Introduction and brief review of prior studies

Sharing of syringes by injecting drug users (IDUs) is an important mode of global transmission of blood borne viruses, such as HIV and hepatitis C virus (HCV) [3, 4]. Both HIV and HCV infection are associated with significant morbidity and mortality [5, 6]. Needle and syringe programs (NSPs) are a public health measure designed to reduce the spread of these infections among IDUs. There are large differences in HIV epidemics among IDUs between different international settings [3, 4, 7]. Ecological studies suggest that where NSPs are not easily accessible, HIV prevalence tends to be substantially greater than in locations where NSPs are available [8-16]. In contrast to HIV infection, prevalence of HCV among IDUs is generally high in all locations regardless of the existence of NSPs [4].

Overview of Needle and Syringe Programs (NSPs)

NSPs provide a range of services that include the provision of injecting equipment, education and information on reduction of drug-related harms, referral to drug treatment, medical care and legal and social services [17]. Equipment provided by NSPs includes needles and syringes, swabs, sterile water, and sharps bins for the safe disposal of injecting equipment. The primary aim of NSPs is to prevent the shared use of injecting equipment, in order to reduce the risk of acquiring blood borne infections among IDUs. IDUs are unlikely to use another person's syringes if they have convenient access to sterile needles and syringes [18, 19]. NSPs also provide condoms and safer sex education to reduce the potential for sexual transmission of infections. Additionally, NSPs add the opportunity for early uptake of treatment and increased access to HCV treatment education.

The first NSP in Australia began as a pilot study in 1986 in Sydney, New South Wales [20]. In 1987 the NSW government endorsed NSPs through policy, and other Australian States and Territories were quick to follow. The first National HIV/AIDS Strategy, released by the Commonwealth Government in 1989, provided a framework for an integrated response to the HIV epidemic and NSPs were identified as a key component of the education and prevention strategy [21]. NSPs continue to be supported by the latest National Strategy on HIV/AIDS and National Hepatitis C Strategy 2005-2008.

There are now more than 3000 NSP sites across Australia, with the sector comprising primary and secondary NSP outlets, mobile and outreach services, syringe vending machines and a significant number of pharmacies that offer NSP services [22]. More than 30 million syringes are distributed each year through Australian NSPs [23].

NSPs operate from three major outlet types and four service delivery modalities. The following outlet types and service modalities operate to varying degrees within the Australian States and Territories.

Primary NSPs

Primary NSPs are services dedicated to the provision of a wide range of sterile injecting equipment and other services to IDUs. Primary NSPs deliver information and education on issues relating to injecting drug use and health and make referrals for IDUs to a range of other services including drug treatment. Primary NSPs may also liaise with a range of local stakeholders including police, other criminal justice service providers and local government in addition to health and community services.

Secondary NSPs

Secondary NSPs operate within existing health or community services but are not directly funded to employ staff to deliver NSP services. Staff providing NSP services do so in addition to the roles for which they are primarily employed. Secondary NSPs may provide the same range of services that primary NSPs do but typically have limited capacity to deliver services other than the delivery of sterile injecting equipment and disposal facilities.

Pharmacy NSPs

Pharmacy NSPs are community retail pharmacies that choose to act as NSP services. Pharmacy NSPs distribute a range of injecting equipment, including disposal containers, to IDUs sometimes on a commercial basis. In addition to the provision of injecting equipment pharmacy NSPs may collect data, provide information and offer referral to IDUs. Pharmacy NSPs are a critical component of NSP service delivery in Australia accounting for approximately 15% of syringes used for injecting drugs.

Service Modalities

Fixed-site NSP services account for the majority of NSPs in Australia. These services operate from a designated building within identified hours including those that operate 24 hours a day. Fixed-site NSPs are often co-located in a variety of settings including hospitals, pharmacies or community health services.

Syringe Vending Machines (SVMs), also known as Needle dispensing Machines (NDMs), are self-contained units that dispense sterile injecting equipment in most cases for a small fee.

