EXPLANATORY DOCUMENT FOR CHANGES TO AUSTRALIAN HEPATITIS B MODELLED ESTIMATES

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BACKGROUND TO PROJECT

- Estimates of hepatitis B in Australia are produced as part of the Surveillance for Hepatitis B Indicators Project, supported by the Australian Government Department of Health and Aged Care, and have been the basis for measurement of Australia's progress toward National Strategy Targets since 2016. They are reported on in the National Surveillance for Hepatitis B Indicators Report, published annually. The estimates are also used as the basis for hepatitis B estimates in the National Viral Hepatitis Mapping Report and are incorporated into the Kirby Institute Annual Surveillance Report.
- The project is conducted with the guidance of the WHO Collaborating Centre for Viral Hepatitis Research Advisory Group, which contains representation from government, community organisations, workforce development, people with lived experience, epidemiological and modelling research, and clinical experience.

BACKGROUND TO MODEL

- The number of people living with chronic hepatitis B (CHB) in Australia is estimated using a deterministic, age-structured dynamic mathematical model. The model accounts for diversity in prevalence and impact of overseas migration, incorporating detailed disease phase dynamics and examining the impact of vaccination and antiviral treatment on mortality attributable to CHB at a population level.
- Over time, the estimated number of people living with CHB in Australia has been subject to incremental changes as the model has been updated. As new research is published and new data sources relevant to the model become available, they are assessed and incorporated if appropriate; this includes clinical data regarding disease progression in hepatitis B, prevalence according to country of birth and year of birth and immunisation coverage both in Australia and overseas.
- As the estimated number of people living with CHB is used as the denominator for key indicators such as treatment uptake and care uptake, changes to this estimate can have follow-on impacts on these indicators. For instance, if the estimated number of people living with CHB decreases due to changes in the model, then the estimated proportion of people receiving treatment and care will increase, even if the number of people receiving treatment or care remains the same. This emphasizes the importance of regularly updating the model in response to new data sources becoming available to ensure accurate and reliable estimation of all hepatitis B indicators.

- In each National Surveillance for Hepatitis Indicators report, estimates are provided together with a plausible range that is generated through sensitivity analysis. Input data have unavoidable uncertainties, and this gives an indication of the likely range in which the true indicator values fall. The presentation of both the mid-point estimates and plausible range provides further transparency around uncertainty and ensures accurate interpretation.
- Sensitivity analysis has shown that the model is strongly affected by the prevalence of CHB in people migrating to Australia, and updates to these estimates can have substantial impact on the final number of people living with CHB. These estimates are continually changing as new studies are conducted, and new data become available.

CHANGES IN 2022 AND IMPACT

- The CHB mathematical model underwent annual review and revision in 2022. These revisions included:
    - Updates to historic CHB prevalence for countries of birth of migrants with the highest numbers of people living with CHB in Australia. This led to a downward revision of prevalence estimates (see Table 1). The number of people estimated to be living with CHB in Australia 2021 decreased by approximately 10% (from 223,220 to 200,385) which is a similar proportional change as has previously occurred[1-4].
    - Decreased the transition rate from HCC to resolved for those living with CHB and receiving treatment for their HCC diagnosis. This has led to an increase in the estimated number of annual deaths due to CHB. This estimate increased by approximately 23.2% (from 367 to 453).

Table 1: Comparison of estimates of key indicators for hepatitis B in 2021, before and after the incorporation of model revisions

Indicators	**Previous estimate**	**New estimate**	**Percent change**	**2022 Target**
Number of people living with CHB	223,220	**200,385**	-10.2%	-
Proportion of people living with CHB who are diagnosed	67.1%*	**72.5%***	8.0%	80.0%
Proportion of people living with CHB who are in care	23.3%	**26.0%**	11.3%	50.0%
Proportion of people living with CHB who are receiving treatment	11.4%	**12.7%**	11.6%	20.0%
CHB attributable mortality	367 deaths; 10.7% decrease since 2017	**453 deaths;** **6.3% increase since 2017**	23.2%	30% reduction from 2017

** Estimate assumes that 8% of notifications are duplicates*

- The revision to the estimated number of people living with CHB consequently changed the estimated uptake of treatment and care, though the impact was minimal. Using the previous denominator, care and treatment uptake were estimated to be 23.3% and 11.4% respectively; after this revision, they were estimated to be 26.0% and 12.7% respectively, and these revised

estimated were very close to the previous upper plausible range (25.3% and 12.3%, respectively).

- These changes make very limited impact in relation to progress toward National Strategy Targets for care and treatment, of 50% and 20% respectively; both the previous and the new estimates reflect that treatment uptake is less than two-thirds the target level, and care is less than half the target level. The overall message, that substantial numbers of people are not currently receiving necessary CHB treatment or care, remains unchanged.

