Estimating the cost-effectiveness of needle-syringe programs in Australia

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Objective: To evaluate the impact and cost-effectiveness of needle-syringe programs (NSPs) with respect to HIV and hepatitis C virus (HCV) infections among Australian injecting drug users (IDUs).

Design/Methods: A health economic analysis was conducted incorporating a mathematical model of HIV and HCV transmission among IDUs. An empirical relationship between syringe availability and receptive syringe sharing (RSS) was assessed. We compared the epidemiological outcomes and costs of NSP coverage (status quo RSS of 15–17%) with scenarios that had no NSPs (RSS of 25–50%). Outcomes included numbers of HIV and HCV infections averted, lifetime health sector costs, and cost per quality-adjusted life year (QALY) gained. Discounting was applied at 3% (sensitivity: 0%, 5%) per annum.

Results: We estimated that NSPs reduced incidence of HIV by 34–70% (192–873 cases) and HCV by 15–43% (19,000–77,000 cases) during 2000–2010, leading to 20,000–66,000 QALYs gained. Economic analysis showed that NSP coverage saved A$70–220 million in healthcare costs during 2000–2010 and will save an additional A$340–950 million in future healthcare costs. With NSPs costing A$245 million, the programs are very cost-effective at A$416–8,750 per QALY gained. Financial investment in NSPs over 2000–2010 is estimated to be entirely recovered in healthcare cost savings by 2032 with a total future return on investment of $1.3–5.5 for every $1 invested.

Conclusions: Australia's early introduction and high coverage of NSPs has significantly reduced the prevalence of HIV and HCV among IDUs. NSPs are a cost-effective public health strategy and will result in substantial net cost savings in the future.

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Keywords: Australia, cost-effectiveness, HCV, HIV, Injecting drug use, mathematical model, needle-syringe programs

Introduction

In many parts of the world, the sharing of injecting equipment, including needle-syringes, among injecting drug users (IDUs) is a major mode of transmission of blood-borne viruses such as HIV and HCV [1,2]. To reduce the spread of HIV and HCV infections through needle-syringe sharing, Australia introduced needle-syringe programs (NSPs) in 1986 [3]. HIV prevalence among IDUs in Australia has since remained relatively low and stable at ~1% [4]; however, HCV prevalence has remained relatively high at 50–70% [4]. At present, there are more than 3,000 NSP sites across Australia, comprising primary and secondary NSP outlets, mobile and outreach services, syringe vending machines, and

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pharmacies that sell or provide injecting equipment free of charge.

Globally, there are significant differences in HIV epidemics among IDUs. Ecological studies suggest that where NSPs are not easily accessible, HIV prevalence tends to be substantially higher than in settings where NSPs are available and easily accessible. For example, Hurley et al. [5] identified studies which estimated HIV seroprevalence among IDUs in the United States between 1988 and 1993 and estimated an average annual increase in HIV prevalence of 5.9% in cities without NSPs, whereas seroprevalence decreased by an average of 5.8% per year in cities with NSPs. HIV acquisition among IDUs has been shown to be significantly associated with non-use of NSPs [6,7].

In this study, we aimed to: (1) estimate the likely impact of NSPs in preventing HIV and HCV transmission at the population-level in Australia over the period 2000–2010, and (2) estimate the cost-utility of NSPs. To estimate the effect of an intervention, one could compare epidemiological indicators in the population of interest with a relevant control population. Another approach to impact evaluation is to compare observed conditions with a counterfactual scenario described by an epidemiological model. The counterfactual is intended to represent what the epidemics would look like in the absence of the intervention. The epidemiological model is used to generate an estimate for the counterfactual in lieu of a "real" comparison case. Here, we examined available empirical data to inform assumptions about the counterfactual with respect to the dominant behavioral factor of HIV and HCV transmission, namely, extent of receptive syringe sharing (RSS). We developed an epidemiological model, which we then calibrated to reflect the historical HIV and HCV epidemics among Australian IDUs. This model was then compared with the epidemics that would have been expected according to the counterfactual conditions.

Methods

Relationship between NSP distribution and receptive syringe sharing

NSPs aim to reduce the rate of RSS. We examined the relationship between NSP distribution and reported levels of RSS with others in the past month. The numbers of syringes distributed across Australia through NSPs were collected from each Australian state and territory health department for the period 1993–2008 [8]. Syringe distribution in Australia has increased over time (Fig. 1a, circles). Currently, approximately 200 syringes are distributed per IDU per year on average, based on an estimated IDU population size of 170,000 [8]. The frequency of RSS among IDUs has been estimated annually since 1995 through the Australian Needle and Syringe Program Survey (ANSPS), a serial cross-sectional seroprevalence survey of IDUs attending NSPs throughout Australia [4,9]. Over the period 1995 to 1999, reported prevalence of RSS decreased from 31% to 17% but has since remained steady [4]. During 2000–2010, levels of pharmacy purchasing of needle-syringes (Fig. 1a, rectangles) have been relatively constant despite large increases in the distribution of syringes from NSPs (Fig. 1a, triangles); therefore, we assume that increases or decreases in NSP distribution are not offset by changes in pharmacy purchasing.

