



5<sup>th</sup> February 2015

The House of Representatives Standing Committee on Health

## **Inquiry into Hepatitis C in Australia**

21<sup>st</sup> January 2015  
Parliament of Victoria  
Spring Street, Melbourne

Prepared on behalf of the Australasian Society for Infectious Diseases (ASID) by:

**A/Prof Joseph Torresi,**  
*MBBS, B.Med.Sci, FRACP, PhD*

NHMRC Practitioner Fellow  
Department of Microbiology and Immunology  
The Peter Doherty Institute for Infection and Immunity  
The University of Melbourne

Infectious Disease Physician  
Department of Infectious Diseases  
Austin Hospital

Chair,  
Viral Hepatitis Special Interest Group, ASID



## Summary statement

### *A. Prevalence rates of Hepatitis C in Australia*

Hepatitis C Virus (HCV) infects 2% of the world's population and is the leading cause of liver transplantation globally.

Currently, the overall prevalence of HCV infection in Australia is 1.3% (308 110 cases). The total number of viremic cases is 230 000, with a viremic prevalence of 1.0% and approximately 13,000 people with hepatitis C related cirrhosis.

Our efforts need to be directed towards achieving each of the objectives of the Fourth National Hepatitis C Strategy if we are to control HCV in Australia.

Although the estimated number and rate of diagnosis of hepatitis C infection per 100 000 population has fallen from 11 480 and 52.7 in 2009 to 10 698 and 46.3 in 2013. The incidence of hepatitis C among people who inject drugs, has increased from 5.4 to 13.0 per 100 person years between 2009 and 2013.

### *B. Hepatitis C early testing and treatment options available through:*

**Testing:** In Australia, approximately 80 per cent of people with hepatitis C infection have been diagnosed. However, it is estimated that up to 50,000 Australians remain unaware that they are chronically infected with hepatitis C.

Increased testing of hepatitis C should be targeted towards priority populations including injecting drug users, in prisons and Aboriginal and Torres Strait Islander people.

**Treatment options:** The options available for treating hepatitis C are undergoing rapid changes with the advent of highly efficacious, easier to tolerate and shorter duration Direct Acting Antivirals (DAAs). This change in treatment will significantly increase the demand for treatment from those living with hepatitis C.

It also expected that as treatment duration decreases and tolerance to antiviral drugs improves significantly, it will be essential to transition treatment from specialist tertiary based centers to more involvement of primary care health professionals in order to greatly facilitate access to treatment. This should include general practice, prisons, drug and alcohol settings and Aboriginal Medical Services.

One important advance that DAAs will deliver in the treatment of chronic hepatitis C is that these drugs will provide effective options for patients with cirrhosis who often tolerate interferon-based therapies poorly. DAAs offer an effective and safe alternative that for these patients will be life saving and avoid the impending path to liver transplantation.

Finally, Aboriginal and Torres Strait Islander peoples have a higher rate of hepatitis C, and lower rates of treatment than non-Indigenous Australians. It will therefore be essential to develop specific approaches to improve the management and treatment of hepatitis C in these communities.

### *C. The costs associated with treating the short term and long term impacts of Hepatitis C in the community.*

The number of people with compensated cirrhosis is predicted to increase from 13 850 in 2013 to 38 130 people in 2030.

With this will come an almost quadrupling of the number of people with decompensated cirrhosis (ie liver failure) and HCC will by 2030.

We would therefore expect that with the rising number of patients with complicated hepatitis C that the associated costs required to manage these individuals will be projected to increase from



\$224 million for the year 2013 to \$305 million per year by 2030. The estimated total cumulative costs for the period between 2013 and 2030 will rise to almost \$5 (\$4.934) billion.

By targeting treatment towards patients with advanced liver disease results in the lowest overall cost with an annual cost of \$143 million in 2030 and a cumulative cost from 2013 to 2030 of \$3.629 billion.

If we are to prevent an increase in the burden of HCV-related advanced liver disease complications, deaths and costs a fivefold increase in HCV treatment uptake over and above current levels will be necessary.

***D. Methods to improve prevention of new Hepatitis C infections, and methods to reduce the stigma associated with a positive diagnosis through:***

**Improving public health awareness:** Approaches to improving the prevention of hepatitis C infection will be an essential component to the overall success of managing hepatitis C in Australia. Prevention of hepatitis C transmission will require a combination of harm reduction strategies with health promotion activities such as education and communication.

