Validation and Interpretation of Neurological Registry Data

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This section of the guideline addresses considerations with respect to the validation and interpretation of registry data. In developing this section of the guideline we consulted with registry, disease, and statistical experts in addition to reviewing the available literature.

Relevant Literature

Methods of Validation

Several methods can be used to assess completeness of registry data. Completeness of registration can serve as an indicator of registry effectiveness - an ideal registry will capture all cases of a given disease within a defined population. Completeness is defined as the proportion of diagnosed cases that are registered. Possible methods for estimating completeness include:

1. Estimates based on cases confirmed through death certificates and the mortality to incidence ratio
2. The historic data method: comparing current rates of registration to appropriate numbers of cases from the past within the same registry
3. Comparison to a reference registry with complete ascertainment
4. Capture-recapture methodology
5. Independent case ascertainment (linking registry data to an independent database)
6. The flow method
7. Estimating completeness based on mortality/incidence ratios.[222]

Schmidtmann et al[222] performed a survey of 195 cancer registries in Europe to determine which methods were most commonly applied to estimate data completeness. The survey found that the historic data method, comparison to a reference registry, estimates based on death certificates and the mortality to incidence ratio, and mortality/incidence ratio were the most commonly used methods. The quality of these indicators of completeness was not assessed.

Although comparative studies on the performance of indicators of completeness are lacking,[222] there are many studies that assessed individual methods of validation. The literature suggests that record-linkage methods and comparison with other data sources were most frequently used to investigate data quality. For validation purposes, registry data has been compared to medical records,[19196,201,203-205,207,209,214,216,220,221.223-225] a national population-based registry,[102,200,202,227,232] a clinic-based registry,[233] a regional database,[219,234] multiple registries,[221,235-237] administrative records,[210,232,238,239] or independent sources such as a quality improvement project,[199] study data,[240,241] in-person or telephone queries,[242] and a research project database.[243] The common variables assessed were case ascertainment, data completeness, data accuracy, reliability and sensitivity.

Several studies reported using the capture-recapture method to estimate completeness of registered cases and degree of under-reporting.[218,228,235,237,244,245] Schmidtmann et al[246] performed a simulation study to evaluate capture-recapture methods for estimating completeness of cancer registries under real conditions. They concluded that all capture-recapture methods underestimated completeness. The flow method,[218,247] mortality incidence ratio,[218] and historic data method[218] were less commonly reported to estimate completeness of case ascertainment.

In order to ensure consistency of data collection and reliability of registry data, a number of approaches have been employed by registries. These include examining inter-rater reliability,[248] comparisons of independent recoding or refilling of data,[249,250] and test-retest reliability.[251] In all cases, the data were found to be accurate, thus allowing for generalizability, research, audit, and review.

Byrne et al performed a systematic review of studies that investigated the validity of administrative registers in psychiatric

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research.[252] Studies varied by validity methods and quality. Methods included applying diagnostic criteria to registry data, comparing registry data with case notes, or applying diagnostic criteria with case notes. In two studies, clinical interviews and case note reviews were assessed using operationalized criteria. The review found no gold standard for the assessment of registry data validity.

Having an objective process of data validation can improve data accuracy and staff accountability of data collection. Protech and Chappel implemented a data validation system to improve the data accuracy of a trauma registry.[253] The data validation model included staff participation in a review of key areas of registry data trends and errors and development of a standardized rating tool included as part of the data abstraction process. The validation method required data abstractors to use an electronic signature for each data abstract and the validity of abstracts were checked using an objective rating system. This process assisted with training of new staff members by providing email summaries of assigned ratings for each data abstract and any detected errors on a weekly basis. The validation tool was useful for providing performance feedback of data collectors and analyzing overall accuracy of data.

Studies that compare the feasibility of various methods of assessing data quality and validating data is limited,[222] thus, future studies are needed that evaluate the performance of different methods of data validation.

Lessons Learned from Improving the Validation of Registry Data

As mentioned earlier, there are a number of different methods that can be used for data validation and these may be associated with varying degrees of data accuracy and reliability. To improve methods of validation, a number of strategies have been proposed. It has been suggested that auditing be undertaken at regular intervals.[199,204,215,223] Frequent assessment of registry data can identify culprits that jeopardize accuracy and/or reliability. Using multiple sources of data can allow for retrieval of missing data and continuous validation.[204,223] Furthermore, randomly selecting participating sites[223] and at random time points[215] is appropriate for the proper evaluation of data quality. If registry staff from the coordinating center visit participating sites, errors may be more easily detected.[196] Selecting clear, objective, and easy-to-evaluate outcomes and variables for validation has been frequently suggested to improve the validation process.[202,223] Lastly, using patient identifiable data for linkage can improve the validation of data.[102]

Other Considerations

Registry Design

Registries evaluating safety, effectiveness, or evaluating an association between specific exposures and outcomes should specify hypotheses a priori to improve design, execution, and acceptance of results. It is important to have some a priori hypotheses. Without an a priori hypothesis, there is concern that the registry may be too broad in terms of its scope or may neglect to collect key information and evaluate specific outcomes. Disease registries with descriptive goals (e.g., clinical features, natural history, disease progression) often will not have an a priori hypothesis. In this case, the registry may serve as a platform through which hypotheses may be generated. Long term project funding for a descriptive registry may allow hypotheses to evolve and new objectives to be generated in a prospective fashion.

