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Combination prevention for persons who inject drugs in the HIV epidemic in a transitional country: The case of Tallinn, Estonia

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Abstract

The study was undertaken to assess the potential effectiveness of combination HIV prevention on the very high seroprevalence epidemic among persons who inject drugs (PWID) in Tallinn, Estonia, a transitional country. Data from community-based cross-sectional (respondent driven sampling) surveys of PWID in 2005, 2007, 2009 and 2011 were used together with mathematical modeling of injection-associated HIV acquisition to estimate changes in injection-related HIV incidence during this period. Utilization of one, two or three of the interventions available in the community (needle/syringes exchange, antiretroviral treatment (ART), HIV testing, opioid substitution therapy) was reported by 42.5%, 30.5%, 11.5% of HIV+ and 34.7%, 36.4%, 5.7% of HIV- PWIDs, respectively in 2011. The modeling results suggest that the combination of needle/syringe programs and provision of ART to PWID in Tallinn substantially reduced the incidence of HIV infection in this population, from an estimated 20.7/100 person-years in 2005 to 7.5/100 person-years in 2011. In conclusion, combination prevention targeting HIV acquisition and transmission-related risks among persons who inject drugs in Tallinn has paralleled the downturn of the HIV epidemic in this population.

Keywords

Persons who inject drugs; intervention; HIV; needle/syringe exchange; antiretroviral treatment; opioid substitution therapy; Estonia

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Introduction

The variety of available HIV prevention interventions for persons who inject drugs (PWID)—which includes needle/syringe exchange programs, opiate substitution treatment; antiretroviral treatment, and most recently, pre-exposure prophylaxis—poses a challenge to the scientific community to develop the knowledge base needed to determine optimal combinations of these prevention interventions for specific populations of PWID. In addition, research and surveillance methodologies that enable monitoring and adjusting combination prevention packages to rapidly respond to epidemiological exigencies are urgently needed.

High seroprevalence HIV epidemics among PWID—with seroprevalence reaching 40% or higher—have occurred in many different areas throughout the world, including high-income countries, transitional countries, and middle/low-income countries (Mathers et al., 2008). The implementation of combined HIV prevention interventions, particularly needle/syringe programs (NSPs), opiate substitution treatment (OST), and anti-retroviral treatment (ART) for HIV infection have helped to control the HIV epidemic among PWID in a number of high income areas—with HIV incidence among persons who inject drugs reduced to < 1/100 person-years at risk, including Amsterdam (de Vos, Prins & Kretzschmar, 2012), New York City (Des Jarlais et al., 2010) and Vancouver, Canada (Montaner et al., 2012).

Injection drug use is driving HIV epidemics in many countries in Eastern Europe, Central Asia, and Southeast Asia (European Center for Disease Control [ECDC], 2008). Whether combined prevention programming will bring these high seroprevalence epidemics under control in resource-limited settings (transitional and low and middle-income countries) is a critical question in HIV prevention.

There are several aspects of HIV epidemics among PWIDs in transitional/low/middle income countries that make implementation of combined HIV prevention programs particularly challenging, including limited resources, marked stigmatization of PWID, and discrimination due to PWID belonging to ethnic minority groups (Des Jarlais et al., 2013a). Further, in many countries, injecting drug use is viewed as a “foreign,” “Western” practice that undermines the traditional values of the society. In some countries, programs such as syringe exchange and opiate substitution treatment are viewed as perpetuating drug use. In such situations, national leaders may oppose evidence-based HIV prevention programs. The Russian opposition to methadone maintenance therapy is an example of this (Elovich & Drucker, 2008).

This report provides preliminary evidence of the potential effectiveness of combination HIV prevention on the very high seroprevalence epidemic among PWID in Tallinn, Estonia, a transitional country. First we describe the history of the HIV epidemic among PWID in Tallinn. We then review the implementation history of interventions to reduce HIV transmission among PWID in Tallinn, as well as epidemiological particulars, obtained from community-based cross-sectional surveys of PWID in 2005, 2007, 2009 and 2011. Based on these data, we then apply a mathematical model of injection-associated HIV transmission to

estimate the impact of combination prevention on the HIV epidemic among PWID in Tallinn.

