Benefits of hepatitis B treatment in Australia: health and economic impacts of nucleos(t)ide analogues

SEAMAN CP, XIAO Y, HOWELL J, SCOTT N

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Declarations

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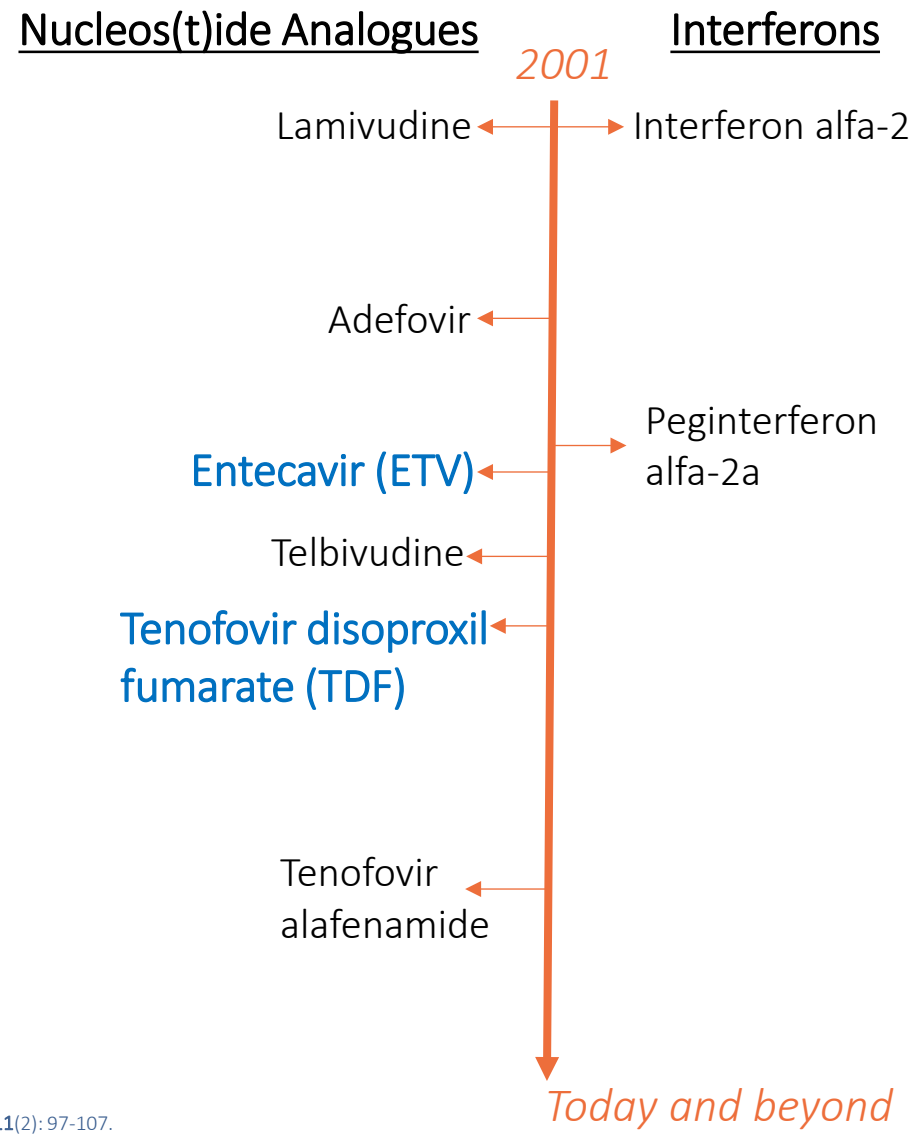
No other conflicts of interest to declare.

