

Integrating Mendelian Randomization With Real-World Evidence: Cost-Effectiveness of Lipoprotein (a) Testing for Primary Prevention of Cardiovascular Disease in High-Income Countries

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1 Background

- Lipoprotein(a) [Lp(a)] is an important risk factor for cardiovascular disease (CVD).
- Cost-effectiveness of Lipoprotein(a) [Lp(a)] testing is not established.
- We aimed to evaluate the cost-effectiveness of Lp(a) testing in the CVD primary prevention population from healthcare and societal perspectives.

2 Methods

- The model Lp(a) testing in individuals not initially classified as high-risk based on age, diabetes status, or the SCORE-2 algorithm. Those with an Lp(a) level ≥ 105 nmol/L (50 mg/dL) were treated as high risk (initiation of a statin plus blood pressure lowering). The Lp(a) testing intervention was compared to standard of care (**Figure 1**).

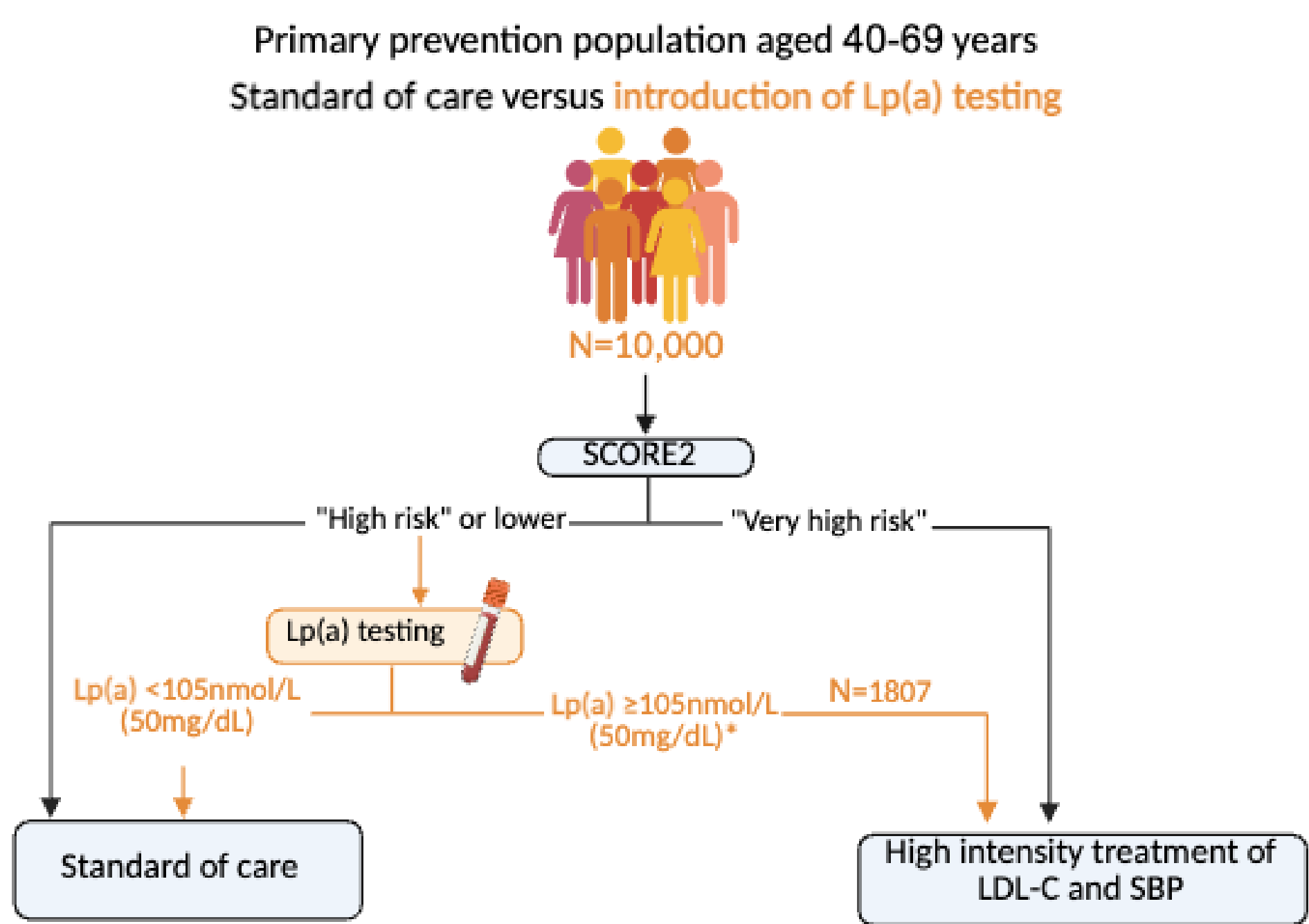


Figure 1. Standard of care versus intervention

- We constructed and validated a multi-state microsimulation Markov model for a population of 10,000 individuals aged between 40 and 69 years without CVD, selected randomly from the UK Biobank (**Figure 2**).
- The primary analyses were conducted from the **Australian and UK** healthcare perspectives in 2023AUD/GBP. A cost adaptation method estimated cost-effectiveness in multiple European countries, Canada, and the USA.
- The effects of LDL-C, SBP, Lp(a), and smoking on the risk of MI, stroke, and death from other causes was proportional to both magnitude and duration of exposure (i.e., the concept of cholesterol-years, pack-years, etc.), using Mendelian Randomisation.

