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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

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Abstract

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)

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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.

Keywords

Hepatitis C; methadone; drug treatment; drug injection; Viet Nam; Estonia; opioid substitution treatment; buprenorphine

Introduction

Approximately 185 million people globally are chronically infected with hepatitis C virus (HCV). Chronic HCV infection causes substantial mortality and morbidity including cirrhosis and hepatocellular carcinoma. (Alter & Seeff, 2000; Thomas, et al., 2000) People who inject drugs (PWID) are central to the HCV epidemic in many countries. (Aceijas & Rhodes, 2007; Hope, Eramova, Capurro, & Donoghoe, 2014; Nelson, et al., 2011) There are an estimated 13 million people globally who have ever injected drugs. (Mathers, et al., 2008) Many PWID acquire HCV infection early in their injection experience, but HCV risk persists during all periods of non-sterile injection drug use. (Hagan, Pouget, Des Jarlais, & Lelutiu-Weinberger, 2008) HCV incidence rates range from 2.7–66/100 person years of observation (PYO) (Maher, Li, Jalaludin, Chant, & Kaldor, 2007; Mehta, et al., 2011; Wiessing, et al., 2014) and prevalence among PWID globally has been estimated to be 67%. (World Health Organization, 2014)

Advances in the treatment of HCV have led to considerations of the elimination (zero incidence requiring continued prevention efforts) or eradication of HCV (zero incidence with no further prevention control efforts). (Grebely & Dore, 2014) Opioid substitution treatment (OST) of opioid dependence has the potential to play a significant role in public health efforts to control HCV by serving 1) as an HCV prevention intervention among PWID, 2) by treating noninjection opioid dependent people who use drugs (PWUD) who might otherwise transition to non-sterile drug injection, and 3) by serving as a platform to engage HCV infected PWUD in the HCV care continuum and link them to HCV treatment. Taken together these efforts can serve as community-level prevention and treatment as prevention (TasP), and can contribute to reduced HCV-related morbidity and mortality.

Modeling studies suggest that OST of opioid dependence, such as methadone maintenance treatment (MMT), can potentially contribute to significant reductions in HCV incidence and prevalence among PWIDs. (Turner, et al., 2011; Vickerman, Martin, Turner, & Hickman, 2012) Modeling studies have shown that scale-up of OST, in combination with the scale-up of needle and syringe exchanges programs (NSP) has the potential to serve as a core component of HCV prevention, reducing HCV prevalence to <30% over a decade. (Vickerman, Martin, Turner, & Hickman, 2012) However, despite this potential there are

currently substantial structural and programmatic gaps in availability of OST globally, and hence in its ability to be used to its full potential as HCV prevention.

As with HIV, the theoretic potential exists to further reduce the incidence and prevalence of HCV by reducing the population HCV viral load through TasP. (Martin, et al., 2013) Modeling suggests that OST, NSP and TasP would have to be significantly scaled up in order for combination HCV prevention to reduce HCV prevalence by three fourths within 15 years; much greater proportions of PWIDs would have to be engaged in HCV treatment, achieve SVR and not get re-infected. (Martin, et al., 2013) There are also significant gaps for PWID in each of the steps in the HCV care continuum: testing, linkage to care, completion of clinical evaluations, and initiation and completion of treatment. Recent estimates are that only 1.0–9.5% of HCV infected PWID initiate treatment, (Grebely & Dore, 2014) dramatically reducing the real world effectiveness of HCV therapy both for individual treatment and as TasP. (Linas, et al., 2014)