Aboriginal and Torres Strait Islander people are at particular risk of HCV transmission through injecting drug use.

The prevalence of hepatitis C is also disproportionately higher among people in custodial settings.

**Approaches to harm minimization to reduce transmission:** Needle and syringe programs (NSPs) have been shown to be cost-efficient and highly effective at reducing transmission of hepatitis C. However, the rate of people reusing needles and syringes has remained high (25%) over the past 5 years. This indicates there a more concerted effort is essential to reduce the sharing of injecting equipment.

**Prevention through vaccination:** A vaccine for hepatitis C is not yet available. However, the Fourth National Hepatitis C Strategy has highlighted that ‘even with the advent of new therapies, a vaccine for hepatitis C is of critical importance to prevent hepatitis C transmission and to enhance current prevention strategies’. The strategy has prioritized research in vaccine development, research into means of implementing vaccine delivery and issues including acceptability and likelihood of uptake by those most affected as essential elements to significantly reducing the transmission of hepatitis C.

Currently the number of new notifications each year (approximately 8000 cases) is more than twice the number of patients who receive treatment in Australia. This means that relying on antiviral treatment strategies alone will be inadequate to control this disease. Furthermore, the high cost of these treatments will inevitably restrict the number of individuals who will ultimately be treated *notwithstanding the fact that these drugs will not prevent reinfection*. Modeling studies have shown that the introduction of a vaccine will have a dramatic impact on reducing the incidence of hepatitis C. Therefore approaches directed at preventing and reducing the transmission of HCV by developing of an effective vaccine is critical to the overall success of controlling HCV transmission.



## Detailed evidence to the terms of reference for the Inquiry into Hepatitis C in Australia

### A. Prevalence rates of Hepatitis C in Australia

Hepatitis C Virus (HCV) infects 2% of the world's population and is the leading cause of liver transplantation globally<sup>1</sup>. Recent advances in the treatment of HCV with directly acting antiviral agents (DAAs) have significantly improved sustained virological response (SVR) rates. However, these treatments will not prevent re-infection<sup>2,3</sup> and transmission of HCV continues to occur at alarming rates<sup>4</sup>.

The Fourth National Hepatitis C Strategy has identified five objectives which, in combination, are aimed at reducing the burden of hepatitis C in Australia<sup>5</sup>. Achieving these objectives will have a significant impact on hepatitis C in Australia but will require a sustained commitment by government. The objectives of the Fourth National Hepatitis C Strategy are to:

1. Reduce the incidence of hepatitis C
2. Reduce the risk behaviours associated with the transmission of Hepatitis C
3. Increase access to appropriate management and care for people with chronic hepatitis C
4. Reduce burden of disease attributed to chronic hepatitis C
5. Eliminate the negative impact of stigma, discrimination, legal and human rights issues on people's health

The estimated number of HCV infected cases (anti-HCV antibody positive) in Australia is 308 110 (range 242 760–328 280), with a prevalence of 1.3% (range 1.1–1.4%). Of these, 80 000 people were estimated to have cleared their infection. The total number of viraemic cases (HCV RNA positive) is 230 000 (range 180 900–244 600), with a viraemic prevalence of 1.0% (0.7–1.1%)<sup>6</sup>. The latest data of the Kirby Institute has reported that in 2013, of the individuals with chronic hepatitis C, 155 000 (115 000 – 165 000) had early liver disease (stage F0/1), 64 000 (43 600 – 79 000) had moderate-to-severe liver disease (stage F2/3), and 11 400 (7 100 – 17 000) were living with hepatitis C related cirrhosis. These data indicate that the estimated number of people with at least moderate liver disease has more than doubled (115% increase) over the last 10 years. In addition the estimated incident cases of decompensated cirrhosis has increased from 210 (130 – 300) in 2003 to 520 (310 – 800) in 2013 while the estimated number of incident cases of liver-related deaths has risen from 250 (170 – 340) in 2003 to 630 (400 – 880) in 2013<sup>5,7</sup>.

The Kirby Institute data has also shown that the estimated number and rate of diagnosis of hepatitis C infection per 100 000 population has fallen from 11 480 and 52.7 in 2009 to 10 698 and 46.3 in 2013. The reductions have occurred in all age groups but have been most prominent in the 25 – 29 and 20 – 24 year age groups, falling by 50% and 43% respectively. However, newly acquired hepatitis C infections continue to occur at the highest rate among adults in these two age groups. Furthermore, the incidence of hepatitis C among people who inject drugs, has increased from 5.4 to 13.0 per 100 person years between 2009 and 2013<sup>7</sup>. In 2013 there were an estimated 5 400 (range 5 000 – 5 800) incident cases of hepatitis C in Australia.

