSION: Mono and dual infections with HIV-1 and HCV is high among IHUs in Malindi, but ART coverage is low. The co-infected IHUs have elevated risk of immunodeficiency due to significantly depressed CD4 T-cell numbers. Coinfection screening, treatment-as-prevention for both HIV and HCV and harm reduction should be scaled up to alleviate infection burden.

M Hickman, D De Angelis, P Vickerman, S Hutchinson, NK Martin (**2015**). "Hepatitis C virus treatment as prevention in people who inject drugs: testing the evidence." Curr Opin Infect Dis **28**(6): 576-582.

PURPOSE OF REVIEW: The majority of hepatitis C virus (HCV) infections in the United Kingdom and many developing countries were acquired through injecting. New clinical guidance suggests that HCV treatment should be offered to people with a transmission risk - such as people who inject drugs (PWID) - irrespective of severity of liver disease. We consider the strength of the evidence base and potential problems in evaluating HCV treatment as prevention among PWID. RECENT FINDINGS: There is good theoretical evidence from dynamic models that HCV treatment for PWID could reduce HCV chronic prevalence and incidence among PWID. Economic evaluations from high-income settings have suggested HCV treatment for PWID is cost-effective, and that in many settings HCV treatment of PWID could be more cost-effective than treating those at an equivalent stage with no ongoing transmission risk. Epidemiological studies of older interferon treatments have suggested that PWID can achieve similar treatment outcomes to other patient groups treated for chronic HCV. Impact and cost-effectiveness of HCV treatment is driven by the potential 'prevention benefit' of treating PWID. Model projections suggest that more future infections, end stage liver disease, and HCV-related deaths will be averted than lost through reinfection of PWID treated successfully for HCV. However, there is to date no empirical evidence from trials or observational studies that test the model projections and 'prevention benefit' hypothesis. In part this is because of uncertainty in the evidence base but also there is unlikely to have been a change in HCV prevalence due to HCV treatment because PWID HCV treatment rates historically in most sites have been low, and any scale-up and switch to the new direct acting antiviral has not yet occurred. There are a number of key uncertainties in the data available on PWID that need to be improved and addressed to evaluate treatment as prevention. These include estimates of the prevalence of PWID, measurements of HCV chronic prevalence and incidence among PWID, and how to interpret reinfection rates as potential outcome measures. SUMMARY: Eliminating HCV through scaling up treatment is a theoretical possibility. But empirical data are required to demonstrate that HCV treatment can reduce HCV transmission, which will require an improved evidence base and analytic framework for measuring PWID and HCV prevalence.

M Hellard, E McBryde, RS Davis, DA Rolls, P Higgs, C Aitken, A Thomson, J Doyle, P Pattison, G Robins (**2015**). "Hepatitis C transmission and treatment as prevention - The role of the injecting network." Int J Drug Policy **26**(10): 958-962.

BACKGROUND: The hepatitis C virus (HCV) epidemic is a major health issue; in most developed countries it is driven by people who inject drugs (PWID). Injecting networks powerfully influence HCV transmission. In this paper we provide an overview of 10 years of research into injecting networks and HCV, culminating in a network-based approach to provision of direct-acting antiviral therapy. METHODS: Between 2005 and 2010 we followed a cohort of 413 PWID, measuring HCV incidence, prevalence and injecting risk, including network-related factors. We developed an individual-based HCV transmission model, using it to simulate the spread of HCV through the empirical social network of PWID. In addition, we created an empirically grounded network model of injecting relationships using exponential random

graph models (ERGMs), allowing simulation of realistic networks for investigating HCV treatment and intervention strategies. Our empirical work and modelling underpins the TAP Study, which is examining the feasibility of community-based treatment of PWID with DAAs. RESULTS: We observed incidence rates of HCV primary infection and reinfection of 12.8 per 100 person-years (PY) (95%CI: 7.7-20.0) and 28.8 per 100 PY (95%CI: 15.0-55.4), respectively, and determined that HCV transmission clusters correlated with reported injecting relationships. Transmission modelling showed that the empirical network provided some protective effect, slowing HCV transmission compared to a fully connected, homogenous PWID population. Our ERGMs revealed that treating PWID and all their contacts was the most effective strategy and targeting treatment to infected PWID with the most contacts the least effective. CONCLUSION: Networks-based approaches greatly increase understanding of HCV transmission and will inform the implementation of treatment as prevention using DAAs.

M Harris, E Albers, T Swan (**2015**). "The promise of treatment as prevention for hepatitis C: Meeting the needs of people who inject drugs?" Int J Drug Policy **26**(10): 963-969.

Treatment as prevention (TasP) is a concept common to the HIV sector. In this commentary we draw on the literature addressing HIV and HCV TasP, alongside qualitative HCV research, to critically appraise the promise of TasP for HCV and assess the needs of PWID in the future of HCV care. With the advent of highly effective direct-acting antiviral HCV treatments, TasP is now under consideration for HCV. A growing body of literature documents numerous social structural barriers to HCV treatment access and uptake for PWID, among whom HCV is highly prevalent. Yet these barriers - and suggestions for surmounting them - are rarely included in emergent literature on HCV TasP. Although HCV TasP has important advocacy potential for increasing treatment access among PWID, critical reflection on its implications are warranted. We outline potential limitations of TasP for HCV and the conditions under which it might be optimised. We argue that HCV treatment as a prevention strategy can only be realisable in a context of enhanced harm reduction access, meaningful community engagement, and enabling environment interventions informed by the needs and perspectives of PWID.

AS de Vos, M Prins, MEE Kretzschmar (**2015**). "Hepatitis C virus treatment as prevention among injecting drug users: who should we cure first?" Addiction **110**(6): 975-983.

BACKGROUND AND AIMS: Treatment of injecting drug users (IDU) for hepatitis C virus (HCV) infection may prevent onward transmission. Treating individuals who often share injecting equipment is most likely to prevent new infections. However, these high-risk IDU are also more likely to become re-infected than low-risk IDU. We investigated to which group treatment is best targeted. DESIGN: We modelled the expected benefits per treatment of one chronically HCV-infected IDU in a population of low- and high-risk IDU. The benefits of treating one low- or one high-risk IDU were compared. MEASUREMENTS: Benefits included the probability for the treated IDU to become and remain uninfected, as well as the expected number of prevented infections to others (i.e. we quantified the total expected decrease in chronic infections). FINDINGS: We found a threshold in HCV-RNA prevalence above which treating low-risk IDU, and below which treating high-risk IDU, resulted in the greatest benefits. This threshold was at 50% of exchanged syringes being HCV contaminated. When 42% of IDU engaged in high-risk behaviour (borrowing and lending out syringes 7.3 times more frequently than low-risk IDU), the corresponding threshold of HCV-RNA prevalence among IDU was at 32%. Larger-risk heterogeneity led to a lower corresponding threshold among IDU. A combination of HCV treatment and 50% risk reduction was best directed at high-risk IDU for prevalence among syringes up to 59%. The threshold was marginally sensitive to changes in disease and treatment variables. CONCLUSIONS: When more than half of all exchanged syringes in a population of injecting drug users (IDU) are contaminated by hepatitis C virus, it is most efficient to treat low-risk IDU first. Below this threshold, it is most efficient to treat high-risk IDU first.

GJ MacArthur, E van Velzen, N Palmateer, J Kimber, A Pharris, V Hope, A Taylor, K Roy, E Aspinall, D Goldberg, T Rhodes, D Hedrich, M Salminen, M Hickman, SJ Hutchinson (**2014**). Interventions to prevent HIV and Hepatitis C in people who inject drugs: a review of reviews to assess evidence of effectiveness. Int J Drug Policy. Jan;25(1):34-52. doi: 10.1016/j.drugpo.2013.07.001. Epub 2013 Aug 21.

