5 QUALITY OF LIFE (QOL) EFFECTS OF NSPS

5.1 INTRODUCTION

Since both HIV and HCV are potentially life-threatening conditions, one of the main benefits from averting infections is the prevention of premature mortality. However, there are considerable contrasts in the natural history of these two chronic viral infections, particularly in the rate of progression to advanced disease and related complications.

Prior to the introduction of improved antiretroviral therapy in the mid-1990s, a half of people with HIV would have developed advanced immunodeficiency and associated AIDS illness complications during the first 10 years of infection. Although a small proportion of people – possibly 5% – were considered long-term non-progressors the majority of the other half would have had evidence of immune function deterioration, and were at risk of progression to AIDS in subsequent years. Survival following development of AIDS was approximately 18 months. Thus, it was expected that very few people with HIV would have been alive or free of AIDS after 15-20 years infection. Although several pre-AIDS HIV conditions are associated with considerable morbidity, the major morbidity associated with HIV infection was as a result of the development of specific AIDS illnesses.

Since the introduction of highly active antiretroviral therapy (HAART), HIV disease progression has markedly slowed, both for people prior to and following development of AIDS illnesses. Morbidity and mortality associated with AIDS illnesses have declined by 50-80% in settings where access to HAART is widespread. On the other hand, there has been an increase in morbidity associated with side effects of therapy. This effect, however, is relatively modest when compared with prior AIDS illness-related morbidity. The sustainability of the effect of HAART on immune function, and longer-term therapeutic toxicity are two areas where there is some uncertainty regarding levels of morbidity and mortality that will be experienced by people with HIV in the next decade.

The natural history of HCV infection varies with HIV in many areas. First, a proportion of people – possibly 20-40% – do not develop chronic infection and are therefore not at risk of advanced liver disease complications. Second, progression to advanced disease is both slower than HIV and not inevitable. An estimated 20% of people with chronic hepatitis C will develop cirrhosis over 15-40 years and be at risk of liver failure and liver cancer. Although the remaining 80% will not develop morbidity associated with advanced liver disease complications, many people suffer considerable morbidity related to a range of relatively non-specific symptoms. These include chronic lethargy, abdominal discomfort, and headaches. There is also recent evidence that HCV may cause cognitive impairment including difficulties with concentration. Pre-advanced liver disease morbidity in chronic hepatitis C is unrelated to the extent of liver damage.

As with HIV, antiviral therapy for HCV has improved in recent years. Currently, 50% of people with chronic hepatitis C who commence standard of care antiviral therapy (interferon and ribavirin combination) develop a sustained response that equates to a probable cure of their infection. Antiviral therapy therefore has the potential to considerably reduce morbidity and mortality related to chronic hepatitis C, however, for several reasons uptake to date has been relatively limited.

HIV and HCV may also have psychosocial effects among infected persons, some of which may be associated with discrimination and social stigma. These will also impact on the person's quality of life, regardless of whether the disease progresses or not.

Given the above, it is likely that gains in quality of life are one of the major health benefits of the prevention of HIV and HCV infections.

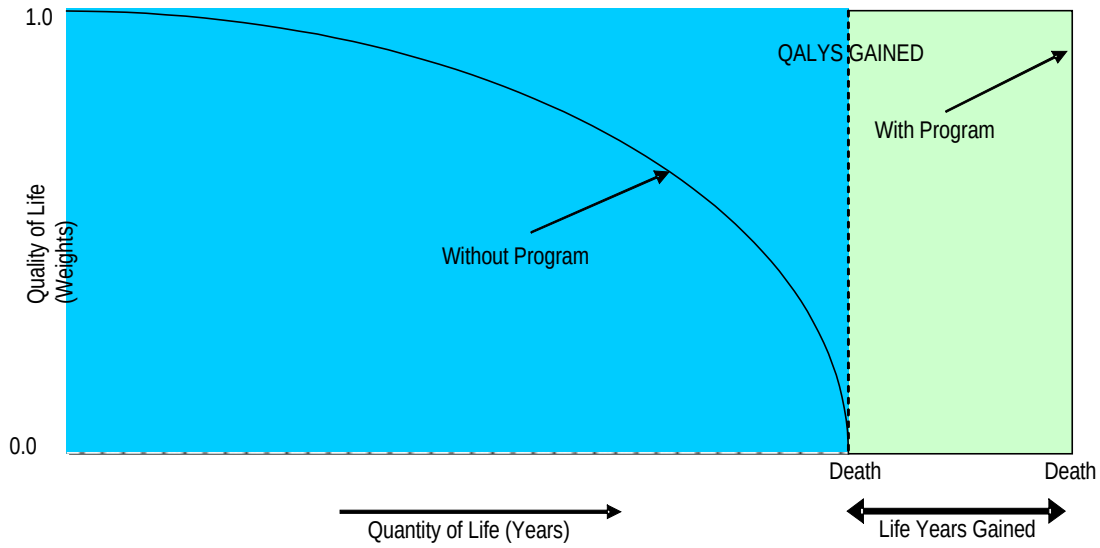
5.2 QUALITY-ADJUSTED LIFE-YEARS (QALYS)

The most widely used approach for estimating quality of life benefits in economic evaluations is the quality-adjusted life-year (QALY). In this approach, states of health are assigned a health state preference or 'utility' value, on a scale including 1.0 (full health) and 0 (death). The amount of time an individual spends in a given health state is then multiplied by the health state preference value to calculate the quality-adjusted life-years (QALYs) gained.

