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 2019

WHO Collaborating Centre for Viral Hepatitis, Doherty Institute for Infection and Immunity
Prepared by: Nicole Romero, Karen McCulloch, Nicole Allard,
Jennifer MacLachlan and Benjamin Cowie

Contact Information

WHO Collaborating Centre for Viral Hepatitis
Victorian Infectious Diseases Reference Laboratory, Doherty Institute for Infection and Immunity
Contact: Nicole Romero
Level 5, 792 Elizabeth Street, Melbourne VIC 3000
Tel: 03 9342 9670 Fax: 03 9342 9380
Email: nicole.romero@mh.org.au

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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
GHSS	Global Health Sector Strategy
HCC	Hepatocellular carcinoma
LHS	Latin-hypercube sampling
MBS	Medicare Benefits Schedule
National Strategy	Australia's 3rd National Hepatitis B Strategy 2018-2022
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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Executive Summary

Number of people living with chronic hepatitis B:

- In 2019 an estimated 230,154 people were living with chronic hepatitis B (CHB) in Australia, representing 0.90% of the population.
- The prevalence of CHB has continued to increase in Australia from 0.74% in 2004.
- A decrease in prevalence can be seen from 1991 onwards in under 20-year olds, highlighting the achievements of hepatitis B vaccination uptake.

Chronic hepatitis B diagnosis:

- An estimated 158,435 people living with CHB in Australia in 2019 had been diagnosed, representing 68.8% of the total.
- The proportion diagnosed in 2019 remains below the National Strategy target of 80%, with 33,696 more people living with CHB requiring diagnosis to reach this by 2022.

Chronic hepatitis B engagement in care:

- During 2019, an estimated 50,897 people were engaged in care for their CHB, receiving either antiviral treatment or monitoring, representing 22.1% of the total.
- The proportion engaged in care in 2019 remains below the National Strategy target of 50%, with 69,185 more people required to be in care to reach this by 2022.

Chronic hepatitis B treatment:

- In 2019, 22,587 people were dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme, which is an estimated 9.8% of all people living with CHB.
- The proportion on treatment in 2019 remains below the National Strategy target of 20% with 25,446 more people requiring treatment to reach this target by 2022.

Burden attributable to chronic hepatitis B:

- The number of deaths attributable to CHB in 2019 was estimated to be 427. Most deaths were attributable to hepatocellular carcinoma (HCC), which was responsible for 316 deaths, while 111 people died due to decompensated cirrhosis (DC).

Jurisdictional disparities:

- Substantial differences in estimated prevalence, access to care and burden of disease in 2019 are noted between states and territories, and in trends over time:
    - Prevalence of CHB ranged from 0.32% to 1.78%
    - The proportion diagnosed ranged from 48.7% to 78.7%
    - The proportion in care ranged from 9.7% to 26.7%, with the proportion of all those living with CHB receiving antiviral treatment ranging from 5.4% to 12.4%
    - The drop in estimated deaths due to CHB between 2011 and 2019 ranges from 0% to 31% (however accurate estimation is difficult particularly in jurisdictions with relatively low populations of people living with CHB).

Introduction

Chronic hepatitis B (CHB) is a significant public health burden and is now the most prevalent blood-borne viral infection in Australia.[1] CHB is a leading cause of liver cancer, the 6th most common cause of cancer mortality in Australia.[2] Substantial improvements in access to appropriate care, monitoring and treatment are required to address hepatitis B related mortality nationally.

Australia's National Hepatitis B Strategies have been fundamental to guiding the response to hepatitis B since 2010, with significant progress being achieved over this period. The 3rd National Hepatitis B Strategy 2018-2022[3] (National Strategy), released in 2018 sets goals to make significant progress towards eliminating hepatitis B as a public health threat, including reducing the burden of disease and eliminating the negative impact of stigma, discrimination, and legal and human rights issues on people's health. The National Strategy highlights priority areas and populations, and outlines targets to measure progress throughout the span of the strategy.

These targets 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 when compared to the end of 2017**
7. Minimise the reported experience of stigma among people living with hepatitis B, and the expression of stigma, in respect to hepatitis B status.

Only bolded targets are reported in this report

Measuring the progress towards the targets of the National Strategy will allow current gaps to be identified, and priority areas to be highlighted to help shape the public health and policy response to hepatitis B in Australia.

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

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 objective of this project 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 3rd National Hepatitis B Strategy 2018-2022 and reporting against Hepatitis B Indicators in the National Blood-borne Viruses and Sexually Transmissible Infections Surveillance and Monitoring Plan 2018 - 2022. This report will not report against vaccination, reduction in local transmission or stigma targets specifically. Further reporting against these indicators can be found in the National Viral Hepatitis Mapping Report, and the Kirby Institute's Annual Surveillance Reports.[5]

This report for the year 2019 is the third publicly available National Surveillance for Hepatitis B Indicators Annual Report. The report can be accessed at: https://www.doherty.edu.au/whoccvh/centre-activities/research/blood-borne-viruses-and-sexually-transmissible-infections-surveillance-and-research-programme

Report Updates

Indicator data estimates have been derived using a mathematical model for the natural history of hepatitis B in Australia extending on previous work.[6-8] The model accounts for diversity in prevalence and impact of overseas migration, incorporating detailed disease phase dynamics, and examining the impact of domestic and overseas vaccination programs, together with the impact of antiviral treatment on mortality attributable to CHB at a population level. Further information regarding the model can be found in the associated paper.

No major methodological changes were made to the model since the 2018 estimates were reported, however updates from previously reported 2018 estimates include:

- Data for the number of people receiving treatment through the PBS and monitoring through MBS for 2018 were updated after the publication of the previous National Surveillance for Hepatitis B Indicators Report[9]. This results in updated estimates for the 2018 HBV cascade of care which now aligns with the 2018 Viral Hepatitis Mapping Report[10].
- Additional output estimates have been incorporated into this report including:
    - Breakdown by age and disease phase of the number of people living with CHB in Australia.
    - Sensitivity analysis on the impact of migration on future estimates of people living with CHB in Australia.
    - Sensitivity analysis on the estimated proportion diagnosed to assess potential impact of duplicate notifications.
    - Scenarios for the impact of future treatment uptake on mortality attributable to CHB, including estimating treatment uptake to reach mortality targets.
    - Future projection estimates for indicators extended to 2030 for each jurisdiction.

Deriving specific modelled indicator estimates for Aboriginal and Torres Strait Islander populations remains a priority of ongoing work and will be included in future reporting.

Due to previous methodological updates, estimates may differ from previous outputs reported in the Kirby Institute's Annual Surveillance Reports[5], the Doherty Institute's National Viral Hepatitis Mapping Project Reports[1], National Surveillance for Hepatitis B Indicators National Report[9], and publications.

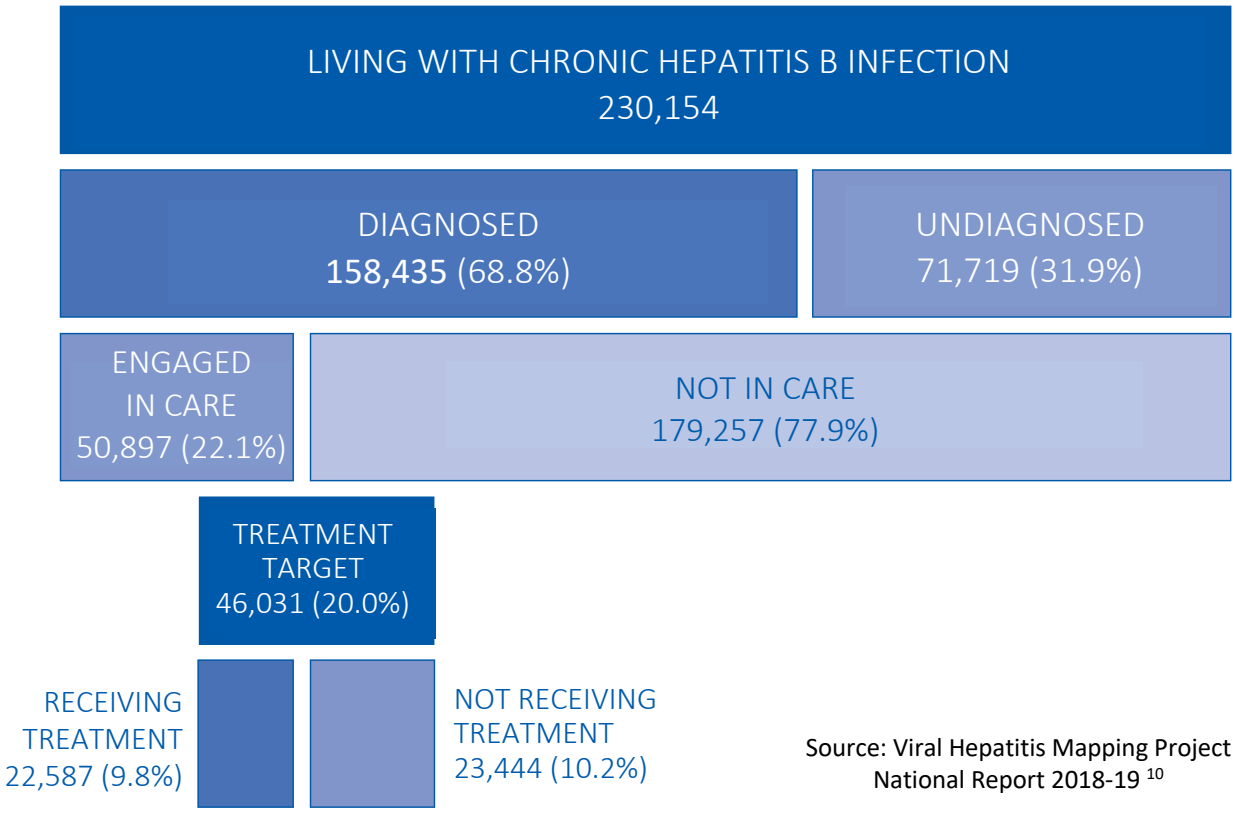
A. National

A.1 Summary National Estimates

Table 1. Australian summary for hepatitis B indicator estimates, 2019

Indicators	Point estimate	Plausible range	
		Minimum	Maximum
1. People living with CHB	230,154	193,799	285,804
2. Proportion of people living with CHB in Australia who have been diagnosed	68.8%	50.8%	86.3%
3. Proportion of people living with CHB in Australia who are receiving care	22.1%	17.8%	26.3%
4. Proportion of people living with CHB who are dispensed drugs for the treatment of hepatitis B	9.8%	7.9%	11.7%
5. Number of attributable deaths due to CHB	427	302	646
6. Number of deaths due to hepatocellular carcinoma attributable to CHB	316	231	471
7. Number of deaths due to attributable to decompensated cirrhosis CHB	111	71	175

Figure 1. Chronic hepatitis B cascade of care, Australia, 2019



Source: Viral Hepatitis Mapping Project National Report 2018-19 [10]

A.1.1 Progress Towards National Cascade of Care Targets

Despite the continued increase 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[12]. Profound increases to existing levels of diagnosis, treatment and care will be required to achieve the 2022 targets contained in the current National Strategy.

Figure 2. Progress towards the 3rd National Hepatitis B Strategy 2018 – 2022 targets

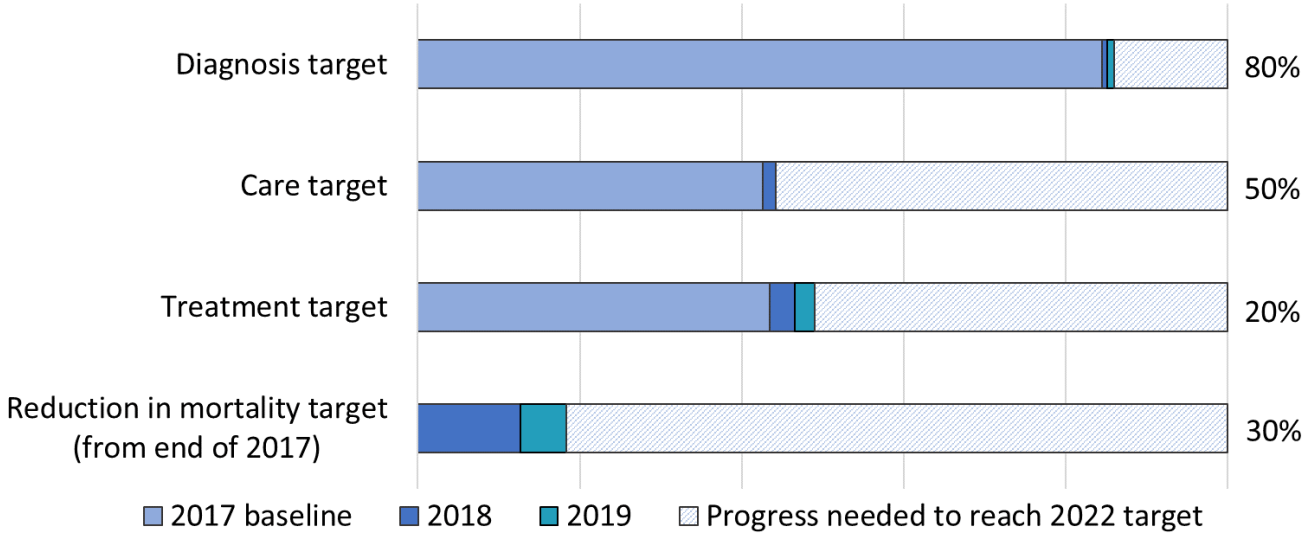


Table 2. Tracking the 3rd National Hepatitis B Strategy 2018-2022 targets

Indicator	2017	2018	2019	2022 Target
Proportion of people living with CHB who have been diagnosed	67.6%	68.1%	68.8%	80.0%
Proportion of people living with CHB who are in care	21.3%	22.1%	22.1%	50.0%
Proportion of people living with CHB who have been treated	8.7%	9.3%	9.8%	20.0%
Reduction of hepatitis B attributable mortality (from end of 2017)	-	3.8%	5.5%	30.0%

A.1.2 Progress Towards Global Health Sector Strategy Targets

We also measure progress towards the WHO's 2030 targets outlined in the Global Health Sector Strategy (GHSS) on Viral Hepatitis 2016 – 2021[4] targets, which are to:

- diagnose 90% of people living with hepatitis B by 2030
- treat 80% of eligible persons with CHB and
- achieve a 65% reduction in hepatitis B related deaths when compared to 2015.

