Title

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The HCV epidemics in key populations (including PWID, prisoners, and MSM): the use of DAAs as treatment for prevention

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Abstract

Purpose of Review—The burden of HCV is high among people who inject drugs (PWID) and prisoners, and increasing among HIV-infected men who have sex with men (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 increasing interest in the use of HCV antiviral treatment for prevention in these populations.

Recent Findings—Numerous theoretical modeling 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. Additionally, 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.

Keywords

hepatitis C Virus; prevention; antiviral treatment; people who inject drugs; prison; men who have sex with men

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Introduction

HCV infection is efficiently transmitted through injecting drug use, and therefore people who inject drugs (PWID) are a key risk group. In many high-income countries, PWID are thought to be responsible for the majority (estimated at >80%) of ongoing HCV transmission (1–3), In many low and middle-income countries, transmission among PWID has also emerged as a contributor to HCV epidemics, although in many of these settings iatrogenic transmission may play a greater role(4), HCV prevalence among PWID is heterogeneous both within and between countries, but globally it has been estimated that approximately 65% of PWID are anti-HCV positive (an estimated 10 million PWID), with >80% prevalence reported in 12 countries(4). HCV incidence among PWID ranges from 5 to 45% per year. Additionally, there are high numbers and proportions of PWID among the prison population(5). As a consequence, the burden of HCV is high among prisoners, with a recent meta-analysis estimating over one-quarter of inmates are positive for anti-HCV, equating to approximately 1.65 million with chronic HCV infection(6). Furthermore, HCV transmission within prison is a common occurrence, often due to a lack of access to harm reduction interventions(6). Finally, there increasing concern surrounding the epidemic of HCV among HIV-infected men who have sex with men (MSM), who contribute less towards the overall HCV epidemic but are in urgent need of HCV treatment and prevention interventions due to accelerated liver disease progression and mortality(7).

Despite the effectiveness of traditional harm reduction interventions such as opiate substitution therapy (OST) and high coverage needle and syringe programmes (NSP) at reducing an individual's risk of HCV acquisition(8, 9), HCV chronic prevalence among PWID remains high. Additionally, many prisons do not provide harm reduction, and the vast majority do not provide comprehensive programs (i.e. NSP and OST). Among MSM, there is a lack of evidence-based behavioral interventions to reduce risk behaviors which have been associated with HCV transmission (such as sexual and drug practices associated with mucosal trauma). Therefore, additional prevention interventions in these populations are urgently needed.

Following on from the worldwide interest in the use of HIV antiretoroviral treatment as prevention(10), there is emerging interest in the potential of HCV antiviral treatment as prevention. Importantly, there is insufficient evidence to date of any impact of HIV treatment as prevention among marginal at risk populations such as PWID(11, 12). However, in theory, HCV treatment as prevention could be more effective than HIV treatment as prevention because HCV treatment is finite and curative. In particular, the dramatic improvement in SVR rates, once-daily dosing, and short therapies (8–12 weeks) with interferon-free direct acting antiviral therapies (IFN-free DAAs) has led many to speculate whether HCV treatment could feasibly be scaled-up sufficiently to be used as an effective prevention strategy among those at risk of transmission(3, 13–16). In this paper we discuss the evidence surrounding HCV treatment for prevention among PWID, prisoners, and MSM.

Potential Impact of HCV treatment as prevention among PWID

International guidelines (such as the US National Institutes of Health, AASLD/IDSA, European Association Study for the Liver, International network on Hepatitis in Substance Users, and the World Health Organization) all advocate for the inclusion of people who use drugs in HCV treatment(17–20). Nevertheless, the reality in the IFN-free DAA era may be different. A recent study in the US found that 88% of states include drug and/or alcohol use in their eligibility criteria, with 50% requiring a period of abstinence, and 64% requiring urine drug screening(21). This is despite increasing evidence that treatment for PWID is highly effective; two systematic reviews suggest that sustained viral response rates (SVR) among PWID are comparable to those reported by large randomized controlled trials of pegIFN/RBV treatment (22, 23). Additionally, reported rates of reinfection among PWID are low (1–5% per year)- though very likely subject to considerable selection bias for interferon based treatments (22, 24). HCV treatment rates among PWID are generally reported as low (<3%) even in high income country settings(25–27).

To date, no trials or empirical observational studies have explored whether HCV treatment can reduce HCV prevalence among PWID and prevent onwards transmission. However, several theoretical modelling studies have explored the potential impact and benefits of HCV treatment for prevention among PWID populations(27–41). It is important that models of the impact of HCV treatment are dynamic in order to account both for “prevention benefit” (i.e. averting further transmission) and risk of re-infection. Simple models of disease burden at a country level without HCV transmission can show that increasing HCV treatment will reduce HCV chronic prevalence through treatment(42), but these models neglect the potential risk of reinfection, or the potential prevention benefits of treatment.