These machines are usually nondescript, do not advertise their contents, and may operate after NSP service hours or provide 24-hour access to sterile injecting equipment.

Outreach/mobile services operate from vehicles, such as a cars, vans or buses, or, in a small number of cases, use a 'foot outreach' model that involves NSP staff carrying backpacks to deliver injecting equipment and educational information. These services can operate on a specific timetable, to be present at designated locations at scheduled times, or may respond to direct requests which are usually made by phone.

Silent or unadvertised services are discrete NSPs that are often targeted at specific subgroups of injectors.

Review of previous NSP economic evaluations

The cost effectiveness of NSPs has been considered in a number of publications including the previous Return on Investment Report [24]. The Return on Investment Report (2002) economic analysis demonstrated that there had been significant financial savings accruing from the expenditure on NSPs and that savings were likely to continue in the future [24]. The net present value (present value of a series of amounts over time) was estimated to be more than $2 billion dollars (discounted at 5%). NSP cost data was collected from jurisdictions and the lifetime cost of treatment for HIV and HCV were obtained from studies in the pre-ARV era but updated with more recent data from the Australian HIV Observational Database. An ecological analysis estimated the effect of NSPs across numerous international cities and the results of the analysis were applied to estimate the impact in Australia. It was estimated that:

- ~25,000 HIV infections were prevented among injecting drug users (IDUs) by the year 2000 due to the introduction of NSPs.
- The cumulative number of HIV/AIDS deaths by the year 2000 in injecting drug users (IDUs) would be ~200 with the NSPs and ~700 without the NSPs.
- ~21,000 HCV infections were prevented among IDUs by the year 2000 due to the introduction of NSPs (of which 16,000 would have developed chronic HCV).

The cumulative number of IDUs living with HCV in 2000 was estimated to be ~200,000 with NSPs in place; it was estimated that the number would have been ~220,000 without NSPs.

In a systematic review of the international literature, 13 economic evaluation studies of NSPs were identified, most based in North America [25]. The studies all concluded that NSPs were

cost-saving or cost-effective compared to the lifetime cost of HIV. A range of approaches were used in the economic analyses, depending on the research question of technical efficiency or value for money.

In a value for money or allocative efficiency analysis, Cohen modelled the impact of a range of public health decisions on women living in the Southern United States [26]. The most cost-effective interventions were alcohol taxes, needle sale/possession, and needle syringe programs, with a cost per HIV infection averted of $3600-$9000. In a previous study, she found that needle exchange and needle deregulation programs were relatively cost-effective only when injection drug users have a high HIV prevalence [27].

Holtgrave used a hypothetical cohort of one million active IDUs in the United States, to estimate the cost-effectiveness of policies to increase access to sterile syringes and syringe disposal at various levels of coverage. A mathematical model of HIV transmission was employed to link programmatic coverage levels with estimates of numbers of HIV infections averted. A policy of funding NSPs, pharmacy sales, and syringe disposal to cover all injections would have cost just over US$423 million for one year. One third of this cost would have been paid for as out-of-pocket expenditures by IDUs purchasing syringes in pharmacies. Compared with the status quo, this policy would cost an estimated $34,278 US per HIV infection averted, a figure that was well under the estimated lifetime costs of medical care for a person with HIV infection. At very high levels of coverage (>88%), the marginal cost-effectiveness of increased program coverage became less favourable [28].

Drucker found that the failure of the federal government in the USA to implement a national needle-exchange program, despite six government-funded reports in support of needle exchanges, might have led to 4000-9700 HIV infections among IDUs, their sexual partners, and their children, during the period 1987-1995. The cost-savings of NSPs could have been between $244m and $538m [29].

A recent analysis from the UK on the cost-effectiveness of NSPs in decreasing HIV and HCV infections showed that increasing the number of IDUs receiving full NSP coverage might be cost-effective if the costs of delivering the increased intervention were not too high and the intervention achieved a moderate decrease in syringe sharing [30]. Results suggested that the impact and the cost-effectiveness of NSPs alone were likely to be greater in settings of lower HCV prevalence [30].