The problem of hepatitis C in travellers to countries of high endemic rates has also been under appreciated. A recent study has shown that the incidence of hepatitis C in Australian travellers visiting South East Asia may be as high as 1.8 infections per 10,000 traveler-days<sup>8,9</sup>. Travel associated hepatitis C infection could therefore pose an additional disease burden. Hepatitis C infection is also not infrequent in immigrants and refugees from countries of high hepatitis C endemic rates. In an Australian study examining the health problems of African immigrants HCV antibodies were detected in 4% of study participants, of whom 80% were viraemic with detectable HCV RNA in their blood<sup>10,11</sup>. Immigrants and refugees will warrant special attention in order to further understand the burden of hepatitis C in this population.



The large number of hepatitis C cases in Australia poses a major burden for the health system nationally. In addition, the high incidence of injecting drug use-acquired infection in the 1980s and 1990s means that as this population ages the rates of HCV-related cirrhosis, liver failure, and HCC are projected to increase substantially over the next two decades, posing an even greater burden on future health budgets.

***B. Hepatitis C early testing and treatment options available through:***

- i. primary care*
- ii. acute care*
- iii. Aboriginal Medical Services*
- iv. prisons*

**Testing:** The successful management of hepatitis C is critically dependent on appropriate referral and linkage to assessment, treatment and support options. At present treatment of chronic hepatitis C is predominantly undertaken in tertiary centers with minimal involvement of primary or acute care facilities and even more limited availability of treatment through Aboriginal medical services and prisons. Services offering testing are in primary care and need to be both accessible and acceptable for priority populations for hepatitis C.

Australia does not have population screening programs for hepatitis C. Early testing for hepatitis C means timely testing of individuals who have risk factors associated with the transmission of HCV at an asymptomatic stage of disease; as per the indications for testing set out in the national hepatitis C testing policy. Early diagnosis reduces the risk of further transmission and allows for the implementation of clinical management, lifestyle changes and treatment in order to minimise progression of disease and liver damage.

Early diagnosis of individuals who are infected with hepatitis C, available through primary care services, is essential for the success of strategies aimed at preventing hepatitis C transmission. In Australia, approximately 80 per cent of people with hepatitis C infection have been diagnosed. However, it is estimated that up to 50,000 Australians remain unaware that they are chronically infected with hepatitis C<sup>5</sup>. Identifying these individuals through effective testing policies will be essential to the overall success of reducing the burden of hepatitis C in Australia. The National Hepatitis C Testing Policy<sup>12</sup> provides important guidance on testing for hepatitis C, is readily available and is based on an assessment of the presences of risk factors for transmission.

Increased testing of hepatitis C should be targeted towards priority populations including injecting drug users, in prisons and Aboriginal and Torres Strait Islander people. Primary care services accessible to these populations require support to increase voluntary testing for hepatitis C and initiate a pathway to care. To accomplish this it will be necessary to implement strategies to increase the involvement of primary healthcare professionals in the management of people with hepatitis C and improve the referral process and access to high-quality support services at the time of diagnosis. In addition the Fourth National Hepatitis C Strategy has identified the necessity of implementing targeted initiatives for priority populations and local health care services to promote awareness and increase HCV testing and in assessing the feasibility, accessibility and cost-effectiveness of the range of existing and emerging testing methods<sup>5</sup>. The implementation of point of care testing, once available, would significantly facilitate the ease of broader access to testing.

**Treatment options:** The options available for treating hepatitis C are also undergoing rapid changes with the advent of DAAs. These antiviral drugs are highly efficacious when used in combination, will involve single daily oral doses eventually removing the need for injections, and treatment duration will be substantially reduced<sup>13</sup>. This change in treatment modalities will significantly increase the demand for treatment from those living with hepatitis C and has



implications for health systems which must adapt to the changing treatment landscape and the associated costs of using new generation antiviral drugs.

It is also expected that as treatment duration decreases and tolerance to antiviral drugs improves significantly, it will be essential to transition treatment from specialist tertiary based centers to more involvement of primary care health professionals in order to greatly facilitate access to treatment<sup>5</sup>.

