Appendix 1 (as supplied by the authors): Full details of input parameters and data sources for the model used to determine the cost-effectiveness of Vancouver's supervised injection facility

Methods

Transitions between model compartments

We modeled three kinds of transmission between states – development of HIV infection, development of hepatitis C infection, and transitions into and out of injection drug use and addiction treatment (Figure 1). We assumed that infection with HIV or hepatitis C was possible through either sexual transmission or needle sharing.

Sexual transmission of HIV and hepatitis C

The literature includes a wide range of estimates for the risk of HIV transmission per sexual act.[1] Given that viral load suppression is associated with lower rates of HIV transmission and assuming that a significant portion of HIV-infected individuals would receive antiretroviral therapy, we used an estimate in the low range of possible values in our base case (0.1%), but tested a wide range of values in sensitivity analysis. Assuming 100 sex acts per year, we estimated the annual per-partner risk at 1%. This estimate is concordant with the observed transmission rate for discordant couples when the viral load level is low.[1]

Sexual transmission of hepatitis C is rare, although the exact rate is not well-defined.[2] In our base case example, we assumed that couples having sex approximately twice a week would transmit hepatitis C to each other at a rate of 0.3% per year.[2, 3] We included the probability of no sexual transmission in our range for sensitivity analysis.

We assumed that condoms would be effective in preventing transmission of both HIV and hepatitis C. We made the simplifying assumption that the efficacy of condoms for preventing both infections was similar and assumed that the relative risk of transmission with condom use, compared to no condom use, was 0.13.[4] We also estimated the proportion of time that condoms were used in sexual acts. Data from a national survey of the general public indicated that condoms were used in approximately 19% of all sexual encounters.[5] We used this estimate for uninfected (HIV-/hepatitis C -) non-users as well as for hepatitis C + (but HIV-) non-users, consistent with guidelines that hepatitis C discordant couples need not change their sexual practices.[6] In the non-user HIV+ population, we assumed a rate of 82%, similar to that observed in HIV+ gay men.[4] In the injection drug user population (hereafter referred to as "users"), data from VIDUS (the Vancouver Injection Drug Use Study) indicates that condom use was higher among those who were HIV+ (68%) than among those who were negative (47%) (VIDUS, personal communication). These estimates are consistent with reports in the literature.[4]

We assumed preferential random mixing when modeling sexual transmissions [7], in which users were more likely to mix with other users than with members of the general public. In a survey of sexually active male injection drug users, 32% reported that the person with whom they injected most often was a sex partner; accordingly, we used a slightly higher proportion than this (40%) as our estimate of the proportion of sex partners of users who are also users.[8]

HIV transmission also depends on the number of sexual partners. Data from VIDUS indicates that the mean number of annual sexual partners is about 2; we assumed that this estimate did not differ by HIV or hepatitis C status (VIDUS, personal communication). For the non-injection-drug using population, we assumed an average of 1 sexual partner per year.[4]

Needle-sharing transmission of HIV and hepatitis C

We modeled transmission of HIV and hepatitis C through needle sharing and prevention of such transmissions through the use of safe injection practices such as use of bleach to sterilize needles. We based our estimate of the probability of transmitting HIV through sharing a needle with an HIV-infected partner on an estimated per-act transmission risk of 0.8% in a previous model.[9] This estimate is slightly higher than a previous estimate [4, 10] but lower than an estimate which accounted for population use of antiretroviral medications but extrapolated from needlestick injuries.[11] The corresponding rate for hepatitis C was 4.0%.[12]

The efficacy of bleach in reducing HIV transmission remains controversial. Although laboratory data suggest that rinsing syringes with bleach is very effective at decreasing the viability of HIV (<1% with undiluted bleach) [13], bleach is not always used properly and some epidemiological data question its effectiveness in real world settings.[14] In our base case model, we made assumptions consistent with a previous model, that HIV transmission would decrease by 85% when bleach was used [10] and that bleach was somewhat less effective (65%) for decreasing hepatitis C transmission.[15] In a scenario analysis, we assumed that use of bleach had no effect on the transmission of HIV or hepatitis C.[14] We assumed that bleach was used in 50% of injections, based on a finding that 50% of control participants in an observational study of drug users used safe injection practices.[16] This estimate is commensurate with an earlier estimate from Vancouver that 39% of needle exchange users received bleach kits when exchanging needles.[17]