A number of studies have examined the technical efficiency of different programs and their delivery. An HIV prevention program based on the distribution of kits and a needle exchange service which had been in operation in Navarra, Spain was found to cost $16,000 to $88,000 per HIV infection averted [31]. A program including mobile NSPs in Hamilton, Canada returned cost-savings four times greater than the program cost [32]. Another program evaluation in Edmonton, Canada estimated that an HIV infection was averted for every C$4,800 spent [33]. A study in Belarus found that harm reduction activities among IDUs could be cost-effective, but relatively small shortfalls in funding reduced the impact and cost-effectiveness of NSPs [34]. New York State NSPs were cost-saving at $20,947 per HIV infection averted [35]. The geographical location of NSPs in a city affected cost-effectiveness: sites needed to be located where the density of IDUs was highest and the number of syringes exchanged per client needed to be approximately equal across sites [36].

Pinkerton evaluated the cost-effectiveness of a behavioural risk reduction intervention with injection drug users that emphasised safer sex and injection practices, rather than needle syringe programs alone. The intervention had been implemented in 1996 at 28 sites across the USA; he examined eight of the sites. In a threshold analysis, he found that the program would have been cost-saving if it had cost less than $2,100 per person to implement and would have been cost-effective (assuming a societal willingness to pay of $50,000 /QALY) if it had cost less than $10,300 per person [37].

In Odessa, Ukraine, with NSP coverage of 20%-38% and HIV prevalence among IDUs of 54%, projections suggested 792 HIV infections were averted, a 22% decrease in HIV incidence among IDUs, but a 1% increase in IDU HIV prevalence. The cost per HIV infection averted was estimated at $97. Scaling up the intervention to reach 60% of IDUs remained cost-effective and reduced HIV prevalence by an estimated 4% over five years [38].

One study of the cost-effectiveness of NSPs for the reduction of HCV used a random-mixing epidemiological model to examine the potential impact of harm reduction interventions. NSPs were predicted to have little impact on HCV incidence and prevalence within realistic populations of IDUs. The authors concluded that short-term incidence analysis substantially overstated syringe exchange program effectiveness and cost-effectiveness in preventing HCV [39].

Introduction to the current analysis

The previous Return on Investment report estimated that $141 million was spent on NSPs across Australia between 1991 and 2000 [24]. From a conservative financial perspective, only the direct costs of treatment saved by the avoidance of HIV and HCV were considered. But the analysis indicated that there had been significant financial savings accruing to government from the expenditure on NSPs and that these savings were expected to continue. The study demonstrated that NSPs have also yielded a significant public health benefit in terms of avoidance of deaths and gains in the duration of life and improvements in the quality of life of IDUs.

Although NSPs are effective, viral transmission still occurs among IDUs in Australia. Each year at least 30 to 40 new HIV infections and 8,000 to 10,000 HCV infections occur through the sharing of syringes [6]. The current coverage of injections with sterile syringes is ~50%. In this context, it is important to re-assess the impact of NSPs and estimate the cost-effectiveness of current programs, as well as the cost-effectiveness of increasing or decreasing the allocation of resources to NSPs and the programs that they deliver. The Australian Government Department of Health and Ageing commissioned the National Centre in HIV Epidemiology and Clinical Research (NCHECR) to undertake a study to update and extend the return on investment analysis on the cost-effectiveness of NSPs in Australia.