The QALYs gained from a given health care intervention are estimated by considering the difference in progression, through the various health states, with and without the intervention concerned. This is shown schematically in Figure 5.1. Here the intervention leads to QALY gains both by increasing or maintaining quality of life and by extending life. The main advantage of the QALY approach is that it provides one combined measure of the benefits of a program that both extends life and maintains quality of life.

In the context of HIV or HCV, we might expect that the health state values for early stages of disease, such as early HIV (CD4 count above 500/mm^3) or mild chronic hepatitis, are higher than those for the later stages of disease, such as AIDS or liver failure. Therefore, if the NSP reduces the probability of infection, or increases the average time to infection, we would expect fewer individuals in a cohort of IDUs to progress to the later stages of disease during their lifetime. Under the QALY approach this will lead to QALY gains.

Figure 5.1 Quality-adjusted life years



5.3 METHODOLOGY FOR ESTIMATING THE QALYS GAINED FROM THE PREVENTION OF HIV AND HCV INFECTIONS

In order to calculate the QALYs gained it is necessary to estimate the duration of time individuals will experience particular health states and the 'utility' values for those states. The durations of time spent in particular health states for someone with HIV or HCV has been estimated from the epidemiological literature and Australian data. These have been incorporated into the calculation of the number of cases prevented by stage of disease and the projections of survivors beyond 2000, as outlined in Section 3, and presented in Tables 3.4.5 and 3.5.5 in Appendix C.

Health state preference values for the disease stages are not readily available. One approach would be to undertake a free-standing study to estimate the values by standard gamble or time trade-off (Drummond, et al, 1997). However, this approach was considered beyond the scope of the current project.

Rather, it was decided to use values for health states existing in the literature. For example, Tengs et al (2000) report more than 1,000 health state values, many of which relate to HIV or HCV. In addition, there have been some papers published specifically relating to HIV (Holtgrave and Pinkerton, 1997) and HCV (Bennett, et al, 1997)

5.3.1 QALY VALUES FOR HIV

The quality of life estimates for HIV have been based on a review updating costs of HIV illness and quality of life estimates since the introduction of combination antiretroviral therapy (Holtgrave & Pinkerton 1997). Their estimates were based on an extensive review of studies, in which HIV-infected patients formed the study population of almost all identified studies. There are some differences in the disease phases they used and those we have employed. We have divided the undiagnosed HIV phase into two, one with "early HIV disease" and one with "progressive HIV disease". In Holtgrave & Pinkerton (1997) all people with undiagnosed HIV were given a quality of life rating of 0.94. We have assumed that people with "progressive HIV disease" who remain undiagnosed would in general have a slightly lower quality of life rating than those with earlier HIV disease. We have assumed that all people with AIDS are diagnosed.

Definitions for disease states and associated quality of life adjustments for HIV are presented in Table 5.3.1:

Table 5.3.1 Quality of life values by disease stage of HIV

Disease Stage	Description	QALY Value
Early HIV Disease – Undiagnosed.	HIV infection with CD4 count above 500/mm^3, unaware of HIV serostatus.	0.94
Early HIV Disease – Diagnosed.	HIV infection with CD4 count above 500/mm^3, aware of HIV serostatus and no antiretroviral therapy.	0.87
Progressive HIV Disease – Undiagnosed.	HIV infection with CD4 count below 500/mm^3, unaware of HIV serostatus.	0.90
Progressive HIV disease – Diagnosed.	HIV infection with CD4 count nadir below 500/mm^3 and commenced on antiretroviral therapy.	0.76
AIDS	AIDS as defined by clinical condition.	0.62

5.3.2 QALY VALUES FOR HCV

Quality of life adjustments for HCV were partly based on previous published estimates from a panel of hepatologists (Bennett et al. 1997). However, recent evidence from quality of life assessments among patient assessments was used to adjust the ratings provided by Bennett et al (1997). For example, studies indicate no significant difference in quality of life based on either degree of hepatic inflammation (as measured by ALT/AST) or extent of hepatic fibrosis (Bonkovsky et al. 1999). Therefore, we have used the same quality of life adjustment for diagnosed mild and moderate chronic hepatitis. Undiagnosed categories have higher quality of life estimates for two reasons. Firstly, development of symptomatic disease may often be a reason for HCV testing. Secondly, recent evidence suggests that quality of life impairment increases following diagnosis of hepatitis C (Rodger et al. 1999). We have combined the quality of life adjustments from Bennett et al (1997) for ascities (0.35), variceal haemorrhage (0.28), and hepatic encephalopathy (0.30), to produce a category for liver failure (0.32). We have assumed that all people with liver failure and HCC are aware of their HCV status. For the 25% of HCV infections that do not progress to chronic hepatitis, we have allocated a quality of life value of 1.0. This is a conservative estimate, as many people with hepatitis C who have not progressed to chronic infection are unaware of their non-viraemic status and may suffer significant impairment in quality of life related to psychosocial mechanisms.