We also collated data on RSS among Australian IDUs from other surveys conducted during 1970–1995 which are comparable to data from the ANSPS. Four studies were identified which also reported on proportions of surveyed IDU populations who receptively shared in the last month: 27% in Sydney [10] and 32% in Perth [11] in year 1993, 37% in Melbourne [12] during 1990–1995 and 27% in Perth [13] in 1995, corresponding with an estimated NSP distribution of 39 and 48 syringes per IDU per year in year 1993 and 1995 [14]. In Fig. 1b we presented the relationship between RSS and NSP distribution of needle-syringes for years in which both RSS prevalence and syringe distribution data are available [10–13]. In comparison to data presented in Figure 1b, it has been estimated that RSS levels in the 1970 s and 1980 s, with no or limited NSP coverage, could have been 70–90% among groups of IDUs [15–17]. However, considering the impact that increased awareness of blood-borne infections would likely have had on risk behaviors, we assumed that RSS prevalence would be 25–50% in the absence of NSPs during 2000–2010 (Fig. 1b). For the counterfactual scenario we assumed that parameters other than RSS would remain unchanged.

Model

A mathematical model was developed to describe HIV and HCV transmission, the distribution of the IDU population across health states over time, and the associated healthcare costs under actual conditions and according to the counterfactual scenario. Full details of the model are provided in the Appendix. Briefly, the model consists of a number of linked subpopulations ("compartments"), categorized by infection, diagnosis, disease progression (in terms of CD4 categories for HIV and stages of fibrosis and clinical states for HCV), and treatment states, as shown in Fig. 2. IDUs who are successfully treated for HCV become susceptible again, and can thus be re-infected. The rates of transition between compartments are defined by parameters based on available data. These can be divided into biological parameters (including HIV and HCV transmission probabilities, HIV- and HCV-related death rates, transition probabilities, and treatment effectiveness) and behavioral parameters (including the frequency of injections, the fraction of IDUs who engage in RSS,

