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THE BOSTON CONSULTING GROUP

The Economic Impact of Hepatitis C in Australia

Commissioned by

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AT A GLANCE

Foreword

Hepatitis Australia's mission is to ensure the needs of Australians affected by, or at risk of viral hepatitis are met. We do this by providing national leadership and advocacy on viral hepatitis and forming partnerships with organisations that share our goals.

The hepatitis C virus attacks the liver, and can lead to long-term, potentially life-threatening liver disease. The very low level of hepatitis C treatment uptake in Australia contributes to a growing burden of disease and rising health care costs.

This Report comes at a critical time. The outlook is bright for many people living with hepatitis C. New hepatitis C medications with significantly improved cure rates are becoming a reality after many years of minimal change in the treatment landscape.

We commend this Report to you. It clearly explains how investment in new hepatitis C treatments will cure more people of a chronic and costly condition and provide substantial economic benefits for society in the longer term.

Helen Tyrrell

CEO, Hepatitis Australia

Disclaimer

While every care has been taken to ensure the accuracy of the information in this report, it is for general information only, is not intended as medical advice, and is not intended to be relied upon by individual readers. Appropriate independent advice should be taken before making any decisions based on this information. The authors, The Boston Consulting Group and Janssen Australia do not accept any liability for any loss suffered by readers as a result of any decisions made.

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1. EXECUTIVE SUMMARY

1.1. 300,000 Australians Have Been Infected With the Hepatitis C Virus

In Australia, a population more than four-fifths the size of Canberra has been exposed to the hepatitis C virus (HCV). This virus has a chronic, insidious, decades-long course, which has serious potential consequences for the health of those who are infected as a result of progressive fibrosis or scarring of the liver, culminating in cirrhosis, liver failure and an increased risk of liver cancer. While HCV is one of the few viruses that can be cured, no vaccine against it is available.

The analysis showed that using protease inhibitors would avoid ~2,438 cases of liver cancer and 2,237 premature deaths"

1.2. HCV Imposes a $252m Burden Each Year on the Government

With a current annual cost to the Commonwealth and State/Territory budgets of $252 m, and a projected five-year cost of $1.5 billion, HCV imposes a significant charge on taxpayers. For every dollar spent to treat chronic HCV infection, four more are spent to deal with the consequences of a failure to prevent, treat and cure it. Over the five-year, medium term, 44 percent of the cost of HCV, or $640 m, will be spent by DEEWR and FaHCSIA to assist those who are disabled by their illness, who are too ill to work or who have lost t heir jobs for HCV-related reasons.

For every dollar spent to treat HCV, four more are spent to combat the consequences of a failure to treat and cure it.

Although the most severe consequences of HCV are very costly (a liver transplant, for example, costs more than $120,000), life-threatening health issues only account for an estimated 17 percent of all medium-term costs, (including the cost of death). Almost 37 percent of five-year costs are generated by those with mild and moderate liver fibrosis, simply because these people are so numerous: 72 percent of all patients are at this stage of disease. Following the 300,000 people who have ever been infected over their remaining lifetimes, 600,605 discounted quality-adjusted life years (QALYs) will be lost, measured against a healthy comparison group, and, on the basis of today's treatment standard, poor health and social costs will impose a $13.4 billion charge on the Commonwealth and State/Territory governments.

1.3. Treatment Outcomes are About to Improve at Reasonable Cost With Protease Inhibitor Medications

A chronically infected person's prospect of cure depends on the genotype, or strain, of the virus with which they are infected. While no treatment is completely effective against HCV, the cure rate for those with genotypes 2 and 3, who constitute about 45 percent of those infected, is about 80 percent. For the 55 percent subset of people who are infected with genotype 1 of the virus, the picture is less rosy. Only 37 percent of a group of people with genotype 1 can be cured with the current treatment, or 'standard of care'.[1] Recently, however, Australia has approved registration of two protease inhibitors, which are innovative antiviral medications, for this group. Taken in addition to the standard medication regimen, the new antivirals would increase the percentage of people cured from 37 percent to 67 percent.[2] Looking at just the group who are currently infected, and including future tax revenue from those who will gradually be cured and return to work, the cost to the government of protease inhibitors over the coming 60 years would be $186 m.

The introduction of protease inhibitor treatment would cost the Government $186m over the lifetime of the cohort of people exposed to infection as of 2012

Since most severe health states occur in the long term, we took the group of people who have currently been exposed to the virus and projected the course of their hepatitis forward over the course of their lifetimes, assuming that the percentage of those treated and treatment success rates remained constant. (We included protease inhibitors for those people who have genotype 1 and will be eligible for treatment.)[3] The analysis showed that using protease inhibitors would avoid approximately 9,474 cases of severe liver damage, or cirrhosis, and about 4,829 instances of liver failure, ~2,438 cases of liver cancer, and ~873 liver transplants. If introduced, the protease inhibitors would avoid 2,237 premature deaths that would occur if only the standard of care were available, and add 55,271 non-discounted quality-adjusted life years to those available under the standard of care. At $17,300 for each additional discounted QALY gained over standard treatment (a figure which does not take savings on government benefits into account), the new medications appear to be a very cost-effective investment in future health. A significant number of additional HCV treatments are expected over the coming decade, and these should improve cure rates further.

DAN: TREATMENT TRIGGERS A LIFESTYLE CHANGE

Now in his late 40s with grown children, Dan* is a sheet-metal worker who fell into despondency when he lost his job after an injury several years ago. Beginning to drink more frequently, he became increasingly depressed. In 2007, when things seemed bleak, he saw his GP. His doctor ordered a panel of blood tests, which showed that Dan was positive for HCV. Faced with the prospect of his liver continuing to decline, Dan opted for immediate treatment.

Dan doesn't discount the difficulty of treatment – "I was tired, I had a headache, and I felt as though I had the flu" - and treatment was especially onerous for him because the first attempt at curing his illness, using the standard medications, was unsuccessful. In a second attempt, he was treated with a protease inhibitor, and cleared the virus.

Dan credits his HCV diagnosis with turning his life around: when he realised he didn't have to put up with gradually worsening health, he dramatically changed his lifestyle, greatly reducing the amount of alcohol he consumed and committing to becoming fitter. Now, he feels much healthier, and his liver condition has improved.

To anyone with the virus who is considering treatment, Dan has this to say:

"There is a cure out there, and you'd be very stupid to knock it back."

*Dan is a pseudonym

PBAC submissions are usually performed from a healthcare provider perspective and therefore only direct healthcare costs were included in the cost per QALY analysis. The incremental cost-effectiveness ratio (ICER, or discounted cost per QALY) of $17,300 presented here differs from those reported in the PBAC submissions for telaprevir[4] and boceprevir[5], which both report ICERs in the range of $15,000-$45,000 per QALY. The difference is reasonable, as the cost per QALY shown here was calculated on the basis of publicly-available data, and without reference to the models and assumptions used by the manufacturers of the two medications, or to the unit costs and duration of treatment in treatment-naive and treatment-experienced settings.

The new medications for Hepatitis C cost $17,300 per incremental QALY gained

Since the aim of this analysis was also to estimate the impact of HCV on the Australian economy, a broader societal perspective has also been used. As a result, this analysis incorporates the whole-of-government costs associated with disability support and unemployment benefit resulting from chronic HCV.

1.4. Outlook

Hepatitis C is a costly illness that places significant demands on the budgets of Australia's Commonwealth and State/Territory governments. In the Third National Hepatitis C Strategy 2010-2013, the Commonwealth's overarching plan for managing HCV, the government set itself these goals:

- Reducing the morbidity and mortality caused by hepatitis C
- Reducing the burden of disease attributed to chronic hepatitis C
- Increasing access to clinical care for people with chronic hepatitis C.

Fortunately, additional tools with which to achieve these goals and treat chronic HCV infection are expected to be introduced in Australia. With them, Australia can restore health, reduce premature death, and improve quality of life at reasonable cost to many of those whose future is now uncertain.

2. PURPOSE OF THE REPORT

The aim of this report is to estimate the cost impact of hepatitis C on the budget of the Commonwealth and State/Territory governments in Australia, and investigate how these would be affected by the introduction of new treatment regimes, and alternative treatment models. A societal perspective has been used, so that the report incorporates the whole-of-government costs associated with disability support and unemployment benefit resulting from chronic HCV.

The report surveys the current infection and treatment landscape and reviews the potential impact of new medications. The estimates provided in this report are based on analyses conducted by The Boston Consulting Group that draw on a range of sources. Population data is taken from Australian Bureau of Statistics data on the size, geographic distribution and ethnic composition of the population of Australia. Patient and outcomes information is based on data collected in the Kirby Institute's Annual Surveillance Report (2011), on findings from Phase III registration trials for telaprevir and boceprevir, on publicly available MBS and PBS cost data, and on a literature review of relevant medical and policy papers using PubMed, open-ended search and a targeted, site-specific review of patient, clinical and policy bodies active in the field in Australia and abroad. This research formed the basis of the economic model that we built to analyse the costs and the health outcomes of the current treatment standard and practice, and selected modifications to it.

In the course of our research, we also spoke to ten nurses who worked with hepatitis C patients and to more than 25 medical specialists (hepatologists, gastroenterologists and infectious diseases physicians) involved in treating HCV. We also surveyed 251 GPs to understand their practice as it related to HCV, and interviewed patients to capture their experience of the illness.

3. THE MEDICAL PICTURE

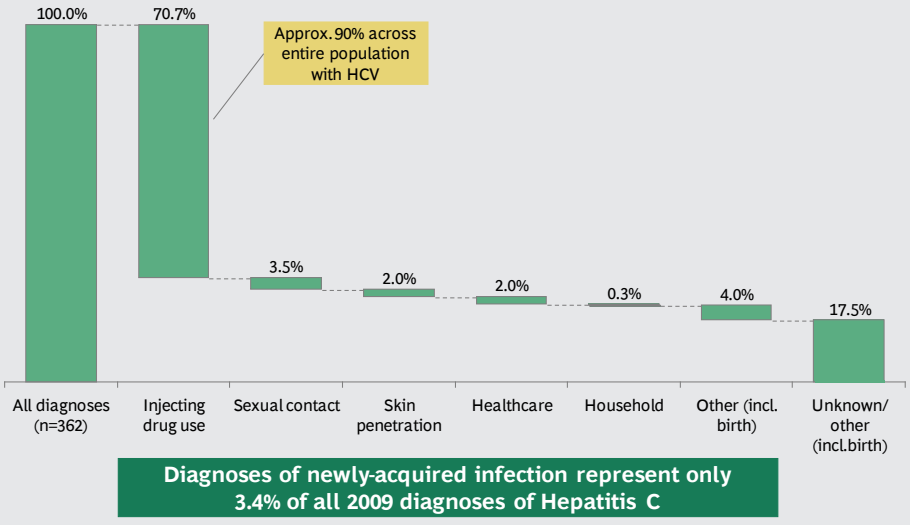
3.1. Introduction to Hepatitis C

Hepatitis C is a small, rapidly-mutating RNA virus. It is one of five viruses that primarily cause inflammation of the liver, or hepatitis, and was first identified in 1988. The hepatitis C virus (HCV) poses a serious threat to public health: since 2006, it has overtaken HIV as the leading viral killer in the US[6] and deaths from hepatitis C have also overtaken HIV-related deaths in Australia[7].

HCV is transmitted by blood-to-blood contact – primarily through sharing contaminated injecting equipment, but also, overseas, by receiving a transfusion of infected blood. (In Australia, all donated blood is routinely screened for HCV, and no one has been infected through transfusion since the latest generation of screening was introduced in 2000.) The virus is highly infectious and can survive in blood outside the body for hours to days – a longer period than some other viruses, such as HIV. After infection, about 25 percent of people clear the virus naturally;[8] the rest remain chronically infected for life unless the virus is eliminated with medication.

In 2009, 11,474 people were diagnosed with hepatitis C in Australia[9], just 3.4 percent of who, or 385, had acquired the infection within the last two years[10]. Approximately 90 percent of them are thought to have acquired the virus through intravenous drug use, generally by sharing needles. Fewer than 3 percent acquired it through sexual contact, but the infections that occurred by that route happened particularly among men who have sex with men (MSM), particularly those who were concurrently infected with HIV. (The degree to which HCV can be transmitted through sexual contact is still being studied, and HCV is not classified as a sexually transmissible infection). Transmission is also possible by other routes.[11]

EXHIBIT 1 | Diagnoses of Newly-Acquired Hepatitis C (2009) by Route of Exposure



Source: The Kirby Institute (2011) HIV, viral hepatitis and on sexually transmissible infections in Australia, 2011, table 2.1.13

HCV has six genotypes, or strains, each with many subtypes. In Australia, the most common is genotype 1, which accounts for 55 percent of all cases. Under the current treatment regimen, it is also, out of the genotypes common in Australia, the one with the worst prospects of cure, with just 37 percent of people with this genotype eliminating the virus under the current standard of treatment. [12]

The current approach to treatment is lengthy – lasting six to 12 months-and can be very arduous for patients as side effects are common and sometimes severe. It also has varying degrees of effectiveness against different strains of the virus. No vaccine is currently effective against HCV, although early-stage work in Canada has shown promising results,[13] and research elsewhere is underway. [14]

3.1.1. Effects of the Virus on People Living with Chronic HCV

The course of the illness is prolonged and people chronically infected with HCV are often unaware that they have it. While the symptoms experienced vary from person to person, exhaustion, irritability, depression and abdominal pain are the most frequently mentioned effects of chronic infection.

EXHIBIT 2 | Five Most Frequently Mentioned Symptoms With Potential Relevance to HCV

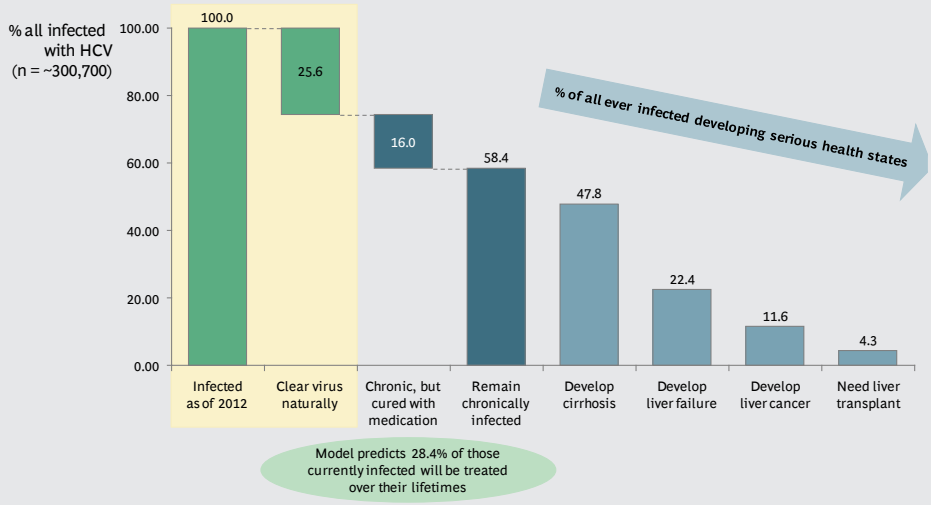
Source: Queensland Health Communicable Diseases Unite, (2003). Quality of life among people living with the chronic Hepatitis C infection (n=188)

The prognosis for HCV varies widely, ranging from the absence of any symptoms through to rare, but more serious cases that can result in death.