MMT programs are potentially critical settings for engaging PWID in HCV care and a variety of models for doing so have been developed. (Bruggmann & Litwin, 2013; Masson, et al., 2013; Sylvestre, 2002) These models include referral from primary care or harm reduction settings to specialty clinics with multidisciplinary teams and addiction specialists, (Bruggmann & Litwin, 2013; Masson, et al., 2013) co-locating hepatology and addiction providers in primary care settings, (Arora, et al., 2011; Seidenberg, Rosemann, & Senn, 2013) community-based treatment models using telemedicine, (Katzman, et al., 2014; Khatri, Haddad, & Anderson, 2013) and on-site treatment within MMT programs. (Litwin, Berg, Li, Hidalgo, & Arnsten, 2011; Litwin, et al., 2012; Sylvestre & Zweben, 2007) Few HCV linkage to care interventions have been evaluated in randomized designs, (Evon, et al., 2011; Larrey, et al., 2011; Masson, et al., 2013) none have been compared, and none have been consistently implemented. While different models may fit different settings, (Litwin, et al., 2012) most MMT programs have limited clinical infrastructure and are not funded to provide HCV services, (Schackman, et al., 2013; Strauss, et al., 2008) potentially limiting the generalizability of on-site HCV treatment in MMT programs to select settings. (Litwin, et al., 2012; Sylvestre & Zweben, 2007)

In addition to gaps introduced by the inconsistent implementation of HCV testing and linkage to care from drug treatment settings, significant limitations in the potential for OST to contribute to HCV control stem from gaps in access to drug treatment services throughout the world. Access to OST is inadequate, despite evidence of efficacy of OST for treatment of opioid dependence, (World Health Organization, 2010a) as a potent form of HIV prevention, (Gibson, Flynn, & McCarthy, 1999) as well as its potentially central role of OST for control of the HCV epidemic. (Nolan, et al., 2014) In 2009, the World Drug Report estimated that 38 million people had problematic drug use and only 4.9 million had access to drug dependence treatment and care. (United Nations Office on Drug Control, 2009)

In addition to the importance of issues of OST access, there are considerations related to improving the quality of, satisfaction with, and impacts of OST services. The specific ways in which OST may be delivered, and in which OST settings are frequently configured in health systems, can be perceived by PWID, and can sometimes be, stigmatizing, controlling

and demoralizing. (Bourgois, 2000; Fraser, 2006) The physical and operational separation of OST treatment settings from other aspects health care, embodying the marginalization and stigmatization of drug use and the treatment of opioid dependence, and systems which rely on surveillance, control and power differentials between PWID and staff, (Bourgois, 2000; Fraser, 2006; Harris, Rhodes, & Martin, 2013; Rance, Newland, Hopwood, & Treloar, 2012) have implications for trust, ethics, and use of OST for HCV prevention and care engagement (as well as for HIV prevention, overdose prevention, and the reduction of other adverse consequences of drug use).

The extent to which OST can function as either HCV prevention or as a platform for engaging HCV infected PWID in the HCV care continuum will depend on structural and programmatic factors that vary among countries throughout the world. Countries vary with regard to the legality of OST; the extent to which participation in OST is stigmatized or subject to criminal justice harassment despite legality; the number of OST slots compared to the number of PWID or opioid dependent persons; and the extent to which OST includes additional forms of harm reduction, is free, is covered by health insurance, is reimbursed on a fee-for-service basis, or is mandated for opioid dependent persons (e.g., by court order).

Six countries on three continents account for half of the global population of PWID (China, Viet Nam, Malaysia, Russia, Ukraine and the United States) (Degenhardt, et al., 2014); this paper will examine programmatic, financial and policy considerations for using OST as a platform to improve the HCV prevention and care continuum in 3 countries, one from each of these continents — the United States (U.S.), Estonia (an Eastern European “transitional” country) and Viet Nam (a Southeast Asian middle income country).

United States

In the U.S., injection drug use is both highly stigmatized and highly criminalized. (Ahern, Stuber, & Galea, 2007; Drucker, 2012) The perception that illicit drug use is a moral weakness and a social evil rather than a behavior with medical consequences occurring in a social dimension is prevalent, has been frequently politicized, and is common in the mainstream media. (Lancaster, Hughes, Spicer, Matthew-Simmons, & Dillon, 2011; Montagne, 2011; Taylor, 2008) From a public health perspective this has been counterproductive, complicating and limiting treatment of opioid dependence and limiting the expansion of OST. From the 1930s to the mid-1960s many PWUD identified by police were sent to Federal compulsory drug treatment centers. (Courtwright, Joseph, & Des Jarlais, 1989) The closure of these centers was followed shortly thereafter by a dramatic rise in the incarceration of PWUDs, and particularly of poor and racial- ethnic minority PWUDs, that continues to this day. (Singer, 2007) Stigma regarding drug use, and the use of stigmatized representations of drug use in the political process, have contributed to ongoing restrictions of wider scale implementation of OST, as well as to an ongoing ban against the use of federal funds to support NSPs. The delivery of health care and preventive services to PWUDs is limited by these restrictions, which complicates the implementation of an effective public health approach to HCV among PWUDs in the U.S. (Des Jarlais, 1995; Des Jarlais, Friedman, & Ward, 1993)