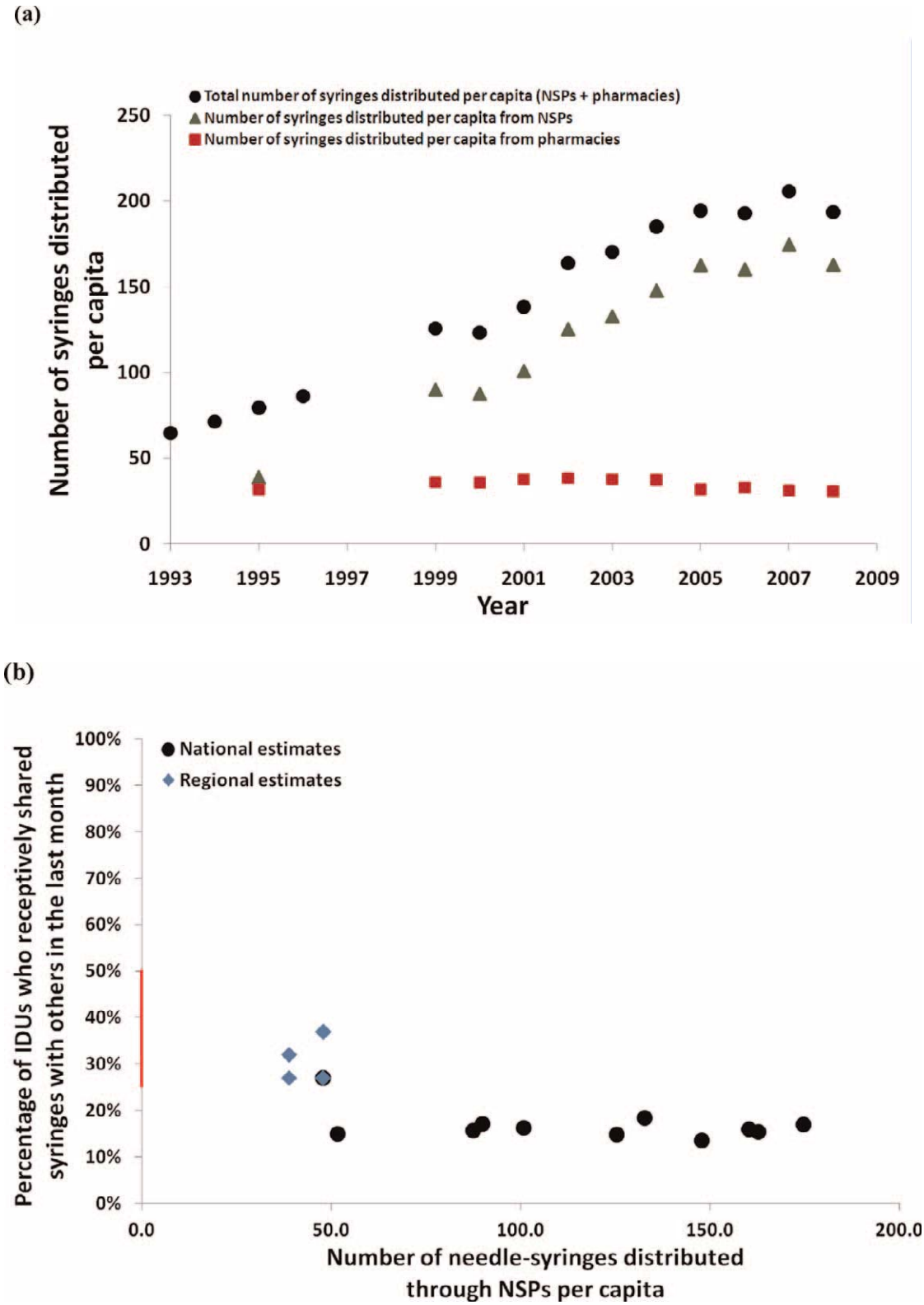

Fig. 1. ??. (a) Syringe distribution trends in Australia from NSPs and pharmacies. (b) Percentage of people who receptively shared needle-syringes in the last month versus annual per capita needle-syringes distributed through NSPs; the red bar on the y-axis indicates the assumed range of sharing rates in the absence of NSPs (20–45%); blue diamonds indicate regional estimates of sharing rate in Sydney [10] (27%) and Perth [11] (32%) in 1993, and in Melbourne [12] (37%) and Perth [13] (27%) in 1995; black circles indicate national estimates of sharing rates from 1995–2010.

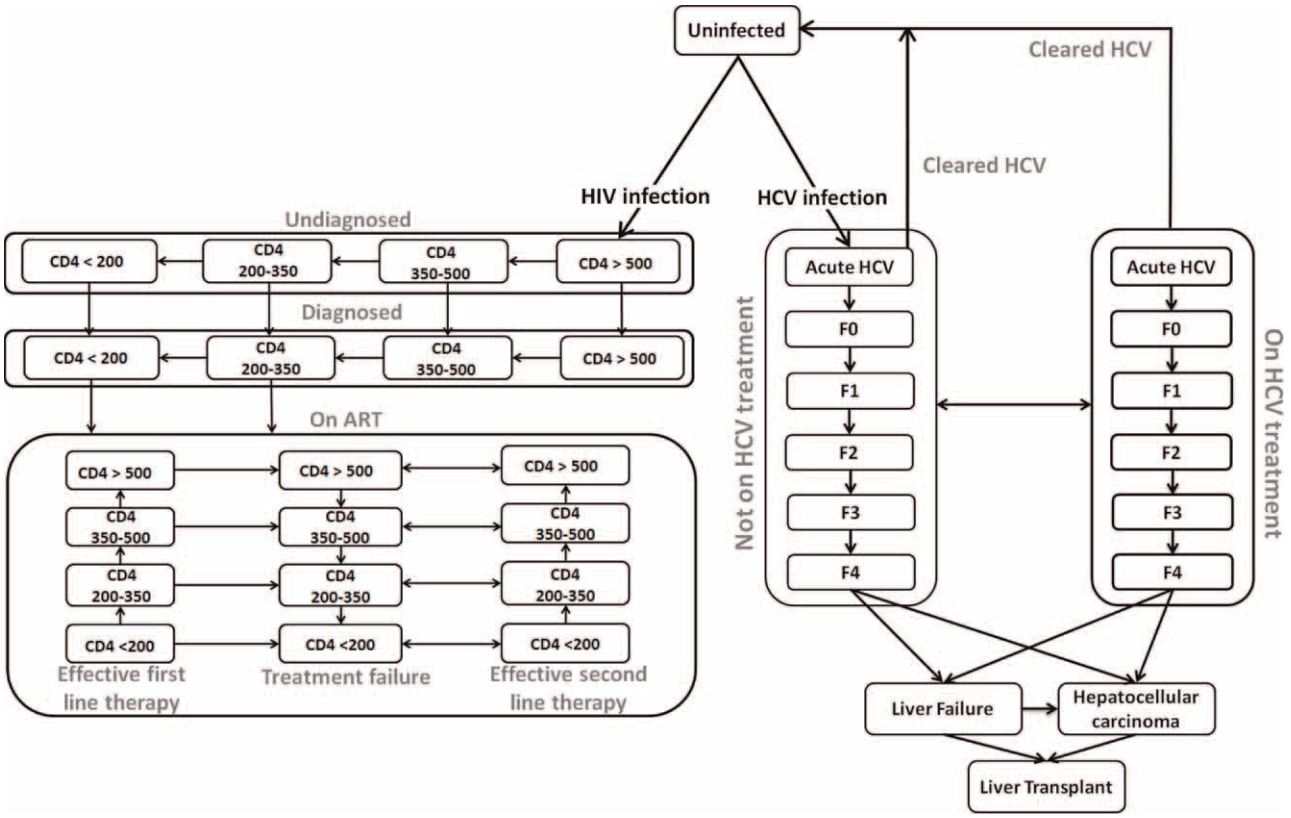

Fig. 2. Schematic diagram of HIV and HCV disease progression among IDUs in Australia. Each arrow represents the number of people in the population moving from one health compartment state to the other compartment.

and the fraction of syringes that are cleaned prior to sharing). The model estimates the change in the number of IDUs in each compartment due to disease progression, initiation of treatment, death or aging, and incidence of infection. The model also calculates the expected numbers of HIV and HCV transmissions through probabilities associated with risk behaviors. The model incorporates time-dependent parameters for factors in which comparable trend data are available, including the frequency of injections, RSS, testing rates, and the number of HIV- / HCV-infected current and former IDUs initiating HIV or HCV treatments. Full descriptions of all model parameters, and their defined range of values and justifications, are provided in the Appendix.