Among users not in methadone treatment, we assumed that needle sharing occurred 13% of the time, as observed in VIDUS (VIDUS, personal communication). This estimate represents the background rate when a needle exchange program is already in place. In our model, participants in methadone treatment shared needles while injecting about 70% less (relative risk = 0.30) than those not in treatment.[18]

A wide range of estimates are available regarding the frequency of injection, but many studies may be biased upward due to overrepresentation of frequent injectors when

sampling from sites such as needle exchange programs. Since the average number of daily injections is an important determinant of HIV incidence, we calibrated the number of injections to yield an incidence of approximately 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.[19, 20] This approach yielded an average of 711 injections per year per user, or about 2.0 injections per day, on average. In sensitivity analysis, we tested a range up to 4 injections per day. We assumed a reduction in injection frequency of approximately 6-fold for users receiving methadone treatment.[18]

HIV and hepatitis C prevalence

Data from the facility indicate that the prevalence of HIV among users of the facility was 17% and the prevalence of hepatitis C was 88% [21]; we assumed similar rates among the general injection drug user population. Similar estimates have been reported by the federal government's expert advisory committee.[22] We estimated the proportion using methadone treatment from the VIDUS, in which the proportion of users using methadone was approximately 11%, consistent with data from other studies.[23, 24] To estimate the prevalence of HIV among the non-injection drug using population, we subtracted infections among injection drug users from the total number of known cases and divided by the total population, using estimates from the Greater Vancouver Area, yielding an estimated prevalence of HIV among the non-injecting drug users of 27 per 10,000.[19, 20] For hepatitis C calculations, we used an estimated prevalence among non-injection drug users of 80 per 10,000 which is the average value for all of Canada.[25, 26]

Mortality

To estimate the mortality rate among non-injection-drug users, we averaged the annual mortality rate for the 15 to 64 year old British Columbia population, weighted by the Vancouver population distribution (21 per 10,000).[27, 28] Recent estimates from Denmark indicate that, after the advent of effective antiretroviral therapy, the additional annual mortality rate among HIV-infected individuals without hepatitis C co-infection was 1.9 per 100.[29] Natural history studies have estimated the relative mortality risk for untreated hepatitis C to be about 1.5.[30] We used a slightly lower value, 1.35, to reflect that some patients will have a sustained virologic response with treatment.[31]

We estimated an additional mortality estimates of 3 per 100 associated with injection drug use [4] and a relative hazard of 0.38 for drug users receiving addiction treatment.[4] We also assumed that hepatitis C +/HIV- users had no increase in mortality risk compared to hepatitis C -/HIV- users.[32] We further assumed that co-infected individuals had a 3-fold higher mortality rate than corresponding hepatitis C -/HIV+ population in each group.[29,32]

Size of the injection drug using population

We estimated that there were 7000 injection drug users in Vancouver. The most concentrated number of drug users is in the Downtown Eastside neighbourhood, where there are an estimated 5000 users. To estimate the number of users in outside of the Downtown Eastside, we assumed that there were 12,000 users in the Greater Vancouver Area [20] who would be proportionally distributed between the city of Vancouver (population 578,040) and the remainder of the Greater Vancouver Area (total population of Greater Vancouver approximately 2,000,000).[28] Accordingly, we estimated about 30% of 7000 (approximately 2000) users resided in the city of Vancouver and outside of the Downtown Eastside, yielding a total size of 7000 injection drug users. This number is consistent with the observation that about 8000 individuals have used the facility, which likely includes individuals from across Greater Vancouver.[22]

Population dynamics

We derived two parameters to meet modeling assumptions. First, we assumed that the population of Vancouver would grow by approximately 1.6% per year,[28] which required a migration rate into the population of 1.7% per year. We assumed that migration into the drug using population occurred at a higher rate than migration into the general population, although estimates for this assumption are difficult to find. In the base case, we assumed that migration rates were 50% higher. In sensitivity analyses we explored a wide range of possible values, from equivalent migration rates to rates that were 3-fold higher.