There are an estimated 774,000–1.5 million lifetime PWID in the U.S. (Lansky, et al., 2014; Tempalski, et al., 2013) The U.S. has had a high prevalence HCV epidemic among PWID since at least the 1970s and between 43–48% have HCV infection. (Armstrong, et al., 2006; Lansky, et al., 2014) Transitions from opioid analgesic use to injection drug use are leading to an emerging epidemic of HCV among young PWID in the U.S. (Havens, et al., 2013; Lankenau, et al., 2012)

Despite evidence of superior effectiveness for OST versus non-OST based opioid dependence treatment, stigma and political factors sometimes favor the implementation of non-OST based drug treatment; current evidence suggests that non-OST drug treatment is also not effective HCV prevention. (Hagan, Pouget, & Des Jarlais, 2011) In virtually all U.S. locales for which there are data, the OST available is insufficient to treat all persons needing it. OST using methadone has been legal for decades in the U.S. and buprenorphine became licensed for use in 2002. As of 2011 there were 1,459 opioid treatment programs serving 304,000 opioid dependent persons daily. (Frimpong, 2013) Of 2.6 million persons 12 years of age and older with opioid dependence in 2010, only an estimated 1 million received OST in that year. (National Institute of Drug Abuse, 2010)

Structural barriers to accessing OST stem in part from specific characteristics of health insurance in the U.S. For many years, third party payment for treatment of substance use disorders was more restrictive than that for other forms of medical care in the U.S., limiting access to substance use treatment. (Buck, 2011; McLellan & Woodworth, 2014) The 2008 Mental Health Parity and Addiction Equality Act, and the 2010 Affordable Care Act (ACA), have reduced these barriers to OST, but have not eliminated restrictions on OST coverage; the full impact of the ACA is not yet clear. (Wen, Cummings, Hockenberry, Gaydos, & Druss, 2013) Medicaid, the U.S. healthcare insurance for low-income persons, is a state-administered program. State Medicaid coverage for OST is highly variable; several states do not cover outpatient OST, and some states have limits on the duration of coverage. (American Society of Addition Medicine, 2013) Commercial health plans are also highly variable as to their coverage of OST. (American Society of Addition Medicine, 2013) These differences in coverage may impede long-term or consistent receipt of OST even among those dichotomously considered “insured” by either private or public payers.

OST programs in the U.S. are highly variable as to their medical infrastructure. The proportion of opioid treatment programs in the U.S. offering access to HCV testing increased from 73% to 90% from 2005 to 2011, but an increasing proportion did so by referring participants for off-site testing. (Frimpong, D’Aunno, & Jiang, 2014) Receipt of revenue from federal funding is associated with increased on-site HCV testing. However, the proportion of programs receiving federal funding decreased; only 34% of opioid treatment programs in the US offered any on site HCV testing in 2011, a decline from 53% in 2005. (Frimpong, et al., 2014)

OST programs with an academic or hospital affiliation have been found to be more likely to offer on-site HCV testing. (Frimpong, et al., 2014) However, the proportion of OST programs having academic, or even hospital, affiliations decreased from 18% to 12%. Point of care HCV tests have the potential to allow widespread testing in OST settings where

medical infrastructure is limited. Currently these tests are not routinely conducted or funded at OST programs, and since positive point of care tests require subsequent viral load testing and linkage to care, gaps in the HCV care are often introduced at these steps. (Morano, et al., 2014; Perlman & Jordan, 2014) Regardless of whether HCV testing is done on site or off site by effective linkage, its potential contribute to HCV control (through primary prevention and through enhancing TasP) would be enhanced by strategies to address identified barriers to, and to utilize identified facilitators of, HCV testing among PWID. (Harris & Rhodes, 2013; Jordan, et al., 2013; Lally, Montstream-Quas, Tanaka, Tedeschi, & Morrow, 2008)