M Hellard, DA Rolls, R Sacks-Davis, G Robins, P Pattison, P Higgs, C Aitken, E McBryde (**2014**). "The impact of injecting networks on hepatitis C transmission and treatment in people who inject drugs." Hepatology **60**(6): 1861-1870.

J Grebely, GJ Dore (**2014**). "Can hepatitis C virus infection be eradicated in people who inject drugs?" Antiviral Res **104**: 62-72.

AS de Vos, ME Kretzschmar (**2014**). "Benefits of hepatitis C virus treatment: a balance of preventing onward transmission and re-infection." Math Biosci **258**: 11-18.

L Wiessing, M Ferri, B Grady, M Kantzanou, I Sperle, KJ Cullen, EMCDDA DRID group; A Hatzakis, M Prins, P Vickerman, JV Lazarus, VD Hope, C Matheï. Hepatitis C Virus Infection Epidemiology Among People Who Inject Drugs in Europe: A Systematic Review of Data for Scaling Up Treatment and Prevention. PLoS One. **2014** Jul 28;9(7):e103345

J Grebely, GV Matthews, AR Lloyd, GJ Dore (**2013**). "Elimination of hepatitis C virus infection among people who inject drugs through treatment as prevention: feasibility and future requirements." Clin Infect Dis **57**(7): 1014-1020.

P Bruggmann (**2013**). "Treatment as prevention: the breaking of taboos is required in the fight against hepatitis C among people who inject drugs." Hepatology **58**(5): 1523-1525.

3. HCV Treatment as prevention in Prisoners

EJ Aspinall, JV Fernandez-Montero (**2020**). Commentary on Bretana et al. (2020): Prevention and treatment in the prison setting will be key to achieving HCV elimination. Addiction. May;115(5):915-916. doi: 10.1111/add.14995. Epub 2020 Mar 4.

Comment on: https://pubmed.ncbi.nlm.nih.gov/31633853/

L Lafferty, J Rance, J Grebely, GJ Dore, AR Lloyd, C Treloar, SToP-C Study Group (**2020**). Perceptions and concerns of hepatitis C reinfection following prison-wide treatment scale-up: Counterpublic health amid hepatitis C treatment as prevention efforts in the prison setting. Int J Drug Policy. Mar;77:102693. doi: 10.1016/j.drugpo.2020.102693. Epub 2020 Feb 8.

Background: Hepatitis C (HCV) infection is highly prevalent within the prison setting. Direct-acting antiviral (DAA) therapies have changed the HCV treatment landscape, offering simple treatment (with minimal side-effects) and high efficacy. These advances have enabled the first real-world study of HCV treatment as prevention (TasP), the Surveillance and Treatment of Prisoners with hepatitis C (SToP-C) study. This paper draws on data from qualitative interviews completed with SToP-C participants following prison-wide DAA treatment scale-up.

Methods: Semi-structured interviews were undertaken with 23 men in prison following HCV treatment completion to identify ongoing risk practices, perceptions of strategies for HCV prevention within the prison setting, experiences of HCV treatment (as prevention), and perceptions of reinfection following cure. Analysis was undertaken using a counterpublic health lens to identify risks and perceptions of reinfection among people treated for HCV within the prison setting.

Results: Participants identified a number of challenges of meaningful HCV 'cure' in the absence of increased access to prevention strategies (e.g., opioid agonist therapy and prison needle syringe programs) along with concerns that 'cure' was only temporary whilst incarcerated. 'Cure' status included self-perceptions of being "clean", while also imposing responsibility on the individual to maintain their 'cure' status.

Conclusion: HCV DAA treatment is provided somewhat under the guise of 'cure is easy', but fails to address the ongoing risk factors experienced by people who inject drugs in prisons, as well as other people in prison who may be at risk of blood-to-blood exposure. Health messaging regarding HCV treatment and treatment for reinfection should be tailored to ensure patient-centred care. Health interventions in prison must address the whole person and the circumstances in which they live, not just the illness.

L Lafferty, TC Wild, J Rance, C Treloar (**2018**). "A policy analysis exploring hepatitis C risk, prevention, testing, treatment and reinfection within Australia's prisons." Harm Reduct J **15**(1): 39.

BACKGROUND: Hepatitis C (HCV) is a global public health concern. There is a global prevalence of 15% among the world's prisoner population, suggesting the need for priority HCV treatment among this population group. New highly efficacious therapies with low side effects, known as directing-acting antivirals, became available under Australia's universal healthcare scheme on 1 March 2016. This creates an opportune time to trial treatment as prevention as an elimination strategy for HCV in prison settings. This paper examines whether policies in Australian jurisdictions support treatment scale-up to achieve elimination among this priority population. METHODS: A comprehensive search was conducted using Google and other web-based search functions to locate all publicly available policies in each Australian state and territory related to HCV health and HCV-related prison health. Ministers (corrections and health) were contacted from each jurisdiction to identify any additional policies. Inductive and deductive analyses were conducted for each jurisdiction, with documents being assessed against a set of four a priori criteria. Documents included in the analysis were current at 1 September 2017, or 18 months following treatment availability. RESULTS: A total of 18 documents were located, including both health (n = 12) and corrections/prison health (n = 6) documents relevant to HCV. Jurisdictions ranged in their commitments for delivering HCV harm reduction strategies and treatment availability within the prison

setting. CONCLUSION: Few jurisdictions have updated or published HCV-related health or prisoner health policies following availability of directing-acting antivirals. Current policies do not provide effective support for implementing treatment scale-up that could be possible under universal access to HCV treatment among this priority population.

J Stone, NK Martin, M Hickman, SJ Hutchinson, E Aspinall, A Taylor, A Munro, K Dunleavy, E Peters, P Bramley, PC Hayes, DJ Goldberg, P Vickerman (**2017**). Modelling the impact of incarceration and prison-based hepatitis C virus (HCV) treatment on HCV transmission among people who inject drugs in Scotland. Addiction. Jul;112(7):1302-1314. doi: 10.1111/add.13783. Epub 2017 Mar 3.

Background and aims: People who inject drugs (PWID) experience high incarceration rates, and previous incarceration is associated with elevated hepatitis C virus (HCV) transmission risk. In Scotland, national survey data indicate lower HCV incidence in prison than the community (4.3 versus 7.3 per 100 person-years), but a 2.3-fold elevated transmission risk among recently released (< 6 months) PWID. We evaluated the contribution of incarceration to HCV transmission among PWID and the impact of prison-related prevention interventions, including scaling-up direct-acting antivirals (DAAs) in prison.

Design: Dynamic mathematical modelling of incarceration and HCV transmission, using approximate Bayesian computation for model calibration.

Setting: Scotland, UK.

Participants: A simulated population of PWID.

Measurements: Population-attributable fraction (PAF) of incarceration to HCV transmission among PWID. Decrease in HCV incidence and chronic prevalence due to current levels of prison opiate substitution therapy (OST; 57% coverage) and HCV treatment, as well as scaling-up DAAs in prison and/or preventing the elevated risk associated with prison release.