We estimated the rate at which individuals would age into the population by dividing the estimated number of individuals turning 15 by the 15 to 64 year old population size, using Vancouver data (1.2%).[28] We used a similar method to estimate the rate of aging out of the population, focusing on individuals turning 65 (1.0%). We made the simplifying assumption that there was no migration out of the population, but tested this assumption in sensitivity analyses. We further assumed that no HIV- or hepatitis C-infected individuals would initiate drug injecting if they were not already doing so. Finally, we assumed that the injection drug using population would grow by at approximately the same rate as the general population (1.6%) if there were no facility. With these assumptions, we calculated that 13 non-injection drug users per 10,000 people would initiate injecting drugs ever year. In sensitivity analyses, we also investigated the assumption that the drug using population would remain stable or fall an average of 1% per year over time.

Analysis of VIDUS data indicated that about 31% of participants initiated methadone maintenance therapy with a median follow-up of about 4.5 years.[24] Hence, we calculated approximately 8% of users would initiate methadone treatment each year. With a median time on methadone of 14.4 months, we calculated that about 44% of these individuals would discontinue methadone therapy each year, assuming a constant transition rate over this time period. This estimate is similar to previous estimates of 35%.[4,24] We further

assumed that 10% of patients leaving methadone treatment (4.4% of the total population receiving therapy) would discontinue injection drug use altogether.[4]

Other assumptions

In addition to the assumptions listed above, we also made several other conservative assumptions regarding the efficacy of methadone treatment and the facility. First, we assumed no increase in condom use, more effective condom use, or decrease in the number of sexual partners upon entering methadone treatment. Second, we assumed that the number of sex partners remained unchanged upon entering methadone treatment or using the facility. Third, we assumed that there was no limit to the capacity of methadone treatment services to include new patients. Fourth, many possible scenarios are possible that reflect the initial distribution of the population among the model compartments described above. We selected the scenario that maximized the expected number of HIV/hepatitis C co-infected individuals.

Costs

We expressed all costs in 2008 Canadian dollars using the Bank of Canada Consumer Price Index.[33] The most recent estimate of HIV-related costs comes from a comprehensive costing study in Alberta. In this analysis, the annual cost of treating HIV, expressed in 2008 dollars, is $15,564.[34], consistent with a recent review.[35] A United States modeling study indicated that the cost of care was considerably higher (average annual undiscounted cost of $25,574), but this estimate may double-count costs attributed to injection drug users; we used this estimate to set an upper bound for our sensitivity analysis of $30,000.[36] No published study has evaluated hepatitis C costing from a Canadian perspective, although a recent estimate of the cost-effectiveness of a potential hepatitis C vaccine extrapolated United States data to a Canadian setting; the United States study estimated a discounted lifetime cost of $35,000 to $40,000.[37,38] Assuming a life expectancy of about 22 years and adjusting for inflation and exchange rates, we calculated the annual undiscounted cost to be about $2650. To estimate costs associated with injection drug use, we extrapolated from two sources. A Vancouver study estimated that the annual cost of hospitalization for an HIV- user, expressed in 2008 dollars, was 2,724;[39] a study of the cost of substance abuse in Canada estimated that hospital costs accounted for approximately 69% of all costs.[40] Accordingly, we estimated the cost of treating an injection drug user at $3922 per year which is similar to recent U.S. estimates.[4] We estimated the treatment costs for users using methadone treatment would be about 20% less,[4] but that methadone treatment incurred an additional cost; one Canadian study estimated methadone maintenance costs of $6000 per year.[41] Finally, we estimated the facility cost as a fixed annual cost of $2.984 million based on data provided by the Scientific Evaluation of Supervised Injecting (SEOSI) investigators. This is comparable to estimates by the federal expert advisory committee.[22]

Calculation of cost-effectiveness ratios

We calculated incremental cost-effectiveness ratios by subtracting the expected discounted cost without the facility over the model time horizon from the expected discounted cost with the facility; we similarly calculated the expected health outcome by calculating the expected years of life gained in each scenario. The incremental cost-effectiveness ratio is calculated by dividing the incremental cost by the incremental health benefit.