Early IFN/RBV based modelling studies explored the potential of treatment as prevention initiatives in generic settings of varied HCV prevalence among PWID (28, 29) or high income country settings like Australia(32, 33, 43) and the UK(44). These generally found that, even with SVR for IFN/RBV of around 60%, modest levels of HCV treatment for PWID could result in marked reductions in HCV chronic prevalence among PWID within 10–15 years for a range of prevalence settings(29). Additionally, HCV treatment for PWID is likely to be more cost-effective than treatment of non or ex-injectors due to the additional prevention benefit in low to moderate chronic HCV prevalence settings(44).

Only one modeling study has explored the implications of HCV treatment for PWID in a low or middle income country setting(34). This study, based in Vietnam, found substantial benefits of scale-up of both HCV treatment with pegIFN/RBV, along with traditional harm reduction interventions(34). This is supported by another analysis which found that scale-up of combination prevention (OST, high coverage NSP, and HCV treatment) could provide even greater prevention impact(31).

More recently, modeling analyses have focused on the potential additional impact of HCV treatment as prevention with direct-acting antiviral therapies with SVR >80%. A modelling analysis in Edinburgh, Scotland; Melbourne, Australia; and Vancouver, Canada reported that scale-up of IFN-free DAA therapy with 90% SVR could lead to substantial reductions

in HCV prevalence in the population(41). For example, in Edinburgh (PWID chronic HCV at 30%) a doubling of HCV treatment rates (to 15 per 1000 PWID annually or 5% of PWID with chronic HCV infection) could halve chronic HCV prevalence and incidence within 10 years(41). However, in settings with higher baseline HCV chronic prevalence among PWID such as Melbourne (50%) and Vancouver (60%), a halving of chronic HCV prevalence could be achieved through a scale-up of treatment by 13–15 fold, with annual treatment rate of 40 per 1000 PWID and 76 per 1000 PWID required, respectively.

Another analysis considered switching to IFN-free DAA (90% SVR) and increasing HCV treatment to the highest currently observed treatment rate in the UK (~26 per 1000 PWID annually). They showed this could lead to a halving of chronic prevalence within a decade in 3 sites in the UK (Plymouth, Dundee, and North Wales), with less impact observed in other sites. Additionally, a recent analysis in France found that due to relatively high current HCV treatment rates among PWID, the introduction of DAAs with 81% SVR could reduce HCV chronic prevalence among PWID from 43% at baseline to 25% within 10 years(35). Finally, modeling has indicated that scale-up of OST or high coverage NSP alongside HCV treatment could reduce the number of expensive IFN-free DAA antiviral treatments required to halve HCV prevalence in a range of settings(31).

However, despite these studies indicating that only modest levels of HCV treatment are required, it seems likely that in many settings (with the exception of France) current treatment rates for PWID are so low that measurable declines in HCV prevalence or incidence among PWID will not be measurable unless further scale-up is achieved, even if IFN-free DAAs are available with high SVR. For example, a recent evaluation of selected services in the UK found highly heterogeneous treatment rates among PWID (from <5 to 26 per 1000 PWID per year). Model projections indicate that in general current HCV treatment rates of PWID have been insufficient to lead to an observable decline in HCV prevalence and maybe insufficient in future, especially given the uncertainty in several important parameters (such as PWID prevalence, and chronic HCV prevalence)(27). Similarly, another modeling analysis indicates that estimated current treatment rates will cause little impact on the epidemic among PWID in Edinburgh, Vancouver, and Melbourne(41).

There is increasing debate on how to best optimize treatment delivery to maximize treatment as prevention benefits. Several studies in Australia(36, 38, 39) have used an individual-based network model to identify the optimal HCV treatment allocation strategy. The Australian analyses use detailed epidemiological data on injecting network connections among PWID in Melbourne to suggest that undertaking a strategy to treat all the contacts of an infected case (treat your friends') could improve the impact of an HCV treatment program over one that treats PWID at random(36, 38, 39). Other modeling analyses have explored the different impact achieved if HCV treatments are allocated towards low or high risk PWID(31, 37, 40, 41) or to those on opiate substitution therapy (31, 33). These analyses have not provided consistent findings, with some suggesting that at moderate to high chronic HCV prevalence among PWID treatment should be targeted to low risk individuals for maximum benefit(37, 40), but another suggesting the opposite(33), or that there is likely to be minimal difference in impact(31, 41). These results primarily differ based on assumptions regarding duration at risk and movement between risk stages or intervention coverage, with

less difference seen in impact the more turnover is present in the population. One study explored the optimization of HCV treatment program timing and implemention to maximize economic and health benefits, finding that the optimal program varied depending on economic or political target(30).