Hepatitis B treatment in Australia

- Treatment is an essential part of hepatitis B elimination efforts in Australia
  - 15-40% lifetime risk of liver failure or liver cancer in absence[1]
  - Only ~44% of eligible Australians receiving treatment in 2022[2,3]
- Treatment of hepatitis B is an evolving landscape
  - Treatment eligibility criteria
  - Pharmaceutical interventions
- As this landscape evolves, we need appropriate evidence to inform the best way of proceeding

PBS/PBAC approval of hepatitis B treatments[4]



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Economic evaluation of NUCs in Australia

- Most extensive cost-effectiveness data for hepatitis B treatment in Australia is for, or compared to, lamivudine
  - $2,028* per QALY gained (lamivudine vs natural history)[1]
  - $10,700* per QALY gained (entecavir [ETV] vs lamivudine); more cost-effective in HBeAg+ adults[2]

- Several more recent cost-effectiveness analyses include ETV and/or tenofovir disoproxil fumarate (TDF), but as part of broader elimination questions
  - Expanding TDF coverage from 2.9% to 15% cost-saving over a 10-year time horizon in South Australia[3]
  - Reaching WHO elimination targets (90% diagnosed, 80% treated) using ETV and TDF by 2030 would cost $14,482 per DALY averted[4]

- Progress toward changes in hepatitis B treatment landscape (including a cure) means establishing cost-effectiveness of treatments in the current Australian context is essential

*CPI adjusted to 2023 Australian Dollars (A$)

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Study Aims

This study aimed to:

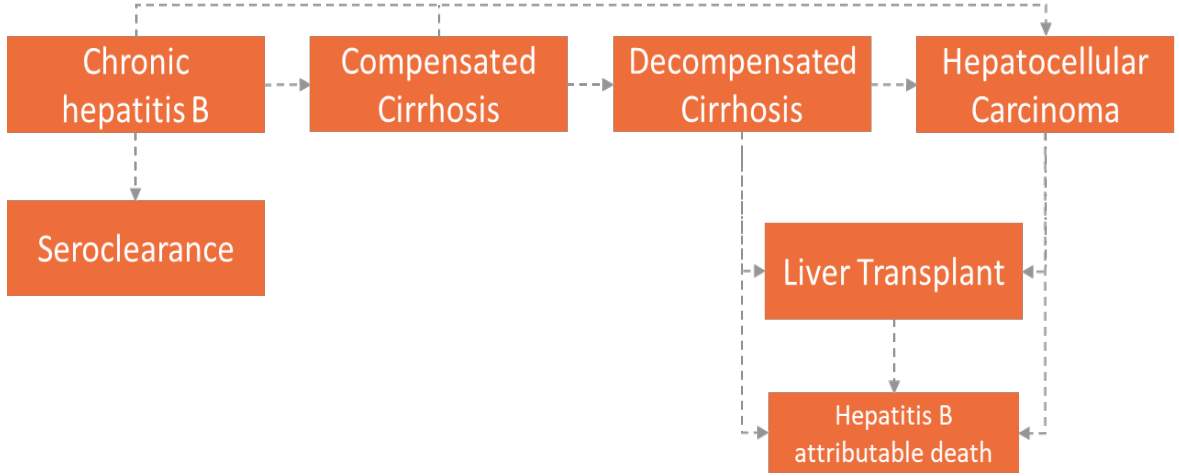
(1) Estimate the health benefits and cost-effectiveness of ETV and TDF (NUC) use among a cohort of Australians living with treatment-eligible chronic hepatitis B

