Walking the tightrope: cardiovascular risk prediction in patients after acute coronary syndrome

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The global burden of cardiovascular disease is significant. In 2015, there were an estimated 17.9 million deaths attributable to cardiovascular disease worldwide.[1] Whilst age-standardised cardiovascular disease mortality has declined over the past decade, the absolute number of deaths attributable to cardiovascular disease has risen by 12.5%.[1] Reliably predicting future cardiovascular disease is therefore an important public health priority. This is especially relevant for low- and middle-income countries, which bear the majority of cardiovascular disease burden[2 3] due to a high prevalence of both traditional and non-traditional cardiovascular risk factors.[4 5]

Numerous cardiovascular disease risk assessment models have been developed in the past five decades. The majority of these have focused on the prediction of incident cardiovascular disease in the general population.[6] This is despite reports that almost half of cardiovascular disease events occur in individuals with a history of prior cardiovascular disease.[7] Indeed, such patients have a 20% higher absolute risk of cardiovascular disease events than patients with no history of prior cardiovascular disease. In their *Heart* paper, Poppe and colleagues[8] tackle in an important research gap, describing the development and validation of a cardiovascular disease risk prediction model for patients with a history of prior cardiovascular disease.

Many national guidelines do not advocate the risk assessment of patients with a history of prior cardiovascular events.[9 10] At first glance this seems reasonable, because such patients are already deemed to be at a high risk of future cardiovascular events. Therefore, the substantial risk experienced by these individuals is essentially considered non-modifiable. However, the problem with this approach is that it may disincentivise the active management of contributory, modifiable risk factors (eg, smoking cessation), or lead to poor compliance with preventative pharmacotherapies due to perceived futility. Both these factors are likely to contribute to an increased cardiovascular disease burden in this population, resulting in poorer patient outcomes.

The authors first identified a 'derivation' cohort of over 13 000 primary care patients recruited to the PREDICT database who had previously been diagnosed with acute coronary syndrome (figure 1).[11] Using routinely collected, linked national healthcare data, patients were automatically followed up for cardiovascular events (defined as hospital admissions due to acute coronary syndrome, heart failure, stroke or peripheral vascular disease, or death from cardiovascular causes), which were then used to inform the development of a cardiovascular disease risk prediction score. This predictive model was then validated on the Coronary Disease Cohort Study cohort, which recruited patients with acute coronary syndrome attending Christchurch or Auckland City hospitals (New Zealand) between 2002 and 2009. Overall, the predictive model performed equally well in both real-world settings.

Usefully, the predictive model contained only variables that were prespecified by Poppe and colleagues to ensure they were both clinically relevant and routinely available in clinical practice. The strongest predictors of a recurrent cardiovascular disease event within 5 years were age 60 years or older (especially age 70–79 years), deprivation (especially being in the most deprived quintile) and history of heart failure, poorly controlled diabetes (haemoglobin A1c ≥65 mmol/mol) or renal impairment (serum creatinine ≥150 μmol/L). The importance of time since prior acute coronary syndrome on the subsequent risk of a recurrent cardiovascular disease event was also recognised by the authors. Notably, patients evaluated within 1 year of their initial acute coronary syndrome event were at the highest risk of recurrence.

Crucially, the patient cohorts used by Poppe and colleagues are contemporaneous, which reduces the likelihood of their predictive model overestimating cardiovascular disease risk. This is a problem often associated with the development and validation of predictive models using historic patient cohorts, which have an inherently higher baseline risk due to a decline in the incidence of cardiovascular disease and improved survival following cardiovascular events over the last three decades.[12 13] Therefore, as the authors point out, the derivation cohort is likely to be representative of the type of patient routinely evaluated in primary care in New Zealand in the current era.

Poppe and colleagues should be commended for following best practice with regards to the development and reporting of a risk prediction model and especially for externally validating their model in a separate cohort of patients.[14] Indeed, this is a step that only a minority of published studies have performed.[6] The impressive performance of their predictive model in the validation cohort, which comprised a different ethnic mix, also suggests that some of the concern regarding the model's external applicability may be unfounded.

Further, the authors should be commended for using the sound statistical principles outlined by Royston *et al*.[15] These include the incorporation of a baseline survival hazard and the centring of the prognostic index from the derivation cohort on the mean prognostic index in the transformation of multivariable relative risk to absolute risk. Similar methodological approaches have been shown to improve model performance in the primary prevention setting and accordingly they improved the performance of the model derived by Poppe and colleagues in the present study.[8 16] Future research should build on this impressive work by focusing on the external validation of this predictive model in contemporary cohorts from distinct geographical regions.