Hepatitis C reproduces in the liver. Chronic infection is often asymptomatic, but hepatitis occurs when the liver becomes inflamed as a result of the virus replicating. Over time, chronic infection can lead to scarring of the liver (fibrosis) and ultimately to cirrhosis, which generally becomes apparent years to decades after the initial

infection. Cirrhosis occurs when healthy liver tissue and structure is replaced by widespread scarring, leading to a loss of liver function. Those with cirrhosis may go on to develop liver cancer or liver failure, with manifestations such as bleeding oesophagal varices, abdominal fluid accumulation (ascites), and a reduced level of consciousness or even coma (encephalopathy), as well as primary liver cancer (hepatocellular carcinoma, or HCC). If liver failure develops, a transplant is the only option for survival. Of the 192 liver transplants performed in Australia in 2010, 25 percent (48 transplants) were due to HCV-related complications,[15] and, of those, 13, or almost one in three, were due to HCC. Liver cancer is often fatal: it does not respond well to chemotherapy or radiotherapy, and the five-year survival rate after surgical removal of the tumour (the most promising treatment available), is only 35 percent.[16] If surgery is not possible because the cancer has spread within the liver or the person's liver function has deteriorated, HCC is incurable, and has usually caused death within three to six months, although the kinase inhibitor sorafenib, now funded in Australia in restricted circumstances, is providing limited improvements in outcomes.

Exhibit 3 | Almost Half of All Those Infected With HCV Develop Serious Liver Damage



Note: The baseline patient population is structured on the basis of the telaprevir studies
Source: The Kirby Institute (2010) "Epidemiological and economic impact of potential increased hepatitis C treatment uptake in Australia"

Note to Exhibit 3: Because we wanted to assess the whole-of-life impact of HCV, our model follows the population who have been exposed to HCV as of 2012 for the remainder of their lives, although for a maximum of 60 years, with eligibility for treatment ceasing at 85. [17] *Because other studies generally model a maximum of 40 years, the model we have used will show a higher incidence of poor health states than those studies.*

Although many people who are chronically infected with hepatitis C show no symptoms of illness, the absence of symptoms is not a reason not to seek assessment for treatment. People who are asymptomatic commonly accumulate silent liver damage that will result, decades later, in liver failure and HCC. This is an issue of concern and anxiety with regard to longer term health problems. Moreover, they could – without knowing it – infect others. This is likely among the small population of those with HCV who share needles while using intravenous drugs, and it is also possible if instruments are re-used without being sterilised in procedures which pierce or break the skin, such as tattooing.

LANA: A LONG-DELAYED DIAGNOSIS LEAVES A STIGMA

Lana* is a teacher of behaviourally-challenged children in NSW. She doesn't know which of the eight blood transfusions she needed while pregnant carried HCV. In 1986, the virus causing HCV hadn't been conclusively identified, and blood wasn't screened.

Over time, Lana became exhausted and her body ached. Doctors thought it might be chronic fatigue or the Epstein-Barr virus. It wasn't until 2002, when she asked her GP whether there was really nothing left to test for, that he checked for HCV.

Lana treatment was long and difficult, but she's adamant that the side effects she experienced pale beside the stigma she felt. Except for her husband and one brother, she felt that she couldn't even confide in her family at the time. Nor could she draw on the support of her friends.

Even now, after being cured, she's noticed that some of those she's since confided in treat her differently.

To anyone else undergoing treatment, Lana says: ***"Think positive, don't adopt the sick role, and, remember, there's an end in sight."***

To their friends and relatives, she has this to say: "When someone you know is always tired and not feeling too good, don't judge them as being lazy and not wanting to help. Like me, they may have Hep C without knowing it."

Since the first treatment, in 2004, failed to eliminate the virus, Lana was treated in 2009 with protease inhibitors. That treatment succeeded, and she now has a healthy liver.

*Lana is a pseudonym

3.1.2. The Global Burden of Hepatitis C

Calculating the total number of people infected with HCV worldwide is a complex exercise, as infection rates vary by country and the quality of the surveillance ranges from almost nil to sophisticated epidemiology. Common estimates range between 2.2 percent and 3 percent of the population being infected with hepatitis C globally.[18] Overall, the World Health Organisation estimates that between 130 and 170 million people are chronically infected with the virus.[19]

In some regions, such as eastern Africa and Mongolia, the prevalence is estimated at more than 10 percent, which is mainly due to unsafe injecting practices and contaminated blood products. In developing economies, hospital-based transmission, due to a lack of sterile medical practices, also contributes to the rate of infection.

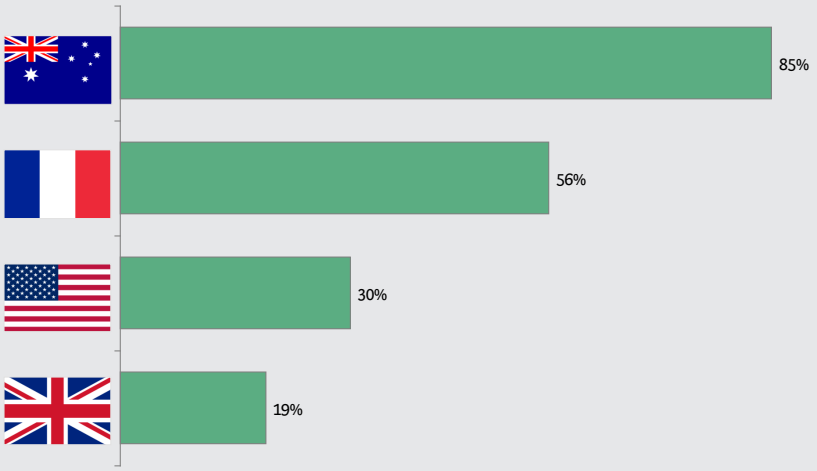
3.1.3. The Burden of Hepatitis C in Australia[20]

According to the National Centre in HIV Epidemiology and Clinical Research (NCHECR), now called the Kirby Institute, approximately 300,000 people in Australia have been infected with HCV at some point in the past. [21]

Of these 300,000 people, a quarter is estimated to clear the virus naturally – that is, they recover from the infection without medical intervention. Once these people have eliminated the virus, they are free from ongoing health concerns related to their exposure to HCV, and can no longer transmit HCV to others. They carry antibodies to the virus, which mark a past infection, but which do not give protection against a future infection. Everyone else who has been infected – 224,000 people, or approximately 1.4 percent of the total population – remains chronically infected.[22] This rate is similar to, or very slightly higher than, that of other OECD countries.

Australia's rate of diagnosis – 85 percent – is significantly higher than that of most other developed countries. For example, in the United States, it is thought that only 30 percent of those infected with HCV have been diagnosed, while in the UK the figure is estimated at approximately 20 percent.[23] Australia's comparatively high rate of diagnosis is likely to result from the extensive ancillary screening programs that check for the virus in settings such as substance abuse centres, prisons, sexual health clinics, and antenatal clinics.

EXHIBIT 4 | Australia's Rate of Diagnosis is High in International Comparison



Source: Australia: Annual Surveillance Report (2010), National Strategy for Hepatitis C (2010), France, UK: Eurasian Harm Reduction Network (2007): "HCV infection in Europe", USA: JP Morgan, report #17911463 (2011)

Projecting transmission rates of hepatitis C into the future is challenging. In particular, the fact that the illness can exist without symptoms for so long, so that diagnosis may be delayed, makes it difficult to assess the effect of needle exchange programs and blood screening tests introduced more than two decades ago, even though these initiatives are widely thought to be effective in reducing infections. We used a mathematical model to project future diagnosis rates on the basis of the Kirby Institute's work. This involved taking the compound annual growth rate of new diagnoses in 2005-2009 (which is 0.2 percent) and assuming it remained constant. Using the model, we projected a figure of 301,000 people in Australia infected with HCV this year, and 318,000 in 2017. [24]

Three quarters of all diagnoses are made in those aged thirty or older. [25] The long, often asymptomatic course of the virus means many of the people diagnosed with HCV in recent years are likely to have acquired the disease in the 1980s or early 1990s.

3.1.4. The HCV Population

This year, the prevalence of HCV is estimated at 301,000. This population includes several distinct segments. To better understand how the disease affects specific groups, we looked more closely at gender, geographic location, imprisonment status and ethnicity. We also examined the extent to which different groups had access to, and took up, therapy for HCV.

In terms of gender, women accounted for 37 percent of those diagnosed with hepatitis C in 2010 (a total of 2,778 women) and men accounted for the remaining 4,722 people.[26] However, among incarcerated populations, women were more than one and a half times as likely to be infected as men – likely to reflect the fact that a higher proportion of women inmates than male inmates have been imprisoned for drug-related crimes.

In terms of geography, New South Wales has the highest absolute numbers, with 3,955 diagnoses made in 2009.[27] However, HCV is most concentrated in the Northern Territory, where 71.6 cases were diagnosed per 100,000 people in 2010, versus just 52 cases per 100,000 people for Australia as a whole.

EXHIBIT 5[28] | HCV Diagnoses Across States and Territories (2009)

State/Territory	Diagnoses 2009	Diagnoses 2009 / 100,000 population
NSW	3,955	55.5
QLD	2,696	60.7
VIC	2,513	45.5
WA	1,144	49,8
SA	553	34.9
TAS	282	60.8
NT	166	71.6
ACT	165	43.8

Source: The Kirby Institute (2011) "HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report"
Note: 2009 figures were used because 2010 numbers for NSW were unavailable at time of going to press

We were also able to break down treatment rates of HCV into urban and rural areas within jurisdictions, based on sales data of the medicines currently used to treat HCV (pegylated interferon and ribavirin). Our analysis showed that 60 percent of people being treated for HCV live in capital cities, 17 percent live in regional areas (centres outside capital cities that have populations over 90,000) and the remaining 23 percent live in rural areas (despite rural areas accounting for only 18 percent of the total population).[29]

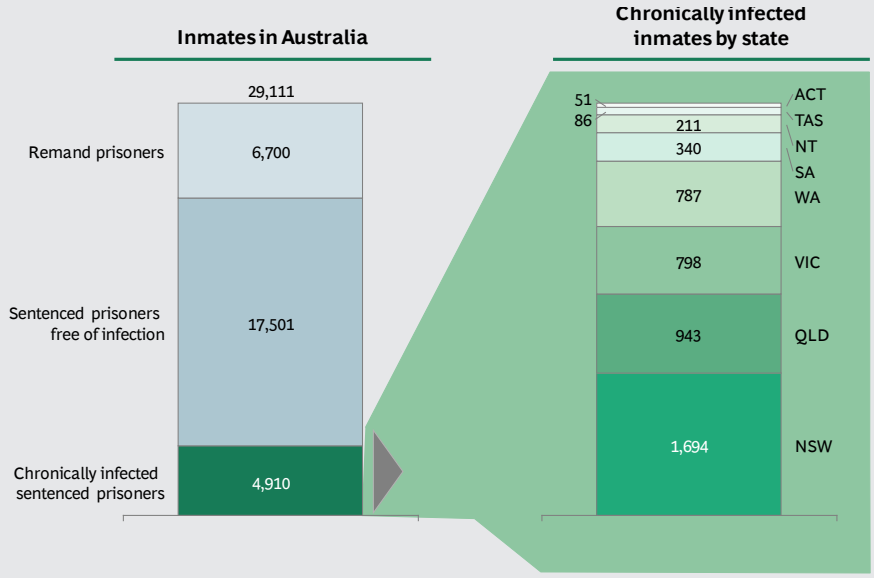
While the absolute number of people with HCV is higher in cities than in rural areas, treatment rates are much lower rurally. Only 13 percent of people diagnosed with HCV present for treatment in rural areas, compared with 33-34 percent in regional and urban centres.[30] A prime cause of rural under-treatment is likely to be due to a lack of skilled treatment capacity, such as hepatologists, hepatology nurses, gastroenterologists and infectious diseases physicians, outside Australia's cities.

In the next sections, we discuss the two priority groups from the National Strategy on Hepatitis C 2010-2013 -- prison inmates and indigenous Australians who face particular difficulties accessing treatment.

3.1.4.1. Prison Inmates [31]

Injecting drug use (IDU), imprisonment and HCV infection are closely interwoven. Accordingly, HCV infection is much more prevalent in Australia's prisons than in the general population. Among male inmates, 21 percent are infected with hepatitis C. Infection rates among female inmates are even higher, which is probably due to the fact that HCV is primarily passed on by equipment-sharing between users of intravenous drugs, and to the fact that a much higher proportion of female inmates than male inmates are incarcerated for drug-related crime. At least 34 percent of female inmates (1,623 women) are infected, versus 21 percent of males.[32]

EXHIBIT 6 | Inmates Chronically Infected With HCV



Source: Australian Bureau of Statistics, 47150DO001_2011 Prisoners in Australia, 2011; The Kirby Institute and The National Drug Research Institute. (2011). National Prison Entrants' Blood borne Virus and Risk Behaviour Survey Report, 2004, 2007 and 2010 – Prevalence of HIV, hepatitis C, sexually transmitted infections, and risk behaviours among Australian prison entrants.

Prisons also feature high rates of other common medical and psychiatric disorders. Accordingly, many prisoners diagnosed with HCV also have a psychiatric diagnosis. This is an important factor in HCV treatment decisions, as psychiatric symptoms, particularly mood disorders, can be made worse by pegylated interferon, which is one of the medications that make up the current treatment standard.

Recent work by Professor Andrew Lloyd of the University of New South Wales provides a large-scale proof of concept for a prison-based HCV treatment program, showing that it is possible to treat HCV infection safely and effectively within a prison setting. In the prison setting, personal, psychological and social factors that make it harder to adhere to a medication regimen, such as active injecting drug use, untreated psychiatric disorders, and lack of stable housing, are better controlled, and it is therefore potentially easier and more cost-effective, to monitor patients closely and supportively.