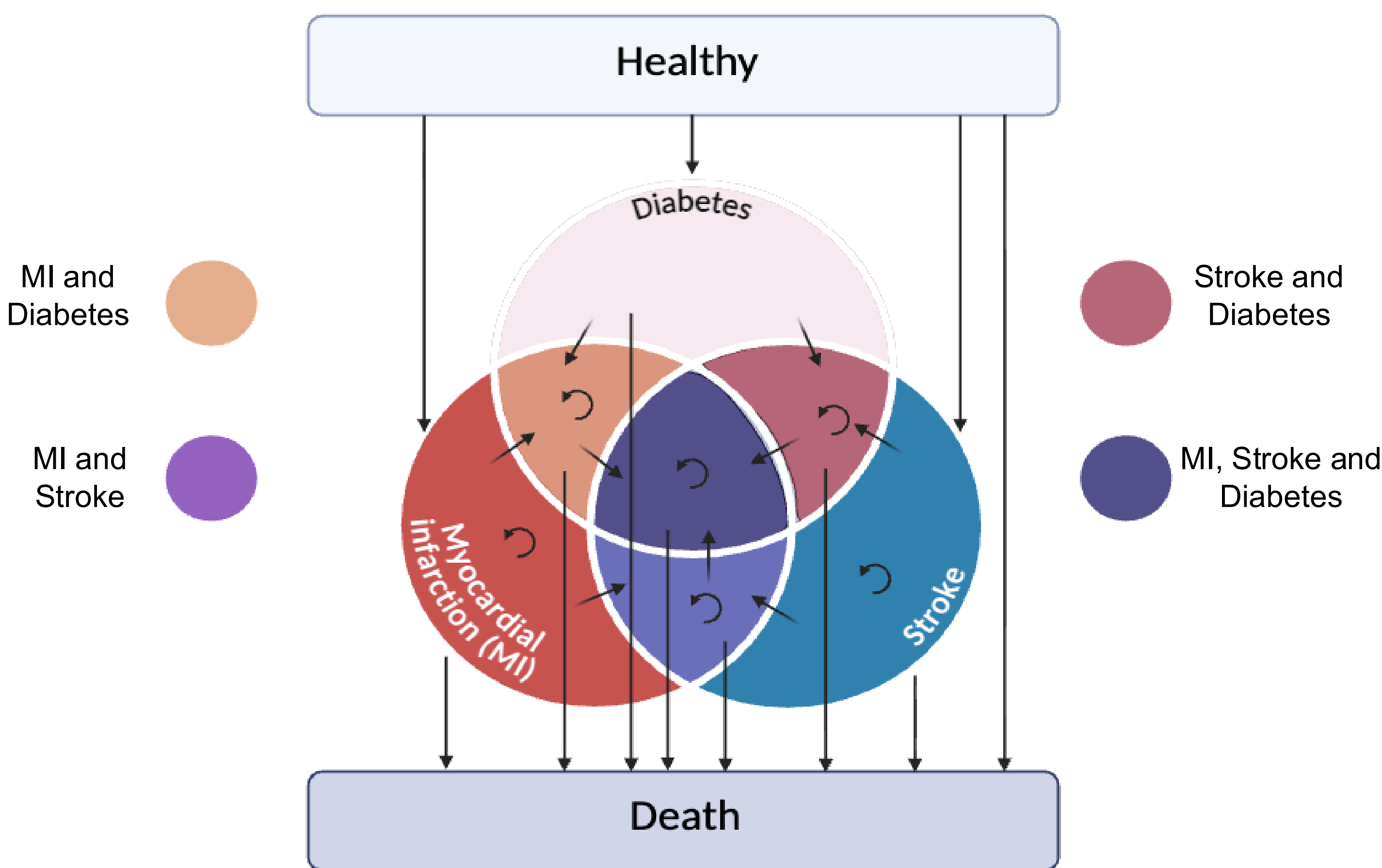