Finally, it is unclear how the prioritization of DAA therapy will affect HCV treatment scale-up among PWID, even in high income countries. International guidelines in 2014 recommended treatment prioritisation for moderate to severe liver disease stages only (F2–F4) (45, 46), whereas updated 2015 European guidelines also include a recommendation for prioritization for those at a risk of HCV transmission(20). A recent dynamic modelling analysis in France explores the impact of HCV treatment as prevention among PWID, and implications of restricting HCV treatment to PWID with moderate or advanced liver disease stages. They show that an expansion of eligibility to include treatment for all at the mild stage would have a dramatic impact on HCV incidence and prevalence due to a substantially increased pool of eligible PWID and therefore higher treatment rates(35). Another modeling analysis in the UK estimated that prioritizing early HCV treatment with IFN-free DAAs as compared to delay until cirrhosis was cost-effective in low-moderate chronic prevalence settings among PWID due to the substantial prevention benefits accrued(47, 48).

HCV treatment as prevention in prison

Prisons could provide an important public health and harm reduction role for PWID, and could provide the opportunity to assess the feasibility of HCV treatment as prevention. PWID have high rates of incarceration due both to the illegal nature of drug use and frequency of drug related crime to support drug use. As a result, HCV infection is very common among prisoners(6). Additionally, the lack of harm reduction interventions in most prisons means that HCV transmission rates can be extremely high, with a meta-analysis estimating incidence rates at 16 per 100 person years among inmates with a history of injecting drug use(6), but ranging from < 1 to over 34 per 100 person years in prisons in Scotland and Australia(5, 49). Prisons also could have a role in HCV case finding and treatment - especially as PWID with an ongoing risk of HCV transmission and who may not yet be in long-term OST programmes can be detected and treated.

To date, the short duration of sentences for PWID (predominately incarcerated for drug related crimes) in many settings may have limited the impact of HCV treatment as prevention among prisoners. For example, a UK based analysis showed that HCV testing and treatment in prisons using 24–48 week PEGIFN/RBV therapy was not cost-effective unless sufficient continuity of care (>=40%) between prison and community can be guaranteed(50). In other words, due to the relatively short incarceration times for many PWID (on average 4 months in the UK), it is crucial to 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. In addition, robust systems to ensure effective referral onto 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. These issues have mitigated against scaling up HCV treatment in the prison setting.

However, highly curative, all-oral shorter duration treatments (8–12 weeks) should greatly enhance HCV treatment as prevention feasibility through increased demand by inmates, ease of delivery and increased treatment completion rates, and therefore could be more cost-effective(51).

HCV treatment as prevention among men who have sex with men (MSM)

In recent years there has been a rapid spread of HCV among HIV-positive men who have sex with men (MSM) documented in Europe, Australia, and the US(7). The burden of HCV is currently much lower than among PWID (HCV prevalence is <10% among HIV-positive MSM although there is evidence of increasing incidence rates in some settings such as Switzerland(7, 52)). In contrast to PWID, the absolute numbers of HCV-HIV coinfected MSM are small and most diagnosed HIV-positive MSM are linked with care, closely monitored, and frequently tested. Additionally, high uptake of HCV treatment among HIV-positive MSM has been reported, with over 40% of HIV/HCV coinfected MSM treatment experienced in European cohorts(53-55). Hence, HCV treatment for prevention may be particularly feasible in this group. However, documentation of high rates of reinfection after treatment among HIV/HCV coinfected MSM (9-15 per 100 person years(56-58)) as well as evidence of a highly connected global network of HCV transmission due to travel may limit the effectiveness of treatment as prevention strategies. Recent modeling work from the UK predicts an expanding HCV epidemic, and that existing levels of treatment are unlikely to reduce HCV chronic prevalence(53). However, scaled-up rates of DAA therapy for everyone (newly diagnosed, those with a previous diagnosis, and those who have previously failed treatment) could substantially reduce both HCV prevalence and incidence within a decade, with further impact achieved if combined with an intervention to reduce behavioral risk(53). Another recent modeling study of the Swiss cohort modeled continued increases in HCV incidence among HIV-positive MSM, and found that reductions in HCV incidence could only be achieved through both stabilization and increased HCV treatment rates, or substantial reductions in high risk behavior with current treatment rates(59).

Treatment as Prevention: Key Issues

Several editorial pieces have discussed the implications of HCV treatment as prevention among PWID(3, 13-16) and prisoners (60, 61). These have highlighted a number of key issues surrounding an effective HCV treatment as prevention response. The importance of a strong foundation of harm reduction intervention strategies, and the possibility of coupling HCV treatment with harm reduction provision to maximize benefit and reduce the risk of reinfection have been highlighted (3, 13, 15, 16). Additionally, the most successful HCV treatment programmes for PWID have often been provided through community based treatment models co-located within specialist drug treatment services (62).