To achieve WHO's 2030 targets outlined in the GHSS on Viral Hepatitis 2016 – 2021, and taking into account future trends, Australia must:

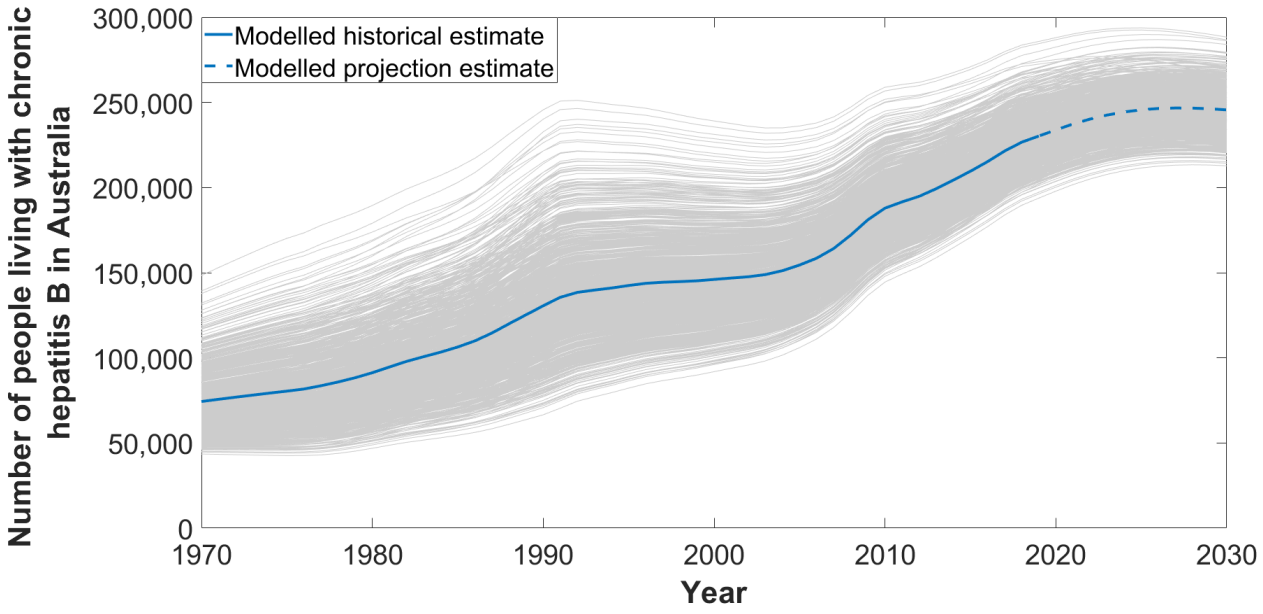
- Increase the number of people diagnosed from 158,435 in 2019 to 221,076 by 2030
- Increase the number of people treated from 22,587 in 2019 to 63,892 by 2030
- Decrease the number of deaths attributable to CHB from 427 in 2019 to 173 by 2030

A.2 National Estimates for Hepatitis B Indicators

A.2.1 Number of people living with chronic hepatitis B in Australia.

During 2019, an estimated 230,154 (plausible range (PR) 193,799 to 285, 804) people were living with CHB in Australia, representing 0.90% of the population. Modelled estimates show that the number of people living with CHB has increased over time in Australia, with an additional 84,290 people living with CHB in 2019 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 245,640 (212,788 to 288,373) people will be living with CHB in Australia by 2030 (Figure 3).

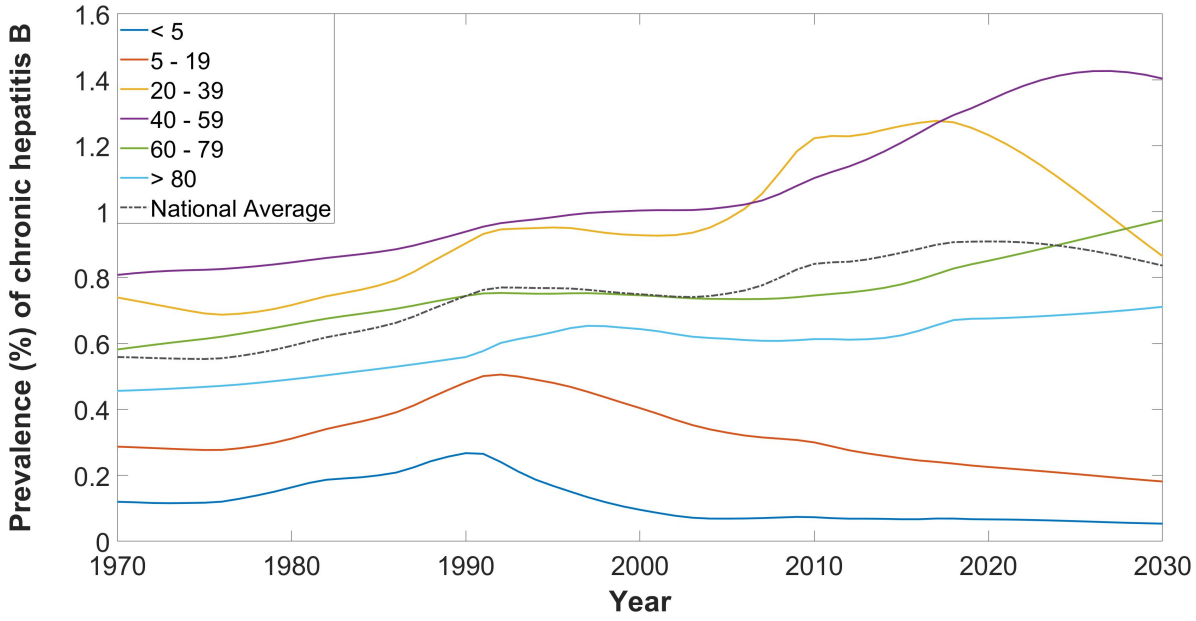
Figure 3. Estimated number of people living with chronic hepatitis B in Australia, 1970-2030.



Grey lines show plausible ranges of estimates.

The prevalence of CHB has increased substantially over time, from 0.6% in 1970 to 0.9% in 2019 (Figure 4). Changes in prevalence vary across age groups, with a decrease in prevalence observed from 1991 onwards in the under 5-year age group and the 5-19 year age group. This highlights the impact of childhood hepatitis B vaccination programs both domestically and internationally, with vaccination mediated reductions in CHB prevalence extending to older age groups over time. The majority of people living with CHB in Australia were born overseas and acquired hepatitis B in childhood prior to migration, and therefore changes in total numbers, countries of origin and age distributions of Australia's migrant population will affect the projections of hepatitis B in Australia. Further detailed information on the epidemiology of CHB in Australia according to priority groups can be found in the Viral Hepatitis Mapping Project National Report.[1, 10]

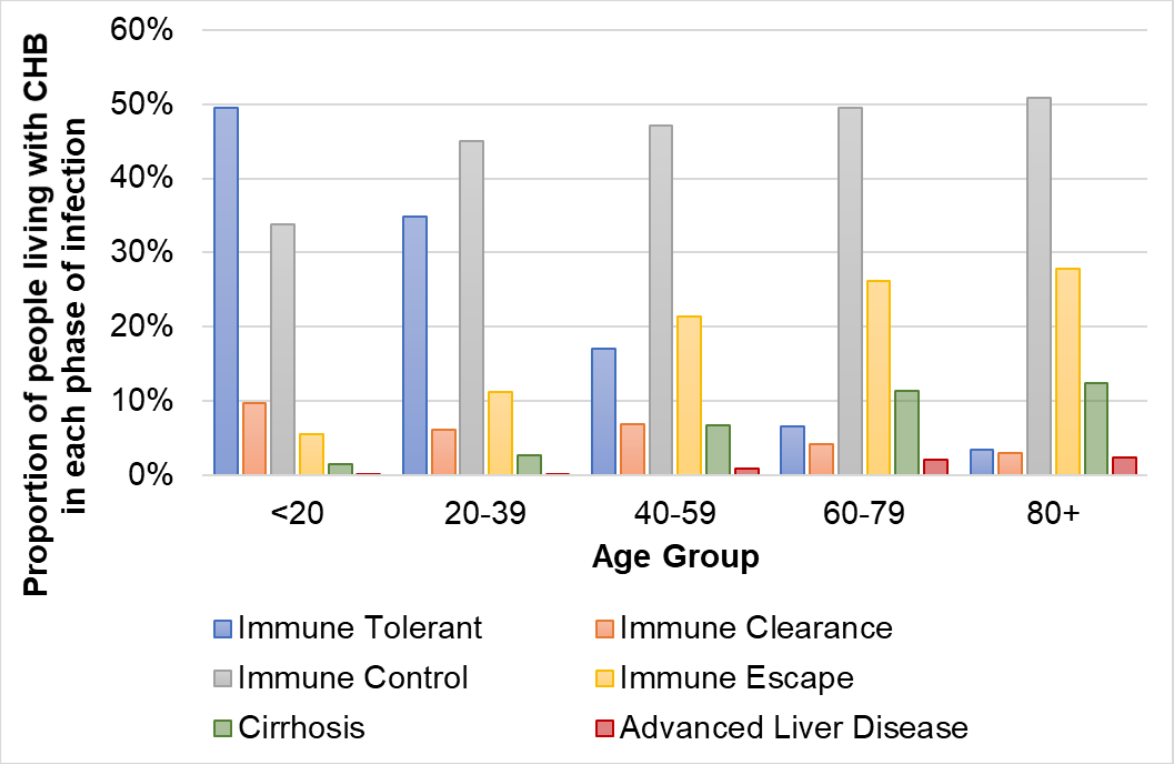
Figure 4. Estimated prevalence of chronic hepatitis B in Australia by age group, 1970-2030.



A.2.1.1 Phases of infection for people living with chronic hepatitis B

People living with CHB can transition in and out of different phases over time so it is important to estimate the distribution of phases at a population level. During 2019, the distribution of people living with CHB in each disease phase was estimated to be 23.6% in immune tolerant, 6.1% in immune clearance, 46.1% in immune control and 17.6% in immune escape phase. In addition, an estimated 5.8% of people living with CHB had cirrhosis and 0.8% had advanced liver disease (hepatocellular carcinoma or decompensated cirrhosis). The proportion of people living with CHB in each disease phase varies by age group (Figure 5) with the majority of people under 20 years old in the immune tolerant phase (49.4%). For all other age groups, the majority of people living with CHB were in immune control, and this was seen to increase with age. The proportion of people with CHB living with cirrhosis in 2019 also increases with age from 1.4% in those under 20 years old to 12.5% in those aged above 80 years. Similarly, the proportion of people living with advanced liver disease increases from 0.1% in those under 20 years to 2.4% in those aged above 80. These estimates have implications for public health messaging around CHB management and treatment eligibility to prevent liver disease and the importance of engaging particular populations, allowing prioritisation of those at greatest risk of disease progression.

Figure 5. Estimated proportion of people living with chronic hepatitis B in each phase of infection by age group, 2019.



A.2.1.2 Sensitivity analysis on estimated future number of people living with CHB in Australia

Migration patterns and overseas vaccination campaigns in countries with endemic CHB, among other factors, will have a significant impact on projections of the number of people living with CHB in Australia. These future migration patterns are dependent on various factors including local and international economic conditions and Governmental policy. Based on current trends, the Australian Bureau of Statistics (ABS) generate three different estimates for future migration projections which can be considered as a low (series A), intermediate (Series B) and high (Series C)[13]. Within this report, we assumed intermediate migration for our future projections. The impact of varying the total number of people migrating into Australia as generated by the ABS projections is substantial (Figure 6), with estimates for 2030 ranging between 235,865 and 255,494 when using the lowest and highest series, respectively. This highlights how changes in

migration patterns and policies could greatly impact future projections of the number of people living with CHB in Australia.

Given the recent changes in arrivals and departures due to the COVID-19 pandemic[14] and likely ongoing shifts in migration patterns, we anticipate 2020 estimates and future projections will be profoundly affected by these changes.

Figure 6: Impact of future migration numbers on estimated number of people living with CHB in Australia.

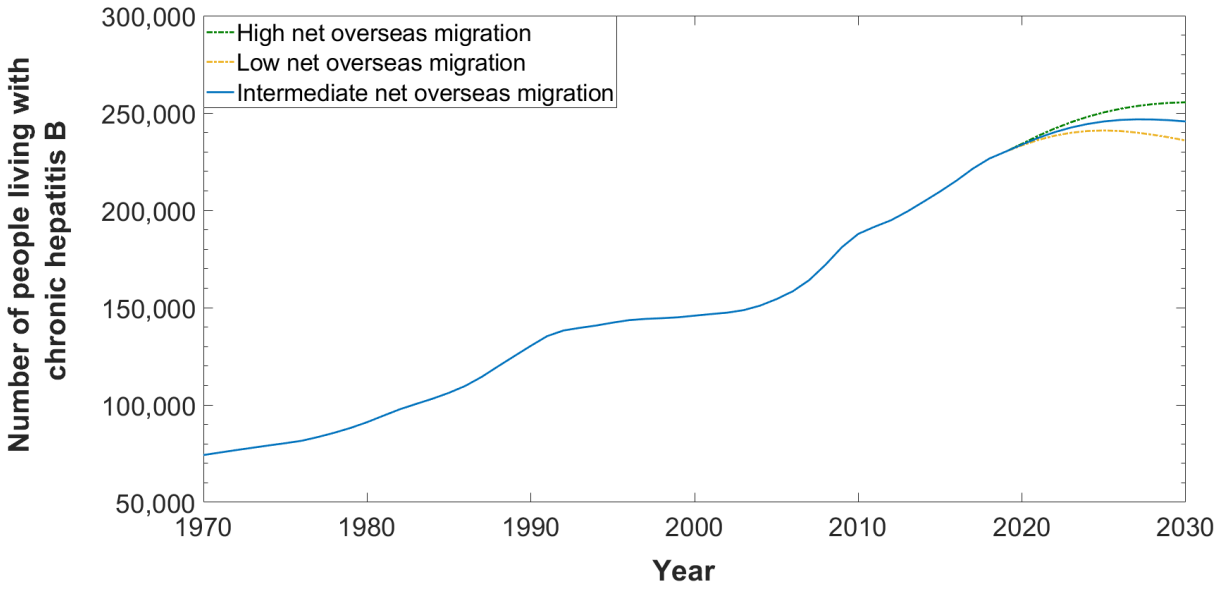
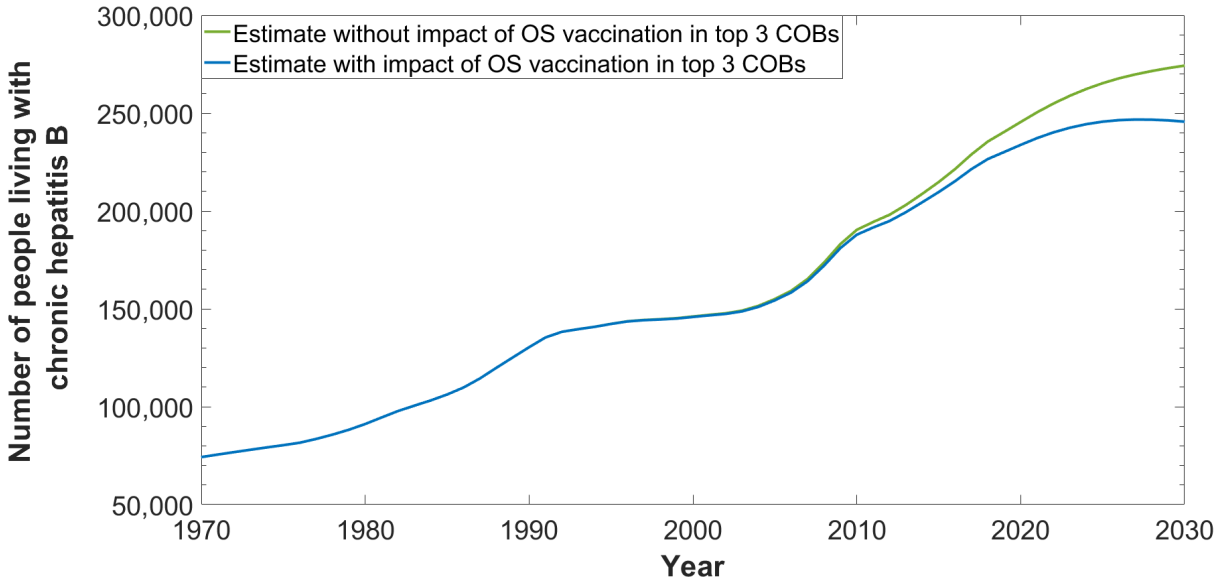


Figure 7 highlights the importance of overseas vaccination campaigns on reducing the prevalence of CHB. The figure represents changes to the projected number of people living with CHB if the prevalence of CHB did not decrease over time due to vaccination impact in three countries where CHB is endemic; China, Philippines and Vietnam. These three countries represent countries which have the highest number of people living with CHB in Australia who were born overseas. If the model did not incorporate the decrease in prevalence in these countries over time due to vaccination, we estimate that an additional 30,000 people would be living with CHB in Australia in 2030 (assuming intermediate future migration projections).