With the advent of highly efficacious regimens of shorter duration, such programs may overcome barriers to treatment in prisons such as variable sentence length; frequent movement of prisoners; limited communication between and within custodial settings; and lack of specialist providers. Successful treatment integrated with harm minimisation interventions will reduce the risk of transmission to other prisoners and the general community.

*One important advance that DAAs will deliver in the treatment of chronic hepatitis C is that these drugs will provide effective options for patients with cirrhosis who often tolerate interferon-based therapies poorly. In addition, for patients with advanced liver disease and liver failure who simply cannot be treated safely with pegylated interferon, DAAs offer an effective and safe alternative that for these patients will be life saving and avoid the impending path to liver transplantation.*

Finally, Aboriginal and Torres Strait Islander peoples have a higher rate of hepatitis C, and lower rates of treatment than non-Indigenous Australians. It will therefore be essential to develop specific approaches to improve the management and treatment of hepatitis C in these communities.

***C. The costs associated with treating the short term and long term impacts of Hepatitis C in the community.***

Estimating the costs associated with the management of hepatitis C in both the short and long term is challenging. However, important information on predicted costs can be gained by examining the outcomes of carefully conducted modeling studies in Australia<sup>1, 6, 14</sup>.

A recent study by Sievert and coworkers provides important insight in to the expected costs hepatitis C will pose for Australia over the next two decades. These investigators predicted that the prevalence of chronic HCV will peak at 255 500 in 2025 followed by a decline to 251 970 by 2030. However, the number of people with compensated cirrhosis will increase from 13 850 in 2013 to 38 130 people in 2030. Predictably the number of people with decompensated cirrhosis in this model will increase to 4170 and the number of cases of HCC will rise to 2040 by 2030 compared with 1430 and 590 respectively in 2013.

Liver related deaths are also expected to increase from 530 in 2013 to 1740 in 2030<sup>6</sup>. These changes will result in a significant increase in the overall burden of disease that will be imposed on the Australian health system, in particular tertiary liver clinics and liver transplant services.

With the rising number of patients with complicated hepatitis C associated liver the costs required to manage these individuals are projected to increase from \$224 million for the year 2013 to \$305 million per year by 2030. The estimated total cumulative costs for the period between 2013 and 2030 will rise to a staggering \$4934 million<sup>6</sup>.

Regimens including combinations of new generation DAAs are expected to increase treatment efficacy to 80–90%. With the advent of highly effective DAAs it might be expected that the introduction of these drugs will minimize the impact of the rising number of patients with more complicated liver disease. Sievert and coworkers addressed this question by examining the three treatment scenarios based on anticipated introduction of DAA regimens. In the first scenario the impact of increased treatment efficacy alone was evaluated without an increase in annual treated



population. This was compared to a second scenario which evaluated increased efficacy and increased treatment uptake and a third scenario that considered the same increases as scenario 2 but with treatment limited to patients with greater than stage 3 fibrosis during 2015–2017 and then unrestricted (ie, patients with any level of fibrosis included) from 2018.

In the first scenario the number of people with chronic HCV was predicted to fall by 12 300 in 2030 and this was accompanied by a 4% reduction in HCV-related mortality. In addition, the prevalence of compensated and decompensated cirrhosis and HCC also fell by 4% respectively. These reductions in hepatitis C disease burden were only associated with modest reductions in overall costs. By 2030, annual costs were estimated at \$305 million, a 4% reduction from the base case, while cumulative costs over the time period were estimated at \$4826 million, a 2% reduction from the base case<sup>6</sup>.

In the second scenario 2, the number of people with chronic HCV fell by 60% (150 290 cases) and this was associated with a 43% reduction in HCV-related mortality (3710 cases), a 52% and 48% fall in compensated and decompensated cirrhosis respectively and a 45% reduction in the number of cases of HCC. The cumulative costs from 2013 to 2030 were estimated at \$3755 million, a 24% reduction<sup>6</sup>.

The third scenario resulted in a 56% fall in the number of people with chronic HCV (141 400 cases) while HCV-related mortality fell by 52% (6320 deaths averted), the number of cases of compensated cirrhosis fell by 56% (21 360 cases), decompensated cirrhosis by 54% (2410 cases) and HCC by 51% (1100 cases) by 2030. These reductions were associated with an annual cost of \$143 million in 2030 (a 55% reduction) and a cumulative cost from 2013 to 2030 of \$3629 million (a 26% reduction)<sup>6</sup>. *This scenario argues strongly for the case to make DAAs more readily available for patients with hepatitis C associated cirrhosis and advanced liver disease.*

This study demonstrated that despite improved treatment outcomes with DAA regimens, the impact on HCV-related liver disease burden and mortality in Australia over the next two decades will be modest if current treatment levels are maintained. The more targeted strategy directed at patients with more advanced liver disease outlined in the third scenario resulted in only a modest reduction in the HCV-associated disease burden compared to scenario 2 although the cumulative cost was substantially lower.