Background

Estonia is a small country in northeastern Europe with a population of 1,340,000 (Statistics Estonia, 2012). A very rapid HIV epidemic began in Estonia in the late 1990s and reached peak incidence in 2001 (108 infections per 100,000 person years; ECDC, 2008). Though lessened, the epidemic continues. In 2011 Estonia had the third highest per capita HIV incidence in Europe (27.3 / 100,000; ECDC, 2012). According to a global review of injection drug use and HIV epidemiology, Estonia has one of the highest concentrations of injection drug users among people aged 15-64 years (1.5% in 2007), which is coupled with a very high HIV prevalence among PWIDs (Mathers et al., 2008). Studies conducted among PWID in Estonia have found very high HIV prevalence rates (40–90%) (Platt L et al., 2006; Wilson, Sharma, Zilmer, Kalikova & Uusküla, 2007). In Tallinn, Estonia's capital and largest city, approximately 50% of the city's 5,000 - 7,000 PWIDs are already infected with HIV (Uusküla, Rajaleid, Talu, Abel-Ollo & Des Jarlais, 2013a).

Estonia's capacity to manage its response to HIV and AIDS has increased greatly over the past decade, particularly through funding from the Global Fund to Fight HIV/AIDS, Tuberculosis, and Malaria (The Global Fund, 2011). Global Fund support was also instrumental in building capacity for the governmental and nongovernmental sectors to interact constructively with each other. These cooperative actions included establishing systems for channeling funds through the government to NGOs and mechanisms for cooperation (Drew et al., 2008). These collaborative efforts resulted in several initiatives, including efforts to reduce the risk of harm faced by PWIDs by scaling-up syringe exchange programs and drug treatment programs. Antiretroviral treatment (ART) is available free of charge to all HIV-infected persons in need, including those without health insurance. There has been a significant increase in the number of persons on ART over the past years: from 250 (Rüütel, Trummal, Salekesin & Pervilhac, 2011) in 2005 to 2156 (Estonian Ministry of Social Affairs, 2012) in 2011.

In Estonia, HIV prevention services are provided by non-profit organizations, mainly funded by the state according to the operating plan of the national HIV/AIDS strategy (Rüütel, Trummal, Salekesin & Pervilhac, 2011). Table 1 presents information on the major HIV prevention services provided for PWID in Tallinn. These services are described further below.

Needle and syringe exchange programs

Needle and syringe exchange programs (NSP) were initiated in 1997 in Estonia. In 2009, there were nine organizations providing syringe exchange and HIV and drug counseling services (3 in Tallinn). Persons who inject drugs may obtain sterile syringes either directly at an exchange site or from syringe exchange community outreach workers. In order to protect confidentiality, exchanges do not record information on the persons obtaining sterile needles and syringes. Based on the numbers of syringes distributed and the estimated numbers of

PWID in Tallinn (~6000 at the end of 2000s), we estimate that about 120 syringes per PWID per year have been distributed in Tallinn since 2008.

Free condom distribution

Syringe exchange programs also provide free condoms at fixed site locations and through community outreach workers. As with syringes, information is not collected by the program about persons obtaining free condoms.

Opioid substitution treatment (OST)

Methadone maintenance therapy was officially introduced to Estonia in 2001. Because HIV/AIDS and illicit drug use in Estonia are interrelated, methadone treatment is state financed, in accordance with the national HIV/AIDS strategy. At the end of 2011, there were 5 institutions (7 centers) for substitution treatment with 690 patients on methadone maintenance treatment, 280 of whom were in Tallinn. Daily attendance is required for methadone patients to receive medication.

