3 THE IMPACT OF NSPS ON HIV AND HCV

3.1 EFFECTIVENESS OF NSPS FOR PREVENTING TRANSMISSION OF HIV AND HCV INFECTION

3.1.1 INTRODUCTION

Measures to prevent HIV infection among people who inject drugs generally focus on preventing blood contact during injection by reducing injection, promoting use of sterile equipment when injecting, or adopting safer injecting practices. Consequently, Needle and Syringe Programs (NSPs) are a key strategy for preventing transmission of HIV infection in several countries, including Australia. In other countries, implementation has been limited by uncertainty about their effectiveness.

Randomised trials of the effectiveness of NSP in preventing HIV transmission have not been conducted. Several observational studies have assessed the impact of NSPs on self-reported risk behaviours, in particular use of sterile syringes or re-use of one's own syringe (Drucker et al. 1998). A few studies have compared HIV incidence or HIV, HBV or HCV prevalence in participants and non-participants of NSPs (Bruneau et al. 1997; Des Jarlais et al. 1995; Hagan et al. 1999; van Ameijden et al. 1994). One study compared NSP implementation in countries with sustained low HIV prevalence to those with high HIV prevalence (Hurley et al. 1997). While another used an ecological study design to compare changes in HIV prevalence in cities with and without NSPs (Hurley et al. 1997). The data generally, but not always, show NSPs to be effective in preventing HIV transmission.

In contrast to HIV infection, prevalence of HCV infection among injecting drug users is universally high, regardless of whether the studies were done in cities with or without NSPs (MacDonald et al. 1996). It is likely that HCV prevalence was already very high among injecting drug users before NSPs were introduced. However, there are no studies that quantify the impact of NSPs on HCV infection. In this study, we have repeated the ecological study of change in HIV prevalence in cities with and without NSP because several countries have introduced NSP since the previous study (Hurley et al. 1997). We have also used a similar methodology to assess the effectiveness of NSP for prevention of HCV infection. A discussion on the rationale behind the approach adopted in this study is presented in Appendix B.

3.1.2 METHODS

The ecological study design was used to compare HIV and HCV infection among injecting drug users in countries with and without NSPs. Data recorded on HIV and HCV infection included both seroprevalence and seroincidence studies. NSPs were defined as programs distributing needles and syringes, either free or with minimal charge, irrespective of whether they operated from a fixed or mobile site, whether return of a used syringe was mandatory, or the range of other HIV and HCV prevention and treatment services provided.

Several sources were used to identify published reports of HIV and HCV prevalence and incidence among injecting drug users and implementation of NSPs. Three electronic databases that indexed relevant journals were searched from January 1984 to June 2001. Both Medline and Embase databases were used because each placed an emphasis on research from different continents, that is, North America and Europe respectively. The Current Contents database was also used because it included literature from Social Science and Psychology journals. Additional studies were obtained from country specific surveillance reports, the HIV/AIDS Surveillance Database (US Census Bureau & UNAIDS, 2000), relevant websites, and through review of the index of journals frequently cited in the electronic searches.

All studies with sample size of at least 50 were included. Cities with HIV prevalence studies were only included if HIV was measured among injecting drug users in two or more calendar years. Studies of HIV or HCV among incarcerated injecting drug users were excluded because very few countries provide NSP during imprisonment.

Studies reported in journals published in languages other than English were only included if sufficient information was provided in the abstract to determine whether the study was suitable for inclusion and all required data points were reported in the abstract. References used in the analysis are provided in Appendix F.

Number of injectors tested per calendar year, percentage with HIV and /or HCV, presence or absence of NSP, and recruitment site were recorded for all studies. If studies reported data aggregated for more than one calendar year, the mid-point of the study period was used as the survey date. Data were also recorded on HIV and HCV prevalence among new and young injectors where available. Studies of HCV incidence were included if they reported numbers of incident HCV infections and person-years of follow-up.

Analysis compared change in HIV and HCV prevalence between cities with and without NSPs at the time of the surveys. For HIV prevalence, city-specific change in prevalence was used in the analysis. For HCV prevalence, however, it was not possible to use city-specific change because relatively few cities had more than one estimate of prevalence.

For each city, the annual rate of change of HIV seroprevalence was estimated by fitting a regression line on a logit scale, with calendar years centred to 1990. The annual rate of change of HIV seroprevalence was also estimated using regressions weighting the comparison of cities with and without NSPs according to one over the variance of the regression estimator (Hurley et al. 1997). The effect of NSPs was assessed by comparing the annual rate of change in HIV seroprevalence in cities that had ever introduced NSPs with cities that had never introduced NSPs. Analyses of HIV seroprevalence were performed comparing all cities, and also in the subset of cities which had an initial HIV seroprevalence of less than 10%, and had results from at least three surveys available over at least three years. Analyses were repeated using regressions weighted according to survey sample size, and also excluding cities in developing countries.

A random effects regression model was used for analyses of HCV seroprevalence because few cities had data points before and after NSPs were introduced, and to allow appropriately for within and between city effects. The analysis model fits regression equations of the form:

$$\text{Logit(HCV prevalence)} = \zeta + \eta^{*}(\text{calendar year}) + \nu^{*}(\text{year since NSPs started})$$

The parameter estimate for ν can then be directly interpreted as the modifying effect of NSPs on logit(HCV prevalence) levels per year. The effect of NSPs on HCV prevalence was estimated using all data from all cities, excluding studies that used blood stored since 1981, and for cities that introduced NSP between the first and last available study. A random effects regression model was also used to estimate the effect of NSPs on HCV prevalence using data available for people reporting less than three years of drug injection. Other regression models, such as ML random effects, and GEE, were also used on the sampled HCV prevalences and gave identical results (data not reported).

Two sets of analyses were performed to assess the effect of NSPs on HCV incidence. In the first set of analyses, random effects and GEE negative-binomial models were used to compare cohorts in cities with and without NSPs, allowing for within and between city effects in the analysis and for over-dispersion effects. In the second analysis, an overall incidence rate was calculated for each city by summing the numbers of incident infections and person-years of follow-up. Straightforward negative-binomial regression models were then used to compare cities with and without NSPs.

3.1.3 HIV SEROPREVALENCE

There were 778 calendar years of data from 103 cities with HIV seroprevalence measurements from more than one year and information on NSP implementation. Studies were from 67 cities without NSP, 23 cities that implemented NSP between the first and last study, and 13 cities that already had NSP when the studies were carried out (Table 3.1.1).

HIV prevalence ranged from zero to 79% at the first data point for each city (median 18%), with 53 cities reporting first HIV prevalence 10% or less. Data were reported from 1978 to 1999. Studies with first HIV prevalence 10% or less were available from 23 cities without NSP, 19 cities that implemented NSP between the first and last study, and 13 cities that already had NSP when the studies were carried out

The fitted HIV prevalence regression lines are presented for those cities that had never introduced NSPs in Figure 3.1a, and for those cities that had ever introduced NSPs in Figure 3.1b. To illustrate the fitting procedure, the fitted regression lines and the reported HIV seroprevalence survey results are shown for two sites (Songkla Province, Thailand and Sydney, Australia) in Figures 3.1c and 3.1d respectively.