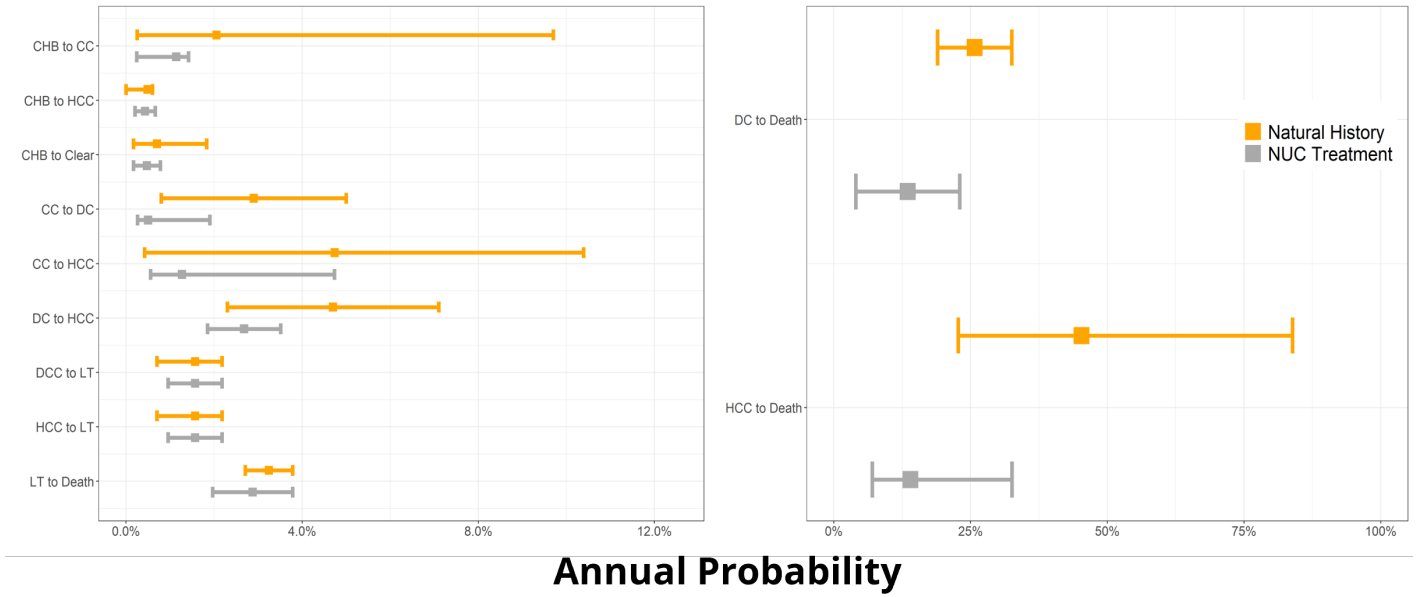
(2) Estimate the total health system costs of treatment-eligible hepatitis B in Australia, and the impact NUC treatment has on costs

(3) Identify key drivers of NUC treatment cost-effectiveness in Australia

Methods: disease progression modelling

- Representative cohort of 1000 Australians living with ***treatment-eligible*** chronic hepatitis B[1]
  - Average Age: 43 years
  - ~70% male
- Previously validated Markov model used to simulate disease progression under:
  (1) Natural history (no treatment)
  (2) NUC (TDF/ETV) treatment
- Liver transplants occurred at rate consistent with national data[2,3]
- Each disease state associated with a quality-of-life weight, informed by review of evidence in comparable high-income countries.