Definitions for disease states and associated quality of life adjustments for HCV are presented in Table 5.3.2:

Table 5.3.2 Quality of life values by disease stage of HCV

Disease Stage	Description	QoL Value
HCV antibody positive – non-chronic hepatitis C.	HCV infected but does not progress to chronic hepatitis.	1.00
Mild chronic hepatitis – Undiagnosed	Chronic hepatitis C, unaware of HCV status, with stage 0-1 (no-minimal) hepatic fibrosis.	0.94
Mild chronic hepatitis – Diagnosed.	Chronic hepatitis C, aware of HCV status, with stage 0-1 (no-minimal) hepatic fibrosis.	0.82
Moderate chronic hepatitis – Undiagnosed.	Chronic hepatitis C, unaware of HCV status, with stage 2-3 (moderate-severe) hepatic fibrosis.	0.94
Moderate chronic hepatitis – Diagnosed.	Chronic hepatitis C, aware of HCV status, with stage 2-3 (moderate-severe) hepatic fibrosis.	0.82
Compensated cirrhosis – Undiagnosed	Chronic hepatitis C, unaware of HCV status, with associated cirrhosis but no evidence of liver failure or hepatocellular carcinoma (HCC).	0.84
Compensated cirrhosis – Diagnosed	Chronic hepatitis C, aware of HCV status, with associated cirrhosis but no evidence of liver failure or hepatocellular carcinoma (HCC).	0.74
Liver failure	Chronic hepatitis C associated cirrhosis that has progressed to de-compensation.	0.32
Hepatocellular Carcinoma (HCC)	Chronic hepatitis C associated cirrhosis that has progressed to HCC.	0.10

5.3.3 ADDITIONAL ELEMENTS OF THE QALY CALCULATIONS

Although somewhat more controversial than discounting costs, it is conventional to discount QALYs by the same rate. This has the effect of slightly reducing the estimate of the total QALYs gained from NSPs, as many of the QALYs are gained in the future.

5.4 NUMBER OF CASES OF HIV AND HCV AVOIDED

The estimates of the number of cases of HIV and HCV avoided as a result of the availability of NSPs during the 1990s are detailed in Section 3, and in Tables 3.4.5 and 3.5.5 in Appendix C. The outcomes have also been illustrated previously in Figures 4.2 and 4.3.

In summary, approximately 25,000 cases of HIV infection and 21,000 cases of HCV infection are estimated to have been avoided as result of NSP activities during the 1990s. Of those with HCV infection, approximately 16,000 persons would develop chronic hepatitis C. By the year 2010, some 4,500 deaths from HIV are estimated as being avoided, approximately 650 fewer people would be living with cirrhosis and 90 HCV-related deaths would have been prevented.

5.5 NUMBER OF LIFE YEARS GAINED

The number of life years gained provides a measure of the additional number of years by those persons who would otherwise have been infected with HIV and HCV, but for the effect of NSPs. This is estimated by deducting the number of life years they would have lived with HIV or HCV from the number of years they are expected to live without the disease. The results are indicative of the effect of the mortality rate for HIV/HCV on the target population, compared to that for the same population without these diseases.

The effect of NSPs on HIV and HCV is illustrated in Figures 5.2 and 5.3, with detailed tables provided in Table 5.5.1 (See Appendix E).

