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Commentary

The promise of treatment as prevention for hepatitis C: Meeting the needs of people who inject drugs?

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ABSTRACT

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.

The HIV field offers real-life experience of treatment as prevention (TasP). The concept of TasP for HIV stems from study findings that antiretroviral therapy (ART) associated viral suppression significantly reduces HIV sexual transmission (Cohen et al., 2011; Rodger et al., 2014). This evidence is reflected in revised international guidelines recommending early ART commencement for people with HIV in serodiscordant relationships (World Health Organisation, 2013), although there are few jurisdictions where these guidelines are implemented in a sustained or systematic manner. While HIV TasP has demonstrated significant benefits in transmission reduction, it has also been subject to sustained critique for overly medicalising the prevention response, to the detriment of primary and community driven prevention initiatives for HIV-negative individuals (Adam, 2011; Johnson, 2014; Nguyen, Bajos, Dubois-Arber, O'Malley, & Pirkle, 2011). Unlike HIV, treatment for hepatitis C (HCV) offers a cure. The development of new, more tolerable and effective, HCV treatments creates the potential for a TasP (or cure as prevention) response. 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 the conditions under which it might be optimised.

The promise of treatment as prevention for HCV

We are in the midst of a changing HCV treatment landscape. Oral direct-acting antivirals (DAAs) have cured up to 100% of clinical trial participants from HCV, fuelling considerable optimism in the sector (Afdhal et al., 2014; Sulkowski et al., 2014). References to HCV eradication and elimination are now commonplace (Grebely & Dore, 2014; Ryder & Dillon, 2014). One key strategy in the HCV elimination toolbox is TasP. HCV TasP involves prioritisation and scale up of HCV treatment provision to people who are currently injecting, with each cure reducing onward transmission opportunities in the population. This, coupled with scaled up primary prevention initiatives, has the potential to substantially reduce HCV population prevalence, making concepts such as HCV elimination feasible. In a context of low levels of HCV treatment access and uptake among PWID (<1% in most countries) TasP for HCV has the potential to be a powerful treatment access advocacy tool.

Modelling work by Martin, Hickman, Hutchinson, Goldberg, and Vickerman (2013), is widely cited as illustrating the potential efficacy of TasP for HCV. Their dynamic models project the

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population impact of increasing HCV treatment for PWID, with treatment scenarios modelled against different contexts of baseline prevalence. In a scenario of DAA therapy (90% SVR, 12 weeks duration) scale-up, treatment provision per 1000 PWID would need to be increased from 7 to 22 in Edinburgh (25% baseline prevalence), 3 to 22 in Melbourne (50% baseline prevalence) and 5 to 98 in Vancouver (65% baseline prevalence) for HCV prevalence among PWID to halve within 15 years. Based on current United States DAA prices this would require annual treatment budgets of approximately US$3.2 million in Edinburgh and US$50 million in Melbourne and Vancouver (Martin, Vickerman, et al., 2013).

Durier, Nguyen, and White (2012) use Vietnam as a case study (72% prevalence among PWID) to model the impact of treatment scale up in resource poor settings. They illustrate that early treatment provision at relatively low treatment coverage (with lower associated costs) can have effective impact. For example, 25% treatment coverage targeting people in the first year of HCV infection is projected to reduce prevalence by 60% in 11 years, whereas 50% coverage for people 4 years after transmission provides a 37% reduction. Increased needle and syringe program (NSP) and opiate substitution therapy (OST) provision can also enhance HCV treatment intervention efficacy, reducing costs. Given a Vietnam scenario of 50% HCV treatment coverage 2.5 years after infection (52% prevalence reduction) scaled up OST and NSP can increase impact by 13% (OST) and 20% (NSP), providing a total 85% prevalence reduction in 11 years (Durier et al., 2012). Additional strategies to increase intervention impact include network approaches, employed by proof of concept studies in Scotland and Melbourne. Here a 'treat your friends' strategy aims to minimise reinfection risks by treating networks of people who inject together. Rolls et al. (2013) project that the effect of treating 35 PWID (per 1000) using a network ring strategy will be the same as treating 47 PWID at random (see also Hellard, Doyle, Sacks-Davis, Thompson, & McBryde, 2014).