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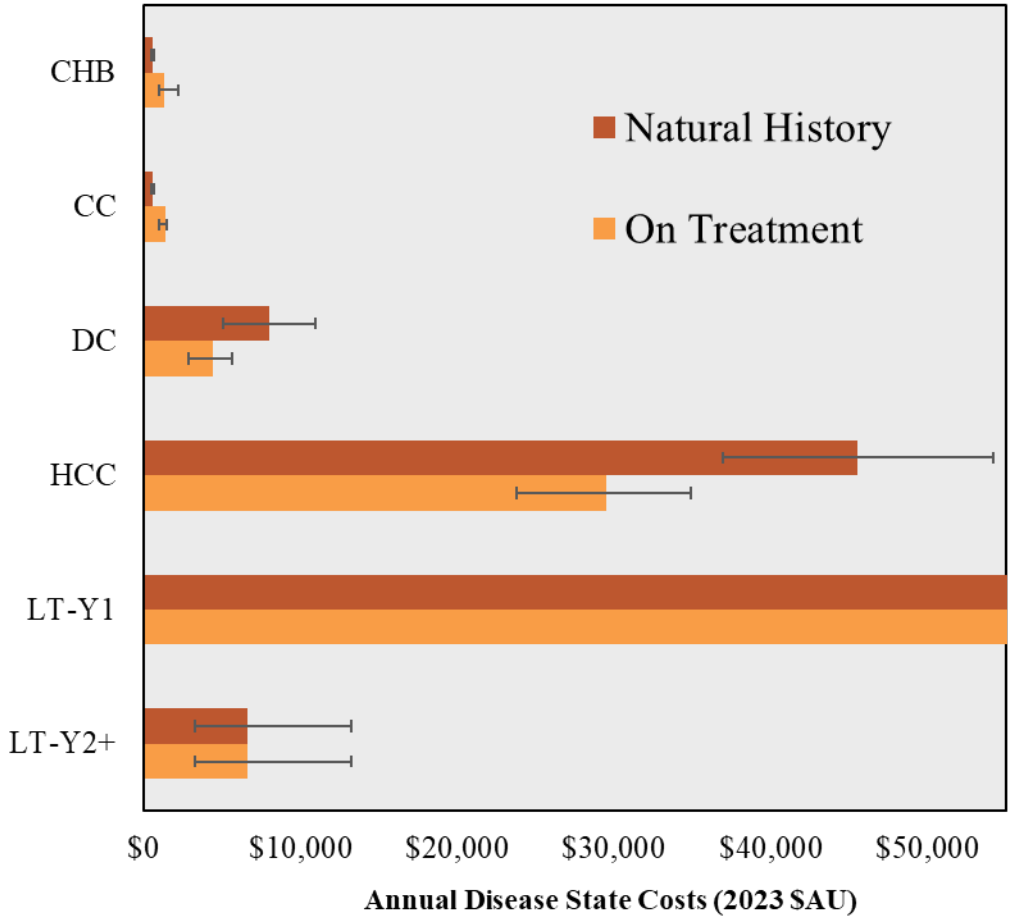
Methods: economic and cost modelling

- Annual costs of each health state derived using an ingredients-based methodology
  - Disease monitoring and HCC surveillance applied to best approximate national guidelines; equal in both cohorts
- 70% ETV : 30% TDF ratio for NUC use
  - TDF incurred bi-annual renal function test costs