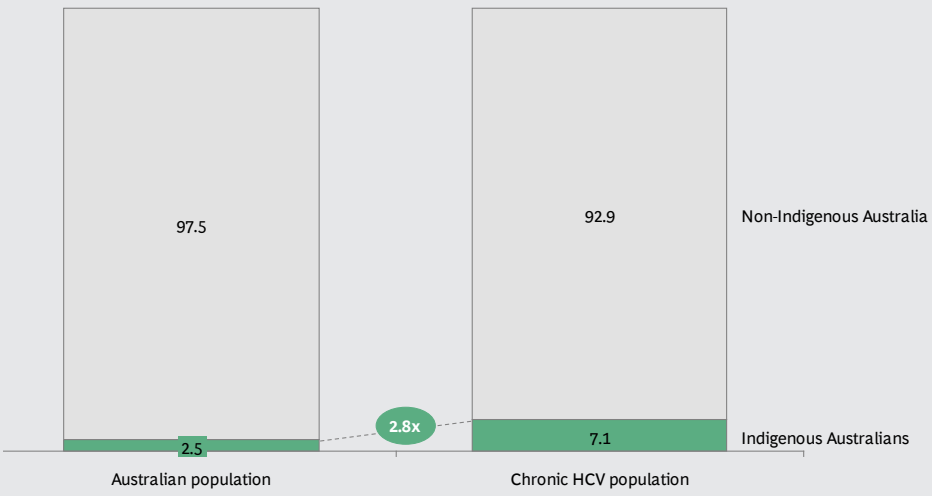
With prisons managed at the State/Territory level, HCV treatment of prison inmates falls to State/Territory authorities. (In some jurisdictions, like Western Australia, health care provision to inmates falls within the Corrective Services portfolio; in others, a separate health authority for prisoners has been established, such as NSW's Justice Health, while the prison in the ACT is managed privately. The decentralised nature of prison health in Australia means that the treatment of HCV among inmates has not advanced in sync, with Professor Lloyd's initiative in

NSW a best-practice outlier. If an initiative to treat inmates with HCV were coordinated Australia-wide, however, either nationally or between the states, it is likely that it would contribute significantly towards achieving the goal of the Third National Hepatitis C Strategy to reduce HCV infection in the population at large.

3.1.4.2. Indigenous Australians [33]

About 22,000 indigenous Australians have been infected with hepatitis C and of these 16,000 (3 percent of Australia's total indigenous population) [34], live with chronic infection. This percentage is almost three times that of Australia's non-indigenous populations. The Third National Hepatitis C Strategy includes the priority areas of reducing harm among Indigenous Australians, and increasing their access to peer education, health care and welfare services. Increasing treatment uptake and completion among these groups is also a priority for the *Third National Aboriginal and Torres Strait Islander Blood-Borne Viruses and Sexually Transmitted Infections Strategy 2010-2013.*

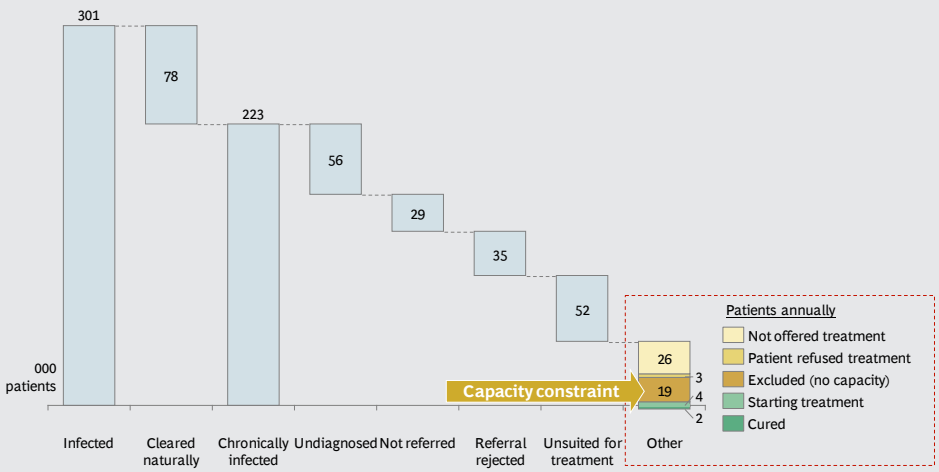
EXHIBIT 7 | Indigenous Australians Infected Almost Three Times as Often as One Would Expect Based on Their Proportion of Population



Source: Australian Bureau of Statistics (population data as at 30 June 2010), Third National Hepatitis C Strategy 2010 - 2013. (2010)

3.2. Treating HCV

EXHIBIT 8 | The 2012 HCV Patient Pipeline (in Thousands of Patients)



Source: Australian Bureau of Statistics; National Hepatitis C Strategy, 2010-2013; survey of 251 GPs, September 2011; interviews with medical specialists and nurses, September 2011; Annual Surveillance Reports; HCV Projections Working Group, October 2006.

Patients face a long pathway from infection with HCV through to diagnosis, treatment and, for some, a cure. Currently, only a small fraction of people who are chronically infected – about 2 percent each year – will progress along the entire route to successful treatment and eradication of the virus. In some cases, this is because of poor access to treatment facilities, or because people are not offered treatment by health care providers. In other cases it is due to patients being unwilling or unable to undertake a year-long, uncomfortable treatment regimen, with a less than even prospect of cure. In our view, the treatment bottleneck is the easiest bottleneck to address, because the lever most open to adjustment by the Commonwealth and State/Territory authorities, is the lack of capacity of skilled health care staff to administer treatment. It is also the most critical, since, unless treatment capacity is widened, no amount of increase in capacity further back along the pipeline towards treatment will flow through to greater numbers of patients receiving antiviral therapy. Finally, it is targeted at a stage of treatment at which patients have been found medically suitable for treatment, and where they are willing to undergo treatment. What is needed is a way to enable the current number of clinicians to cure more people, and then to add clinical capacity so that even more cures are available. Secondarily, incorporating treatments that reduce the overall time to treat would increase the number of patients who could be treated each year. As capacity increases, education targeted at GPs and clinicians in other related areas, such as drug and alcohol clinics or sexual health centres, is likely to ensure that treatment reaches those for whom it is most appropriate.

3.2.1. Current Treatment is Hospital-Based and Led by Specialists[35]

Approximately 90 percent of HCV treatment is currently administered in hospitals (overwhelmingly in public hospitals), usually in outpatient clinics. Care is provided by medical specialists, predominantly hepatologists, gastroenterologists, and infectious diseases physicians. The remaining 10 percent of treatment is divided equally between specialist private practices and community centres. Relevant specialists are expensive and relatively rare (there are only about 400 gastroenterologists in Australia, for example, many of whom do not treat HCV, as their practices are focused on other prevalent disorders, such as peptic disease). Antiviral drug prescriptions currently need to be issued by specialists (unless a GP has taken a qualifying course) a model that also limits the supply of treatment.

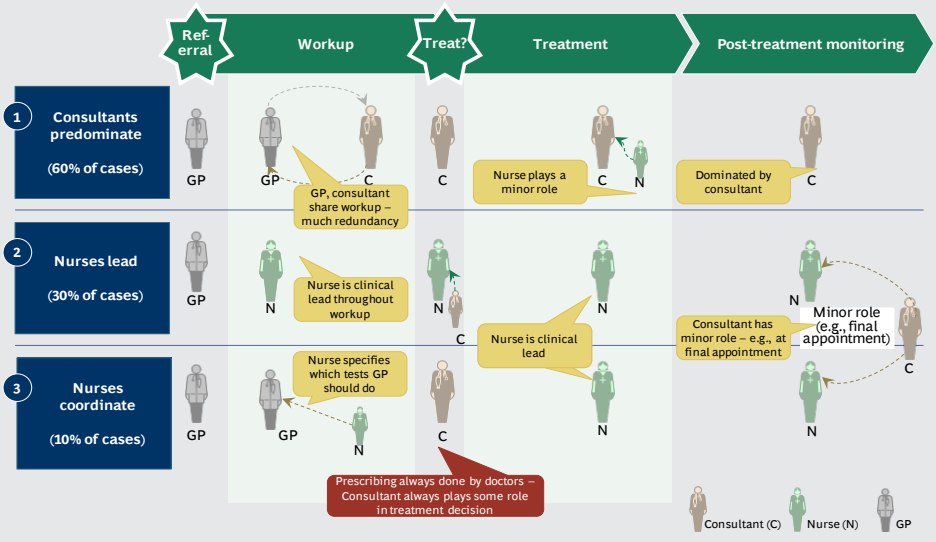
The hepatology nurses and hepatologists, gastroenterologists and infectious diseases physicians with whom we spoke were highly critical of continuing the concentration of treatment in the public hospital setting. In their view, the rigid scheduling and official setting were at odds with the needs of many HCV-infected patients, who can struggle with fixed appointments, and who often feel alienated by an institutional setting. If this is the case, it is likely that the current hospital-based approach reduces demand for treatment and also makes it more difficult for some patients to complete their treatment. Some hospitals do offer drop-in or outreach clinics, but the practice is not widespread.

"By treating HCV patients in a large institutional setting, we're asking them to come into the environment which is most alienating and intimidating to them"

Hospital gastroenterologist, Sydney

We observed three general hospital-based treatment models, illustrated in Exhibit 9. The most common relies on the intensive use of specialists.

EXHIBIT 9 | Three Models Of HCV Treatment Observed, With Consultant-Led Model Dominating



Source: Interviews with physicians and nurses, September 2011

In Australia, specialist hepatologists, gastroenterologists and infectious diseases physicians are the main prescribers of the two medications that comprise the current treatment for HCV (pegylated interferon and ribavirin). Only relatively few GPs have been approved to prescribe these medications (in shared care arrangements with specialist physicians). To gain approval, GPs must train and qualify to be registered as prescribers of highly specialised drugs under section 100 of the Schedule of Pharmaceutical Benefits. Currently, only about 70 GPs have this registration, of whom only a small number actually initiate treatment. Many do not even prescribe maintenance treatment, though qualified to do so. [36]

3.2.2. Australia Has Very Low Rates of Treatment

The most significant problem in treating HCV is the low proportion of infected people who are actively assessed, offered treatment, and can access therapy without lengthy waiting periods. As we have seen, many people self-select out of treatment because they are deterred by the likely side effects, which are not only unpleasant, but can make it difficult to keep a regular job.

In 2010, about 3,760 people received treatment (that is, antiviral medication) for HCV,[37] which amounts to only 2 percent of people with chronic hepatitis C. This is substantially lower than for other chronic viral illnesses. For example, if we examine another chronic viral illness, HIV, we see that 87 percent of those infected received treatment in 2010.[38] A comparison between the two diseases is difficult, since those with HIV are treated continuously, whereas those with HCV usually receive only one course of treatment, for a finite period. Moreover treatment is not effective for everyone, with many unable to clear the virus despite treatment, and widespread adverse effects. Nonetheless, the difference in treatment rates is dramatic.

3.2.2.1. Barriers to Receiving Care From a Specialist

Even patients who present to a GP for diagnosis will not necessarily end up receiving treatment. In this setting many patients fail to move to the next stage of the pathway, which involves specialist appointments. Some specialists partly attribute this to under-diagnosis by GPs, who may not screen for HCV when faced with symptoms familiar to a clinician working in hepatology or infectious diseases. However, since Australia's rate of diagnosis is relatively high by OECD standards, under-diagnosis is only likely to play a minor role.

Another reason that fewer patients attend specialist appointments may be that their GPs do not refer them, either because:

- the patient appears to be well, or
- the GP (wrongly) concludes that treatment is unnecessary, or that the patient is ineligible for treatment on the basis of stringent eligibility criteria which no longer apply, or
- the GP (wrongly) views HCV as chronic and largely untreatable, or
- the GP prioritises other pressing medical needs over the referral, or believes that the patient's life is too unstructured to make treatment realistic, or
- the person with HCV does not have a GP whom he or she sees regularly, or, in a

small minority of cases, the person is a migrant who is not eligible for Medicare.

GPs who believe that HCV is largely untreatable may be influenced by the low rates of effectiveness of antiviral therapies in the past, not being aware of the new treatment modalities that have emerged. Standard treatment in the 1990s required three injections of interferon each week, and cleared the virus in 30 percent of people with genotypes 2 and 3, but only 9 percent of those with genotype 1. Cure rates were raised to the current level (37 percent for genotype 1 and approximately 80 percent for other genotypes) in the late 1990s, when a combination of slow-release (pegylated) interferon and the antiviral ribavirin was introduced.

Not all of those specialists who are capable of providing care to patients with HCV do so: as discussed above,[39] many of the 400 gastroenterologists in Australia work in the private sector and do not provide practice-based treatment for HCV, referring patients instead to a hospital outpatients' department. Some rural areas are completely without gastroenterologist coverage.

Finally, part of the reason that not all patients see specialists is likely to lie with patients themselves. Though many treatment clinics have a reminder system, the 251 GPs we surveyed estimated that one in six of patients they referred did not take up the referral. GPs and specialists were generally in agreement that transparency over what happened once a referral had been written by a GP was poor.

3.2.2.2. Barriers to Receiving Treatment

The most common bottleneck to receiving treatment for those whose liver condition would otherwise warrant it occurs when specialists do not recommend treatment because the patient has a significant contraindication. This may be either a medical condition, such as a psychiatric disorder, or a social behaviour, such as alcohol and drug use. As illustrated earlier, only about half of those who are referred to treatment are actually suited to undergo it. [40]

For example, in patients with a history of psychosis and mood disorders, the potential for depression and other mood symptoms caused by pegylated interferon make some clinicians reluctant, albeit to varying degrees, to initiate treatment. Some doctors will not treat these patients even if their difficulties are resolved and medication that guards against their psychiatric symptoms reappearing while they are being treated for HCV is available. One clinician interviewed, for example, would not accept a patient with any psychiatric comorbidity, including an isolated past incident of depression or controlled bipolar disorder, because of pegylated interferon's potential to worsen mood, while others saw no barrier in treating people with either condition. Treatment is also not initiated in pregnant women or women planning to conceive, in order to prevent harm to the foetus.

Some doctors are unwilling to treat patients who are still actively injecting. Since the majority of the HCV population acquire the virus through sharing needles for intravenous drug use, this is problematic. No doctors we spoke to would treat those who injected on a daily basis, while some were prepared to treat those who injected weekly. In part, their reluctance reflects a pragmatic assessment that an individual

patient who is still injecting is more likely to be re-infected at a later date. However, the primary reason not to treat is based on the belief that a person who is injecting drugs on a daily or almost-daily basis will lack the resources necessary to manage the demands of treatment. Equally, a person without a stable support system or accommodation is unlikely to be able to sustain the rigours of treatment and a fixed dosing schedule for what may be up to 48 weeks, under the current standard of treatment.

3.2.3. Current Approach to Treatment

For people infected with HCV who do not clear the virus naturally, antiviral medication is the only way to eliminate the virus and cure HCV. As noted above,[41] 55 percent of all those infected with HCV carry genotype 1 of the virus, which is the strain with the lowest prospects of cure.

3.2.3.1. An Onerous Regimen

In Australia, the current treatment is to use a slow-release form of (pegylated) interferon, injected on a weekly basis, in combination with the antiviral ribavirin, which is taken in tablet form twice a day. This treatment is designed to eliminate the virus but carries onerous side effects for patients. genotype 1 patients, who make up the majority of those infected, are treated for 48 weeks.