Economic analysis

Economic analysis was carried out to estimate the cost-effectiveness of NSPs from a health sector perspective. NSP costs were collated from all state and territory health departments in Australia in 2008 for 2000–2008; 2009–2010 costs were assumed to be the same as the 2008 costs. Costs included consumable items (syringe distribution, syringe disposal, and safe sex packs) and support costs (primary NSP operations, support for secondary NSPs, transport, and vending machines). We also derived estimates of average annual costs for different HIV and HCV health states using published literature and local data (estimated from activity-based analysis and national databases) [8]. The annual healthcare cost for a person living with HIV varied from A$1,523–$2,731 (excluding antiretroviral drugs), depending on the health state. In addition, the annual cost of antiretroviral therapy (ART) was estimated to be A$14,613 for first-line therapy, A$15,178 for second-line and A$27,776 for subsequent lines of ART per person per year. The annual healthcare cost for a person living with HCV was estimated to range A$288–114,411, from early HCV infection to liver transplantation, respectively. The unit costs of hospital admission were estimated by searching health department data on the frequency and proportions of admission to hospital with different health states of HCV and HIV [18] and then deriving a weighted average cost per admission in a health state using cost weights for admission to an Australian public hospital [19]. Outpatient items were valued from the Australian Medicare Benefits Schedule [20] and Pharmaceutical Benefits Scheme [21]. Client costs for the purchase of injection equipment were estimated from data on the number of sterile injection equipment packs provided through pharmacies and average client out-of-pocket cost for these packs. However, indirect healthcare costs were not included in the analyses. All costs were estimated in 2008 Australian dollars and inflated to 2010 Australian dollars using the

health consumer price index [22]. The annual healthcare costs per person are summarized in the Appendix.

Cost-utility analysis was performed to compare the costs and outcomes between the counterfactual no-NSP scenario and the status quo. Health state utilities were used to adjust the absolute life expectancy to derive quality-adjusted life years (QALYs) [23,24]. Healthcare costs were also calculated based on the number of people in each health state. The incremental cost-effectiveness ratio (ICER), expressed as cost per QALY gained, is the difference in costs between the counterfactual no-NSP scenario (HIV and HCV health care costs) and the status quo (NSP costs plus HIV and HCV health care costs) divided by the difference in QALYs between the same two scenarios. Analyses were performed for two time frames: 2000–2010 to study the return obtained over the period of investment, and 2010–2100 to examine the lifetime costs and consequences for the population related to the investment over the period 2000–2010. Costs were adjusted by an annual rate of 3% for the past ten years and then discounted over future time by three choices of rate: 0%, 3%, and 5% for sensitivity analysis.

Calibration, uncertainties, and sensitivity analysis

The model was calibrated using a Bayesian melding procedure [25] to reflect the HIV and HCV epidemics among Australian IDUs over the period 2000–2010. Credible intervals and upper and lower bounds for each parameter were derived from empirical data. These were used to define cumulative distribution functions (CDFs) for each model parameter (i.e., the priors). CDFs for each prevalence data point were defined similarly. A total of 1,000 simulations were conducted, with parameter values chosen randomly based on the parameters' inverse CDFs.