Findings: Incarceration contributes 27.7% [PAF; 95% credible interval (CrI) -3.1 to 51.1%] of HCV transmission among PWID in Scotland. During the next 15 years, current HCV treatment rates (10.4/6.8 per 1000 incarcerated/community PWID annually), with existing prison OST, could reduce incidence and chronic prevalence among all PWID by a relative 10.7% (95% CrI = 8.4-13.3%) and 9.7% (95% CrI = 7.7-12.1%), respectively. Conversely, without prison OST, HCV incidence and chronic prevalence would decrease by 3.1% (95% CrI = -28.5 to 18.0%) and 4.7% (95% CrI = -11.3 to 14.5%). Additionally, preventing the heightened risk among recently released PWID could reduce incidence and chronic prevalence by 45.0% (95% CrI = 19.7-57.5%) and 33.3% (95% CrI = 15.6-43.6%) or scaling-up prison HCV treatments to 80% of chronic PWID prison entrants with sufficient sentences (>16 weeks) could reduce incidence and prevalence by 45.6% (95% CrI = 38.0-51.3%) and 45.5% (95% CrI = 39.3-51.0%), respectively.

Conclusions: Incarceration and the elevated transmission risk following prison release can contribute significantly to hepatitis C virus transmission among people who inject drugs. Scaling-up hepatitis C virus treatment in prison can provide important prevention benefits.

L Azbel, JA Wickersham, MP Wegman, M Polonsky, M Suleymanov, R Ismayilov, S Dvoryak, S Rotberga, FL Altice (**2015**). "Burden of substance use disorders, mental illness, and correlates of infectious diseases among soon-to-be released prisoners in Azerbaijan." Drug Alcohol Depend **151**: 68-75.

BACKGROUND: Despite low HIV prevalence in the South Caucasus region, transmission is volatile. Little data are available from this region about addiction and infectious diseases among prisoners who transition back to communities. METHODS: A nation-wide randomly sampled biobehavioral health survey was conducted in 13 non-specialty Azerbaijani prisons among soon-to-be-released prisoners. After informed consent, participants underwent standardized health assessment surveys and testing for HIV, hepatitis B and C, and syphilis. RESULTS: Of the 510 participants (mean age = 38.2 years), 11.4% were female, and 31.9% reported pre-incarceration drug injection, primarily of heroin. Prevalence of HCV (38.2%), HIV (3.7%), syphilis (3.7%), and HBV (2.7%) was high. Among the 19 HIV-infected inmates, 14 (73.7%) were aware of their HIV status, 12 (63.2%) were receiving antiretroviral therapy (ART), and 5 (26.3%) had CD4 < 350 cells/mL (4 of these were on ART). While drug injection was the most significant independent correlate of HCV (AOR = 12.9; p = 0.001) and a significant correlate of HIV (AOR = 8.2; p = 0.001), both unprotected sex (AOR = 3.31; p = 0.049) and working in Russia/Ukraine (AOR = 4.58; p =

0.008) were also correlated with HIV. CONCLUSION: HIV and HCV epidemics are concentrated among people who inject drugs (PWIDs) in Azerbaijan, and magnified among prisoners. A transitioning HIV epidemic is emerging from migration from high endemic countries and heterosexual risk. The high diagnostic rate and ART coverage among Azerbaijani prisoners provides new evidence that HIV treatment as prevention in former Soviet Union (FSU) countries is attainable, and provides new insights for HCV diagnosis and treatment as new medications become available. Within prison evidence-based addiction treatments with linkage to community care are urgently needed.

Levy, M. H. and S. Larney (**2015**). "The ethics of hepatitis C "treatment as prevention" among prisoners." Hepatology **61**(1): 402.

Hepatitis C virus (HCV) infection is highly prevalent among prisoners. The development of new therapeutics for HCV infection has given rise to recommendations (including by one of us, S.L.) that opt-out HCV testing be implemented in correctional settings, with infected individuals linked to treatment. Increasing testing and treatment of HCV infection in prisons is in line with the paradigm of "treatment as prevention": that by reducing the pool of prevalent HCV infection through treatment, onward transmission will cease. There are two important issues to consider in discussions of HCV treatment as prevention in the prison context.

First, prisoners are in unequal power relationships with custodial and health staff. How can we be sure that consent for HCV testing in an opt-out environment is truly voluntary and free from coercion? Requiring prisoners to choose to not opt-out of an HCV test, and opt-in to an HCV test, may be an effective approach to ensuring voluntariness that also maximizes testing uptake. Furthermore, ensuring that the responsible staff do an adequate job of pretest counseling in an opt-in setting may be a more ethical approach to increasing testing uptake than imposing a policy of opt-out testing.

Second, an important aspect of "treatment as prevention" is the converse: "prevention as treatment," or the prevention of reinfection of treated individuals. In community settings, people successfully treated for HCV infection can usually obtain treatment for substance use disorders, including opioid substitution therapy, to assist in reducing or ceasing injecting drug use, or can access sterile needles and syringes if they do inject. Implementation of these interventions and other harm reduction measures is poor in prisons. The limited options for prisoners wishing to protect themselves against reinfection pose a significant challenge to the success of HCV "treatment as prevention" in prison settings. Anecdotally, prisoners are choosing to defer treatment entry in the absence of the ability to protect themselves from reinfection.

NK Martin, P Vickerman, D Goldberg, M Hickman (**2015**). "HCV treatment as prevention in prison: key issues." Hepatology **61**(1): 402-403.

There are high numbers and proportions of people who inject drugs (PWID) among the prison population—and therefore, inevitably high rates of hepatitis C virus (HCV) among prisoners.1 Therefore, the proposal of using HCV treatment as prevention in prison settings is compelling. Indeed, our theoretical modeling studies have indicated that treatment of those with ongoing HCV transmission risk could prevent onward transmission and reduce HCV chronic prevalence.2, 3 In their letter ("The Ethics of Hepatitis C 'Treatment as Prevention' Among Prisoners"), Levy and Larney rightly highlight the need for truly voluntary HCV testing. We would also like to emphasize that voluntary HCV testing is not enough; our recent cost-effectiveness analysis4 of HCV testing and treatment in the prison health systems highlighted the need to also ensure that infected individuals are referred to treatment and remain in referral contact or on treatment after release or transfer. The high turnover of incarcerated populations and frequent prison transfers in some prison settings therefore poses a challenge. Systems to ensure effective referral into treatment and continuity of care are often not in place, which can substantially limit the effectiveness and cost-effectiveness of a prison-based treatment as prevention strategy.

Levy and Larney also call for greater access to harm reduction interventions within prison for those who successfully complete treatment to protect themselves against reinfection, and caution that reinfection may limit the effectiveness of treatment as prevention in prisons. In a recent study in Scotland the risk of

HCV transmission in prisons was lower than the community, due primarily to widespread access to opiate substitution treatment (OST).5 We agree that greater access to OST is required within prisons, and that if HCV incidence remains high then further harm reduction interventions should be made available for all individuals, not just those who undergo treatment. However, it should be remembered that the time in prison is comparatively short in relation to the overall duration of injecting risk in the community, so the risk of reinfection may well be greater in the community than in prison. We have shown that a combination prevention approach (OST, needle and syringe programs, and HCV treatment) could have a substantial impact on the HCV epidemic in the population.6 HCV case finding and treatment in prison could provide a substantial boost to "treatment as prevention" in the community, precisely because individuals with an ongoing risk of transmitting infection to others may be detected and treated. To date, however, the duration of HCV treatment, problems of ensuring continuity of care in the community, and average durations of imprisonment have mitigated against scaling up HCV treatment in the prison setting.

Many of these issues could be overcome with the advent of highly potent all-oral, interferon-free, direct-acting antiviral regimens for HCV. In particular, these shorter-course treatments with much reduced side effects may substantially increase the feasibility of increasing HCV treatment availability within prison settings. To inform policy, evaluations are needed to gauge the effectiveness and acceptability, particularly from an ethical perspective, of HCV treatment among prisoners, for both individual and population benefit.