In order to secure long-term funding, registries might need to develop new hypotheses or questions over time. Consider beginning the registry with an initial question, but constructing the registry in a manner to allow adding of questions in a prospective manner that can be answered through the registry's work.

Registry Development

It is essential to be transparent about the goals of the registry and methodology employed by the registry. A key question is how well do the study results apply to the target population? Are the results generalizable to them? Can they be extrapolated to other populations that are of interest? Case ascertainment must also be considered. It is important to minimize selection bias and determine whether the registry is capturing data across the entire applicable spectrum of the target population (i.e. not just the sickest or most disabled patients are included). Case ascertainment may be improved through partnering with patient organizations and recent census data. It is important to have a mechanism for assessing/tracking disease severity in order to ensure that the entire spectrum of the disease is represented.

With respect to assessing data quality, it is important to ensure relevant variables are collected, whether data collection is complete, and how missing data were handled. Assessment of completeness and accuracy of data has to make sense with respect to the disease. It has to be acknowledged that data assessment methods will evolve with increasing knowledge of the disease.

Sometimes registries are used for purposes other than those that were pre-specified. It is important to ensure that when a registry database is used for a purpose that was not pre-specified, that the registry contains all the information necessary to answer the new question. It is often difficult to ascertain what and how much to ask initially. Flexibility to modify what is asked is beneficial. As registries can help address new questions, the ability to add new modules/concepts is beneficial.

Validating Completeness, Accuracy and Quality of Data

It is important for registries to define how missing data will be handled, and develop a strategy to try to minimize missing data. For example, some registries use the internet (online contact information) to facilitate the collection and follow up of missing data. However, internet data collection may be less accurate than face to face data collection. Completeness must be balanced against accuracy. Collecting data from multiple sources may ensure completeness but can potentially compromise data accuracy. It is important for the registry to report data completeness, especially if data are being published.

Registry completeness can also be assessed across different demographics (e.g. age, Socioeconomic status, rural/urban) so that any biases in the registry are apparent. Additionally, there should be plans for site monitoring, quality assurance and data verification. Data review is and should be a standard practice.

With respect to hypothesis-driven registries, it is important to have a plan for statistical analyses that describes the analytic principles and statistical techniques employed to address the primary and secondary objectives. Statistical analyses need to be planned at appropriate intervals while considering the possible time dependency of data within the registry. It is important to ensure that a sufficient number of events have occurred and that sufficient time has passed in order to ensure that it is biologically plausible for a specific event to have occurred. It may be necessary to consider the natural history of the disorder. Registry analyses should provide information on: (1) patient population, (2) exposure or treatment, (3) endpoints or outcomes, (4) time, and (5) potential for bias.

For analyses, the use of internal comparator groups is preferable. If they cannot be found, an effort should be made to use external comparator groups. For internal comparator groups, one can make comparisons of individuals with varying disease severity, different disease subtypes, or by individuals presenting with disease at different times. Non-diseased spouses may be used as a comparator but they are potentially exposed to the same environment. It may be necessary to find an alternately derived control group. One potential concern with external comparators is that the data is not collected the same way. In order for the use of the external comparator to be fair, outcomes must be "hard", such as death, institutionalization, or hospitalization.

There is the potential that analyses performed by different investigators using data from multi-site registries may address the same question but produce different results. Methodological differences may explain the deviations. It is important to ensure that centers are interpreting things in the same way (standardization of responses).

Recommendations

✓ A priori hypotheses may improve the design, execution, and acceptance of results and serve to clearly define the scope and nature of the information being collected by a registry. Registries which seek to prove a premise need hypotheses; registries with descriptive goals do not need hypotheses.

✓ Registries should consider a design and permissive policies that allow for new hypotheses to be generated and followed up on as the registry develops. This may generate opportunities to obtain new funding and may ensure long-term viability.

✓ Be transparent about the goals and methodology of the registry.

✓ Ensure the entire spectrum of the disease or condition is represented if registry results are to be generalized.

✓ Ensure data collection includes important and relevant variables.

✓ Address confounding variables where possible.

✓ Clearly define inclusion/exclusion criteria to maximize data quality and maximize target population capture.

✓ Use internal comparator groups where possible. If external comparator groups are being used, recognize potential limitations and try to utilize unambiguous outcomes.

✓ Have a plan in place to minimize the amount of missing data. Where data are missing, ensure that this is addressed. Ensure the risks associated with supplementary data collection modalities have been addressed.

✓ Ensure that registry completeness and potential sampling biases are reported.

✓ Ensure that resources are in place for proper and thorough data analyses. Registry analyses should provide information on: (1) patient population, (2) exposures, (3) endpoints or outcomes, (4) time, (5) potential for bias.

✓ Address deviations in data collection and interpretation that occur between sites.