- NUCs reduced frequency of hospitalisation in decompensated cirrhosis and HCC health states[1]
- Costs presented in 2023 Australian Dollars ($A) and discounted at 5% per annum[2]



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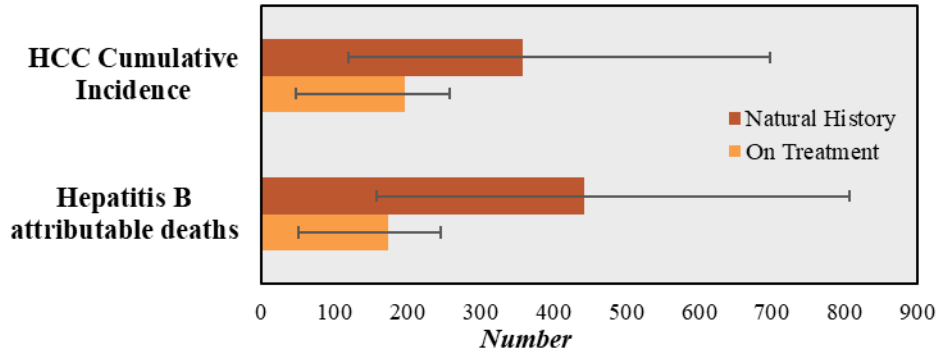
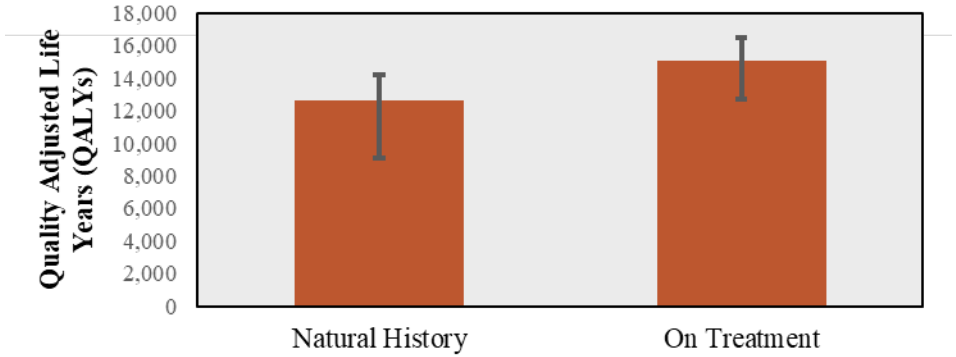
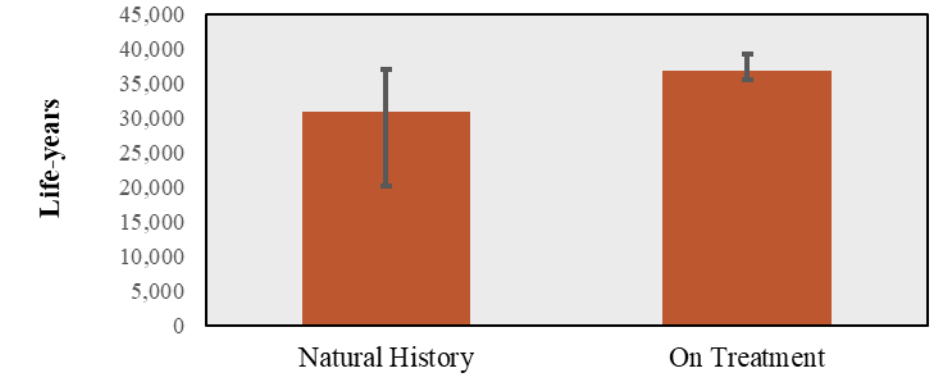
Results: health benefits of NUC treatment