Figure 5.2 Life Years Gained for HIV cases avoided

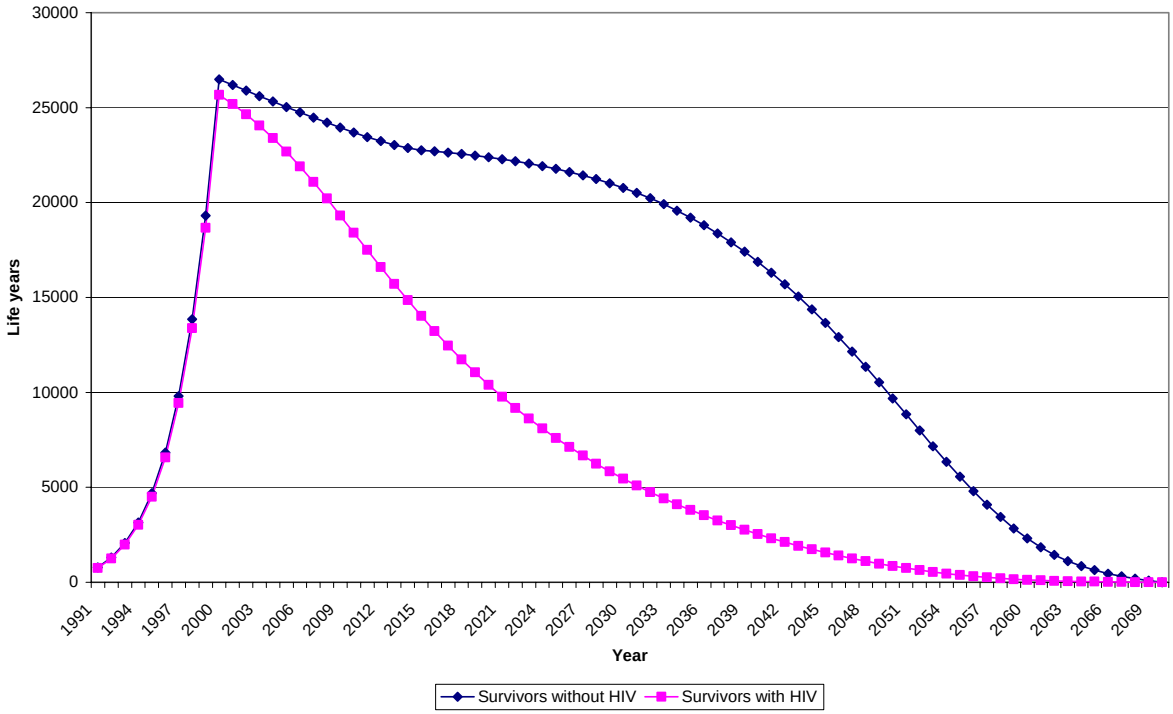
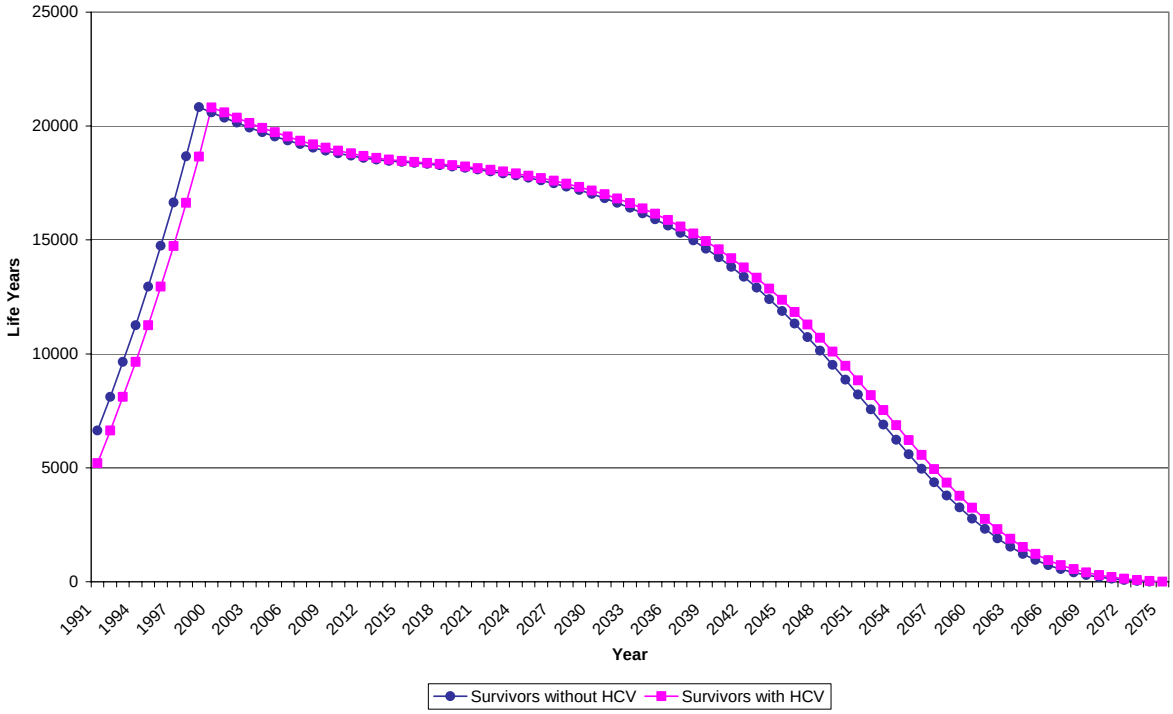


Figure 5.3 Life Years Gained for HCV cases avoided



In the figures, the gap between the curves "Survivors without HIV/HCV" and "Survivors with HIV/HCV" represents the number of life years saved over the lifetime of those affected. As is evident from both the figures and the tables, the effect of NSPs in terms of life years saved is much greater for HIV than for HCV. The 25,000 persons avoiding HIV are expected to gain an additional 588,000 life years (about 23 years each) than if they had contracted HIV. In comparison, the 21,000 persons avoiding HCV are expected to gain only about 1,200 life years

over their lifetime. The difference in these outcomes is essentially due to the different mortality rates associated with each disease and their rate of progression through the various stages, both of which have been incorporated into the analysis.