Supplementary results

In the base case model (no facility), we assumed that the population of Vancouver experienced cumulative growth of about 17.2%. The prevalence of injection drug use in Vancouver remained relatively constant at between 121 and 127 individuals per 10,000 persons. Much of the growth occurred over the first 7 years, after which the size of the user population stabilized at about 8,200 users (Figure 2). With implementation of the facility, the size of the user population would continue to increase due to decreased HIV and hepatitis C infection and less associated mortality. Prevalence increased to a high of about 127 individuals per 10,000 persons after 5 years and then fell slightly thereafter; the absolute number of individuals grew to nearly 8,600 users.

We assumed that the presence of the facility did not increase the rate at which individuals entered methadone treatment. In the base case, the number of users receiving methadone treatment increased to about 1160 individuals and then stabilized at this value, representing 14.2% of all injection drug users (Figure 3). With the facility, the number of individuals entering drug treatment increased to about 1211 individuals at 10 years, representing 14.1% of all injection drug users.

HIV prevalence

The prevalence of HIV, including co-infected individuals, grew over the 10 year time horizon. In the base case, HIV prevalence in the entire population increased from about 0.40% at baseline to 0.81% after 10 years. With the presence of a facility, the prevalence of HIV after 10 years was 0.70% (Figure 4). The prevalence of HIV among injection drug users also increased in both scenarios. Without a facility, the prevalence increased from 17% at baseline to 50% after 10 years, whereas the growth with the facility was to 40% after 10 years.

Hepatitis C prevalence

The prevalence of hepatitis C in the overall population, including co-infected individuals, also increased over the timeframe of our model. The prevalence in the entire population increased from 1.64 % at baseline to 1.87 % after 10 years (Figure 4). With the presence of the facility, the prevalence of hepatitis C after 10 years was about 1.92 %. While the facility averted some hepatitis C infections, enhanced survival and subsequent hepatitis C transmission among users increased hepatitis C prevalence. Within the user population,

the prevalence of hepatitis C without the facility, increased from 88% at baseline to a peak of about 97.5% after about 3 years and then remained stable. With the facility, the prevalence peaked at about 97.0% after 4 years and remained stable.

Co-infection prevalence

The prevalence of HIV/hepatitis C co-infection increased in our model in the overall population, including users, from about 18.2 cases per 10,000 at baseline to 61.8 cases per 10,000 after 10 years. With the presence of a facility, the prevalence of HIV/hepatitis C co-infection after 10 years was 51.5 cases per 10,000. The prevalence of HIV/hepatitis C co-infection among injection drug users increased in both scenarios. Without a facility, the prevalence increased from 15% at baseline to 51% after 10 years, whereas the growth with a facility was to 41% after 10 years.

Sensitivity to the cost of HIV care

If the average annual cost of HIV care exceeded $10,339, the facility would result in a net cost saving (Figure 5). Only at very low costs of HIV care ($1000 per year), the incremental cost-effectiveness of the facility was $28,000 per life year gained.

Alternative scenario regarding bleach efficacy

We performed an additional set of analyses in which we assumed that bleach had no efficacy in preventing HIV or hepatitis C transmission. Under these assumptions, the number of HIV infections averted was 606, the number of hepatitis C infections averted was 34, and the undiscounted gain in life expectancy was 1,822 years. Focusing solely on facility operating costs, the undiscounted incremental cost per HIV case averted over 10 years was $39,500 and per hepatitis C case averted was $711,600. Discounted incremental costs were -$12.7 million (saving) and discounted health benefits were 1294 life years; thus, the facility dominated the alternative. Further incorporating effects of increased referral to addiction treatment yielded a discounted cost saving of $11.4 million and a survival benefit of 1476 years.