Brief description of the methods and key assumptions

Mathematical epidemic transmission model

A mathematical epidemic model was developed to simulate HIV and HCV transmission among IDUs in Australia. The model was used to determine the population-level effectiveness of NSPs in preventing transmissions of HIV and HCV. A detailed description of the model is provided in Appendix A and a complete listing of the parameters and assumptions of the model and explanation of values used in the analysis are provided in Appendix B. Briefly, the model considered heterogeneity in injecting behaviour, including frequency of injecting and sharing of injecting equipment as well as rates of cleaning equipment. Mathematical associations were derived to describe the coverage of injecting equipment among IDUs for different levels of NSP distribution of sterile injecting equipment. The model tracked the changing number of IDUs in the population, including the entry of new injectors and the rate of ceasing injecting behaviour. The structure of the analysis was a compartmental model based on a large system of ordinary differential equations (see Appendix A). The infection of IDUs with HIV and/or HCV was simulated based on injecting

behaviour and mixing in the population. The model also tracked the natural history of disease progression for people infected with HIV and/or HCV. The model was used to estimate the number of people in each HIV and HCV health state, including important clinical endpoints (as well as drug-related, disease-related, and background death rates), for various NSP-delivery and behavioural scenarios (see Appendix A). All available Australian behavioural and epidemiological data and international disease-related data were used as inputs to calibrate the model to the relevant Australian population (see Appendix B). The model also accounted for the total number of needles and syringes distributed to IDUs in each population, as informed by each State and Territory health department. Uncertainty and sensitivity analyses were carried out by varying all input parameters over plausible ranges, using Latin Hypercube Sampling implemented in the SaSAT software package [40], and running the mathematical model 10,000 times. One hundred model simulations for each population were chosen for the full analysis that best matched HIV and HCV notifications data as well as the prevalence of both infections, number of HIV- and HCV-infected IDUs receiving treatment, annual incidence of HCV-related fibrosis, liver failure, and hepatocellular carcinoma (HCC).

Separate analyses were carried out for Australian IDUs at a national level and by each Australian state and territory, as well as for Aboriginal and Torres Strait Islander populations. The same mathematical structure was used to describe the interaction and epidemiology of HIV and HCV among IDUs in each Australian state and territory and in Australian Aboriginal and Torres Strait Islander populations. Population-specific behavioural and epidemiological data were used to inform the inputs for the model simulations (see Appendix A). The mathematical model was calibrated in order to accurately reflect the unique HIV and HCV epidemiology (incidence and prevalence of infection and each disease outcome/health state) in each population. The model's epidemiological outputs were aligned with available national surveillance data and NSP survey data with estimations from the HCV Projections Working Group study [41]. The numbers of people in each health state over time were used to inform the economic analyses of NSPs. The decade from 2000-2009 was investigated to determine the effectiveness, and cost-effectiveness, of NSPs in the past. Analyses were also conducted to simulate what is likely to have occurred over the last decade, had NSPs not been in place or if the coverage of syringes among IDUs had been different. The model was then used to forecast epidemic trajectories over the next 70 years (2010-2079) under assumptions that behaviour of IDUs or funding and services of NSPs remain unchanged or according to changes in conditions. Epidemic projections are shown over the period 2010-2019.

Economic analysis methods

The economic analysis was designed to calculate the net present value and future values and cost-effectiveness of NSPs with respect to their benefits in averting HIV and HCV infections from a health sector (government as third party payer) perspective. Therefore, the analysis is the most conservative and rigorous estimate of the true return on investment as the many other benefits of NSPs were not factored into the analysis (support, referral, education etc.). The analysis used budget data provided by State and Territory health departments to derive the cost of NSPs and their associated interventions. Healthcare costs saved for HIV and HCV prevented by the intervention were derived from models of service delivery, calibrated with data from local and international research on utilisation and valued using appropriate government cost sources. All costs were in 2008 Australian dollars, adjusted by the consumer price index for previous costs and by 3%, 0% and 5% for costs in the future. Outcomes of interest included the life years gained, disability adjusted, of the current expenditure on NSPs, compared to a range of alternatives, including an absence of program or 'partial null'. The time horizon of the economic model was varied to reflect different decision contexts: the period 2000-2009 to reflect past investment in NSPs, 2010 to 2019 and 2029 to reflect the impact of choices made in 2009 in relation to the next 10-20 years, and 2010-2059 and 2010-2079 to consider whole of lifetime impacts.