Although some settings have achieved high rates of diagnosis, many PWID and prisoners are undiagnosed and unlinked to care(63). Simplified diagnostic and assessment tools need to be further evaluated, including non-invasive methods of HCV testing (oral saliva or dried blood spot testing), point of care HCV RNA assessment, and liver fibrosis assessment (via transiet elastrography) (64–66).

A number of ethical issues regarding HCV testing and treatment in prison have been raised(60, 61, 67). There is a need to ensure HCV testing in prison is truly voluntary, due to potential unequal power relationships between prisoners and staff. Furthermore, as in the community, HCV treatment should be offered alongside other harm reduction interventions (such as OST) to reduce the risk of infection/reinfection(67).

Additionally, other key populations may contribute more towards HCV transmission in low and middle income countries than PWID or prisoners(68). For example, those accessing unsafe medical injections may be a key population where HCV treatment for prevention could also play a role(69).

A key barrier to rolling out treatment as prevention to PWID and prisoners, however, is the high costs of DAA therapy (USD$7000 per week) even in high income countries. The recent introductions of restrictions on access to sofosbuvir-based regimens due to illicit drug use in a majority of United States jurisdictions, presumably as a cost-saving measure, are clearly non-evidence based and highly stigmatizing(21). Further, they undermine efforts at reducing individual-level liver disease burden among PWID and compromise potential HCV treatment as prevention strategies. In many countries there remains a large difference between the number of treatments currently delivered and the number required to observe a reduction in HCV prevalence, and these sorts of restrictions place further barriers to HCV treatment among PWID.

Among MSM, the highly connected international transmission network and uncertainty surrounding potential HCV transmission to or from other groups (such as HIV-negative MSM, or HIV-positive but undiagnosed MSM) remain key questions surrounding the potential impact of HCV treatment as prevention in this community. Additionally, it is unclear how potential changes in risk behavior among MSM due to widespread provision of HIV antiretroviral treatment or interventions such as pre-exposure prophylaxis will impact on the HCV epidemic and subsequent prevention interventions.

Conclusions

Traditional primary prevention is unlikely to reduce HCV prevalence among PWID to low levels as evidenced in settings with high coverage of these interventions but continued high transmission rates(70). Other effective and cost-effective interventions to stop HCV transmission are required. A number of theoretical modeling studies have shown that modest levels of HCV treatment, especially with DAA therapy, could markedly reduce HCV incidence and chronic prevalence among PWID in a variety of settings. Nonetheless these “ modest” rates of treatment are generally higher than current rates and to achieve an impact require switching to new DAA therapies. Among MSM coinfected with HCV and HIV, further HCV treatment scale-up is likely required despite high treatment rates in this population.

There is an urgent need for empirical studies to test HCV treatment as prevention hypotheses. Rolling out and scaling up HCV treatment in populations at risk of transmission is likely to require reductions in the cost of the new DAA therapies.