Figures

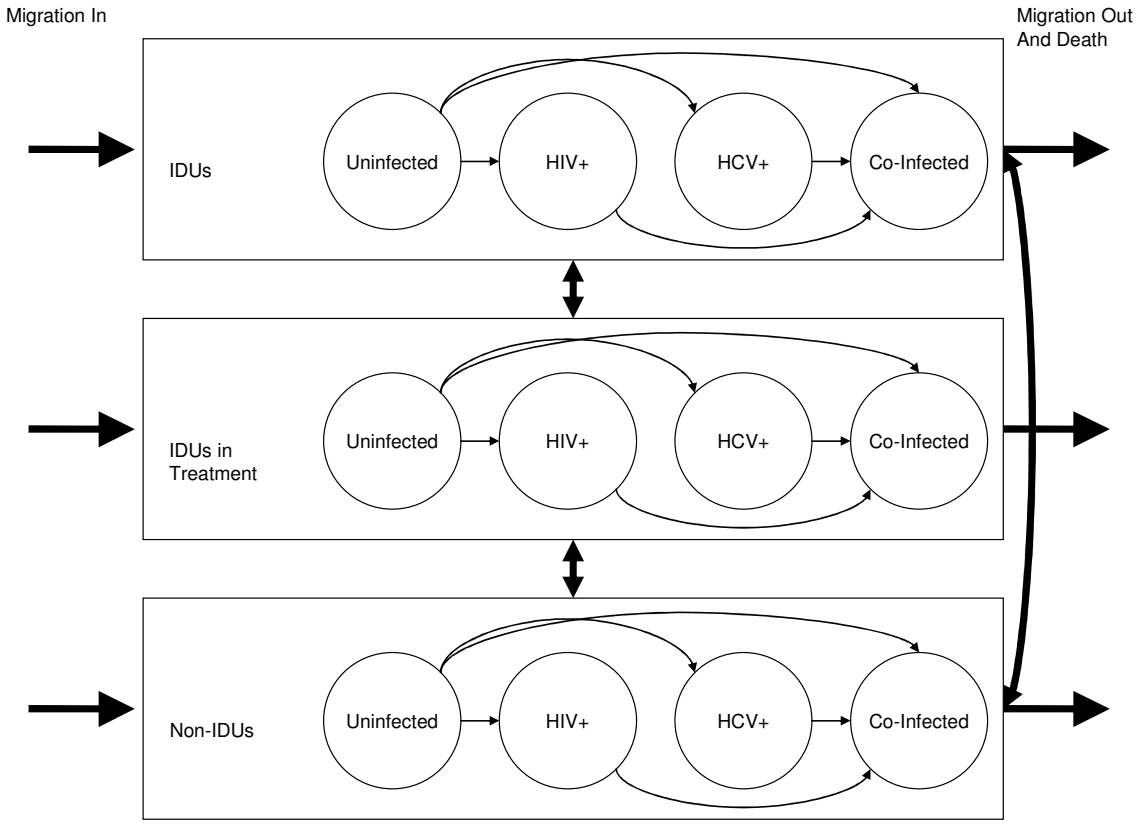

Figure 1: Simplified schematic of the model. Each circle represents one compartment in the model and each block represents injection drug user (IDU) status – active users (top), users receiving methadone maintenance treatment (middle), and non-injection drug users (bottom). Arrows indicate potential transitions between states, although some transitions are assumed to not occur in the base state model but explored in sensitivity analysis (such as migration or aging into the "IDU in Treatment block". Large arrows indicate that individuals from any state within a block can move to another state in another block. Thus, individuals move between states as they develop new infections, including Human Immunodeficiency Virus (HIV) infection, hepatitis C Virus (HCV) infection, or HIV–HCV co-infection, start or stop using injection drugs, and start or stop methadone. Movement into and out of the population is also represented. Deaths and aging out of the cohort may occur from any model compartment.