4. HCV Treatment as prevention in MSM

T Elliott, GS Cooke, L Garvey (**2020**). "Interventions to reduce acute hepatitis C virus in HIV-positive MSM." Curr Opin Infect Dis **33**(1): 1-9.

PURPOSE OF REVIEW: The WHO has set ambitious targets for hepatitis C virus (HCV) elimination by 2030. In this review, we explore the possibility of HCV micro-elimination in HIV-positive (+) MSM, discussing strategies for reducing acute HCV incidence and the likely interventions required to meet these targets. RECENT FINDINGS: With wider availability of directly acting antivirals (DAAs) in recent years, reductions in acute HCV incidence have been reported in some cohorts of HIV+ MSM. Recent evidence demonstrates that treatment in early infection is well tolerated, cost effective and may reduce the risk of onward transmission. Modelling studies suggest that to reduce incidence, a combination approach including behavioural interventions and access to early treatment, targeting both HIV+ and negative high-risk groups, will be required. HCV vaccine trials have not yet demonstrated efficacy in human studies, however phase one and two studies are ongoing. SUMMARY: Some progress towards the WHO HCV elimination targets has been reported. Achieving sustained HCV elimination is likely to require a combination approach including early access to DAAs in acute infection and reinfection, validated and reproducible behavioural interventions and an efficacious HCV vaccine.

SR Bartlett, TL Applegate, BP Jacka, M Martinello, FM Lamoury, M Danta, D Bradshaw, D Shaw, AR Lloyd, M Hellard, GJ Dore, GV Matthews, J Grebely (**2019**). "A latent class approach to identify multi-risk profiles associated with phylogenetic clustering of recent hepatitis C virus infection in Australia and New Zealand from 2004 to 2015." J Int AIDS Soc **22**(2): e25222.

INTRODUCTION: Over the last two decades, the incidence of hepatitis C virus (HCV) co-infection among men who have sex with men (MSM) living with HIV began increasing in post-industrialized countries. Little is known about transmission of acute or recent HCV, in particular among MSM living with HIV co-infection, which creates uncertainty about potential for reinfection after HCV treatment. Using phylogenetic methods, clinical, epidemiological and molecular data can be combined to better understand transmission patterns. These insights may help identify strategies to reduce reinfection risk, enhancing effectiveness of HCV treatment as prevention strategies. The aim of this study was to identify multi-risk profiles and factors associated with phylogenetic pairs and clusters among people with recent HCV infection. METHODS: Data and specimens from five studies of recent HCV in Australia and New Zealand (2004 to 2015) were used. HCV Core-E2 sequences were used to infer maximum likelihood trees. Clusters were identified using 90% bootstrap and 5% genetic distance threshold. Multivariate logistic regression and latent class analyses were performed. RESULTS: Among 237 participants with Core-E2 sequences, 47% were in a pair/cluster. Among HIV/HCV co-infected participants, 60% (74/123) were in a pair/cluster, compared to 30% (34/114) with HCV mono-infection (p < 0.001). HIV/HCV co-infection (vs. HCV mono-infection; adjusted odds ratio (AOR), 2.37, 95% confidence interval (CI), 1.45, 5.15) was independently associated with phylogenetic clustering. Latent class analysis identified three distinct risk profiles: (1) people who inject drugs, (2) HIV-positive gay and bisexual men (GBM) with low probability of injecting drug use (IDU) and (3) GBM with IDU & sexual risk behaviour. Class 2 (vs. Class 1, AOR 3.40; 95% CI, 1.52, 7.60), was independently associated with phylogenetic clustering. Many clusters displayed homogeneous characteristics, such as containing individuals exclusively from one city, individuals all with HIV/HCV co-infection or individuals sharing the same route of acquisition of HCV. CONCLUSIONS: Clusters containing individuals with specific characteristics suggest that HCV transmission occurs through discrete networks, particularly among HIV/HCV co-infected individuals. The greater proportion of clustering found among HIV/HCV co-infected participants highlights the need to provide broad direct-acting antiviral access encouraging rapid uptake in this population and ongoing monitoring of the phylogeny.

DL Braun, B Hampel, R Kouyos, H Nguyen, C Shah, M Flepp, M Stöckle, A Conen, C Béguelin, P Künzler-Heule, D Nicca, P Schmid, J Delaloye, M Rougemont, E Bernasconi, A Rauch, HF Günthard, J Böni, JS Fehr, Swiss HIV Cohort Study (**2019**). "High Cure Rates With Grazoprevir-Elbasvir With or Without Ribavirin Guided by Genotypic Resistance Testing Among Human Immunodeficiency Virus/Hepatitis C Virus-coinfected Men Who Have Sex With Men." Clin Infect Dis **68**(4): 569-576.

Background: This study was performed to investigate the efficacy and safety of grazoprevir-elbasvir guided by baseline resistance-associated substitutions (RASs) in the Swiss HCVree Trial. Methods: We performed hepatitis C virus (HCV) RNA screening among all men who have sex with men (MSM) enrolled in the Swiss HIV Cohort Study. Individuals with replicating HCV genotype 1 or 4 infection were eligible for grazoprevir-elbasvir treatment. Genotype 1a-infected individuals with baseline RASs and genotype 4-infected individuals with prior failure of HCV treatment received 16 weeks of grazoprevir-elbasvir combined with ribavirin. All other individuals received 12 weeks of grazoprevir-elbasvir alone. Patients reporting unprotected sex with occasional partners were offered a HCV risk reduction-oriented behavioral intervention. Results: We screened 3722 MSM and identified 177 (4.8%) with replicating infection. A total of 122 individuals (3.3%) were eligible for study treatment. Six of 76 patients infected with genotype 1a (7.3%) harbored baseline RASs. Sustained virological response after 12 weeks of follow-up was achieved in 121 patients (99%), including all with genotype 1a infection. Overall, 8 serious adverse events occurred, none of which was related to the study drug. Seventy-five percent of eligible MSM participated in the risk counseling program. Conclusions: Grazoprevir-elbasvir for 12 or 16 weeks, with or without ribavirin, achieved high cure rates and had an excellent safety profile. Unique to other studies, the treatment duration was guided by the presence of baseline RASs among genotype 1a-infected individuals, and the treatment phase was accompanied by an HCV risk reduction-oriented behavioral intervention. This successful population-wide treatment approach lays the groundwork to achieve HCV elimination in coinfected MSM. Clinical Trials Registration: NCT02785666.

L Brener, DA Murphy, J Ellard, E Cama, N Fraser, J Murray (**2019**). "Knowledge, attitudes and practices related to hepatitis C among gay and bisexual men in the era of direct-acting antivirals: implications for treatment and prevention." Cult Health Sex: 1-17.

Increases in hepatitis C (HCV) infections among gay and bisexual men have recently been reported in a number of countries, with sexual transmission being the primary route of infection. Given that in countries such as Australia most gay and bisexual men living with HIV are already engaged in clinical care - as are an increasing number of HIV-negative men - there is potential for reducing onward HCV transmission through proactive testing and treatment. This study explored knowledge, attitudes and practices related to HCV among 194 gay and bisexual men collected through an online survey in Australia. Overall, respondents had high levels of HCV knowledge; however, only 76% knew about the availability of new treatments for HCV. Men's knowledge of their own HCV testing history was uncertain, with one in six unaware if they had ever been tested. Among men who reported recent drug injecting, one-third had been injected by someone else, and two-thirds had injected someone else, indicating a subculture of cross-administering within sexualised drug-use networks. We argue that the robust sexual, socio-cultural and clinical infrastructure that has been developed by - and for - gay and bisexual men around HIV care and prevention creates the potential for reducing HCV in this group.