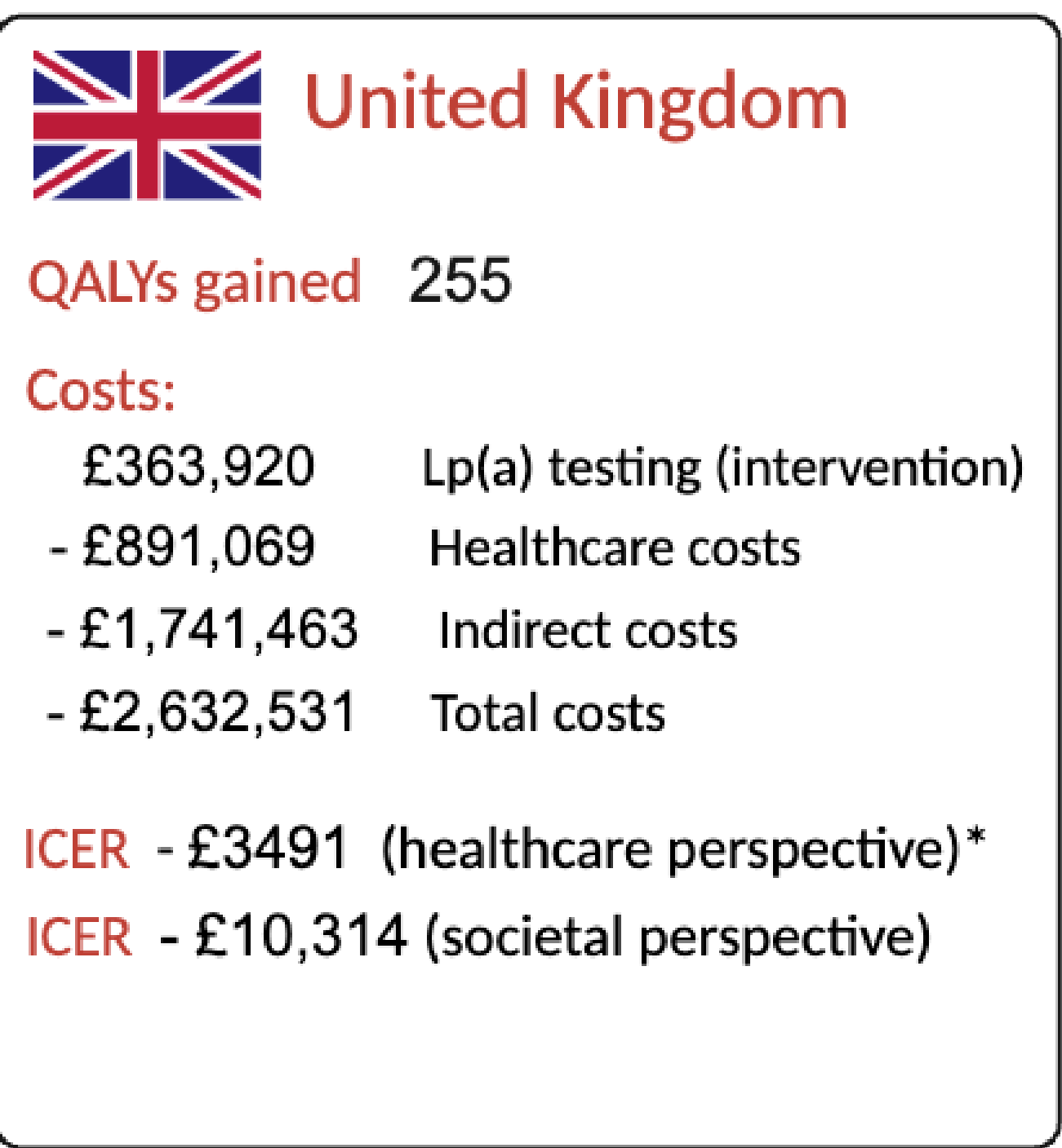
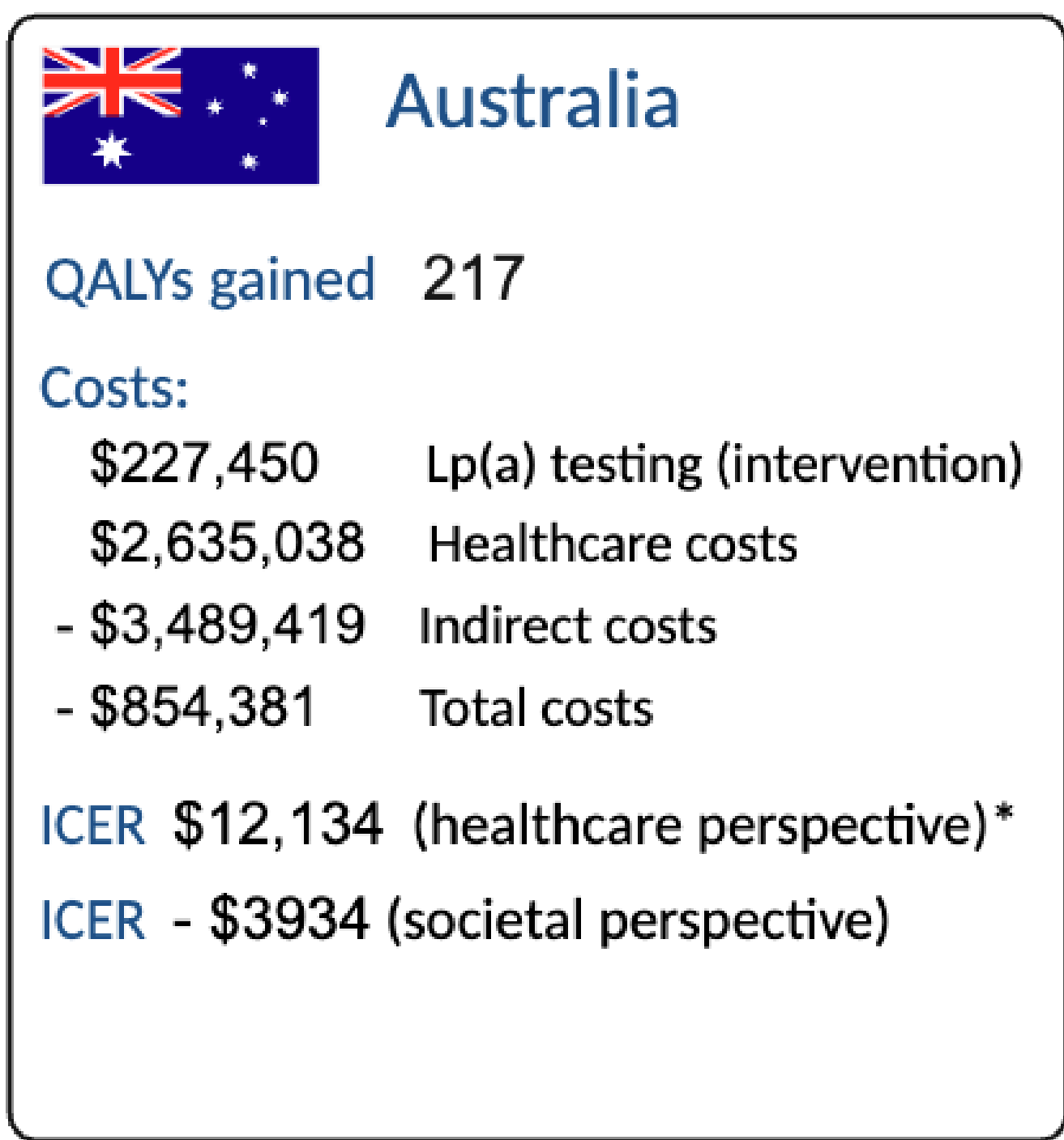