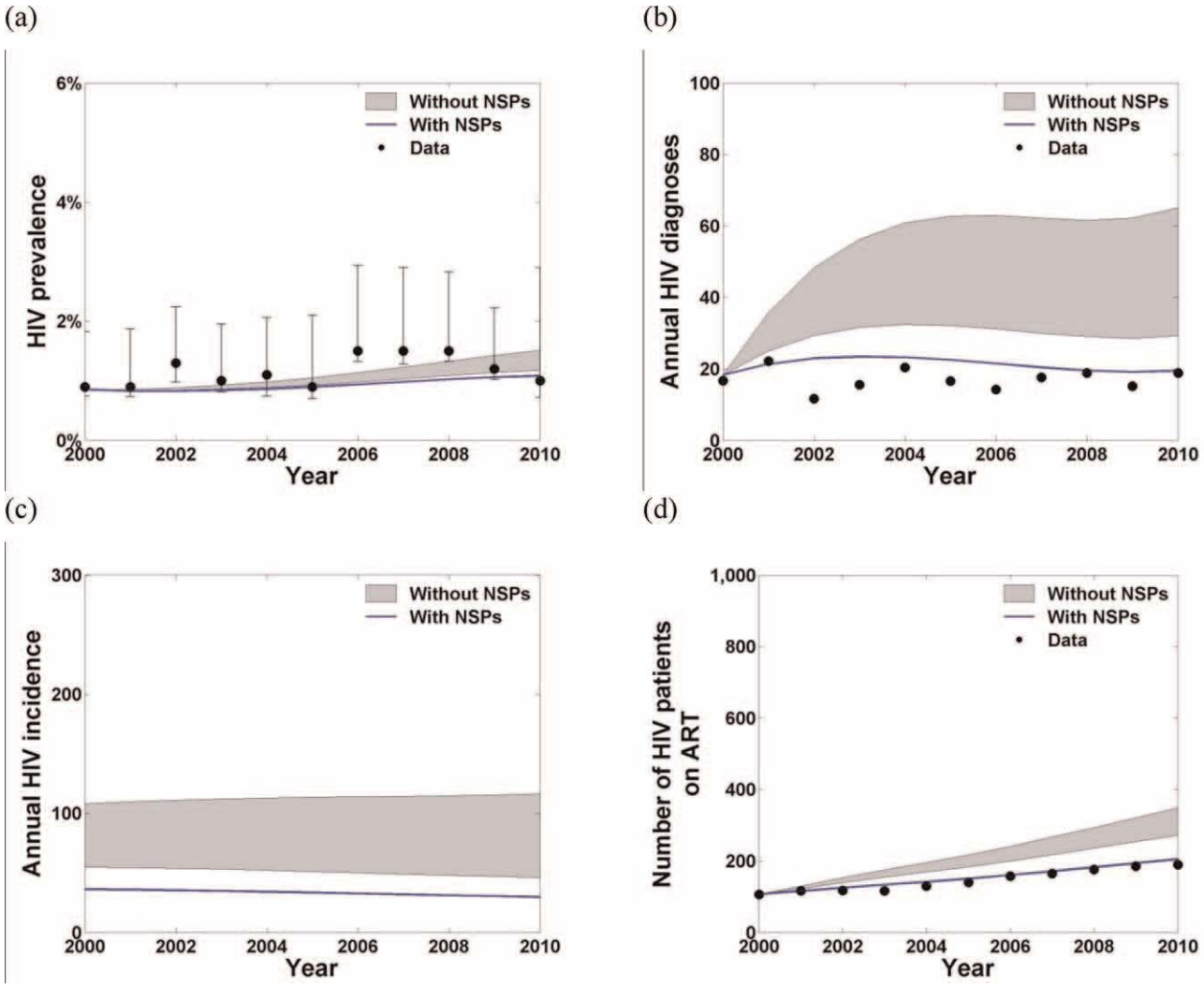

Fig. 3. Annual number of cases of HIV among IDUs given historical NSP distribution trends (blue curve: model; black dots: observed data [4,41]), versus projected cases in the absence of NSPs (shaded region: 25–50% RSS) for (a) HIV prevalence, (b) annual number of HIV diagnoses, (c) annual number of incident cases of HIV, and (d) number of people on ART. Median model simulations are shown.

The likelihood, as a measure of goodness-of-fit, of each simulation was defined as the product of the likelihood of each parameter value and the likelihood of each prevalence point, as defined by their respective CDFs. The posterior parameter distribution was obtained by randomly sampling 1,000 times over the original simulations, with each simulation weighted by its likelihood. This resulted in 100 unique simulations being used for the final analysis. The values and interquartile ranges (IQRs) quoted in the remainder of the paper are derived from this posterior distribution of simulations.

For sensitivity analysis, partial rank correlation coefficients (PRCCs) were calculated between incidence in 2010 and the sampled model parameters. All simulations and analyses were performed in MATLAB 2010a (The Mathworks, Natick, Massachusetts).

Results

The model accurately reproduced historical trends in the prevalence among IDUs for HIV and HCV in Australia from 2000 to 2010 [4] (Figs. 3 and 4). With the current distribution of syringes, modeled HIV prevalence was relatively low and stable, reaching 1.1%, with IQR of 1.0–1.3% in 2010 (Fig. 3a). The model also matched HCV prevalence, which changed over time between 50% and 60% (Fig. 4a).

The model estimated substantial increases in both HIV and HCV infections according to the counterfactual assumptions in the absence of NSPs (with RSS levels between 25% and 50%). During 2000–2010, approximately 559–1,240 new HIV infections and 120,000–178,000 new HCV infections would have occurred among IDUs without NSPs, resulting in prevalence levels of 1.2–1.5% and 66–80%, respectively (the lower and upper bounds represent the medians of the counterfactual scenarios with 25% and 50% levels of RSS, respectively). Thus, we estimate that NSPs resulted in the aversion of 192–873 HIV cases (34–70%) and 19,000–77,000 HCV cases (15–43%). The prevention of these infections would have resulted in a gain of 20,000–66,000 QALYs during 2000–2010, and 48,000–145,000 additional QALYs over a lifetime horizon (3% discounted).

