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# Congenital diaphragmatic hernia: The role of multi-institutional collaboration and patient registries in supporting best practice

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ABSTRACT

Among congenital malformations, congenital diaphragmatic hernia (CDH) is distinguished by its relatively low occurrence rate, need for resource intensive, integrated multidisciplinary care, and widespread variation in practice and outcome. Although randomized controlled trials (RCTs) are considered the gold standard for generating evidence, they are poorly suited to the study of a condition like CDH due to challenges in illness severity adjustment, unpredictability in clinical course and the impact limitations of studying a single intervention at a time. An alternative to RCTs for comparative effectiveness research for CDH is the patient registry, which aggregates multi-institutional condition-specific patient level data into a large CDH-specific database for the dual purposes of collaborative research and quality improvement across participating sites. This article discusses patient registries from the perspective of structure, data collection and management, and privacy protection that guide the use of registry data to support collaborative, multidisciplinary research. Two CDH-specific registries are described as illustrative examples of the "value proposition" of registries in improving the evidence basis for best practices for CDH.



One of the major challenges to studying congenital diaphragmatic hernia (CDH) for the purpose of generating "best practice" evidence, is its relatively low incidence (2.7 per 10,000 live births),[1] and the prolonged period of time necessary to collect sufficient numbers of cases for analysis. An obvious solution is to combine cases from multiple centers, so that accrual periods are relatively short, and therefore more likely to be representative of current practice. There are clear advantages to multi-center collaboration for the purpose of outcomes analysis, particularly if the data collected can be standardized, and the knowledge gained from research can be used to the benefit of clinical care at the data-sharing sites. This justification is foundational to the value proposition of patient registries as a source of high-quality evidence guiding best practice for a rare, complex condition such as CDH.

## What are patient registries?

A patient registry is a collection of standardized information about a group of patients who share a condition or experience that serves a predetermined scientific, clinical, or policy purpose.[2] The use of the word "patient" signifies that the focus of the data is on health information and health care delivery. Other terms such as clinical registries, clinical data registries, disease registries, and outcomes registries are also used. A key attribute of patient registries is the encouragement of multi-institutional collaboration guided by data collecting and sharing policies, and the use of data for research which credits the registry, as well as the individuals who conduct the research.

### *Key elements*

#### *Data*

High-quality data are essential to all patient registries. A key to data quality is standardization, which is important when combining data from different hospitals where interpretation of the meaning or value of a specific variable could vary. A "data dictionary" in which every variable is explicitly defined is critical to standardization. There are a number of models of data collection, including manual collection by formally trained, task-dedicated abstractors, as is currently done by National Surgical Quality Improvement Program (NSQIP)'s surgical clinical reviewers.[3] This ensures high data quality, but at high cost. The lower cost alternatives are for the data to be abstracted from patient charts by providers or untrained abstractors, or in some instances, as

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direct excerpts from the electronic health record (EHR). Alternative sources, such as administrative or billing data lack clinical granularity and validity, and generally are not appropriate sources of data for patient registries. Another desirable data management function is data cleaning, which involves identifying and modifying or deleting incomplete, inaccurate or irrelevant data.[4] This involves the identification of missing fields, and the automatic flagging of quantitative fields in which the entered data are outside of an acceptable clinical range. One of the challenges associated with a blank datafield is whether to assign it as "unknown" or "missing"; the assignment of a default value may make the data complete, but not necessarily accurate.

*Privacy protection*

In the United States, the Health Insurance Portability and Accountability Act (HIPAA) and its implementation regulations (known collectively as the Privacy Rule), assures legal protection of the privacy of "individually identifiable health information."[5] This includes an individual's past, present, or future physical or mental health condition, the provision of health care to an individual or payment for that health care. Legislation that ensures similar oversight for privacy exists in most countries. It is therefore essential that patient registries comply with jurisdictional privacy regulations by ensuring that all patient identifiers (name, searchable health information numbers, and date of birth) are completely dissociated from the registry record. Another consideration for registries is whether consent is required for data collection. Institutional Review Boards (IRBs) may offer differing points of view, but in general, as long as the data are "observational" (data entered into a patient's chart during the provision of care, and not used to influence care), and is not linked to biological samples, then the need for consent may be waived. This is especially important for rare diseases like CDH, where the potential value to society of improved care and outcomes enabled by a complete dataset, must be balanced with the autonomy of individuals in controlling their data, even if it is de-identified. When multiple institutions contribute data, the de-identified aggregate dataset must be protected (firewall and encryption), and its use informed by inter-institutional data-sharing agreements and a data use policy.