Another recent Australian modeling study examining various scenarios with annual treatment rates of 13, 17, or 25 per 1000 PWID (people who inject drugs) predicted reductions the relative prevalence of hepatitis C or 20%, 30%, and 50%, respectively, within 30 years. With the introduction of highly effective antiviral therapies like DAAs that result in higher sustained viral response rates this study also estimated that the impact of increased treatment rates would result in a further reduction in hepatitis C prevalence of 21%–23% after 15 years and 17%–38% after 30 years<sup>14</sup>.

These studies highlight that in order to prevent an increase in the burden of HCV-related advanced liver disease complications, deaths and costs a fivefold increase in HCV treatment uptake over and above current levels will be necessary.

***D. Methods to improve prevention of new Hepatitis C infections, and methods to reduce the stigma associated with a positive diagnosis through:***

- i. the public health system*
- ii. public health awareness and prevention campaigns to reduce morbidity and mortality caused by Hepatitis C*
- iii. non-government organisations through health awareness and prevention programmes.*



**Improving public health awareness:** The introduction of more effective antiviral drugs and treatment regimens alone will be insufficient to completely address the burden of hepatitis C-associated disease. Approaches to improving the prevention of hepatitis C infection will therefore be an essential component to the overall success of managing hepatitis C in Australia. Hepatitis C transmission is preventable. It is estimated that 90 per cent of new hepatitis C infections in Australia are caused by sharing or reuse of injecting equipment<sup>5</sup>. Effective prevention interventions can reduce hepatitis C transmission and the subsequent impact of infection on both individuals and the community. Prevention of hepatitis C transmission will require a combination of harm reduction strategies with health promotion activities such as education and communication. Approaches to prevention must include engagement with priority populations to ensure these strategies reach the priority populations adequately<sup>5</sup>.

An important part of hepatitis C prevention will include a significant effort to improving the knowledge of hepatitis C transmission in the general population and those 'at risk' of injecting. This will be achieved through effective health promotion, education and awareness activities, which include up to date information about hepatitis C, transmission risk and prevention strategies<sup>5</sup>.

Aboriginal and Torres Strait Islander people are at particular risk of HCV transmission through injecting drug use. The rate of hepatitis C infection among indigenous injecting drug users is up to 13 times higher than the non-indigenous IDU population<sup>5</sup>.

The prevalence of hepatitis C is also disproportionately higher among people in custodial settings. This is primarily due to a high rate of imprisonment for drug-related offences and unsafe injecting drug use in prisons. Effective prevention strategies, like needle and syringe programs, in custodial settings are needed to reduce risk behaviors and to access treatment services<sup>5</sup>.

**Approaches to harm minimization to reduce transmission:** Needle and syringe programs (NSPs) have been shown to be cost-efficient and highly effective at reducing transmission of hepatitis C. It has been estimated that over the decade 2000 – 2009 NSPs have directly averted 97,000 new hepatitis C infections<sup>15</sup>. However, the rate of people reusing needles and syringes has remained stable at 25-28% over the past 5 years. This indicates there a more concerted effort is essential to reduce the sharing of injecting equipment<sup>5</sup>. This could be accomplished through;

- (1) increasing access and availability of sterile injecting equipment among people who inject drugs
- (2) continued support of increased access to opioid pharmacotherapy programs and harm reduction and drug treatment programs
- (3) building knowledge and skills in priority populations, health care professionals and the community of hepatitis C transmission risks, testing and treatment

**Prevention through vaccination:** A vaccine for hepatitis C is not yet available. However, the Fourth National Hepatitis C Strategy has highlighted that 'even with the advent of new therapies, a vaccine for hepatitis C is of critical importance to prevent hepatitis C transmission and to enhance current prevention strategies'. The strategy has prioritized research in vaccine development, research into means of implementing vaccine delivery and issues including acceptability and likelihood of uptake by those most affected as essential elements to significantly reducing the transmission of hepatitis C.