The overall comparison of annual rates of change of HIV seroprevalence in cities that never introduced NSPs with cities that did introduce NSPs are summarised in Table 3.1.2. Cities that introduced NSPs had a mean annual 18.6% decrease in HIV seroprevalence, compared with a mean annual 8.1% increase in HIV seroprevalence in cities that had never introduced NSPs (mean difference –24.7% [95% CI: –43.8%, 0.5%], p=0.06).

In cities with an initial HIV prevalence less than 10% and with sero-surveys over a period of at least three years, the mean annual decrease in HIV prevalence was 4.0% in cities that introduced NSPs, compared with a mean annual 28.6% increase in cities without NSPs (mean difference –25.3% [95% CI:-50.8%, 13.3%], p=0.2).

Variability of the point estimate was markedly reduced and statistical significance markedly increased when the analyses for all cities and cities with HIV prevalence less than 10% were weighted according to one over the regression estimate (The better fit implies a smaller variance, and therefore its reciprocal is larger, representing a larger weight). However, a disadvantage of the weighted analyses is that it tends to put much greater weight on the few cities in which the linear regression gives a very good fit to the available HIV seroprevalence estimates. For this reason, and because the unweighted results are qualitatively very similar and, for all cities, the point estimate is smaller than the weighted analysis, estimates of NSP effectiveness were based on the unweighted analysis.

3.1.4 HCV SEROPREVALENCE

There were 190 calendar years of HCV seroprevalence data from 101 cities. Data were from 41 cities without NSP, 9 cities that implemented NSP between the first and last study, and 51 cities that already had NSP when the studies were carried out (Table 3.1.3). There were 71 cities with data available for one calendar year, 13 cities with data for two calendar years and 17 cities with data for three or more calendar years. In the 30 cities with HCV seroprevalence data available for more than one year, 60% had already implemented NSPs before the first year of measurement and 30% introduced NSP between the first and last year of measurement.

Median HCV prevalence was 75% (range 24% to 96%) in studies from cities without NSP and 60% (range 17% to 98%) in cities with NSP (NPtrend p=0.01). Data were reported from 1973 to 2000 (Figure 3.2). HCV results from stored samples collected between 1973 and 1989 were reported by 21 cities. There were 44 cities with their first study carried out between 1990 and 1994 and 36 cities with their first study between 1995 and 1999.

Overall the results indicated little change in HCV prevalence before NSPs were introduced, followed by a decline after introduction of NSPs (Table 3.1.4). If HCV prevalence was 75% or 50% respectively before NSPs were introduced, the results correspond to around a 1.5% or 2% decline in HCV prevalence per annum.

Similar results were obtained when two studies based on samples from the 1970s and one from 1980 were excluded from analysis and when analysis was limited to nine cities that implemented NSP between the first and last study (Table 3.1.4). Other analyses, using different regression models, such as ML random effects, and GEE, gave similar results (data not presented).

3.1.5 HCV SEROPREVALENCE AMONG NEW INJECTORS

There were 48 studies, from 19 cities, with HCV seroprevalence estimated among people reporting less than three years of injecting drug use (Figure 3.3). Most studies were from nine Australian cities (n=35, 73%). There were also two studies from both Baltimore and New York, and one study each from Chicago, Dublin, Lille, Liverpool, Manipur, Padua, New Zealand (four cities combined), and Valencia.

Most studies were carried out in cities with NSPs (43 studies from 16 cities). Five studies were carried out in four cities without NSPs. Before and after NSP data were only available from one city. Studies were carried out between 1985 and 2000, with half since 1996 (Figure 3.3). Sample size ranged from 14 to 303, median 53.

Median HCV prevalence was substantially lower in cities with than without NSPs (19% vs 71%; Table 3.1.5). On average, HCV prevalence in cities with NSPs was 37% lower than in cities without NSPs using random effects regression modelling (mean (sd): 25% (+18%) vs. 66% (+15%), $p<0.001$; Table 3.1.6).

3.1.6 HCV INCIDENCE

HCV incidence was reported for 27 time periods from nine countries. All three studies in cities without NSP were from Italy (Naples, Padua and Rome) in early 1990. HCV incidence studies in cities with NSPs were from six Australian cities (nine data points), Amsterdam (four data points), Baltimore (three data points), Berlin (one data point), Czechoslovakia (one data point), Geneva (two data points), Malmo (one data point), New Zealand (one data point), and Seattle (one data point).

On average, HCV incidence was 25 per 100 person years in studies from cities without NSPs compared with 16 per 100 person years in studies from cities with NSPs (Table 3.1.7). Similar rates were obtained when HCV incidence was aggregated for each city (Table 3.1.9). Analyses consistently indicated a non-statistically significant protective effect for HCV incidence in cities with NSPs using random effects and GEE negative-binomial regression models for all data points and straightforward negative-binomial regression modelling for data aggregated by city (Table 3.1.8).

3.1.7 DISCUSSION

On average, HIV seroprevalence decreased in studies of injecting drug users in cities with NSPs whereas in studies from cities without NSPs, HIV seroprevalence increased. Seroprevalence of HCV also decreased annually in studies carried out after NSPs were introduced. HCV prevalence was substantially lower among people reporting less than three years of drug injection in cities with NSPs compared to cities without NSPs. There was also a non-statistically significant protective effect for HCV incidence in cities with NSPs when compared to those without NSPs.

There are several limitations associated with the ecological study design that should be considered when interpreting the findings from these studies. Seroprevalence data used in the analyses were collected according to different protocols and in diverse populations. It is unlikely that estimates of HIV and HCV seroprevalence in cities with NSPs would differ systematically from those in cities without NSPs, so any such sampling bias would underestimate the effectiveness of NSPs. Because cities were selected for analysis by the existence of published HIV and HCV serological surveys, bias may have been introduced by the decision to do a survey in a particular city at a particular time.

Data on NSPs used in the analyses were based on presence or absence of NSPs rather than on the extent and uptake of these services. Given the positive findings, however, it is likely that inclusion of these parameters would result in a dose response effect on HIV and HCV seroprevalence from NSPs. In addition, it is not possible to separate the effects of implementation of NSPs from the other HIV prevention strategies (Benedikt et al. 2000). In most settings, introduction of NSPs is one component of a broader harm reduction package to reduce the risk of transmission of blood-borne viruses and other harm associated with injecting drug use. Other components include education and counselling, drug dependency treatment strategies such as methadone maintenance

therapy, and provision of clean injecting equipment through other outlets in particular pharmacies. Adequate data was not available on individual components of harm reduction strategies to allow an evaluation of the impact of components other than provision of clean injecting equipment (NSPs). Sensitivity analysis has been conducted to determine the outcome of lower rates of NSP effect on HIV (See Section 4.8).

The excess risk of HIV in people who inject drugs is not due solely to sharing needles, other injecting practices and sexual behaviour patterns increase HIV risk. In contrast to HIV, HCV infection is rarely spread through sexual transmission (MacDonald et al. 1996).

It is also possible that HIV seroprevalence may have remained low in some of the cities with NSPs, irrespective of their introduction. HCV infection, however, is universally high among drug injectors. In most countries HCV infection became endemic among this population before there was widespread publicity about transmission of blood borne viruses through injecting practices. Because HCV infection remains asymptomatic for longer than HIV infection, it is also possible that people with HCV infection remain in the population of injectors for longer than those with HIV infection, therefore increasing the prevalence of HCV infection in seroprevalence surveys of injectors.