A Boerekamps, GE van den Berk, FN Lauw, EM Leyten, ME van Kasteren, A van Eeden, D Posthouwer, MA Claassen, AS Dofferhoff, DWM Verhagen, WF Bierman, KD Lettinga, FP Kroon, CE Delsing, PH Groeneveld, R Soetekouw, EJ Peters, SJ Hullegie, S Popping, DAMC van de Vijver, CA Boucher, JE Arends, BJ Rijnders (**2018**). "Declining Hepatitis C Virus (HCV) Incidence in Dutch Human Immunodeficiency Virus-Positive Men Who Have Sex With Men After Unrestricted Access to HCV Therapy." Clin Infect Dis **66**(9): 1360-1365.

Background: Direct-acting antivirals (DAAa) cure hepatitis C virus (HCV) infections in 95% of infected patients. Modeling studies predict that universal HCV treatment will lead to a decrease in the incidence of new infections but real-life data are lacking. The incidence of HCV among Dutch human immunodeficiency virus (HIV)-positive men who have sex with men (MSM) has been high for >10 years. In 2015 DAAs became available to all Dutch HCV patients and resulted in a rapid treatment uptake in HIV-positive MSM. We assessed whether this uptake was followed by a decrease in the incidence of HCV infections. Methods: Two prospective studies of treatment for acute HCV infection enrolled patients in 17 Dutch HIV centers, having 76% of the total HIV-positive MSM population in care in the Netherlands. Patients were recruited in 2014 and 2016, the years before and after unrestricted DAA availability. We compared the HCV incidence in both years. Results: The incidence of acute HCV infection decreased from 93 infections during 8290 person-years of follow-up (PYFU) in 2014 (11.2/1000 PYFU; 95% confidence

interval [CI], 9.1-13.7) to 49 during 8961 PYFU in 2016 (5.5/1000 PYFU; 4.1-7.2). The incidence rate ratio of 2016 compared with 2014 was 0.49 (95% CI, .35-.69). Simultaneously, a significant increase in the percentage positive syphilis (+2.2%) and gonorrhea (+2.8%) tests in HIV-positive MSM was observed at sexual health clinics across the Netherlands and contradicts a decrease in risk behavior as an alternative explanation. Conclusions: Unrestricted DAA availability in the Netherlands was followed by a 51% decrease in acute HCV infections among HIV-positive MSM.

L Salazar-Vizcaya, RD Kouyos, J Fehr, D Braun, J Estill, E Bernasconi, J Delaloye, M Stöckle, P Schmid, M Rougemont, G Wandeler, H F Günthard, O Keiser, A Rauch, Swiss HIV Cohort Study (**2018**). "On the potential of a short-term intensive intervention to interrupt HCV transmission in HIV-positive men who have sex with men: A mathematical modelling study." J Viral Hepat **25**(1): 10-18.

Increasing access to direct-acting antiviral (DAA) treatment for hepatitis C virus (HCV) infection and decelerating the rise in high-risk behaviour over the next decade could curb the HCV epidemic among HIV-positive men who have sex with men (MSM). We investigated if similar outcomes would be achieved by short-term intensive interventions like the Swiss-HCVree-trial. We used a HCV transmission model emulating two 12-months intensive interventions combining risk counselling with (i) universal DAA treatment (pangenotypic intervention) and (ii) DAA treatment for HCV genotypes 1 and 4 (replicating the Swiss-HCVree-trial). To capture potential changes outside intensive interventions, we varied time from HCV infection to treatment in clinical routine and overall high-risk behaviour among HIV-positive MSM. Simulated prevalence dropped from 5.5% in 2016 to </=2.0% over the intervention period (June/2016-May/2017) with the pangenotypic intervention, and to </=3.6% with the Swiss-HCVree-trial. Assuming time to treatment in clinical routine reflected reimbursement restrictions (METAVIR >/=F2, 16.9 years) and stable high-risk behaviour in the overall MSM population, prevalence in 2025 reached 13.1% without intensive intervention, 11.1% with the pangenotypic intervention and 11.8% with the Swiss-HCVree-trial. If time to treatment in clinical routine was 2 years, prevalence in 2025 declined to 4.8% without intensive intervention, to 2.8% with the pangenotypic intervention, and to 3.5% with the Swiss-HCVree-trial. In this scenario, the pangenotypic intervention and the Swiss-HCVree-trial reduced cumulative (2016-2025) treatment episodes by 36% and 24%, respectively. Therefore, intensive interventions could reduce future HCV treatment costs and boost the benefits of long-term efforts to prevent high-risk behaviour and to reduce treatment delay. But if after intensive interventions treatment is deferred until F2, short-term benefits of intensive interventions would dissipate in the long term.

NK Martin, A Thornton, M Hickman, C Sabin, M Nelson, GS Cooke, TCS Martin, V Delpech, M Ruf, H Price, Y Azad, EC Thomson, P Vickerman (**2016**). "Can Hepatitis C Virus (HCV) Direct-Acting Antiviral Treatment as Prevention Reverse the HCV Epidemic Among Men Who Have Sex With Men in the United Kingdom? Epidemiological and Modeling Insights." Clin Infect Dis **62**(9): 1072-1080.

BACKGROUND: We report on the hepatitis C virus (HCV) epidemic among human immunodeficiency virus (HIV)-positive men who have sex with men (MSM) in the United Kingdom and model its trajectory with or without scaled-up HCV direct-acting antivirals (DAAs). METHODS: A dynamic HCV transmission model among HIV-diagnosed MSM in the United Kingdom was calibrated to HCV prevalence (antibody [Ab] or RNA positive), incidence, and treatment from 2004 to 2011 among HIV-diagnosed MSM in the UK Collaborative HIV Cohort (UK CHIC). The epidemic was projected with current or scaled-up HCV treatment, with or without a 20% behavioral risk reduction. RESULTS: HCV prevalence among HIV-positive MSM in UK CHIC increased from 7.3% in 2004 to 9.9% in 2011, whereas primary incidence was flat (1.02-1.38 per 100 person-years). Over the next decade, modeling suggests 94% of infections are attributable to high-risk individuals, comprising 7% of the population. Without treatment, HCV chronic prevalence could have been 38% higher in 2015 (11.9% vs 8.6%). With current treatment and sustained virological response rates (status quo), chronic prevalence is likely to increase to 11% by 2025, but stabilize with DAA introduction in 2015. With DAA scale-up to 80% within 1 year of diagnosis (regardless of disease stage), and 20% per year thereafter, chronic prevalence could decline by 71% (to 3.2%) compared to status quo in 2025. With additional behavioral interventions, chronic prevalence could decline further to <2.5% by 2025. CONCLUSIONS: Epidemiological data and modeling suggest a continuing HCV epidemic among HIV-diagnosed MSM in the United Kingdom driven by high-risk

individuals, despite high treatment rates. Substantial reductions in HCV transmission could be achieved through scale-up of DAAs and moderately effective behavioral interventions.

5. HIV Prep and Hepatitis C

M Martinello, J Yee, SR Bartlett, P Read, D Baker, JJ Post, R Finlayson, M Bloch, J Doyle, D Shaw, M Hellard, K Petoumenos, L Lin, P Marks, T Applegate, GJ Dore, GV Matthews, CEASE study team (**2019**). "Moving towards hepatitis C micro-elimination among people living with HIV in Australia: the CEASE study." Clin Infect Dis.

