WHO Collaborating Centre for Viral Hepatitis VIDRL

Doherty Institute

National Surveillance for Hepatitis B Indicators

Measuring the progress towards the targets of the National Hepatitis B Strategy – Annual Report 2017

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Abbreviations

ABS	Australian Bureau of Statistics
ACT	Australian Capital Territory
CHB	Chronic hepatitis B
DC	Decompensated cirrhosis
DSS	Department of Social Services
FoI	Force of infection
HCC	Hepatocellular carcinoma
LHS	Latin-hypercube sampling
National Strategy	Australia's 2nd National Hepatitis B Strategy 2014-2017
NNDSS	National Notifiable Diseases Surveillance
NOM	Net overseas migration
NSW	New South Wales
NT	Northern Territory
PBS	Pharmaceutical Benefits Scheme
PR	Plausible range
QLD	Queensland
SA	South Australia
TAS	Tasmania
VIC	Victoria
WA	Western Australia
WHO	World Health Organization

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Contents

Executive Summary

Number of people living with chronic hepatitis B:

- In 2017 an estimated 233,947 people were living with chronic hepatitis B (CHB) in Australia, representing 0.97% of the population.
- The prevalence of CHB in 2017 varied considerably between each state and territory from 0.28% in Tasmania to 1.17% in Victoria.

Chronic hepatitis B diagnosis:

- An estimated 149,118 people living with CHB in Australia had been diagnosed in 2017, representing 63.74% of the total.
- In 2017, the Northern Territory and New South Wales had the highest proportion of people living with CHB who had been diagnosed, with all other jurisdictions falling below the national average.
- Australia did not reach the 2017 National Strategy target of increasing the proportion of all people living with CHB who are diagnosed to 80%. No individual jurisdiction reached this 80% target either.

Chronic hepatitis B treatment:

- In 2017, 18,851 people were dispensed drugs for the treatment of hepatitis B which is an estimated 8.06% of all people living with CHB.
- The estimated proportion of people living with CHB receiving treatment was higher than the national average in the Australian Capital Territory and New South Wales in 2017, with all other jurisdictions falling below the national average.
- Australia did not reach the 2017 National Strategy target of increasing the proportion of people living with chronic hepatitis B who are receiving antiviral treatment to 15%. No individual jurisdiction reached this 15% target either.

Burden attributable to chronic hepatitis B:

- The number of deaths attributable to CHB in 2017 was estimated to be 479. Most deaths were attributable to hepatocellular carcinoma (HCC), which was responsible for 327 deaths in 2017, while 152 people living with CHB died due to decompensated cirrhosis (DC).
- The total number of deaths attributable to CHB in each state and territory varied from 4 to 154 in 2017.

Introduction

Chronic hepatitis B is a significant public health burden and is now the most prevalent chronic blood-borne viral infection in Australia. Chronic hepatitis B (CHB) is a leading cause of liver cancer, the 6th most common cause of cancer mortality in Australia(1). Without substantial improvements in access to appropriate care, monitoring and treatment hepatitis B related mortality will continue to increase.

Australia's National Hepatitis B Strategies have been fundamental to guiding the hepatitis B response since 2010. The 2nd National Hepatitis B Strategy 2014-2017 (National Strategy)(2) included aspirational targets to measure progress towards the overall goal to reduce the burden of hepatitis B. These targets were, by 2017, to:

1. Achieve HBV childhood vaccination coverage of 95 per cent
2. Increase hepatitis B vaccination coverage of priority populations
3. Increase to 80 per cent the proportion of all people living with chronic hepatitis B who are diagnosed
4. Increase to 15 per cent the proportion of people living with chronic hepatitis B who are receiving antiviral treatment.

The 3rd National Hepatitis B Strategy 2018-2022(3) was released in 2018 and contains new objectives and targets to guide Australia's response to the needs of people living with CHB. These targets have been expanded following the previous National Strategy, and are by the end of 2022 to:

1. Achieve and maintain hepatitis B childhood vaccination coverage of 95 per cent at 12 and 24 months
2. Reduce the number of newly acquired hepatitis B infections across all age groups by 50 per cent, with a focus on priority populations
3. Increase the proportion of people living with chronic hepatitis B who are diagnosed to 80 per cent
4. Increase the total proportion of people living with chronic hepatitis B receiving care to 50 per cent
5. For people living with chronic hepatitis B, increase the proportion receiving antiviral treatment to 20 per cent
6. Reduce hepatitis B attributable mortality by 30 per cent
7. Minimise the reported experience of stigma among people living with hepatitis B, and the expression of stigma, in respect to hepatitis B status.

Australia has also endorsed the World Health Organization (WHO) Global Health Sector Strategy on Viral Hepatitis 2016 – 2021(4), which calls for the elimination of hepatitis B as a public health threat by 2030. Global targets for 2030 include 90% of people living with hepatitis B diagnosed, 80% of eligible persons with CHB treated and a 65% reduction in hepatitis B related deaths compared to 2015.

Report Background

A key aspect of Australia's National Hepatitis B Strategy 2014-2017 was the identification of specific measurable aims and targets, including increasing the proportion of people living with CHB who have been diagnosed, increasing treatment uptake in those affected, and reducing the burden of attributable morbidity and mortality associated with the disease. Measuring the progress towards the objectives and targets of the National Strategy will allow for identification of priority areas in order to shape the public health and policy response to hepatitis B in Australia.

This report summarises work undertaken by the WHO Collaborating Centre for Viral Hepatitis at the Doherty Institute on the Surveillance for Hepatitis B Indicators Project funded by The Australian Government Department of Health. The project objective is to develop disease burden estimation and mathematical modelling approaches to inform the surveillance, monitoring and evaluation of progress towards achieving the objectives of the 2nd National Hepatitis B Strategy 2014-2017 and reporting against Hepatitis B Indicators in the National Blood-borne Viruses and Sexually Transmissible Infections Surveillance and Monitoring Plan 2014-2017. Future reports will report against the objectives and targets of the 3rd National Hepatitis B Strategy 2018-2022.

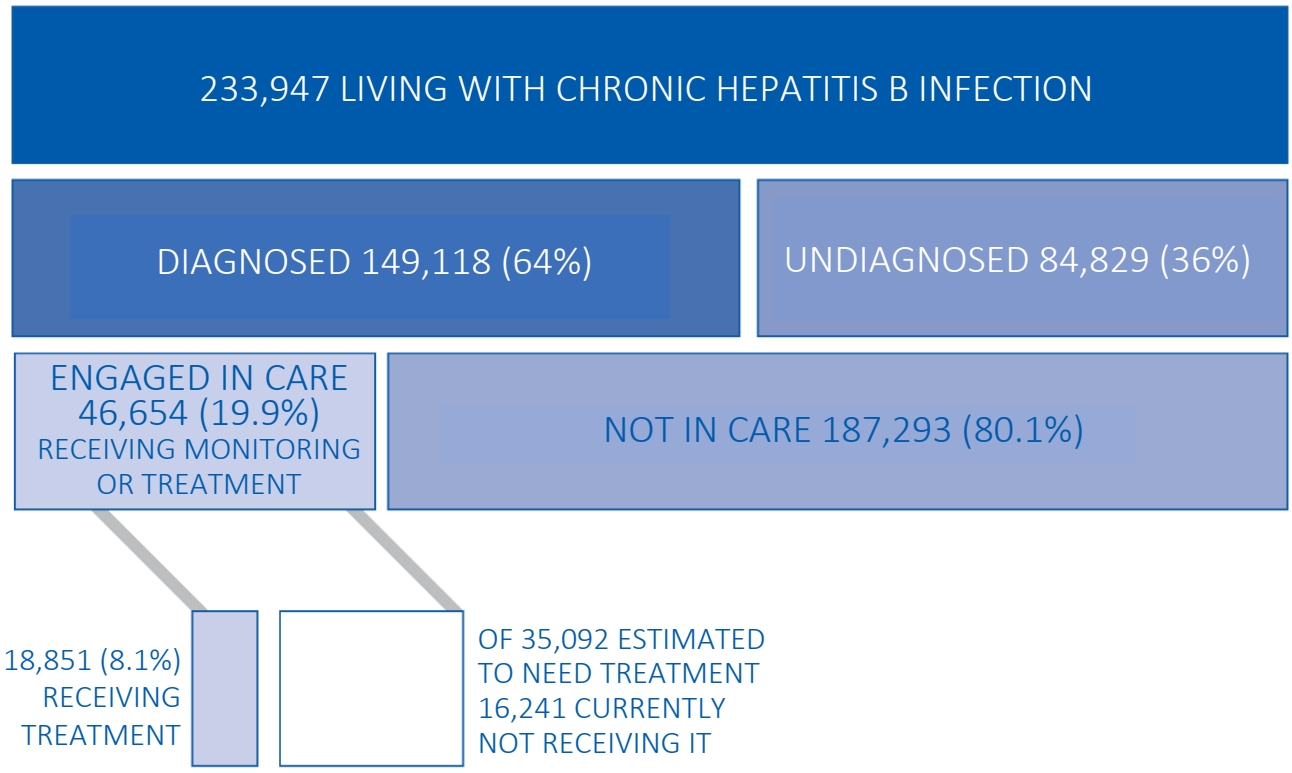
This is the first publicly available Summary Report of Hepatitis B Indicator 2017 Estimates. Indicator data estimates have been derived from new mathematical modelling for CHB in Australia, and are an extension of our previous modelling work. These new simulations use additional population information and incorporate increased complexity including disease transition states, treatment uptake and treatment impact. The new estimates differ in some respects from previous outputs, and more accurately reflect the current epidemiological and clinical pattern of CHB in Australia. Estimates have been incorporated into The Kirby Institute's Annual Surveillance Reports(5) and the Doherty Institute's National Viral Hepatitis Mapping Project Reports(6), along with supporting interpretive and methodological information.