If NSPs decrease the incidence of HIV and HCV, the rate of increase in seroprevalence should decrease, although the seroprevalence itself may not decrease, at least initially. It is likely that the lower effect of NSP on HCV than HIV seroprevalence can be attributed to the generally higher prevalence of HCV compared to HIV before the introduction of NSPs.

NSPs influence HIV and HCV transmission by increasing use of sterile syringes for injection and lowering the rate of syringe sharing thereby reducing contact with each virus. Some NSPs also provide referrals to drug treatment centres, condoms and education about minimising risk. The difference in rate of change of HIV seroprevalence between cities with and without NSPs and the decrease in HCV prevalence in cities after the introduction of NSPs may not be due solely to NSPs. Nonetheless, the study provides evidence that NSPs reduce the spread of HIV and HCV infection.

Table 3.1.1 Location of cities and sites of recruitment for cities with at least two HIV prevalence studies according to NSP status from the time of first to last study

Location of studies		No. cities without NSP	No. cities with & without NSP	No. cities with NSP
Asia	China	3	0	0
	India	1	1	0
	Malaysia	4	0	0
	Myanmar	4	0	0
	Nepal	0	0	1
	Thailand	22	2	0
	Vietnam	0	1	0
Australia		0	2	8
Canada		0	3	0
Europe	Austria	0	1	0
	Czech Republic	1	0	0
	Denmark	0	1	0
	France	0	0	1
	Germany	0	1	0

Location of studies		No. cities without NSP	No. cities with & without NSP	No. cities with NSP
	Greece	0	1	0
	Israel	1	0	0
	Italy	10	0	0
	Netherlands	0	0	2
	Spain	3	0	0
	Switzerland	0	1	0
South America	Argentina	0	1	0
	Brazil	5	0	0
United Kingdom		0	4	1
United States		13	4	0
Total cities		**67**	**23**	**13**
Recruitment sites				
Deceased		0	4	0
Detoxification/rehabilitation		226	18	0
Drug treatment agency		95	72	8
Entry to treatment		33	17	0
Field & snowball		16	25	7
Health service		0	2	0
HIV testing centre		6	17	0
Infectious diseases hospital		14	1	0
Multiple sites		15	61	6
NSP/pharmacy		0	27	35
Sexual health clinics		4	12	2
Other/not reported		26	25	3
Total studies		**435**	**281**	**61**

Table 3.1.2 Estimated annual rate of change in HIV seroprevalence according to weighting of analysis and sample selection for cities without and with NSPs

Weighting of analysis/ Sample selection	Cities without NSPs	Cities with NSPs
No weighting of analysis		
All cities		
Number	63	36
Mean	8.1%	-18.6%
(95% CI)	(-2.8%, 20.1%)	(-42.6%, 15.3%)
Mean difference (95%CI)	-24.7% (-43.8%, 0.5%), p=0.057	

Weighting of analysis/ Sample selection	Cities without NSPs	Cities with NSPs
Cities with initial HIV prevalence <10%, three calendar years of data		
Number	19	25
Mean	28.6%	-4.0%
95% CI	(-4.9%, 73.8%)	(-28.5%, 29.0%)
Mean difference (95%CI)	-25.3% (-50.8%, 13.3%), p=0.165	
Weighting of analysis		
All cities		
Number	63	36
Mean	5.1%	-29.2%
(95% CI)	(1.4%, 9.1%)	(-30.8%, -27.6%)
Mean difference (95%CI)	-32.7% (-37.5%, -27.6%), p=<0.001	
Cities with initial HIV prevalence <10% and three calendar years of data		
Number	19	25
Mean	32.1%	7.8%
95% CI	(22.1%, 42.8%)	(-4.8%, 22.0%)
Mean difference (95%CI)	-18.4% (-32.0%, -2.0%), p=0.030	

Table 3.1.3 Location of cities and sites of recruitment for cities with HCV prevalence studies according to NSP status from the time of first to last study

Location of studies		Number of cities without NSP	Number of cities without & with NSP	Number of cities with NSP
Asia	China	2	0	0
	Bangladesh	1	0	0
	India	0	0	1
	Japan	3	0	0
	Malaysia	1	0	0
	Nepal	0	0	1
	Taiwan	1	0	0
	Thailand	3	0	1
Australia		0	2	10
Canada		0	0	1
Europe	Austria	1	1	0
	Belgium	1	0	2
	Croatia	1	0	0

	Denmark	0	0	1
	France	1	0	4
	Germany	1	0	2
	Greece	1	0	0
	Hungary	1	0	0
	Iceland	1	0	0
	Israel	1	0	0
	Italy	7	0	1
	Luxembourg	0	0	1
	Netherlands	0	0	1
	Norway	1	0	0
	Poland	2	0	0
	Portugal	0	1	0
	Saudi	1	0	0
	Slovenia	0	0	1
	Spain	3	1	2
	Sweden	0	1	1
	Switzerland	0	1	1
New Zealand		0	0	5
South America	Argentina	0	0	1
	Brazil	2	0	0
United Kingdom		0	0	11
United States		5	2	4
Total cities		**41**	**9**	**51**
Recruitment sites				
Detoxification/rehabilitation		12	2	5
Drug treatment agency		14	9	10
Field & snowball		6	2	9
HIV testing /Sexual health centre		4	5	14
Multiple sites		2	5	15
NSP/pharmacy		0	11	37
Other		6	11	11
Total studies		**44**	**45**	**101**

Table 3.1.4 Estimation of the effect of NSPs on HCV prevalence per year using random effects regression

Inclusion criteria	logit(HCV)	Coefficient	Std. Error	p value	95% CI
All cities and all data points					
	Calendar year	-0.008	0.02	0.7	-0.05, 0.04
	Years since NSP	-0.079	0.03	0.003	-0.13, -0.02
	Constant	1.040	0.24	<0.001	0.56, 1.52
	sigma_u	0.5637			
	sigma_e	0.8082			
	rho	0.3275	(fraction of variance due to u_i)		
All cities and excluding data points before 1981					
	Calendar year	-0.0460	0.03	0.1	-0.10, 0.12
	Years since NSP	-0.0576	0.03	0.05	-0.11, -0.001
	Constant	92.775	59.3	0.1	-23.5, 209.1
	sigma_u	0.5627			
	sigma_e	0.8084			
	rho	0.3264	(fraction of variance due to u_i)		
All nine cities with data points before and after NSP					
	Calendar year	0.0446	0.04	0.2	-0.03, 0.11
	Years since NSP	-0.1317	0.05	0.01	-0.24, -0.03
	Constant	-87.17	70.8	0.2	-226, 51.6
	sigma_u	0.2255			
	sigma_e	0.8245			
	rho	0.0696	(fraction of variance due to u_i)		

Table 3.1.5 Summary of HCV prevalence rates among people reporting less than three years of drug injection according to availability of NSPs

NSP	Number of studies	Mean HCV prevalence	Standard deviation	Median HCV prevalence	Inter-quartile range
No NSP	5	66%	15%	71%	5%
With NSP	43	25%	18%	19%	21%

Table 3.1.6 Estimation of the effect of NSPs on HCV prevalence among people reporting less than three years of drug injection using random effects regression