For more information about the distribution of chronic hepatitis B by priority population in Australia refer to the 2018-2019 Mapping Project Report [10].

Figure 7: Impact of overseas vaccination campaigns on estimated number of people living with CHB in Australia.



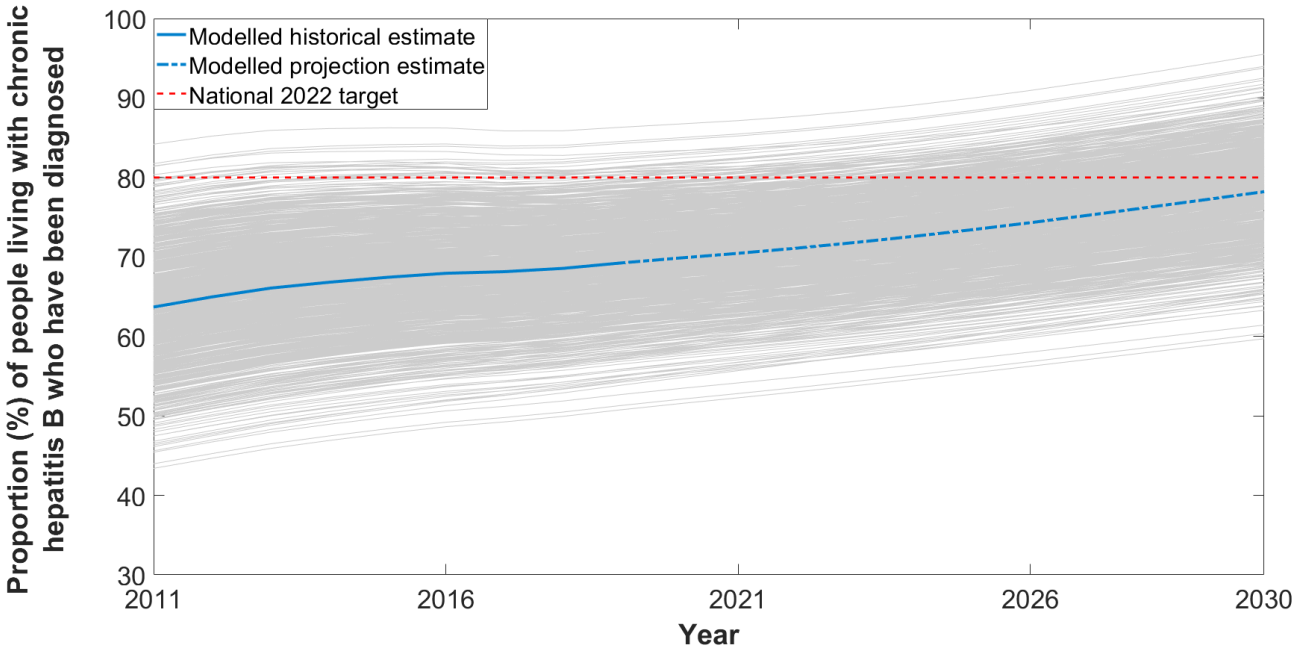
A.2.2 Proportion of people living with chronic hepatitis B in Australia who have been diagnosed

In 2019, an estimated 158,435 people living with CHB in Australia had been diagnosed, representing 68.8% (PR 50.8% to 86.3%) of all Australians living with CHB. Historical trends show modest improvements in this proportion, having increased from 63.0% diagnosed in 2011 (Figure 8, Appendix Table A2). Although thousands of individuals are diagnosed with CHB in Australia each year, the population living with CHB also continues to increase (Figure 3), and a proportion of those previously diagnosed die either due to complications of CHB, or other causes - therefore the rate of diagnosis must increase substantially to have an impact on the total proportion diagnosed.

The proportion diagnosed in 2019 remains below the National Strategy target of 80%, with 33,696 more people living with CHB requiring diagnosis to reach this target by 2022. Since 2010 the annual number of national notifications has been fluctuating, but following a decreasing trend [15]. By combining this information with modelled outputs, we estimate the proportion diagnosed will increase on average 0.82% per year to reach 77.8% diagnosed in 2030 (Figure 6). Following these trends, Australia will not reach the proportion diagnosed target of 80% until 2033.

To reach WHO's Global Health Sector Strategy of 90% diagnosed by 2030, the proportion diagnosed would need to increase by an average of 1.9% every year to reach 221, 076 people diagnosed, representing an additional 62,641 people living with CHB requiring diagnosis (or an average of 5,695 new diagnoses per year).

Figure 8. Estimated proportion of people living with chronic hepatitis B in Australia who have been diagnosed, 2011-2030.



Grey lines show plausible ranges of estimates.

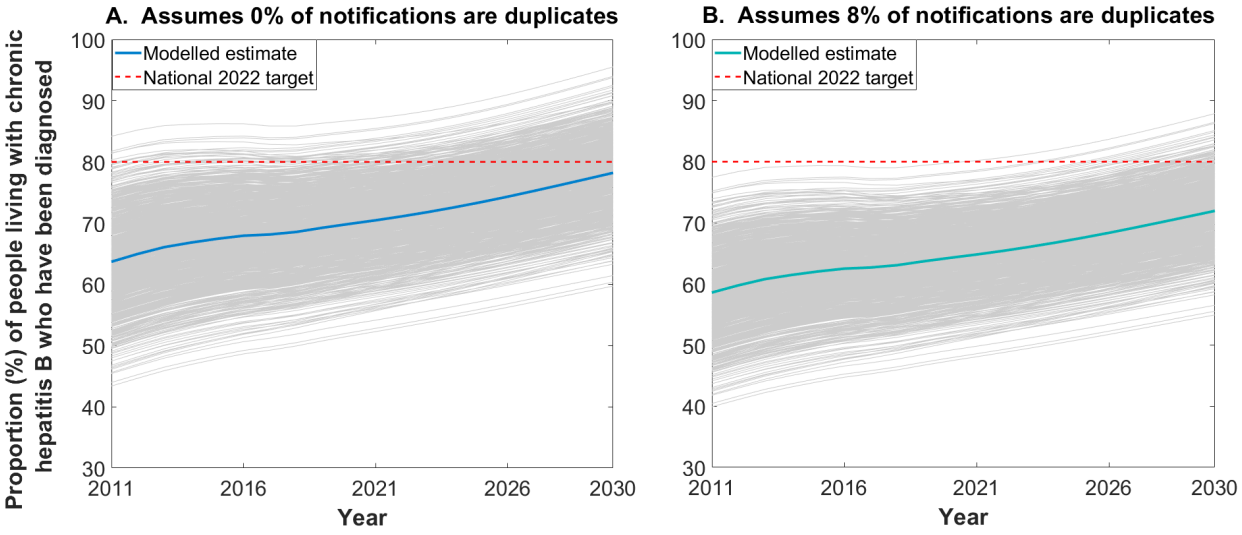
Considering the plausible range, the proportion diagnosed in 2019 could be as small as 50.8% and as large as 86.3% - which in the latter case would mean that Australia has already reached the 2022 diagnosis target. However, the likelihood that the 2022 diagnosis target has been achieved in 2019 is low, as the target was not achieved in 97.8% of model simulations. These estimates may be considered optimistic and further analysis below highlights the impact of uncertainties in source data on the proportion diagnosed.

A.2.2.1 Sensitivity Analysis for duplicate notifications

The number of people living with CHB who have been diagnosed is calculated by using the number of notifications, which is sourced from the National Notifiable Diseases Surveillance (NNDSS) system [15]. However, NNDSS data may contain duplicates if individuals have been diagnosed in multiple jurisdictions, inflating the number of people diagnosed. Data linkage projects in New South Wales and Victoria estimated that approximately 8% of notifications were duplicates, occurring in both jurisdictions. While we do not yet know what the proportion of duplicate notifications will be nationally, we conducted a sensitivity analysis to consider the impact this could have on the estimated proportion diagnosed nationally (Figure 9). Assuming 8% of national notifications are duplicates reduces the estimated proportion diagnosed in 2019 from 68.8% (PR 50.8% to 86.3%) to 63.3% (PR 46.7% to 79.4%). Furthermore, only 0.1% of model simulations estimated the 2022 diagnosis target could be reached in 2022 when assuming 8% of notifications are duplicates, compared to 4.6% of simulations if we assumed no duplicate notifications (Figure 10).

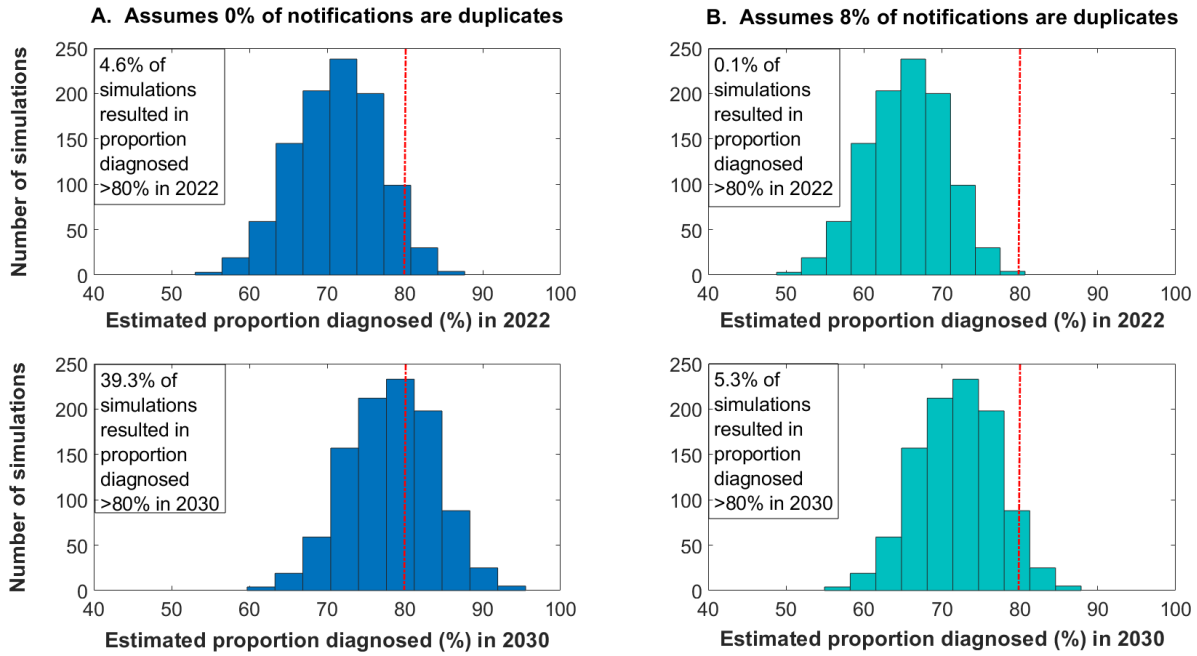
This sensitivity analysis highlights the importance of estimating the proportion of duplicate notifications for accurately estimating the true proportion diagnosed, particularly across states and territories.

Figure 9: Comparison of estimated proportion diagnosed when assuming none of the national notifications are duplicates (Figure A) and when assuming 8% of national notifications are duplicates (Figure B).



Grey lines show plausible ranges of estimates.

Figure 10: Distribution of estimated proportion diagnosed in 2022 and 2030 based on model output of 1,000 simulations. Figure A graphs assume no duplicate notifications, Figure B assumes 8% of national notifications are duplicates.

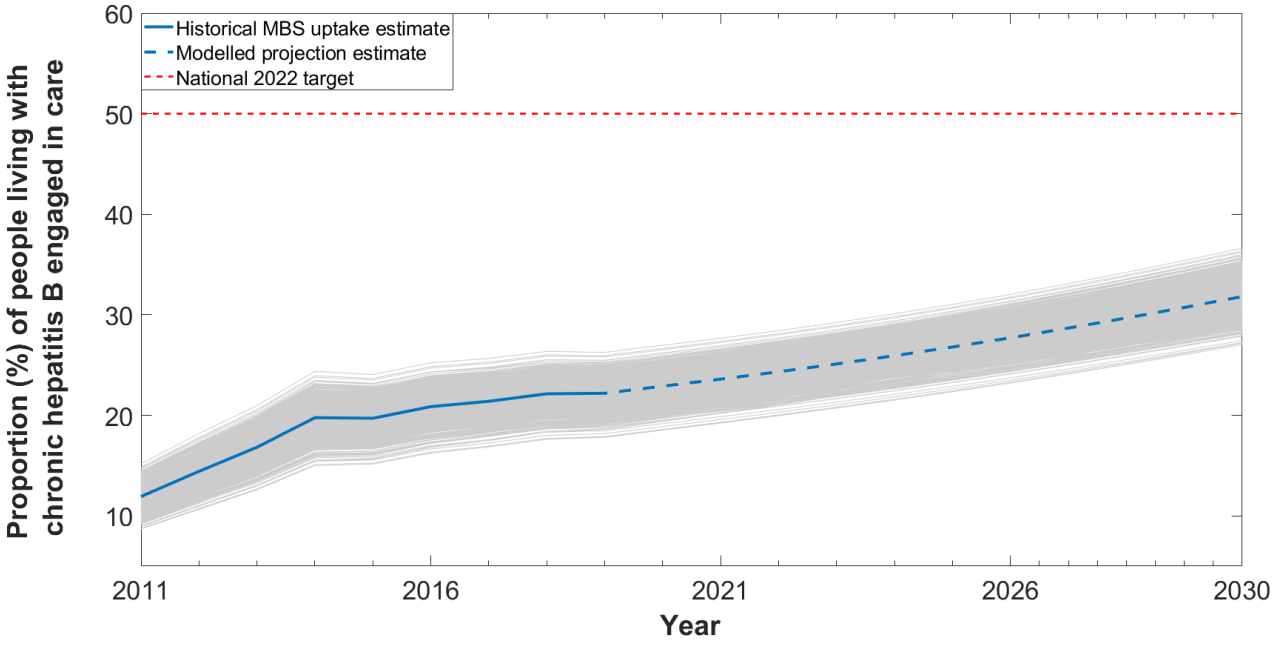


A.2.3 Proportion of people living with chronic hepatitis B who are engaged into care, receiving either treatment or monitoring

During 2019, 50,897 people were engaged in care for their CHB, receiving either antiviral treatment or monitoring without antiviral treatment. As a result, total uptake of care is an estimated 22.1% (PR 17.8% to 26.3%) of all people living with CHB. Modelled trends show substantial improvement in this proportion over time, increasing from 11.8% since 2011 (Figure 11, Appendix Table A3). Although this increase was relatively rapid between 2011 to 2014, the rate of increase has been substantially slower since 2015. While the total number of people engaged in care has increased each year, the population living with CHB also continues to increase (Figure 3), therefore engagement in care must increase substantially to have an impact on this proportion.

Clinical guidelines recommend that all people living with CHB should be engaged in care, and Australia currently falls well short of accomplishing this. The proportion engaged in care also remains below the National Strategy target of 50%, with 69,185 more people required to be in care to reach this target by 2022. If the current average annual increase of 0.82% since 2015 were to remain stable, Australia will not reach the 50% target until 2053.