Summary National Estimates

Table 1. Australian summary for hepatitis B indicator estimates, 2017

Indicators	Point estimate	Plausible range	
		Minimum	Maximum
1. People living with CHB	233,947	190,250	265,760
2. Proportion of people living with CHB in Australia who have been diagnosed	63.74%	52.65%	80.57%
3. Proportion of people living with CHB who are dispensed drugs for the treatment of hepatitis B	8.06%	7.09%	9.91%
4. Number of attributable deaths due to CHB	479	352	658
4. Number of deaths due to hepatocellular carcinoma attributable to CHB	327	245	445
4. Number of deaths due to attributable to decompensated cirrhosis CHB	152	107	213

Figure 1. Chronic hepatitis B cascade of care, Australia, 2017



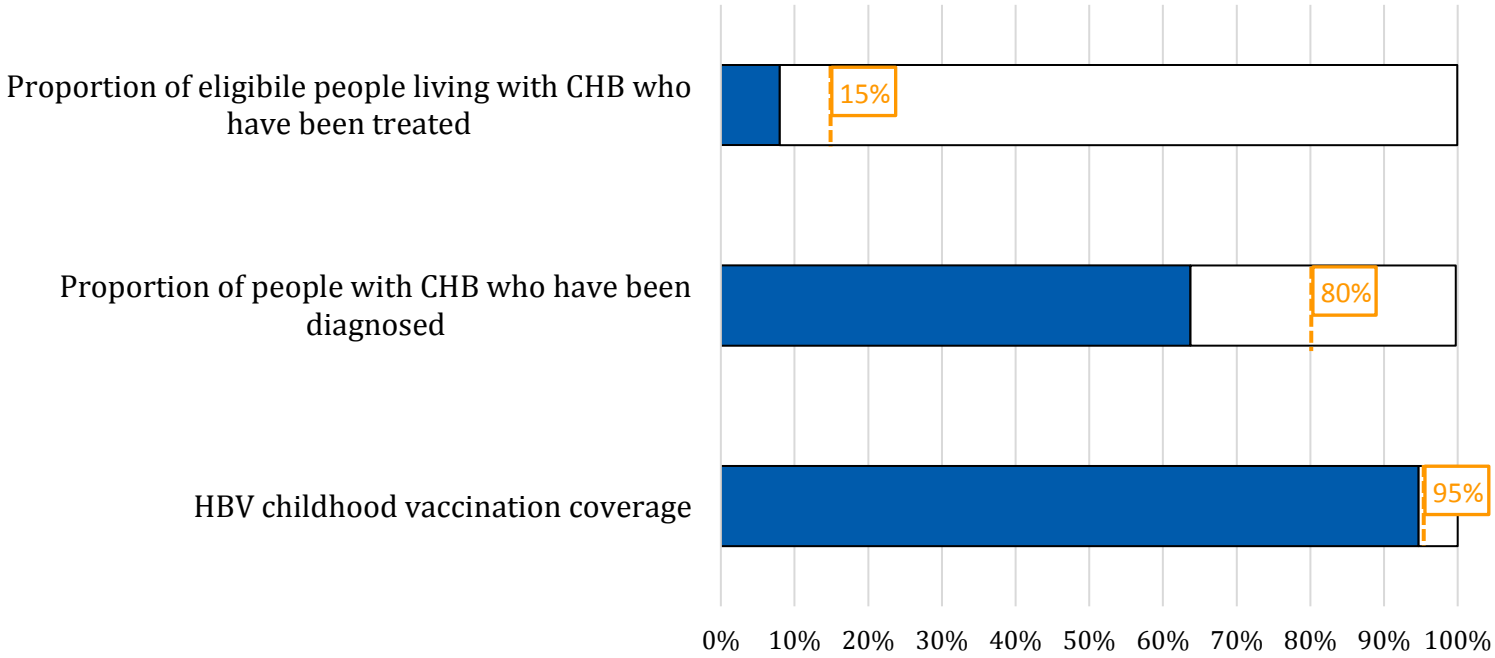
Source: National Hepatitis B Mapping Report

Summary Progress Towards Targets

Despite notable increases in the number of people having been diagnosed with chronic hepatitis B, and in those receiving antiviral treatment, Australia did not reach the 2017 diagnosis and treatment uptake targets set in the 2nd National Hepatitis B Strategy 2014-2017, with progress needed to achieve the 2022 targets set in the 3rd National Hepatitis B Strategy 2018-2022.

Hepatitis B infant immunisation coverage among 12-month children nationally reached 94.7% in 2017, just short of the National Strategy target of 95% by 2017. HBV vaccination coverage data is collected by the Australian Immunisation Register and further explored in the National Hepatitis B Mapping Report.

Figure 2. 2017 progress towards the 2nd National Hepatitis Strategy 2014 – 2017 targets



To achieve WHO's 2030 targets outlined in the Global Health Sector Strategy on Viral Hepatitis 2016 – 2021, and taking into account future trends, Australia needs to:

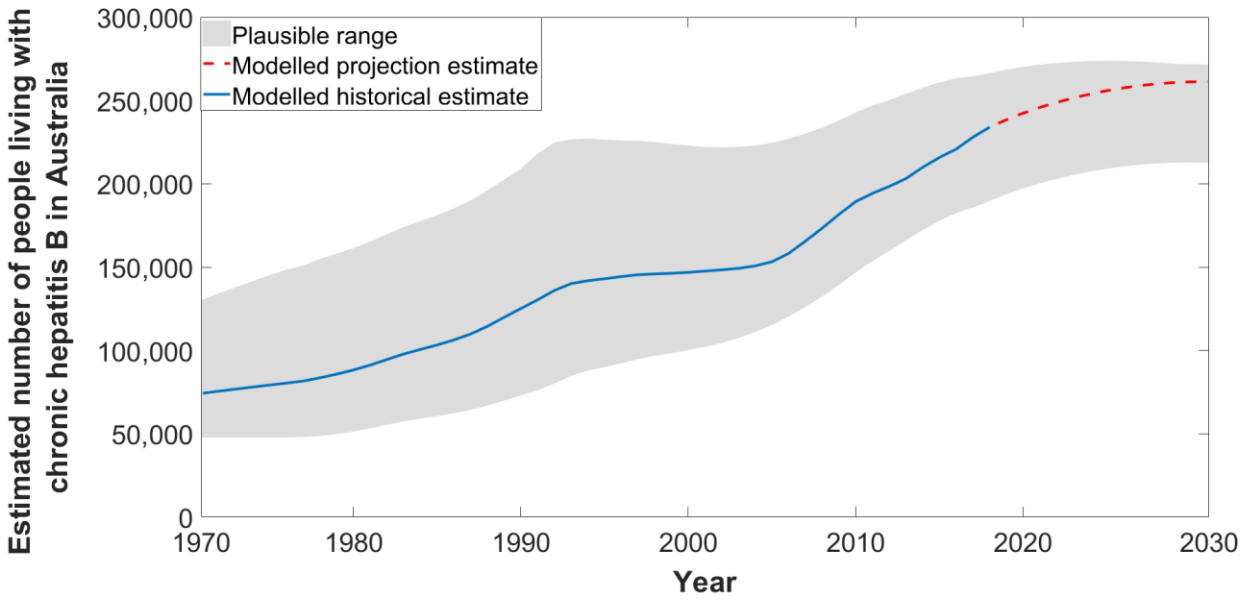
- Increase the number of people diagnosed from 149,118 in 2017 to 235,141 by 2030
- Increase the number of people treated from 18,851 in 2017 to 65,317 by 2030
- Decrease the number of deaths attributable to CHB from 479 in 2017 to 184 by 2030

Detailed National Estimates

1. Number of people living with chronic hepatitis B in Australia.

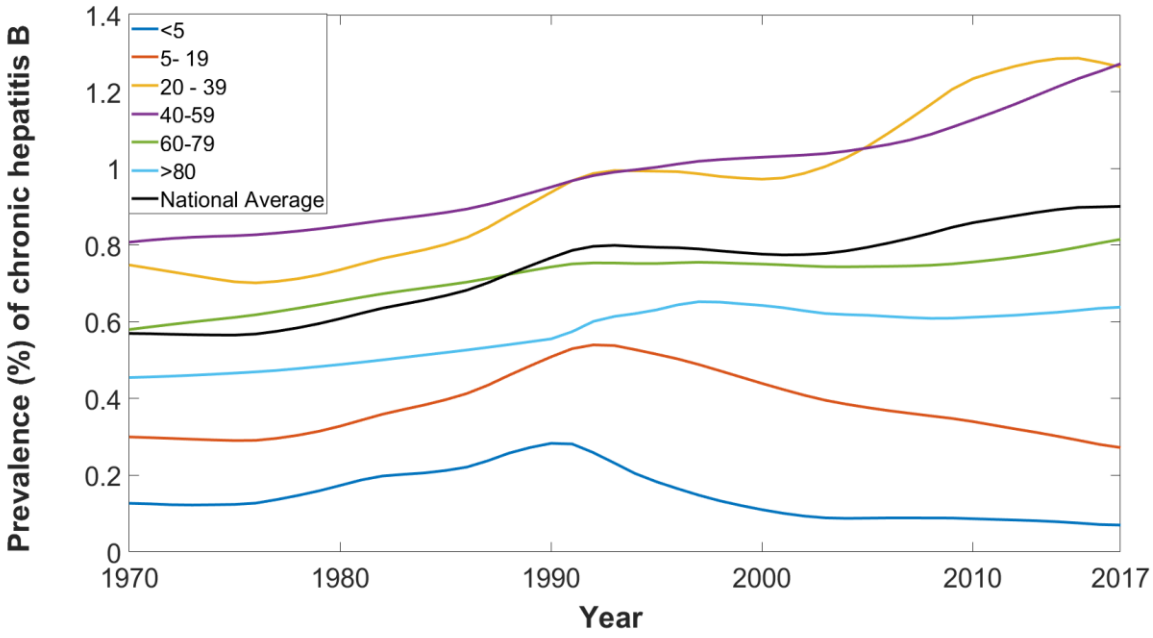
During 2017, an estimated 233, 947 (plausible range (PR) 190,250 to 265,760) people were living with CHB in Australia. Modelled estimates show that the number of people living with CHB has increased over time in Australia, with an additional 86,355 people living with CHB in 2017 when compared to 2000 (Figure 3, Appendix Table A1). Following current trends, including migration, treatment uptake and historical and current vaccination uptake both in Australia and overseas, an estimated 261,268 (213,170 to 270,970) people will be living with CHB in Australia by 2030 (Figure 3).

Figure 3. Estimated number of people living with chronic hepatitis B in Australia over time, 1970-2030



The increase in estimated numbers of people living with CHB is partly driven by the increased population in Australia over time, however the prevalence of CHB has nearly doubled from 0.57% in 1970 to 0.97% in 2017 (Figure 4). Changes in prevalence over time varies across age groups. A decrease in prevalence can be seen from 1991 onwards in the under 5 year age group and the 5-19 year age group. This highlights the achievements of hepatitis B vaccination uptake especially among infants both domestically and internationally, the impact of which will extend into older age groups over time. The majority of people living with CHB in Australia were born overseas and acquired hepatitis B in their country of origin, and therefore changes in the size, country of origin and age distribution of Australia's migrant population will affect the epidemiology and future projections of hepatitis B in Australia.