HCV prevalence	Coefficient	Std. Error	p value	95% CI
NSP	-37.06	7.75	<0.001	-52.25, -21.86
Constant	64.50	8.41	<0.001	48.01, 80.98
sigma_u	22.74			
sigma_e	8.70			
rho	0.87	(fraction of variance due to u_i)		

Table 3.1.7 HCV incidence rates per 100 person years for cohorts according to availability of NSPs

NSP	Number of studies	Mean HCV incidence	Standard deviation	Median HCV prevalence	Inter-quartile range
No NSP	3	24.7/100py	16.9	28.6/100py	33.1
With NSP	24	16.4/100py	9.9	15.0/100py	10.6

Table 3.1.8 Comparison of HCV incidence in cohorts with and without NSP using negative binomial regression modeling

Type of model/ scnumber	IRR	Std. Error	p value	95% CI
Random effects negative binomial model				
NSP	0.55	0.25	0.18	0.23, 1.32
Total pyrs	(exposure)			
/ln_r	2.38	0.95		0.52. 4.24
/ln_s	3.45	1.17		1.16, 5.75
r	10.81	10.27		1.68, 69.53
s	31.62	37.01		3.19, 313.5
GEE negative binomial model				
NSP	0.69	0.47	0.58	0.19, 2.54
Total pyrs	(exposure)			

Table 3.1.9 HCV incidence rates per 100 person years for each city overall according to availability of NSPs

NSP	Number of studies	Mean HCV incidence	Standard deviation	Median HCV prevalence	Inter-quartile range
No NSP	3	24.7/100py	16.9	28.6/100py	33.1
With NSP	14	18.5/100py	11.4	15.9/100py	16.2

Table 3.1.10 Comparison of HCV incidence for each city with and without NSP using negative binomial regression modeling

Type of model/ scnumber	IRR	Std. Error	p value	95% CI
Random effects negative binomial model				
NSP	0.73	0.30	0.44	0.32, 1.64
Total pyrs	(exposure)			
/lnalpha	-1.28	0.45		-2.16. -0.40
alpha	0.28	0.13		0.12, 0.67

Figure 3.1a Fitted HIV prevalence in cities without NSPs.

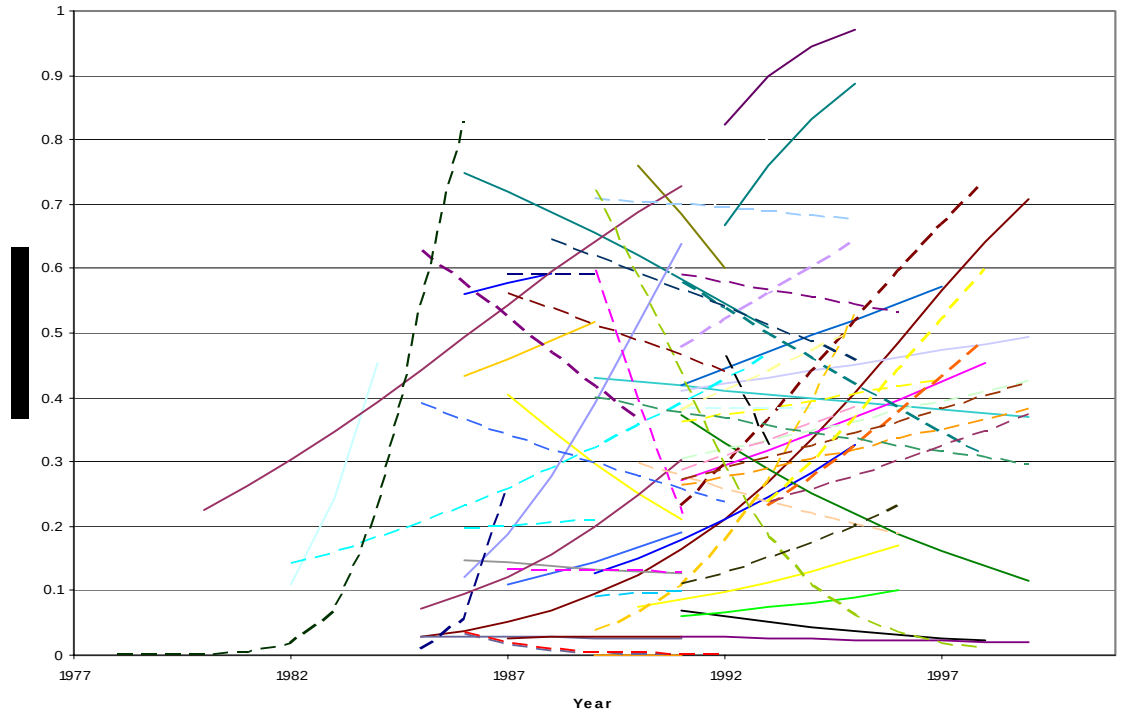


Figure 3.1b Fitted HIV prevalence in cities with NSPs.

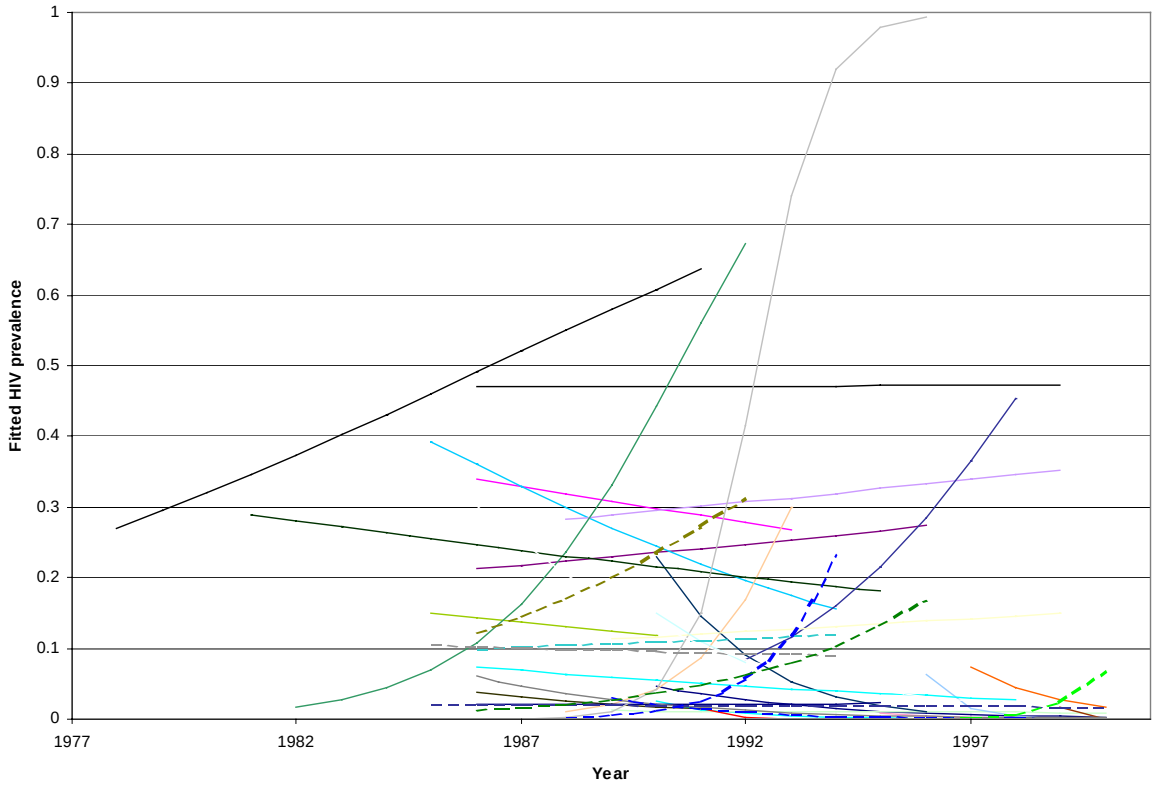


Figure 3.1c HIV seroprevalence in injecting drug users per year of survey for a city without NSP, Songkla Province, Thailand. (Lines represent fitted values from the logistic regression model)

