Appendix 2 (as supplied by the authors): Additional details regarding the models' methods, calibration and results

1. Estimation of transmission

Our model uses principles of dynamic compartmental modeling to estimate transmission of HIV and HCV. The most important assumption is the following equation, which is used to calculate the number of new infections in each time step:

(# injections, target group) $\times \frac{(\text{# injections, infected group})}{(\text{total # injections})} \times P(\text{transmission per injection})$

The terms with "# injections" in their description in the above equation represent the number of risky, shared injections. It is through such injections that infection could be transmitted. In our base case analysis, we distinguished between two types of risky injections depending on whether or not bleach was used, reflecting our assumption of reduced transmission risk associated with bleach use. We further defined similar equations to model sexual transmission, incorporating sexual contact with and without condoms.

To illustrate our approach, we focus on the number of new infections caused by needlesharing ("risky injections") between HIV-infected drug users and HCV+/HIV- drug users (the largest subgroup defined by HIV/HCV status among injection drug users). We focus only on those not using bleach.

Number of injections among infected group:

- Number of HIV+ injection drug users not in treatment after migration and aging in first 0.1 year: 1043
- Number of injections per user per month: 71.08
- Proportion of injections where needles are shared: 0.13
- Proportion of injections in which bleach is used: 0.5
- Risky injections among HIV+ injection drug users per month: **4820** (1043*71.08*0.13*0.5)

Number of injections among target group:

- Number of HIV-/HCV+ injection drug users not in treatment after migration and aging in first 0.1 years: 4509
- Number of risky injections among HIV-/HCV+ infected injection drug users who don't use bleach per 0.1 year: **20,832** (4509*71.08*0.13*0.5)

<u>Total number of risky injections: 29,028 (calculations not shown, includes uninfected</u> *co-infected individuals and those in treatment*)

New HIV infections (among injection drug users; from injections where bleach is not used):

• New HIV infections from HIV+ injected drug users not in treatment to HIV-/HCV+: 4820 * 20,832 / 29,028 * 0.008 = 28

These new HIV cases represent the bulk of new cases. Other cases occur among participants in treatment, those using bleach, and due to sexual transmission. We estimate that in the first 0.1 year, there are 37.1 transmissions due to needle-sharing (without the facility).

The SIF reduces transmissions due to decreased needle sharing among those injectors who use the SIF. We estimated 31.9 new transmissions due to needle-sharing in the first 0.1 year. (Among 21% who use the SIF, rate of transmission is decreased by about 70% (slightly less, since the odds ratio only approximates the relative risk), hence the number of transmissions decreased by about 14% (0.21*0.7). Accordingly, about 5.2 HIV transmissions (5.2/37.1 = 14%) are averted in the first 0.1 year and about 62 in the first year.

2. Calibration of our model with estimated HIV incidence among injection drug users

In the first 24 months, we estimated 865 new HIV infections among injection drug users (IDUs) for a crude incidence rate of about 12% over this time period (this number is approximate because it also accounts for aging and migration). The VIDUS cohort estimated that the cumulative incidence rate in the cohort over the first 24 months was about 10 to 12%, with a much lower incidence rate thereafter.¹

As outlined in the appendix to our manuscript, our model was calibrated such that the it yielded 350 cases in the first year of the model when the Safe Injection Facility was operative, which we estimated from observational data that the incidence rate for HIV infection in Vancouver was about 0.4 cases per 1000 people, the population was 578040, and an estimate that approximately one-third of people who become positive are unaware of their status.

3. Incidence over time

Although we estimate 62 HIV infections averted in the first year, it is important to note that our model is dynamic; hence, it accounts for increasing HIV prevalence over time and changes in population size. Accordingly, the number of HIV infections averted will change in a time-dependent manner, with more infections averted as HIV prevalence increases. Thus, the estimated total number of infections averted (1191) exceeds the estimate from multiplying those averted in year 1 by the model duration (620).

4. Core groups in epidemics

The notion that core groups can be important in understanding the spread of an epidemic has long been understood by mathematical modelers²⁻⁴ and epidemiologists.⁵ Several models have

estimated that an intervention targeted to a relatively small core group can have a much greater impact because of mixing with non-core individuals. For example, an intervention targeted to 1,000 female commercial sex workers in Kenya was estimated to prevent 6,000-10,000 new HIV infections per year. A dynamic compartmental model was used to analyze expansions of methadone maintenance programs and included both IDUs and the general non-IDU population.⁶ The authors found that, in addition to providing benefits for IDUs, significant benefits accrued to the general non-IDU portion of the population. Two scenarios were considered, corresponding to high and low prevalence of HIV among IDUs. Significant benefits accrued to the general population in both instances: "58% of the QALYs gained and 28% of the QALYs infections averted" in the high-prevalence scenario, and "71% of the QALYs gained and 36% of infections averted" in the low prevalence scenario. These benefits were so significant that even when the benefits that accrued to IDUs were completely ignored, the intervention was found to be cost effective in both scenarios. A compartmental model used to analyze expansions of HAART in St. Petersburg, Russia, found significant benefits in terms of infections prevented, with approximately 75% of the benefit accruing to non-IDUs even in cases when the intervention was targeted towards IDUs.⁷

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