Figure 11. Estimated proportion of people living with chronic hepatitis B in Australia who were engaged in care (receiving either treatment or monitoring), 2011-2030.



Grey lines show plausible ranges of estimates.

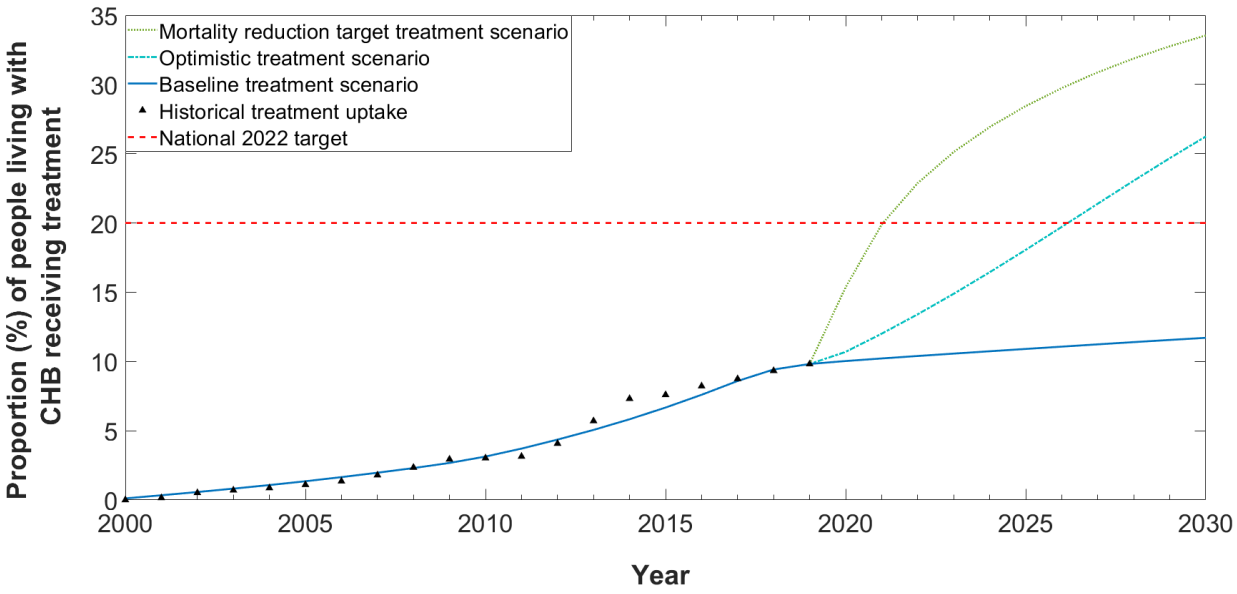
A.2.4 Proportion of people living with chronic hepatitis B who are dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme

During 2019, 22,587 people were dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme (PBS), which is an estimated 9.8% (PR 7.9% to 11.7%) of people living with CHB. Modelled trends since 2015 show an ongoing modest increase in this proportion (average increase 0.56% per year) (Figure 12, Appendix Table A4).

For Australia to achieve the National Strategy target of 20%, an additional 25,446 people living with CHB will need to receive antiviral treatment by 2022. Three scenarios were modelled to consider future treatment uptake and the impact on future mortality: (i) Mortality reduction target treatment scenario: a treatment scenario under which the 2022 mortality target is reached, (ii) Optimistic treatment scenario: an optimistic but plausible scenario based on the high treatment uptake trends seen in the NT since 2014 (Figure 20), and (iii) Baseline treatment scenario: a scenario which assumes treatment uptake will continue following the trends since 2018.

Only one of these scenarios (the mortality reduction target treatment scenario) reached the National Strategy target of 20% receiving treatment, and requires a substantial average annual treatment increase of 4.4% from 2019 to 2022, compared to our current increase of 0.49% from 2018 to 2019.

Figure 12. Estimated proportion of people living with chronic hepatitis B in Australia who were dispensed drugs for the treatment of hepatitis B through the Pharmaceutical Benefits Scheme, 2011-2030.



A.2.4.1 Treatment eligibility

Although the number of people dispensed drugs for treatment of CHB through the PBS is usually reported as a proportion of the total number of people living with CHB, it is important to highlight not all people living with CHB are eligible for treatment. This is because the dynamic natural history of hepatitis B and the various phases of infection mean 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.[16] These guidelines emphasize the importance of generating estimates of the proportion of people living with CHB by phase (refer to section A.2.1.1 on page 13)[11].

Based on limited overseas data, it has previously been estimated that 10-30% of people living with CHB are eligible for treatment.[17-19] The true proportion of people living with CHB who require treatment will vary by hepatitis B genotype, age group, sex, and other factors, and had not previously been estimated for Australia. The modelling undertaken for this project, which incorporates the phase of CHB and the proportion of people living with cirrhosis, enabled estimation of the number of people living with CHB eligible for antiviral treatment in Australia for the first time. We are able to track this over time in response to population changes.

In 2019, an estimated 69,827 (PR 53, 415 to 94,630) people living with CHB were eligible for antiviral treatment, representing 30.3% (PR 27.6% to 33.1%) of the total. This suggests the National Strategy target of 20% of people living with CHB receiving antiviral treatment by 2022 remains conservative (Figure 12). Based on this modelling, Australia treated a third of those estimated to require treatment in 2019 and would have needed to treat an additional 47,240 people to reach everyone who was eligible. 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 will need to increase from 22,587 in 2019 to 63,892 in 2030. Since 2015, an average annual increase of 1.8% in treatment uptake for eligible people was observed; if this trend were to remain stable, Australia will not reach the WHO 2030 elimination target until 2046.

A.2.5 Burden of disease attributable to chronic hepatitis B in Australia

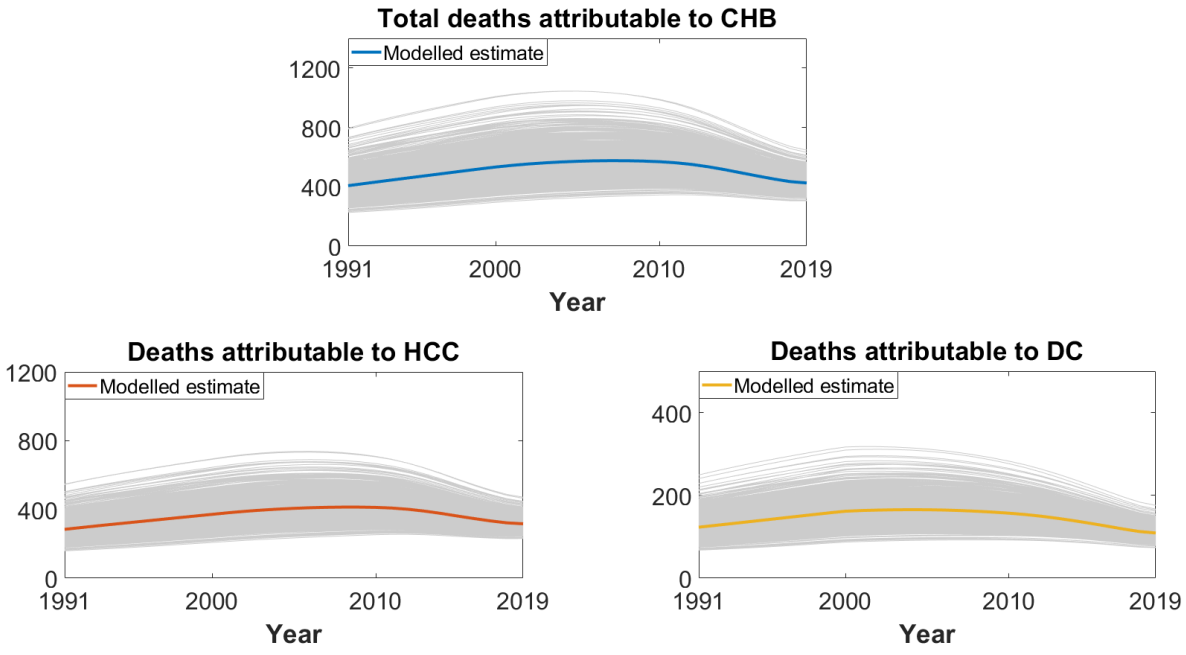
In 2019 an estimated 427 (PR 302 to 646) people died due to complications of CHB in Australia. The total number of estimated attributable deaths has changed over time, increasing from 407 in 1991 to a peak of 575 deaths in 2007 followed by a gradual decline (Figure 13, Appendix Table A5). This decrease 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 at greatest 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 was responsible for 316 (PR 231

to 471) deaths in 2019, while 111 (PR 71 to 175) people were estimated to have died due to DC. Deaths due to both causes have decreased over the last decade, however the decline has been more pronounced for DC (32.7% reduction, from peak of 165 in 2004, Figure 13) than for HCC (23.5% reduction, from the peak of 413 in 2008, Figure 13).

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 substantially reduce the risk of development of HCC, this effect is not immediate and antiviral therapy has limited impact on survival once HCC has already been diagnosed. In contrast, antiviral treatment not only prevents progression to cirrhosis and then to DC, but additionally 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) can be expected to accelerate the reduction in HCC attributable deaths.

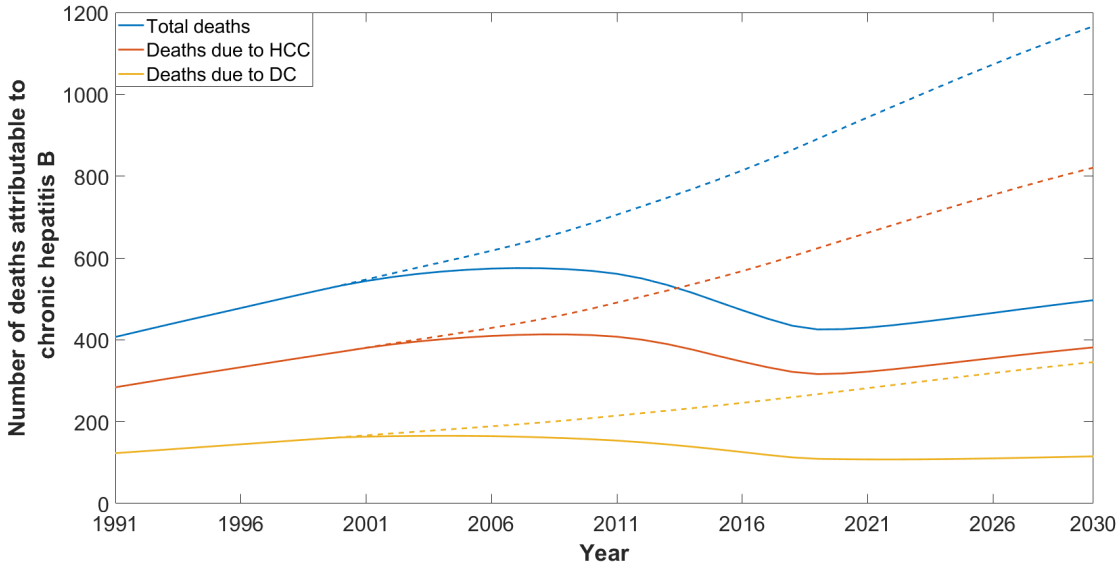
Figure 13. Estimated number of deaths attributable to chronic hepatitis B in Australia over time, 1991-2019.



Grey lines show plausible ranges of estimates.

The results of the modelling undertaken for this project suggest that without the availability of antiviral treatment in Australia, the number of attributable deaths would have continued to increase over time, to 891 CHB attributable deaths estimated in 2019 (Figure 14). Our assessment estimates that in 2019, 464 lives were saved due to treatment, with a total of 3,172 lives saved since the introduction of antiviral treatment for CHB in Australia from 2000.

Figure 14. Estimated number of deaths attributable to chronic hepatitis B in Australia, baseline treatment vs no treatment, 1991 – 2030.



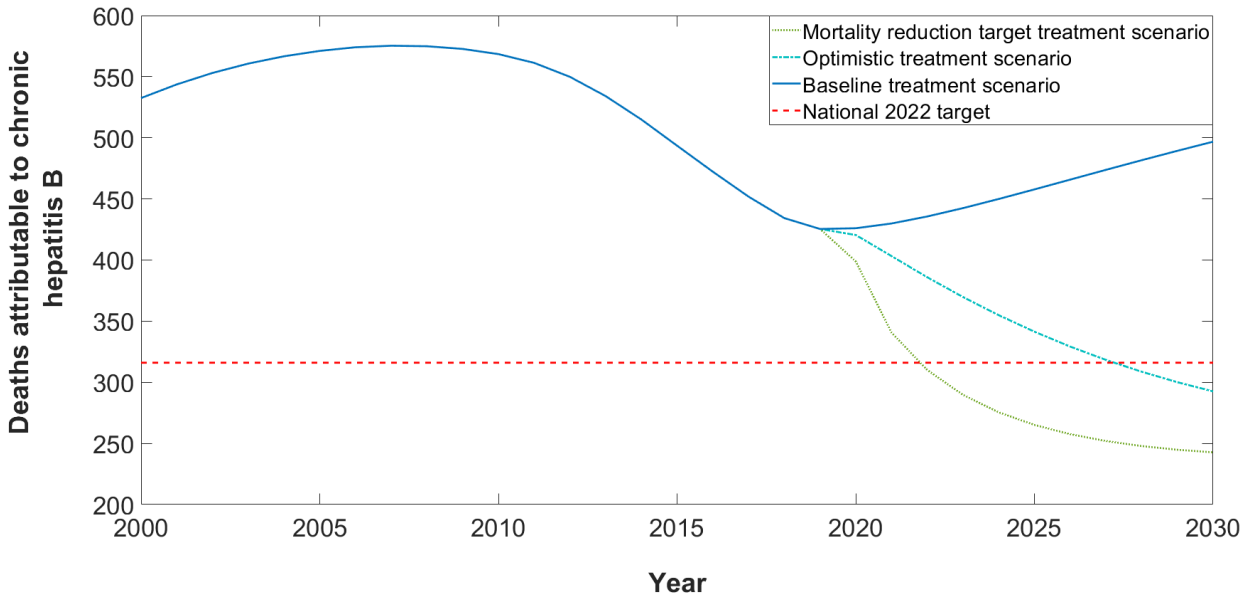
Dotted lines show estimated deaths per year without treatment for CHB

A.2.5.1 Impact of treatment on mortality

The reduction in deaths attributable to CHB at the end of 2019 relative to the end of 2017 was 5.5%, with considerable progress still needed to reach the National Strategy target of a 30% reduction in hepatitis B attributable mortality by 2022. To reach this target, the total number of CHB attributable deaths must fall to 316 deaths. Although the reduction in deaths has been pronounced since the introduction of antiviral treatment, future reductions depend on future treatment uptake. In 2022, the estimated reduction of attributable deaths in Australia when compared to 2017 under the baseline, optimistic and mortality reduction target scenarios (Figure 12) will be 3.1%, 14.6% and 31.4% respectively (Figure 15). The mortality reduction target scenario was chosen to ensure the 2022 mortality target of a 30% reduction when compared to 2017 was achieved. The optimistic treatment scenario was chosen as an optimistic but plausible treatment uptake scenario based on the high treatment uptake trends seen in the NT since 2014.

To reach the WHO Global Health Sector Strategy 2030 target of a 65% reduction in hepatitis B related deaths compared to 2015, the total number of CHB attributable deaths must fall to 173 deaths by 2030.

Figure 15: Impact of future treatment uptake on estimated number of deaths attributable to chronic hepatitis B in Australia, 2000 – 2030.