HIV testing

Free, voluntary HIV testing is available to the population groups who are at the most risk at several AIDS counseling and testing (VCT) clinics (including two VCT clinics in Tallinn) and via prevention and harm reduction service providers.

Medical HIV care and antiretroviral treatment

In Estonia, ART typically is initiated when CD4 cell counts fall below 350cells/mm² (European AIDS Clinical Society [EACS], 2013). HIV treatment is provided by the government healthcare system through infectious disease departments in five major hospitals (one in Tallinn).

Methods and Data Sources

Empirical data about the HIV epidemic among PWID in Tallinn were obtained from a series of community-based cross-sectional surveys of persons who inject drugs in Tallinn in 2005, 2007, 2009 and 2011. These surveys used respondent driven sampling (RDS) for subject recruitment. Potential participants were eligible to be included in the study if they were 18 years of age or older, were Estonian or Russian language speakers, reported having injected in the previous two months, and were able and willing to provide informed consent.

Each wave of data collection utilized a structured questionnaire based on the WHO Drug Injecting Study Phase II survey (version 2b (rev.2); Des Jarlais, Perlis, Stimson & Poznyak, 2006) that elicited information on respondents' demographics, drug use, and sexual behaviors. Additional questions elicited information on participants' utilization of various HIV-related services, including being tested for HIV in the previous 12 months, visiting an NSP with the last 4 weeks, currently receiving methadone treatment, and, for HIV-positive respondents, currently receiving ART.

Data on the volume of HIV prevention services (NSP; OST, and VCT)) were obtained from the Estonian National Institute for Health Development (National Institute for Health Development [NIHD], 2011). All study protocols were approved by the Research Ethics Committee of the University of Tartu, Estonia.

Modeling the effectiveness of combined prevention programs

We estimated the effectiveness of combined HIV prevention for PWID in Estonia using a mathematical model of injection-associated HIV acquisition based on Edward Kaplan's "needles that kill" modeling framework (Kaplan, 1989). In our model, the incidence of new HIV infections among PWID is a direct function of the number of injections with borrowed syringes and the proportion of borrowed syringes that are contaminated with HIV:

$$\text{Incident Infection Rate} = bct,$$

where b is the average number of injections with borrowed syringes per PWID per year; c is the proportion of borrowed syringes that are contaminated with HIV; and t denotes the per-injection probability of HIV transmission from a contaminated syringe to a previously-uninfected PWID (further explication of the model is provided in (Pinkerton, 2010). The proportion of contaminated syringes, c , depends upon the rate at which used syringes are exchanged for sterile ones—the greater the exchange rate, the shorter the average time each syringe spends in circulation, hence the less likely it is to become contaminated with HIV before (potentially) being used by another person. Specifically,

$$\text{Contamination Rate} = bp(1 - s) / (x + bp(1 - s)),$$

where p is the prevalence of existing infection among PWID, x denotes the number of syringes exchanged per PWID per year and s represents the percent of PWID on ART who have suppressed viral load. Persons with suppressed viral load were assumed incapable of effectively contaminating a syringe with HIV. Both the new infection rate and the contamination rate are measured in years, so that the model estimates the rate of incident cases of HIV per 100/person-years.

Results

Cross-sectional RDS studies recruiting PWID were conducted in Tallinn in 2005 ($n=350$), in 2007 ($n=350$), in 2009 ($n=329$) and in 2011 ($n=350$). Table 2 presents data on HIV prevalence, HIV testing, and ART coverage among study participants during these years. Table 2 indicate that the proportion of HIV-seropositive PWID in Tallinn receiving ART has increased greatly over the period of the 4 RDS surveys, reaching 40% among HIV-seropositive persons in 2011.

Combined prevention participation among current injection drug users

In 2011, 350 PWIDs (174 of whom were living with HIV) were surveyed. One third (18.5%) of study participants were on OST, two thirds (68.9%) were current users of NSP, 40% of HIV-infected respondents were on ART, and over half (55.7%) of HIV-uninfected

PWID reported being tested for HIV within the 12 months prior to study participation. (OST included both short-term detoxification programs and long-term maintenance programs in these analyses.)