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References

1. De Angelis D, Sweeting M, Ades AE, Hickman M, Hope V, Ramsay M. An evidence synthesis approach to estimating Hepatitis C Prevalence in England and Wales. Statistical Methods in Medical Research. Aug 1; 2009 18(4):361–79. [PubMed: 19036917]
2. Williams IT, Bell BP, Kuhnert W, Alter MJ. Incidence and transmission patterns of acute hepatitis c in the united states, 1982–2006. Archives of Internal Medicine. 2011; 171(3):242–8. [PubMed: 21325115]
3. Grebely J, Dore GJ. Can hepatitis C virus infection be eradicated in people who inject drugs? Antiviral Research. 2014 Apr.104:62–72. [PubMed: 24468275]
4. Nelson PK, Mathers BM, Cowle B, Hagan H, Des Jarlais DC, Horyniak D, et al. Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews. The Lancet. 2011; 378:571–83.
5. Dolan K, Teutsch S, Scheuer N, Levy M, Rawlinson W, Kaldor JM, et al. Incidence and risk for acute hepatitis C infection during imprisonment in Australia. European Journal of Epidemiology. 2010; 25:143–8. [PubMed: 20084429]
6. Larney S, Kopinski H, Beckwith CG, Zaller ND, Jarlais DD, Hagan H, et al. The incidence and prevalence of hepatitis C in prisons and other closed settings: Results of a systematic review and meta-analysis. Hepatology. 2013; 58(4):1215–24. Systematic review and meta-analysis of HCV incidence and prevalence in prisons. [PubMed: 23504650]
7. Bradshaw D, Matthew G, Danta M. Sexually transmitted hepatitis C infection: the new epidemic in MSM? Current Opinions in Infectious Diseases. 2013; 26(1):66–72.
8. Van Den Berg D, Smit D, Van Brussel G, Coutinho R, Prins M, Amsterdam C. Full participation in harm reduction programmes is associated with decreased risk for human immunodeficiency virus and hepatitis C virus: evidence from the Amsterdam Cohort Studies among drug users. Addiction. 2007; 102(9):1454–62. [PubMed: 17697278]
9. Turner K, Hutchinson S, Craine N, Hope V, Palmateer N, Vickerman P, et al. The impact of needle and syringe provision and opiate substitution therapy on the incidence of Hepatitis C virus in injecting drug users: pooling of UK evidence. Addiction. 2011; 106(11):1978–88. [PubMed: 21615585]
10. Cohen M, Chen Y, McCauley M, Gamble T, Hosseinipour M, Kumarasamy N, et al. Prevention of HIV-1 Infection with Early Antiretorival Therapy. N Engl J Med. 2011; 365:493–505. [PubMed: 21767103]
11. Wood E, Kerr T, Marshall BDL, Li K, Zhang R, Hogg RS, et al. Longitudinal community plasma HIV-1 RNA concentrations and incidence of HIV-1 among injecting drug users: prospective cohort study. BMJ. 2009 2009-04-30 00:00:00;338.
12. Miller WC, Powers KA, Smith MK, Cohen MS. Community viral load as a measure for assessment of HIV treatment as prevention. The Lancet Infectious Diseases. 2013 May; 13(5): 459–64. [PubMed: 23537801]
13. Hellard M, Doyle JS, Sacks-Davis R, Thompson AJ, McBryde E. Eradication of hepatitis C infection: The importance of targeting people who inject drugs. Hepatology. 2014; 59(2):366–9. [PubMed: 23873507]
14. Hagan LM, Wolpe PR, Schinazi RF. Treatment as prevention and cure towards global eradication of hepatitis C virus. Trends in Microbiology. 2013 Dec; 21(12):625–33. [PubMed: 24238778]

15. Grebely J, Matthews GV, Lloyd AR, Dore GJ. Elimination of Hepatitis C Virus Infection Among People Who Inject Drugs Through Treatment as Prevention: Feasibility and Future Requirements. Clinical Infectious Diseases. Oct 1; 2013 57(7):1014–20. [PubMed: 23728143]

16. Bruggmann P. Treatment as prevention: The breaking of taboos is required in the fight against hepatitis C among people who inject drugs. Hepatology. 2013; 58(5):1523–5. [PubMed: 23728921]

17. AASLD/IDSA/IAS-USA. Recommendations for testing, managing, and treating hepatitis C. 2015. http://www.hcvguidelines.org

18. World Health Organization. Guidelines for the screening, care and treatment of persons with hepatitis C infection. 2014. http://apps.who.int/iris/bitstream/10665/111747/1/9789241548755_eng.pdf

19*. Robaeys G, Grebely J, Mauss S, Bruggmann P, Moussalli J, De Gottardi A, et al. Recommendations for the Management of Hepatitis C Virus Infection Among People Who Inject Drugs. Clinical Infectious Diseases. Aug 15; 2013 57(suppl 2):S129–S37. Study highlighting the frequent restrictions on access to DAA therapy due to illicit drug use in the US. [PubMed: 23884061]

20. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C. 2015. http://www.easl.eu/medias/cpg/HEPC-2015/Full-report.pdf

21. Barua S, Greenwald R, Grebely J, Dore G, Swan T, Taylor L. Restrictions for Medicaid reimbursement of sofobuvir in the treatment of hepatitis C virus infection in the United States. Annals of Internal Medicine. 2015 in press.

22. Aspinall A, Corson S, Doyle J, Grebely J, Hutchinson S, Dore GJ, et al. Peginterferon and ribavirin treatment for chronic hepatitis C virus in people who inject drugs: A systematic review and meta-analysis. Clinical Infectious Diseases. 2013; Suppl 2(57)

23*. Dimova RB, Zeremski M, Jacobson IM, Hagan H, Des Jarlais DC, Talal AH. Determinants of Hepatitis C Virus Treatment Completion and Efficacy in Drug Users Assessed by Meta-analysis. Clinical Infectious Diseases. Mar 15; 2013 56(6):806–16. Study highlighting the continued low uptake of HCV treatment among PWID in Vancouver, Canada. [PubMed: 23223596]

24*. Grady BP, Schinkel J, Thomas XV, Dalgard O. Hepatitis C Virus Reinfection Following Treatment Among People Who Use Drugs. Clinical Infectious Diseases. Aug 15; 2013 57(suppl 2):S105–S10. Study highlighting the continued low uptake of HCV treatment among PWID in Australia. [PubMed: 23884057]