B. State and Territories

B.1 Summary State and Territory Estimates

Table 3. Australian summary for hepatitis B indicator point estimates by jurisdiction, 2019

State/ Territory	People living with CHB	Diagnosed (%)	In care (%)	Treatment uptake (%)	Total deaths attributable to CHB	HCC deaths attributable to CHB	DC deaths attributable to CHB
ACT	3,470	65.7%	22.2%	11.0%	5	4	1
NSW	81,483	78.7%	26.7%	12.4%	133	100	33
NT	4,355	74.5%	24.9%	8.3%	11	8	3
QLD	35,305	70.8%	17.8%	7.0%	73	53	20
SA	12,243	64.6%	16.4%	7.8%	25	18	7
TAS	1,692	48.7%	14.8%	5.4%	4	3	1
VIC	68,819	60.5%	24.0%	9.7%	124	92	32
WA	22,787	58.9%	9.7%	6.6%	52	38	14
Australia	230,154	68.8%	22.1%	9.8%	427	316	111

Note: Jurisdictional estimates were standardized to ensure the sum of indicator variables across the jurisdictions matches the modelled national estimate.

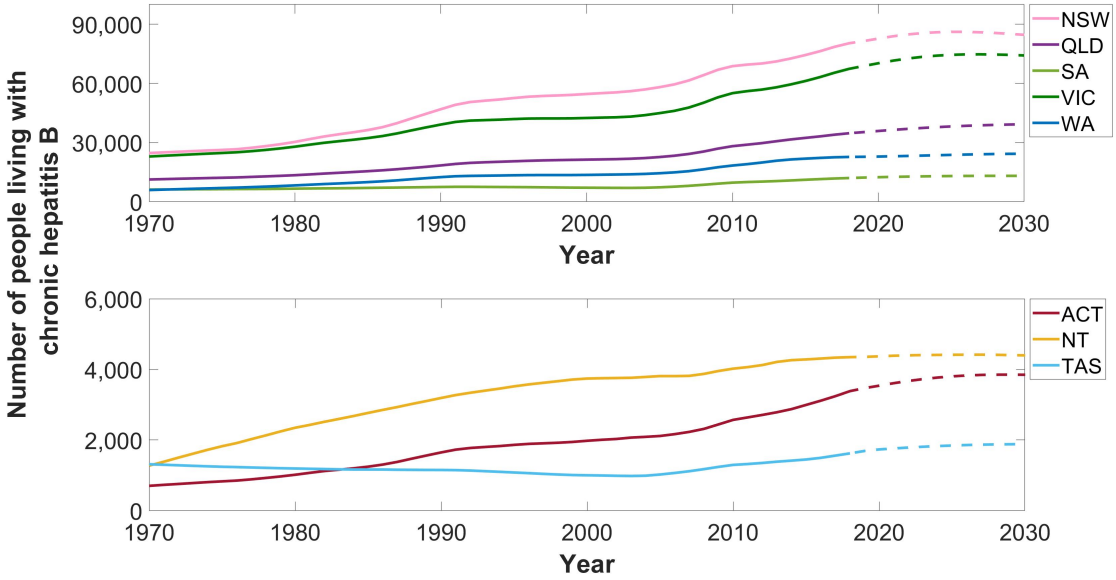
B.2 State and Territory Estimates for Hepatitis B Indicators

B.2.1 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, aside from TAS (Figure 16, Appendix Table A1). Similar to national estimates, differences in overseas migration patterns affect the epidemiology and future projections of hepatitis B across jurisdictions and is demonstrated in differential changes over time. This is particularly highlighted in TAS, which is the only jurisdiction to historically show a gradual decline in the number of people living with CHB (Figure 16). Despite steady increases in this number after 2004, TAS still had the lowest estimate in 2019 with 1,692 number of people living with CHB. The effect of migration has also been seen in NSW and VIC which had the highest estimates of people living with CHB in 2019 (81,483 and 68,819 respectively), and historically saw relatively high increases after increased migration in 1990 (Table 4, Appendix Table A1).

Prevalence across jurisdictions varies according to differing population demographics, with the highest prevalence in 2019 estimated in NT (1.78%) and the lowest was in TAS (0.32%). Among other jurisdictions, VIC (1.03%) and NSW (1.00%) had estimated prevalence above the national average (0.90%) in 2019, WA (0.86%) was equivalent, and ACT (0.81%), SA (0.70%) and QLD (0.69%) were below (Table 4).

Figure 16. Estimated number of people living with chronic hepatitis B by jurisdiction, 1970-2030



Dotted lines represent modelled projection estimates.

Table 4. Estimated number of people living with chronic hepatitis B and prevalence by jurisdiction, 2019

State/Territory	People living with CHB	Plausible range		Prevalence (%)
		Minimum	Maximum	
ACT	3,470	2,916	4,239	0.81%
NSW	81,483	68,518	100,064	1.00%
NT	4,355	4,015	4,952	1.79%
QLD	35,305	31,070	40,520	0.69%
SA	12,243	10,427	15,517	0.70%
TAS	1,692	1,442	2,049	0.32%
VIC	68,819	56,768	90,200	1.03%
WA	22,787	18,643	28,263	0.86%
Australia	230,154	193,799	285,804	0.90%

Note: Jurisdictional estimates were standardized to ensure the sum of indicator variables across the jurisdictions matches the modelled national estimate.

B.2.2 Proportion of people living with chronic hepatitis B in Australia who have been diagnosed

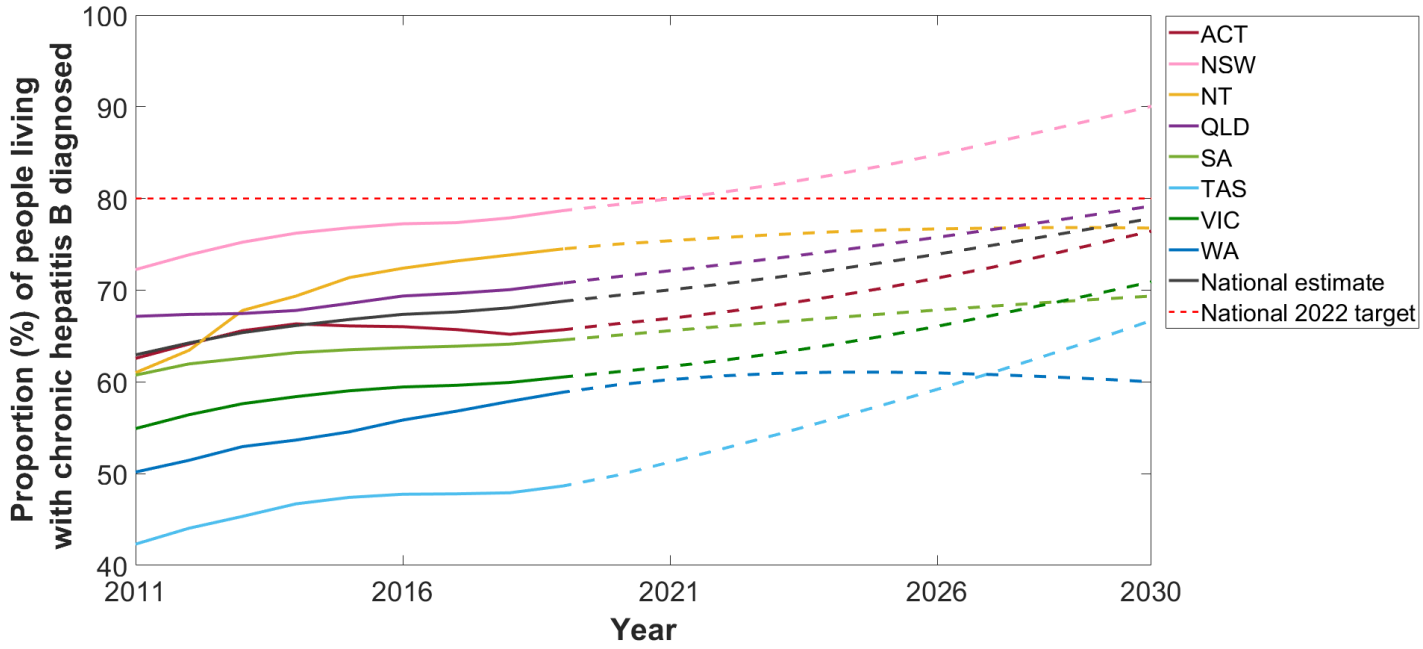
Since 2011 modest increases in the estimated proportion of people living with CHB who have been diagnosed have been observed in all jurisdictions (Figure 17, Appendix Table A2). The estimated proportion diagnosed varied greatly between jurisdictions, with NSW (78.7%), NT (74.5%) and QLD (70.8%) having the highest proportion diagnosed in 2019 (Table 5). Estimates for all other states

and territories were below the national average of 68.8%, with ACT (65.7%), SA (64.6%), VIC (60.5%) and WA (58.9%) exceeding 50%. The estimate for TAS (48.7%) suggests that the majority of the people living with CHB in this jurisdiction remain undiagnosed.

No jurisdiction has yet reached the 2022 National Strategy target of 80% of people living with CHB being diagnosed. Following trends in notifications since 2010, the only jurisdiction due to reach the 80% diagnosed target by 2022 is NSW, which is estimated to reach the target in 2021 (Figure 17). All other jurisdictions would reach the target after 2030. A significantly increased rate of diagnosis is required in all these jurisdictions to reach the National Strategy target by 2022.

As the proportion diagnosed is dependent on routinely collected surveillance data, disparities between states and territories will be impacted by variations in screening practices, underlying population differences in each jurisdiction and duplicate notifications. Please see section *A.2.2.1 Sensitivity analysis for duplicate notifications* for more information.

Figure 17. Estimated proportion of people living with chronic hepatitis B who have been diagnosed by jurisdiction, 2011-2030.



Dotted lines represent modelled projection estimates.

Table 5. Estimated proportion of people living with chronic hepatitis B who have been diagnosed by jurisdiction, 2019

State/Territory	Proportion diagnosed	Plausible range	
		Minimum	Maximum
ACT	65.7%	49.5%	90.7%
NSW	78.7%	59.3%	87.2%
NT	74.5%	61.8%	89.0%
QLD	70.8%	59.2%	89.2%
SA	64.6%	44.4%	88.7%
TAS	48.7%	38.9%	62.2%
VIC	60.5%	41.3%	84.7%
WA	58.9%	43.8%	82.1%
Australia	68.8%	50.8%	86.3%

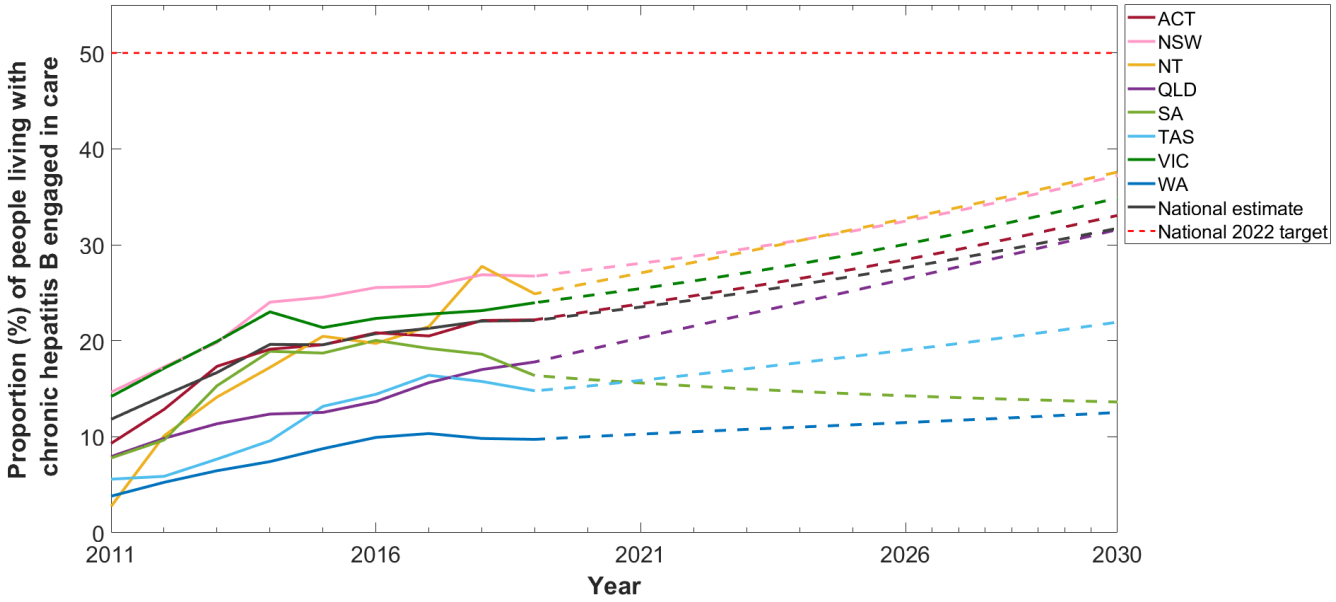
B.2.3 Proportion of people living with chronic hepatitis B who are engaged into care, receiving either treatment or monitoring

Since 2011, the proportion of people living with CHB who were engaged in care varied greatly between state and territories (Figure 18, Appendix Table A3). Despite some fluctuations, generally the proportion of people living with CHB who are engaged into care has been increasing in most states and territories since 2011. However, since 2017 there has been a more pronounced decreasing trend in the proportion receiving care in SA, TAS and WA (Figure 18), this may be due to changes in accurate data reporting, as anomalies in the expected number of viral load tests performed in some jurisdictions have been observed in the Viral Hepatitis Mapping Project National Report[1, 10].

It can be observed that jurisdictions with a higher proportion diagnosed also had a higher proportion engaged in care. In 2019 NSW (26.7%), NT (24.9%), VIC (24.0%) and ACT (22.2%) had the highest proportions of people living with CHB engaged in care (Table 6). All other jurisdictions, who also had lower diagnosis proportions, fell well under the national average of 22.1% engagement in care: QLD (17.8%), SA (16.4%), TAS (14.8%), WA (9.7%).

No jurisdiction has yet reached the 2022 National Strategy target of 50% of people living with CHB engaged in care. Following current trends since 2015, NT, QLD, NSW and ACT will not reach this target until 2029, 2042, 2049 and 2053 respectively. All other jurisdictions will reach the 2022 target after the national estimate, in 2053. Although the National Strategy target is set to 50%, clinical guidelines recommend that all people living with CHB should be engaged in care, so drastic improvements need to be made across all jurisdictions to engage all people living with CHB.

Figure 18. Estimated proportion of people living with chronic hepatitis B who were engaged into care, receiving wither treatment or monitoring by jurisdiction, 2011-2030



Dotted lines represent modelled projection estimates.

Table 6. Estimated proportion of people living with chronic hepatitis B who were engaged in care by jurisdiction, 2019

State/Territory	Proportion in care	Plausible range	
		Minimum	Maximum
ACT	22.2%	18.2%	26.4%
NSW	26.7%	21.8%	31.8%
NT	24.9%	21.9%	27.0%
QLD	17.8%	15.5%	20.2%
SA	16.4%	12.9%	19.2%
TAS	14.8%	12.2%	17.4%
VIC	24.0%	18.3%	29.1%
WA	9.7%	7.8%	11.9%
Australia	22.1%	17.8%	26.3%

B.2.4 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 Viral Hepatitis Mapping Project National Report,[1, 10] the proportion of people living with CHB receiving antiviral treatment has increased over time in all states and

territories (Figure 19, Appendix Table A4). Treatment uptake varied greatly between jurisdictions, with NSW (12.4%) and ACT (11.0%) estimated to have the highest proportion of people with CHB receiving treatment in 2019 (Table 7). All other states and territories were below the national average (9.8%) for treatment uptake, including VIC (9.7%), NT (8.3%), SA (7.8%), QLD (7.0%), WA (6.6%) and TAS (5.4%). A relatively rapid increase in treatment uptake was observed in most jurisdictions until 2014 to 2015, when the rate of increase slowed. Uniquely, NT has seen the opposite pattern over time, with substantial treatment uptake seen in more recent years compared to other jurisdictions. In 2019, no jurisdiction had reached the 2022 National Strategy target of 20% treatment uptake.