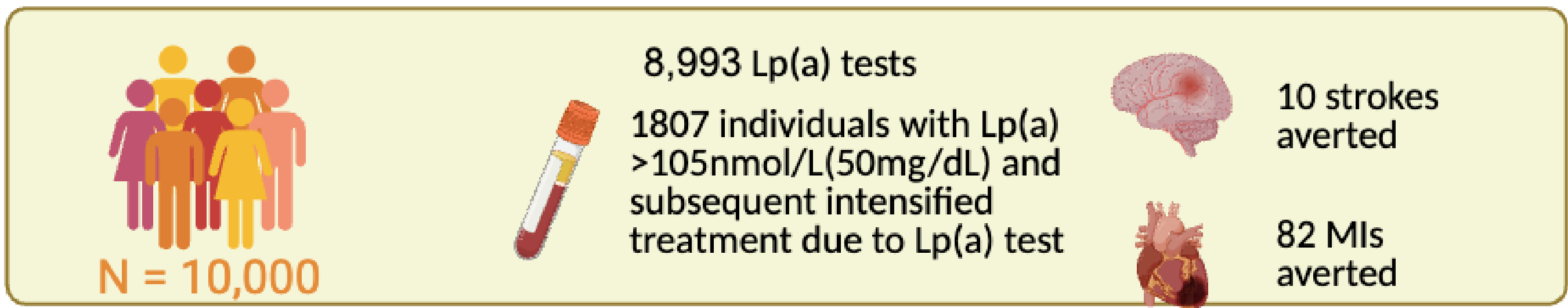