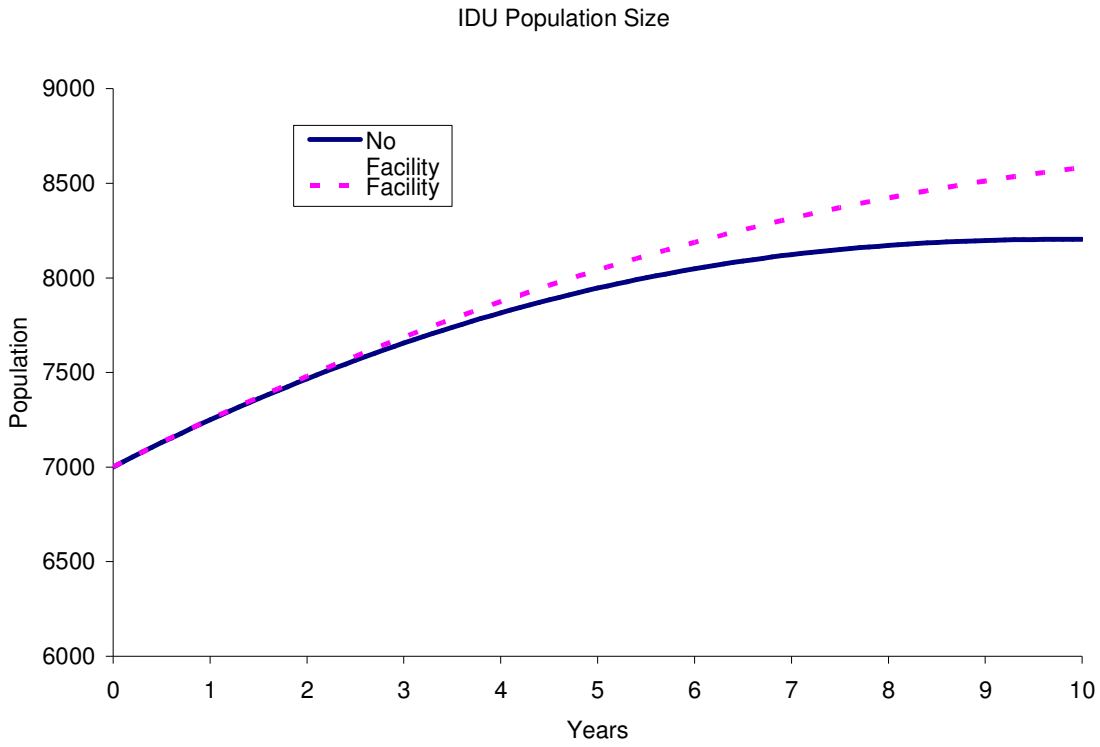

Figure 2: Projected increase in the population of injection drug users with and without a safe injection facility (SIF).