25. Alavi M, Raffa JD, Deans GD, Lai C, Krajden M, Dore GJ, et al. Continued low uptake of treatment for hepatitis C virus infection in a large community-based cohort of inner city residents. Liver International. 2014; 34(8):1198–206. [PubMed: 24164865]

26. Iversen J, Grebely J, Topp L, Wand H, Dore G, Maher L. Uptake of hepatitis C treatment among people who inject drugs attending Needle and Syringe Programs in Australia, 1999–2011. Journal of Viral Hepatitis. 2014; 21(3):198–207. [PubMed: 24438681]

27. Martin NK, Foster GR, Vilar J, Ryder SE, Cramp M, Gordon F, et al. HCV treatment rates and sustained viral response among people who inject drugs in seven UK sites: real world results and modelling of treatment impact. Journal of Viral Hepatitis. 2015; 22(4):399–408. [PubMed: 25288193]

28. Martin NK, Vickerman P, Hickman M. Mathematical modelling of Hepatitis C Treatment for Injecting Drug Users. Journal of Theoretical Biology. 2011; 274:58–66. [PubMed: 21236265]

29*. Martin NK, Vickerman P, Foster GR, Hutchinson SJ, Goldberg DJ, Hickman M. Can antiviral therapy for hepatitis C reduce the prevalence of HCV among injecting drug user populations? A modelling analysis of its prevention utility. Journal of Hepatology. 2011; 54:1137–44. Modelling study evaluating the impact of combination interventions (HCV DAA treatment, OST, and NSP) on HCV incidence and prevalence among PWID. [PubMed: 21145810]

30. Martin NK, Pitcher AB, Vickerman P, Vassall A, Hickman M. Optimal Control of Hepatitis C Antiviral Treatment Programme Delivery for Prevention Amongst a Population of Injecting Drug Users. PLoS One. 2011; 6(8):e22309. Epub 2011 Aug 11. [PubMed: 21853030]

31. Martin NK, Hickman M, Hutchinson SJ, Goldberg DJ, Vickerman P. Combination interventions to prevent HCV transmission among people who inject drugs: modeling the impact of antiviral

treatment, needle and syringe programs, and opiate substitution therapy. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. Aug; 2013 57(Suppl 2):S39–S45. [PubMed: 23884064]

32. Vickerman P, Martin N, Hickman M. Can Hepatitis C virus treatment be used as a prevention strategy? Additional model projections for Australia and elsewhere. Drug and Alcohol Dependence. 2011; 113(2–3):83–5. [PubMed: 20832198]
33. Zeiler I, Langlands T, Murray JM, Ritter A. Optimal targeting of Hepatitis C virus treatment among injecting drug users to those not enrolled in methadone maintenance programs. Drug Alcohol Depend. 2010; 110(3):228–33. [PubMed: 20430537]
34. Durier N, Nguyen C, White LJ. Treatment of Hepatitis C as Prevention: A Modeling Case Study in Vietnam. PLoS ONE. 2012; 7(4):e34548. [PubMed: 22511949]
35. Cousien, A.; Tran, VC.; Jauffret-Roustide, M.; Deuffic-Burban, S.; Dhersin, J-S.; Yazdanpanah, Y. IMPACT OF NEW DAA-CONTAINING REGIMENS ON HCV TRANSMISSION AMONG INJECTING DRUG USERS (IDUS): A MODEL-BASED ANALYSIS (ANRS 12376). European Study of the Liver Conference (EASL 2014) Oral Abstract; 2014. http://wwwnataporg/2014/EASL/EASL_87htm
36*. Rolls D, Sacks-Davis R, Jenkinson R, McBryde E, Pattison P, Robins G, et al. Hepatitis C transmission and treatment in contact networks of people who inject drugs. PLoS ONE. 2013; 8(11):e78286. Network modelling study showing the additional impact of the ‘treat a friend’ approach for HCV treatment as prevention among PWID. [PubMed: 24223787]
37. de Vos AS, Kretzschmar MEE. Benefits of hepatitis C virus treatment: A balance of preventing onward transmission and re-infection. Mathematical Biosciences. 2014; 258:11–8. [PubMed: 25242609]
38. Hellard M, Rolls DA, Sacks-Davis R, Robins G, Pattison P, Higgs P, et al. The impact of injecting networks on hepatitis C transmission and treatment in people who inject drugs. Hepatology. 2014; 60(6):1861–70. [PubMed: 25163856]
39*. Rolls DA, Daraganova G, Sacks-Davis R, Hellard M, Jenkinson R, McBryde E, et al. Modelling hepatitis C transmission over a social network of injecting drug users. Journal of Theoretical Biology. 2012 Mar 21.297:73–87. Modelling study exploring the impact of IFN-free DAA treatment as prevention among PWID in Canada, Australia, and the UK. [PubMed: 22185979]
40. de Vos AS, Prins M, Kretzschmar MEE. Hepatitis C virus treatment as prevention among injecting drug users: who should we cure first? Addiction. 2015 n/a-n/a.
41. Martin N, Vickerman P, Grebely J, Hellard M, Hutchinson S, Lima V, et al. HCV treatment for prevention among people who inject drugs: modeling treatment scale-up in the age of direct-acting antivirals. Hepatology. 2013; 58(5):1598–609. [PubMed: 23553643]
42. Gane E, Kershenobich D, Seguin-Devaux C, Kristian P, Aho I, Dalgard O, et al. Strategies to manage hepatitis C virus (HCV) infection disease burden –volume 2. Journal of Viral Hepatitis. 2015; 22:46–73. [PubMed: 25560841]
43. Hellard M, Jenkinson R, Higgs P, Stoové M, Sacks-Davis R, Gold J, et al. Modelling antiviral treatment to prevent hepatitis C infection among people who inject drugs in Victoria, Australia. Med J Aust. 2012; 196(10):638–41. [PubMed: 22676879]
44. Maher L, White B, Hellard M, Madden A, Prins M, Kerr T, et al. Candidate hepatitis C vaccine trials and people who inject drugs: Challenges and opportunities. Vaccine. 2010 Oct 21; 28(45): 7273–8. [PubMed: 20831914]
45*. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C. 2014. http://fileseasleu/easl-recommendations-on-treatment-of-hepatitis-CpdfEconomic evaluation showing that early DAA treatment for PWID is cost-effective and guidelines which recommend prioritization should incorporate both risk status and disease stage
46. AASLD/IDSA. Recommendations for Testing, Managing, and Treating Hepatitis C. 2014.
47. Martin N, Vickerman P, Dore G, Grebely J, Miners A, Cairns J, et al. How should HCV antiviral treatment be prioritized in the direct-acting antiviral era? An economic evaluation including individual and prevention benefits. 2015 Submitted.