5.6 QUALITY ADJUSTED LIFE YEARS GAINED

The preceding analysis of life years gained takes into account the mortality effect of HIV and HCV on persons within the target population, namely injecting drug users. However, this analysis does not take into account any differences in the quality of life for those with HIV or HCV compared to those without the disease. As discussed in Section 5.2, the application of an adjustment factor to take account of the quality of life effects of these diseases leads to a measure referred to as Quality Adjusted Life Years (QALYs). Comparing this measure to the number of life years that the affected population lives in a disease-free state (i.e. by avoiding HIV and HCV) provides a measure of the QALYs gained as a result of NSPs. QALYs gained therefore incorporate both the quantity of life gained, and the quality of life gained by avoiding HIV and HCV.

The outcomes of this analysis are presented in Table 5.5.1 (See Appendix E) and in Figures 5.4 to 5.7.

Figure 5.4 Life Years and QALYs gained by HIV survivors

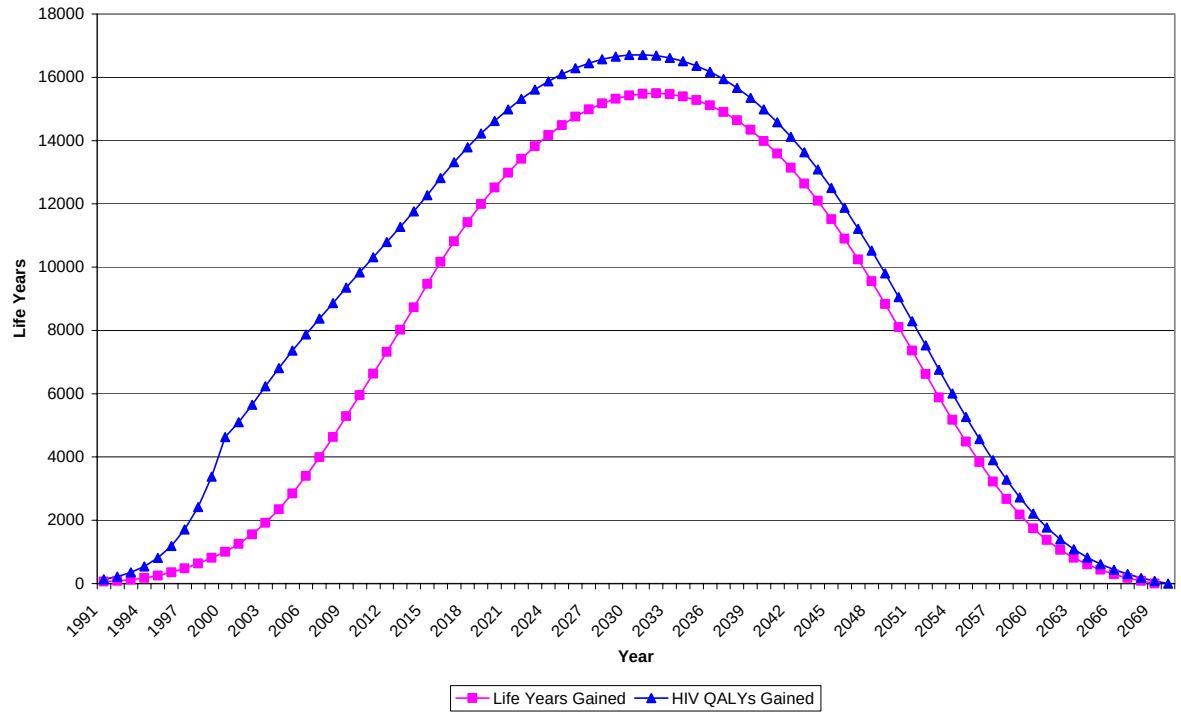
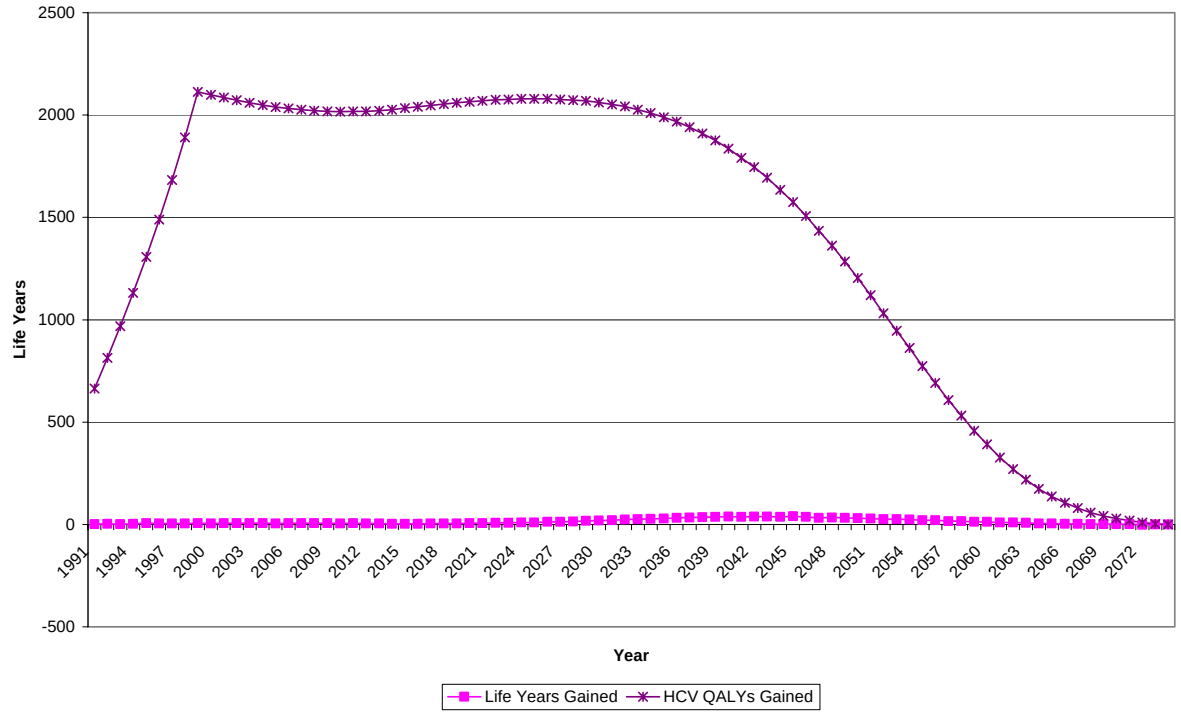