Co-located models of HCV care avoid the need for linking infected persons from MMT to other HCV care sites, but given the limited medical infrastructure in most MMT programs other strategies, such as linkage support or telemedicine, may be more practical ways to leverage OST for HCV care. A recent study showed that a linkage to HCV care intervention for MMT patients can significantly improve linkage to off-site HCV care compared to education and traditional referral only (OR: 4.10; 95% CI: 2.35–7.17). (C. L. Masson, et al., 2013) However, neither co-located models nor linkage models are widely implemented. (Bruggmann & Litwin, 2013; Masson, et al., 2013; Perlman, et al., 2014)

In the U.S., in addition to available MMT slots, buprenorphine is also available by prescription for opioid dependence. However, the implementation of buprenorphine as OST has been limited by variations in State regulations governing its use, by costs and insurance coverage limitations, by limitations in the number of providers who are credential to prescribe it and actually do so, and by caps in the number of patients any given credential provider can treat. Of the approximately 625,000 physicians eligible to do so, a total of 25,388 are certified to prescribe buprenorphine; 5,300 primary care physicians (just 2.5% all primary care physicians) and only 1,200 addiction specialists (less than one-third of the total) are burprenorphine certified, sharply limiting access for patients, especially in less populous areas where there may be no certified providers at all. (SAMHSA, 2014) While buprenorphine affords the potential to expand OST options for opioid dependent persons, and to potentially expand use OST for HCV services, due to limitations in provider capacity as well as in insurance coverage this potential has not yet been realized.

How HCV treatment is paid for in the U.S. health insurance system is highly relevant to plans to address the HCV epidemic among PWID and specifically to using OST to do so. Commercial insurance plans generally cover drugs approved by the Food and Drug Administration and generally follow standard treatment guidelines, but generally with prior approval processes and variable patient co-payment requirements. Whether Medicaid will pay for HCV treatment is decided separately by each state program. Some states have added new direct acting antiviral agents (DAA) such as sofosbuvir to their Medicaid formularies and will pay for them when prescribed by HCV providers; others have not done so out of cost concerns (e.g., as of February 2015 neither Michigan nor Texas Medicaid plans cover sofosbuvir). Some states Medicaid plans have established a need for rigorous prior approvals (e.g., California, Florida, Massachusetts, Illinois, Pennsylvania and New York as of February 2015) (National Institute of Health, 2014), and some limit treatment or access to DAAs to patients with grade 3 or 4 liver fibrosis. Particularly relevant to PWUDs are new (or under consideration) requirements for a ‘readiness for treatment’ assessment that

includes measures of abstinence. Previous U.S. National Institute of Health HCV treatment guidelines had suggested that PWID not be offered HCV treatment until or unless they had ceased illicit drug use for at least 6 months; these unethical guidelines led to fewer HCV infected PWID being treated. (Edlin, et al., 2001) While these recommendations in treatment guidelines had been removed, the reinstitution of guidelines that include abstinence measures as a requirement for assessing 'readiness for treatment' in many ways represents a throwback to an era of prior HCV treatment guidelines that discouraged treatment for persons with recent or current illicit drug use. (Edlin & Winkelstein, 2014)