48. Martin, N.; Vickerman, P.; Dore, G.; Grebely, J.; Miners, A.; Cairns, J., et al. How should HCV antiviral treatment be prioritized in the direct-acting antiviral era? An economic evaluation including individual and prevention benefits. 2015; EASL Conference 2015 Poster 96206;

49. Taylor A, Munro A, Allen E, Dunleavy K, Cameron S, Miller L, et al. Low incidence of hepatitis C virus among prisoners in Scotland. Addiction. 2013 n/a-n/a.

50. Linas B, Wong A, Schackman B, Kim A, Freedberg K. Cost-effective Screening for Acute Hepatitis C Virus Infection in HIV-infected Men Who Have Sex With Men. Clin Infec Dis. 2012; 55:279–90. [PubMed: 22491339]

51. Martin, NK.; Vickerman, P.; Brew, I.; Williamson, J.; Irving, W.; Sakshena, S., et al. Is increased HCV case-finding when combined with 8 or 12 weeks interferon-free direct-acting antiviral treatment cost-effective in UK prisons? A cost utility analysis including treamtent as prevention benefits. European Association for the Liver Conference (EASL); 2015; 2015.

52. Wandeler G, Gsponer T, Bregenzer A, Günthard HF, Clerc O, Calmy A, et al. Hepatitis C Virus Infections in the Swiss HIV Cohort Study: A Rapidly Evolving Epidemic. Clinical Infectious Diseases. Nov 15; 2012 55(10):1408–16. [PubMed: 22893583]

53. Martin N, Hickman M, Nelson M, Thornton A, Sabin C, Lattimore S, et al. Understanding and Preventing the HCV Epidemic among Men Who Have Sex With Men in the UK: A Mathematical Modelling Analysis. 2015 EASL 2015 eposter.

54. Ingiliz P, Boyd A, Steininger K, Caranico A, Dupke S, Krznaric I, et al. Long-term follow-up of HIV-positive men who have sex with men (MSM) with acute hepatitis C virus (HCV) infection: high rates of treatment and low rates of liver-related complications. 2015 CROI 2015 poster 671.

55. Wandeler G, Schlauri M, Jaquier M-E, Rohrbach J, Metzner KJ, Fehr J, et al. Incident Hepatitis C Virus Infections in the Swiss HIV Cohort Study: Changes in Treatment Uptake and Outcomes Between 1991 and 2013. Open Forum Infectious Diseases. 2015 03/25 11/03/received 02/12/accepted;2(l):ofv026.