Comparators

The current provision of NSPs was compared to a scenario where publically funded NSPs did not exist (the no program or partial null scenario). In this scenario, it is assumed that needles were available only through client purchase at pharmacies, comprising 15% of the current needle availability in Australia. This was based on the estimates of private needle purchase provided by the States and Territories. It is important to note that community pharmacies are a critical component of needle and syringe programs. If publicly funded access to sterile injection equipment had not been put in place, but simply the enabling legislation enacted, or was at some stage removed. there would most likely be substantial migration to pharmacy outlets or the numbers of IDUs utilising pharmacies would more likely have been greater.

Potential changes in the number of sterile injection equipment units provided were considered in a series of scenarios. Supply was assumed to increase or decrease by 10%, 25% or 50%. In all scenarios the cost of consumables and support for the sector increased or decreased by 10%, 25% or 50%.

NSP costs

State and Territory health departments provided data on the budgets for NSPs in responses to a standardised questionnaire developed after a stakeholder meeting. Two main categories of costs were identified that related to the activities of NSPs: (i) consumables including sterile injecting equipment, disposal costs and safe sex-equipment, and (ii) support for the NSP sector including primary NSP operations, support of secondary sites, transport and vending machines. Some jurisdictions separately identified costs such as grants, peer-support programs, and telephone information services on safe disposal of needles and training. These costs were included in the support for primary NSPs subcategory unless identified as relating to one of the other subcategories.

All jurisdictions were given the option to reflect on their initial answers in comparison with their peers and provide further data in order to ensure consistency in responses. Four jurisdictions were not able to provide complete data back to the year 2000. Missing data was imputed by applying the changes in the consumables and support in the four jurisdictions with complete data. Data related to financial years were applied to the calendar year that the financial year started. Specific funding for primary healthcare or drug and alcohol programs that occurred at the same site was not included; the human resource cost of providing sterile injection equipment at secondary sites was not included due to data uncertainty, except where specific support for enhanced secondary sites was provided.

Healthcare costs

The healthcare costs of HIV and Hepatitis C were identified through the creation of a model of service delivery reflecting current practice by the authors, who included doctors experienced in HIV and HCV. Utilisation data was derived for different health states from the literature and local data by four CD4 strata and three antiretroviral strata in HIV and by seven disease and treatment states in HCV. Assumptions and data sources are listed in Appendix C.

Outpatient items were valued from the Medicare Benefits Schedule [42] and Pharmaceutical Benefits Schedule [43] in 2008 dollars. The unit costs of 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 [44] and then deriving a weighted average cost per admission in a health state using cost weights for admission to an Australian public hospital [45]. Health care costs are summarised in Table 1. Further details of costs are provided in Appendix C.

Table 1: Summary healthcare costs of HIV and HCV

HIV Healthcare	Annual Cost
CD4 > 500	$1,523
350 < CD4 < 500	$2,055
200 < CD4 < 350	$2,731
CD4 < 200	$5,500
1st line therapy	$14,613
2nd line therapy	$15,178
3rd line therapy	$27,776
HCV Healthcare	**Annual Cost**
Precirrhosis stage of chronic hepatitis C (fibrosis stage 0 to 3) - 1st year	$798
Precirrhosis stage of chronic hepatitis C (fibrosis stage 0 to 3) - successive years	$288
Compensated cirrhosis (fibrosis stage 4)	$827
Decompensated cirrhosis (liver failure)	$12,764
Hepatocellular carcinoma	$17,033
Liver transplant - 1st year	$114,411
Liver transplant - successive years	$12,764
Treatment of acute HCV patients with pegylated interferon and ribavirin (24 weeks)	$10,782
Treatment of chronic HCV patients with pegylated interferon and ribavirin (24 weeks)	$10,829
Treatment of chronic HCV patients with pegylated interferon and ribavirin (48 weeks)	$18,835

Patient/client costs

Client costs for the purchase of injection equipment were estimated from data on the number of sterile injection equipment provided through pharmacies and average client out-of-pocket cost of packs of sterile injection equipment. Patient and family healthcare costs for people living with HCV and HIV were approximated from studies in Canada [46] and New Zealand [47], converted to 2008 Australian dollars using the appropriate consumer price index and purchasing power parities [48]. These data were used in a secondary analysis. Time costs for the attendance at NSPs to collect equipment were not included in the client cost, because the economic analysis aimed to examine the value for money of NSPs rather than the technical efficiency of alternative provision and delivery mechanisms. Patient/client out-of-pocket costs were included in a secondary analysis of investment in NSPs because there was an absence of local recent data.