Viet Nam

In 1986 Viet Nam began a series of policy changes referred to as *Doi Moi* (Boothroyd & Phạm, 2000) which included a gradual transition from a socialist economy to a more capital-based economy. These transitions were temporally accompanied by a rise in injection drug use, and by an expanding HIV epidemic among PWIDs. The population of PWIDs is estimated to have increased 70% between 2000–2004. (Quan, et al., 2011) As of 2012, Viet Nam had 171,000 registered PWUDs. (Nguyen, Nguyen, Pham, Vu, & Mulvey, 2012) While *Doi Moi* has been accompanied by significant cultural transformations, injection drug use has remained highly criminalized and stigmatized (national law labels it a "social evil"), informed in part by collective historical memory of the impact of the British imperialistic opium trade on the Vietnamese population. (Dao, Hirsch, Giang le, & Parker, 2013; Reid & Higgs, 2011) In 2006 the Vietnamese government formally endorsed harm reduction interventions, yet the expansion of MMT for opioid dependence met with greater resistance than did the expansion of NSP, for reasons including these historical memories and caution in establishing a national dependence on externally produced medication. (Edington & Bayer, 2013) PWUDs identified by police may be sent to compulsory drug treatment centers, estimated to hold 50,000–60,000 PWUDs in which drug treatment is non-OST-based. (World Health Organization, 2009) In 2008 MMT was piloted in 2 cities, Hai Phong and Ho Chi Minh City, with police playing a role in referring some PWUDs to the expanding number of MMT programs, and referring other PWUDs to the compulsory treatment centers. (Jardine, Crofts, Monaghan, & Morrow, 2012)

In Viet Nam, estimates of HCV prevalence among PWID range from 31% to 97.2% (Ye, Pang, Wang, & Liu, 2014) and a U.N. document estimated an average prevalence of 74% among PWID. (United Nations Office on Drug Control, 2013) Hence Viet Nam has a high prevalence HCV epidemic among PWID. Rates of HIV infection and HCV infection were 28.4% and 56.9%, respectively among 965 eligible patients in a MMT program in Ho Chi Minh City and Hai Phong in the first year of the MMT pilot. (Hoàng Đình Cảnh, 2013) HCV incidence among PWIDs with a recent onset of injection (<4 years) in one study was 23.35 per 100 person-years and the mean time between first injection and first positive HCV test was 1.2 years. (Clatts, Colón-lópez, Giang, & Goldsamt, 2010)

MMT was expanded in Viet Nam in response both to the large population of PWID, and the drug use-driven HIV epidemic. In 2011 Viet Nam announced plans to domestically produce methadone, however thus far methadone used is imported. (Edington & Bayer, 2013) The Vietnamese government also authorized the Ministry of Health (MOH) to expand MMT to

at least 30 provinces to provide treatment for more than 80,000 drug users by 2015. (Government of Vietnam, 2014) MMT is being expanded in Viet Nam with support by the Viet Nam MOH, as well as international agencies, non-governmental organizations (NGOs), and with co-payments from PWUD being treated. In anticipation of decreases in international funding, the Vietnamese National HIV Strategic Plan identified a need for increased revenue streams to promote sustainable HIV prevention, and conducted studies of PWUDs' willingness to pay for drug treatment. These studies have concluded that PWUD are willing to pay co-payments and this approach is being built into the national expansion of MMT. (Tran, 2013) As of September 2014, Viet Nam had established 122 MMT in 38 provinces and cities and has provided treatment for 30,850 PWUDs. Buprenophine is not currently available in Vietnam.

In 2010, Viet Nam initiated a nationwide campaign for liver health which includes plans for increased screening for HCV, and expanded linkage to care and treatment for HCV. (Gish, et al., 2012) One modeling study estimated that even 25% HCV treatment coverage in Viet Nam could decrease HCV incidence and prevalence among PWID. (Durier, Nguyen, & White, 2012) HCV antibody testing is available in Viet Nam, but HCV testing in MMT settings is available only to patients who can self-pay. HCV viral load testing is available in Hanoi and Ho Chi Minh City, and generally not in the provinces. The Viet Nam MOH issued HCV treatment guidelines in November 2013, and recommends treatment with interferon, ribavirin and either telaprevir or boceprevir; national guidelines do not yet address the use of newer DAAs. For those who can pay for treatment, HCV treatment is available in national hospitals, but generally not in provincial hospitals. Yet currently virtually no HCV treatment is provided for HIV-HCV co-infected patients in HIV care settings, HCV treatment is not provided in MMT settings, and overall few PWID are treated. Costs of treatment, payment requirements, limitations in provider capacity and stigmatization of PWID all contribute to this situation. Whether recent changes in licensing deals for new DAAs will translate to increased numbers of PWID being treated remains to be seen.

