The role of national registries

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This editorial refers to ‘Cardiovascular risk in post-myocardial infarction patients: nationwide real world data demonstrate the importance of a long-term perspective’, by T. Jernberg et al. on page 1163.

In this issue of the journal, Jernberg and colleagues describe the long-term outcomes of the universe of patients admitted between 2006 and 2011 to Swedish hospitals with a diagnosis of acute myocardial infarction.1 Over a median follow-up of 2.5 years, the study identified relatively higher rates of subsequent cardiac events, almost double those described in contemporary clinical trials.2–5 Using their national hospital claims and vital status registries, the work finds a 10% death rate within 7 days of discharge, 12% mortality at 1 year among the initial survivors, and 7% mortality over the second year. Approximately two-thirds of these deaths were considered cardiovascular. The composite endpoint of cardiovascular death, myocardial infarction, or stroke between 1 week and 1 year post-discharge was 18%, with an additional 20% of patients experiencing this combined endpoint in the second year. These event rates are substantially higher than the 2–12% rates seen in contemporary trials such as the Study of Platelet Inhibition and Patient Outcomes (PLATO), Dual Antiplatelet Therapy (DAPT), TAXUS Liberté Post Approval Study (TL-PAS), and the Thrombin Receptor Antagonist in Secondary Prevention of Atherothrombotic Ischemic Events (TRA 2P) studies. Sponsored and partly authored by AstraZeneca, one would expect the work was designed to highlight potential targets for dual antiplatelet therapy beyond 1 year applied to the general population of acute coronary syndrome patients. The higher event rates are probably driven by at least three factors: the inclusive nature of the national registry with far greater representation of elderly patients; clinical trial inclusion criteria that sometimes rely on selection for coronary stenting; and the differences in claims data and clinical trials in establishing subsequent myocardial infarctions. For the latter point, the Swedish registry considers hospitalizations that include a diagnosis code for myocardial infarction to represent such complications, possibly counting events that may have been excluded by more specific criteria of the clinical trial event adjudication process that include symptoms and ECG abnormalities as diagnostic criteria. Of particular concern is the potential for higher event rates due to discharge diagnoses of myocardial infarction based upon oxygen demand and supply mismatch, or type 2 myocardial infarction.6 The International Classification of Diseases claims that codes are unable to differentiate such events from myocardial infarction due to atherosclerosis and plaque rupture typically counted in clinical trials.7

While claims data have a number of limitations, their advantages for comprehensive epidemiology studies such as this work far outweigh their limitations. Strengths include accurate identification of age, gender, and events that influence payment, including hospitalizations and change in vital status. With the comprehensive nature of the Swedish health system, the greatest benefit of these studies involves their ability to describe the universe of patients and ‘real world’ practice. Entry into clinical trials is biased according to having to survive long enough to be enrolled, and being viable enough to be considered for study enrolment and of adequate mental status to provide informed consent. Procedural trials involve further bias in selection for coronary intervention. These biases favour younger patients such that the average ages of patients in the large trials cited above were 10–12 years less than those identified in global studies such as this report. The age group that predominantly stands out in the Swedish registry is those over age 75, almost half the population of this study, including 19% of patients over age 85 years. Only 3–15% of patients are over age 75 in the corresponding clinical trials.

The significance of including a representative sample of elderly patients is nicely illustrated in the figure depicting Kaplan–Meier risk of events stratified by age. There is almost a doubling of event rates for patients in the 70- to 79-year-old cohort compared with younger patients, and another doubling of event rates for those patients over age 80. Thus, the cardiovascular event rates among post-myocardial infarction patients in the general population in Sweden are much higher than those found in clinical trial populations, largely driven by events in elderly patients.

The high event rates raise issues regarding the extension of the findings of clinical trials to everyday practice. As therapies move from clinical trials to the general population, the higher event rates in the most elderly patients suggest the potential for even greater benefit. Such benefit may come at the cost of higher complication rates, particularly for older patients with increased risk of bleeding.

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Once again, a Swedish national registry serves as a beacon by which we can gauge the inclusiveness and outcomes of clinical trials, and highlights the need to understand efficacy in older patients. The authors wisely avoid making potentially confounded treatment comparisons in these observational data. Such efficacy can only be tested in randomized clinical trials, underscoring the importance of redoubling efforts to enrol more representative cohorts with particular focus on the inclusion of elderly patients, those at greatest risk for cardiovascular events. Lacking adequate representation of elderly acute coronary syndrome patients in clinical trials, we must remain prudent and circumspect in our application of evidence-based therapies to this age group.

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References