In 2000–2010, an average of approximately 30 million syringes was distributed annually through NSPs in Australia, at an estimated cost of A$245 million (Table 1). The total healthcare costs attributed to HIV and HCV infections among IDUs over the same period were A$2.8 billion (IQR: $2.3–3.7 billion) and A$5.1 billion (IQR: $4.4–6.5 billion) when including future costs for current IDUs living with these infections (3% discounted). If NSPs did not exist in Australia, an estimated extra A$70–220 million would have been spent over 2000–2010 on HIV and HCV healthcare and A$340–950 million on additional future healthcare (3% discounted). The incremental cost-effectiveness ratio for the current program compared to no program ranged from A$416 -8,750/QALY (25%-50% RSS) over 2000–2010. If one uses a maximum willingness to pay for healthcare interventions threshold of A$50,000 per QALY gained, as is commonly used in Australia, NSPs in Australia are cost-effective. Comparing future costs and outcomes, the investment in NSPs over the period 2000–2010 would be cost-saving from 2032 onwards. In the lifetime model, each dollar spent on NSPs in 2000–2010 would have a return on investment of A$1.3–5.5 ((cost benefit – cost investment)/cost investment) in averted healthcare costs. Our uncertainty analysis findings are provided in the Appendix.

Our sensitivity analysis revealed that the transmission probability per injecting episode using a contaminated syringe is the most important biological factor in determining both HIV and HCV incidence (PRCC: 0.78 for HIV and 0.60 for HCV), while the RSS level was the most sensitive behavioral factor (PRCC: 0.62 for HIV and 0.42 for HCV), followed by the frequency of injecting (PRCC: 0.51 for HIV and 0.27 for HCV). A full listing of parameter sensitivities is provided in the Appendix.

Discussion

In this study, we evaluated the cost-effectiveness of syringe distribution in Australia, a country in which NSPs have been well-established for over two decades. Using available biological, behavioral, and program data in a mathematical modeling framework, we showed that NSPs are likely to have averted a substantial number of HIV and HCV infections.

Importantly, our evaluation suggests that NSPs have facilitated consistently low prevalence of HIV among IDUs in Australia. In many other regions of the world, HIV prevalence is very high among IDUs [26]. In contrast to their success in preventing an epidemic of HIV among IDUs, NSPs have not effectively controlled HCV in Australia. This is likely due to greater biological transmissibility of HCV compared with HIV [27] and that HCV was already well-established in the Australian IDU population before NSPs were introduced [28]. Despite high NSP coverage in Australia, RSS is still relatively common among new IDUs and has been demonstrated to be strongly associated with increased risk of HCV infection [29].

In 2002, a cost-effectiveness analysis of the effect of NSPs in preventing HIV and HCV transmission among Australian IDUs was conducted to assess impact over

