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Opiate substitution treatment and HCV prevention: Building an evidence base?

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The beneficial effects of opiate substitution treatment (OST) for people who inject drugs (PWID) encompass multiple domains and outcomes. This includes decreasing HIV acquisition risk by half[1], reducing drug related mortality[2, 3], possibly enhancing adherence to HIV anti-retroviral treatment[4], diminishing crime[5] and the societal costs associated with drug use[6], increasing quality of life[5] and sometimes employment status[7, 8]. However, until recently, the evidence for OST or any harm reduction intervention reducing the risk of hepatitis C virus (HCV) acquisition was classified as insufficient[9, 10]. This situation started to change three years ago when a pooled UK analysis of selected observational studies suggested for the first time that OST could reduce HCV acquisition risk amongst PWID by over 50% and that the combination of OST and high coverage needle and syringe distribution could reduce HCV acquisition risk by up to 80%[11]. In recent months, there has been a further strengthening of the evidence base, with results from the Vancouver Injecting Drug Use Study (VIDUS) published in this issue of Addiction[12] and two other prospective studies of PWID from Australia[13] and San Francisco, in USA,[14] each reporting that OST can reduce the risk of HCV acquisition by 50–80% (Table 1). Despite a similar effect size across all four studies, an important difference between the Australian paper[13], from the HITs-c cohort, and the analyses from Vancouver and San Francisco is that White et al. only included PWID for whom OST was potentially indicated – i.e. those who reported primarily injecting heroin or other opioids[13]. In contrast, both the Vancouver and San Francisco papers were inclusive of all cohort participants, including those for whom OST may not be indicated (such as methamphetamine and cocaine injectors), so the protective effects may be under-estimated. While it is encouraging that the size of the protective effect is consistent across the studies in multiple sites, we recognise that these studies are all observational and at greater risk of selection bias and confounding than randomised controlled trials. For instance, in the Nolan

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study[12] there was a considerable difference in the HCV prevalence among people receiving and not receiving OST at baseline (24% vs 76%)as well as differences in drug using patterns which may suggest the difference in risk may not be entirely due to the direct effects of OST on injecting behaviours. Importantly, methadone and buprenorphine are essential medicines that cannot be randomised in future studies and so the evidence base will have to be built from non-randomised observational studies such as these.

So what are the implications of these results for designing HCV prevention strategies? Firstly, as highlighted by a recent modelling analysis[15], OST averts infections, with projections from the UK suggesting that current high coverage levels of OST (50% of PWID are currently on OST in the UK) may have contributed to reducing the chronic HCV prevalence from 57% to 40%. OST may also have an accumulating effect – the longer the average duration on OST the greater the impact on reducing HCV risk[12] and drug related mortality[2]. Indeed, because economic analyses suggest that OST could be cost saving when societal benefits are accounted for[6], or at least highly cost-effective if just health benefits are considered[6], then it seems there should be no argument against scaling up OST in all settings.

There is a long way to go until we achieve the high levels of OST coverage that currently exist in some settings such as the UK and Australia. Data from the last systematic review of intervention coverage among PWID suggested that the worldwide coverage of OST was at best 8%[16], and although many countries have since initiated OST programmes, recent data continue to show inadequate coverage of OST in most settings[17]. This raises the spectre of the potential enormous size of the global prevention gap. For example, adapted results from our previous modelling analysis[15] suggest scaling up OST worldwide could avert between 1 and 2 million HCV infections over the next 10 years if it was scaled up from less than 10% to 50% coverage (8 million) of all PWID. Although these calculations warrant more detailed modelling to capture the heterogeneities in different epidemics, they nonetheless highlight the substantial potential prevention benefit of scaling up OST.

It is important to note, however, that although recent results suggest that OST is an essential component of any future HCV prevention strategy, it is not the only answer to HCV prevention. HCV prevalence remains persistently high in many countries despite high coverage of OST and needle and syringe distribution. It is likely that only by also scaling up antiviral treatment and prophylactic vaccine development for HCV that prevalence can be significantly reduced[18, 19].

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Table 1

Summary of findings from recent studies showing protective effect of OST on HCV acquisition.

Setting	Person years	Incident infections	Incidence without OST†	Incidence with OST†	Adjusted hazard or odds ratio	Reference
UK multisite	189	40	26.4	11.5	0.41 (0.21–0.82)	[11]
Vancouver, Canada	2911‡	184	5.5 (4.7–6.4)	0.5 (0.3–0.9)	0.47 (0.29–0.76)	[12]
Sydney, Australia	215	17	26.9 (14.5–50.0)	3.3 (1.1–10.2)	0.18 (0.04–0.77)	[13]
San Francisco, USA	680	171	28.2 (23.9–33.4)	8.6 (4.1–18.1)	0.39 (0.18–0.87)	[14]

†HCV incidence per 100 person years for those PWID without or with OST in last time period except for Vancouver study where it is HCV incidence for PWID never and ever on OST;

‡person years not given in study so estimated from number of incident infections and estimated HCV incidence