Pegylated interferon can cause insomnia, a lack of appetite and prominent flu-like symptoms. More seriously, it can also cause mood swings and induce suicidal thoughts, making it particularly problematic for patients with a history of psychiatric illness.

Ribavirin can also cause a variety of side effects especially anaemia (which causes fatigue), but also nausea. It can also cause a rash, which is generally not severe. In a closely monitored setting like a prison, side effects can be managed to ensure patients adhere to the dosing schedule. In less stable environments, the rigours of treatment may make patients less likely to adhere to the dosing schedule, jeopardising their chances of being cured.

Many patients with chronic HCV experience psychiatric and neurological symptoms. In some cases, these symptoms will be made more severe by the personal and social factors that accompany high levels of intravenous drug use. In a survey of 188 Queenslanders living with HCV that Queensland Health conducted early last decade, exhaustion and mood difficulties were common. [42] These symptoms are significant because they make it more difficult for patients to comply with a regular and burdensome treatment regimen. Previous or existing psychiatric symptoms, especially those which are mood-related, are also likely to be exacerbated by treatment. The onerous nature of treatment for HCV is a particular barrier for those with psychiatric and neurological symptoms, as it represents a burden beyond those they already carry.

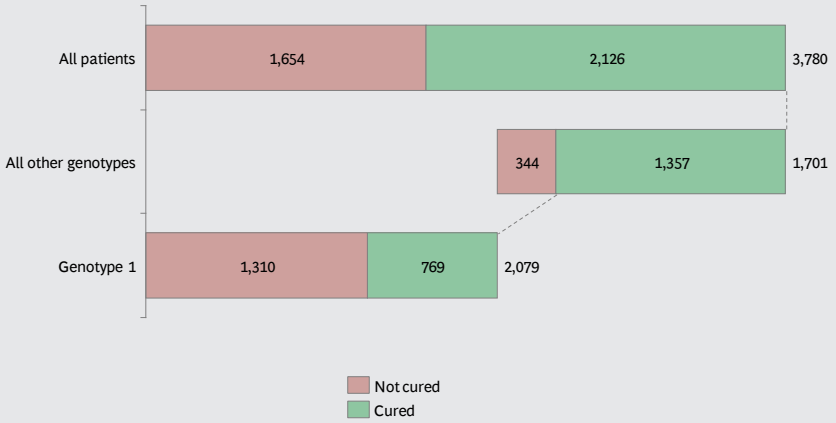
3.2.3.2. Treatment Efficacy

The effectiveness of the current approach to treatment depends on which genotype is being treated.

As noted earlier, patients with genotypes 2 and 3 who do not have cirrhosis or bridging fibrosis (about 40 percent) are treated for six to twelve months. They have an 82 percent chance of being cured. All other patients (60 percent) are currently treated for 48 weeks, and have a ~37 percent success rate.[43]

Applying these rates to the 2010 data suggests that, of the 3,760 patients treated[44], 2,126 people, or 56 percent of those infected, were cured.

EXHIBIT 10 | Cure Rates by Genotype (2012) Under Current Standard of Treatment



Source: Genotype 1: ADVANCE study (comparator arm), REALIZE study, assuming patients are treatment naive (ADVANCE cure rates) and 50% are treatment experienced (REALIZE cure rates). Other genotypes: The Kirby Institute (2011) HIV, viral hepatitis and sexually transmissible infections in Australia: Annual Surveillance Report 2011 (74%-84% cure rate for genotypes 2-3, depending on fibrosis status). We assumed an 84% cure rate for patients with mild or no fibrosis, a rate of 74% for patients with cirrhosis, and the average of the two figures for patients with moderate fibrosis. These rates were multiplied by the proportion of patients treated, for an overall genotype 2/3 cure rate of 80%.

Although this figure suggests that half of those who undertake treatment are cured, it masks a much lower rate of cure in patients infected with genotype 1, the most common strain in Australia. Of approximately 2,079 patients treated with this genotype, only ~769 (37%) will be cured. However, new pharmaceutical treatments are becoming available that can significantly improve the prospects of a cure for people with genotype 1 HCV.

3.2.4. Imminent Treatment Developments

3.2.4.1. Overview

Two new drugs have recently been introduced to treat the predominant HCV genotype. Boceprevir (marketed by the pharmaceutical company Merck Sharpe and Dohme as Victrelis™) and telaprevir (marketed by Janssen Australia as Incivo™) are first-in-class protease inhibitors that target the HCV protease enzyme, and thus prevent the genotype 1 virus from replicating.

Telaprevir has marketing or regulatory approval in the US, Canada, Japan, the UK, the EU, Switzerland and Australia, although it is not yet listed here on the Pharmaceutical Benefits Schedule (PBS) for subsidised provision to Australians with chronic HCV infection. Boceprevir is approved in all of these countries except Japan; it, too, is not yet listed on the PBS. Both telaprevir and boceprevir have been used in five separate Phase III clinical trials, including two in Australia. [45]

3.2.4.2. Improved Rates of Cure for Genotype 1 Patients

Both telaprevir and boceprevir will dramatically improve cure rates for patients with genotype 1, pushing them from ~37 percent to ~67 percent.

The new medications are taken in addition to the existing treatment (pegylated interferon and ribavirin). They will dramatically improve cure rates for patients with genotype 1, increasing them from ~37 percent to ~67 percent overall.[46] As Exhibits 11 and 12 show, however, response rates vary, depending on whether the patient has been treated before, and how he or she has responded. Those who respond to medication are divided into those who respond fully, those who respond only partially and those who do not respond at all.

Had the new agents been available for genotype 1 patients in Australia in 2010, and had the treatment rate been the same, the number of overall cures would have increased by 29 percent, from 2,128 to 2,750.

The new medications may also shorten the duration of treatment for many genotype 1 patients. Telaprevir can also shorten the overall length of treatment for genotype 1 patients who respond early to treatment (~58 percent of all patients) from 48 to 24 weeks. Trial data for boceprevir suggests that the treatment time reduces 48 to 28 weeks for approximately 44 percent of patients who are early responders. Patients whose illness has progressed to cirrhosis need 48 weeks' treatment, however, and their cure rates are lower, at approximately 62 percent. [47]

EXHIBIT 11 | Telaprevir[48]

	Percentage of patients eliminating the virus			
	No prior treatment	Previous releasers	Previous non-responders	Prior null responder
Telaprevir-based triple therapy	79%	84%	61%	31%
Taking Standard of Care	46%	22%	15%	5%

- **Data relating to Telaprevir is sourced from the ADVANCE (first column in above table) and REALIZE studies**
- **Previous relapsers** are people whose viral load was undetectable while on treatment with pegylated interferon and ribavirin, but whose viral load became detectable again within six months of the end of treatment (week 48 for Genotype 1).
- **Prior partial responders** are people whose viral load never became undetectable, but whose viral load sustained a >2 log drop by week 12 during prior treatment with pegylated interferon and ribavirin.
- **Prior null responders** are people whose viral load had a <2 log drop by week 12 during prior treatment with pegylated interferon and ribavirin.

Note: No study has compared telaprevir and boceprevir, and the above table should not be understood as a comparison. Moreover, an indirect comparison between the products does not show any statistically significant differences in terms of overall efficacy of results.

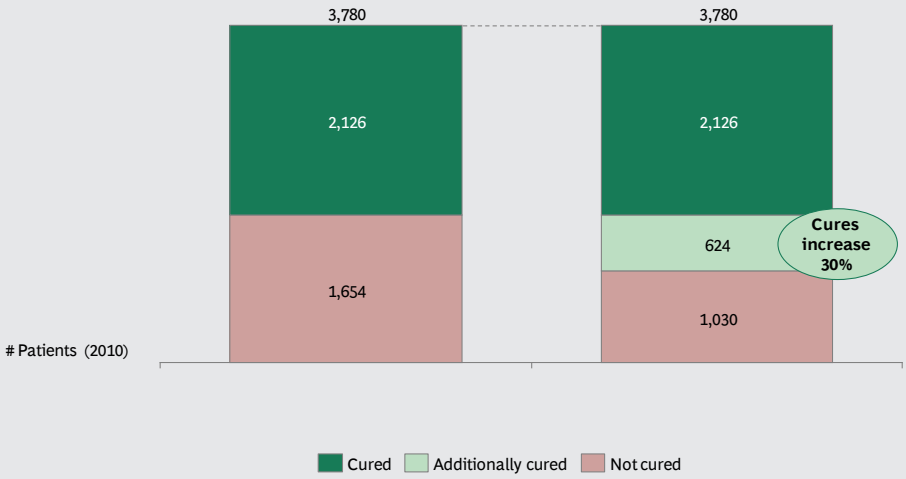
EXHIBIT 12 | Boceprevir[49]

	Percentage of patients eliminating the virus			
	No prior treatment	Previous releasers	Previous non-responders	Prior null responder
Boceprevir-based triple therapy	63%-66%[50]	69%[51] – 75%[52]	40%[53] – 52%[54]	n/a[55]
Taking Standard of Care	38%	32%	33%	n/a

- **Data relating to Boceprevir is sourced from the SPRINT-2 (first column in the above table) and RESPOND 2 studies**
- **Previous Relapser:** Subject who failed to achieve SVR after at least 12 weeks of previous treatment with peginterferon alfa and rabiviron, but had undetectable HCV-RNA at the end of treatment.
- **Previous non-responders:** Subject who failed to achieve SVR after at least 12 weeks of previous treatment with peginterferon alfa and rabiviron, but demonstrated a ≥ 2 log reduction in HCV-RNA by Week 12.

Note: No study has compared telaprevir and boceprevir, and the above table should not be understood as a comparison. Moreover, an indirect comparison between the products does not show any statistically significant differences in terms of overall efficacy of results.

EXHIBIT 13 | Addition of New Agents Has the Potential to Increase Overall Cure Rates by 30%



Source: ADVANCE, REALIZE studies; The Kirby Institute (2011) HIV, viral hepatitis and sexually transmissible infections in Australia: Annual Surveillance Report 2011 (applying analysis outlined in Exhibit 11)

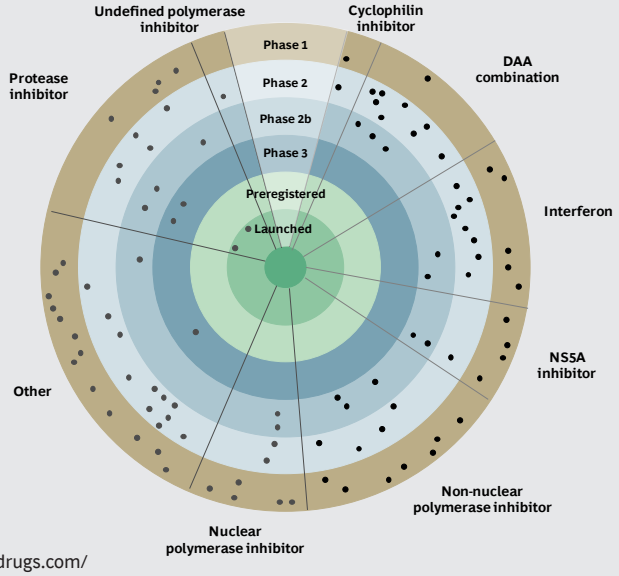
3.2.4.3. The Side Effect Profile of Triple Therapies

The new drugs are added individually to the existing two-medication regimen, making up a three-medication regimen that is called 'triple therapy'. Their side effects can exacerbate those caused by the other two medications. Clinical trial data suggests that up to half of those taking telaprevir experience a rash, which is severe in approximately 5 percent of cases. The main side effect of boceprevir, based on trial data, is anaemia, which is experienced by about half of patients. It can also leave a metallic taste in a patient's mouth.

Doctors we interviewed had differing views over whether side effects from the new drugs would affect patients' ability to complete a course of treatment. Many felt that patients currently faced with taking medication for 48 weeks, would find the prospect of reduced treatment time very motivating, and that, as observed in the telaprevir Phase III program, it would actually be easier to adhere to a treatment plan overall, any additional side effects notwithstanding. Others noted that the main side effects (rash, anaemia) of the new agents were simply an exacerbation of existing side effects, for which they already had treatment procedures in place, such as a consulting dermatologist on call, and which they knew how to manage.

3.2.5. The Longer-Term Treatment and Diagnosis Outlook

EXHIBIT 14 | The Hepatitis C Treatment Outlook (Compounds in Development)



Source: http://hcvdrugs.com/

Beyond telaprevir and boceprevir, the long-term outlook for HCV therapy is bright, with over 100 agents from more than eight therapeutic classes in development.[56] The classes of medication in the HCV pipeline are provided around the edge of Exhibit 14, above, and the clinical drug development phases progress towards the target at the centre, from Phase I (safety and pharmacology) through Phases 2 and 3 to pre-registration and launch.

The next wave of medications is likely to be approved within three years, with another wave likely to follow two years later. By the end of the decade, if not sooner, pegylated interferon, which requires a weekly injection and causes the most burdensome side effects of the current treatment regimen, is unlikely to form a part of HCV treatment, as interferon-free therapies with enhanced safety benefits emerge. As always, with drug development, it is impossible to predict with certainty when – or, indeed, if at all – the new treatments will be approved for general use.

Until 2006, a liver biopsy was needed to verify that patients seeking to start HCV treatment had moderate to severe liver damage. Liver biopsies were generally only available in large teaching hospitals, which limited patients' ability to access treatment. While a biopsy is no longer required, knowing the degree of damage (fibrosis) to the liver is still beneficial for clinical management. There are now two non-invasive options to do this.

Blood-based biomarker assays, such as FibroTest™, were thought by several clinicians to offer a similar diagnostic value to a biopsy at much less discomfort for patients. Ultrasounds of the liver have also become possible, such as the FibroScan™ devices manufactured by EchoSens. At ~$60,000 for even a portable unit, they represent a significant investment for hospitals, but do offer a non-invasive alternative to biopsies. Both approaches were regarded by clinicians we spoke to as promising advances in the diagnosis and staging of fibrosis and cirrhosis that would enable them to categorise patients seen in clinic and prioritise them for treatment.

3.3. Policy Issues

Treating hepatitis C effectively at the population level relies on managing two aspects of the treatment model. First, patients must present for treatment in sufficiently high numbers. Second, the health system must have sufficient clinical and allied capacity in place including doctors, nurses, psychologists, social workers, and infrastructure. At present, Australia can improve on both dimensions.

3.3.1. Supply Issues in Treatment: Adding More Clinical Capacity

We estimate that less than one in every five patients (17 percent) who would like to start treatment can do so.[57] At a national level, the system operates with a constant backlog: while there are pockets of success, waiting lists in Queensland can stretch for years, and treatment in rural areas is often wholly absent because of a lack of clinical expertise. The Australian government's commitment to telehealth could go some way towards mitigating rural areas without specialist support or any HCV service, but better provision for HCV patients is likely to require a coordinated approach between the different clinical and infrastructural supporters who currently deal with pieces of the HCV puzzle.