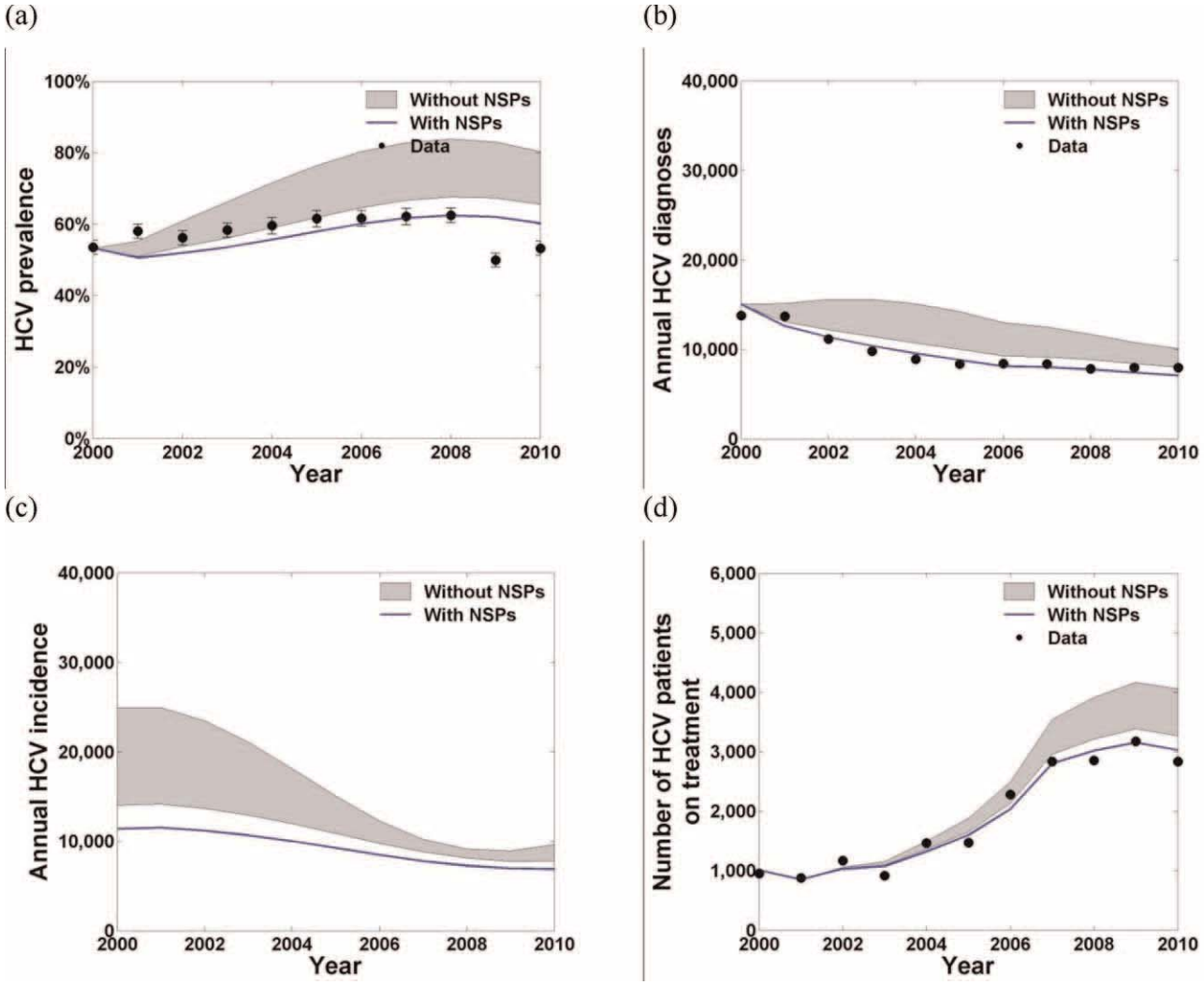

Fig. 4. Annual number of cases of HCV among IDUs given historical NSP distribution trends (blue line: model; black dots: observed data [4,41]), versus projected cases in the absence of NSPs (shaded region: 25–40% RSS) for (a) HCV prevalence, (b) annual number of HCV diagnoses, (c) annual number of incident cases of HCV, and (d) number of people on HCV treatment. Median model simulations are shown.

the period 1991–2000 [30]. It was estimated that around 25,000 HIV and 21,000 HCV infections were prevented, with a net cost-saving of A$20 million. In a recent report [8], we estimated that greater numbers of infections and healthcare costs would be saved according to less conservative assumptions regarding the counterfactual RSS.

Our model demonstrates that NSPs have been beneficial in preventing both HIV and HCV transmission among IDUs, are cost-effective in the short-term, and are cost-saving when future health outcomes and costs are considered. It is important to note that this study assesses only the impact of NSPs in averting HIV and HCV infections among IDUs. It does not include other benefits such as preventing injecting-related injuries, psychosocial support and referral, education and prevention. Several other studies have demonstrated similar results in other contexts. In a systematic review of the international literature published in 2006, 13 economic evaluation studies of NSPs were identified [31]. The studies all concluded that NSPs were cost-saving or cost-effective compared to the lifetime cost of HIV.

Representatives from all Australian jurisdictions were asked to provide the costs of NSPs for this analysis that related only to NSPs but this was not always possible. It should also be noted that there are only small changes in some outcomes over the period 2000–2010, such as number of people who receive ART, develop hepatocellular carcinoma or liver failure, and receive liver transplantation. The benefits in these outcomes become more marked over a long time period as infections averted

Table 1. Estimated HIV- and HCV-related outcomes with and without NSPs.

Outcome (median, interquartile range)	With NSPs[a]	Without NSPs	
		Scenario 1: 25% RSS	Scenario 2: 50% RSS
Prevalence of HIV among IDUs (2010)	1.08% (0.97–1.34)%	1.17% (1.01–1.45)%	1.52% (1.47–1.68)%
Cumulative incidence of HIV	367 (159–747)	559 (323–895)	1,240 (687–2,110)
Cumulative number of new HIV diagnoses	175 (76–372)	251 (130–440)	505 (246–939)
Cumulative number of new AIDS diagnoses	57 (44–78)	66 (50–85)	91 (62–130)
Cumulative number of people receiving first-line ART	1,560 (1,410–1,710)	1,920 (1,690–2,160)	2,310 (1,980–2,690)
Cumulative number of people receiving second-line ART	132 (125–142)	135 (126–147)	138 (127–152)
Cumulative number of HIV-related deaths	548 (517–583)	543 (514–573)	552 (518–593)
Prevalence of HCV among IDUs (2010)	60% (53–67)%	66% (63–67)%	80% (78–81)%
Cumulative incidence of HCV	101,000 (41,000–199,000)	120,000 (64,000–197,000)	178,000 (104,000–274,000)
Cumulative number diagnoses of HCV	106,000 (54,000–194,000)	116,000 (65,000–193,000)	149,000 (84,000–242,000)
Cumulative number of people receiving HCV treatment	21,000 (9,700–37,000)	22,000 (10,000–37,000)	26,000 (12,000–44,000)
Cumulative number of people with liver failure or HCC	71,000 (54,000–88,000)	71,000 (54,00–88,000)	71,000 (54,000–89,000)
Cumulative number of people who received a liver transplant	423 (217–634)	424 (217–635)	425 (218–641)
Cumulative number of liver-related deaths	13,000 (7,800–19,000)	13,000 (7,800–19,000)	13,000 (7,800–19,000)
Cost-effectiveness of Australian NSPs (2000–2010)[b]			
Total QALYs (unadjusted)	3.68m (3.06–4.44)m	3.66m (3.04–4.43)m	3.62m (3.01–4.41)m
Total QALYs (adjusted)	4.35m (3.62–5.23)m	4.33m (3.59–5.22)m	4.29m (3.56–5.20)m
Total healthcare costs ($, unadjusted)	1,880m (1,530–2,500)m	1,930m (1,580–2,540)m	2,040m (1,648–2,722)m
Total healthcare costs ($, adjusted)	2,830m (2,330–3,740)m	2,900m (2,380–3,800)m	3,050m (2,480–4,040)m
Cost-effectiveness of Australian NSPs (2000-Lifetime)[b]			
Total QALYs (undiscounted)	28.0m (23.1–34.7)m	28.0m (23.0–34.6)m	27.9m (22.9–34.5)m
Total QALYs (3% discounted)	12.7 m (10. 5–15.5)m	12.6m (10.4–15.5)m	12.5m (10.3–15.4)m
Total healthcare costs ($, undiscounted)	5,600m (5,000–6,800)m	6,210m (5,600–7,290)m	7,250m (6,430–8,630)m
Total healthcare costs ($, 3% discounted)	5,130m (4,390–6,510)m	5,470m (4,690–6,780)m	6,080m (5,140–7,620)m
Total NSP costs (adjusted for CPI)	$245m		
Incremental cost-effectiveness ratio (ICER)[c]	2000–2010	2000-Lifetime	
Scenario 1 ($, 3% discounted)	8,750	Cost-saving	
Scenario 2 ($, 3% discounted)	416	Cost-saving	