Figure 19. Estimated proportion of people living with chronic hepatitis B who were dispensed drugs for the treatment of hepatitis B through the PBS by jurisdiction, 2011-2019.

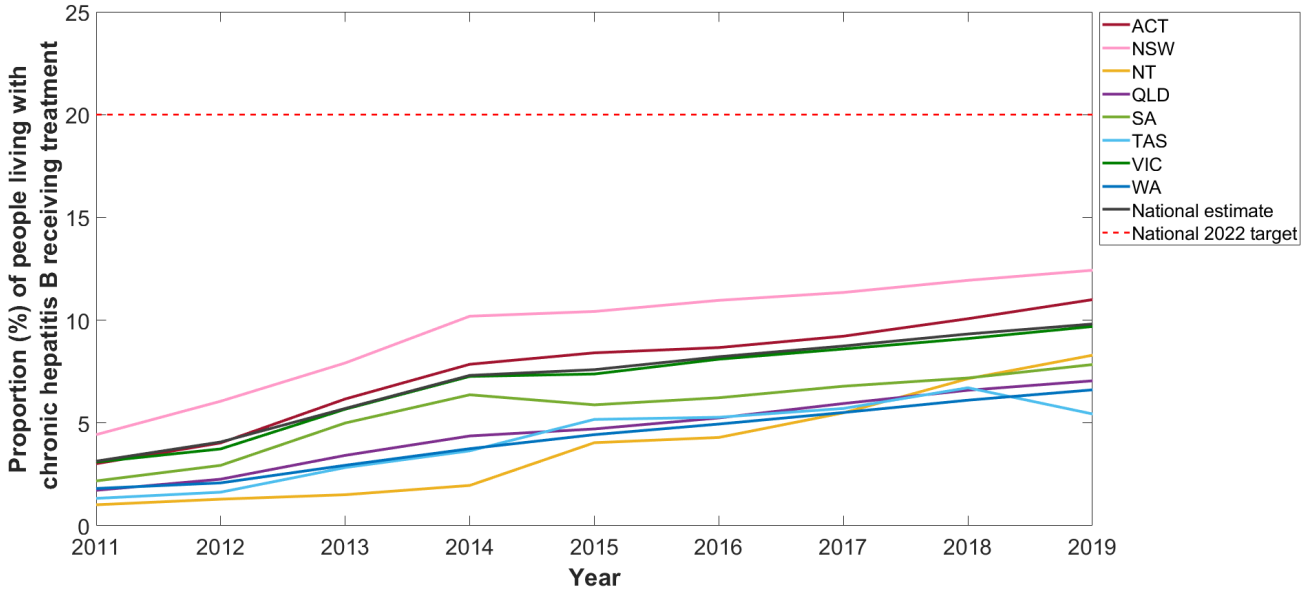
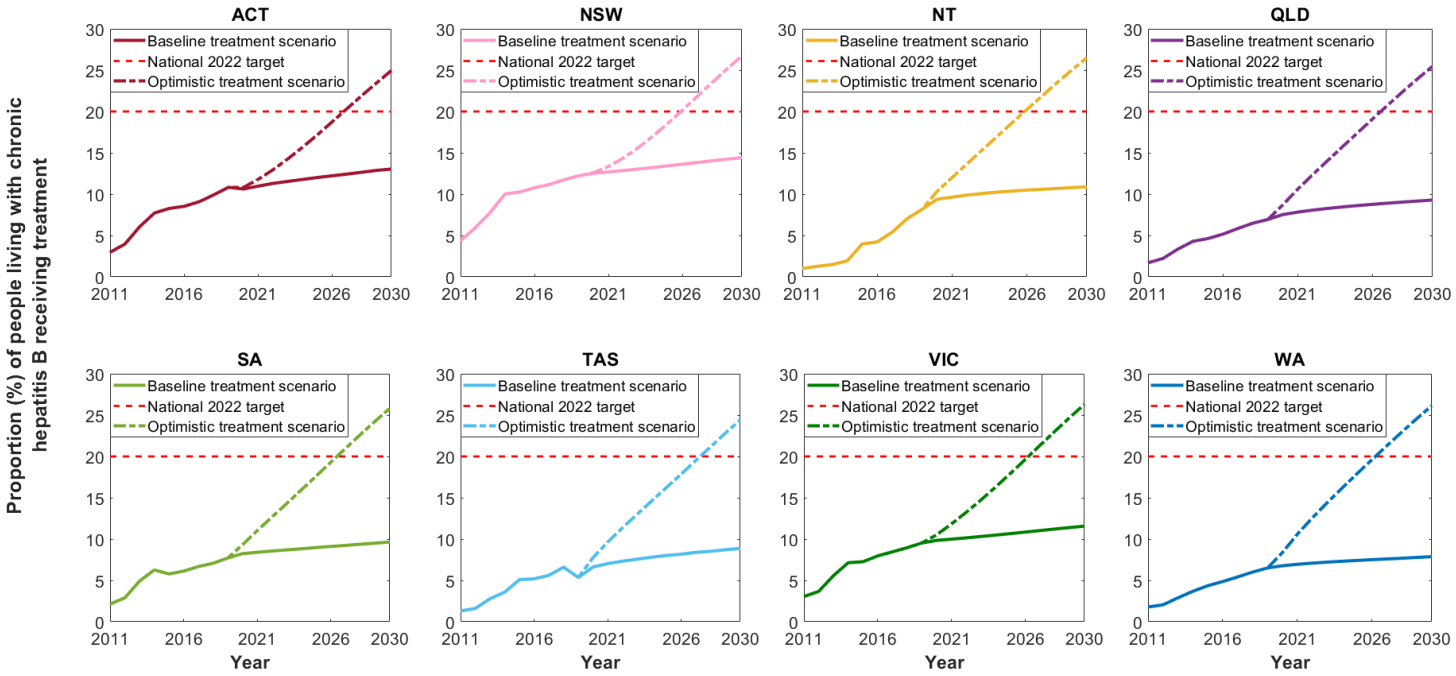


Table 7. Estimated proportion of people living with chronic hepatitis B who were dispensed drugs for the treatment of hepatitis B through the PBS by jurisdiction, 2019

State/Territory	Proportion receiving treatment	Plausible range	
		Minimum	Maximum
ACT	11.0%	9.0%	13.1%
NSW	12.4%	10.1%	14.8%
NT	8.3%	7.3%	9.0%
QLD	7.0%	6.1%	8.0%
SA	7.8%	6.2%	9.2%
TAS	5.4%	4.5%	6.4%
VIC	9.7%	7.4%	11.7%
WA	6.6%	5.3%	8.1%
Australia	9.8%	7.9%	11.7%

To explore future treatment uptake, two scenarios were modelled for each jurisdiction: (i) Baseline scenario assumes treatment uptake will continue following the trends since 2018 and (ii) Optimistic scenario assumes an optimistic but plausible scenario based on the high treatment uptake trends seen in the NT since 2014 (Figure 20). Under the baseline scenario no jurisdiction reached the 2022 treatment target with NSW and ACT estimated to have the highest proportion of people living with CHB receiving treatment in 2030, 14.4% and 13.0% respectively. Under the optimistic scenario jurisdictions only reach the 2022 target of 20% treatment uptake between 2026 and 2028, however this requires a significant increase in uptake from 2020 onwards (Figure 20).

Figure 20: Estimated proportion of people living with chronic hepatitis B in Australia receiving treatment by jurisdictions, Baseline vs Optimistic future treatment uptake scenarios



B.2.4.1 Treatment eligibility

As described in the National Estimates section of this report (Page 21), not all people living with CHB are eligible for treatment due to the dynamic natural history of hepatitis B. Based on limited overseas data, it is estimated that 10-30% of people living with CHB are eligible for treatment.[17-19] The true proportion of people living with chronic hepatitis B who require treatment will vary by hepatitis B genotype or country of birth as a proxy, age group, sex, and other factors. This has been highlighted when comparing the proportion eligible for treatment in each state and territory. In 2019, NT (32.4%), WA (30.6%) and NSW (30.5%) were estimated to have the highest proportion of people living with CHB who are eligible for treatment, followed by VIC (30.3%), SA (30.1%), QLD (30.0%), ACT (28.7%) and TAS (28.1%).

B.2.5 Burden of disease attributable to chronic hepatitis B in Australia

While national estimates demonstrated a gradual decline in deaths attributable to CHB from 2006 onwards, this was largely driven by those jurisdictions with the largest number of people living with CHB receiving treatment (NSW and VIC), with this trend not being observed in all states and territories (Figure 21, Appendix Table A5).

NSW and VIC were estimated to have the highest burden of CHB attributable deaths in 2019 (133 and 124 deaths respectively, Table 8). Although burden is currently similar in NSW and VIC, this has not always been the case, with NSW historically having the highest numbers of deaths and experiencing a larger and earlier peak (204 in 2006) compared to VIC (174 in 2007). The more profound decline in total estimated deaths in NSW reflects the relatively higher treatment uptake in NSW when compared with VIC. In NT, SA and TAS, jurisdictions with lower treatment uptake, the total number of deaths attributable to CHB has only marginally declined. Similar trends can be seen for both HCC (Figure 22, Appendix Table A5) and DC (Figure 23, Appendix Table A6) attributable deaths.

The reduction in deaths attributable to CHB at the end of 2019 relative to the end of 2017 was variable between jurisdictions and is difficult to reliably estimate in states and territories with smaller populations of people living with CHB. Some jurisdictions with larger populations showed a similar reduction in deaths when compared to the national estimate of 5.5%, with VIC and WA estimated to have reductions of 6.8% and 5.5%, respectively. However, QLD and NSW estimated to have reductions below the national estimate with 5.2% and 5.0% respectively.

Figure 21. Estimated number of deaths attributable to chronic hepatitis B by jurisdiction, 1991-2019.

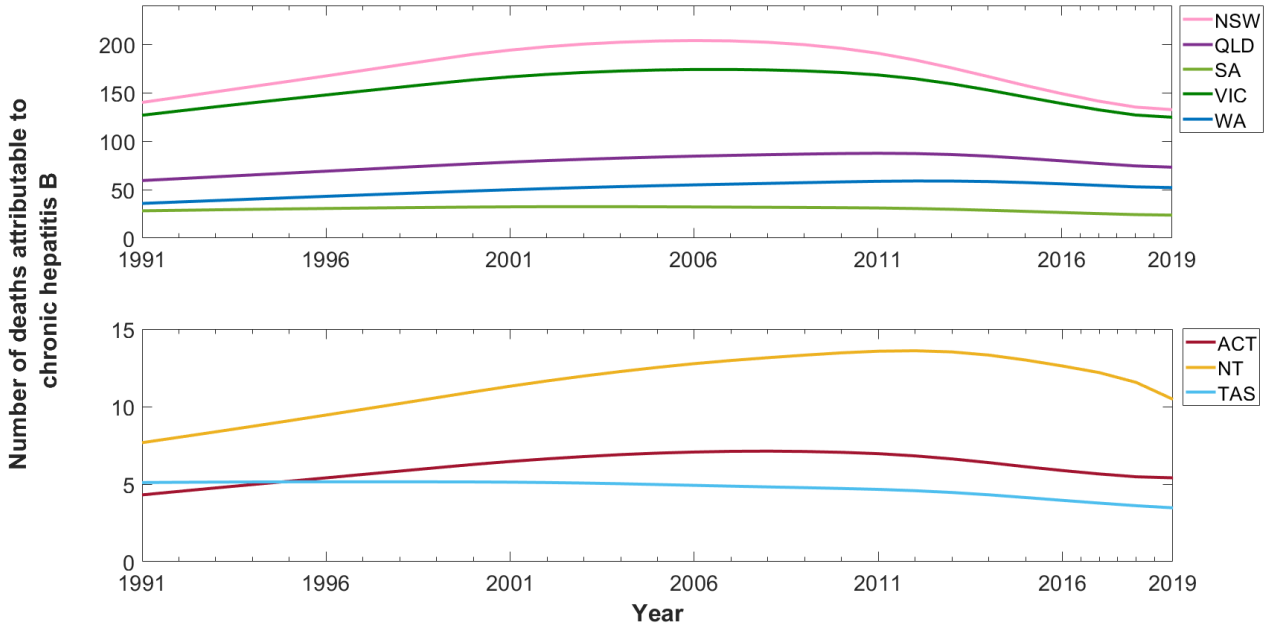


Table 8. Estimated number of total deaths attributable to chronic hepatitis B and population numbers by jurisdiction, 2019

State/Territory	Total deaths attributable to CHB	Plausible range		People living with CHB
		Minimum	Maximum	
ACT	5	3	8	3,470
NSW	133	96	197	81,483
NT	11	8	14	4,355
QLD	73	56	97	35,305
SA	25	17	39	12,243
TAS	4	2	6	1,692
VIC	124	84	206	68,819
WA	52	36	79	22,787
Australia	427	302	646	230,154

Figure 22. Estimated number of HCC deaths attributable to chronic hepatitis B across jurisdictions, 1991-2019.

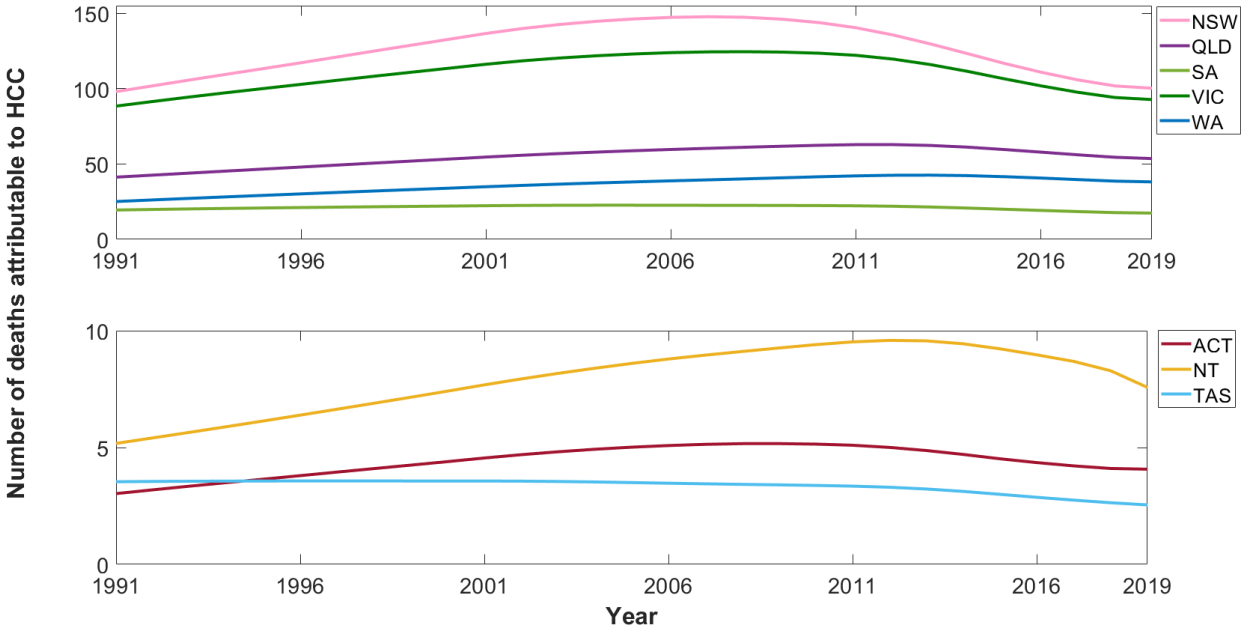


Figure 23. Estimated number of DC deaths attributable to chronic hepatitis B across jurisdictions, 1991-2019.