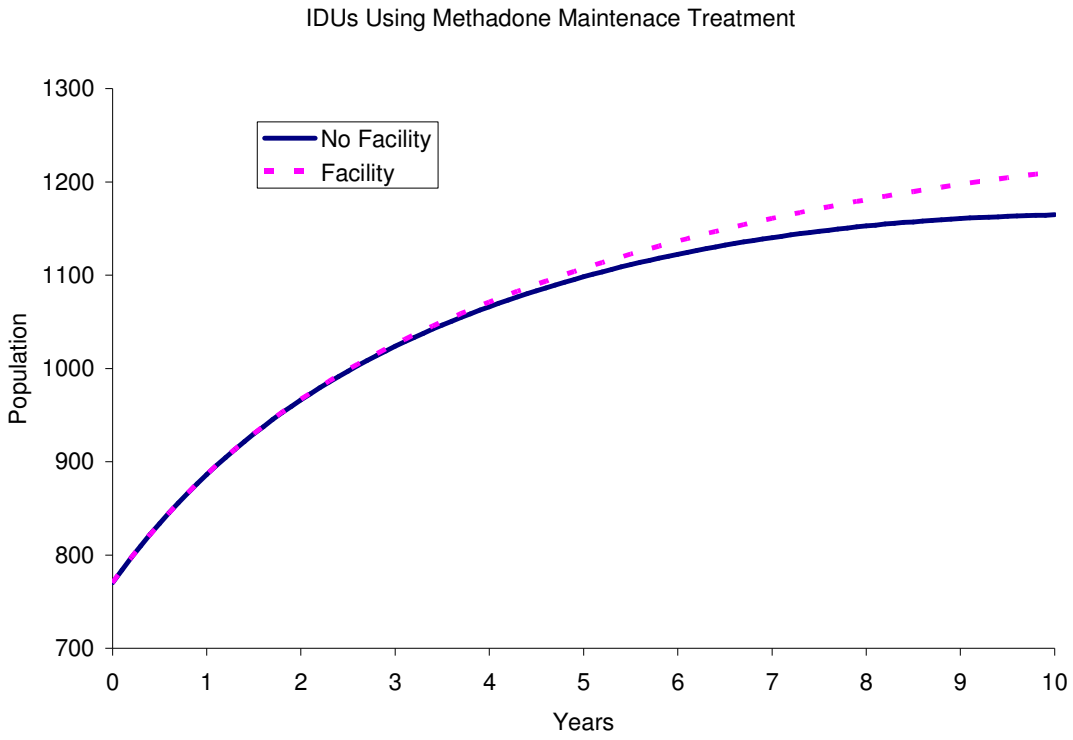

Figure 3: Projected increase in the population of injection drug users using methadone treatment with and without a safe injection facility (SIF).