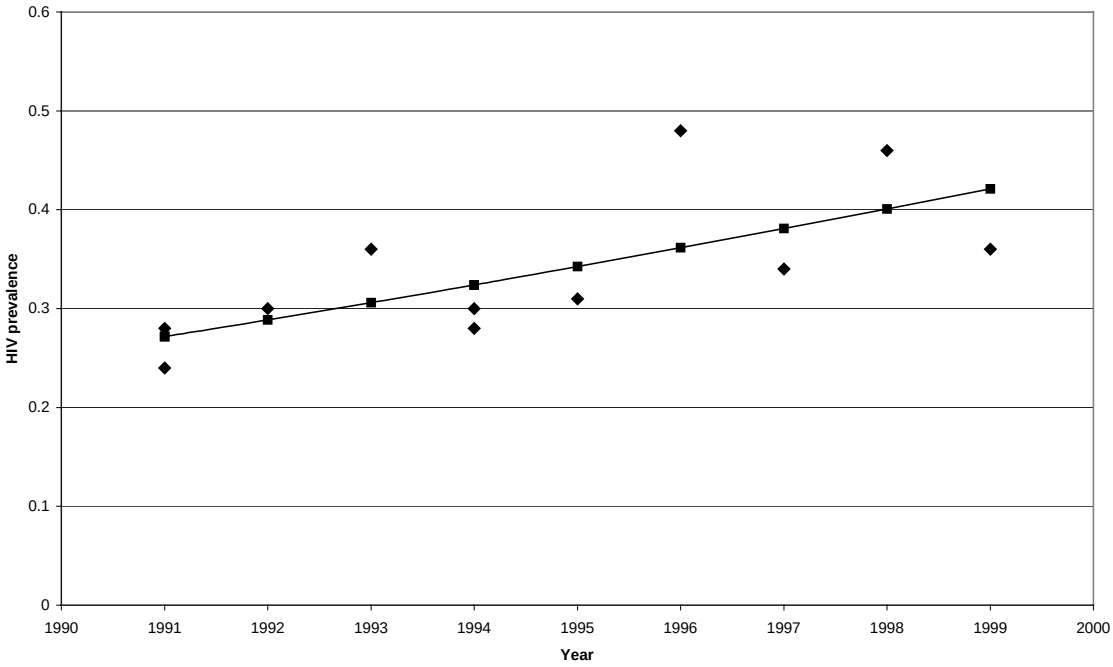


Figure 3.1d HIV seroprevalence in injecting drug users per year of survey for a city with NSP, Sydney, Australia. (Lines represent fitted values from the logistic regression model)

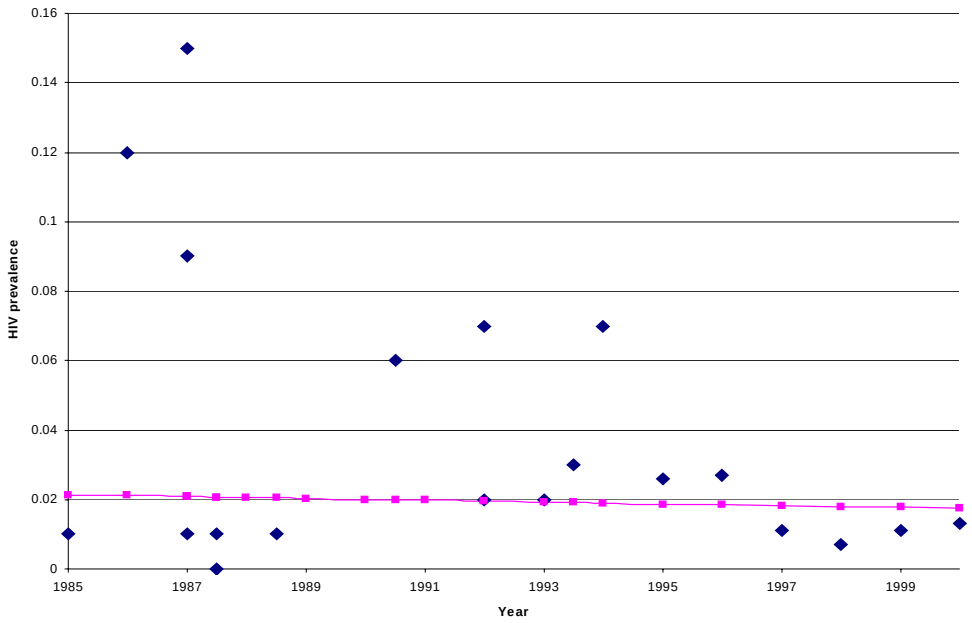


Figure 3.2 HCV seroprevalence among injecting drug users according to NSP status of city and year of study

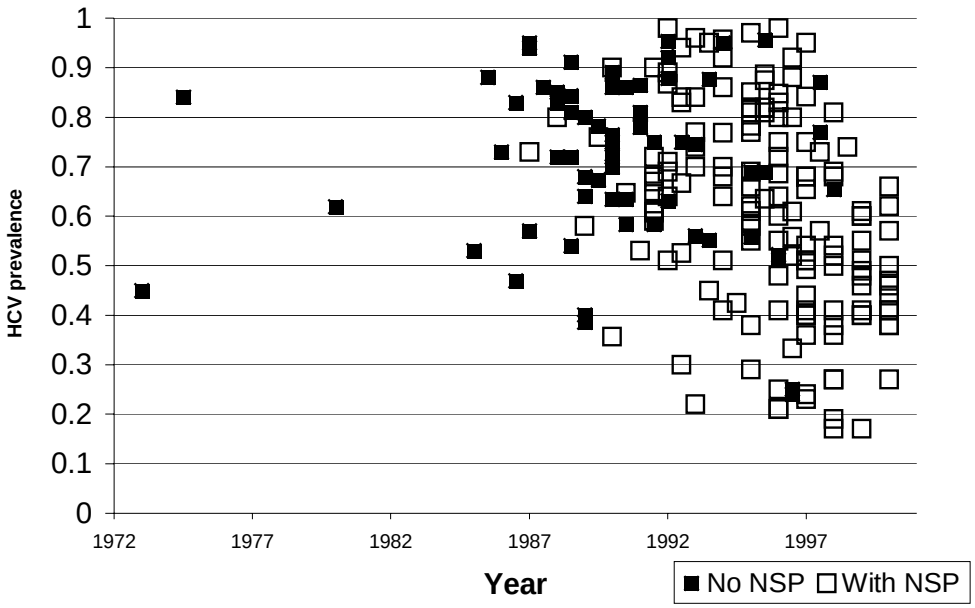
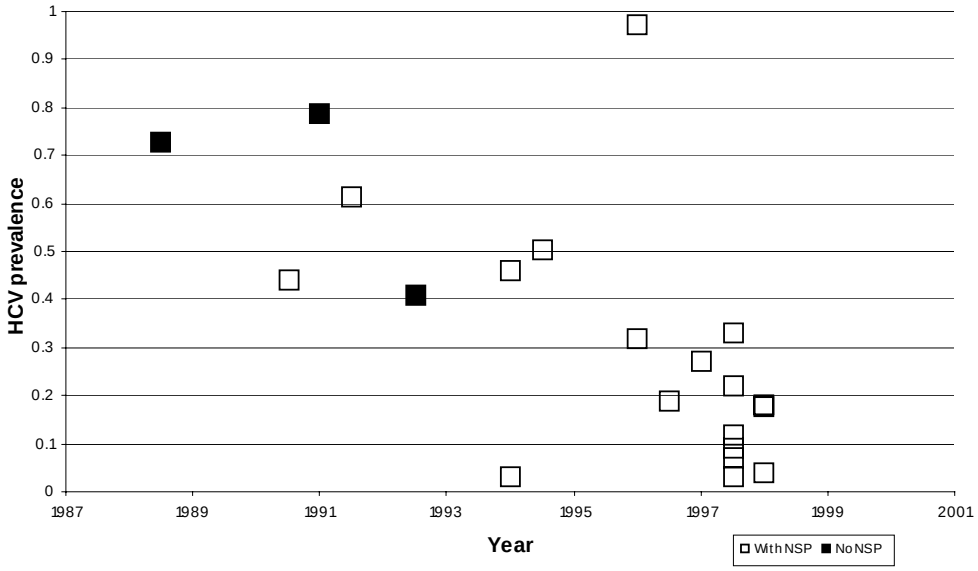