VERIFICATION WITH OTHER SOURCES

Verification is an important complement to modelling, to ensure that outputs are consistent with other data sources. Our modelling outputs have been validated against a number of external data sources, as described below.

- CHB prevalence estimates are most commonly available from studies done in pregnant women, as they are a population that is the subject of near-universal testing uptake in the setting of antenatal care. Antenatal seroprevalence studies in Australia have shown a prevalence among women giving birth during 2000-2016 of 0.7%-0.8% in NSW[5, 6]. This is broadly consistent with the estimated prevalence using modelling, after adjusting for the lower prevalence seen in women compared to men[7].

- A national study of residual diagnostic blood samples found a CHB prevalence of 0.7% in 2002[8], which is consistent with the current modelled estimate of 0.6% for that year.

- Analysis of blood donor data has demonstrated that there is a significant correlation between CHB prevalence in blood donors and estimated prevalence using the modelling method, validating the estimated variations observed according to region[9].

- The current estimated proportion of individuals diagnosed with late-stage disease in hepatitis B, in both NSW[10] and VIC is consistent with the current modelled estimate of the proportion of individuals who remain undiagnosed.

- The modelled estimate of the number of HCC deaths attributable to CHB is in line with nationally reported estimates of liver cancer, and the estimated proportion attributable to hepatitis B[11, 12].

KEY RESOURCES

Hepatitis B Indicators Project Reports available at: https://www.doherty.edu.au/whoccvh/centre-activities/bbv-sti-surveillance-and-research-programme-surveillance-for-hepatitis-b-indicators

Viral Hepatitis Mapping Project Report available at: https://ashm.org.au/vh-mapping-project/

More details on model structure and parameters available in the following publication: https://aasldpubs.onlinelibrary.wiley.com/doi/full/10.1002/hep.30899

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REFERENCES

1. McCulloch K, Romero N, MacLachlan JH, Cowie BC. National Surveillance for Hepatitis B Indicators: Measuring the progress towards the targets of the National Hepatitis B Strategy – Annual Report 2020. Melbourne: WHO Collaborating Centre for Viral Hepatitis, The Doherty Institute; 2021.

2. Romero N, McCulloch K, Allard N, MacLachlan JH, Cowie BC. National Surveillance for Hepatitis B Indicators: Measuring the progress towards the targets of the National Hepatitis B Strategy – Annual Report 2019. Melbourne: WHO Collaborating Centre for Viral Hepatitis, The Doherty Institute; 2020.

3. Romero N, McCulloch K, MacLachlan JH, Cowie BC. National Surveillance for Hepatitis B Indicators: Measuring the progress towards the targets of the National Hepatitis B Strategy – Annual Report 2017. Melbourne: WHO Collaborating Centre for Viral Hepatitis, The Doherty Institute; 2019

4. Romero N, McCulloch K, Allard N, MacLachlan JH, Cowie BC. National Surveillance for Hepatitis B Indicators: Measuring the progress towards the targets of the National Hepatitis B Strategy – Annual Report 2018. Melbourne: WHO Collaborating Centre for Viral Hepatitis, The Doherty Institute; 2019

5. Deng L, Reekie J, Ward JS, Hayen A, Kaldor JM, Kong M, et al. Trends in the prevalence of hepatitis B infection among women giving birth in New South Wales. The Medical Journal of Australia. 2017 Apr 17;206(7):301-5.

6. He WQ, Duong MC, Gidding H, MacLachlan J, Wood J, Kaldor JM, et al. Trends in chronic hepatitis B prevalence in Australian women by country of birth, 2000 to 2016. Journal of Viral Hepatitis. 2020;27(1):74-80.

7. Cowie B, Karapanagiotidis T, Enriquez A, Kelly H. Markers of hepatitis B virus infection and immunity in Victoria, Australia, 1995 to 2005. Australian and New Zealand Journal of Public Health. 2010 Feb;34(1):72-8.

8. Gidding HF, Warlow M, MacIntyre CR, Backhouse J, Gilbert GL, Quinn HE, et al. The impact of a new universal infant and school-based adolescent hepatitis B vaccination program in Australia. Vaccine. 2007 Dec 12;25(51):8637-41.

9. MacLachlan JH, Cowie BC. Blood counts: the epidemiology of chronic hepatitis B is reflected in routinely collected donor data. J Clin Epidemiol. 2014 Mar;67(3):357-8.

10. Samji H, Yu A, Kuo M, Alavi M, Woods R, Alvarez M, et al. Late hepatitis B and C diagnosis in relation to disease decompensation and hepatocellular carcinoma development. Journal of Hepatology. 2017 Nov;67(5):909-17.

11. Australian Institute of Health and Welfare. Cancer in Australia 2021. Canberra: Australian Institute of Health and Welfare; 2021.

12. Hong TP. An Australian population-based study of the incidence and outcomes of hepatocellular carcinoma: the Hepatomas of Melbourne Epidemiological Research (HoMER) study; 2019.