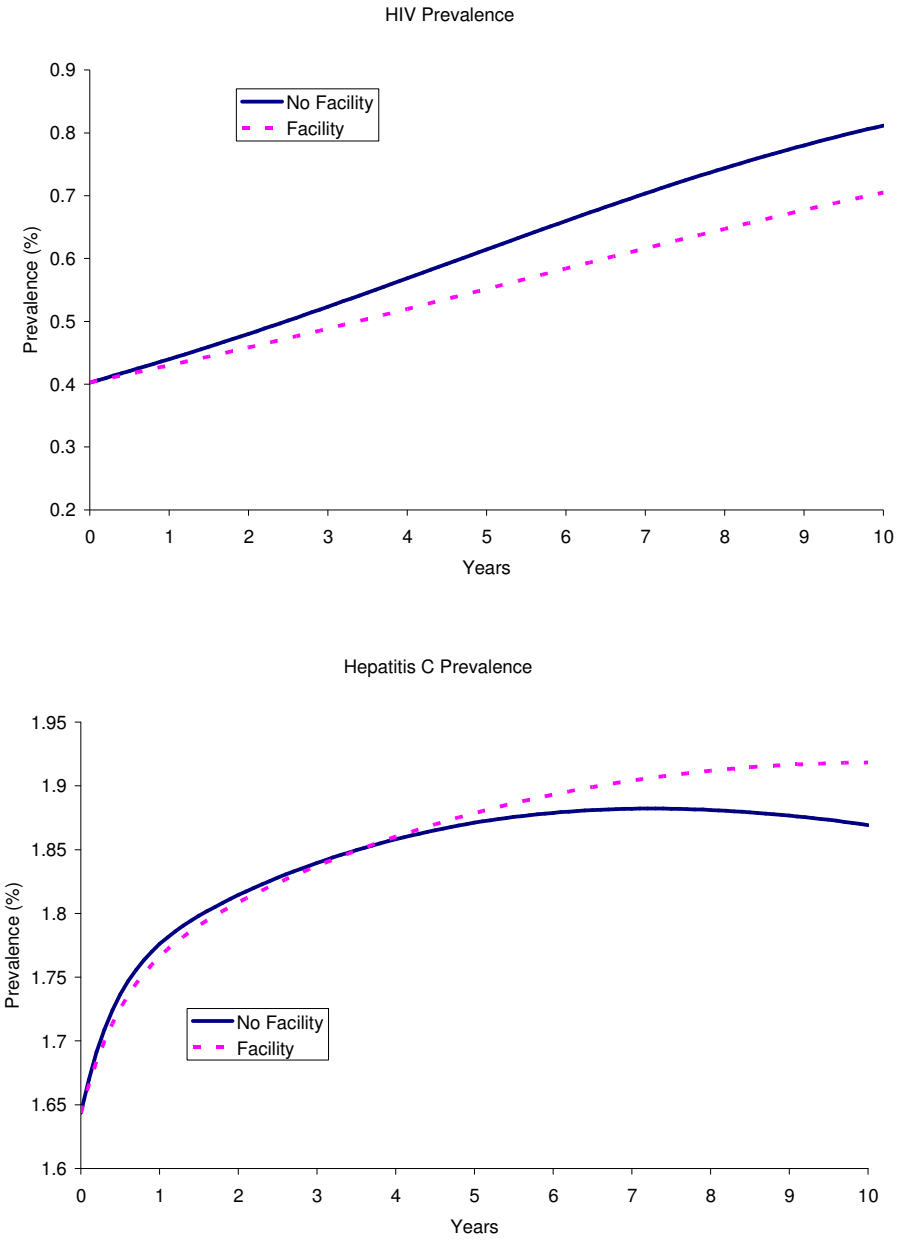

Figure 4: Projected change in HIV (top) and hepatitis C (HCV, bottom) prevalence in the total Vancouver population with and without a safe injection facility (SIF).

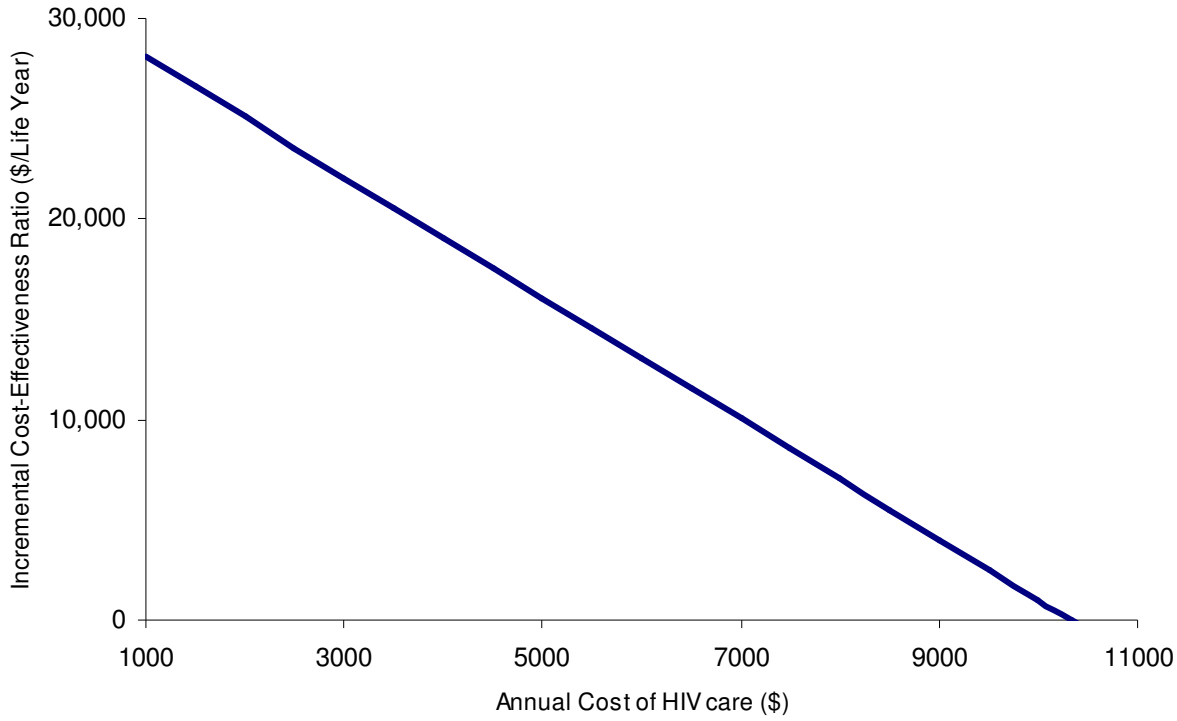

Figure 5: Sensitivity analysis to the annual cost of HIV care.

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