Figure 3.3 HCV seroprevalence among people reporting less than three years of drug injection according to NSP status of city and year of study



3.2 METHODOLOGY FOR ESTIMATES OF NUMBERS OF PEOPLE LIVING WITH HIV ACQUIRED THROUGH INJECTING DRUGS

3.2.1 ESTIMATES AND PROJECTIONS OF HIV/AIDS INCIDENCE

Estimates of past HIV incidence and future AIDS incidence as a result of injecting drug use were obtained using back-projection methods. The method uses observed AIDS incidence data (adjusted for reporting delay), and knowledge of the rate at which HIV infected people progress to AIDS, to reconstruct the likely pattern of past HIV incidence. It is then also possible to estimate future AIDS incidence. The form of back-projection used was that suggested by Becker et al (1991), as modified by Marschner and Watson (1992). Because of the relatively small numbers of AIDS cases reported due to injecting drug use, back-projection analyses were applied to annual AIDS counts.

The baseline rate of progression to AIDS was modelled using a Weibull-with-levelling distribution (Rosenberg et al. 1992), corresponding to a median time to AIDS of just under 10 years and a progression rate of 11.2% at four years (Alcabes et al. 1993). The extended definition of AIDS, adopted in Australia in January 1988, was assumed to result in a 10% increase in the rate of progression to AIDS (Rosenberg et al. 1992).

Because of the uncertainties surrounding both the effect of combination antiretroviral treatments in reducing the rate of progression to AIDS, and the numbers of people living with HIV infection taking up such treatments, back-projections were performed using the following methods. First, a back-projection based on AIDS cases diagnosed to the end of 1994 was performed to estimate the pattern of HIV incidence up to this time. Over this period only moderately effective antiretroviral treatments were available, assumed to correspond to an overall 10% reduction in the rate of progression to AIDS, so the pattern of past HIV incidence can be reliably reconstructed. Second, the effects of improved combination treatments since the beginning of 1995 were then estimated, based on the estimated pattern of HIV incidence, so as to closely approximate AIDS incidence observed between 1996 and 2000.

The effects of improved combination treatments on reducing the overall rate of progression to AIDS were estimated based on cases of AIDS reported due to injecting drug use, and are summarised in the Table 3.2.1 below.

Table 3.2.1 Estimated percentage effect of combination antiretroviral treatments in reducing the overall rate of progression to AIDS between 1995 and 1999

Year	1996	1997	1998	1999	2000
Estimated reduction in progression rate (%)	77	69	60	52	44

Projections of AIDS incidence from 2001 onwards were made by assuming that the effect of treatments on the rate of progression to AIDS continued at the year 2000 level.

In analyses HIV incidence was fixed at 20 cases per year from 1994 onwards. The level at which HIV incidence was fixed was decided on the basis of the number of HIV diagnoses and diagnoses of newly acquired HIV infection reported to the National HIV Database, and was also chosen to be consistent with the estimated HIV incidence obtained from the back-projection analyses.

Back-projection estimates of HIV incidence need to be adjusted for underreporting of AIDS diagnoses, and deaths prior to AIDS. Reporting of AIDS cases was thought to be relatively complete in Australia, with completeness estimated to be at least 95% (Grulich et al. 1999). Deaths among IDUs are estimated to be approximately 1% per annum (Thorley 1981; English et al. 1995). The median time to AIDS is thought to be just

under 10 years, so, taken together, HIV incidence was inflated by 15% to allow for underreporting of AIDS and deaths prior to AIDS.

3.2.2 ESTIMATES OF THE NUMBER OF INJECTING DRUG USERS LIVING WITH HIV INFECTION

Estimates of the number of IDUs living with HIV infection by disease stage (CD4+ cell count more than 500/σl, a CD4+ cell count of less than 500/σl and AIDS free, or living with AIDS) were based on the estimated pattern of past HIV incidence. The rate of progression to a CD4+ cell count fewer than 500/σl was modelled using a similar Weibull-with-levelling distribution to that used to model the time from HIV infection to AIDS. The median time from HIV infection to a CD4+ cell count of 500/σl was assumed to be 4 years, with 95% below 500/σl by 10 years. Survival following AIDS among IDUs in Australia was reasonably consistent between 1988 and 1995. The effect of combination antiretroviral treatment in improving survival following AIDS from 1996 was assumed to be similar to the effect of treatment in reducing the rate of progression to AIDS in Table 3.2.1, and to continue at the year 2000 rate from 2001 onwards. Background death rates were based on ABS life tables, assuming that the mean age at HIV seroconversion among IDUs was 30 years, and that there were 3 male HIV-infected IDUs for each female HIV-infected IDU (ABS 1995).

3.2.3 ESTIMATING THE NUMBER OF INJECTING DRUG USERS LIVING WITH HIV WITHOUT NSPS

The effect of needle and syringe programs (NSPs) in reducing HIV transmission among IDUs has been estimated to correspond to an annual reduction in (logit) HIV prevalence of 0.28 (see Section 3.1).

HIV prevalence among IDUs in Australia between 1980 and 2000 was based on the estimated numbers of IDUs living with HIV described above, and estimates of the numbers of IDUs in Australia.

Numbers of IDUs in Australia were estimated as follows. The number of dependent heroin users in Australia in 1997 was assumed to be 75,000 (Hall et al. 2000). A reasonable fit to available estimates over the previous two decades was obtained by assuming a constant net 8% increase in dependent heroin users per year. To allow for injecting of other drugs, the total number of regular IDUs was assumed to be 33% greater than the number of dependent heroin users (i.e. 100,000 regular IDUs in 1997 (Law 1999). The number of occasional IDUs was assumed to be 175,000 in 1997 (Law 1999) with the same annual percentage increases.