BACKGROUND: Micro-elimination of HCV among people living with HIV may be feasible in Australia, given unrestricted access to direct-acting antiviral (DAA) therapy from 2016. Our aim was to evaluate progress towards elimination goals within HIV/HCV co-infected adults in Australia following universal DAA access. METHODS: The CEASE prospective cohort study enrolled HIV/HCV positive adults, irrespective of viremic status, from 14 primary and tertiary clinics in Australia. Annual and cumulative HCV treatment uptake, outcome, and HCV RNA prevalence were evaluated, with follow-up through May 2018 (median follow-up: 2.63 years). Factors associated with DAA uptake were analysed. RESULTS: Between July 2014 and March 2017, 402 HIV/HCV antibody-positive participants were enrolled (95% male [80% gay and bisexual men,], 13% cirrhosis, 80% history of injecting drug use [39% current injecting]). Following universal DAA access, annual HCV treatment uptake in those eligible increased from 7% and 11% per year in 2014 and 2015, respectively, to 80% in 2016. By 2018, cumulative HCV treatment uptake in those ever eligible for treatment was 91% (336/371). HCV viremic prevalence declined from 82% (95%CI 78%, 86%) in 2014 to 8% (95%CI 6%, 12%) in 2018. Reinfection was reported in only five participants for a reinfection incidence of 0.81 per 100-person years (95% CI 0.34, 1.94). CONCLUSIONS: High uptake and effectiveness of unrestricted DAA therapy in Australia has permitted rapid treatment scale-up, with a dramatic reduction in HCV infection burden and low reinfection rate among people living with HIV, suggesting that micro-elimination is feasible.

E Hoornenborg, L Coyer, A Boyd, RCA Achterbergh, MF Schim van der Loeff, S Bruisten, HJC de Vries, J Koopsen, TJW van de Laar, M Prins, Amsterdam PrEP Project team in the HIV Transmission Elimination AMsterdam (H-TEAM) Initiative. (**2019**). "High incidence of HCV in HIV-negative men who have sex with men using pre-exposure prophylaxis." J Hepatol.

BACKGROUND AND AIMS: Hepatitis C virus (HCV) has emerged as a sexually transmitted infection (STI) among HIV-positive men who have sex with men (MSM). We evaluated HCV-incidence and its risk-factors among HIV-negative MSM using HIV pre-exposure prophylaxis (PrEP). METHODS: Participants of the Amsterdam PrEP project were tested for HCV antibodies or HCV-RNA every 6 months. Participants used daily or event-driven PrEP and could switch regimens during follow-up. We calculated incidence rates (IRs) for overall HCV-infection and separately for primary and re-infection. A univariable Bayesian exponential survival model was used to identify risk-factors associated with incident HCV-infection. The HCV NS5B gene fragment (709 bp) was sequenced and compared to HCV isolates from HIV-positive MSM and other risk groups (n=419) using phylogenetic analysis. RESULTS: Among 350 participants contributing 653.6 person-years (PY), we detected 15 HCV infections in 14 participants (IR=2.30/100PY). There were eight primary infections (IR=1.27/100PY) and seven re-infections (IR=27.8/100PY). IR was 2.71/100PY in daily and 1.15/100PY in event-driven PrEP-users. Factors associated with incident HCV-infection were higher number of receptive condomless anal sex acts with casual partners (posterior Hazards Rate (HR)=1.57 per ln increase, 95% Credibility Interval (CrI)=1.09-2.20), anal STI (posterior HR=2.93, 95%CrI=1.24-7.13), injecting drug use (posterior HR=4.69, 95%CrI=1.61-12.09) and sharing straws when snorting drugs (posterior HR=2.62, 95%CrI=1.09-6.02). We identified robust MSM-specific HCV clusters of subtypes 1a, 4d, 2b and 3a, which included MSM with and without HIV. CONCLUSIONS: HIV-negative MSM on PrEP are at risk for incident HCV-infection, while identified risk-factors are similar to those in HIV-positive MSM. Regular HCV-testing is needed, especially for those with a previous HCV-infection and those reporting risk-factors.

Krakower, D. S. and K. H. Mayer (**2019**). "Routine screening for hepatitis C in MSM on HIV PrEP." Nat Rev Urol **16**(5): 272-274.

A Boerekamps, K Wouters, HSM Ammerlaan, HM Götz, M Laga, BJA Rijnders (**2018**). "Case series on acute HCV in HIV-negative men in regular clinical practice: a call for action." Neth J Med **76**(8): 374-378.

> BACKGROUND: The evidence that HIV treatment as prevention (TasP) and HIV pre-exposure prophylaxis (PrEP) reduces the risk of HIV transmission is overwhelming. But as PrEP and TasP can lead to increased sexual mixing between HIV positive and negative men who have sex with men (MSM), sexually transmitted infections such as acute hepatitis C (HCV), which were thought to be limited to HIV-infected MSM, could become more frequent in HIV uninfected MSM as well. The objective of this study was to describe a series of cases of sexually transmitted HCV infections in HIV-uninfected MSM in the Netherlands and Belgium. METHODS: Through the Dutch Acute HCV in HIV Study (a Dutch-Belgian prospective multicentre study on the treatment of acute HCV infection, NCT02600325) and the Be-PrEP-ared study (a PrEP project in Antwerp, EudraCT2015-000054-37) several acute HCV infections were detected in HIV-negative men. RESULTS: A newly acquired HCV infection was diagnosed in ten HIV-negative MSM. HCV was diagnosed at a sexually transmitted infection (STI) clinic (n = 2), by their general practitioner (n = 2), by their HIV physician (n = 1) or at a PrEP clinic (n = 5). Ten patients reported unprotected anal intercourse and four had a concomitant STI at the time of HCV diagnosis. Six patients reported using drugs during sex. CONCLUSIONS: Our observation calls for a larger nationwide epidemiological study on the prevalence, incidence and risk factors of HCV infection in HIV-uninfected MSM. In the changing landscape of TasP and PrEP, reliable and up-to-date epidemiological data on HCV among HIV-uninfected MSM are needed and will help in developing evidence-based testing policies.

RN Werner, M Gaskins, A Nast, C Dressler (**2018**). "Incidence of sexually transmitted infections in men who have sex with men and who are at substantial risk of HIV infection - A meta-analysis of data from trials and observational studies of HIV pre-exposure prophylaxis." PLoS One **13**(12): e0208107.

> BACKGROUND: Men who have sex with men (MSM) and who engage in condomless anal intercourse with casual partners are at high risk of acquiring sexually transmitted infections (STIs), but reliable epidemiological data are scarce. Studies on HIV pre-exposure prophylaxis (PrEP) enrol MSM who indicate that they engage in behaviour that puts them at high risk of acquiring HIV. Because they also screen for STIs at regular intervals, these studies may serve as a valuable source to estimate incidence rates of STIs in this subpopulation of MSM. METHODS: We systematically searched for trials and observational studies of PrEP in MSM that reported data on the incidence of STIs during the study period. Incidence rates were calculated as events per 100 person-years (py) with 95% confidence intervals (CI). Data from individual studies were pooled building subgroups along study types and geography. We performed sensitivity analyses, including data only from studies that met pre-defined quality criteria. RESULTS: Twenty-four publications on 20 studies were included. The majority of studies reported that sexual behaviour and/or STI incidence remained stable or decreased during the study period. For syphilis, incidence rates ranged from 1.8/100py to 14.9/100py, the pooled estimate was 9.1/100py (95%-CI: 7.7-10.9). Incidence rates for gonorrhoea and chlamydia of any site ranged from 13.3/100py to 43.0/100py and 15.1/100py to 48.5/100py, respectively. Considering only studies that met the criteria for sensitivity analysis yielded pooled estimates of 39.6/100py (95%-CI: 32.9-47.6) and 41.8/100py (95%-CI: 33.9-51.5), respectively. The overall estimate for hepatitis C incidence was 1.3/100py (95%-CI: 1.0-1.8). CONCLUSIONS: Despite partly heterogeneous results, the data depict high incidence rates of STIs among MSM who engage in higher-risk sexual behaviours such as condomless sex with casual partners. This subpopulation of MSM requires access to STI screening at close intervals. By offering access to structures that provide regular STI monitoring and prompt treatment, PrEP may not only decrease HIV incidence but also have beneficial effects in decreasing the burden of STIs.