Estonia

In Eastern Europe, drug use was not unknown during the socialist era, (Lagerspetz & Moskalewicz, 2002) and was labeled as a moral problem, stigmatized and criminalized. Injection drug use epidemics emerged in the 1990s and have led to some of the highest HCV prevalence rates among PWID (Nelson, et al., 2011) reported in the world. Drug use is highly criminalized; ("Act on Narcotic Drugs and Psychotropic Substances and Precursors," 1997) over two thirds of PWID have been imprisoned at least once during their lifetime. (Abel-Ollo, et al., 2009; Uuskula, et al., 2010; Vorobjov, Uuskula, et al., 2012)

Injection drug use grew rapidly in Estonia at the same time as the political and market reforms of the 1990s. (Lagerspetz & Moskalewicz, 2002) The transition from Soviet occupation to autonomy brought about major societal upheaval. Employment fell by one fifth, the gross domestic product decreased by nearly 40% (Lauristin & Pettai, 2011; Staehr, 2004) and there were cuts in social services linked to loans from international lenders. There were concomittant increases in several communicable diseases, most notably HIV, HCV,

sexually transmitted diseases, and tuberculosis. (Uuskula, Plank, Lassus, & Bingham, 2001; Uuskula, Silm, & Vessin, 1997) While comparable pre- and post-transition data are scant, by the mid 1990s a high prevalence HCV epidemic was established among PWIDs the preceeded the HIV epidemic by several years. (Stuckler, King, & Basu, 2008; Uuskula, Kalikova, Zilmer, Tammai, & DeHovitz, 2002)

Although stigmatization of drug use has been identified an obstacle to the expansion of harm reduction services for PWID, (Vorobjov, Uuskula, Abel-Ollo, Talu, & Jarlais, 2009) NSP services were expanded in Estonia (in the capital, Tallinn, and in cities in the North East). Studies have identified HCV serorprevalences of 74%–94% among PWIDs, and rates of chronic HCV of 64%– 88%. (World Health Organization, 2010b) Among PWID attending a NSP in the mid 2000s the prevalence of HCV antibodies was 96%. (Vorobjov, Uuskula, Abel-Ollo, Talu, Ruutel, et al., 2009) The expansion of NSPs and increases in syringe coverage was associated with a significant reduction in HIV incidence among PWID, from 21/100 PYO to 9/100 PYO between 2005 and 2009. (Jarlais, Feelemyer, Modi, Abdul-Quader, & Hagan, 2013; Uuskula, et al., 2011) Yet recent injectors still have a high HCV incidence (77/100 PYO) (A Uuskula, DC Des Jarlais, personal communication).

Healthcare in Estonia is funded through a system in which employers are obliged to fund health insurance for their employees through the Estonian Health Insurance Fund (EHIF). In addition, certain groups of unemployed persons (e.g., pregnant women, persons under 19 years of age) are covered directly by the EHIF. As of 31 December 2013, EHIF had 1,231,203 members representing 93.4% of the Estonian population. However, fewer than 50% of Estonian PWIDs have health insurance. (Vorobjov, Des Jarlais, et al., 2012)

Methadone detoxification has been available in Estonia since 1998, and MMT was initiated in 2001 and has expanded as part of the national HIV prevention strategy. (Mounteney & Griffiths, 2014) State government funding is the primary payment mechanism for MMT. (World Health Organization, 2010b) In 2012 there were 685 treatment slots and approximately 1157 PWUDs received MMT, but overall OST coverage of the opioid dependent population is estimated to be less than 15%. (Mounteney & Griffiths, 2014) The majority of MMT is provided by NGOs and to small extent in the capital, Tallinn, by local health care providers. Most MMTs refer participants for off site HCV (and HIV) testing by other health care providers. Burpenorphine is generally not available in Estonia.

