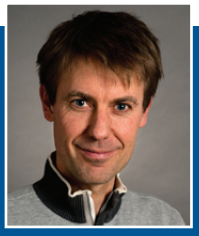
The Nordic Health Care Registries–Real Improvement to Outcomes Research?

Lars Pedersen, MSc, PhD, Department of Clinical Epidemiology, Aarhus University, Aarhus, Denmark

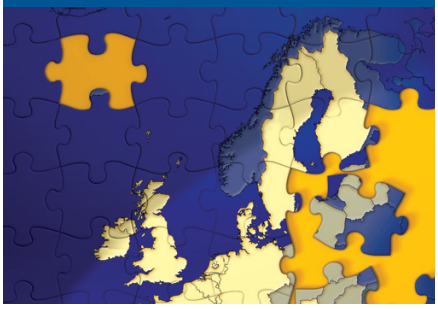


KEY POINTS . . .

The Nordic system offers long-term follow-up of patients and complete control of censoring due to emigration or death.

Combining large health care registries with clinical trial data is a unique opportunity in the Nordic countries.

Utilizing the Nordic registries to their full potential requires involvement of local experts who understand the data and the context in which the data are generated.



Health care in Nordic countries is free and tax-supported. The service includes free access to general practitioners, hospitals, and outpatient specialty clinics, and partial reimbursement of prescribed medications. The equal access to health care implies equal probability of being recorded in many national health care registries, regardless of socioeconomic status.

The Nordic countries have a long tradition of using registries, and some of the oldest disease registries are still in use today; including cancer registries dating back to the 1940s and hospital discharge registries dating back to the 1970s. The numerous nationwide registries, based on a combined population of approximately 25 million people, provide valuable resources for outcomes research.

A prerequisite for utilizing the registries to their full potential is the ability to link and enrich them via a unique personal identifier. This identifier, a unique civil registration code, was introduced more than 50 years ago and has since been assigned to every person at birth. In outcomes research, the unique identifier allows linkage to primary collected data and surveys. It facilitates detection of events in randomized trials conducted in the Nordic countries and sampling of comparison groups. It also provides full control over individual data on migration, residence, and vital status, which is a prerequisite for an optimal study design. As a result, the entire Nordic population is often considered as a cohort in epidemiological research.

Use of health care registries to detect events in randomized clinical trials is a unique application of the Nordic system. For instance, in interventional cardiology in Denmark data have been utilized with notable success in the past years.

A major strength of the Nordic system is the ability to follow persons over long periods of time. For instance, all Danes can be traced from the establishment of the Civil Registration System in Denmark from April 1, 1968 (or date of birth or immigration, whichever came last) until the date of death, emigration, or end of follow-up (which is often an administrative fixed date set at the latest data cut-off). Although currently approximately 5.5 million Danish inhabitants are alive, close to 9 million individuals can be tracked through the Danish Civil Registration System back to 1968, and close to 25% of these can be followed for more than 40 years. This ability to conduct studies with such a long follow-up, linked to other data sources and with complete control of censoring due to emigration or death, is really a unique feature of the Nordic system.

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In addition to the classical registries like the cancer registries and cause of death registries, the Nordic countries have over the past 25 years established a large number of other health care databases originating from existing routinely collected health care data. These databases have originally been established for the purpose of planning, management, claims, and—albeit less often—research. One example of such a health care database is the various national prescription databases, which are now used extensively in epidemiological research. They have been available since 1994 in Finland and Denmark, since 2004 in Norway, since 2005 in Sweden, and since 2006 in Iceland.

Because of the administrative nature of these routinely collected data, they often lack detailed clinical data, have low precision of measurements, and do not contain all data necessary to address a given research question. On the other hand, they offer many advantages; the main ones being readily collected data, low costs,

and data collection independent of any research hypothesis, which leaves less room for certain types of bias. In addition, the relatively large completeness of some of these databases with respect to capturing the members of the target population largely prevents selection bias.

Researchers affiliated with universities or other public institutions can gain access to individual-level health care data for research purposes, but raw data from national registries and health care databases are not stored in one common server and therefore, combined Nordic datasets are not readily accessible for researchers. In fact, data are stored and maintained by several data organizations within each country and the export of raw data between countries is often restricted and sometimes impossible because of legal issues. In addition, these data are often recorded on the basis of non-standardized web formulas and interfaces, including adoption of different disease classification systems in each country.

To overcome the hurdle of pooling and harmonizing data across borders, distributed database network approaches are increasingly being utilized. Adoption of this approach allows national researchers and data experts to maintain full control of their available national data, while enabling sharing of standard aggregated data for meta-analyses on a Nordic level. In this setup, the local researchers are responsible for mapping and transforming the data into a standardized framework, the so-called set of "input files." One set of standardized software programs is then shared for site-specific aggregation, quality checks, and initial analyses. At each site, the aggregated data can subsequently be uploaded to a common platform for further analysis. This approach is similar to the approach used in many other research consortia doing large-scale outcomes research. For instance, the EU-ADR group has established a comprehensive framework for observational research based on a distributed database network. This network includes a number of linked data sources originating from primary care and population-based record-linkage systems in Spain, Italy, the Netherlands, the United Kingdom, and Denmark.

The Nordic registries and health care databases have a large utilization potential, and when combined, the total population is approximately 25 million living individuals per year. Such a large collection of data enables studies of rare diseases, drug exposures, and drug interactions. Large studies increase the statistical precision by narrowing the confidence intervals relating to the risk estimates. Even so, these large studies can produce misleading results if validity issues like confounding and measurement error are not well understood and effectively managed. It is important to understand that these issues are not eliminated just because of a large study size. Utilizing the Nordic registries to their full potential requires involvement of local experts who understand the data, and are aware of the pitfalls and the context in which the data are generated. This is just as important as the statistical and epidemiological expertise. ■

Additional information:
The preceeding article is based on a presentation given during the Third Plenary Session, "Health Care Evidence: Can We Get To the 'Real World'?" at the ISPOR 17th Annual European Congress, 8-12 November 2014.

To view Dr. Pedersen's presentation, go to: http://www.ispor.org/Event/ReleasedPresentations/2014Amsterdam