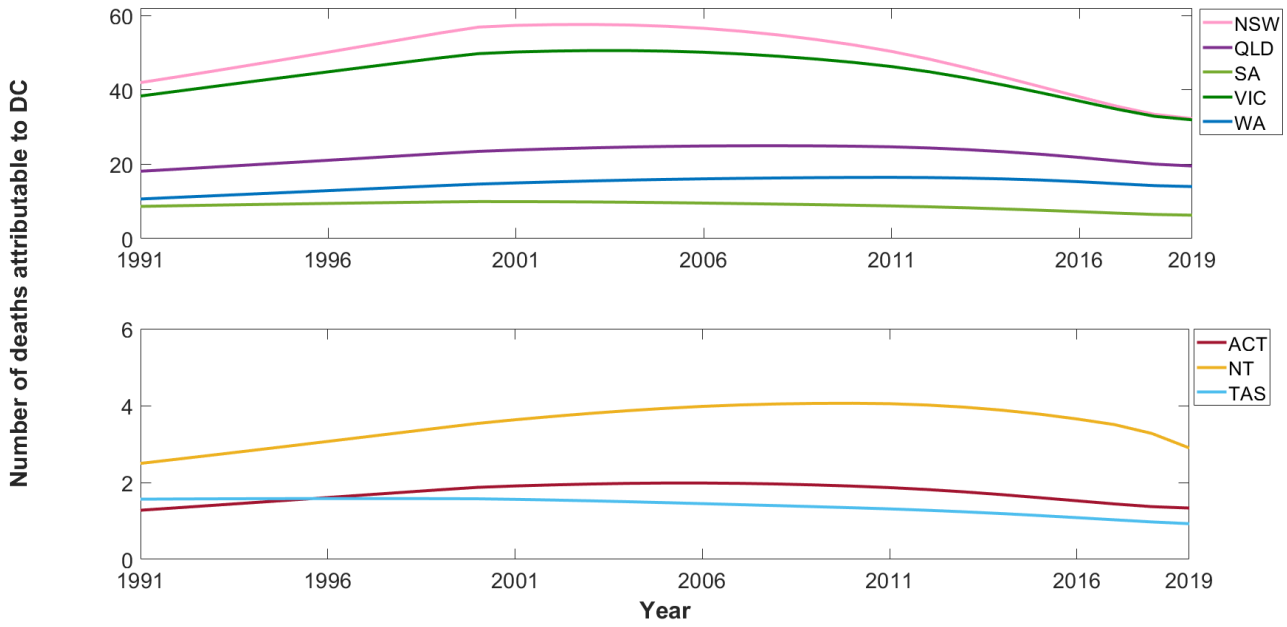


Table 9. Estimated number of HCC deaths and DC deaths attributable to chronic hepatitis B by jurisdictions in 2019

State/Territory	HCC deaths attributable to CHB	HCC Plausible range		DC deaths attributable to CHB	DC Plausible range	
		Minimum	Maximum		Minimum	Maximum
ACT	4	3	6	1	0	2
NSW	100	74	146	33	22	51
NT	8	6	10	3	2	4
QLD	53	42	70	20	14	27
SA	18	13	28	7	4	11
TAS	3	2	4	1	0	2
VIC	92	64	150	32	20	56
WA	38	27	57	14	9	22
Australia	316	231	471	111	71	175

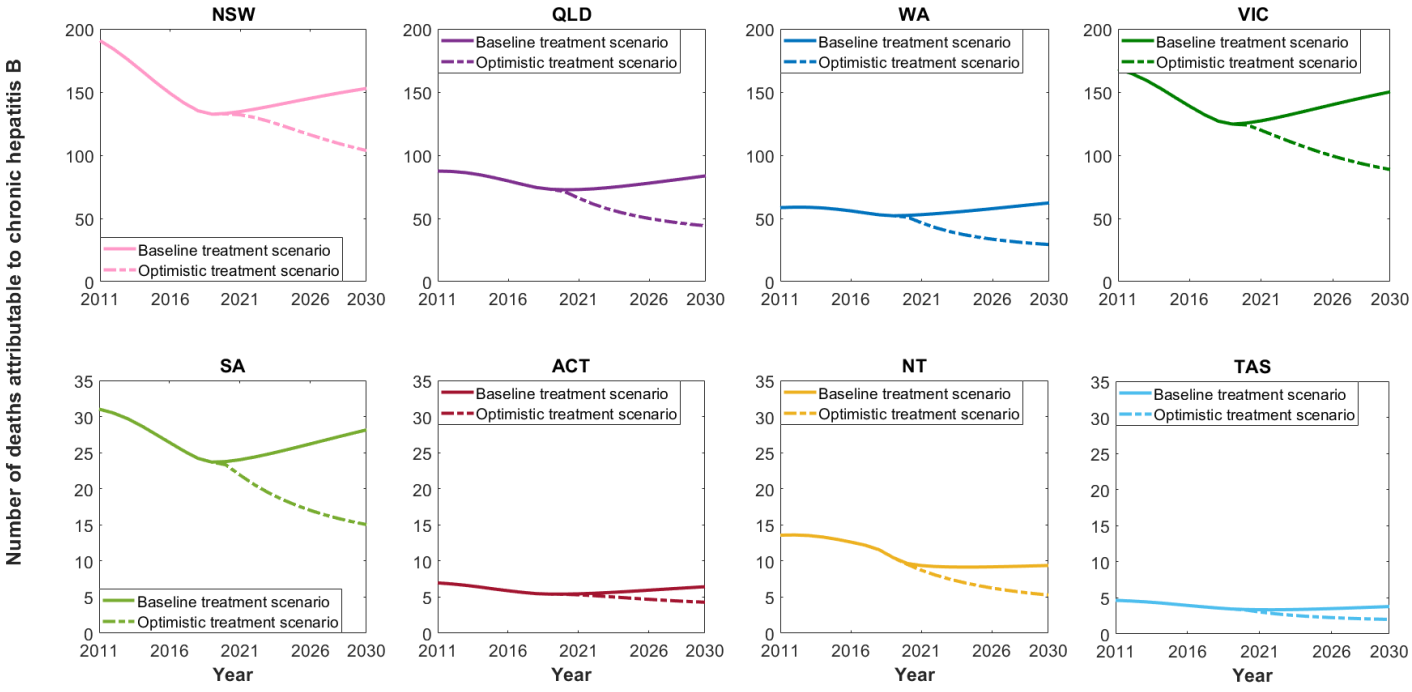
B.2.5.1 Impact of treatment on mortality

Considerable progress will be required in all jurisdictions to reach the National Strategy target of a 30% reduction in hepatitis B attributable mortality by 2022 compared to 2017. The estimated future mortality attributable to chronic hepatitis B depends on the future treatment uptake. Two

treatment scenarios were modelled (Figure 20 and page 31) - the baseline and optimistic scenarios – which result in very different reductions in future mortality.

Under the baseline treatment scenario, it is estimated that despite previous decreases, most jurisdictions will start to again see an increase in the number of deaths attributable to chronic hepatitis B (Figure 24). This projection is due to the fact that treatment uptake is increasing at a slower rate when compared to 2011 to 2015, combined with the continual increase in the estimated number of people living with CHB and an ageing population (Figure 20). Future estimates to 2022 show QLD, VIC and NSW will have the highest estimated reduction in mortality when compared to 2017 of 5.2%, 2.3% and 2.1% respectively. Unlike the baseline treatment scenario, estimates from the optimistic scenario showed mortality continues to decline. The highest estimated reduction in mortality in 2022 when compared to 2017 is seen in WA (21.8%), QLD (20.8%), VIC (12.8%) and NSW (7.1%) (Figure 24). However, this requires substantial increase in the treatment uptake in jurisdictions from 2020 onwards (Figure 20).

Figure 24: Comparison of estimated total number of deaths attributable to chronic hepatitis B in each jurisdiction under the baseline and optimistic treatment scenarios.



Note the difference in y-axis bounds between top and bottom rows.

C. Methodological Notes

To ensure estimates most accurately reflect the current epidemiology and clinical pattern of CHB in Australia, data inputs and assumptions are updated regularly to incorporate new information. For that reason new estimates may differ in some respects from previous outputs reported in the Kirby Institute's Annual Surveillance Reports,[5] the Doherty Institute's National Viral Hepatitis Mapping Project Reports,[1, 10, 20] and the National Surveillance for Hepatitis B Indicators: 2018 Annual Report[9].

C.1 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 – 2019 2020– 2050	 Federation to Century's End Australian Bureau of Statistics Department of Social Services, Australian Bureau of Statistics Australian Bureau of Statistics
CHB prevalence by country of birth	Published literature
CHB phase distribution	Published and grey literature, expert opinion
Treatment uptake	Pharmaceutical Benefits Scheme
Vaccination uptake	Australian Immunisation Register data

C.2 Mathematical Model

The estimates presented in this report were derived from the recently published mathematical model [11]. The model is a dynamic, age-structured deterministic mathematical model that incorporates important demographic features such as births, migration, deaths and aging over time. To optimise accurate representation of the transmission, epidemiology and progression of hepatitis B, the 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 no-cirrhosis and cirrhosis classifications and stratified by those receiving treatment and those not receiving treatment. This results in the model consisting of a total of 21 health states. Each health state is broken down into 18 age categories (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 exploration of age-specific and health-state specific estimates, such as disaggregated mortality estimates for DC and HCC.

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 generated based predominantly on a review of published and grey literature. Details of these transition estimates have been published elsewhere.[11]

Transmission
A dynamic, age-adjusted measure of the force of infection is incorporated in the model to account for local transmission over time. The impact of vaccine uptake over time was modelled using the Australian Immunisation Register data by age and year. Measures of vaccine efficacy by age group were used to estimate the proportion of individuals receiving effective vaccination for hepatitis B in the Australian population.

Demographic data
The Australian Bureau of Statistics (ABS) provided the majority of the demographic data used in the model. This included total population numbers[21, 22], births[21], deaths[23, 24] and life tables[25] used to derive age-group mortality rates 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. Data regarding net overseas migration (NOM) produced by the ABS provided the total number of people entering the population from 1951 to 2019 as well as estimates of future NOM from 2020 to 2050.[26] Age and country of birth distributions within this were calculated using different sources dependent on time period and data availability:

- *2005 to 2019,* ABS NOM by country of birth data were used to estimate the total number of people entering the population each year. Department of Social Services (DSS) settlement data[27] were used to estimate the age distribution by country of birth and applied to the ABS NOM country of birth to estimate the number of people by age group and country of birth migrating into the population.
- *1991 to 2004,* DSS settlement data[27] were used to estimate total migrant arrival numbers by country of birth by age by year.
- *1975 to 1990,* ABS migration data[28] were used to determine the number of migrants entering by country of birth. National age distribution data were not available prior to 1991, so data from the state of Victoria (representing 25% of Australia's population) on age distribution during 1975 to 2006 were applied as they were found to be a reasonable approximation.

- *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.[29]

Prevalence

At the start of the modelled period (1951), the baseline prevalence of the Australian population was assumed to be 0.5%,[30] representing a low prevalence country. The number of people living with CHB migrating to Australia each year was derived using the estimated prevalence of CHB according to country of birth. To account for changing age-specific source population prevalence over time (due predominantly to infant vaccination programs), we derived varying prevalence estimates across different time periods and applied these to migration data according to age group and year of arrival for country of birth for the majority of 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). Different data sources were used for different time periods:

- *1991 to 2018,* For those migrating into Australia born in 1991 or later, prevalence estimates derived for the Viral Hepatitis Mapping Project National Report 2017 [1] were applied. These prevalence estimates were taken predominately from local seroprevalence surveys,[31, 32] supplemented with global systematic reviews.[33, 34] Antenatal estimates were adjusted upwards to correct for the discrepancy in CHB prevalence by sex.[35]
- *1951 to 1990,* For those migrating into Australia born prior to 1991, prevalence estimates derived by the CDC as of 2008 were applied.[30] Countries were divided into three categories, based on the prevalence during this period; low prevalence (0.5%), intermediate prevalence (5%) and high prevalence (10%). These estimates are higher compared to those during 1991-2017 which takes into account prevalence estimates in the pre-vaccination era.

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 Philippines.[20, 33, 36-39] Specific prevalence estimates by country and year of birth were applied to incoming migrants.

Phase distribution

Individuals living with CHB migrate into Australia in different disease phases. The proportion of individuals living with CHB 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.[40-42] All source countries were categorised into three world regions (Asia/Pacific, Africa, and Other) to account for differences in natural history.

Treatment

This model incorporates the impact of treatment by estimating differential uptake rates by disease phase, with proportions according to disease phase determined using expert opinion and literature reviews, which were then fitted to treatment uptake derived from PBS data.

Data obtained from PBS records were used to derive the number of people on treatment in Australia each year since 2000. It excludes individuals prescribed lamivudine or tenofovir for HIV infection.

Plausible range

The plausible ranges reported were derived by allowing the force of infection, migrant population prevalence, proportion of migrants with CHB living with cirrhosis, CHB mortality, and other disease transition estimates to vary according to prior knowledge of possible distributions.[11] This was achieved using Latin-hypercube sampling (LHS), as described by Marino et al.[43] The mathematical model was run using 1000 different combinations of these varied parameters, 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. Some of the data sources differed from the national model due to availability and appropriateness of data. For years when ABS NOM by jurisdiction was not available, we imputed total numbers entering the population for each jurisdiction by applying a proportion (derived from available jurisdiction NOM breakdown) to the national NOM by year. The age distribution of incoming migrants by country of birth was imputed for missing years based on the overall age distribution of permanent settlers arriving in 1991 (obtained from DSS settlement data) which were applied back to 1951.

Although the national model does not currently explicitly model the differential prevalence among Aboriginal and/or Torres Strait Islander peoples, this was incorporated into the model for state and territories where this proportionally has the greatest effect on the number of people living with CHB (QLD and NT). This also ensures that estimates in QLD and NT more accurately reflect the true population. This was incorporated by adjusting the prevalence among the proportion of Aboriginal and/or Torres Strait Islander peoples living in both jurisdictions.[44-46]

Prior to 1990, Census data poorly reflect the actual number of Aboriginal and/or Torres Strait Islander peoples living in Australia,[47] which underestimates the population and has a substantial impact on output estimates. To better reflect total population numbers in the years prior to 1990, reported populations and number of births were adjusted upwards each year in accordance with the proportion of Aboriginal and/or Torres Strait Islander population and births during the 1991 to 2016.[48] Differential phase information for Aboriginal and/or Torres Strait Islander peoples living with CHB was estimated[49] to reflect the differences in natural history. Data were provided from the Hepatitis B Sero-Coding Project, Northern Territory Government. Further model development will incorporate adjustments for the remaining states and territories, dependent on the availability of appropriate data.

Each jurisdiction was modelled separately to adequately capture trends in the epidemiology of CHB over time. Jurisdictional estimates were then standardized to ensure the sum of indicator variables across the jurisdictions matches the modelled national estimate.