For every 1000 Australians living with treatment-eligible chronic hepatitis B, we found NUC treatment:

- Averted 163 (95%CrI: 19, 546) HCC cases, and reduced incidence by 0.6 (95%CrI: 0.1, 2.9) cases per 100 person-years.
- Reduced hepatitis B attributable mortality by 60%, averting 269 (95%CrI: 54, 679) deaths
- Increased survival by an average 5.8 (95%CrI: 1.3, 17.3) years, and gained 2.5 (95%CrI: 1.3, 5.4) QALYs per person







Results: health system costs and cost-effectiveness

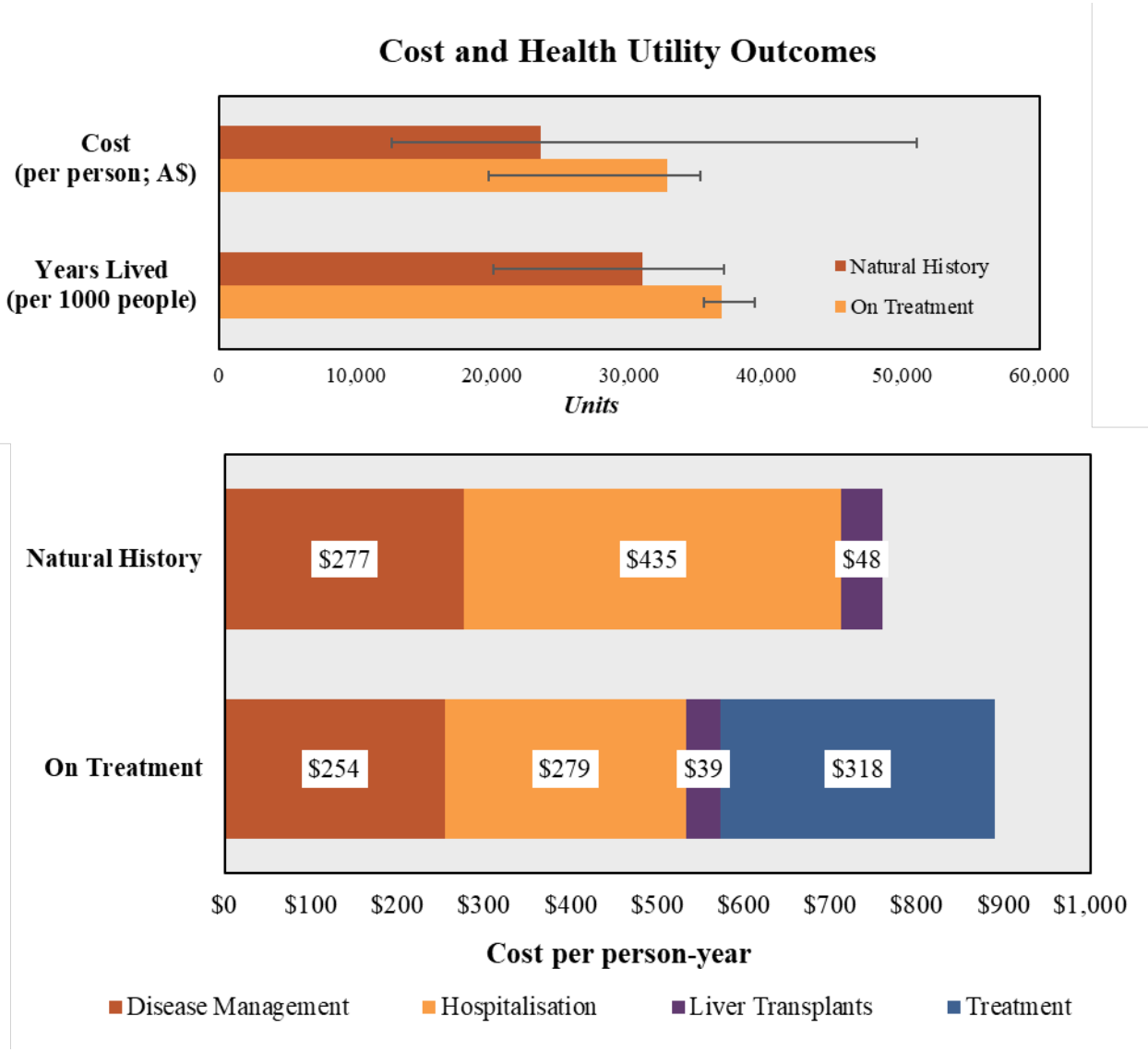
On average, NUC treatment **increased** the cost of treatment-eligible chronic hepatitis B in Australia by almost $10,000 per person.

Higher per-person costs persisted when adjusted for survival benefits of NUC treatment:

- **Natural History:** $760 (95%CrI: 347, 2,191) per-person-year
- **On Treatment:** $890 (95%CrI: 509, 960) per-person-year
- Additional $318 per-person-year partially (~60%; $188) offset by savings elsewhere in the health-system

Despite additional costs, use of NUCs in current Australian context is **highly** cost-effective:

- $34,401 (95%CrI: cost-saving, $184,092) per death averted
- $1,585 (95%CrI: cost-saving, $8,115) per life-year gained
- $3,736 (95%CrI: cost-saving, $9,186) per QALY gained