Figure 2. Multi-state microsimulation Markov model for a population of 10,000

3 Results

- Among 10,000 individuals, 1,807 had their treatment modified from Lp(a) testing.



Cost adaptation

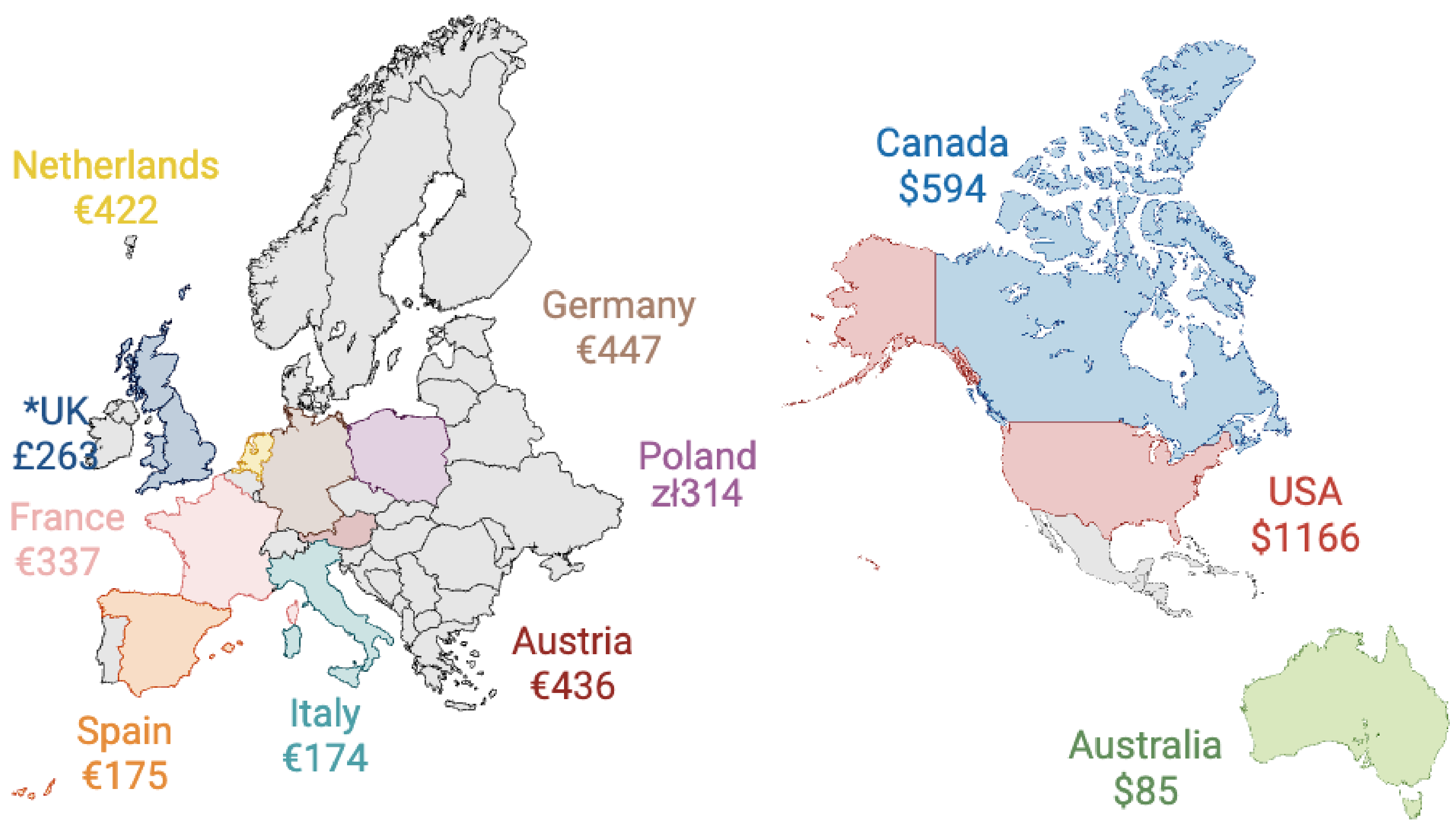
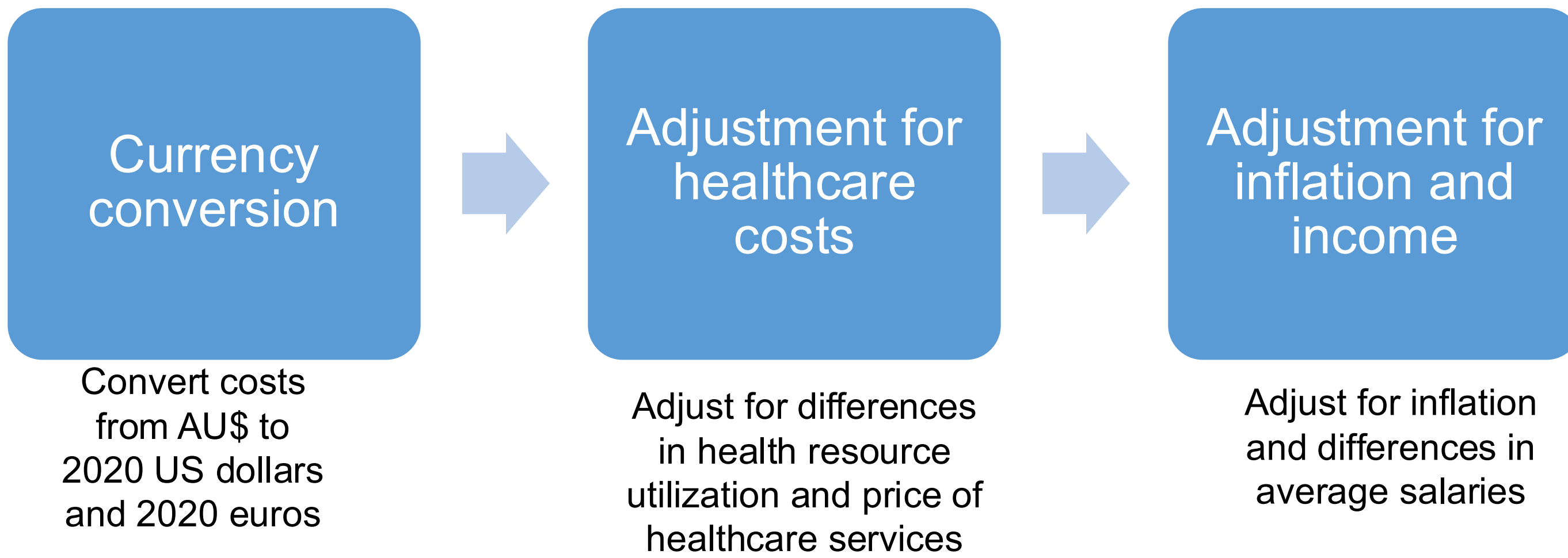


Figure 3. Cost saved per person Total Healthcare + indirect costs/10,000

4 Conclusions

- Lp(a) testing in the primary prevention population to reclassify CVD risk and treatment is cost-saving and warranted to prevent CVD.
- Adapted ICERs should be viewed as approximate estimates rather than precise country-specific outcomes.

References:

1. Florian, K. Eur Heart J. 2022; 43:3925-3946.
2. Nordestgaard BG. Lancet. 2024; 404:1255-1264.
3. Ademi Z. Swiss Med Wkly. 2018; 148, w14626

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