HCV treatment was introduced into Estonia in 2001, yet while HCV treatment agents are available, cost, insurance coverage, insurance policies, stigmatization of drug use and PWUDs, and the reflection of that stigmatization in policy, are barriers to expanded treatment. HCV treatment is accessible to those insured by the EHIF or otherwise able to pay. The EHIF will cover HCV treatment for persons who are insured by the fund, yet current national HCV treatment guidelines consider injection drug use as a contraindication for HCV treatment, and do not specify any period of abstinence to qualify for treatment. (Margus, Salupere, & Ott, 2010; World Health Organization, 2013) Nevertheless, 12 % (Tuuling, 2011) to 28% (Brjalin, et al., 2012) of people in HCV treatment attribute their HCV infection to past injection drug use.

Conclusions

In this paper we have outlined several social, program and structural level factors relevant to controlling the HCV epidemics in the U.S., Estonia and Viet Nam, and in particular those factors relating to the use of OST as part of HCV public health control. In each country examined, a range of interconnected factors affects the use OST as HCV prevention and as a means to improve the HCV care continuum. These factors include 1) that OST is not yet provided on the scale needed to adequately address illicit opioid dependence itself, 2) inconsistent use of OST as a platform for HCV services, 3) the high costs of HCV treatment, and health insurance systems and policies that affect access to both OST and HCV treatment, and 4) the stigmatization of drug use and PWID.

In developing plans for future HCV control efforts, and of utilizing OST as a platform HCV control, it is helpful to consider the experience with efforts to control HIV infection among PWID in these three countries. While the current obstacles to controlling HCV in the U.S., Estonia, and Viet Nam are certainly considerable, the initial obstacles to controlling HIV infection may well have been more formidable. In particular, political opposition to NSPs in the U.S., and financial resource and other resource constraints in Estonia and Viet Nam were much greater. Despite these barriers—which have been reduced but certainly not eliminated—HIV transmission has been greatly reduced in the US (Centers for Disease Control Prevention, 2012) and Estonia (Jarlais, et al., 2013; Uuskula, et al., 2011) and has stabilized in Viet Nam. (Des Jarlais, et al., 2007) Thus, we do believe that there is also a reasonable prospect for controlling HCV among PWID in these three—and many other—countries.

We see the following steps as the most likely route for eventually controlling HCV transmission among PWID:

1. Maintaining current HIV prevention efforts, with increased attention to HCV prevention. Because HIV prevention has been quite successful, there is a danger that funding for these programs may be reduced. Reductions in HIV prevention (OST and NSPs) would probably lead to new outbreaks of HIV, and because HCV is so efficiently transmitted through sharing injection equipment, would make control of HCV among PWID close to impossible. In addition, increased attention to issues of particular relevance to HCV, such as reducing sharing of drug preparation equipment, aspects of injection relationships and contextual aspects of injection, and injection cessation and ‘breaks’ are needed. (Page, Morris, Hahn, Maher, & Prins, 2013)

2. Expand systematic efforts to reduce the societal stigma attached to drug use and PWUDs. In each country discussed, the stigmatization of drug use and of PWUDs, and political manipulation of this stigmatization, has resulted in laws and policies that constrain implementation of evidence-based public health approaches to HCV. (Edington & Bayer, 2013; Edlin & Winkelstein, 2014) Individual stigmatization and structural stigmatization are interrelated and mutually reinforcing; stigma is best conceived of as a multilevel construct. (Angermeyer, Matschinger, Link, & Schomerus, 2014; Cook, Purdie-Vaughns, Meyer, & Busch, 2014) Structural stigma and stigmatizing social environments contribute to HIV and HCV risk