Figure 5.5 Life Years and QALYs gained by HCV survivors



In figures 5.4 and 5.5 the curves "HIV/HCV QALYs Gained" represent the quality adjusted life years for persons who would have had HIV/HCV, but for the effect of NSPs. The gap between these curves and the curves "Life Years Gained" represents the quality effect of HIV and HCV on their lives. The 25,000 persons avoiding HIV are expected to gain an additional 715,000 quality adjusted life years than if they had contracted the disease. In comparison, the 21,000 persons avoiding HCV are expected to gain about 120,000 quality adjusted life years over their lifetime. The difference between the two groups is largely attributable to the greater effect of HIV on the "quantity" of life compared to HCV, rather than the "quality" effect.

In the case of HIV, the number of life years gained each year increases up to the year 2033, and thereafter continues at a progressively slower rate. The curve for QALYs gained generally follows a similar pattern, reflecting the dominant effect of the "quantity" component.

In contrast, the number of life years gained for persons avoiding HCV is relatively small. However, when considering the effect of HCV on the quality of life, considerable gains are evident. These gains are relatively constant up to the year 2035, then decline each year to death.

Figures 5.6 and 5.7 illustrate the cumulative number of life years and QALYs gained by avoiding HIV and HCV. The shape of the curves "Life Years Gained" illustrates the progressive effect of the different mortality rates and is considerably steeper for HIV than for HCV. The increasing gap between "Life Years Gained" and "QALYs Gained", and the timing of its emergence, illustrates the differences in quality of life effect between the two diseases.