*Data access*

The registry should be overseen by a committee, which controls how, to whom, and for what purpose registry data is released. It is reasonable that sites that contribute data should also be able to access it. Requests for data for a research project should clearly describe the research question, data fields required, methodology (including biostatistical analysis) and a knowledge translation plan. Once the steering committee has approved a study, the data can be released in a manner that complies with jurisdictional privacy requirements. Use of registry data for research should be done under the auspices of the IRB obtained through the principal investigator's home institution.

*Registry infrastructure*

A data registry is frequently an essential underpinning of a "clinical research network," which usually consists of a consortium of providers, researchers, administrators, policy makers, and patients (Figure 1). The network uses the data it collects to conduct observational research around a population of patients, a specific disease or condition (such as CDH), or based upon a specific interventional methodology (e.g., clinical trials). Depending on its size, a clinical research network may require significant infrastructure including information management/technology (IM/IT), project management (e.g., research coordinators), methodology (clinical trials and biostatistics) support and knowledge translation

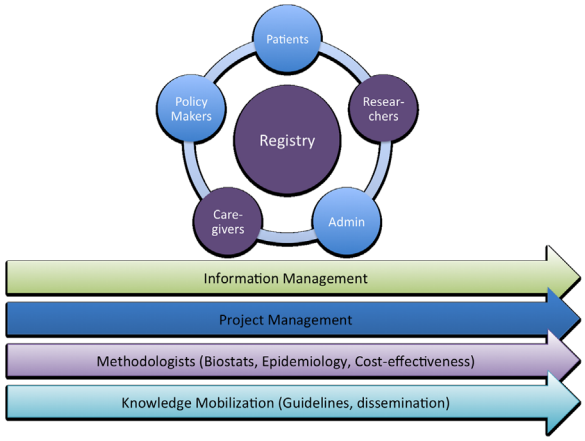


**Fig. 1.** Structure and function of a clinical research network.

capacity. Increasingly, the importance of patient engagement at every level, including informing proposals from a patient or community member perspective, serving in key leadership roles, and encouraging self-reporting of personal health data to the registry: these networks are often referred to as "patient-powered" research networks.[6]

The dissemination of an annual report describing aggregate case numbers and outcomes, as well as anonymized, individual site case numbers and outcomes provides valuable "benchmarking" to individual sites and a foundation for quality assurance (QA) and quality improvement (QI) activities. The value of registries as enablers of hospital QI activity (an accreditation mandate), supports the argument that hospitals should pay for the data to be collected.

## Registries and comparative effectiveness research

The gold standard for generating high-quality evidence to inform best practice is the randomized controlled trial (RCT). However, the challenges of large sample sizes, extreme costs, the need for highly controlled and often exclusionary enrollment criteria, and the lack of infrastructure and expertise required to conduct trials in the context of clinical care all limit the value of the RCT as the primary evidence source for many conditions. For a complex condition like CDH, which requires highly integrated multidisciplinary care (including surgery), the RCT, which generally targets one intervention at a time, is poorly suited to the creation of generalizable evidence which can be widely and safely implemented outside of the constrained trial environment. Disease-specific registries offer a pragmatic alternative to the RCT for evidence creation: the large numbers of patients accrued over a short time period, the existence of treatment and outcome variation, and the ability to risk adjust for severity of the condition allow patient registries to produce high quality, actionable, best practice evidence. Furthermore, the capacity for registries to conduct knowledge translation through their integrated care communities frequently improves the efficiency of uptake of best practices. Recently, the feasibility of conducting an interventional trial within a patient registry was demonstrated in Sweden.[7] The registry RCT, which has been described as the "next disruptive technology" in clinical research is facilitated by registry enrollment at the point of care.[8] Swedish citizens are given unique identifiers that allow linkage of their health information across the health services that they access, and so treatment and outcomes data can be obtained without additional data collection. Whether such registry trials could be conducted in countries without supportive health information policies and IT infrastructure remains to be seen.