Within the existing treatment pathway, the largest bottleneck is the public hospital-based model led by medical specialists – in part, because of the historical requirement for a liver biopsy. Hepatologists, gastroenterologists and infectious diseases specialists are highly specialised expert resources that could be better used to make key treatment decisions and advise other clinicians, rather than run the entire, treatment program from beginning to end. In our view, the best lever to increase treatment numbers is to increase the supply of generalist clinicians (doctors and nurses) able to provide HCV treatment under the supervision of a specialist.

3.3.2. Demand Issues in Treatment: Increasing Patient Presentation Rates

Encouraging more diagnosed patients to present for treatment is a complex issue that lies at the heart of Australia's low treatment numbers. Compared to the United Kingdom and the USA, Australia has a high rate of diagnosis, yet less than 2 percent of patients present for treatment each year.

The population living with chronic HCV in Australia is heterogeneous, and the known barriers to treatment are numerous, so that a multi-pronged and

collaborative approach between all stakeholders in the HCV field is needed to encourage increased presentation rates, involving Government, hospitals, clinicians, community organizations and private industry.

At an individual level, readiness for treatment can be viewed as a complex interplay of numerous factors driving a person towards treatment that are counterbalanced by perceived and real barriers to treatment. For a well-informed patient, the tipping point at which treatment is chosen is influenced by, for example, their disease stage, their life circumstances, their knowledge of treatment options and their likelihood of achieving a cure, as well as their ease of access to treatment and considerations around disclosure.

The factors impacting on individual demand for treatment are quite specific, however. At a population level poor awareness of the benefits of treatment and fear of disclosure due to stigma and discrimination are two of the major barriers which currently hold people back from treatment.

Knowledge about HCV treatment among the patient population is patchy. While some are very well informed about the availability of treatment and recent improvements in cure rates, many others retain misconceptions that the infection is benign or that treatment is unlikely to benefit them. HCV treatment has evolved significantly over the last decade, but community level perceptions of treatment have not kept pace with the changes. Some patients may have been told, when diagnosed many years ago, that there was no effective treatment for HCV or that they were not eligible for treatment, and this perception has held to this day. Other people with HCV do not prioritise hepatitis C treatment because they feel well and do not understand that despite feeling well progressive liver disease may be occurring. Improving treatment knowledge across the whole community is thus a prerequisite to individual considerations of treatment.

Clinician education is also paramount. Primary health providers in particular are the principal avenue for specialist referral and have a key role to play in improving specialist presentation rates.

Stigma and discrimination continue to be a major concern for people with HCV. For some, their transmission of HCV is deeply and emotionally tied to a period of their lives that they have moved on from and seeking treatment dredges up unpleasant memories, concerns about disclosure and fears of how they may be judged. Addressing widespread stigma and discrimination and creating more supportive environments within which people with HCV find it easier to talk about their condition openly with family, employers, and healthcare providers will help to reduce one of the identified barriers to treatment which is considered along with many other factors when individuals assess their own particular threshold point for choosing treatment.

4. COST ANALYSIS OF THE HCV DISEASE BURDEN

All the costs referred to in this report are directly attributable to Commonwealth or State/Territory budgets

Disease burden is the impact of a health problem in an area measured by financial cost, mortality, morbidity, or other indicators. The mortality and morbidity effects are often quantified in terms of quality-adjusted life years (QALYs) or disability-adjusted life years (DALYs), which combine the burden due to both death and morbidity into one index. This allows for the comparison of the disease burden due to various risk factors or diseases. It also makes it possible to predict the possible impact of health interventions.

4.1. Cost Impact of HCV Today

4.1.1. Understanding The Cost Impact of Hepatitis C

HCV infection generates costs in several ways. First, it causes direct healthcare costs associated with both the treatment of the disease and its longer term consequences. These costs include the cost of medication, the cost involved in employing medical personnel to treat the virus, and the cost of nursing care. A second set of costs is generated indirectly by the fact that some of those who have chronic HCV are disabled and unable to work, or must reduce their hours of work. These costs include costs to the government in providing social benefits and the cost of lost production. While important, costs in this last category are difficult to measure and value. They include the cost of lost production when people who are ill are unable to go to work, and they include the cost of carers' time in looking after those infected when they are ill.

In this report, we look only at the direct costs of treating HCV and at the cost to the Commonwealth of paying social benefits.

We have restricted our cost analysis to those costs borne by the Commonwealth or State/Territory governments because the data basis on which to quantify those costs was more extensive and more reliable than the figures with which we could estimate lost production costs for the private sector. Since we did not consider productivity costs or the costs of patient time, and did not consider patient co-payments, all the costs referred to in this report are directly attributable to Commonwealth or State/Territory budgets.

4.1.1.1. Medical and Non-Medical Costs

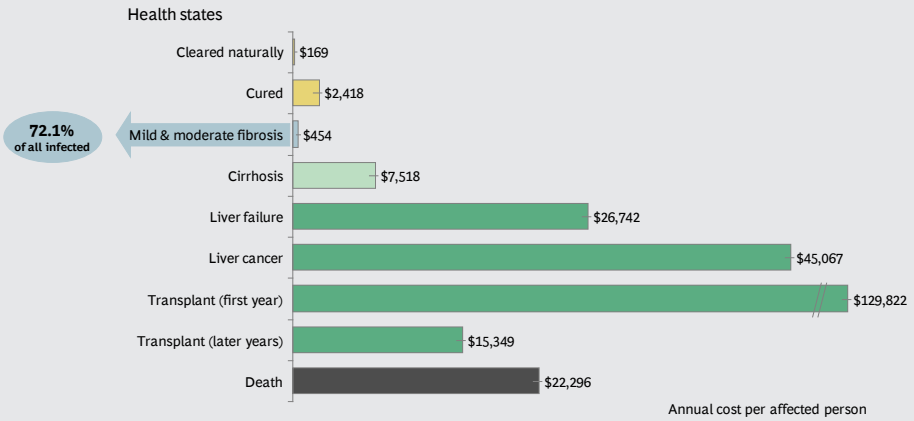
To assess the financial costs of HCV, we first looked at the medical costs caused by HCV. These included the cost of nurses, doctors and medicines that were necessary when attempting to cure the illness and to treat its consequences, like liver failure, liver cancer, or the need for a liver transplant. We also looked at hospital costs, using values for the public sector, where the overwhelming majority of HCV treatment occurs. We did not subtract patient co-payments from our costs: as most HCV treatment takes place in hospital outpatient clinics, they are likely to be negligible.

Secondly, we looked at non-medical costs that were incurred where people needed government support for reasons closely related to their hepatitis. Here, we looked

at the Newstart Allowance for jobseekers, the Sickness Allowance (paid to those in work who need to take time off for illness) and the Disability Pension, which is paid to those who cannot work. We included these non-medical costs when evaluating the burden of the disease on the government, but, as they are transfer payments, we did not include them in the economic analysis that went into calculating the cost per additional QALY gained through the use of protease inhibitors. We excluded the effect of lost productivity due to illness, and we did not include the cost of patient and carer time (for example, in waiting for appointments) because we did not believe that the data available allowed us to estimate them accurately enough to include them. Nor did we consider the cost of carers' time, as it is difficult to obtain reliable information about the number of carers who look after people with hepatitis C or the amount of time involved. Our analysis thus represents a conservative estimate of the economic impact of the disease.

EXHIBIT 15 | Annual Cost (Including Social Cost) of HCV-Related Health States

Calculated on number of people in health states in any one year



Source: MBS, PBS schedule costs; social benefit provisions, cost of Newstart benefit and Sickness Allowance (Department of Education Employment and Workplace Relations); cost of Disability Pension (Department of Families, Housing, Community Services and Indigenous Affairs); administration costs (Human Services)

4.1.1.2. The Cost of Health States

Along a second dimension, we broke costs down in a different way by looking at the costs associated with different medical conditions (referred to as "health states") which can occur after infection with HCV. To estimate the total cost of each health state, we considered both the medical and pharmaceutical burden, and the cost of government support. We counted the cost of these health states for everyone infected with HCV, whether or not they were in treatment.

As Exhibit 15 makes clear, the more severe health states are also the most costly. 72 percent of the people who are infected with HCV have only mild or moderate

fibrosis, and, even though the annual cost to manage each individual case of fibrosis is only approximately $500, people in this group account for most of the one-year costs of HCV. This is simply because there are so many of them, in contrast to the less than one percent of people who are in the very severe states of cirrhosis, liver cancer and liver transplantation in any given year.

We calculated costs over three time-periods: annually, on a five-year (medium-term) basis, and in an analysis that followed the cohort of all those who have currently been infected for the rest of their lives, but for a maximum of 60 years.

4.1.1.3. Cost Allocation Structure

Once we had established the costs caused by HCV, we looked at which part of the Commonwealth or State/Territory administration bore each cost. In our analysis, all of these costs, along with the cost of treating the disease, were allocated to the agency responsible for paying them.

EXHIBIT 16 | Cost Categories Considered

Commonwealth				State/Territory
DoHA Department of Health and Ageing	DEEWR Department of Education, Employment and Workplace Relations	FaHCSIA Department of Families, Housing, Community Services and Indigenous Affairs	DHS Department of Human Services	Health Departments
Pharmaceuticals 40% hospitals (inpatient, outpatient); MBS	Newstart Allowance; Sickness Allowance	Disability Benefit	Cost of administering payments and rebates	60% hospitals; Prison inmates' treatment

We calculated government assistance for the following three benefits: the Newstart Allowance, provided by DEEWR to jobseekers; the Sickness Allowance, provided by DEEWR to those temporarily unable to work; and the Disability Pension, provided by FaHCSIA. Because the number of people drawing a Carer Allowance for reasons related to HCV was considered too low to be reliably estimated, it was excluded from our analysis.

To estimate the cost of government assistance, we sought to gauge the proportion of patients in each health state who were able to (and were) working, and how many would need support in the form of government benefits. We based our estimations on a series of interviews with nurses and specialists.

A significant proportion of patients who present for treatment draw a disability pension for a complex set of interrelated needs, of which hepatitis C is only one. Because of this, we assumed that hepatitis C was a significant contributing cause for 0.6 percent of the HCV patient group who receive a Disability Pension.[58] Likewise,

we assumed that the same number of patients received the Newstart Allowance due to their hepatitis C status, which created difficulties for them in qualifying for and sustaining employment. (The actual number of patients on these benefits is much higher, but many of them draw assistance for a complex set of reasons, only a part of which relates to their HCV. In all, we estimated that ~29 percent of those who had mild or moderate fibrosis drew government support, but not for reasons primarily related to their hepatitis. We used disability measures and clinician interviews to estimate the proportion of those who had been employed and needed to draw the Sickness Allowance during treatment or in the advance stages of the disease. An overview of our estimate of the distribution of patients across social benefits and employment at various stages of their illness is given in Appendix 6.3)

4.1.1.4. Quality-Adjusted Life Years (QALYs)

Finally, we looked at how many years the virus takes away from a person's life – or, in the case of a treatment for the disease, how many years it gives back to a person. We did not focus on absolute years, but on the length of life lived and on its quality, using so-called quality-adjusted life years (QALYs). In general, a year of perfect health (as enjoyed, for example, by a young adult) is given a QALY value of 1, and each state of illness or disability is given a value that is less than 1. We used a value of .82 for a person who has cleared or been cured of the virus (we did not use 1, since most mid-life adults carry some comorbidity, and the population with HCV may have more morbidity than the general population, given the role that intravenous drugs play in its transmission). We then assigned a QALY value of .55 to cirrhosis, and .45 to liver failure, liver cancer or the first year of a liver transplant.[59] (The full list of our QALY values is in Appendix 6.4, Quality-Adjusted Life Year Utility Values). We have discounted QALYs and costs (at five percent per annum) where we have calculated costs per QALY, but we have not discounted QALYs where they appear as standalone figures.

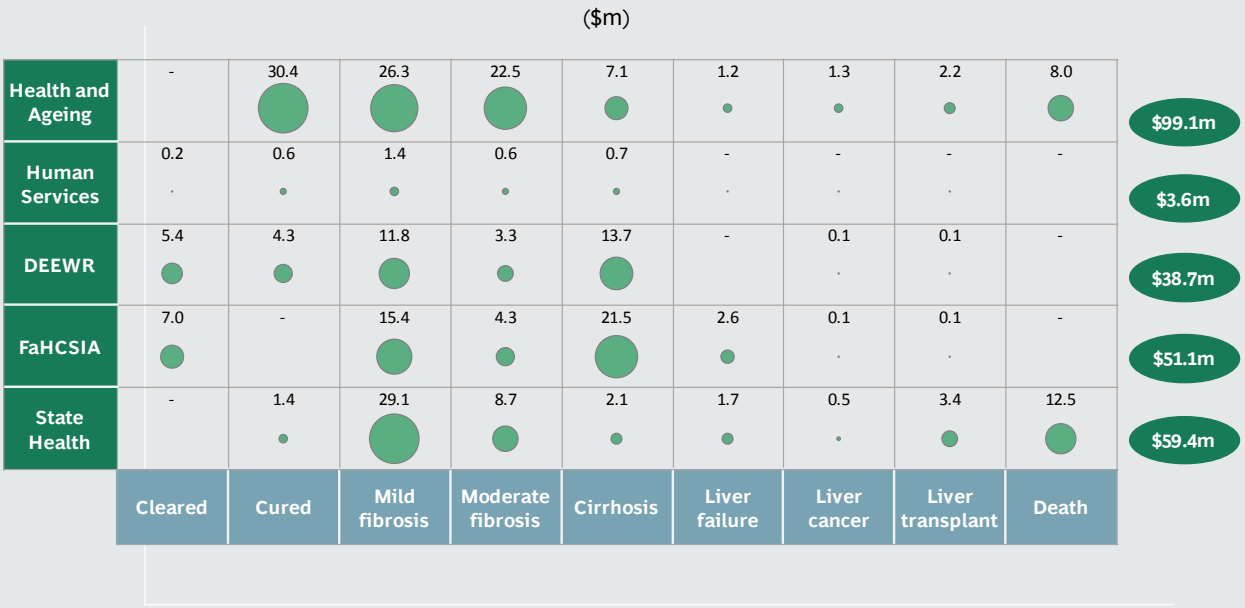
Knowing that a year lived with HCV and cirrhosis is worth only 0.55 (or just over half) the quality of a year lived as a healthy young adult, or two thirds of the quality of a year lived as an adult who is cured (0.82) makes it possible to estimate the number of QALYs that each treatment secures, and so to compare treatments.

4.1.2. Annual Cost Calculation: One-Year Costs Estimated at $252 million

In Australia, each year HCV is likely to result in approximately 213 cases of liver failure, (costing $5.6 m), ~44[60] liver transplants (costing $5.8 m), and ~48 cases of liver cancer (costing $2.2 m).