N Scott, M Stoové, DP Wilson, O Keiser, C El-Hayek, J Doyle, M Hellard (**2018**). "Eliminating hepatitis C virus as a public health threat among HIV-positive men who have sex with men: a multi-modelling approach to understand differences in sexual risk behaviour." J Int AIDS Soc **21**(1).

INTRODUCTION: Outbreaks of hepatitis C virus (HCV) infections among HIV-positive men who have sex with men (MSM) have been observed globally. Using a multi-modelling approach we estimate the time and number of direct-acting antiviral treatment courses required to achieve an 80% reduction in HCV prevalence among HIV-positive MSM in the state of Victoria, Australia. METHODS: Three models of HCV transmission, testing and treatment among MSM were compared: a dynamic compartmental model; an agent-based model (ABM) parametrized to local surveillance and behavioural data ("ABM1"); and an ABM with a more heterogeneous population ("ABM2") to determine the influence of extreme variations in sexual risk behaviour. RESULTS: Among approximately 5000 diagnosed HIV-positive MSM in Victoria, 10% are co-infected with HCV. ABM1 estimated that an 80% reduction in HCV prevalence could be achieved in 122 (inter-quartile range (IQR) 112 to 133) weeks with 523 (IQR 479 to 553) treatments if the average time from HCV diagnosis to treatment was six months. This was reduced to 77 (IQR 69 to 81) weeks if the average time between HCV diagnosis and treatment commencement was decreased to 16 weeks. Estimates were consistent across modelling approaches; however ABM2 produced fewer incident HCV cases, suggesting that treatment-as-prevention may be more effective in behaviourally heterogeneous populations. CONCLUSIONS: Major reductions in HCV prevalence can be achieved among HIV-positive MSM within two years through routine HCV monitoring and prompt treatment as a part of HIV care. Compartmental models constructed with limited behavioural data are likely to produce conservative estimates compared to models of the same setting with more complex parametrizations.

JV Fernandez-Montero, EJ Aspinall, JE Burns (**2017**). "Treatment as Prevention: Should Hepatitis C Learn the Lessons from HIV?" AIDS Rev **19**(4): 212-218.

Long-term experience in the treatment of HIV-infected individuals has shown indirect benefits of early initiation of antiretroviral therapy, particularly in preventing HIV transmission. With the advent of direct-acting antivirals for the treatment of hepatitis C, the strategy of treatment-as-prevention has become feasible. However, economic, clinical, ethical, and public health issues arise from the concept of using therapeutic interventions only as prevention strategies.

Ayoub, H. H. and L. J. Abu-Raddad (**2017**). "Impact of treatment on hepatitis C virus transmission and incidence in Egypt: A case for treatment as prevention." J Viral Hepat **24**(6): 486-495.

Egypt has launched a hepatitis C virus (HCV) treatment programme using direct-acting antivirals (DAAs). Our aim was to assess the impact of five plausible programme scale-up and sustainability scenarios for HCV treatment as prevention in Egypt. We developed and analysed a mathematical model to assess programme impact using epidemiologic, programming and health economics measures. The model was parametrized with current and representative natural history, HCV prevalence and programme data. HCV incidence in Egypt is declining, but will persist at a considerable level for decades unless controlled by interventions. Across the five programme scenarios, 1.75-5.60 million treatments were administered by 2030. Reduction in incidence (annual number of new infections) by 2030 ranged between 29% and 99%, programme-attributed reduction in incidence rate (new infections per susceptible person per year) ranged between 18% and 99%, number of infections averted ranged between 42 393 and 469 599, and chronic infection prevalence reached as low as 2.8%-0.1%. Reduction in incidence rate year by year hovered around 7%-15% in the first decade of the programme in most scenarios. Treatment coverage in 2030 ranged between 24.9% and 98.8%, and number of treatments required to avert one new infection ranged between 9.5 and 12.1. Stipulated targets for HCV by 2030 could not be achieved without scaling-up treatment to 365 000 per year and sustaining it for a decade. In conclusion, DAA scale-up will have an immense and immediate impact on HCV incidence in Egypt. Elimination by 2030 is feasible if sufficient resources are committed to programme scale-up and sustainability. HCV treatment as prevention is a potent and effective prevention approach.

Ishizaki A, Tran VT, Nguyen CH, Tanimoto T, Hoang HTT, Pham HV, Phan CTT, Bi X, Pham TV, Ichimura H. (**2017**). "Discrepancies in prevalence trends for HIV, hepatitis B virus, and hepatitis C virus in Haiphong, Vietnam from 2007 to 2012." PLoS One **12**(6): e0179616.

We previously reported a significant reduction in the prevalence of human immunodeficiency virus type 1 (HIV) from 2007 to 2012 in people who inject drugs (PWID; 35.9% to 18.5%, p < 0.001) and female sex

workers (FSW; 23.1% to 9.8%, p < 0.05), but not in blood donors (BD) or pregnant women, in Haiphong, Vietnam. Our aim in the present study was to assess trends in the prevalence of infection with hepatitis B and C viruses (HBV and HCV, respectively). We also investigated the coinfection rates of HBV and HCV with HIV in the same groups. Between 2007 and 2012, HBV prevalence was significantly decreased in BD (18.1% vs. 9.0%, p = 0.007) and slightly decreased in FSW (11.0% vs. 3.9%, p = 0.21), but not in PWID (10.7% vs. 11.1%, p = 0.84). HCV prevalence was significantly decreased in PWID (62.1% in 2007 vs. 42.7% in 2008, p < 0.0001), but it had rebounded to 58.4% in 2012 (2008 vs. 2012, p < 0.0001). HCV prevalence also increased in FSW: 28.6% in 2007 and 2009 vs. 35.3% in 2012; however, this difference was not significant (2007 vs. 2012, p = 0.41). Rates of coinfection with HBV and HCV among HIV-infected PWID and FSW did not change significantly during the study period. Our findings suggest that the current harm reduction programs designed to prevent HIV transmission in PWID and FSW may be insufficient to prevent the transmission of hepatitis viruses, particularly HCV, in Haiphong, Vietnam. New approaches, such as the introduction of catch-up HBV vaccination to vulnerable adult populations and the introduction of HCV treatment as prevention, should be considered to reduce morbidity and mortality due to HIV and hepatitis virus coinfection in Vietnam.

SR Bartlett, JO Wertheim, RA Bull, GV Matthews, FM Lamoury, K Scheffler, M Hellard, L Maher, GJ Dore, AR Lloyd, TL Applegate, J Grebely (**2017**). "A molecular transmission network of recent hepatitis C infection in people with and without HIV: Implications for targeted treatment strategies." J Viral Hepat **24**(5): 404-411.

