



Why Join a Patient Registry?

The number of patient registries continues to grow, especially in the chronic and rare diseases communities, due to the benefits they provide to both patients and the healthcare community.

By Ronale Tucker Rhodes, MS

What causes a disease — especially a chronic or rare disease? How can clinicians be sure that the medications prescribed to treat a disease are the best ones? Are those medications always safe? How can patients or providers increase the chances that health insurance will cover the cost of medications? How can it be determined what the long-term health prognosis will be for patients diagnosed with a disease? These are but a sampling of questions to which both patients and healthcare providers seek answers when it comes to patient care.

For years, healthcare providers have based their care for patients upon clinical trials that provide data about treatment effects in controlled conditions. While these data are reliable, they often are not applicable to the diverse population, which can result in “evidence gaps

that impede the ability of patients and providers to make informed treatment decisions and of payers to determine what kinds of coverage will be appropriate.”¹ Therefore, to care for their patients based on real-world results, healthcare professionals are now focusing on evidence-based medicine, which is what patient registries provide.

Patient registries are operated by many different entities, including the federal government, state governments, universities, hospitals, non-profit organizations and private groups.² No one knows exactly how many patient registries there are. For instance, ClinicalTrials.gov contains more than 800 patient registries, but according to Elise Berliner, who heads the U.S. Agency for Healthcare Research and Quality’s (AHRQ’s) technology assessment, those probably represent just the “tip of the iceberg.”³ But, it is known

that the number of registries is growing and that they are powerful tools that provide broader results about the course of disease, variations in treatment and outcomes, factors that influence prognosis and quality of life, patterns in the delivery of care, and the effectiveness, safety and quality of care.⁴

Who Is Eligible to Join a Patient Registry?

To participate in a patient registry, a patient must be either diagnosed with the disease or treated with the medicine for which the registry is tracking. For instance, USIDNET, a registry established and managed by the Immune Deficiency Foundation for patients diagnosed with primary immunodeficiency diseases (PIDDs), originally enrolled only patients diagnosed with the more widely known PIDDs, including severe combined immune deficiency, X-linked agammaglobulinemia, common variable immune deficiency, DiGeorge syndrome, Hyper IgM syndrome, Wiskott-Aldrich syndrome and chronic granulomatous disease. However, the registry has now been enlarged to include more than 100 PIDDs.⁵

Patients can register for most registries on their own. However, it is more typical for healthcare providers to be the facilitator between their patients and the registries. Patients' healthcare providers assign someone in their office to input patient data into the registry and keep it updated as is required by the registry. Each registry differs in the types of information collected on patients once they have joined. All registries require patients to sign a consent form. Other forms that may be required include an authorization for the release of health information, a participant intake questionnaire, a family history questionnaire, an affected questionnaire (more in-depth questions about various symptoms, treatments and experiences), a semi-annual or annual update form or others.

How Is the Information in Patient Registries Used?

Registries are intended to collect data for a variety of reasons, including estimating the magnitude of a disease, determining the incidence of disease, examining trends over time, assessing healthcare quality, conducting research, estimating survival analysis, investigating etiological hypotheses, serving as a source of potential participants in clinical trials, and the reasons go on.² But, the four major purposes for patient registries are to evaluate the natural history of disease, determine the clinical effectiveness and cost-effectiveness of treatment, monitor safety of treatment and improve quality of treatment.^{1,4}

When evaluating the natural history of disease, its characteristics, management and outcomes with or without treatment are tracked. The reasons for tracking this may be due to the natural history of a disease not being well-described, to the variation across different groups and geographic regions that often change over time, or to changes in the disease after the introduction of certain therapies.^{1,4} For instance, the CGD (chronic granulomatous disorder) Society established a registry of CGD patients within the UK and Ireland, and in 2011 after evaluating the collected data, it found that younger patients generally are doing fairly well, but older patients still suffer complications and earlier death than unaffected people.⁶

All information in a registry is protected by the HIPAA Privacy Rule.

In contrast to the information that can be gained from clinical trials, registries can determine the clinical effectiveness of a treatment or service by looking at broader population bases (e.g., older versus younger, men versus women, etc.) and longer periods of time (e.g., from childhood into adulthood).^{1,4} Using the CGD registry as an example, it found that many years ago, young boys presenting with what looked like Crohn's disease (a granulomatous inflammation of the gut) would simply be treated as having inflammatory bowel disease, even if it was CGD. Now, however, gastroenterology colleagues always think about CGD. In addition, the CGD registry found that survival is better today than it was 10 or 15 years ago for CGD patients, but it is not normal in most cases, and the quality of life is not always normal.⁶ Another example of how registries can improve clinical effectiveness is the Improve Care Now registry that collects data on children and adolescents with Crohn's disease and ulcerative colitis. Since the registry was started, the percentage of kids with Crohn's disease and ulcerative colitis who are in remission has increased from 50 percent to more than 75 percent — all without new medicines.⁷

Registries also can be designed to collect cost data and effectiveness data to model the comparative value of a treatment's or service's ability to achieve a desired outcome, such as life expectancy or disease-free periods. For providers,

Registries for Patients Whose Treatment May Include Immune Globulin

Below is a short list of the many registries that exist in the U.S. for patients who rely on immune globulin products — patients who suffer from both immune deficiencies and autoimmune disorders. To find a registry for a specific disease that is not listed here, patients can contact their healthcare providers or the organizations listed in the Resources section in the back of this and every issue of *IG Living* magazine, as well as those on our website at www.IGLiving.com.