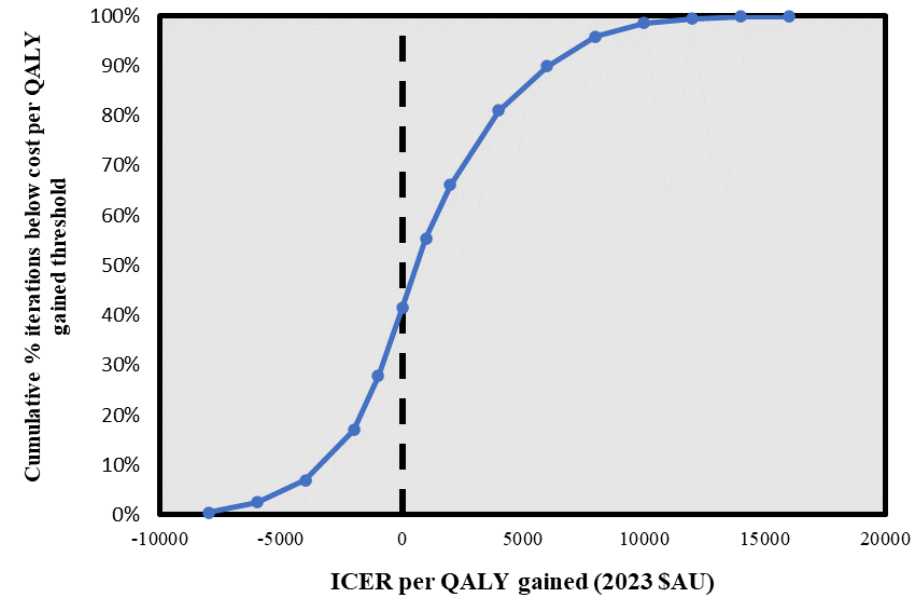


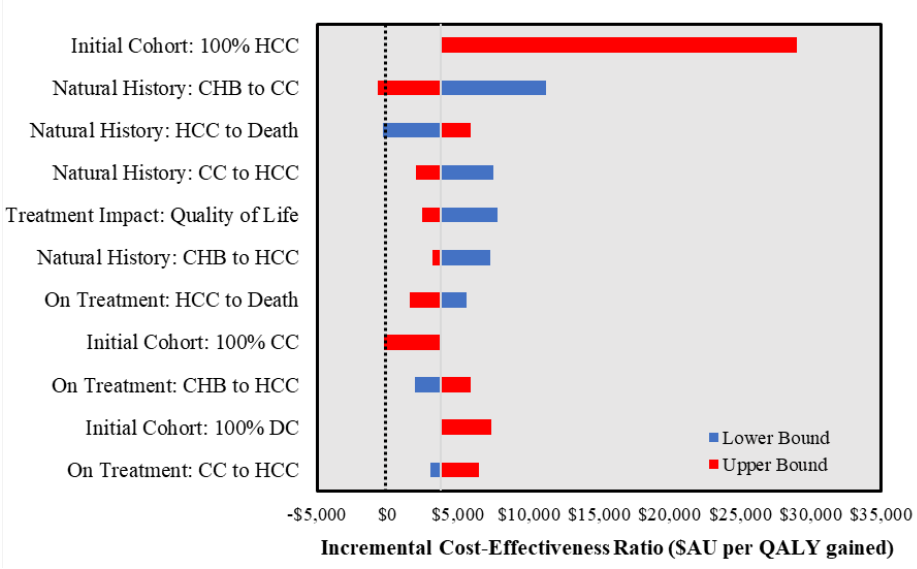
Results: key cost-effectiveness drivers

Cost-savings were seen in **~40%** of model simulations, and PBAC cost-effectiveness threshold of $50,000 per QALY gained exceeded in **0%** of model simulations.

A series of one-way sensitivity analyses demonstrated:

- Treatment could be even more cost-effective if targeted towards those at elevated risk of compensated cirrhosis
- Starting treatment in a younger cohort was modestly more cost-effective than an older cohort
- Starting treatment in decompensated cirrhosis or HCC stages was far less cost-effectiveness (*importance of screening*)
- Non-adherence to treatment (~20%) did not meaningfully alter cost-effectiveness but did reduce health benefits in NUC treatment cohort.
- Annual disease state cost assumptions had a non-significant impact on cost-effectiveness





Limitations

- Disease progression rates informed by small cohort studies, with significant uncertainty on parameter values leading to large error bounds on outputs
- Disease progression rates taken as an average risk over cohort lifetime, not dynamic with aging cohort
- Several benefits of NUCs (transmission reductions, productivity gains) not included in the analysis

Conclusions

- Use of ETV and TDF under current hepatitis B disease management guidelines in Australia may avert ~60% of hepatitis B attributable mortality within eligible cohort

- <$4,000 per QALY gained indicates exceptional cost-effectiveness profile, and one that could be further enhanced with reduced cost of NUCs

- While these results are timely, cost-effectiveness should only be one criteria by which any changes to the treatment landscape are evaluated
    - Broadening treatment eligibility may simplify care-cascade
    - A hepatitis B cure will likely be more expensive but improve individual health outcomes

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Thank you

Dr Chris Seaman
Email: chris.seaman@burnet.edu.au

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