Willingness to pay for healthcare interventions threshold is A$50,000 per QALY gained. m, million.
[a]Sharing rate varied between 15% and 17% over the period 2000-2010.
[b]Adjusted for CPI with 2010 Australian dollars and discounted 3%. Analysis is done with 5% discounting shown in Appendix E.
[c]Incremental cost-effectiveness ratio (ICER) = incremental costs/ incremental QALYs
= (total costs of scenario-(total costs of investment+ total costs of status quo)) /(total QALYs of scenario – total QALYs of status quo).

lead to aversions of these clinical and disease-related outcomes.

While the assumptions of this analysis were based on the best available data, these data consisted of non-random samples and case notifications. This study was limited by reliance on self-reports of behavior from serial cross-sectional surveillance studies which were based on self-administered questionnaires. Self administration of surveys has been shown to reduce social desirability bias but is still not an ideal measure of actual risk [32–34]. Where possible, multiple prospective observational studies using varied methods and sampling techniques were also considered. The most crucial component of our analysis was the counterfactual assumption in the absence of NSPs. Studies conducted prior to the introduction of NSPs could not be used for this analysis due to their use of incomparable survey questions, however, the 70–90% levels of RSS reported in these studies provides an indication of high pre-NSP RSS levels in Australia. International studies provide some support for our counterfactual scenario [35–37]. Canada RSS recently increased from 10% to 23% following the closure of the only fixed NSP in the city of Victoria, but there was no change in RSS in Vancouver where NSPs remained open [38].

Although we incorporated uncertainty in parameter estimates where possible, many of the differences that exist between IDUs could not be captured in this population-based mathematical model. Our model did not include large heterogeneity, such as distinguishing current and former IDUs, and used weighted averages across the distributions of injecting frequencies. We believe the population-based model used in the current analysis is most appropriate for the data available, and represents an advance over previous models of HIV and HCV among IDUs in Australia.

This study used single estimates of HIV and HCV healthcare costs based on national medical benefits schemes. Ranges in utility weights were used to calculate uncertainties in QALYs. Conservatively, the model did not consider the increases in HCV costs that are likely to occur in the future associated with direct-acting antiviral therapy. As it is unlikely that HCV prevalence will decrease substantially over the next 10 years due to the impact of improved HCV treatment unless uptake is enormously enhanced, the increase in the costs should not affect the conclusions related to the cost-effectiveness of prevention programs.

Our model did not consider the reduction of RSS due to opioid substitution therapy, which has been associated

with reductions in opiate use, mortality, and the transmission of HIV [39]. However, since opiod substitution therapy is not an effective treatment for people who inject drugs other than opiates, its potential impact depends on the proportion of IDUs who inject opioids. During the period 2006–2010 in Australia, approximately 30% of IDUs injected opioids [4]. Studies have also shown that HCV transmission can be reduced when NSPs and opioid substitution therapy are delivered in combination [40].

Although NSPs in Australia are effective, there is also a need for a range of complementary evidence-based public health responses to further prevent HIV and HCV transmission among IDUs. These include biomedical and behavioral prevention interventions which target injecting risk behaviors, and interventions designed to increase access to and early uptake of HCV treatment. In conclusion, our study provides evidence that the ongoing implementation of NSPs in Australia has led to substantial public health benefits and cost savings.

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Conflicts of interest

None declared.

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