NSPs were first introduced in Australia in late 1987. Hence, NSPs were assumed to have reduced HIV prevalence among IDUs from 1988 onwards. The pattern of HIV prevalence if NSPs had not been introduced was estimated by increasing (logit) HIV prevalence by 0.28 per year from 1988 onwards. From this, a pattern of HIV incidence if NSPs had not been introduced was derived.

Estimates of the numbers of IDUs living with HIV by disease stage if NSPs had not been introduced were obtained by applying the same models described above regarding rates of progression from HIV infection to CD4+ cell count <500 cells/σl, to AIDS and survival before and following AIDS.

3.2.4 ESTIMATED EFFECT OF NSPS IN REDUCING NUMBERS OF INJECTING DRUG USERS WITH HIV BY DISEASE STAGE

To allow costing of the effect of NSPs in reducing the number of people living with HIV, estimates of the reduction in the number of people living with HIV by disease stage were obtained by subtracting the estimates obtained with NSPs from the corresponding estimates without NSPs. In these analyses, HIV incidence due to injecting drug use was assumed to cease from 2001 onwards, and estimates were projected forward until all people infected with HIV were estimated to have died.

3.3 METHODOLOGY FOR ESTIMATES OF NUMBERS OF PEOPLE LIVING WITH HCV ACQUIRED THROUGH INJECTING DRUGS

3.3.1 ASSUMPTIONS USED IN MODELS OF HCV INCIDENCE

The incidence of HCV in Australia was modelled based on the following assumptions regarding the past pattern of injecting drug use in Australia:

- There were 100,000 regular IDUs in 1997 (Hall et al. 2000), with a constant net increase of 8% per year since 1970, and with 5% stopping injecting each year (Thorley 1981; English et al. 1995).
- There were 175,000 occasional IDUs in 1997, with a constant net increase of 8% per year since 1970, and with 10% stopping injecting each year (Law 1999).
- There were no IDUs in 1960, with a linear increase in the number of both regular and occasional IDUs between 1960 and 1970.

Other assumptions made in modelling HCV incidence were the same as those adopted by the HCV Projections Working Group (Law 1999):

- 65% of IDUs who start injecting regularly have previously injected occasionally (from the Delphi study).
- The HCV incidence rate in uninfected regular IDUs was taken to be 18% per annum from 1960 until 1985, after which it was taken to decrease linearly to 13% in 1989 and thereafter.
- The HCV incidence rate in occasional IDUs was taken to be 20% of that in regular IDUs.
- All people starting or stopping injecting, or becoming regular rather than occasional IDUs, did so independent of their HCV status.
- HCV incidence due to receipt of infected blood or blood products was taken to be 15% of HCV incidence in IDUs until the early 1980s, after which it was assumed to have gradually decreased following the introduction of donor self-deferral related to injecting drugs (which began in 1983), and to be stopped entirely from 1990 onwards with the introduction of blood donor screening for HCV.
- HCV incidence through other transmission routes (such as needle stick injuries in health care workers, or tattoos) was taken to be 10% of HCV incidence in IDUs between 1987 and 1997, reflecting the data on risk factors for recent incident HCV infections. Prior to 1987 it was assumed to increase linearly to 20% of HCV incidence in IDUs in 1977, and then fixed at this absolute number of infections per year prior to this, again broadly consistent with data on risk factors for prevalent HCV infections, and for people with HCV infection attending liver clinics.
- The number of HCV infections between 1950 and 1960 was held constant at a low level proportional to the modelled HCV incidence among IDUs. Any HCV infections prior to 1950 were assumed to have negligible effect on estimates and projections, and were not modelled.

3.3.2 ESTIMATES OF RATES OF HCV-RELATED LIVER DISEASE PROGRESSION

It was assumed that 75% of people exposed to HCV developed HCV chronic infection (i.e. 25% of exposed people cleared HCV) (Law 1999). Of people with chronic HCV infection, it was assumed that one third had normal ALT values, one third abnormal ALT values, and one third abnormal ALT values with further covariates which indicate they would be at increased risk of progression (eg high alcohol intake). Rates of progression from stage 0/1 liver disease to stage 2/3 liver disease, and from stage 2/3 disease to cirrhosis are shown in Table 3.3.1.

Table 3.3.1 Annual rates of liver disease progression

Disease Stage	Stage 0/1 to Stage 2/3	Stage 2/3 to Cirrhosis
Not chronic HCV	0%	0%
Chronic HCV, normal ALT	1%	1%
Chronic HCV, abnormal ALT	2%	2%
Chronic HCV, normal ALT and further cofactors	3%	3%

Note: Stage 0=no hepatic fibrosis, stage 1=minimal hepatic fibrosis; stage 2=moderate hepatic fibrosis; stage 3=severe hepatic fibrosis; stage 4=cirrhosis.

Taken together, these assumptions combine so that of all people exposed to HCV, 5.3% are estimated to develop cirrhosis by 20 years, with 7.1% of people with chronic HCV developing cirrhosis by 20 years. This is consistent with current evidence regarding progression rates to cirrhosis (Freeman et al. 2001).

Rates of developing liver failure or hepatocellular carcinoma (HCC) from cirrhosis were assumed to be 4% and 1% respectively (Fattovich et al. 1997). It was further assumed that HCC could develop following liver failure, but not vice-versa. HCV-related mortality following cirrhosis was taken to be 1.5% per annum (Fattovich et al. 1997).

Mortality unrelated to HCV, both before and after cirrhosis, was assumed to be 1% per year (Thorley 1981; English et al. 1995) due to injecting drug use. Background mortality was based on ABS life tables, assuming that the mean age at HCV seroconversion among IDUs was 25 years, and that there were 2 male HCV-infected IDUs for each female HCV-infected IDU (ABS 1995).

Estimates of the numbers of people living with HCV by disease stage, and the incidence of liver cancer and HCC, were derived by combining these progression rates with the HCV incidence pattern estimated through the models described above.

3.3.3 Estimates of the Number of Injecting Drug Users Living with HCV without NSPs

The modelled estimate of HCV incidence in Australia that has occurred with NSPs described above corresponds to a gradual increase in HCV prevalence among regular IDUs until the mid- to late-1980s, followed by a gradual decline to around 52% HCV prevalence in 2000. NSPs were first introduced in Australia in late 1987. Hence, NSPs were assumed to have reduced HCV prevalence among IDUs from 1988 onwards. The pattern of HCV prevalence if NSPs had not been introduced was estimated by assuming that HCV prevalence would have remained constant at 1988 levels from 1988 onwards. From this, a pattern of HCV incidence if NSPs had not been introduced was derived. It was further assumed that the introduction of NSPs had no effect on HCV transmissions through routes other than injecting drug use.

Estimates of the numbers of people living with HCV by disease stage if NSPs had not been introduced were then derived using the same progression rate distributions described above.