Figure 4. Estimated prevalence of chronic hepatitis B in Australia by age group, 1970-2017



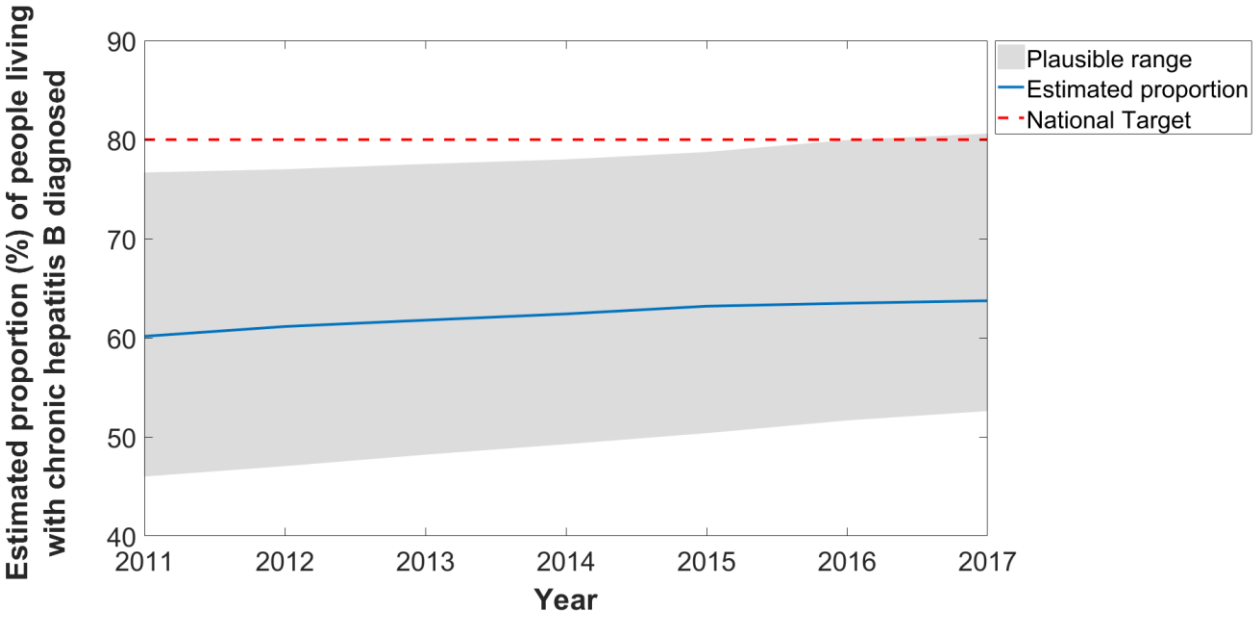
2. Proportion of people living with chronic hepatitis B in Australia who have been diagnosed*

* Please note: To align with targets written in the National Strategy, proportion diagnosed is reported rather than proportion remaining undiagnosed

In 2017, an estimated 149,118 people living with CHB in Australia had been diagnosed, representing 63.74% (PR 52.65% to 80.57%) of the total. Modelled trends show modest improvements in this proportion, increasing by 3.59% since 2011, when the proportion diagnosed was 60.15% (Figure 5, Appendix Table A2). Although the total number of people diagnosed has increased substantially each year, the population living with CHB also continues to increase (Figure 3), therefore the rate of diagnosis must increase substantially to have an impact on the proportion diagnosed.

The proportion diagnosed remains below the 2017 National Strategy target of 80% of people living with CHB being diagnosed, with 38,040 more people living with CHB requiring to be diagnosed to reach this target. If the current average annual increase of 0.39% in proportion diagnosed were to remain stable, Australia would not reach the 80% target until 2059. To reach WHO's Global Health Sector Strategy of 90% diagnosed by 2030, Australia's proportion diagnosed must increase by 2.04% every year, to reach 235,141 from the current level of 149,118 diagnosed in 2017.

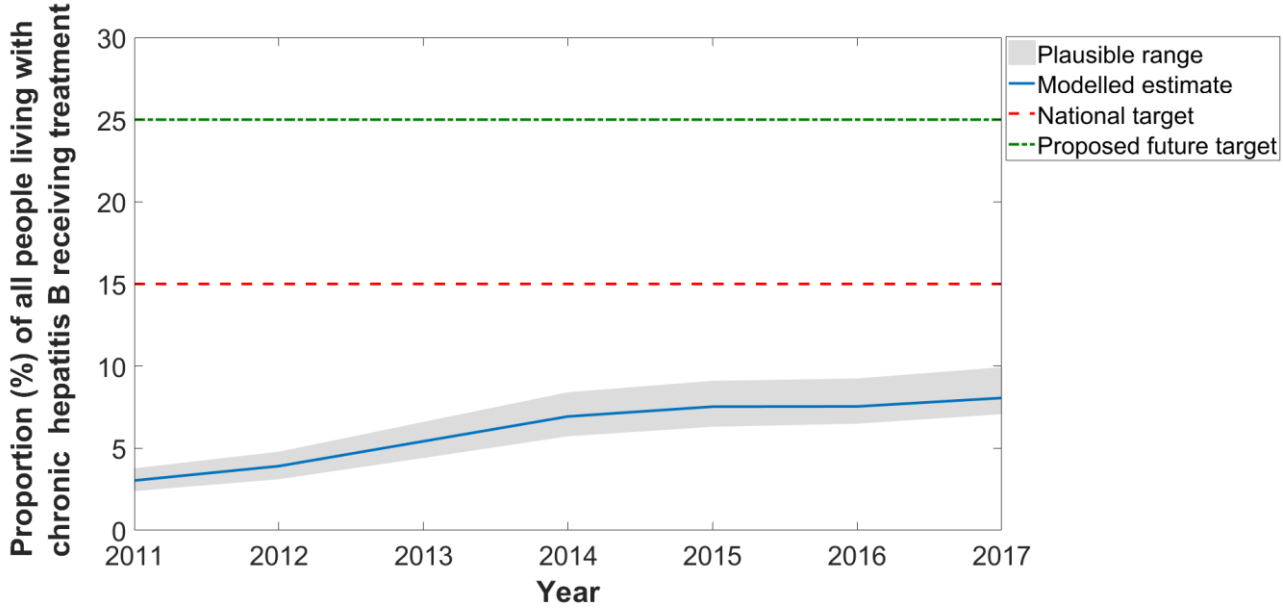
Figure 5. Estimated proportion of people living with chronic hepatitis B in Australia who have been diagnosed over time, 2011-2017



3. Proportion of people living with chronic hepatitis B who are dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme

During 2017, 18,851 people were dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme (PBS), which is an estimated 8.06% (PR 7.09% to 9.91%) of people living with CHB. Modelled trends since 2011 show an ongoing modest increase (average increase 0.72% per year) in this proportion (Figure 6, Appendix Table A3), with the current estimated uptake being half the National Strategy target for 2017 of 15%. To have reached this target an additional 16,242 people living with CHB would need to being receiving antiviral treatment in 2017. With current trends in uptake it will be 2027 before 15% of Australians living with CHB will be receiving treatment.

Figure 6. Estimated proportion of people living with chronic hepatitis B in Australia who are dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme over time, 2011-2017



Treatment target

The number of people dispensed drugs for treatment of CHB is usually reported as a proportion of the total number of people living with hepatitis B. This is because the dynamic natural history of hepatitis B and the various phases of infection mean that the minority of people living with CHB require treatment. Current guidelines recommend antiviral therapy only for those in an immune active phase of CHB (immune clearance, immune escape) or those living with cirrhosis with detectable HBV replication irrespective of phase(7).

The National Strategy included a treatment target of 15% by 2017, representing a conservative estimate of the proportion of people living with CHB who require antiviral treatment. This estimate was based on limited overseas data, and the plausible range for the proportion of people living with CHB who are eligible for treatment has been estimated to be between 10-25%(8-10). The true proportion of people living with chronic hepatitis B who require treatment will vary by hepatitis B genotype, age group, sex, and other factors, and has not been estimated for Australia. The modelling undertaken for this project, which incorporates the phase of CHB and the proportion of people living with cirrhosis, enables estimation of the number of people living with CHB eligible for antiviral treatment in Australia for the first time.

In 2017, an estimated 71,544 (PR 55,622 to 87,649) people living with CHB were eligible for antiviral treatment, representing 30.58% (PR 23.78% to 37.47%) of those living with CHB. This estimate supports the increased treatment target of 20% of people living with CHB being on antiviral treatment as contained in the National Hepatitis B Strategy 2018-2022, while

suggesting this remains a conservative target. In the future, higher treatment targets (for example, 25% of people living with CHB) may more accurately reflect the proportion of Australians living with CHB who require treatment (Figure 6).

Based on this modelling, Australia is currently treating one-quarter of those estimated to require treatment in 2017. To reach the WHO Global Health Sector Strategy of 80% of eligible people with CHB treated by 2030, the number of people receiving antiviral treatment in Australia would need to increase from 18,851 in 2017 to 68,162 in 2030. An average annual increase of 1.73% in treatment uptake was observed in the previous five years; if this trend were to remain stable, Australia would not reach the WHO 2030 elimination target until 2048.

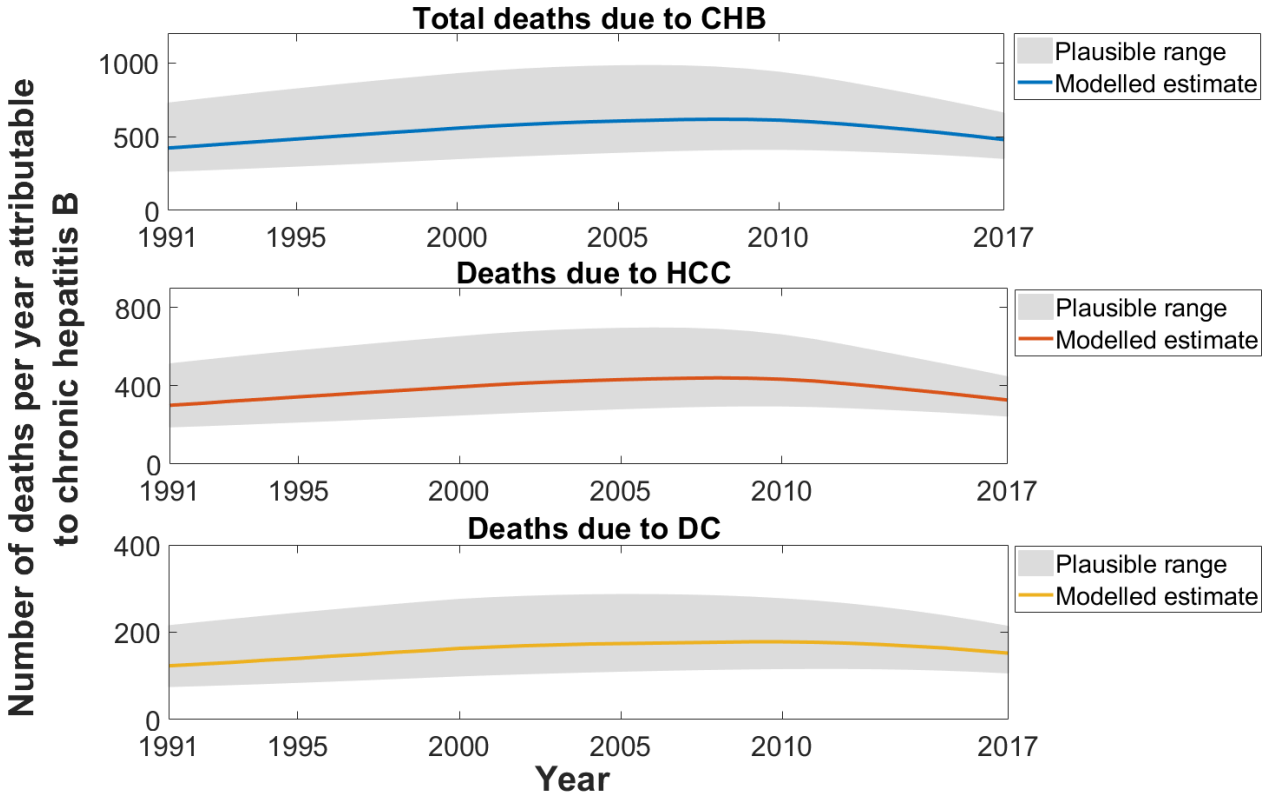
4. Burden of disease attributable to chronic hepatitis B in Australia