behaviors (Rhodes, Singer, Bourgois, Friedman, & Strathdee, 2005; Rhodes & Treloar, 2008) and pose barriers to public health efforts to control HCV. (Rhodes, 2009) Systematic efforts relevant to each country are needed to reduce the stigma attached to drug use and PWUDs, and to revise laws and policies that stigmatize PWUD (e.g., policies which prohibit or discourage HCV treatment based on drug use status), including those relevant to the expansion of OST and of HCV treatment for PWUD. Efforts to address the stigma associated with HIV (e.g., use of a Stigma Index as part of program evaluation) (Tomaszewski, 2012) and the stigmatization of drug users (e.g., such as those of drug users' unions and other forms of community mobilization, efforts of some non-governmental organizations such as the STIGMA Foundation in Indonesia, and those of some governmental organizations such as the United Kingdom Drug Policy Commission) (Drug Policy Commission, 2010; Friedman, et al., 2007; Spratt, 2010) are both directly relevant efforts to decease stigmatization of PWUDs, and can serve as models for further efforts to reduce stigma as it impacts HCV prevention and care. (Mahajan, et al., 2008)

3. Expand and improve use of OST as part of a coordinated public health approach to opioid dependence, HIV prevention, and HCV control efforts. WHO HCV guidelines recognize OST as a critical component of HCV prevention and care efforts. (World Health Organization, 2005) Yet the U.N. estimates that one in 6 PWUDs globally receive any drug treatment in any given year (Burns, 2014) – and gaps in OST forms of drug treatment are even greater. In the three countries examined, however, OST was included in national HIV prevention efforts. The policies that facilitated this decision could potentially serve as models for the further expansion of OST to simultaneously serve multiple public health goals, including both those related to drug use itself, those related to HIV, as well as those related to HCV prevention and care engagement. Expansion of OST should be accompanied by efforts to improve OST services, (Fraser, 2006) including efforts to 'tame systems' though 'negotiated flexibility', to reduce structural stigmatization, and reduce structural reinforcement of criminalization, of PWUD and drug treatment through greater integration of OST in health care systems, to minimize controlling, surveilling, and demoralizing aspects of OST systems to create more enabling and trust promoting (and deserving) environments of care, (Harris, et al., 2013) along with efforts to increase OST options including the expanded use of buprenorphine.

   Current health insurance systems and policies contain elements that both facilitate access and create barriers to OST and the use of OST as a link to HCV care. Efforts to address these systematic barriers, to expand OST access and coverage, and to implement sustained support of OST based HCV services and models to improve retention in the HCV care continuum will be needed to control HCV among PWID.

4. Reductions in the current cost of treatments for HCV infection and expanded coverage of HCV treatment by health insurance systems to allow population level HCV treatment as prevention. Pricing structures for HCV treatment agents pose barriers to significant treatment scale up for low and middle-income countries.

Such price considerations are also relevant in the U.S. where cost considerations affect private and public payer policies governing access to HCV treatment. Thus, substantial price reductions and changes in health insurance policies will be needed if large numbers of HCV infected PWID are to be treated in these countries. Treating substantial numbers of persons infected with HCV would undoubtedly prevent considerable morbidity and mortality. Modeling studies suggest that to reduce the prevalence of HCV by three fourths within 15 years, TasP would have to be significantly scaled up. (Martin, et al., 2013) Both mathematical modeling and lessons learned from the HIV epidemic demonstrate that scaled up "combination prevention" will be required to control the HCV epidemic among PWID. This would include expansion of OST and NSPs, and use of OST to engage HCV infected PWID in treatment.

Great progress has been made in reducing HIV transmission among PWID, including providing antiretroviral treatment to increasing numbers of HIV infected PWID. HCV transmission and the morbidity and mortality associated with HCV infection among PWID can also be greatly reduced. The global expansion of OST, and its use as HCV prevention and as a means of engagement in the HCV care continuum should be a feasible next step in the public health response to the HCV epidemic and is likely to be critical, if not essential to, efforts to eliminate or eradicate HCV.

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Highlights (for review)

We examined the use of mediation assisted treatment of opioid dependence to improve the HCV control.

The stigmatization of drug use is a barrier and should be addressed.

Mediation assisted treatment should be expanded as part of HCV control efforts.

Public health efforts for opioid dependence, HIV and HCV should be coordinated.

Expanded health coverage is needed to allow HCV treatment as prevention.