Hepatitis C poses a significant and growing public health problem in Australia that will only be partially addressed with the introduction of new antiviral therapies. Although the number of reported cases in Australia has fallen in the past 5 years the proportion of individuals with more





significant liver disease has increased<sup>16</sup>. Previous infection and clearance of HCV does not necessarily result in protection against reinfection thereby limiting the long-term ability of antiviral therapy alone to adequately control hepatitis C in Australia<sup>2</sup>. Also, with approximately 90% of HCV cases occurring in injecting drug users<sup>17</sup> and the fact that reinfection in this group is not infrequent<sup>2, 3</sup> the expectation that hepatitis C infection rates can be controlled with antiviral drugs alone is not realistic and instead will need to occur in combination with harm reduction strategies and health promotion activities. However, individuals who have cleared HCV and become reinfected are twice as likely to clear infection compared to individuals with primary infection<sup>3</sup>. These findings indicate that protective immunity does occur and that producing a vaccine to prevent the development of persistent infection is an achievable goal<sup>2, 3</sup>.

Simulation models of hepatitis C dynamics in a high risk population can provide important information to better understand not only disease transmission but also to evaluate the potential population-level benefits of public-health interventions like vaccination. By using such a model it can be predicted that the introduction of a vaccine will have a significant effect on reducing the incidence of hepatitis C<sup>18</sup>. It is important to understand the design of this study in order to fully appreciate the impact of introducing a hepatitis C vaccine will have in a population. In this study investigators examined several scenarios basing the model and parameter estimates on extensive data collected in the UFO Study of young IDU in San Francisco. The scenarios incorporated known rates of spontaneous clearance and reinfection with HCV in an IDU population, predicted reductions in hepatitis C prevalence associated with the introduction of needle and syringe programs and the probability of HCV transmission according to the phase of HCV infection (acute versus chronic). The model also made a number of important assumptions about vaccine immunity, uptake, coverage and efficacy. The investigators assumed that vaccination would confer immunity to all HCV exposures to 31%, 78% and 99% of subjects 30 days after the first, second, and third doses respectively, basing this on the known rates for HBV vaccine. They also predicted that with 25%, 50%, and 25% of those vaccinated completing 1, 2, and 3 vaccine doses respectively, the average modeled effectiveness was 71.5% of the 50%, 65%, and 80% efficacy used in the model. This enabled the investigators to examine the predicted benefits of vaccines of both modest and high efficacy.

This important study highlighted that a vaccine with 50% to 80% efficacy targeted to high-risk or sero-negative IDU at a high vaccination rate could dramatically reduce chronic HCV incidence in IDU to 2–7% per person year (ppy) 30 years after its introduction. In the best case scenario with a sero-targeted or high risk-targeting strategy, a high vaccination rate (1% per month) and a vaccine efficacy of 80%, a predicted drop in the incidence of chronic HCV from an average of 13.5% to 4.3%, 3.2%, and 2.3% ppy at 5, 10, and 30 years, respectively, could be achieved after the initiation of the vaccination program. A vaccine delivered at a moderate rate (0.6% per month) was only a little less effective in reducing incidence of HCV (2.9% at 30 years). Even an untargeted vaccination strategy delivered at a high vaccine coverage rate (1% per month) resulted in a reduction in HCV incidence after 20 years<sup>18</sup>.

The first T cell-based preventative vaccine against HCV was recently trialed in a human Phase I study<sup>19</sup>. This was followed by a second study utilizing a prime-boost strategy with ChAd3 and MVA viral vectors encoding the non-structural proteins of HCV<sup>20</sup>. The adenoviral and MVA-based delivery systems had a good safety profile and induced strong, broad cross-genotype immune responses. This is an encouraging first step for the development of a HCV vaccine and paves the way for Phase II studies and for progression of other vaccine platforms.

Currently the number of new notifications each year (approximately 8000 cases) is more than double the number of patients who receive treatment in Australia, a total of only 2% of the 230,000 chronically infected individuals<sup>5, 16</sup>. This means that relying on antiviral treatment strategies alone will be inadequate. Instead delivering broader access to antiviral drugs will need



to occur in combination with harm reduction strategies, health promotion activities and once a vaccine is available effective strategies for vaccine introduction and promoting vaccine uptake in partnership with the at risk and affected communities. Furthermore, the high cost of antiviral treatments will inevitably restrict the number of individuals who will ultimately be treated notwithstanding the fact that these drugs will not prevent reinfection. However, the introduction of a hepatitis vaccine into an environment where other effective interventions like DAAs are already in place would provide the strongest advance towards eradicating HCV. Therefore approaches directed at preventing and reducing the transmission of HCV by developing of an effective vaccine is critical to the overall success of controlling HCV transmission.