The total one-year cost due to HCV is estimated to be $252 m. The bulk of these costs are generated by people with mild or moderate fibrosis ($84.0 m and $39.5 m respectively) and cirrhosis ($45.1 m). 64 percent of the costs are medical ($162.0 m), while $89.8 m, or a third of the total, is paid out in government assistance by DEEWR ($38.7 m) and FaHCSIA ($51.1 m).

EXHIBIT 17 | Distribution of Annual Costs of Hepatitis C ($252m)



Source: Australian Bureau of Statistics, MBS, PBS data, Human Services PBRS, DEEWR, FaHCSIA.; BCG economic model

4.1.3. Medium-Term Cost Calculation: Five-Year Costs Estimated at $1.5 billon

Since policy planning often assumes a horizon of five to ten years, we also projected the cost of the current burden of HCV forward. Over the five year time-period, we estimated the distribution of people across the poor health states that can follow HCV, in order to simulate the number of people who are currently infected or who will become infected during the next five years, and the cost of their illness to the government.

4.1.3.1. The Medium-Term Impact on Individual Health

We estimated the number of advanced cases of the disease in the next five years by considering the group of currently infected patients and the probability that they will develop a more severe health state. Under the current treatment approach, we can expect to see the following instances of severe health states:

- ~24,668 cases of cirrhosis ($509 m)
- ~1,494 cases of liver failure ($86 m)
- ~332 cases of liver cancer ($33 m)
- ~144 liver transplants ($23 m)

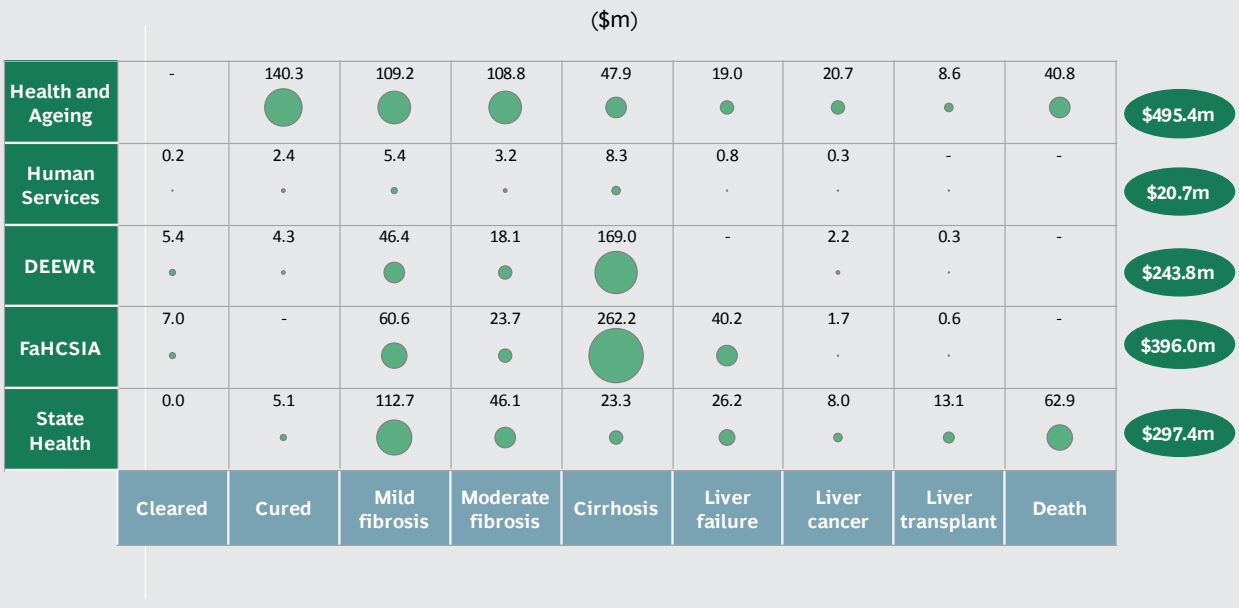
Overall, we also expect 1,064 years of life, and a total of 103,540 QALYs to be lost by the infected group over five years, compared to an equivalent, healthy group. An average of 0.34 QALYs are lost per infected person over those five years. The main driver of this lost quality of life is the poor health states (especially cirrhosis and liver failure) that would have been avoided had patients been cured of HCV.

4.1.3.2. The Medium-Term Cost Structure

The structure of the five-year, medium-term costs consists of the cost to treat 2 percent of the current group of people who are infected, as is the case today, and also the cost of everyone who has HCV having their disease progress during that time. The remaining groups were assumed to generate costs over four years, three years, two years and one year, respectively, taking us to the 2017-18 financial year.

We also factored in the effect of treatment, assuming that some people in early groups who received treatment would not then progress to more expensive health states. Only 17 percent of the medium-term cost is attributable to the most severe states of the disease (liver failure, liver cancer, liver transplants and death). 73 percent of the cost comes from those with advancing liver disease – that is, mild and moderate fibrosis, and fully-developed cirrhosis. The remaining costs are generated by people who have cleared the virus or been cured, in the year that they contracted the illness. These costs come from the fact that those people drew a Newstart or Sickness Allowance, or a Disability Benefit, for a complex of reasons in which hepatitis was a significant contributing factor.

EXHIBIT 18 | Distribution of Five Year Costs of Hepatitis C ($1.5bn)



Source: Australian Bureau of Statistics, MBS, PBS data, Human Services PBRS, DEEWR, FaHCSIA.; BCG economic model

4.1.4. Lifetime Cost Calculation for Currently Infected Group: $13.6 billion

4.1.4.1. The Lifetime Impact on Individual Health

Following the current group for the rest of their lives (but for a maximum of 60 years), we estimate that the following severe health states would occur:

- 143,700 cases of cirrhosis ($623 m)
- 67,462 cases of liver failure ($1.3 billion)
- 34,878 cases of liver cancer ($700 m)
- 12,788 people whose health deteriorated to the point where they needed a liver transplants in order to survive ($950 m).

Overall, we also expect a total of 1,487,457 QALYs, or an average of 4.9 QALYs per person, to be lost by the currently infected group over the remainder of their lives when compared to a healthy group, because of their poor health states. These figures are calculated over the remaining lifetime of the group of people who are currently infected.

4.1.4.2. The Cost Structure of the Currently Infected Group Over Their Lifetime

To calculate the lifetime costs of the currently infected group, we modelled the development of their illness for the remainder of their lives, or 60 years, assuming that the success rates of the current standard of care and protease inhibitors would remain constant, as would current treatment rates, with patients eligible for treatment until the age of 85.[61] This allows us to estimate the average lifetime cost of each person who becomes infected at $44,500. The average lifetime cost of a person with genotype 1 who is treated with pegylated interferon and ribavirin, but not with protease inhibitors, is almost twice that, or $81,000.

50 percent of the costs incurred in the 60-year model are medical and health-related, and come from the severe health states that those with HCV may develop. The remainder, or $6.6 BN, is driven by the cost of social benefits for those unable to work for reasons due to their HCV.

4.2. Impact of Newly-Approved Treatments on HCV

EXHIBIT 19 | Distribution of Lifetime Costs of the Group of People Currently Infected With Hepatitis C ($13.4bn)

Source: Australian Bureau of Statistics, MBS, PBS data, Human Services PBRS, DEEWR, FaHCSIA.; BCG economic model

4.2.1. Genotype 1 Patient Profile

To estimate the economic impact of new treatments, we first looked at the profile of patients who will benefit from them. As we have seen, the protease inhibitors are only effective for patients who carry genotype 1 of the virus, a group that makes up 55 percent of all those who are infected in Australia.

We estimated, based on discussions with medical specialists, that 90 percent of people infected with genotype 1 HCV who receive treatment would be treated with a protease inhibitor. Interviews with clinicians also led us to model a significant increase (we assumed 20 percent) in genotype 1 patients seeking treatment because of the greater chance of success, despite the current capacity constraints.

Doctors we spoke to believed that many genotype 1 patients were deterred from starting treatment because of the low chance of success and difficult side effects. Our interviews with clinicians also suggests that doctors have been anticipating the availability of the new protease inhibitors and as a result, have been sequestering or 'warehousing' their genotype 1 patients till such time as they can be treated with more effective medication.

"We're not putting any genotype 1s through treatment on the standard of treatment any more"

- Gastroenterologist, Sydney, September 2011

The protease inhibitors have an incremental cost per QALY of $17,300 (excluding the cost of social benefits)

4.2.2. Additional Costs From Protease Inhibitors

We next considered the impact on the cost of treatment if the new drugs, boceprevir and telaprevir, were available. Since telaprevir and boceprevir would be in addition to the current treatment regimen, they will increase the cost of treatment for people with genotype 1 HCV.

The cost of a course of treatment on the current treatment regimen for genotype 1 patients is $20,400. Since Australian prices for boceprevir and telaprevir are yet to be finalised, as a baseline, we used prices in the UK to estimate the local price and assumed that the total course of both drugs would be priced equally. [62]

Since no pricing information for boceprevir and telaprevir is available for Australia, we estimated that treating these patients with a protease inhibitor would cost approximately $31,500 over and above the current standard of treatment for a total of about $50,000 per patient. The extra cost is a direct function of price, as no additional costs are incurred. We also took into account the reduction in pegylated interferon and ribavirin due to a shorter length of treatment for some of those with genotype 1.

Although the next wave of medications will increase treatment costs for genotype 1 from ~$20K to ~$50K –, they will accelerate the likelihood of cure from ~37 percent to ~67 percent

4.2.3. Costs Avoided With Protease Inhibitors

Protease inhibitors appear to be cost effective and good value for money when outcomes are measured in QALYs. Over a 60-year time period, the current group of people who have been infected would regain a total of 106,256 additional QALYs, assuming that treatment rates remained constant at just under 2 percent per year.[63] Compared to the current approach to treatment, the new drugs would add an additional discounted $17,300 per QALY gained, without considering social costs, as these are transfer payments.

Some medication costs are avoided by using protease inhibitors. Since 58 percent of patients taking telaprevir require 24 fewer weeks' treatment with interferon and ribavirin, we priced in an overall average direct medication saving of ~$5,912 for every genotype 1 patient treated with telaprevir instead of the current approach to treatment. We then asked what other additional costs would be incurred, and what current costs would be avoided, if protease inhibitors were available.

The new agents begin to reduce social costs in the medium term, with DEEWR and FaHCSIA showing reduced spending for Newstart, the Sickness allowance and the Disability Pension over five years, as patients regain their health and no longer need support from the Commonwealth.

4.2.3.1. Costs to Commonwealth Avoided Over Five Years

EXHIBIT 20 | Five-Year Burden of Costs to Commonwealth in Two Treatment Paradigms

	Commonwealth level				State level	
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health & Ageing	Total
Current treatment	$495 m	$21 m	$244 m	$396 m	$297 m	$1.5 billion
With protease inhibitors	$794 m	$25 m	$239 m	$385 m	$304 m	$1.8 billion
Net extra costs of protease inhibitors	Cost: $299 m	Cost: $5 m	Savings: $5 m	Savings: $11 m	Cost: $7 m	$0.3 billion

Source: BCG economic model

Over the medium term, based on a five-year period, the introduction of new drugs might appear to only deliver modest gains for genotype 1 patients: ~60 fewer cases of liver failure, ~20 fewer cases of liver cancer, and between three and five fewer deaths.

4.2.3.2. Costs Avoided Over the Lifetime of the Group of People Currently Infected

If we project these numbers forward over the lifetime of the currently infected group (for which we have modelled 85,000 people undergoing treatment in the standard of care arm and 91,000 in the protease inhibitor arm), the cost impact of the protease inhibitors diminishes further.

EXHIBIT 21 | Cost to Commonwealth of Currently Infected Group Over Their Lifetimes

	Commonwealth level				State level	
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health & Ageing	Total
Current treatment	$3,442 m	$139 m	$2,180 m	$4,455 m	$3,185 m	$13.4 billion
With protease inhibitors	$4,117 m	$132 m	$2,054 m	$4,191 m	$3,092 m	$13.6 billion
Net impact of protease inhibitors	Cost: $675 m	Savings: $6 m	Savings: $126 m	Savings: $264 m	Savings: $93 m	Net cost: $186 m

Source: BCG economic model

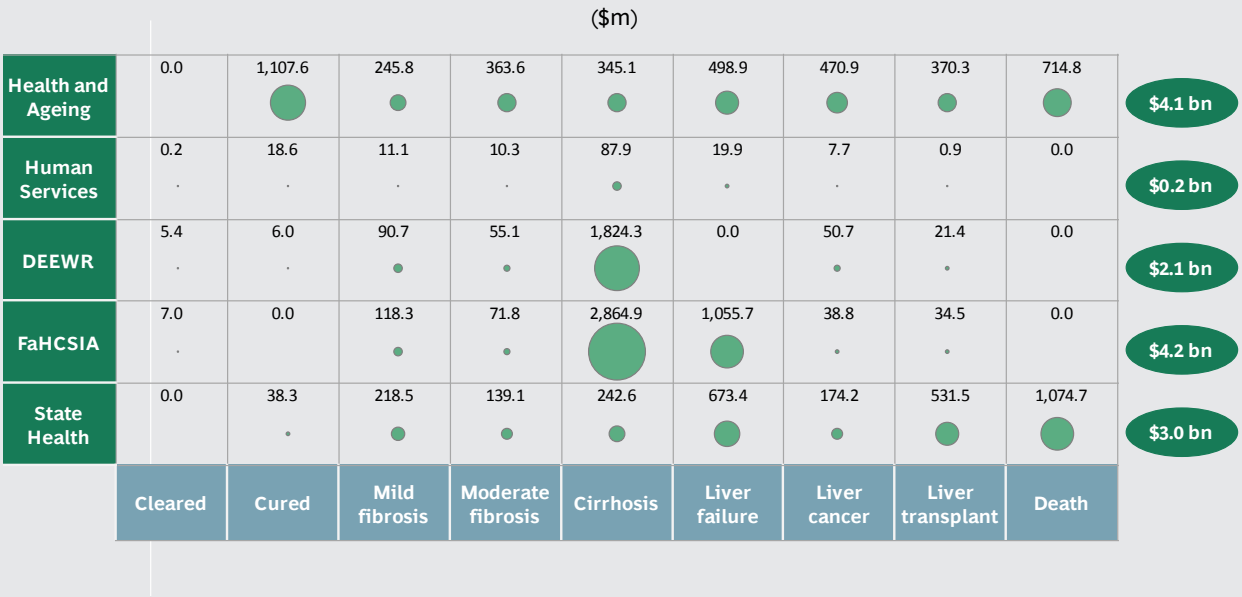
Projecting out across the lifetime of the current group of infected patients, we estimated $13.4 billion in discounted costs for the current standard of treatment, and an additional $186 m for the additional use of protease inhibitors.