Figure 5.6 Cumulative Life Years and QALYs gained by HIV survivors

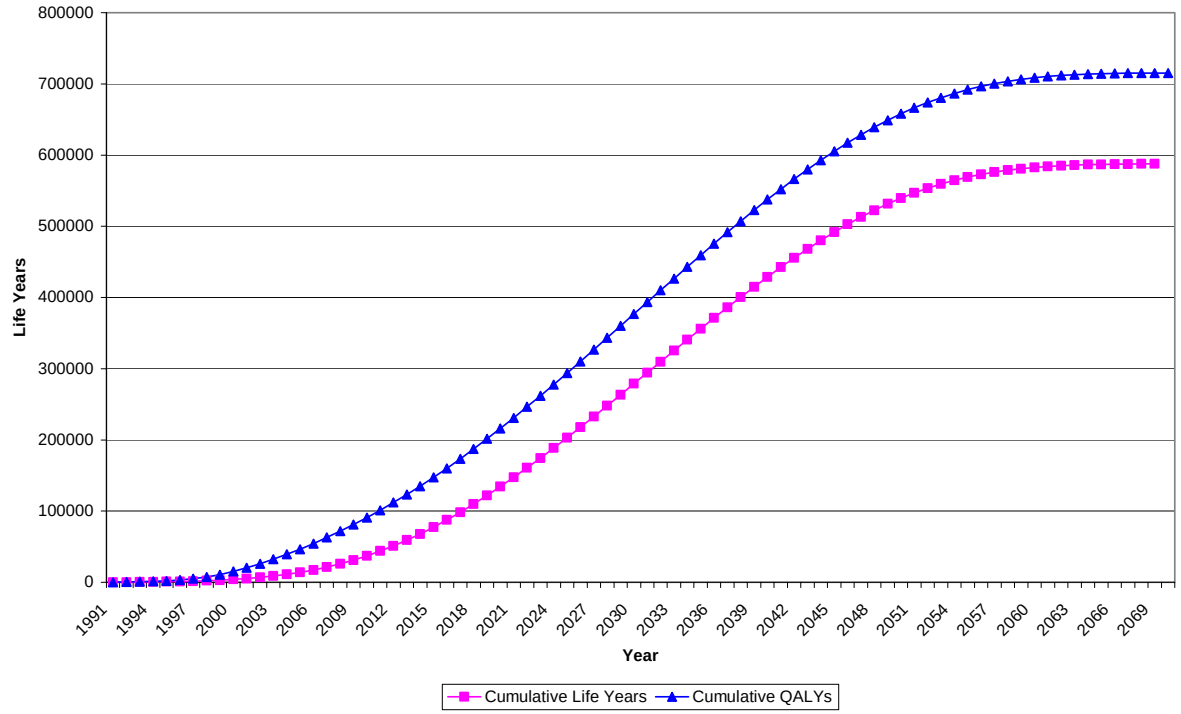
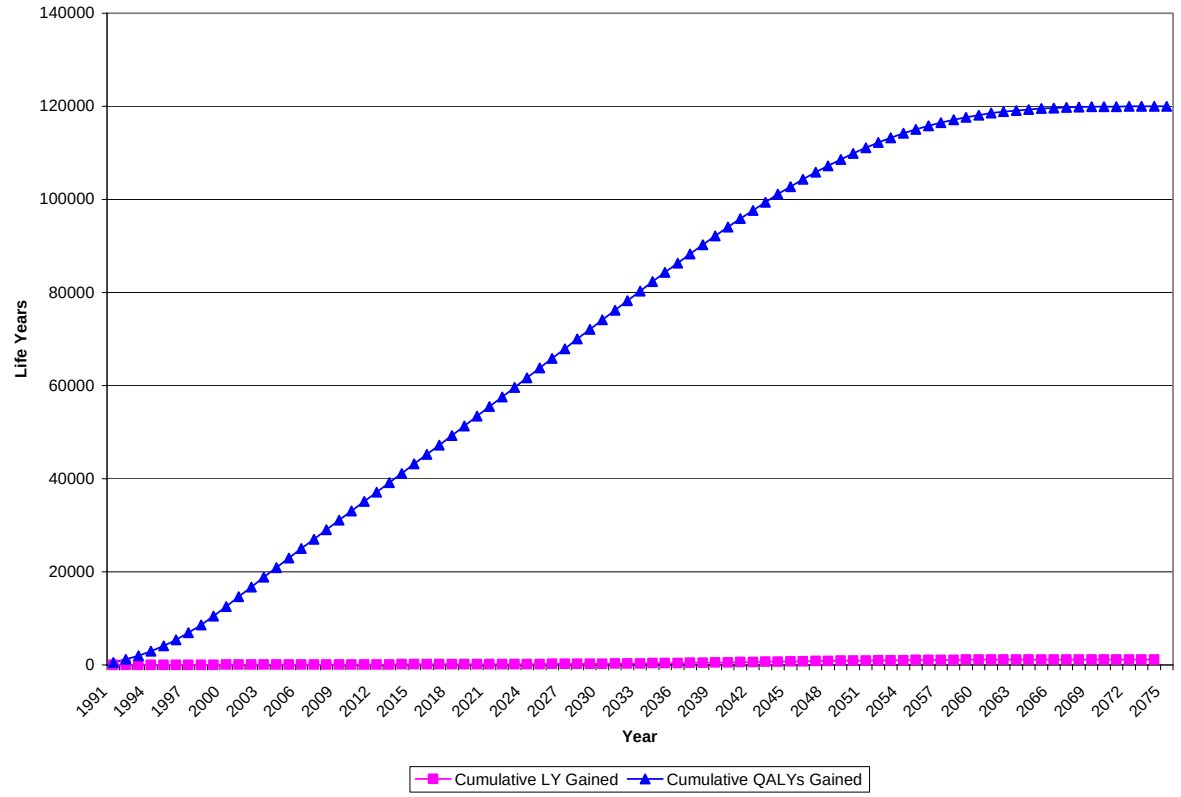


Figure 5.7 Cumulative Life Years and QALYs gained by HCV survivors



As previously noted, it is not uncommon to discount QALYs gained in the future in the same way as we have discounted future financial benefits. This approach is based on the principle that an improvement in the quality of

life is likely to be valued more if it occurs earlier than if it occurs later in life, just as a dollar gained earlier is likely to be valued more than a dollar gained later.