**Concluding key summary points:**

***A. Prevalence rates of Hepatitis C in Australia***

1. Currently there are 230 000 viraemic cases of HCV in Australia and an estimated 11 400 people living with hepatitis C related cirrhosis.
2. The incidence of hepatitis C associated chronic liver disease complications is expected to rise dramatically.
3. The incidence of hepatitis C among people who inject drugs has increased.
4. Hepatitis C continues to pose a major health concern in Australian prisons and in Aboriginal and Torres Strait Islander people.
5. Hepatitis C in Australian travellers abroad, immigrants and refugees is problem that has been under appreciated.

***B. Hepatitis C early testing and treatment options available through:***

1. Services offering testing in primary care need to be expanded, accessible and acceptable for priority populations.
2. Early diagnosis of hepatitis C is critical to reducing the risk of further transmission and for the implementation of clinical management and to reduce the overall burden of HCV in Australia.
3. Increased testing of hepatitis C should be targeted towards priority populations including injecting drug users, in prisons and Aboriginal and Torres Strait Islander people.
4. New highly efficacious antiviral drugs with shorter treatment durations and excellent tolerability are becoming available. Access to these drugs needs to be substantially increased to all individuals with hepatitis C in order to reduce the burden of hepatitis C in Australia.

***C. The costs associated with treating the short term and long term impacts of Hepatitis C in the community.***

1. The estimated total cumulative cost for hepatitis C treatment over the next 2 decades will be approximately \$5 billion (\$300 million/yr).
2. A five-fold increase in the number of people treated annually, particularly in individuals with cirrhosis of the liver, would reduce the prevalence of hepatitis C in Australia by approximately 50% and the total cumulative cost by 25% to approximately \$3.7 billion over the next 2 decades.

***D. Methods to improve prevention of new Hepatitis C infections, and methods to reduce the stigma associated with a positive diagnosis through:***

1. Effective prevention interventions like needle and syringe programs can reduce hepatitis C transmission and the subsequent impact of infection on both individuals and the community.



2. Prevention of hepatitis C transmission require a combination of harm reduction strategies with health promotion activities such as community education and communication, especially in priority populations.
3. Effective prevention strategies, like needle and syringe programs, in custodial settings are needed to reduce risk behaviors and to access treatment services.
4. Antiviral drugs do not prevent reinfection with HCV. However, the availability of a vaccine in the future is predicted to dramatically reduce the incidence of chronic hepatitis C in high-risk populations. Effective strategies for the introduction of a vaccine and promoting vaccine uptake will need to be developed well in advance of a vaccine becoming available commercially.

#### **Supporting submission documents;**

1. Sievert W, Razavi H, Estes C, Thompson AJ, Zekry A, Roberts SK, Dore GJ. Enhanced antiviral treatment efficacy and uptake in preventing the rising burden of hepatitis C-related liver disease and costs in Australia. *Journal of Gastroenterology and Hepatology* 2014;29 Suppl 1:1-9.
2. Hahn JA, Wylie D, Dill J, Sanchez MS, Lloyd-Smith JO, Page-Shafer K, Getz WM. Potential impact of vaccination on the hepatitis C virus epidemic in injection drug users. *Epidemics* 2009;1:47-57.

#### **References:**

1. Dore GJ, Ward J, Thursz M. Hepatitis C disease burden and strategies to manage the burden (Guest Editors Mark Thursz, Gregory Dore and John Ward). *Journal of Viral Hepatitis* 2014;21 Suppl 1:1-4.
2. Grebely J, Prins M, Hellard M, Cox AL, Osburn WO, Lauer G, Page K, Lloyd AR, Dore GJ. Hepatitis C virus clearance, reinfection, and persistence, with insights from studies of injecting drug users: towards a vaccine. *The Lancet Infectious Diseases* 2012;12:408-14.
3. Sacks-Davis R, Aitken CK, Higgs P, Spelman T, Pedrana AE, Bowden S, Bharadwaj M, Nivarthi UK, Suppiah V, George J, Grebely J, Drummer HE, Hellard M. High rates of hepatitis C virus reinfection and spontaneous clearance of reinfection in people who inject drugs: a prospective cohort study. *PLoS One* 2013;8:e80216.
4. Negro F, Alberti A. The global health burden of hepatitis C virus infection. *Liver international*. 2011;31 Suppl 2:1-3.
5. Health. AGDo. Fourth National Hepatitis C Strategy, 2014-2017. Commonwealth of Australia 2014.
6. Sievert W, Razavi H, Estes C, Thompson AJ, Zekry A, Roberts SK, Dore GJ. Enhanced antiviral treatment efficacy and uptake in preventing the rising burden of hepatitis C-related liver disease and costs in Australia. *Journal of Gastroenterology and Hepatology* 2014;29 Suppl 1:1-9.
7. The Kirby Institute for Infection and Immunity in Society. HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Reports 1997–2013. Available at: 2014.
8. Johnson DF, Ratnam I, Matchett E, Earnest-Silveria L, Christiansen D, Leder K, Grayson ML, Torresi J. The incidence of HBV and HCV infection in Australian travelers to Asia. *J Travel Med* 2013;20:203-5.