The reason that we do not see substantial savings through the use of protease inhibitors even though they enable so many patients who are cured to avoid severe health states is that liver failure and liver cancer occur decades into the future. Because we have discounted future costs at 5 percent per annum, the impact of even the most expensive health state, a liver transplant, which we have estimated at just under $130,000 for the first year, is halved if it occurs two decades from now,

and reduced to ~$16,500 – by a factor of almost eight – if it does not take place for another 40 years.

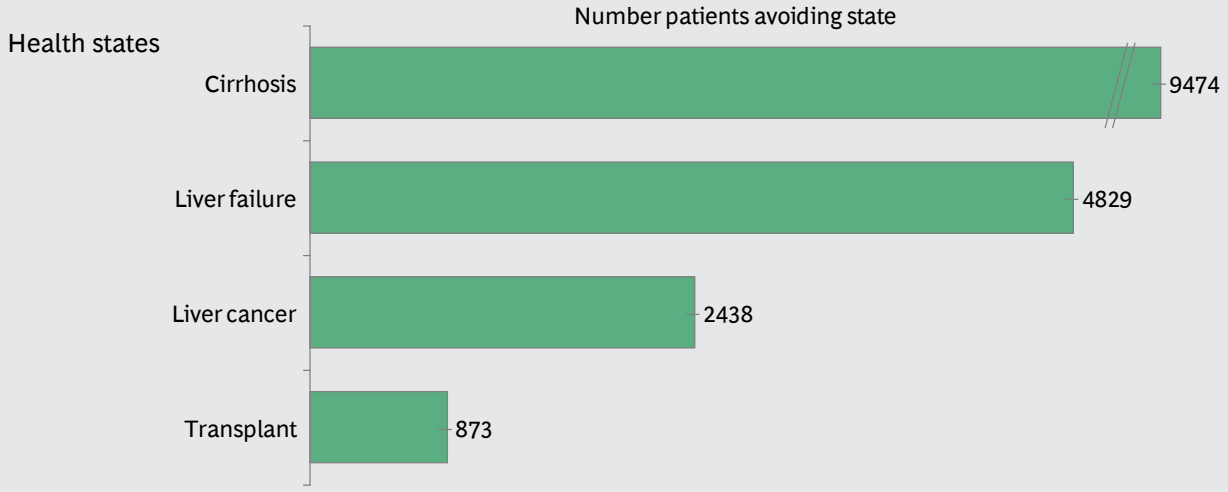
The other reason why we do not see big savings is because some people the cohort are treated each year. So, for example, those treated with a protease inhibitor in the first year of the model build up 60 years' worth of savings. However, those treated much later in the model (for example, in the 20th year), build up only 40 years of savings. Given that hepatitis C progresses slowly, the additional patients who, for example, achieve a cure in the 35th year of the model), are unlikely to accrue any benefits/savings during the remaining 25 year period.

EXHIBIT 22 | Lifetime Cost Burden of the Group of Currently Infected People if Protease Inhibitors Were Available ($13.6bn)



Source: Statistics Australia, MBS, PBS data, Human Services PBRS, DEEWR, FaHCSIA.;BCG economic model

EXHIBIT 23 | Serious Health States Avoided Over Lifetime by Administering Protease Inhibitors to the Current Cohort Of Treated Patients



Note: 91,000 patients treated in protease inhibitor arm; (Genotype 1); 85,000 treated in standard of care arm .
Source: ADVANCE, REALIZE trials, literature review

Over this longer time frame, the new drugs are likely to result in a substantial decrease in the number of severe – and more costly – health states: ~9,474 fewer cases of cirrhosis, ~4,829 fewer cases of liver failure, ~2,438 fewer cases of liver cancer, and ~873 fewer liver transplants.

4.2.4. Additional Taxation Revenue From the Introduction of Protease Inhibitors

A proportion of those in each stage of illness are dependent on government benefits (Appendix 6.3) we also modelled the impact on the government's finances of those who are cured and can move from benefits to employment. As our median age at treatment was 50, those cured had an average of 15 years to work.

Once we had reviewed the costs to the taxpayers that HCV incurs, and looked at how increasing cure rates could avoid costs, we also looked at the increased revenue that would be generated through GST, income and payroll taxes when those who were cured were working, and were no longer on social support.

Based on patient disease progression in trials, we had assumed that 31 percent of those treated had mild fibrosis, 53 percent had moderate fibrosis, and 16 percent had cirrhosis. Of those, we had assumed that 8.6 percent were enrolled on social benefits for reasons related to their HCV. We excluded a further 20 percent of patients who were drawing a benefit for a reason not directly related to HCV. (Further detail of the methodology used to calculate taxation revenue is provided in Appendix 6.5)

EXHIBIT 24 | Proportion of Those in Health States Drawing Benefits Because of HCV

Disease state	Drawing benefits			Employed	(Excluded)
	Proportion on Newstart benefit (DEEWR)	Proportion on sickness allowance (DEEWR)	Proportion on disability support (FaHCSIA)		On benefit, but not because of HCV, or > 65
Mild fibrosis	0.6%	0	0.6%	70%	29%
Moderate fibrosis	0.6%	0	0.6%	70%	29%
Cirrhosis	0.6%	21%	26%	28%	24%

Source: Interviews with specialist clinicians (n = 25) across Australia, September 2011

4.2.4.1. Five-Year Tax Revenue From HCV Cures Due to Protease Inhibitors

First, we assessed the five-year tax revenue from the group of people who are currently affected, and from those who will become infected over each of the next four years. We put this estimated revenue at $13.2 m.

EXHIBIT 25 | $13.2m in Taxation Revenue Estimated From Additional HCV Cures Due to Protease Inhibitors Over Five Years

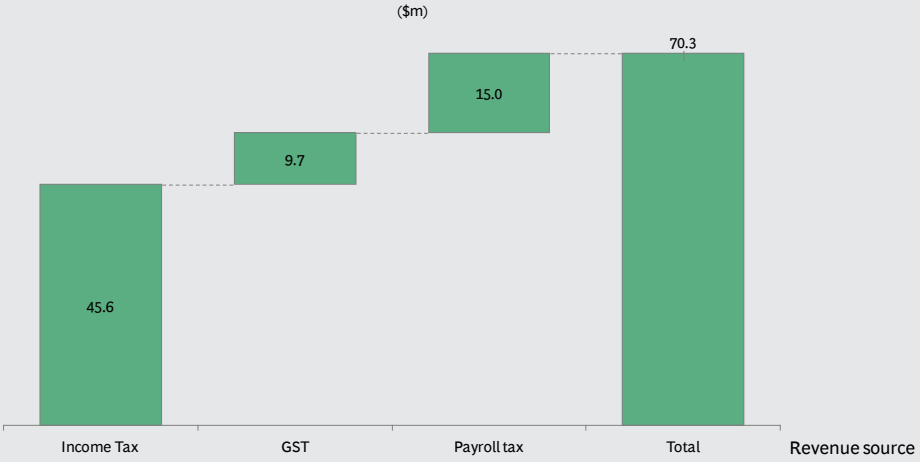
Source: Statistics Australia, Australian Tax Office, ADVANCE, REALIZE trials; BCG economic model.

4.2.4.2. Tax Revenue Over the Remaining Working Life of the Currently Infected Group

Next, we assessed the benefit to government of treatment for the currently infected group, looking at the taxation revenue from following one group of infected people for the rest of their working lives. We estimated their median remaining working life at fifteen years. We then took the number of cures expected over the lifetime of the protease inhibitors, and estimated the taxation revenue expected if the 8.6

percent of those cured who had been on social benefits for reasons relating to their HCV were able, after eliminating the virus, to earn the average Australian wage. We included a small proportion of beneficiaries who were asymptomatic (1.2 percent of those infected), as we understood from clinicians that many patients are on government benefits for a complex of reasons driven by social and medical factors that accompanied the frequent use of intravenous drugs which led to HCV infection.[64] Over that time, the government would benefit by $70.3 m (in today's dollars) in taxation revenue, just over half of which, or $45.6 m in today's dollars, would be income tax.

EXHIBIT 26 | $70.3m in Tax Revenue Estimated From Additional HCV Cures Due to Protease Inhibitors Over Lifetime of Today's Infected Cohort



Source: Statistics Australia, Australian Tax Office, ADVNACE, REALIZE trials

4.2.5. Economic Conclusion

HCV imposes a high burden of costs on taxpayers today: we estimate its five-year cost to the Commonwealth and States/Territories at $1.5 billion, and the lifetime cost of just the group of people who are currently infected at $13.4 billion.

While protease inhibitors are an upfront cost, the improved health that they make possible is inexpensive, at $17,300 per incremental QALY (not counting social costs) over treatment with pegylated interferon and ribavirin. When the group of people who have been exposed to the virus as of 2012 is tracked for the remainder of their lives, or for a maximum of 60 years, introducing protease inhibitors imposes a net cost on the public of $186 m over six decades.

5. CONCLUSION

5.1. The Protease Inhibitors: The First Step Towards Improved Outcomes

The first step towards improving HCV treatment outcomes is to use the new protease inhibitors, telaprevir and boceprevir to improve treatment outcomes for genotype 1 patients. These medications were approved in early 2012, and their manufacturers have lodged applications to list them on the PBS. Over the lifetime of each group of patients treated, the protease inhibitors would cure almost one and a half thousand more people annually compared to today. Each genotype 1 patient treated with a protease inhibitor instead of the current treatment standard would significantly lower his or her risk of developing a poor future health state: the risk of cirrhosis would be reduced from 57 percent to 30 percent, the risk of liver failure would be reduced from 29 percent to 16 percent, the risk of HCC would be reduced from 15 percent to 8 percent, and the risk of transplant would decline from 6 percent to 3 percent.

At $17,300 per incremental QALY gained, the protease inhibitors are a very reasonably-priced way to purchase beneficial health outcomes for the HCV population. Looking just at the group of people who have been exposed to the virus as of today and following them for the remainder of their working and natural lives, the introduction of protease inhibitors would impose a net cost of $186 m over sixty years.

6. APPENDICES

6.1. Five-Year Costs by State/Territory

6.1.1. Overall Five-Year Costs

AUSTRALIA
(All costs in $m)

	Commonwealth	States							Total
		ACT	NSW	NT	QLD	SA	TAS	VIC	WA	
Current treatment standard	1,443.83	0.15	3.14	0.17	2.10	0.45	0.23	2.02	0.91	1,453
With protease inhibitors	1,729.04	0.31	6.65	0.36	4.44	0.96	0.48	4.28	1.98	1,749
Net cost of protease inhibitors	284.94	0.16	3.50	0.19	2.34	0.51	0.25	2.26	1.05	295

Source: BCG economic model

6.1.2. Detailed Breakdown of Five-Year Costs Across States/Territories

ACT
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	8.0	0.3	3.9	6.4	4.7	23.3
With protease inhibitors	12.8	0.4	3.8	6.2	4.7	28.0
Net cost of protease inhibitors	4.8	0.1	-0.1	-0.2	0.0	4.7

Source: BCG economic model

NSW
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	170.9	7.1	83.9	136.2	99.9	498.1
With protease inhibitors	274.3	8.7	82.3	132.5	100.9	598.8
Net cost of protease inhibitors	103.4	1.6	-1.6	-3.7	1.0	100.7

Source: BCG economic model

NT
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	9.2	0.4	4.5	7.3	5.3	26.7
With protease inhibitors	14.7	0.5	4.4	7.1	5.4	32.1
Net cost of protease inhibitors	5.5	0.1	-0.1	-0.2	0.1	5.4

Source: BCG economic model

QLD
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	114.1	4.8	56.0	90.9	66.7	332.4
With protease inhibitors	183.1	5.8	54.9	88.4	67.3	399.6
Net cost of protease inhibitors	69.0	1.1	-1.1	-2.5	0.7	67.2

Source: BCG economic model

SA

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	24.6	1.0	12.1	19.6	14.4	71.8
With protease inhibitors	39.5	1.3	11.9	19.1	14.5	86.3
Net cost of protease inhibitors	14.9	0.2	-0.2	-0.5	0.1	14.5

Source: BCG economic model

TAS

(All costs in $ million)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	12.4	0.5	6.1	9.9	7.2	36.0
With protease inhibitors	19.9	0.6	6.0	9.6	7.3	43.3
Net cost of protease inhibitors	7.5	0.1	-0.1	-0.3	0.1	7.3

Source: NEED SOURCE

VIC

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	109.9	4.6	53.9	87.6	64.2	320.3
With protease inhibitors	176.4	5.6	52.9	85.2	64.9	385.0
Net cost of protease inhibitors	66.5	1.0	-1.0	-2.4	0.6	64.8

Source: BCG economic model

WA

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	50.9	2.1	25.0	40.6	29.8	148.4
With protease inhibitors	81.8	2.6	24.5	39.5	30.1	178.4
Net cost of protease inhibitors	30.8	0.5	-0.5	-1.1	0.3	30.0

Source: BCG economic model

6.2. Lifetime Cost of Currently Infected Group Across States/Territories

ACT

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	55.2	2.2	34.9	71.3	50.7	214.3
With protease inhibitors	66.2	2.1	32.9	67.1	49.1	217.3
Net cost of protease inhibitors	10.9	-0.1	-2.0	-4.2	-1.7	3.0

Source: BCG economic model

NSW

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	1,180.8	47.6	746.3	1,524.8	1,084.6	4,584.2
With protease inhibitors	1,414.8	45.3	703.2	1,434.8	1,049.3	4,647.4
Net cost of protease inhibitors	234.1	-2.3	-43.2	-90.0	-35.3	63.3

Source: BCG economic model

NT

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	63.2	2.6	40.0	81.6	58.1	245.5
With protease inhibitors	75.8	2.4	37.7	76.8	56.2	248.8
Net cost of protease inhibitors	12.5	-0.1	-2.3	-4.8	-1.9	3.4

Source: BCG economic model

QLD
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	788.0	31.8	498.0	1,017.6	723.8	3,059.1
With protease inhibitors	944.1	30.2	469.2	957.5	700.2	3,101.4
Net cost of protease inhibitors	156.2	-1.5	-28.8	-60.1	-23.6	42.2

Source: BCG economic model

SA
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	170.1	6.9	107.5	219.7	156.3	660.6
With protease inhibitors	203.9	6.5	101.3	206.8	151.2	669.7
Net cost of protease inhibitors	33.7	-0.3	-6.2	-13.0	-5.1	9.1

Source: BCG economic model

TAS
(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	85.4	3.4	54.0	110.3	78.5	331.7
With protease inhibitors	102.4	3.3	50.9	103.8	75.9	336.3
Net cost of protease inhibitors	16.9	-0.2	-3.1	-6.5	-2.6	4.6

Source: BCG economic model

VIC

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	759.3	30.6	479.9	980.5	697.4	2,947.7
With protease inhibitors	909.8	29.1	452.2	922.6	674.7	2,988.4
Net cost of protease inhibitors	150.5	-1.5	-27.7	-57.9	-22.7	40.7

Source: BCG economic model

WA

(All costs in $m)

	Commonwealth				State	Total
	Health & Ageing	Human Services	DEEWR	FaHCSIA	Health	
Current treatment standard	351.9	14.2	222.4	454.4	323.2	1,366.1
With protease inhibitors	421.6	13.5	209.5	427.6	312.7	1,385.0
Net cost of protease inhibitors	69.7	-0.7	-12.9	-26.8	-10.5	18.9

Source: BCG economic model

6.3. Estimated Proportion of Those With HCV on Government Benefits

Many of those infected with HCV draw government benefits for a variety of reasons, only one of which is Hepatitis C itself. On the basis of interviews with clinicians and nurses, and using Australian Bureau of Statistics data on the burden of disability, we disaggregated those who drew government benefits for reasons not primarily related to HCV and restricted our cost analysis only to those who drew government benefits primarily because they were infected with the virus. Since many people draw benefits for overlapping and interrelated reasons, our figures represent an estimate; where we were uncertain, we allocated the smallest possible number to the group of those drawing benefits because of HCV in order to ensure our estimate of total cost was as conservative as possible.