Applying the same discount rates used in the financial analysis (viz 5%, 3% and 0%) to QALYs gained results in the figures shown in Table 5.6.1

Table 5.6.1 Net Present Value of QALYs gained for HIV and HCV

Discount Rate	Net Present Value, 1991 (QALYs)		
	HIV	HCV	HIV & HCV
5%	138,072	32,207	170,279
3%	248,364	50,041	298,406
0%	715,245	119,992	835,237

A total of approximately 715,000 QALYs were gained by the avoidance of HIV, the present value of which, at a discount rate of 5%, is 138,000 QALYs (248,000 at a 3% discount rate). The equivalent gains for HCV are 120,000 QALYs over their lifetime, the present value of which (discounted at 5%) is 32,000 QALYs (50,000 at 3%). Discounting has the effect of reducing the present value of gains made in later years relative to those made in earlier years. Consequently, the ratio of the present value of QALYs gained to total QALYs gained for HIV (i.e. 138,072/715,245) is lower than that for HCV (i.e. 32,207/119,992), reflecting the fact that HCV makes a higher proportion of its QALY gains in the earlier years compared to HIV.

5.7 SENSITIVITY ANALYSIS

The QALY adjustment factors used in the analysis of effect of NSPs on the quality of life of injecting drug users have been based on estimates from the literature, as described in Section 5.3.1.

In order to test the effect of different QALY factors on the outcomes demonstrated to date, we have conducted sensitivity analysis by increasing the QALY adjustment factor by 5% across all stages of both HIV and HCV. Such an increase could come about with improved methods of treating each disease, which, while perhaps not altering the rate of disease progression or mortality, improve the quality of life in each stage. The effect of this approach is essentially to reduce the QALYs saved by NSPs, as those who might otherwise be infected by HIV or HCV would enjoy a higher quality of life than under our original assumptions.

The alternative QALY values are shown in Table 5.7.1, and the effects of the application of these values shown in Table 5.7.2.

Table 5.7.1 Alternative quality of life values by disease stage of HIV and HCV

HIV		HCV	
Disease Stage	QALY Value	Disease Stage	QALY Value
Early HIV Disease – Undiagnosed.	0.987	HCV antibody positive – non-chronic hepatitis C.	1.000
Early HIV Disease – Diagnosed.	0.9135	Mild chronic hepatitis – Undiagnosed.	0.987
Progressive HIV Disease – Undiagnosed.	0.945	Mild chronic hepatitis – Diagnosed.	0.861

HIV		HCV	
Disease Stage	**QALY Value**	**Disease Stage**	**QALY Value**
Progressive HIV disease – Diagnosed.	0.798	Moderate chronic hepatitis – Undiagnosed.	0.987
AIDS	0.651	Moderate chronic hepatitis – Diagnosed.	0.861
		Compensated cirrhosis – Undiagnosed.	0.882
		Compensated cirrhosis – Diagnosed.	0.777
		Liver failure.	0.336
		Hepatocellular Carcinoma (HCC).	0.105

Table 5.7.2 Net Present Value of QALYs gained for HIV and HCV, alternative QALY values

Discount Rate	Net Present Value, 1991 (QALYs)		
	HIV	**HCV**	**HIV & HCV**
5%	129,151	22,603	151,754
3%	235,943	35,528	271,471
0%	692,880	87,118	779,998

The effect of increasing the quality of life adjustment factor for HIV and HCV is to raise the total number of QALYs for people with these diseases, and hence to reduce the QALY gains made by avoiding them. It should be noted that the effect on HCV, however, is greater than that for HIV. This reflects the fact that the major component of the QALY gains made in HIV is derived from an improvement in the quantity of life saved, whereas HCV QALY gains are made up almost entirely of quality of life effects.

In both instances, the gains made in terms of quality of life effects of NSPs in HIV and HCV remain considerable, and reinforce the importance of this aspect of their effect.

5.8 DISCUSSION

The analysis of the effects of HIV and HCV on both the quantity of life and the quality of life of persons with these diseases adds a further dimension to the assessment of the effect of NSPs among injecting drug users. As demonstrated in Section 4, the investment in NSPs to date has been shown to be financially beneficial, and satisfies current government investment criteria on financial grounds alone. Any benefits to consumers in terms of the number of lives saved, the number of life years gained, and the improved quality of life are therefore additional to the direct financial benefits to governments previously identified.

Our analysis demonstrates that NSPs have contributed significantly to:

- ☐ The number of cases of HIV and HCV avoided;
- ☐ A reduction in the number of deaths from HIV, and to a lesser extent from HCV;
- ☐ An increase in the number of life years among injecting drug users, particularly from the avoidance of HIV; and
- ☐ An improvement in the quality of life among injecting drug users who would otherwise have contracted HIV or HCV.

Each of these outcomes should be considered over and above the direct financial benefits achieved from the investment in NSPs. It is clear that if we were to place a monetary value against any of these outcomes, the financial gains already demonstrated would be significantly increased.