C.3 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 2018 as the numerator. Notification data has been sourced from the National Notifiable Diseases Surveillance (NNDSS) system.

NNDSS data 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: Estimating the proportion of people living with chronic hepatitis B who are engaged in care, receiving either treatment or monitoring
The proportion of people living with CHB who are receiving care was calculated using the number of people receiving either treatment or monitoring as the numerator and the modelled number of people living with CHB as the denominator.

The number of people receiving monitoring was obtained from Medicare Benefits Schedule (MBS) records and calculated by assessing the number of individuals who received a viral load test in a given year while not receiving treatment items in the past 12 months, in order to identify those undergoing off-treatment monitoring separately from those monitored during treatment. This number was then combined with the number of individuals who were receiving treatment, to generate the number in care. The number of people receiving treatment was obtained from PBS records and excludes individuals prescribed lamivudine or tenofovir for HIV infection.

These data do not include services that were not provided by Medicare, such as those paid for by individual patients, or subsidised by state government services. However, previous analyses and comparison with other source data demonstrate that the vast majority of testing and treatment services for patients with hepatitis B are provided through Medicare and included in these estimates.[50]

4: Estimating 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 CHB 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.

5: Estimating 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.

D. 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	74264	704	24679	1276	11274	6170	1315	22925	5921
1971	75555	732	25018	1386	11459	6211	1301	23309	6139
1972	76801	757	25339	1502	11642	6250	1286	23674	6351
1973	78012	783	25654	1613	11817	6286	1271	24029	6559
1974	79212	809	25966	1724	11988	6324	1257	24381	6763
1975	80352	831	26260	1826	12146	6368	1244	24717	6960
1976	81593	853	26619	1915	12309	6426	1235	25076	7160
1977	83523	888	27333	2026	12579	6445	1224	25621	7407
1978	85729	928	28191	2133	12843	6480	1213	26276	7665
1979	88225	970	29153	2244	13124	6547	1203	27027	7957
1980	91160	1018	30335	2349	13448	6628	1195	27910	8277
1981	94503	1072	31728	2429	13840	6706	1187	28920	8621
1982	97783	1123	33080	2517	14271	6770	1180	29879	8963
1983	100541	1161	34181	2598	14665	6825	1172	30674	9265
1984	103216	1200	35199	2681	15062	6900	1166	31425	9583
1985	106237	1247	36345	2769	15482	7003	1166	32279	9946
1986	109808	1306	37796	2854	15937	7099	1166	33298	10352
1987	114432	1382	39836	2935	16474	7177	1160	34625	10843
1988	119854	1474	42247	3023	17075	7281	1157	36189	11408
1989	125141	1563	44604	3106	17694	7382	1154	37693	11945
1990	130390	1650	46913	3192	18404	7476	1153	39131	12471
1991	135373	1729	49144	3274	19157	7556	1149	40448	12916
1992	138270	1776	50536	3340	19691	7555	1137	41135	13100
1993	139617	1804	51222	3399	19999	7509	1119	41377	13188
1994	140816	1830	51826	3457	20252	7460	1101	41604	13286
1995	142290	1864	52576	3521	20504	7420	1082	41915	13408
1996	143566	1892	53252	3576	20748	7370	1063	42167	13498
1997	144210	1908	53627	3622	20955	7299	1043	42236	13520
1998	144571	1924	53885	3667	21101	7218	1025	42235	13516
1999	145040	1947	54191	3714	21222	7146	1010	42283	13527
2000	145864	1980	54631	3742	21348	7100	1003	42463	13597
2001	146678	2008	55056	3751	21459	7062	997	42651	13694
2002	147422	2031	55445	3757	21588	7020	989	42808	13784
2003	148713	2070	56050	3763	21800	7000	983	43149	13898
2004	151023	2091	56935	3787	22142	7076	991	43898	14103
2005	154361	2116	58087	3812	22657	7299	1025	44925	14440
2006	158393	2168	59479	3811	23314	7620	1069	46055	14877

2007	164131	2232	61469	3818	24213	8057	1118	47739	15485
2008	172065	2317	64150	3874	25421	8582	1177	50143	16401
2009	181059	2444	66908	3956	26926	9155	1241	52942	17487
2010	187890	2572	68748	4022	28164	9679	1297	55055	18353
2011	191574	2642	69528	4066	28921	9978	1322	56072	19045
2012	194883	2712	70087	4124	29697	10198	1352	56851	19862
2013	199419	2788	71129	4213	30661	10463	1388	57999	20778
2014	204494	2877	72633	4263	31584	10788	1418	59500	21431
2015	209687	2996	74389	4283	32369	11136	1450	61217	21847
2016	215264	3115	76323	4308	33135	11468	1497	63199	22219
2017	221420	3243	78557	4334	33994	11773	1560	65424	22535
2018	226566	3386	80363	4348	34726	12019	1624	67391	22709
2019	230154	3470	81483	4355	35305	12243	1692	68819	22787
2020	233778	3540	82712	4370	35873	12430	1735	70221	22897
2021	237236	3611	83890	4388	36424	12590	1763	71526	23044
2022	240163	3673	84821	4400	36935	12730	1788	72606	23210
2023	242532	3726	85500	4408	37397	12850	1811	73454	23386
2024	244352	3770	85936	4413	37812	12945	1830	74078	23568
2025	245641	3804	86142	4417	38173	13019	1846	74493	23747
2026	246425	3829	86132	4420	38486	13072	1859	74709	23918
2027	246720	3846	85917	4421	38748	13106	1870	74740	24072
2028	246652	3851	85579	4417	38965	13121	1877	74647	24195
2029	246287	3852	85148	4410	39143	13119	1882	74456	24277
2030	245640	3850	84627	4402	39280	13100	1883	74172	24326

Table A2. *Model output for the proportion of people living with chronic hepatitis B in Australia who have been diagnosed, 2011-2019*

Year	National (%)	ACT (%)	NSW (%)	NT (%)	QLD (%)	SA (%)	TAS (%)	VIC (%)	WA (%)
2011	63.0%	62.6%	72.2%	61.0%	67.1%	60.7%	42.3%	54.9%	50.2%
2012	64.2%	64.1%	73.9%	63.4%	67.4%	62.0%	44.0%	56.4%	51.5%
2013	65.4%	65.6%	75.2%	67.8%	67.5%	62.6%	45.3%	57.6%	52.9%
2014	66.1%	66.3%	76.2%	69.4%	67.8%	63.2%	46.7%	58.4%	53.7%
2015	66.8%	66.1%	76.8%	71.4%	68.6%	63.5%	47.4%	59.0%	54.6%
2016	67.4%	66.0%	77.2%	72.4%	69.4%	63.7%	47.8%	59.4%	55.8%
2017	67.6%	65.7%	77.4%	73.2%	69.7%	63.9%	47.8%	59.6%	56.8%
2018	68.1%	65.2%	77.9%	73.8%	70.1%	64.1%	47.9%	59.9%	57.9%
2019	68.8%	65.7%	78.7%	74.5%	70.8%	64.6%	48.7%	60.5%	58.9%

Table A3. *Model output for the proportion of people living with chronic hepatitis B in Australia who are engaged in care, 2011-2019*

Year	National (%)	ACT (%)	NSW (%)	NT (%)	QLD (%)	SA (%)	TAS (%)	VIC (%)	WA (%)
2011	11.8%	9.3%	14.6%	2.7%	7.9%	7.8%	5.6%	14.2%	3.8%
2012	14.3%	12.9%	17.3%	10.1%	9.8%	9.7%	5.9%	17.1%	5.3%
2013	16.7%	17.3%	19.8%	14.1%	11.4%	15.3%	7.7%	19.9%	6.5%
2014	19.6%	19.1%	24.0%	17.2%	12.4%	18.9%	9.6%	23.0%	7.4%
2015	19.6%	19.6%	24.5%	20.5%	12.5%	18.7%	13.2%	21.4%	8.8%
2016	20.8%	20.8%	25.6%	19.7%	13.7%	20.0%	14.4%	22.3%	9.9%
2017	21.3%	20.5%	25.7%	21.5%	15.6%	19.2%	16.4%	22.8%	10.3%
2018	22.1%	22.1%	26.9%	27.8%	17.0%	18.6%	15.8%	23.1%	9.8%
2019	22.1%	22.2%	26.7%	24.9%	17.8%	16.4%	14.8%	24.0%	9.7%

Table A4. *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, 2011-2019*

Year	National (%)	ACT (%)	NSW (%)	NT (%)	QLD (%)	SA (%)	TAS (%)	VIC (%)	WA (%)
2011	3.1%	3.0%	4.4%	1.0%	1.7%	2.2%	1.3%	3.1%	1.8%
2012	4.1%	4.0%	6.1%	1.3%	2.3%	2.9%	1.6%	3.7%	2.1%
2013	5.7%	6.2%	7.9%	1.5%	3.4%	5.0%	2.8%	5.7%	2.9%
2014	7.3%	7.9%	10.2%	2.0%	4.4%	6.4%	3.6%	7.3%	3.7%
2015	7.6%	8.4%	10.4%	4.0%	4.7%	5.9%	5.2%	7.4%	4.4%
2016	8.2%	8.7%	11.0%	4.3%	5.2%	6.2%	5.3%	8.1%	4.9%
2017	8.7%	9.2%	11.3%	5.5%	5.9%	6.8%	5.7%	8.6%	5.5%
2018	9.3%	10.1%	11.9%	7.2%	6.6%	7.2%	6.7%	9.1%	6.1%
2019	9.8%	11.0%	12.4%	8.3%	7.0%	7.8%	5.4%	9.7%	6.6%

Table A5. *Model output for the total number of deaths attributable to chronic hepatitis B in Australia, 2011-2019*

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
2011	562	7	192	14	88	31	4	168	58
2012	550	7	183	14	88	31	4	164	59
2013	534	7	176	14	86	29	4	159	59
2014	515	7	166	13	84	29	4	154	58
2015	493	7	157	13	82	28	4	145	57
2016	473	6	149	13	80	26	4	139	56
2017	452	5	140	13	77	25	4	133	55
2018	435	5	134	11	75	25	4	127	54
2019	427	5	133	11	73	25	4	124	52

Table A6. *Model output for the total number of HCC deaths attributable to chronic hepatitis B in Australia, 2011-2019*

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
2011	408	5	141	10	63	22	3	122	42
2012	400	5	135	10	63	22	3	119	43
2013	390	5	130	10	62	21	3	116	43
2014	376	5	123	9	61	21	3	112	42
2015	361	5	116	9	60	20	3	106	42
2016	347	4	111	9	58	19	3	102	41
2017	333	4	105	9	56	18	3	98	40
2018	322	4	101	8	55	18	3	94	39
2019	316	4	100	8	53	18	3	92	38

Table A7. *Model output for the total number of DC deaths attributable to chronic hepatitis B in Australia, 2011-2019*

Year	National	ACT	NSW	NT	QLD	SA	TAS	VIC	WA
2011	154	2	51	4	25	9	1	46	16
2012	150	2	48	4	25	9	1	45	16
2013	144	2	46	4	24	8	1	43	16
2014	139	2	43	4	23	8	1	42	16
2015	132	2	41	4	22	8	1	39	15
2016	126	2	38	4	22	7	1	37	15
2017	119	1	35	4	21	7	1	35	15
2018	113	1	33	3	20	7	1	33	15
2019	111	1	33	3	20	7	1	32	14

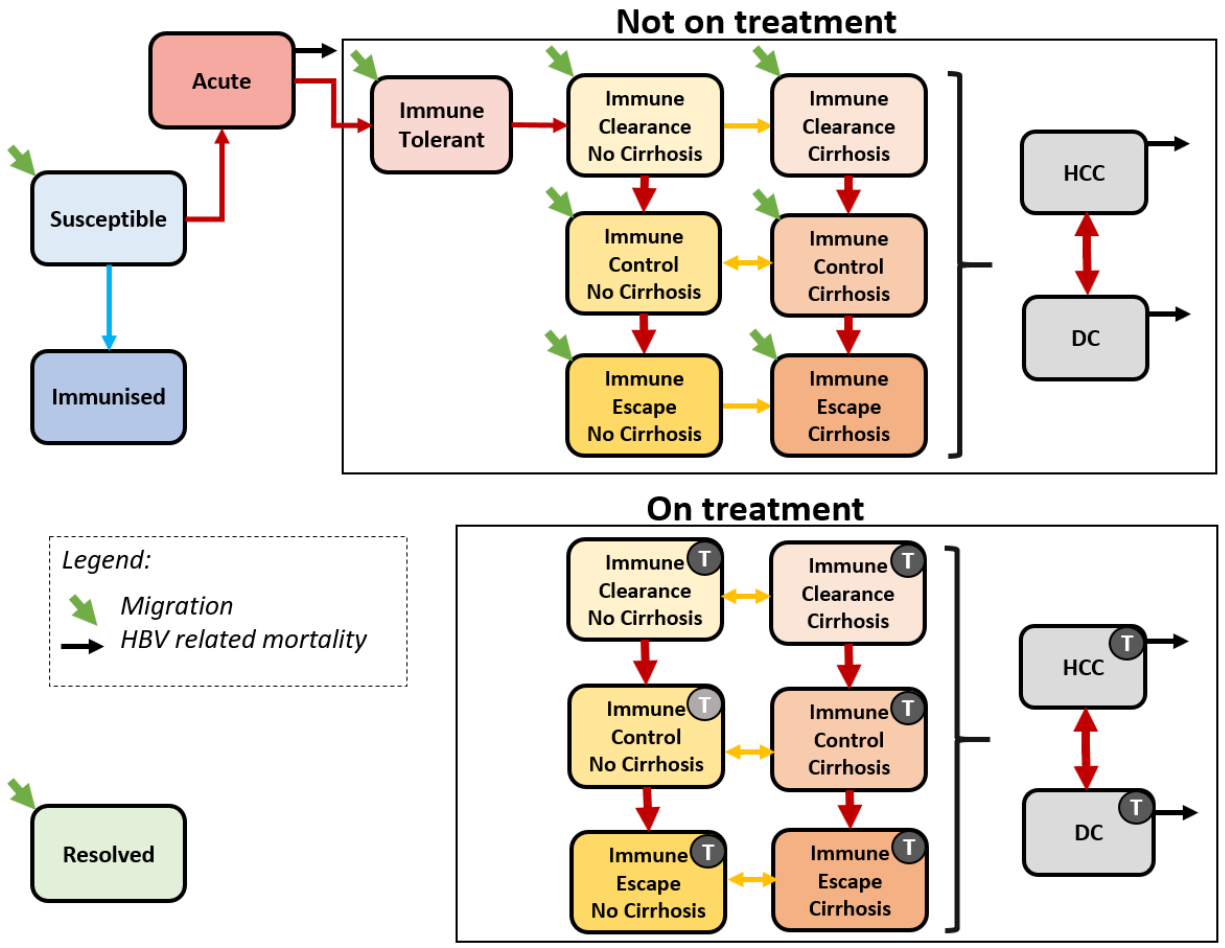


Figure A1: Schematic diagram of the mathematical model describing the progression of hepatitis B infection and indicating key transitions. Chronic hepatitis B phases are within the boxes. Phases with a 'T' indicate individuals in that phase receiving treatment. Light grey treatment icon indicates those who have transitioned into this phase while on treatment. HCC = hepatocellular carcinoma; DC = decompensated cirrhosis. Coloured arrows represent transitions between states. Each health state is stratefied by age. Resolution of infection is possible from acute infection and from CHB phases and results in the transition into the resolved state.

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