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Evaluating Clinical Outcomes from Administrative Databases

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How often in practice do we hear patients ask, “what is going to happen to me?” When they do, how do we to estimate their risk of serious events? Do we consider data from clinical trials, observational studies, or our daily clinical practice? Because of the nature of medical practice in the United States, there is no single reliable source of outcome information for patients, whether they are seen after a procedure or an event or are in stable condition in the clinic.

For many clinicians, the major source of information on risk comes from clinical trials, which may be sponsored by organizations requiring peer review (e.g., the National Institutes of Health), industry, professional societies, or clinical registries. Accurate reporting of clinical events is critical to our understanding of patient risk.

What are the sources of outcome data? Outcomes in clinical trials are usually assessed through follow-up using direct patient contact and electronic health record information, as well as some from local hospital administrative sources and death certificates. Events are then adjudicated by an expert committee that reviews the available data.[1] This process is often seen as the gold standard for evaluating events, although there have been criticisms.[2, 3] A limitation of this process is that the period of follow-up in clinical trials is variable, from short term of a month or so, to intermediate term of a one or two years, to longer term of up to five years. Clinical follow-up beyond this point within the structure of a clinical trial is unusual. This process is similar for clinical trials sponsored by peer review organizations and by industry.

Registries may also be used to assess outcomes. However, registries sponsored by professional societies may only collect short term data, often related to procedures (e.g., percutaneous coronary intervention) or events (e.g., myocardial infarction),[4] and those sponsored by industry are variable in their approach to data collection. Furthermore, events during follow-up in registries are rarely adjudicated. Another source for outcomes data may be long-term epidemiological cohort studies in the United States, some with follow-up to as long as 30 years.[5] Events in these cohorts are usually adjudicated and serve as a particularly rich source of information.

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How then can events during follow-up be determined for patients in registries and clinical trials? One approach is to link the data to commercial or governmental administrative data sources, which at least in principle include these follow-up data.[6–10] This process of linkage can be either what is called deterministic or probabilistic.[7, 11] In deterministic linkage, patients are matched directly using patient identifiers such as Social Security number. Quite often, because of concerns over privacy, Social Security numbers and other patient identifiers are not collected.[12] In such cases, probabilistic matching is used, in which institution, patient age and sex, and date of admission are used. This approach will only match a fraction of the patients (typically about two thirds). There is some danger of false matches, but generally the specificity of the matches is over 0.90.[13]

How do administrative databases acquire the information about events? Generally these data are gathered from insurance claims submitted when billing for care. When there is no claim, an administrative database may not have information on the event. This is particularly relevant for out-of-hospital mortality, which may not be captured in commercial claims databases. Furthermore, commercial databases may not be able to distinguish whether an event is fatal or not (e.g., fatal vs non-fatal myocardial infarction). This is a severe limitation of linking to commercial databases in the United States, and as such it is not commonly done. In the United States, the major claims database to which trials and registries are linked is Medicare.[6, 14] Medicare has event data and obtains mortality data from the National Death Index, generally considered the gold standard for evaluating survival in the United States.[1, 15] However, the National Death Index is of limited accuracy for cause of death.[1] A limitation of Medicare, however, is that it generally only includes those over age 65, and will not include patients over 65 with commercial insurance (e.g., those still working) or patients with Medicare Advantage. Linking of trials and registries to the long-term epidemiologic cohorts in the United States is unusual, as linkage to specific patients is generally not possible and the cohorts have limited numbers of patients. Linkage to similar patients, however, is possible and has recently been accomplished for patients in SPRINT (Systolic Blood Pressure Intervention Trial).[16]

How reliable are the outcomes identified in administrative databases? Butala et al. have addressed this concern in this issue of *JACC: Cardiovascular Interventions*.[17] These investigators linked data from three clinical trials and two registry studies of transcatheter aortic valve replacement to Medicare fee-for-service inpatient claims. Of 5,302 patients older than 65 years in the dataset, 4,229 (79.8%) were deterministically matched to Medicare claims. Non-linked patients were most likely enrolled in Medicare Advantage. Linked and non-linked patients were generally similar. The events considered were death, aortic valve reintervention, and myocardial infarction at one year and permanent pacemaker implantation, acute kidney injury, and bleeding at 30 days. Trial outcomes were all defined by the Valve Academic Research Consortium and adjudicated by an independent clinical events committee.[18] Specific International Classification of Diseases (ICD)-9 or ICD-10 codes were used, noted by the investigators, to find events in the Medicare database. All comparisons were of Medicare claims to the adjudicated events in the clinical database as the standard. For mortality, Medicare claims had a sensitivity of 99.9% and specificity of 99.9%. For reintervention, Medicare claims has a sensitivity of 84.4% and specificity of 99.6%. For myocardial infarction, Medicare claims had a sensitivity of 63.6% and

specificity of 97.2%. For pacemaker implantation, Medicare claims had a sensitivity of 92.2% and specificity of 99.1%. For acute kidney injury, Medicare claims had a sensitivity of 70.2% and specificity of 85.4%. For bleeding, Medicare claims had a sensitivity of 86.4% and specificity of 36.8% (Table 1)

The data reveal that Medicare claims are most useful for mortality and short-term events, such as pacemaker implantation. For longer term events, however, such as myocardial infarction or reintervention, identification of events from Medicare claims will be more limited. For complications such as acute kidney injury or bleeding, Medicare claims is likely to be unreliable. As the investigators note, events during follow-up may be missed even in clinical trial databases, and Medicare claims may prove useful in supplementing clinical trial databases.

This study is most important in understanding how we go about assessing events for research purposes and how the results can be interpreted in clinical practice. There simply is no perfect approach to this issue. Given the complicated nature of the health care system in the United States, there will not be a single source of outcomes data, except perhaps for mortality in the National Death Index, which has its own flaws.[1] Thus, it is imperative for investigators to carefully consider their sources of data for events, be transparent in reporting, and carefully consider where data may be incomplete or erroneous and the impact this could have on their findings. Even clinical event committees are limited by imperfect data with which to evaluate outcomes.[2]

Can the results of this study be generalized to other conditions? The authors rightfully note that additional research is needed in other areas. However, it seems unlikely that this study can be replicated for all conditions where Medicare claims might be used. Indeed, there may not always be a gold standard for comparison. Nonetheless, further studies of this type are certainly justified. Furthermore, Butala et al. offer an excellent prototype for such studies. In any case, follow-up data are almost always going to have limitations. Readers of published clinical research and clinicians should be reasonably skeptical of long-term follow-up data obtained using Medicare claims, excluding mortality, which seems reliable.

How does the United States compare to other countries? Most of the world will have no reliable follow-up data. Some well-developed countries, such as Denmark and Sweden, have whole country hospitalization and mortality databases.[19, 20] These databases will be useful for mortality and presumably events such as myocardial infarction but may also fall short for complications such as acute kidney injury or bleeding. The generalizability of results from Denmark and Sweden to the rest of the world, is at best uncertain.

The problems of how to properly follow up on our patients is real and there will be no perfect solution. Yet decisions must be made for our patients in the absence of truly sound data. Skilled, knowledgeable, skeptical clinicians who are patient advocates will continue to be the basis of sound practice.

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Table 1.

Sensitivity and Specificity of Medicare Claims Identification of Events Compared to Independent Clinical Events Committee Adjudication from Butala et al.

Event	Sensitivity	Specificity
Mortality	99.9%	99.9%
Reintervention	84.4%	99.6%
Myocardial infarction	63.6%	97.2%
Pacemaker implantation	92.2%	99.1%
Acute kidney injury	70.2%	85.4%
Bleeding	86.4%	36.8%