In summary, Poppe and colleagues have demonstrated that risk prediction research is undergoing a paradigm shift in patients with a history of prior cardiovascular disease. Using contemporary, routinely collected clinical data, they have developed, validated and reported a cardiovascular disease risk prediction model specifically for use in patients with a previous history of acute coronary syndrome. The resultant model was clinically relevant and performed well at predicting cardiovascular disease risk in this important population of patients.

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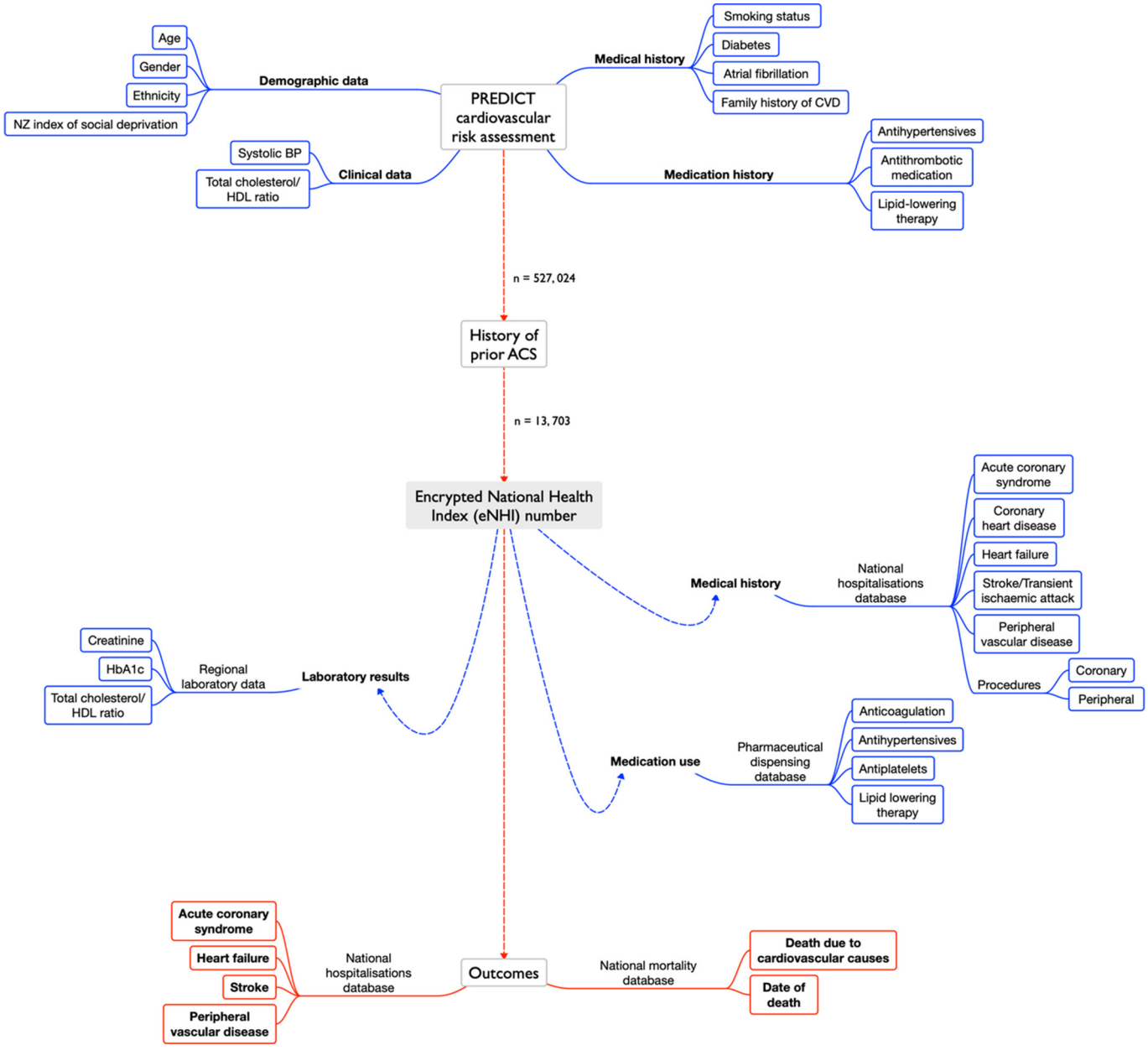

Figure 1 Map summarising linkage of national data assets used by Poppe and colleagues to define the PREDICT-ACS study population and to determine subsequent outcome events. ACS, acute coronary syndrome; CVD, cardiovascular disease; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; NZ, New Zealand.

However, whether it will perform equally well in other case mixes, whilst avoiding subsequent underestimation or overestimation of future cardiovascular risk, and translate to improved patient outcomes, are exciting and as yet unanswered questions.

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