In 2017 an estimated 479 (PR 352 to 658) people died due to CHB in Australia. The total number of estimated attributable deaths has changed over time, increasing from 422 in 1991 to a peak of 617 deaths in 2008 followed by a gradual decline (Figure 7, Appendix Table A4). This decrease in estimated deaths is due to the introduction and scaling up of effective antiviral treatment in Australia during the last two decades, and the resulting reduction in CHB-associated mortality in those most at risk of adverse outcomes.

Deaths due to CHB are caused by the development of decompensated cirrhosis (DC); and/or hepatocellular carcinoma (HCC), the most common form of liver cancer. In Australia, the majority of estimated deaths due to CHB were attributable to HCC, which were responsible for 327 (PR 245 to 445) deaths in 2017, while 152 (PR 107 to 213) people died due to DC. Deaths due to both causes have decreased over the last decade, however the decline has been more pronounced for DC (35% reduction, from peak of 154 in 2002) than for HCC (17% reduction, from the peak of 367 in 2004, Figure 7).

The impact of treatment in reducing the risk of death due to CHB may be more pronounced for DC compared to HCC due to the underlying clinical factors in relation to treatment impact. While antiviral treatment has been demonstrated to reduce the risk of development of HCC, the impact of antiviral treatment once HCC is diagnosed is relatively minor. In contrast, antiviral treatment not only prevents progression to cirrhosis and then to DC, in addition antiviral treatment can be effective even when provided late in the disease course, resulting in re-compensation of liver disease. In coming years, increasing the uptake of timely treatment in people living with CHB (i.e. before the development of cirrhosis) will accelerate the reduction in HCC attributable deaths.

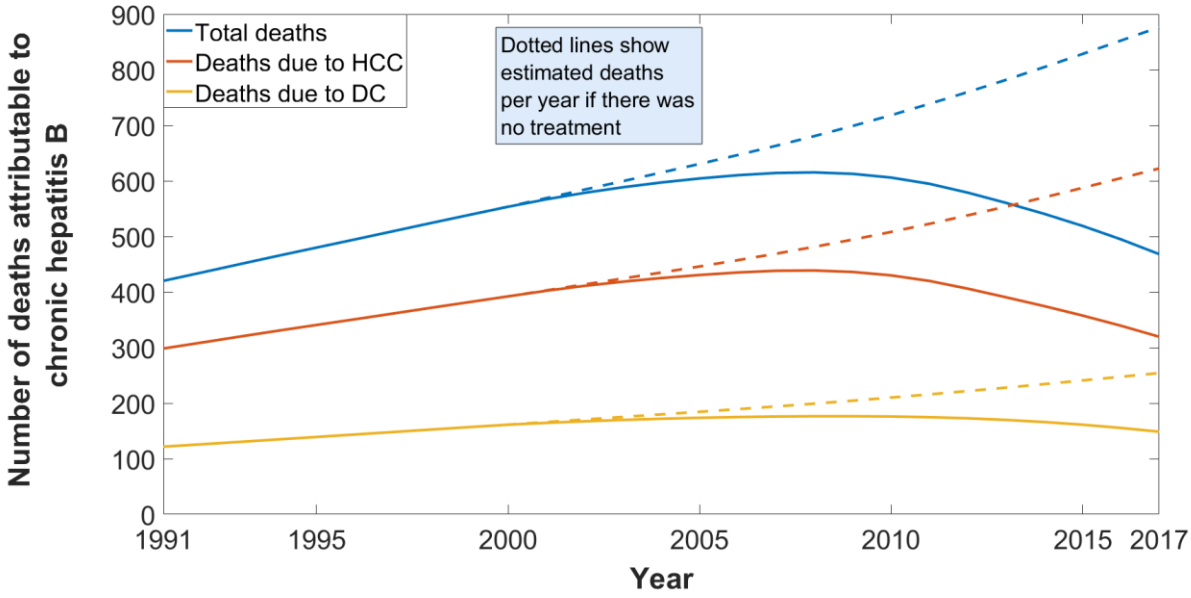
Figure 7. Estimated number of deaths attributable to chronic hepatitis B in Australia over time, 1991-2017



In the modelling undertaken for this activity, deaths due to DC and HCC have been modelled separately. The new modelling approach also allows for estimation of the impact of treatment on these outcomes at a population level. The modelled results suggest that without antiviral treatment, the number of attributable deaths would have continued to increase over time, with 893 CHB attributable deaths estimated in 2017 if no treatment had been available (Figure 8). Our assessment estimates that in 2017, 414 lives were saved due to treatment, with a total of 2,315 lives saved since the introduction of antiviral treatment for CHB.

Although the reduction in deaths has been pronounced since the introduction of antiviral treatment, the current rate of decline in the number of CHB related deaths is insufficient to reach the WHO Global Health Sector Strategy 2030 target of a 65% reduction in hepatitis B related deaths compared to 2015. To reach this target, the total number of CHB attributable deaths must fall to 184 deaths. If the current rate of reduction were to stay stable, Australia would not reach this target until 2042.

Figure 8. Estimated number of deaths attributable to chronic hepatitis B in Australia, treatment vs no treatment, 1991 – 2017



Summary State and Territory Specific Estimates

Table 2. Australian summary for hepatitis B indicator point estimates by jurisdictions, 2017

State/Territory	People living with CHB	Diagnosed (%)	Treatment uptake (%)	Total deaths attributable to CHB	HCC deaths attributable to CHB	DC deaths attributable to CHB
ACT	3,272	55.80%	8.86%	7	5	2
NSW	79,685	71.99%	11.32%	129	88	41
NT	3,708	77.47%	5.96%	12	8	4
QLD	33,585	54.72%	5.72%	86	59	27
SA	12,545	40.14%	6.06%	31	21	10
TAS	1,464	42.64%	5.19%	4	3	1
VIC	70,737	51.63%	7.56%	154	105	49
WA	22,799	46.80%	5.34%	59	41	18
Australia	233,947	63.74%	8.06%	479	327	152

Note: As each state and territory is modelled separately, the sum of indicator variables across states may not equal the modelled National estimate.

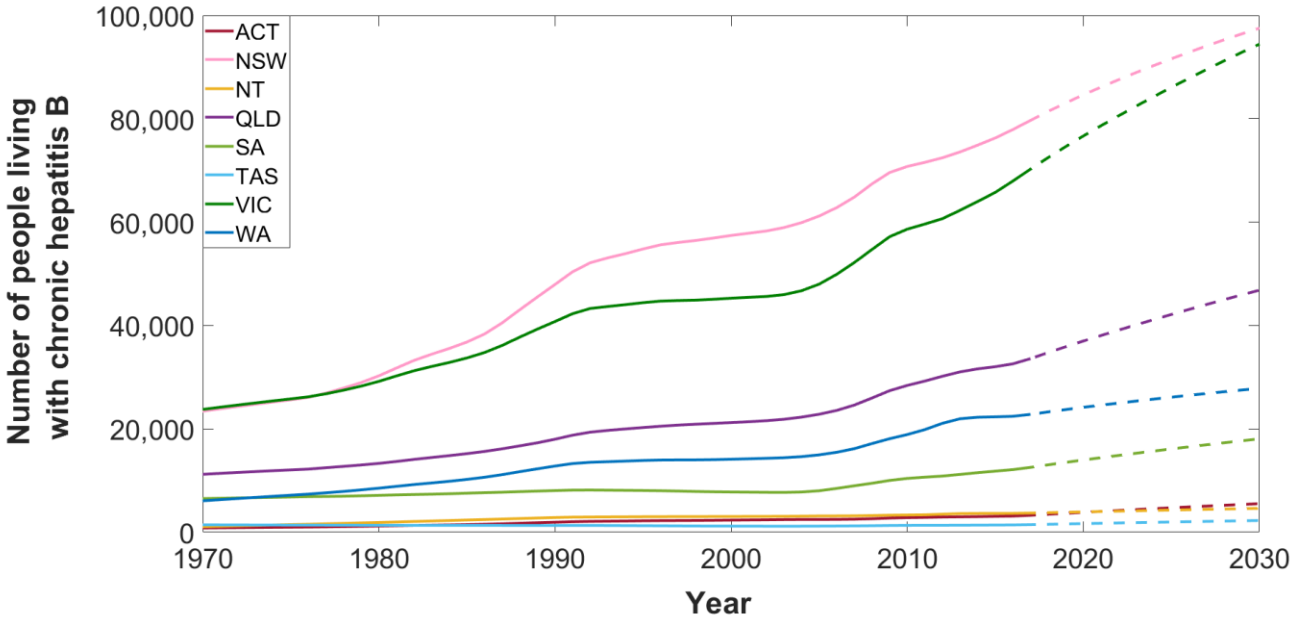
Detailed State and Territory Specific Estimates

1. Number of people living with chronic hepatitis B in Australia.

Modelled estimates show that the number of people living with CHB has increased over time in all jurisdictions (Figure 9, Appendix Table A1). During 2017, NSW and VIC had the highest estimates, with 79,685 and 70,737 people living with CHB respectively (Table 3). Tasmania had the lowest estimate with 1,464 number of people living with CHB.

Similar to national estimates, differences in overseas migration affect the epidemiology and future projections of hepatitis B across jurisdictions, as demonstrated in the differential increases over time (Figure 9).

Figure 9. Estimated number of people living with chronic hepatitis B by jurisdiction over time, 1970-2030



Please note: Dotted lines represent modelled projection estimates.