Coverage with selected preventive interventions (ART, NSP, VCT, and OST) was assessed separately for HIV-infected and uninfected PWIDs. Only 12.1% of HIV-positive study respondents did not participate in any of the 3 applicable interventions (ART, NSP, OST): 42.5% reported utilizing a single intervention, 30.5% participated in 2 interventions, and 11.5% all three interventions. Most HIV-negative PWID (77.3%) utilized one or more of the applicable interventions (VCT, OST, NSP): 34.7% reported utilizing a single intervention, 36.4% participated in 2 interventions, and 5.7% participated in all three interventions. Other than ART, intervention utilization was not significantly different between HIV-positive and at-risk persons.

Modeling the combined effectiveness of syringe exchange and ART

Tallinn's syringe exchange programs have grown rapidly in recent years, from 38 syringes exchanged per PWID in 2005 to 125 syringes in 2011. During this same period, the proportion of PWID receiving ART grew from 0% to 40%.

The results of the modeling analysis of the impact of syringe exchange and ART on the incidence of HIV infection among PWID in Tallinn are presented in Table 3. The modeled incidence decreased rapidly - from 20.7/100 person-years in 2005 to 7.5/100 person-years in 2011 - as ART uptake and the number of syringes exchanged by Tallinn's NSPs increased over this period.

Because the number of methadone maintenance treatment positions (approximately 300) is extremely small compared to the estimated numbers of PWID in Tallinn (~6000), we did not include methadone treatment as a prevention strategy in the combination prevention model. A straightforward method for incorporating methadone maintenance treatment into the incidence estimation model would be to assume that persons in methadone treatment cease injecting drugs. (Note that this is an optimistic assumption, in that many persons in methadone treatment continue to inject). This would reduce the size of the drug injecting population by the number of persons in methadone maintenance treatment. Reducing the population of PWID by 300 (a 5% reduction versus the estimated 6000 PWID in Tallinn) would not have a noticeable effect on the HIV incidence rate among PWID, which also would be reduced by approximately 5%.

Discussion

Research in high income countries has documented that large scale implementation of needle syringe programs may have an impact within a short time period (2-3 years) (Des Jarlais, Feelemyer, Modi, Abdul-Quader & Hagan, 2013b), but achieving the maximal impact at the population level may take 5 -15 years after implementation of combined prevention (Des Jarlais et al., 2005; Des Jarlais, Arasteh & Friedman, 2011).

We conducted a series of community-based cross-sectional surveys of persons who inject drugs in Tallinn in 2005, 2007, 2009 and 2011, and used a mathematical model to estimate the potential impact on HIV incidence of NSP and ART on this high HIV prevalence epidemic. The modeled incidence was high at the beginning of the observation period (20.7/100 person-years in 2005) but decreased rapidly with in 5 years to 7.5/100 person-years in 2011. These estimates indicating a decrease in HIV incidence during the study time period are in the same direction as the Estonian surveillance data (the number of newly-reported HIV cases from all transmission routes in Tallinn decreased from 263 in 2005 to 205 in 2011) (Estonian Health Board, 2012).

Our incidence estimates suggest that, in combination, high but achievable NSP syringe distribution rates (~120 syringes per year per PWID) and moderate levels of ART coverage (20 to 40%) can have a marked effect on HIV incidence among PWID. Additional expansion of NSPs, increasing ART coverage among HIV-infected PWID, and increasing the proportion of persons on ART who achieve viral suppression would further enhance the impact of these interventions.

The set of interventions implemented in Tallinn as part of the combination prevention package was site and epidemic specific. Although scaling up ART (including for PWID) was possible in Estonia, it might not be so in other locations. Estonia has been unable to provide long-term maintenance OST at the public health scale – however OST has been a vital prevention component in several other countries (Gowing, Farrell, Bornemann, Sullivan & Ali, 2011; MacArthur et al., 2012). Further, interventions that reduce the infectiousness of HIV-positive persons needs be combined with strategies that reduce HIV susceptibility in the uninfected.