9. Johnson DF, Leder K, Torresi J. Hepatitis B and C infection in international travelers. *Journal of Travel Medicine* 2013;20:194-202.
10. Gibney KB, Torresi J, Lemoh C, Biggs BA. Isolated core antibody hepatitis B in sub-Saharan African immigrants. *J Med Virol* 2008;80:1565-9.
11. Gibney KB, Mirhshahi S, Torresi J, Marshall C, Leder K, Biggs BA. The profile of health problems in African immigrants attending an infectious disease unit in Melbourne, Australia. *The American Journal of Tropical Medicine and Hygiene* 2009;80:805-11.
12. Committee. NHTPER. National Hepatitis C Testing Policy, 2012. Prepared by a joint working party of the Blood Borne Virus and STI Subcommittee (BBVSS) and the Ministerial Advisory Committee on Blood Borne Viruses and Sexually Transmissible Infections (MACBBVS). Canberra, ACT: Commonwealth of Australia. 2012.
13. EASL Clinical Practice Guidelines: management of hepatitis C virus infection. *Journal of Hepatology* 2014;60:392-420.
14. Hellard ME, Jenkinson R, Higgs P, Stooze MA, Sacks-Davis R, Gold J, Hickman M, Vickerman P, Martin NK. Modelling antiviral treatment to prevent hepatitis C infection among people who inject drugs in Victoria, Australia. *The Medical journal of Australia* 2012;196:638-41.
15. Research. NCiHEaC. Return on investment 2: Evaluating the cost-effectiveness of needle and syringe programs in Australia. Canberra, ACT: NCHECR, University of NSW on behalf of the Australian Government Department of Health and Ageing, 2009.
16. The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia Annual Surveillance Report. The University of New South Wales, Sydney, NSW. 2014.
17. Gidding HF, Topp L, Middleton M, Robinson K, Hellard M, McCaughan G, Maher L, Kaldor JM, Dore GJ, Law MG. The epidemiology of hepatitis C in Australia: notifications, treatment uptake and liver transplantations, 1997-2006. *Journal of Gastroenterology and Hepatology* 2009;24:1648-54.
18. Hahn JA, Wylie D, Dill J, Sanchez MS, Lloyd-Smith JO, Page-Shafer K, Getz WM. Potential impact of vaccination on the hepatitis C virus epidemic in injection drug users. *Epidemics* 2009;1:47-57.
19. Barnes E, Folgari A, Capone S, Swadling L, Aston S, Kurioka A, Meyer J, Huddart R, Smith K, Townsend R, Brown A, Antrobus R, Ammendola V, Naddeo M, O'Hara G, Willberg C, Harrison A, Grazioli F, Esposito ML, Siani L, Traboni C, Oo Y, Adams D, Hill A, Colloca S, Nicosia A, Cortese R, Klenerman P. Novel adenovirus-based vaccines induce broad and sustained T cell responses to HCV in man. *Science translational medicine* 2012;4:115ra1.
20. Swadling L, Capone S, Antrobus RD, Brown A, Richardson R, Newell EW, Halliday J, Kelly C, Bowen D, Fergusson J, Kurioka A, Ammendola V, Del Sorbo M, Grazioli F, Esposito ML, Siani L, Traboni C, Hill A, Colloca S, Davis M, Nicosia A, Cortese R, Folgari A, Klenerman P, Barnes E. A human vaccine strategy based on chimpanzee adenoviral and MVA vectors that primes, boosts, and sustains functional HCV-specific T cell memory. *Science translational medicine* 2014;6:261ra153.