Table 3. Estimated number of people living with chronic hepatitis B by jurisdictions in 2017

State/Territory	People living with CHB	Plausible range	
		Minimum	Maximum
ACT	3,272	3,179	4,355
NSW	79,685	71,260	97,279
NT	3,708	3,698	4,386
QLD	33,585	29,407	37,052
SA	12,545	10,955	14,853
TAS	1,464	1,326	1,847
VIC	70,737	57,685	81,130
WA	22,799	20,037	28,025

2. Proportion of people living with chronic hepatitis B in Australia who have been diagnosed

Since 2011 there have been modest increases in the estimated proportion of people living with CHB who have been diagnosed in all jurisdictions (Figure 10, Appendix Table A2). The estimated proportion diagnosed varied greatly between jurisdictions, with NT (77.47%) and NSW (71.99%) having the highest proportion diagnosed in 2017. Estimates for all other states and territories were below the national average (63.74%), with ACT (55.80%), QLD (54.72%)

and VIC (51.63%) exceeding 50%. Estimates for WA (46.80%), TAS (42.64%) and SA (40.14%) suggest that the majority of the people living with CHB in these jurisdictions remain undiagnosed.

No jurisdiction reached the 2017 National Strategy target of 80% of people living with CHB being diagnosed. Following current diagnostic trends, NT and NSW will reach the 80% diagnosed target in 2019 and 2028, respectively, much sooner than the projected national estimate of 2059.

As the proportion diagnosed is dependent on routinely collected surveillance data, disparities between states and territories will be impacted by variations in screening practices and in underlying population differences in each jurisdiction, such as the level of interstate migration after diagnosis (which may be more common in some jurisdictions) and the number of correctional and detention facilities, which may have high rates of testing.

Figure 10. Estimated proportion of people living with chronic hepatitis B who have been diagnosed over time, by jurisdiction 2011-2017

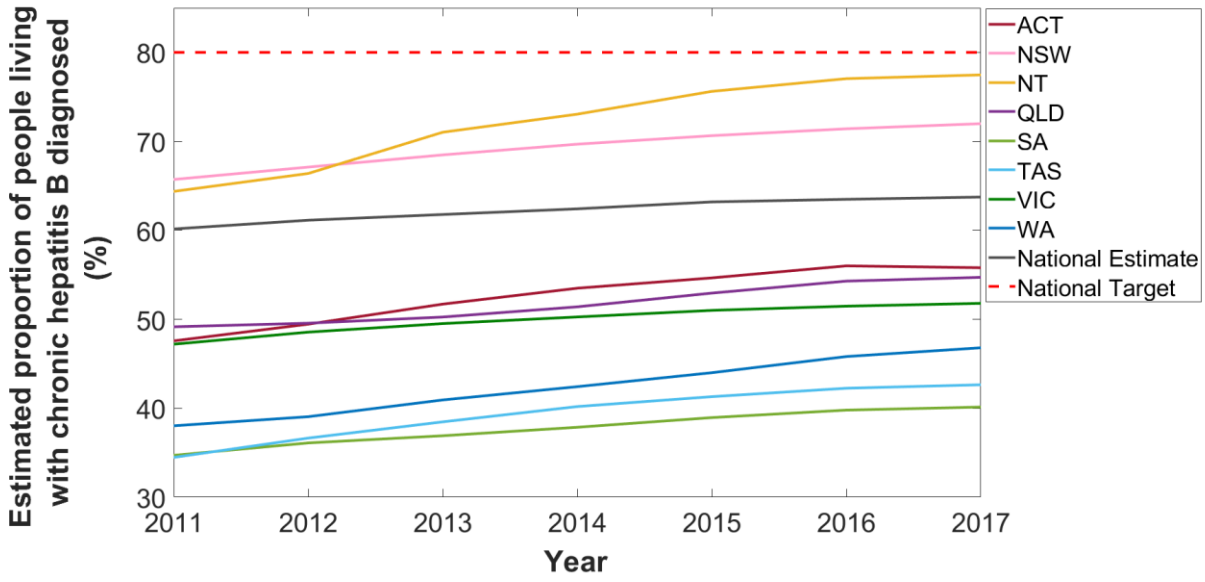


Table 4. Estimated proportion of people living with chronic hepatitis B who have been diagnosed by jurisdictions in 2017

State/Territory	Proportion diagnosed	Plausible range	
		Minimum	Maximum
ACT	55.80%	40.63%	62.19%
NSW	71.99%	55.56%	82.06%
NT	77.47%	63.55%	81.77%
QLD	54.72%	47.26%	64.22%
SA	40.14%	30.38%	48.83%
TAS	42.64%	34.10%	48.82%
VIC	51.63%	40.35%	66.67%
WA	46.80%	36.11%	56.12%
Australia	63.74%	52.65%	80.57%

3. Proportion of people living with chronic hepatitis B who are dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme

As previously described in the National Hepatitis B Mapping Report(6), the proportion of people living with CHB receiving antiviral treatment has increased over time in all states and territories (Figure 11, Appendix Table A3). Treatment uptake varied greatly between jurisdictions, with NSW (11.32%) and ACT (8.86%) estimated to have the highest proportion of people with CHB receiving treatment in 2017 (Table 5). All other states and territories were below the national average for treatment uptake, which was 8.06%; VIC (7.56%), SA (6.06%), NT (5.96%), QLD (5.72%), WA (5.34%), TAS (5.19%).

No jurisdiction reached the 2017 National Strategy target of 15% antiviral treatment uptake. Following current trends, NSW and ACT will reach the 15% treatment uptake target in 2022 and 2026, respectively. For jurisdictions with lower estimated treatment uptake, WA would not reach the target until 2037, and TAS would not reach the 15% target until 2038. Other states varied according to population and treatment uptake trends, with jurisdictions reaching the 15% treatment uptake target in 2030 for NT, 2032 for VIC, 2035 for QLD and 2036 for SA.

Figure 11. Estimated proportion of people living with chronic hepatitis B who are dispensed drugs for the treatment of hepatitis B through the PBS across jurisdictions over time, 2011-2017

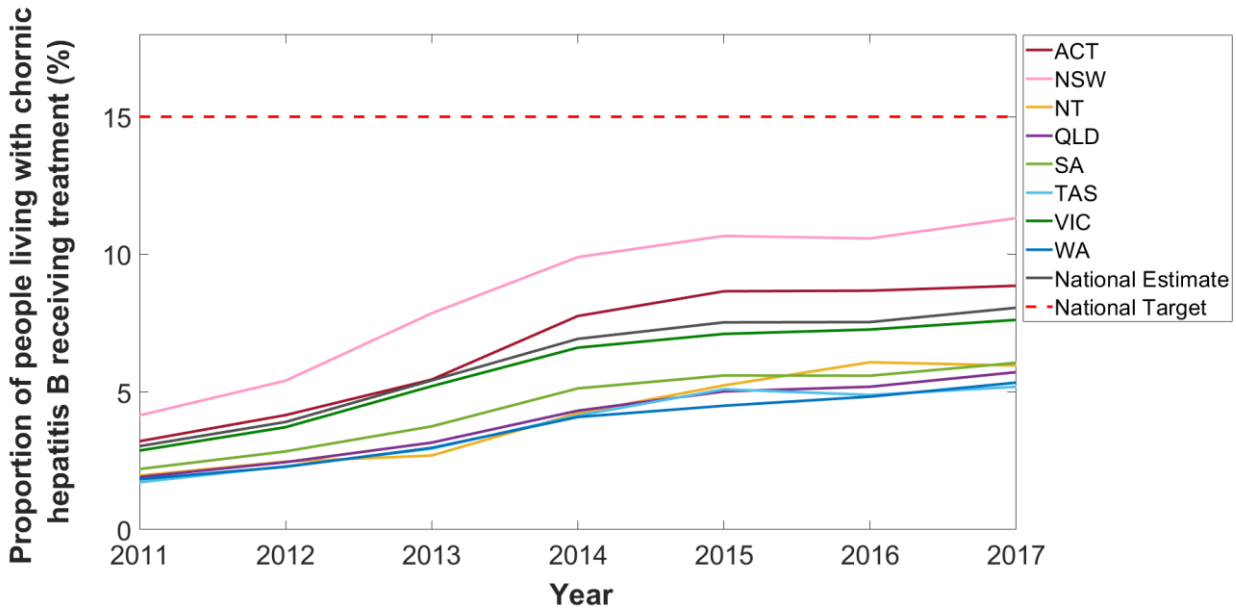


Table 5. Estimated proportion of people living with chronic hepatitis B who received treatment through the PBS by jurisdictions in 2017

State/Territory	Proportion receiving treatment	Plausible range	
		Minimum	Maximum
ACT	8.86%	6.66%	9.12%
NSW	11.32%	9.27%	12.65%
NT	5.96%	5.04%	5.98%
QLD	5.72%	5.18%	6.53%
SA	6.06%	5.12%	6.94%
TAS	5.19%	4.12%	5.73%
VIC	7.56%	6.60%	9.28%
WA	5.34%	4.35%	6.08%
Australia	8.06%	7.09%	9.91%

4. Burden of disease attributable to chronic hepatitis B in Australia

While national estimates demonstrated a gradual decline in the estimated deaths attributable to CHB from 2008 onwards, this was largely driven by those jurisdictions with the largest number of people living with CHB and on treatment (NSW and VIC), however this trend was not observed in all states and territories (Figure 12, Appendix Table A4).

VIC was estimated to have the largest burden of CHB attributable deaths in 2017 (154 deaths), however this has only been the case since 2011 (Table 6). Prior to that year, NSW had the highest number of deaths, however a more profound decline in total deaths were seen after 2006 reflecting the relatively higher treatment uptake in NSW when compared with VIC, where the decline in deaths has been less pronounced. In QLD, WA and TAS, the jurisdictions with the lowest treatment uptake, the total number of deaths attributable to CHB has marginally declined. Similar trends can be seen for both HCC (Figure 13, Appendix Table A5) and DC (Figure 14, Appendix Table A6) attributable deaths.