There is considerable enthusiasm for these approaches in the HCV sector, with linkages between the advent of DAAs, TasP and viral eradication commonly made. For example, in an article titled '*The end of hep C*', Sussman, Remien, and Kanwal state: "in the absence of herd immunity universal eradication of HCV is the only way to prevent reinfection" (2014: 534). Hagan, Wolpe, and Schinazi comment that the availability of DAA treatment "sparks an ethical call for HCV eradication and provides essential tools to spearhead the effort", with the success of TasP depending on "financial will from the public, industry and governmental bodies to deploy the necessary resources" (2013: 625). Notable in these commentaries is not only the premise of HCV eradication[1], but the omission of: (a) the prevention effect of OST and NSP; (b) the role of the affected community and their organisations in an effective TasP response; and (c) social structural barriers to HCV treatment access for PWID. While a number of HCV TasP commentators address the role of NSP and OST in enhancing TasP efficacy (see Durier et al., 2012; Grebely & Dore, 2014; Hellard et al., 2014; Martin, Hickman, et al., 2013) and the impact of health system barriers on TasP feasibility (Bruggmann & Litwin, 2013; Grebely & Dore, 2014) few scholars have focused in any depth on the broader social structural barriers to health care access or the acceptability of population based initiatives for PWID and their community organisations. Fraser and Moore provide a valuable exception, highlighting the common conflation of group and individual rights in prevention initiatives, such that the personal interests of PWID become "indistinguishable from those of society as a whole, despite their evident exclusion from many of the rewards offered by society" (2011: 377). We explore this tension further in the following section.

The limits of a population-based approach

TasP for HCV, as with HIV, has implications for clinical treatment decision-making and for the way health systems prioritise and target treatment provision. This has become a particularly fraught issue since the development and licencing of expensive DAAs. In the context of potential cost-justified rationing of DAAs in the UK, Innes, Goldberg, Dillon, and Hutchinson (2014) project that the prioritisation of treatment for PWID will optimally impact on transmission incidence (a TasP approach), but will have minimal impact on limiting new cases of severe liver morbidity (SLM). Conversely, the prioritisation of people with more advanced liver disease will reduce SLM but not incident transmission. This is because the population targeted by TasP (current 'risky' injectors) are likely to be younger and have minimal fibrosis, whereas those with advanced liver disease are often older and less likely to be injecting unsafely (or at all). Innes et al. pose the question: "what public health outcomes do we value the most?" The two competing population-based considerations provided (reduction of SLM vs transmission incidence) are however, not necessarily those of the individuals who negotiate risk and illness in their everyday lives. They are not necessarily the public health outcomes that matter to 'the public'—nor is there an ethical framework provided for pitting these interests against one another.

Aware that HCV treatment cost-based rationing will need to be justified to those seeking treatment, Innes et al. advise clinicians to "manage expectations" of the benefits of a SVR (sustained virological response or HCV 'cure'), as "more realistic expectations may lead to patients making more conservative treatment choices if the benefits on offer are accepted to be modest" (Innes, Goldberg, Dillon, et al., 2014: 1). The authors draw on a recent simulation model measuring the "patient important benefits of an SVR" in terms of the attainment of additional life years and additional healthy life years (Innes, Goldberg, Dusheiko, et al., 2014). The clinical benefits conferred for older patients with less advanced fibrosis were found to be minimal (<3% gain in life years and healthy life years) whereas younger individuals with compensated cirrhosis demonstrated a greater life years benefit (>50% gain). While this information can inform individual and clinical decision making, it fails to take into account the intensely social nature of what it is to live with and clear HCV.

For many individuals seeking treatment, the benefits on offer are not modest, but profound. This is evident in qualitative study data where 28 people were followed from HCV treatment referral until up to a year after treatment completion[2]. Sam[3], aged 60 with minimal fibrosis, described his HCV diagnosis as bringing an end to life as he knew it. Although aware that the risk of transmission was low, Sam was so fearful of passing HCV on that he ceased all sexual relationships, stopped any physical play with children and described being constantly wary in social interactions. Of the two years between diagnosis and commencing HCV treatment he said: "my life completely stopped". This reduced social interaction and internalised stigma prompted a prolonged drinking binge, resulting in the loss of his job. Three months after completing triple

[1] As Grebely and Dore (2014) explain, HCV eradication is a more ambitious and unrealistic aim than HCV elimination. Eradication: Complete and permanent worldwide reduction to zero of new cases through deliberate efforts with no further control required. Elimination: reduction of incidence of infection to zero in a defined geographic area as a result of deliberate efforts, but requires continued measures to prevent re-establishment of transmission.

[2] The Hepatitis C Treatment Journey Study. London based, NIHR funded [NIHR-PDF-2011-04-031]. Data collection comprised 1–5 interviews with 28 participants from referral to treatment services up to a year post treatment, interviews with 18 providers and stakeholders, and 100 h of HCV clinic observations.

[3] A pseudonym.