56. Lambers F, Prins M, Thomas M, Molenkamp R, Kwa D, Brinkman K, et al. Alarming incidence of hepatitis C virus re-infection after treatment of sexually acquired acute hepatitis C virus infection in HIV-infected MSM. AIDS. 2011; 25(17):F21–7. [PubMed: 21857492]

57. Martin T, Martin N, Hickman M, Vickerman P, Page E, Everett R, et al. Hepatitis C virus reinfection incidence and treatment outcome among HIV-positive MSM. AIDS. 2013; 27(16): 2551–7. [PubMed: 23736152]

58. Hill A, Simmons B, Saleem J, Cooke G. Five-year risk of late relapse or reinfection with hepatitis C after sustained virological response: meta-analysis of 49 studies in 8534 patients. 2015 CROI 2015. Februrary 23,-26, 2015. Abstract 654.

59*. Salazar-Vizcaya L, Kouyos R, Zahnd C, Battegay M, Darling K, Calmy A, et al. Behavioural and Treatment Interventions to Reduce Hepatitis C Virus Transmissions Among HIV-infected MSM: A Cohort-based Modelling Study. 2015 CROI 2015. Poster 675 Modelling study evaluating the potential for HCV treatment as prevention in Egypt, where individuals with a high rate of medical injections are the main driver of the epidemic.

60. Levy MH, Larney S. The ethics of hepatitis C ‘treatment as prevention’ among prisoners. Hepatology. 2014 n/a-n/a.

61. Martin NK, Vickerman P, Goldberg D, Hickman M. HCV treatment as prevention in prison: Key issues. Hepatology. 2014 n/a-n/a.

62. Bruggmann P, Litwin AH. Models of Care for the Management of Hepatitis C Virus Among People Who Inject Drugs: One Size Does Not Fit All. Clinical Infectious Diseases. Aug 15; 2013 57(suppl 2):S56–S61. [PubMed: 23884067]

63. Weissing L, Roy K, Sapinho D, Hay G, Taylor A, Goldberg D, et al. Surveillance of hepatitis C infection among injecting drug users in the European Union. Hepatitis C and injecting drug use: impact, costs and policy options. 2006:91–135.

64. Hickman M, McDonald T, Ali J, Nichols T, Hope V, Skidmore S, et al. Increasing the uptake of hepatitis C virus testing among injecting drug users in specialist drug treatment and prison settings by using dried blood spots for diagnostic testing: a cluster randomized controlled trial. Journal of Viral Hepatitis. 2008; 15(4):250–4. [PubMed: 18086182]

65. Jewett A, Smith BD, Garfein RS, Cuevas-Mota J, Teshale EH, Weinbaum CM. Field-based performance of three pre-market rapid hepatitis C virus antibody assays in STAHR (Study to Assess Hepatitis C Risk) among young adults who inject drugs in San Diego, CA. Journal of Clinical Virology. 2012 Jul; 54(3):213–7. [PubMed: 22560051]

66. Moessner BK, Jørgensen TR, Skamling M, Vyberg M, Junker P, Pedersen C, et al. Outreach screening of drug users for cirrhosis with transient elastography. Addiction. 2011; 106(5):970–6. [PubMed: 21182552]

67. Arain A, Robaeys G, Stover H. Hepatitis C in European prisons: a call for an evidence-informed response. BMC Infectious Diseases. 2014; 14(Suppl 6):S17. [PubMed: 25252822]

68. Woodall, H.; Martin, N.; Hallett, TB.; Cooke, G.; Hickman, M.; Vickerman, P. What is needed to control Hepatitis C (HCV) in different epidemiological settings?. 2015; EASL Conference 2015. Poster 96217;

69. Breban R, Arafa N, Leroy S, Mostafa A, Bakr I, Tondeur L, et al. Effect of preventive and curative interventions on hepatitis C virus transmission in Egypt (ANRS 1211): a modelling study. The Lancet Global Health. 2014 Sep; 2(9):e541–e9. [PubMed: 25304421]

70. Palmateer NE, Taylor A, Goldberg DJ, Munro A, Aitken C, Shepherd SJ, et al. Rapid Decline in HCV Incidence among People Who Inject Drugs Associated with National Scale-Up in Coverage of a Combination of Harm Reduction Interventions. PLoS ONE. 2014; 9(8):e104515. [PubMed: 25110927]

Key points

- The burden of HCV is high among people who inject drugs and prisoners
- Modelling studies have shown modest levels of HCV interferon-free DAA therapy for PWID and prisoners could have a substantial prevention benefit and reduce HCV chronic prevalence/incidence. Among MSM, further HCV treatment scale-up is likely required despite high treatment rates in this population.
- There is an urgent need for empirical studies testing the concept of HCV treatment as prevention among key populations.