Our study has several limitations. The cross-sectional survey data were obtained from a non-probability sample of PWID, which may have implications for the representativeness of the study results. However, the sampling technique used in this study (respondent driven sampling) is known to mitigate some of the limitations of convenience sampling (Malekinejad et al., 2008). It is unlikely that the marked increase we observed in the proportion of HIV+ PWID on ART is due to sampling bias only.

PWIDs in Tallinn can also obtain sterile injection equipment from pharmacies (Vorobjov et al., 2009). We were unable to determine the numbers of syringes obtained from pharmacies over the 2005 to 2009 time period. Despite some imprecision in determining the numbers of sterile needles and syringes obtained by PWIDs in Tallinn over the time period covered by the surveys, it is clear from the data in Table 1 that there was a very substantial increase in the provision of sterile injecting equipment.

Our modeling included injecting-related HIV transmission but not sexual transmission, so that the actual HIV incidence among PWID in Tallinn is likely to be somewhat higher than our estimates suggest. As most of the sexual transmission is likely to be from PWID to non-injecting sexual partners (Uusküla et al., 2013b), sexual transmission to PWID is not likely to be substantial.

Despite these limitations, our findings strongly suggest that, in Tallinn, the combination of NSP, HIV testing, and scaling up ART for those in need has helped to reduce the magnitude of the HIV epidemic and may be vital for keeping the epidemic under control. Combined prevention targeting both acquisition and transmission related risks among those affected by HIV is important. The set of combined interventions should be site and epidemic specific, provided at a public health scale, and responsive to community and governmental stakeholders.

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HIV-positive IDUs (n = 174) **HIV-negative IDUs (n = 176)**

Note: ART – currently on ART; OST – currently on methadone; NSP – using NSP within 4 last weeks; VCT – 'being tested for HIV within the 12 months prior to the study'

Figure 1.

Utilization of the HIV prevention and treatment interventions to reduce infectiousness of HIV-positive persons who inject drugs (PWID) and interventions that reduce HIV susceptibility among HIV- uninfected PWID in Tallinn, in 2011

Table 1

Harm reduction services provided to persons who inject drugs (PWID) in Tallinn, Estonia, 2003 to 2011

	2003	2005	2007	2009	2011
Visits to needle/syringe programs	2341	30,863	63,324	63,333	35,764
Syringes distributed through NSPs	18010	230,409	600,021	774,782	748,384
Condoms distributed through NSPs	16,427	83,975	158,164	131,162	85,744
Treatment slots for opioid substitution treatment	0	103	200	209	280

Table 2

HIV prevalence, testing, and ART coverage among persons who inject drugs (PWID) in Tallinn, Estonia, 2005 to 2011 (data from cross-sectional RDS studies)

	2005	2007	2009	2011
Proportion of PWID infected with HIV (%)	54	55	50	50
Proportion of HIV negative PWID tested for HIV within the last 12 months (%)	54	56	31	49
Proportion of HIV-infected PWID on ART (%)	0	8.4	20	40

Table 3

Modeled HIV incidence rate among persons who inject drugs (PWID) in Tallinn, Estonia, 2005 to 2011

	2005	2007	2009	2011
HIV prevalence among PWID (%)	54	55	50	50
Syringes distributed through NSPs per PWID per year	38.4	100.0	129.1	124.7
HIV-infected PWID on ART (%) ^a	0	8.4	20	40
Estimated HIV incidence rate (%) ^b	20.7	11.1	8.0	7.5

^aViral suppression achieved by 50% of those on ART (Uusküla et al., 2012).

^bIncidence rate estimates assume 65.4 injections with borrowed syringes per year per PWID (Pinkerton, 2011) and a 0.0066 per-injection probability of HIV transmission (Kaplan & O'Keefe, 1993).