Figure 12. Estimated number of deaths attributable to chronic hepatitis B across jurisdictions, 1991-2017

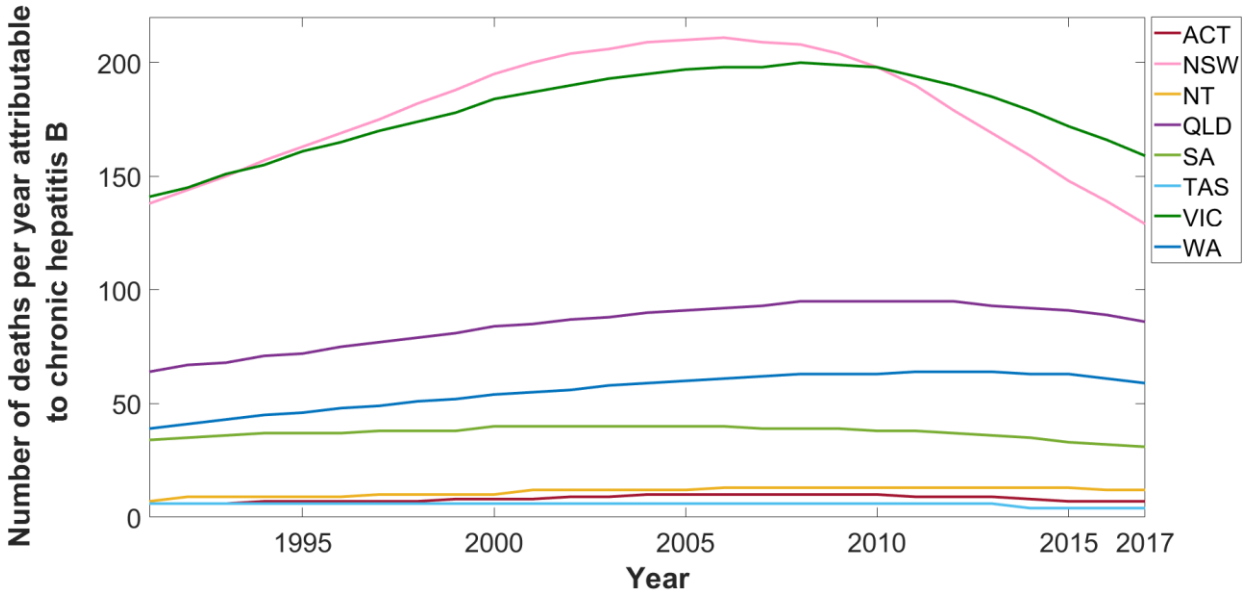


Table 6. Estimated number of total deaths attributable to chronic hepatitis B by jurisdictions in 2017

State/Territory	Total deaths attributable to CHB	Plausible range	
		Minimum	Maximum
ACT	7	6	11
NSW	129	108	188
NT	12	12	17
QLD	86	68	108
SA	31	23	46
TAS	4	3	6
VIC	154	108	226
WA	59	44	84

Figure 13. Estimated number of HCC deaths attributable to chronic hepatitis B across jurisdictions, 1991-2017

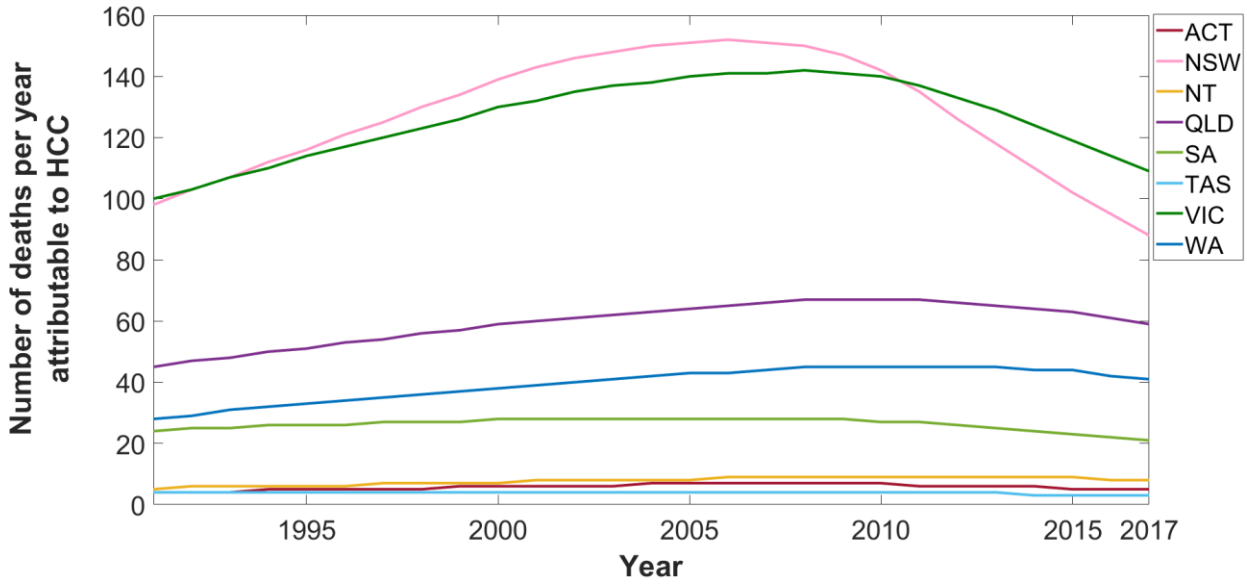


Figure 14. Estimated number of DC deaths attributable to chronic hepatitis B across jurisdictions, 1991-2017

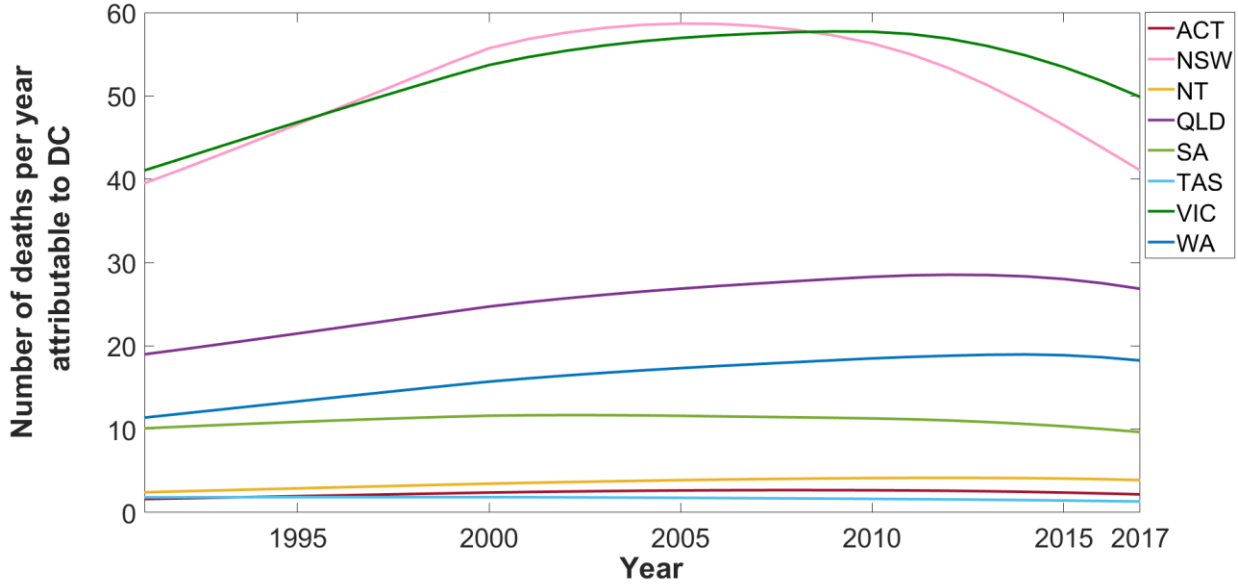


Table 7. Estimated number of HCC deaths and DC deaths attributable to chronic hepatitis B by jurisdictions in 2017

State/Territory	HCC deaths attributable to CHB	HCC Plausible range		DC deaths attributable to CHB	DC Plausible range	
		Minimum	Maximum		Minimum	Maximum
ACT	5	4	7	2	2	4
NSW	88	74	126	41	34	62
NT	8	8	11	4	4	6
QLD	59	47	74	27	21	34
SA	21	16	31	10	7	15
TAS	3	2	4	1	1	2
VIC	105	75	152	49	33	74
WA	41	31	58	18	13	26

Methodological Notes

Summary of mathematical model inputs

Mathematical Model Inputs	Source
Disease progression estimates	Published and grey literature, expert opinion
Australian demographic data	Australian Bureau of Statistics
Migration: Net overseas migration	Australian Bureau of Statistics
Migration: country of birth and age distribution 1951 – 1974 1974 – 1990 1991 – 2017 2018 – 2050	 Federation to Century's End Australian Bureau of Statistics Department of Social Services Australian Bureau of Statistics
HBV prevalence by country of birth	Published literature
HBV phase distribution	Published and grey literature, expert opinion
Treatment uptake	Pharmaceutical Benefits Scheme
Vaccination uptake	Australian Immunisation Register data

Mathematical Model

The estimates presented in this report were generated from new mathematical models based on previous work (11). The model is a dynamic age-structured deterministic mathematical model. The model population incorporates important demographic features such as births, migration, deaths and aging over time. The population is stratified into 18 age groups (those aged between 0 and 84 are grouped into 5-year age categories plus a final 85+ age group). Age groups were chosen to reflect the Australian population and to allow more accurate incorporation of the differential risks in acquiring hepatitis B and progression to chronic hepatitis B by age, plus uptake and impact of vaccination within Australia. The modelled population is dynamic (changes over time) and accounts for births and immigration, all-cause and hepatitis B related mortality, and emigration.

The model has been comprehensively revised and incorporates a large number of different elements to optimise representation of the transmission, epidemiology and progression of hepatitis B. The revised model incorporates 9 exclusive health states, representing the natural history of hepatitis B; susceptible, immune (through vaccination), acute infection, immune tolerant, immune clearance, immune control, immune escape, decompensated cirrhosis, hepatocellular carcinoma and resolved infection. Chronic hepatitis B health states have also been differentiated into non-cirrhotic and cirrhotic classifications and the provision or lack of provision of treatment. This results in the model consisting of a total of 21 health states. Each health state is broken down into age categories, which allows exploration of age-specific and health-state specific estimates, such as disaggregated mortality estimates for DC and HCC.

The new version of the model diagram can be found in Appendix Figure A1. Various data inputs and elements of the model are described below.

Disease progression estimates
Disease progression and transitions between each health state, including the impact of treatment on these, were incorporated based on literature review and expert opinions. Estimates represent annual transmission rates, with age dependent estimates incorporated where relevant and available.

Force of Infection
The force of infection (FoI) takes into account risk of both vertical or horizontal transmission of hepatitis B. Risk of infection between age groups varies. For example, risk of transmission from mother to child is incorporated by increasing the risk of infection from adults aged 20-40 to children aged 0-4 (youngest age group in model population). The force of infection incorporated is dynamic, meaning it is changes over time depending on the number of people who are living with chronic hepatitis B (i.e. those who contribute to the FoI acting on others).

Domestic vaccination
Information on vaccine uptake and vaccine efficacy by age group was used to determine an overall measure of the proportion of individuals receiving effective vaccination for hepatitis B in the Australian population.

Demographic data
Australian demographic data incorporated into the model included population numbers, birth numbers and mortality rates by age since 1951. This information was sourced from Australian Bureau of Statistics (ABS) (Catalogue numbers: 31010, 3105.0.65.001, 32220). Age specific mortality rates were derived from ABS life tables (3302.0.55.001) which report mortality rates by single year of age. Age-group mortality rates were derived by taking the average rate across the 5 years included in each given age group.