Productivity losses and gains

The methods used to estimate productivity losses and gains associated with HIV and HCV infection are described fully in Appendix D. In brief, the workforce participation rate, assumed work absenteeism and premature mortality of individuals acquiring HIV and HCV were compared to participation and mortality of individuals without the disease, similar in age, gender and injection drug use. The productivity losses due to mortality, short-term absenteeism and disability were estimated using the Friction Cost approach that assumed that individuals who left work due to illness or death could be replaced in three months. Productivity cost was discounted at 3%, 0% and 5%. Alternative time periods for replacement of a worker and approaches to costing productivity losses including the Human Capital method are reported in the chapter on productivity losses and gains. Taxation and welfare payments were not included. Due to the significant uncertainty in the parameters used, productivity losses and gains were not included in the primary analysis, but described in a secondary analysis.

Other sectors costs and cost offsets

While other sectors of the government and the economy such as local government, justice and insurance may be affected by expenditure on NSPs, the associated costs and cost-offsets are very difficult to identify, measure or value. Therefore, these costs and cost-offsets have not been included in this analysis.

Injection-related injuries and disease

Injection-related injuries and disease (IRID) may be significantly reduced by the provision of sterile injection equipment. The cost of IRID to the public health system in Victoria, Queensland and New South Wales was estimated at more than $19m in 2005/6 [49]. However there is a lack of data on the effect size of NSPs on reducing IRID, and other factors related to injection site, hygiene, demography and drug type may also be significant [50]. Therefore the potential additional cost-offsets of preventing IRID in the population of NSP users were included as a secondary analysis only.

Disability-adjusted life years

Disability-adjusted life years (DALYs) provide an outcome that takes account of morbidity and mortality associated with disease and may allow comparison between alternative public health interventions [51]. Disability adjustment weights for health states to derive DALYs were taken from data from the Global Burden of Disease project [52]. DALYs were estimated using standard methods from the outputs of the population transmission model of the number of individuals in the population living in each health state.

Economic analyses

Cost and disutility data for different health states were included in the population transmission model that was run 100 times with outputs of the prevalence of each heath state for HIV and HCV. The HIV and HCV cost was applied in an Excel spreadsheet and the cost summed for each of the 100 iterations. For each iteration, the incremental healthcare cost or cost-offset was estimated comparing one alternative with another. The median incremental healthcare cost and interquartile ranges (IQR) were calculated. The expenditure on NSPs was summarised for all jurisdictions and applied in the model. Costs reported for financial years were applied to the population model outcomes by the calendar year in which the financial year commenced, i.e. costs for NSPs in 2002/3 were deemed to be accrued in calendar year 2002. The net financial difference between the NSP expenditure and incremental healthcare cost was calculated for each year, undiscounted and discounted. The net financial value of NSPs for the period 2000-2009 was estimated from year 2000 onwards to reflect hindsight on decisions made in year 2000 and from year 2010 onwards in the analyses for future spending to reflect the perspective of a decision maker in 2009.

The DALYs for each scenario were summed in the population model and the incremental number of DALYs gained or lost estimated for each scenario compared to the no program scenario. The incremental cost-effectiveness ratios between alternative scenarios were estimated by dividing the incremental net cost of the scenarios by the incremental DALYs gained or lost. Incremental cost-effectiveness ratios for alternative options that were cheaper and more effective were not reported, instead the net financial cost-savings and gains in adjusted life years were reported.