Combining phylogenetic and network methodologies has the potential to better inform targeted interventions to prevent and treat infectious diseases. This study reconstructed a molecular transmission network for people with recent hepatitis C virus (HCV) infection and modelled the impact of targeting directly acting antiviral (DAA) treatment for HCV in the network. Participants were selected from three Australian studies of recent HCV from 2004 to 2014. HCV sequence data (Core-E2) from participants at the time of recent HCV detection were analysed to infer a network by connecting pairs of sequences whose divergence was </=.03 substitutions/site. Logistic regression was used to identify factors associated with connectivity. Impact of targeting HCV DAAs at both HIV co-infected and random nodes was simulated (1 million replicates). Among 236 participants, 21% (n=49) were connected in the network. HCV/HIV co-infected participants (47%) were more likely to be connected compared to HCV mono-infected participants (16%) (OR 4.56; 95% CI; 2.13-9.74). Simulations targeting DAA HCV treatment to HCV/HIV co-infected individuals prevented 2.5 times more onward infections than providing DAAs to randomly selected individuals. Results demonstrate that genetic distance-based network analyses can be used to identify characteristics associated with HCV transmission, informing targeted prevention and treatment strategies.

SR Bartlett, B Jacka, RA Bull, F Luciani, GV Matthews, FMJ Lamoury, ME Hellard, B Hajarizadeh, S Teutsch, Bethany White, L Maher, GJ Dore, AR Lloyd, J Grebely, TL Applegate (**2016**). "HIV infection and hepatitis C virus genotype 1a are associated with phylogenetic clustering among people with recently acquired hepatitis C virus infection." Infect Genet Evol **37**: 252-258.

The aim of this study was to identify factors associated with phylogenetic clustering among people with recently acquired hepatitis C virus (HCV) infection. Participants with available sample at time of HCV detection were selected from three studies; the Australian Trial in Acute Hepatitis C, the Hepatitis C Incidence and Transmission Study - Prison and Community. HCV RNA was extracted and Core to E2 region of HCV sequenced. Clusters were identified from maximum likelihood trees with 1000 bootstrap replicates using 90% bootstrap and 5% genetic distance threshold. Among 225 participants with available Core-E2 sequence (ATAHC, n=113; HITS-p, n=90; and HITS-c, n=22), HCV genotype prevalence was: G1a: 38% (n=86), G1b: 5% (n=12), G2a: 1% (n=2), G2b: 5% (n=11), G3a: 48% (n=109), G6a: 1% (n=2) and G6l 1% (n=3). Of participants included in phylogenetic trees, 22% of participants were in a pair/cluster (G1a-35%, 30/85, mean maximum genetic distance=0.031; G3a-11%, 12/106, mean maximum genetic distance=0.021; other genotypes-21%, 6/28, mean maximum genetic distance=0.023). Among HCV/HIV co-infected participants, 50% (18/36) were in a pair/cluster, compared to 16% (30/183) with HCV mono-infection (P=<0.001). Factors independently associated with phylogenetic clustering were HIV co-infection [vs. HCV mono-infection; adjusted odds ratio (AOR) 4.24; 95%CI 1.91, 9.39], and HCV G1a

infection (vs. other HCV genotypes; AOR 3.33, 95%CI 0.14, 0.61).HCV treatment and prevention strategies, including enhanced antiviral therapy, should be optimised. The impact of targeting of HCV treatment as prevention to populations with higher phylogenetic clustering, such as those with HIV co-infection, could be explored through mathematical modelling.

GJ Dore (**2016**). "Hepatitis C treatment as prevention among HIV-infected men who have sex with men: Feasible?" Hepatology **64**(6): 1834-1836.

DL McCollum (**2011**). "Update of the past year: a review from IDSA 2011." Top Antivir Med **19**(5): 187-192.

The Infectious Diseases Society of America Annual Meeting serves as a time of expert review of the year's most important innovations. Important new information on HIV infection incidence was discussed. The remarkable efficacy of "treatment as prevention" in the HIV Prevention Trials Network (HPTN) 052 study and the proper place of oral preexposure prophylaxis were among the important prevention topics. Key engagement-in-care research indicates that only 19% of HIV-infected persons in the United States have a plasma HIV RNA level below the limits of assay detection. Among antiretroviral topics, the role of the newly approved nonnucleoside reverse transcriptase inhibitor (NNRTI) rilpivirine was discussed. Primary care topics for the HIV-infected population included treatment of triglyceride level elevations and bone health. The newly published data on the proper timing of antiretroviral therapy initiation after starting tuberculosis treatment were highlighted. Finally, exciting advances in the treatment of hepatitis C virus (HCV) infection necessitate that practitioners understand the complexities of treating HIV/HCV coinfections.

Part I Treatment As Prevention (TAP) hepatitis C in risk groups

Introduction of the participants
Chairs: Mojca Matitic and Pierre Van Damme

16:30-16h:50   Welcome and opening of the meeting
      • Welcome and opening
      • Introduction of the participants
Greet Hendrickx

1. Hepatitis treatment as prevention in risk groups

Session 1.1: Real-life data of TAP in different risk groups	
16:50-17:10	**Treatment as prevention in risk groups: an overview** *Mojca Matitic*
17:10-17:25	**Treat all or Treatment as prevention in Risk groups** Modelling the potential prevention benefits of a treat-all hepatitis C treatment strategy at global, regional and country levels: A modelling study *Adam Trickey*
17:25- 17:40	**PWID** - Model of care and outcomes in PWID **Iceland** Treatment as Prevention for Hepatitis C (**TraP Hep C)** - a nationwide elimination programme in Iceland using direct-acting antiviral agents.- *Magnus Gottfredsson*
17:40- 17:55	**Scotland** Evaluating the population impact of hepatitis C direct acting antiviral treatment as prevention for people who inject drugs (EPIToPe) - a natural experiment (protocol). *Matthew Hickman,* **Prisoners** - Model of care and outcomes in PWID and prisoners (No speaker confirmed yet) J Stone, NK Martin, M Hickman, SJ Hutchinson, E Aspinall, A Taylor, A Munro, K Dunleavy, E Peters, P Bramley, PC Hayes, DJ Goldberg, P Vickerman (**2017**). Modelling the impact of incarceration and prison-based hepatitis C virus (HCV) treatment on HCV transmission among people who inject drugs in Scotland. Addiction. Jul;112(7):1302-1314. doi: 10.1111/add.13783. Epub 2017 Mar 3
17:55- 18:10	**MSM** - Model of care and outcomes in MSM **The Netherlands –**Declining Hepatitis C Virus (HCV) Incidence in Dutch Human Immunodeficiency Virus-Positive Men Who Have Sex With Men After Unrestricted Access to HCV *Anders Boyd*
17:10- 18:25	**Lessons Learned from HIV TAP program** Treatment as Prevention: Should Hepatitis C Learn the Lessons from HIV? *José Vincent Fernandez-Montero*

Session 1.2: Groups discussion: hepatitis treatment as prevention

Chairs:

18:30-19:30   Groups discussion: hepatitis TAP be included in public health guidelines and recommendations

Questions to be answered:

1. Is there enough scientific evidence to include TAP in hepatitis prevention guidelines in all risks group or in some?

Chair: Thomas Vanwolleghem

2. Should TAP be included in the national hepatitis elimination plan? (responsibilities – resources)

Chair: Daniel Lavanchy

3. Should TAP in risks groups be included in WHO's targets to achieve hepatitis Elimination by 2030? Is Micro elimination the way to go?

Chair: Antons Mozalevskis

PARTICIPANTS LIST

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Duffell	Erika	Sweden
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Kane	Mark	USA
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Lavanchy	Daniel	Switzerland
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