Migration
In addition to Australia specific demographic data, incoming migration by age and country of birth were also incorporated. Estimates of net overseas migration (NOM) produced by the ABS (Catalogue number 3412.0) were used to estimate total number of people entering the population from 1951 to 2050. Age and country of birth distributions were calculated using different sources dependent on time period and data availability, as outlined below.

1951 to 1974
The Department of Immigration resource Federation to Century's End was used to determine the number of permanent settlers to Australia by country of birth from 1951 to 1974(12). The number of settlers arriving from each country of birth were scaled up so that the total numbers equalled the NOM for each year. To estimate the total number in each age group we applied the age-distribution derived from the total number of migrants in Victoria during 1975 to 2006 as age distribution information was not available according to country of birth. Cowie (2) demonstrated the Victorian age distribution was comparable to published modelling studies in low endemic regions of hepatitis B, thus this was used as an approximation.

1975 to 1990
ABS migration data (catalogue number 3421.0) were used to determine the number of migrants entering by country of birth from 1975 to 1990. The number of people arriving from each country of birth were scaled up so that the total numbers equalled the NOM for each year. To estimate the total number in each age group we applied the age-distribution derived from the total number of migrants in Victoria during 1975 to 2006, as age distribution information was not available according to country of birth.

1991 to 2017
Requested Department of Social Services (DSS) settlement data were used to obtain country of birth and age-distributions of incoming migrants in Australia from 1991 to 2016. The number of people arriving from each country of birth were scaled up so that the total numbers equalled the NOM for each year.

2018 - 2050
Estimated NOM for the total number entering the population for 2018 to 2050 were calculated using ABS NOM projections, Series B (Catalogue number 3222.0). The average age distribution of migrants between 2014 and 2016 was used as future projections and country of birth distribution was assumed to equal the same distribution as 2017.

Prevalence
The number of people living with CHB in the population was derived using the estimated prevalence of CHB according to country of birth, obtained from established seroprevalence survey estimates. To take into account changing prevalence over time, due predominately to increases in infant vaccination in migration source countries, this updated model used varying prevalence estimates across different time periods and applied these to migration data according to age group and year of arrival for countries of birth for the majority migrants to Australia. Prevalence for the top 3 countries of birth for CHB was estimated using a separate method (see 'Direct estimation of immunisation impact' section, below).

1951 to 1990
At the start of the model (1951), the baseline prevalence of the Australian population was assumed to be 0.5%, representing a low prevalence country. This proportion was derived in Cowie(11) from published studies and fits with what is known about the historical prevalence of hepatitis B in Australia. The estimated prevalence according to country of birth derived in Cowie(11) were applied to incoming migrants who were born before 1991. Countries were divided into three categories, based on the prevalence during this period; low prevalence (0.5%), intermediate prevalence (5%) and high prevalence (10%). More information on country assignment of categories can be found in Cowie(11). These estimates are higher compared to the 1991-2017 which takes into account prevalence estimates in the pre-vaccination era.

1991 to 2017
For those migrating into Australia born in 1991 or later, prevalence estimates derived for the Hepatitis B Mapping Project: National Report 2016 were applied(6). These prevalence

estimates were taken from a number of local and international seroprevalence surveys. The most widely used source was a cohort of antenatal women diagnosed with CHB in NSW during 2000-2008 (13), supplemented with global systematic reviews of prevalence (14, 15). Antenatal estimates were adjusted upwards to correct for the discrepancy in CHB prevalence by sex(16). More information can be found in the Hepatitis B Mapping Report (see (https://www.ashm.org.au/HBV/hepatitis-b-mapping-reports/)).

Direct estimation of immunisation impact
A literature review was conducted to obtain age- and year-prevalence estimates for the 3 countries which had the highest numbers of people living with CHB in Australia - China, Vietnam and the Philippines(6). Data were extracted from a range of sources including seroprevalence surveys, modelling and review papers(14, 17-19). Specific prevalence estimates by country and year of birth were applied to incoming migrants. This allowed more robust estimations of CHB prevalence, given increasing vaccination uptake and thus lower prevalence in younger age groups, and changing migration age distributions over time. In the next iteration of the model, this method will be extended to additional migration source countries, dependent on data availability and quality.

Phase distribution
Individuals who acquired HBV infection in Australia enter into the model in the acute hepatitis B infection health state and progress through various states according to the transition estimates. However, individuals living with CHB migrate into Australia in different disease phases. The proportion of individuals living with chronic hepatitis B in each disease phase (immune tolerant, immune clearance, immune control and immune escape) by age group were derived for different world regions using published data and expert opinion(20-22). All source countries were categorised into three world regions (Asia/Pacific, Africa, Other) to account for differences in natural history of CHB infection in different populations.

Treatment
This revised model incorporates the impact of treatment for the first time. Differential uptake rates by disease phase were estimated, with proportions according to disease phase determined using expert opinion and literature reviews. To ensure our modelled estimates of the number of people receiving treatment accurately reflect empirical data, modelled estimates were fitted to treatment uptake derived from Pharmaceutical Benefits Scheme (PBS) data (see below).

Data obtained from PBS records were used to derive the number of people on treatment in Australia each year since 2000, in order to parameterise the model and generate update estimates. This source includes all services provided through Medicare. Treatment data represent the number of individuals prescribed any drug listed on the PBS for the treatment of CHB during this time period including: adefovir, entecavir, lamivudine, pegylated interferon alfa-2a, telbivudine and tenofovir. It excludes individuals prescribed lamivudine or tenofovir for HIV infection.

Plausible range
The plausible ranges reported were derived by allowing the FoI, migrant population prevalence, proportion of migrants with CHB living with cirrhosis, HBV mortality and other disease transition estimates to vary according to prior knowledge of possible distributions. This was achieved using latin-hypercube sampling (LHS), as described by Marino et al (23). The mathematical model was run using 100 different combinations of these varied parameters (FoI, migrant populations prevalence, proportion of migrants living with CHB assumed to be living with cirrhosis by age, HBV mortality rates and other disease transition estimates), which produced a range of overall estimates. The minimum and maximum estimates produced were then used to define the plausible range around the point estimate value.

Jurisdictional estimates
The national model was applied to each state and territory using state specific demographic information obtained from the ABS including births, deaths, migration and age distribution. Some of the data sources differed from the national model due to availability and appropriateness of data. For example, with the exception of Victoria, the age distribution of incoming migrants by country of birth during the period 1951 to 1990 was not available. For Victoria we used the age distribution of people immigrating to Victoria between 1975 to 2006 and retroactively applied this back to 1951 (as was also performed for the national model). For all other states and territories, the overall age distribution of permanent settlers arriving in 1991 (obtained from DSS settlement data) were applied back to 1951.

Prior to 1990, Census data poorly reflect the actual number of Aboriginal and Torres Strait Islander people living in Australia(24), which has a particularly substantial impact in the NT, where Indigenous people represent greater than 25% of the population. To better reflect total population numbers in the NT in the years prior to 1990, reported populations and number of births were adjusted upwards each year in accordance with ABS data regarding the proportion of Aboriginal and Torres Strait Islander people resident in the NT (30%) and the proportion of births for Aboriginal and Torres Strait Islander people (40%) during the period 1991 to 2016 (ABS catalogue 3238.0). For those states where the estimated proportion of people living with CHB who were Aboriginal and/or Torres Strait Islander was greater than 15% (QLD and NT), the prevalence among the Australian-born population was adjusted in accordance with local data(25, 26). Further model development will incorporate adjustments for the remaining states and territories, dependent on the availability of appropriate data.

Methodology for Indicators

1: Estimating the number of people living with chronic hepatitis B in Australia
The total number of people living with chronic hepatitis B in Australia and the number according to age group and state and territory are direct outputs of the model. Prevalence of CHB was calculated using the number of people living with chronic hepatitis B as the numerator and the total population according to ABS numbers as the denominator.

2: Estimating the proportion of people living with chronic hepatitis B in Australia who have not been diagnosed

The number of people living with hepatitis B who have been diagnosed is derived using the model output of the number of people who have ever lived with CHB in Australia since 1951 as the denominator and the cumulative number of notifications of hepatitis B from 1971 to 2017 as the numerator. Notification data has been sourced from the National Notifiable Diseases Surveillance (NNDSS) system.

NNDSS data are collated from all states and territories, allowing estimation of the proportion of people diagnosed according to jurisdiction. However, notifications are nationally reported as de-identified records to the NNDSS, and may contain duplicates if individuals have been diagnosed in multiple jurisdictions, inflating the number ever diagnosed. A national linkage study has commenced under the auspices of this project which aims to quantify the extent of duplicate reporting across jurisdictions to the NNDSS for both hepatitis B and hepatitis C, allowing identification of the true number of individuals diagnosed and refining of modelled estimates. When the results of this national notifications linkage project are available the results will be incorporated into this model.

3: Estimate the proportion of people living with chronic hepatitis B who are dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme
The proportion of people living with chronic hepatitis B who are receiving treatment was calculated using the number of people receiving treatment (obtained from PBS data) as the numerator and the modelled number of people living with CHB as the denominator.

The proportion eligible for treatment is derived by dividing the modelled number of people eligible for treatment by the modelled number of all people living with chronic hepatitis B.

4: Estimate the burden of disease attributable to chronic hepatitis B in Australia
The number of deaths attributable to CHB, and specifically due to DC and HCC, in Australia is a direct output of the model.