3.3.4 Estimated Effect of NSPs in Reducing Numbers of Injecting Drug Users with HCV by Disease Stage

To allow costing of the effect of NSPs in reducing the number of IDUs living with HCV, estimates of the reduction in the number of people living with HCV by disease stage were obtained by subtracting the estimates obtained with NSPs from the corresponding estimates without NSPs. In these analyses, HCV incidence due to injecting drug use was assumed to cease from 2001 onwards, and estimates were projected forward until all people infected with HCV were estimated to have died, either from HCV-related or unrelated mortality.

3.4 NUMBER OF HIV INFECTIONS PREVENTED THROUGH THE INTRODUCTION OF NSPS

3.4.1 ESTIMATES OF INJECTING DRUG USERS LIVING WITH HIV/AIDS WITH NSP INTRODUCTION

Estimates and projections of the number of people living with HIV acquired through injecting drug use by disease stage and HIV/AIDS-related deaths from 1981 though 2070 are provided in Table 3.4.1 (See Appendix C). The number of people living with HIV/AIDS is estimated to have peaked in the early 1990s at approximately 470 cases, with a peak in people living with AIDS of less than 100 in the late 1990s. The cumulative number of deaths from HIV/AIDS by 2010 is projected to be approximately 350.

3.4.2 ESTIMATES OF INJECTING DRUG USERS LIVING WITH HIV/AIDS WITHOUT NSP INTRODUCTION

Corresponding estimates and projections of the number of people living with HIV/AIDS by disease stage and HIV/AIDS-related deaths without the introduction of NSPs are provided in Table 3.4.2 (See Appendix C). The number of people living with HIV/AIDS was estimated to peak in 2000 at approximately 26,000, with a peak in people living with AIDS of almost 3,000 in 2010. The estimated cumulative number of deaths from HIV/AIDS by 2010 was approximately 5,000.

3.4.3 ESTIMATES OF HIV INFECTIONS AND HIV/AIDS DEATHS PREVENTED THROUGH NSP INTRODUCTION

Estimates of the number of HIV infections and HIV/AIDS deaths prevented through the introduction of NSPs (over the period 1988 through 2000) are provided in Table 3.4.3 (See Appendix C). By the year 2000, approximately 25,000 HIV infections are estimated to have been prevented since the introduction of NSP in 1988, and by 2010 approximately 4,500 deaths are projected to have been prevented.

3.4.4 ESTIMATES OF HIV/AIDS CASES PREVENTED BY DISEASE STAGE AND DIAGNOSIS CATEGORY

An estimated 90% of the Australian HIV-infected population is diagnosed (NCHECR 2001). We have assumed that the proportion diagnosed is 100% for people with AIDS, and would be higher among people with progressive HIV disease (CD4<500/mm^3) than people with early HIV disease (CD4 >500/mm^3) (Table 3.4.4).

Based on data from the Australian HIV Observational Database (AHOD) over the period January 1997- March 2001, 71% of people with diagnosed HIV infection in Australia were receiving antiretroviral therapy. The proportion of injecting drug users receiving antiretroviral therapy was not significantly different to other risk categories (63% versus 71%, p>0.05). The proportion of people receiving antiretroviral therapy is 90% for AIDS, 50% for CD4 < 500/mm^3, and 69% for CD4 > 500/mm^3. Due to probable selection bias in AHOD for people with early HIV disease who are receiving antiretroviral therapy, the population level proportion is likely to be somewhat lower. Therefore, 40% of people with early stage HIV disease have been estimated to be receiving antiretroviral therapy.

Table 3.4.4 Proportions of people with diagnosed HIV and antiretroviral therapy use by disease stage

Disease stage	Diagnosed/Undiagnosed (%)	Antiretroviral therapy among diagnosed group[1]
Early HIV disease (CD4 >= 500/mm^3)	80/20	40%
Progressive HIV disease (CD4 < 500/mm^3)	90/10	70%
AIDS	100/0	90%

All people with undiagnosed HIV are assumed to not be receiving antiretroviral therapy.

Estimates of the number of HIV/AIDS cases prevented through the introduction of NSP by disease category and diagnosis category are provided in Table 3.4.5 (See Appendix C). These estimates form the basis for the calculation of the health care cost savings provided by the introduction of NSPs.

3.5 NUMBER OF HCV INFECTIONS PREVENTED THROUGH THE INTRODUCTION OF NSPS

3.5.1 ESTIMATES OF INJECTING DRUG USERS WITH HCV AND HCV-RELATED DEATHS WITH NSP INTRODUCTION

Estimates and projections of the number of people living with HCV acquired through injecting drug use by disease stage and HCV-related deaths from 1961 through to 2075 with the introduction of NSPs are provided in Table 3.5.1 (See Appendix C). In 2000, the number of people living with HCV is estimated to be approximately 200,000 (approximately 150,000 with chronic HCV infection). By 2010 an estimated 11,800 people are projected to be living with cirrhosis, and estimated cumulative HCV-related deaths are projected to be 1,800.

3.5.2 ESTIMATES OF INJECTING DRUG USERS WITH HCV AND HCV-RELATED DEATHS WITHOUT NSP INTRODUCTION

Corresponding estimates and projections of the number of people living with HCV by disease stage and HCV-related deaths without the introduction of NSPs are provided in Table 3.5.2 (See Appendix C). In 2000, the number of people living with HCV is estimated to be approximately 220,000 (approximately 165,000 with chronic HCV infection). By 2010 an estimated 12,500 people are projected to be living with cirrhosis, and estimated cumulative HCV-related deaths are projected to be 1,900.

3.5.3 ESTIMATES OF HCV INFECTIONS AND DEATHS PREVENTED THROUGH NSP INTRODUCTION

Estimates of the number of HCV infections and HCV-related deaths prevented through the introduction of NSPs (over the period 1988 through 2000) are provided in Table 3.5.3 (See Appendix C). By the year 2000, approximately 21,000 HCV infections are estimated to have been prevented since the introduction of NSP in 1988, (of which approximately 16,000 would have developed chronic HCV); while by 2010 approximately 650 fewer people are projected to be living with cirrhosis and 90 HCV-related deaths would have been prevented.

3.5.4 ESTIMATES OF HCV CASES PREVENTED BY DISEASE STAGE AND DIAGNOSIS CATEGORY

In Australia, an estimated 70% of people living with hepatitis C are diagnosed (NCHECR 2001). Table 3.5.4 outlines the estimates of diagnosed chronic hepatitis C by stage of liver disease. It was assumed that proportions of diagnosed chronic hepatitis C would increase with disease stage to reach 100% for advanced liver disease complications (HCC, liver failure).

Table 3.5.4 Proportions of people with diagnosed chronic hepatitis C at different disease stages

Disease stage	Diagnosed/Undiagnosed (%)
Mild chronic hepatitis C	60/40
Moderate chronic hepatitis C	75/25
Compensated cirrhosis	80/20
Liver failure	100/0
Hepatocellular carcinoma	100/0

Note: An estimated 70% (140,000/200,000) of people living with hepatitis C in Australia are aware of their HCV status (NCHECR 2001).

Estimates of the number of HCV cases prevented through the introduction of NSP by disease stage and diagnosis category are provided in Table 3.5.5 (See Appendix C). These estimates form the basis for the calculation of the health care cost savings provided by the introduction of NSPs. Although there may be quality of life impairment and health care costs for people who are HCV antibody positive but do not have chronic hepatitis C, we have taken the conservative approach of basing our analyses on cases of chronic hepatitis C only.