To arrive at an initial estimate of the amount of disability caused by HCV, we used Australian Bureau of Statistics data on the burden of disability,[65] combined with a literature review targeting disability and Hepatitis C. We then used interviews with hepatologists, infectious diseases physicians and gastroenterologists to refine our estimate of the percentage of those in each disease state who would draw each benefit.

Proportion of Those in Health States Drawing Benefits because of HCV

Health state	Proportion on Newstart benefit (DEEWR)	Proportion on sickness allowance (DEEWR)	Proportion on disability support (FaHCSIA)	Employed	On benefit, but not because of HCV
Cleared virus naturally	0.6%	0%	0.6%	70%	29%
Cleared (beyond year 1)	0%	0%	0%	80%	20%
Cured (year 1)	0%	18%	0%	63%	20%
Cured (beyond year 1)	0%	0%	0%	80%	20%
Mild fibrosis	0.6%	0%	0.6%	70%	29%
Moderate fibrosis	0.6%	0%	0.6%	70%	29%
Cirrhosis	0.6%	21%	26%	28%	24%
Liver failure	0%	0%	80%	0%	20%
Liver cancer	0.6%	25%	15%	35%	24%
Transplant (year 1)	0%	10%	20%	50%	20%
Transplant (later years)	0%	5%	5%	70%	20%

Source: Australian Bureau of Statistics; interviews with hospital-based hepatologists, infectious diseases physicians and gastroenterologists across Australia, September 2011

6.4. Quality-Adjusted Life Year Utility Values

Health state	Utility
Cleared	0.82
SVR Cure	0.82
Mild HCV	0.77
Moderate HCV	0.66
Compensated cirrhosis	0.55
Decompensated cirrhosis	0.45
HCC	0.45
Liver transplant	0.45
Post liver transplant	0.67
Death	0

Note: A year of perfect health has a utility value of 1, meaning that it is of full benefit to a person. Normal adult health has a utility value of 0.82, and each state of illness or disability is given a value that is less than that.
Source: Wright M. (2006) "Health benefits of antiviral therapy for mild chronic Hepatitis C: randomized controlled trial and economic evaluation", Health Technology Assessment (2006) Vol. 10: No. 21

6.5. Calculation of Taxation Revenue

6.5.1. Sample Size and Structure

We excluded from our analysis all those who did not retrieve treatment with protease inhibitors (that is, those who were not infected with genotype 1 of the virus, or who were infected with genotype 1 but who were not treated with protease inhibitors). We also excluded those who had been working before being cured, as we did not consider that additional tax revenue was generated when they returned to work.

We further restricted the number of eligible people cured by excluding those people who had been receiving social benefits for reasons that did not relate to their HCV status were not returned to employment.

There remained those with genotype 1 of the virus who were treated with protease inhibitors, who had been receiving social benefits for reasons relating directly to their HCV infection and who moved to the median wage. As the median age of those treated in our sample was 50, we modelled income from taxation for 15 years.

6.5.2. Income Tax Calculation

We assumed that those moving to work moved to the median income, and calculated the income tax on that income using data provided by the Australian Tax Office.

6.5.3. GST Calculation

We applied the Australian GST rate of 10 percent to the cost of a basket of goods and services bought by a household in the middle earning quintile, using Australian Bureau of Statistics data #6530.

6.5.4. Payroll Tax Calculation

We assumed that 80 percent of those returning to work were employed, and that 20 percent were self-employed. We then calculated payroll tax for the 80 percent who were employed, for whom we had assumed the median wage.

6.6. Probability of Transitioning Between Health States

FROM Health State	TO Health State	Probability	Source
Mild	Moderate	0.041	Bennett (1997)[67]
Moderate	Compensated cirrhosis	0.073	Bennett (1997) [68]
Compensated cirrhosis	Decompensated cirrhosis	0.039	Villa (1997) [69]
	HCC	0.015	Villa (1997)
Compensated cirrhosis-SVR	Decompensated cirrhosis	0.000	Expert opinion
	HCC	0.006	Estimated using odds ratio from Brady (2007) [70]
Decompensated cirrhosis	HCC	0.015	Villa (1997) [71]
	Liver transplant	0.033	NCHECR (2010) [72]
	Death	0.129	Villa (1997) [73]
HCC	Liver transplant	0.132	Kirby Institute (2011) [74]
	Death	0.335	Cancer Survival Victoria (2007), Cancer Institute NSW (2007). [75]
Liver transplant	Death Yr 1	0.080	Australia and New Zealand Liver Transplant Registry (2010) [76]
Post-liver transplant	Death (subsequent years)	0.023	Australia and New Zealand Liver Transplant Registry (2010) [77]

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8. ENDNOTES

1. The SVR of 37 percent has been taken from the comparator arm of the telaprevir studies (ADVANCE and REALIZE) and assumes that 50 percent of treated patients are treatment naive (using SVR rates from ADVANCE) and 50 percent of treated patients are treatment experienced (using SVR rates from REALIZE).
2. The figure again assumes a 50:50 mix of treatment-experienced and treatment-naïve patients, but uses data from the telaprevir arm of ADVANCE and REALIZE; see above, n. 1.
3. We considered that patients would remain eligible for treatment until they reached the age of 85 or died. In our model, 85,354 patients were treated over 60 years in the arm that used the standard of care (the current treatment standard), and 90,184 patients were treated in the arm using protease inhibitors.
4. The telaprevir submission is available at http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-telaprevir-nov11.
5. The boceprevir submission is available at http://www.health.gov.au/internet/main/publishing.nsf/Content/pbac-psd-boceprevir-july11.
6. Scott Holmberg, MD (Centers for Disease Control and Prevention), to the American Association for the Study of Liver Diseases.
7. Professor Gregory Dore, The Kirby Institute, University of New South Wales, communication to the report project team, May 2012.
8. The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011), Table 6.2.2.
9. 2009 numbers used, as 2010 figures do not include those for New South Wales: The Kirby Institute (2010) Australian Chronic Hepatitis C Observational Study (ACHOS), March 2010, Table 2.1.9, p. 58.
10. Ibid, Table 2.1.12, p. 59.
11. See Topp L, Maher L and Kaldor J, ch. 6, "Transmission of hepatitis C virus" in Dore G, Temple-Smith M and Lloyd A (2009) Hepatitis C – An Expanding Perspective.
12. For a discussion of the composition of the figure of 37 percent, see above, n. 1.
13. Phase I results, 2011, for TG-4040.
14. Barnes and colleagues have shown a broad immune response in humans using vaccines developed with adenoviral vectors: Barnes, E., Folgori, A., Capone, S., Swadling, L., Aston, S., Kurioka, A., Meyer, J., et al. (2012). Novel Adenovirus-Based Vaccines Induce Broad and Sustained T Cell Responses to HCV in Man. Science Translational Medicine, 4(115), 115ra1-115ra1; see also Colloca, S., Barnes, E., Folgori, A., Ammendola, V., Capone, S., Cirillo, A., Siani, L., et al. (2012). Vaccine Vectors Derived from a Large Collection of Simian Adenoviruses Induce Potent Cellular Immunity Across Multiple Species. Science Translational Medicine, 4(115), 115ra2-115ra2.
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17. The baseline patient population is structured on the basis of the telaprevir studies
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22. NCHER Annual Survey Reports 2010, using a 25.6 percent rate of clearance (The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011), table 6.2.2) and projecting growth forward at 0.2 percent p.a. using the CAGR from 2005 to 2009.
23. "HCV Infection in Europe" report, prepared by the Eurasian Harm Reduction Network in 2007; data for US from JPMORGAN report #17911463, compiled in 2011.
24. We applied a linear trend to the prevalence data presented in the Kirby Institute's Annual surveillance reports over a nine-year period to estimate prevalence in future years. The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveil-

lance Report (2002-2011).

25. The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011), table 2.1.12, p. 59.
26. Ibid, table 2.1.10, p. 58.
27. Ibid, Table 2.1.9, Number and rate of diagnosis of Hepatitis C infection, 2006-2010, p. 58 (2010 data not available for NSW).
28. Ibid, table 2.1.9.
29. Calculated from IMS data by dividing sales by average price of treatment. Population of the states, 2004 (Australian Bureau of Statistics):
30. IMS sales data, standard of care medications (2010-11).
31. Calculated from IMS data by dividing sales by average price of treatment. Population of the states, 2004 (Australian Bureau of Statistics): http://www.abs.gov.au/AUSSTATS/abs@.nsf/ProductsbyTopic/3C467E74C23239FFCA256E8A0077ADD9?OpenDocument.
32. The Kirby Institute and The National Drug Research Institute. (2011). National Prison Entrants' Blood borne Virus and Risk Behaviour Survey Report, 2004, 2007 and 2010 – Prevalence of HIV, hepatitis C, sexually transmitted infections, and risk behaviours among Australian prison entrants.
33. Lloyd, "Establishment of a successful assessment and treatment service"; The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011), Table 2.2.7, p. 65.
34. Depending on overall prevalence assumption used for Australia.
35. IMS data; consumer market research.
36. ASHM (NSW, SA), BCG analysis (using ratio).
37. The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011), Table 7.3.2, p. 126.
38. Australian HIV Observational Database.
39. Above, s. 3.2.1 Current treatment is hospital-based and led by specialists.
40. Exhibit 8, S. 3.2, above, p. 19.
41. Above, s. 3.1 Introduction to hepatitis C, p. 9.
42. Communicable Diseases Unit, P. H. S. (2003). Quality of Life Among People Living with Chronic Hepatitis C Infection. Public Health (pp. 1-45).
43. The 37 percent cure rate assumes that 50 percent of patients are treatment-naïve, and that 50 percent are treatment-experienced. This split affects the fibrosis condition of treated patients, and thus their SVR rates; see also above, n. 1.
44. The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011).
45. Telaprevir has been used in the ADVANCE, REALIZE and ILLUMINATE trials, the first two of which included Australian sites; boceprevir was tested in the SPRINT-2 and RESPOND-2 trials.
46. SVR rates are taken from the ADVANCE and REALIZE telaprevir studies, and assume that 50 percent of treated patients are treatment-naive and 50 percent are treatment-experienced. The analysis uses the distribution of patients with mild HCV, moderate HCV and cirrhosis at baseline from the ADVANCE and REALIZE studies. For more detail on how rates were calculated, see above, notes 1-2.
47. ADVANCE trial; see also above, n. 1.
48. INCIVO® approved Product Information, 6 March 2012. Figures given in Fig. 13 also collated in Incivo™ product information.
49. VICTRELIS® approved Product Information, 22 December 2011. Figures given in Fig. 13 also collated in Victrelis™ product information.
50. VICTRELIS® approved Product Information, 6 March 2012.
51. BOC Response Guided Therapy.
52. BOC/PR48.
53. BOC Response Guided Therapy.
54. BOC/PR 48.
55. Null responders were not included in the RESPOND-2 study VICTRELIS® Approved Product Information, 22 December 2011).
56. "New Drugs Pipeline" (http://HCVdrugs.com/).
57. Clinician interviews, September 2011, and survey of 251 GPs, September 2011.
58. We knew from clinician interviews that approximately one in three patients seen was supported by a government benefit. We also used clinical advice to estimate the proportion of patients disabled or unable to work in each disease state, which we estimated on the basis of clinician

interviews. Since we understood from clinicians that many patients draw government benefits even while asymptomatic for a complex of reasons that relate to social and medical factors accompanying the frequent use of intravenous drugs, we also needed to account for those people who are drawing a benefit for reasons related primarily to their hepatitis, and not to other comorbidities. We calibrated our estimate by taking Australian Bureau of Statistics data (cat. no. 4430.0.55.001), according to which 6.7 percent of all disability in Australia is primarily caused by diseases of the digestive system, and assumed conservatively that no more than one in ten of those would relate to hepatitis.

59. Wright M, Grieve R, Roberts J, Main J, Thomas HC on behalf of the UK Mild Hepatitis C Trial Investigators. Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation. Health Technol Assess 2006; 10(21).
60. 2010: 48 (The Kirby Institute, HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report (2011))
61. The medication used to treat HCV will change, and success rates are likely to rise, but no data is available to inform sensible modelling of medication and efficacy over 60 years.
62. Since the market share of these drugs cannot be predicted at the date of publication, we assumed a 70:30 division of patients between telaprevir and boceprevir, based on the latest sales data from the US market.
63. We calculate a treatment rate of 1.7 percent for those taking standard of care medications, and estimate a rate of 1.9 percent for those with Genotype 1, as we assume that presentation and treatment rates for those with Genotype 1 will increase when protease inhibitors become available.
64. See n. 58.
65. Australian Bureau of Statistics, cat. no. 4430.0.55.001.
66. Utility values from Wright M, Grieve R, Roberts J, Main J, Thomas HC on behalf of the UK Mild Hepatitis C Trial Investigators. Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation. Health Technol Assess 2006; 10(21).
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71. Above, n. 69.
72. NCHECR. Epidemiological and economic impact of potential increased hepatitis C treatment uptake in Australia. (2010).
73. Above, n. 69.
74. 202 liver transplants were conducted in 2010, 8 percent of which were due to HCC (ANZLTR 22nd Annual report). There were 122 cases of HCC in 2010 (Table 6.2.2, Kirby Institute HIV Annual Surveillance Report 2011).
75. The probability has been calculated on the basis of the average of 5 year survival rates in NSW (16 percent) and VIC (10 percent). A report by the Cancer Institute NSW (Survival from Cancer NSW 2007) states that the five-year survival rate for patients with HCC is 16 percent. A report by the Victorian Cancer Registry (Cancer Survival Victoria 2007) states that the five-year survival rate for patients with HCC is 10 percent.
76. Australia and New Zealand Liver Transplant Registry, 22nd Annual report 2010, page 19.
77. Ibid.

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