Appendix

Table A1. Model output for the number of people living with chronic hepatitis B in Australia per year, 1970-2030

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
1970	74324	821	23419	1076	11208	6512	1428	23569	6074
1971	75610	854	23882	1157	11389	6575	1419	23982	6301
1972	76852	886	24331	1241	11567	6634	1409	24380	6524
1973	78060	918	24767	1322	11738	6691	1400	24767	6741
1974	79258	949	25200	1404	11903	6747	1390	25149	6955
1975	80395	979	25611	1479	12055	6811	1382	25515	7162
1976	81639	1007	26090	1546	12214	6888	1377	25906	7373
1977	83568	1046	26917	1633	12479	6921	1368	26475	7629
1978	85778	1093	27888	1715	12740	6969	1360	27160	7895
1979	88277	1144	28961	1800	13012	7047	1352	27933	8196
1980	91216	1200	30261	1889	13320	7135	1345	28838	8522
1981	94560	1262	31770	1980	13686	7222	1338	29878	8875
1982	97845	1322	33243	2078	14092	7297	1333	30868	9225
1983	100609	1369	34448	2169	14457	7362	1325	31686	9533
1984	103280	1417	35558	2262	14818	7444	1321	32442	9852
1985	106296	1473	36796	2359	15203	7553	1323	33303	10221
1986	109865	1542	38349	2455	15629	7654	1325	34343	10635
1987	114477	1630	40506	2548	16137	7740	1319	35703	11136
1988	119883	1734	43039	2649	16709	7852	1317	37302	11716
1989	125141	1837	45513	2747	17297	7958	1315	38837	12265
1990	130360	1936	47932	2844	17992	8057	1314	40296	12802
1991	135982	2033	50392	2916	18774	8146	1315	41802	13285
1992	140092	2100	52136	2943	19355	8162	1313	42800	13530
1993	141833	2136	53086	2962	19702	8133	1299	43173	13644
1994	143007	2170	53899	2979	19984	8103	1280	43520	13760
1995	144308	2212	54800	3000	20252	8073	1262	43893	13884
1996	145427	2245	55609	3013	20508	8028	1243	44191	13968
1997	145906	2263	56067	3020	20726	7960	1223	44291	13992
1998	146258	2280	56451	3027	20899	7885	1205	44362	14003
1999	146842	2308	56919	3035	21053	7823	1192	44524	14042
2000	147592	2345	57420	3043	21215	7785	1184	44723	14117
2001	148375	2375	57850	3053	21378	7755	1175	44945	14208
2002	149254	2403	58278	3063	21575	7722	1166	45203	14299
2003	150728	2445	58943	3073	21855	7705	1160	45633	14415
2004	153224	2470	59899	3102	22270	7780	1168	46465	14622
2005	158207	2468	61179	3139	22825	8020	1184	47808	14968
2006	165648	2485	62809	3150	23569	8478	1202	49784	15470

2007	173397	2525	64847	3172	24607	8983	1225	52089	16168
2008	181641	2611	67398	3229	25965	9473	1258	54608	17152
2009	189319	2738	69592	3293	27384	10019	1304	57082	18089
2010	194236	2820	70770	3333	28399	10409	1334	58598	18892
2011	198401	2868	71562	3373	29246	10653	1340	59676	19855
2012	203086	2934	72451	3488	30177	10863	1348	60803	21073
2013	209883	2974	73579	3604	31021	11185	1360	62494	21954
2014	215780	3016	74897	3637	31608	11521	1376	64272	22250
2015	220774	3072	76281	3644	32023	11817	1392	66100	22325
2016	227976	3122	77909	3653	32577	12112	1411	68362	22429
2017	233947	3272	79685	3708	33585	12545	1464	70737	22799
2018	238391	3471	81417	3786	34754	13038	1533	73023	23276
2019	242328	3664	83061	3862	35887	13513	1600	75219	23731
2020	245790	3851	84629	3937	36989	13975	1666	77338	24167
2021	248808	4033	86117	4009	38056	14420	1730	79373	24581
2022	251474	4210	87551	4080	39101	14855	1793	81353	24982
2023	253819	4385	88942	4150	40128	15283	1855	83292	25373
2024	255840	4557	90293	4220	41138	15704	1917	85190	25755
2025	257538	4725	91602	4289	42131	16117	1977	87047	26127
2026	258917	4891	92869	4356	43106	16522	2037	88862	26489
2027	259975	5054	94096	4423	44064	16920	2097	90635	26841
2028	260716	5213	95281	4490	45004	17310	2155	92366	27184
2029	261141	5370	96426	4555	45927	17691	2213	94054	27517
2030	261268	5524	97529	4621	46832	18064	2269	95700	27840

Table A2. Model output for the proportion of people living with chronic hepatitis B in Australia who have been diagnosed, 2011-2017

Year	National (%)	ACT (%)	NSW (%)	NT (%)	QLD (%)	SA (%)	TAS (%)	VIC (%)	WA (%)
2011	60.15	47.57%	65.72%	64.37%	49.16%	34.71%	34.48%	46.95%	38.03%
2012	61.14	49.45%	67.10%	66.39%	49.56%	36.10%	36.65%	48.31%	39.05%
2013	61.78	51.70%	68.48%	71.02%	50.25%	36.91%	38.47%	49.28%	40.93%
2014	62.41	53.49%	69.68%	73.05%	51.40%	37.86%	40.19%	50.04%	42.43%
2015	63.19	54.65%	70.64%	75.62%	52.94%	38.95%	41.30%	50.80%	43.99%
2016	63.49	56.00%	71.41%	77.05%	54.29%	39.79%	42.25%	51.29%	45.81%
2017	63.74	55.80%	71.99%	77.47%	54.72%	40.14%	42.64%	51.63%	46.80%

Table A3. Model output for the proportion of people living with chronic hepatitis B in Australia who are dispensed drugs for the treatment of hepatitis B through the PBS, 2011-2017

Year	National (%)	ACT (%)	NSW (%)	NT (%)	QLD (%)	SA (%)	TAS (%)	VIC (%)	WA (%)
2011	3.03	3.21	4.15	1.96	1.91	2.2	1.72	2.87	1.83
2012	3.91	4.16	5.41	2.47	2.45	2.84	2.3	3.71	2.28
2013	5.42	5.45	7.86	2.69	3.16	3.75	2.94	5.19	2.97
2014	6.93	7.76	9.9	4.23	4.32	5.13	4.14	6.58	4.09
2015	7.53	8.66	10.67	5.24	5.02	5.6	5.1	7.08	4.5
2016	7.54	8.68	10.58	6.08	5.19	5.59	4.89	7.22	4.83
2017	8.06	8.86	11.32	5.96	5.72	6.06	5.19	7.56	5.34

Table A4. Model output for the total number of deaths attributable to chronic hepatitis B in Australia, 2011-2017

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
2011	600	9	190	13	95	38	6	191	64
2012	585	9	179	13	95	37	6	187	64
2013	567	9	169	13	93	36	6	181	64
2014	548	8	159	13	92	35	4	175	63
2015	527	7	148	13	91	33	4	168	63
2016	504	7	139	12	89	32	4	162	61
2017	479	7	129	12	86	31	4	154	59

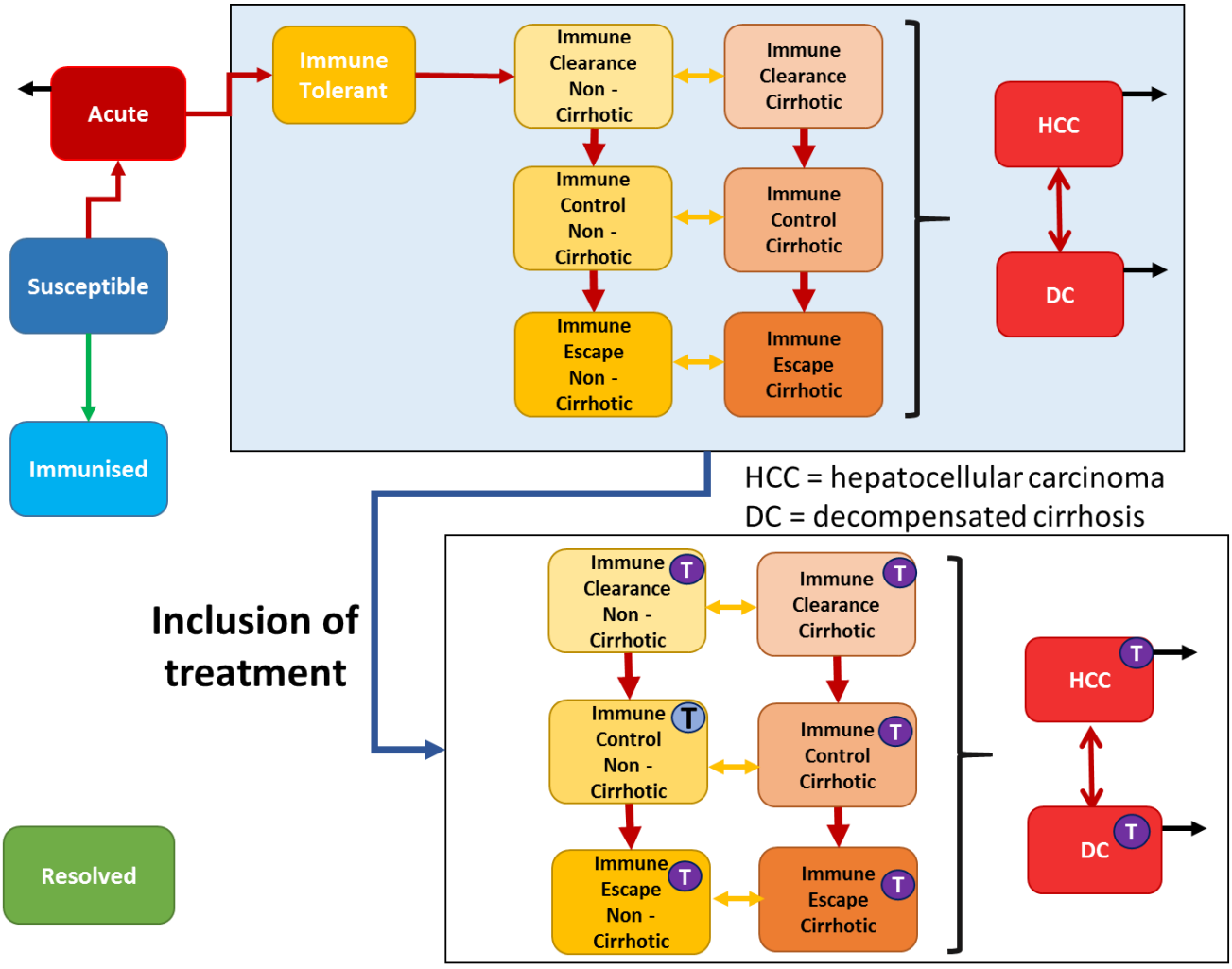
Table A5. Model output for the total number of HCC deaths attributable to chronic hepatitis B in Australia, 2011-2017

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
2011	424	6	135	9	67	27	4	135	45
2012	410	6	126	9	66	26	4	131	45
2013	395	6	118	9	65	25	4	126	45
2014	379	6	110	9	64	24	3	121	44
2015	363	5	102	9	63	23	3	116	44
2016	345	5	95	8	61	22	3	111	42
2017	327	5	88	8	59	21	3	105	41

Table A6. Model output for the total number of DC deaths attributable to chronic hepatitis B in Australia, 2011-2017

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
2011	177	3	55	4	28	11	2	56	19
2012	175	3	53	4	29	11	2	56	19
2013	172	3	51	4	28	11	2	55	19
2014	168	2	49	4	28	11	1	54	19
2015	164	2	46	4	28	10	1	52	19
2016	158	2	44	4	28	10	1	51	19
2017	152	2	41	4	27	10	1	49	18

Figure A1. Mathematical model diagram



*Decompensated Cirrhosis (DC), Hepatocellular Carcinoma (HCC), Compartments with 'T' represent treatment eligible states. Black arrows represent hepatitis B related deaths.

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