USIDNET: www.usidnet.org

USIDNET is a clinical registry for residents of the U.S. who are affected by several different primary immunodeficiency disorders. Established and managed by the Immune Deficiency Foundation, the registry is an outgrowth of a National Institute of Allergy and Infectious Diseases-supported pilot project begun in 1982 to establish a similar registry for U.S. residents affected by chronic granulomatous disease (CGD), which provided considerable information to patients about CGD that had not been previously available. USIDNET's goal is to provide improved access to patients by researchers conducting both basic and clinical studies; accurate and up-to-date profiles useful to clinicians and genetic counselors; and improved access by patients to information about the latest treatments. The registry also will include disease prevalence in the overall population and in various subgroups; the number and types of genetic defects that result in PIDDs, the clinical spectrum of these diseases; the correlation between the genetic defect and clinical picture; effects of current therapy on the course of PIDDs; and causes and incidences of morbidity and mortality. There are 33 enrollment sites in the U.S.

IDEaL (Immunoglobulin, Diagnosis, Evaluation and Key Learnings): www.idealpatientregistry.com

IDEaL seeks physicians to participate as sub-investigators in this

landmark patient registry. All physicians who prescribe immune globulin therapy are encouraged to participate, and physician and patient participation are completely voluntary and can be terminated at any time. The registry is observational in nature, requiring no change to a patient's medical care. Subjects in the registry are contacted approximately every six months to complete various quality-of-life scales.

Rare Diseases Clinical Research Network (RDCRN) **Patient Contact Registry:** rarediseasesnetwork.epi.usf.edu/registry

This registry was created to inform patients and/or parents of patients about clinical research studies. Information contained within the registry is used for recruitment for research studies directed at improving the knowledge and treatment of rare diseases, making it possible for researchers to find new treatments, create new studies and work for the improvement of patients' lives. Supported by the Office of Rare Diseases Research and National Center for Advancing Translational Sciences, RDCRN has more than 150 clinical sites.

MYOVISION: www.myositis.org

MYOVISION is a myositis patient registry designed to capture environmental exposures and other potential triggers of myositis. Utilizing funds from the Centers for Disease Control and Prevention, The Myositis Association will collect information from adults and children with myositis about their disease.

Peripheral Neuropathy Research Registry (PNRR): www.foundationforpn.org/peripheralneuropathyresearch/fpn-data-repository

Launched by the Foundation for Peripheral Neuropathy, the PNRR focuses on diabetic, chemotherapy-induced, HIV/AIDS and idiopathic

this information can be used to alter the way it provides a treatment or service. From a coverage perspective, policy determinations on payment rely on cost-effectiveness data.¹⁴ An example of how cost-effectiveness data can be used is Sweden's registry for hip replacement surgery that was begun in 1979. Since then, Sweden has reduced the number of surgeries that have to be repeated as a share of total hip replacements in a given year to 10 percent, saving some \$14 million per year. Those who examined data from this registry estimated that if the U.S. had in place a similar registry, it would avoid approximately \$2 billion of an expected \$24 billion in total costs for these surgeries in 2015.⁸

Because registries provide data on a broad population, they can be valuable for monitoring patient safety. They can act as surveillance systems to monitor a population for any occurrence of an unexpected or harmful event, which can help to both quantify the risk and to properly attribute it. In fact, FDA noted that "through the creation of registries, a sponsor can evaluate safety signals identified from spontaneous case reports, literature reports or other sources, and evaluate the factors that affect the risk of adverse outcomes such as dose, timing of exposure or patient characteristics. Registries also can be used to monitor safety for products with a known risk factor, which can be acces-

neuropathies. It was created to help researchers better characterize clinical phenotypes of patients with the disorder and will facilitate both the basic and clinical research studies needed for an improved understanding of the etiology and pathogenesis of peripheral neuropathy.

Inflammatory Bowel Disease (IBD) Registry:
www.hasbrochildrenshospital.org/services/pediatric-astroenterology/research/inflammatory-bowel-disease-registry.html

The Pediatric IBD Collaborative Research Group (PIBD CRG) at the Hasbro Children's Hospital formed the IBD Registry to gather demographics, clinical and laboratory information, as well as responsiveness to treatment data on children newly diagnosed with IBD. Twenty-one centers throughout the U.S. and Canada have enrolled more than 600 children to participate in this prospective, observational research program that examines treatments and quality-of-life outcomes to gain a better understanding of how these issues impact children newly diagnosed with IBD.

Improve Care Now Registry: improvecarenow.org

Improve Care Now is a network designed to improve the care and health of children and adolescents with Crohn's disease and ulcerative colitis. The network has developed *Model IBD Care: Guidelines for Consistent Reliable Care* based on carefully analyzed results of thousands of doctor-patient visits, as well as the latest studies and treatments worldwide. Clinicians and patients apply this information, experiences are tracked and studied, results are shared openly and further refinements are made to the guidelines to continually improve care for patients.

sible to the pharmacist and the physician to grant access to the drug only under appropriate circumstances, and to provide a source of data for the manufacturer on the frequency of the adverse event.⁴

Providers are more often using registries as a tool for ensuring adherence to clinical guidelines and assessing performance. This is becoming even more crucial for providers as reimbursement is increasingly tied to performance through programs such as the pay-for-performance initiatives. For patients, then, the data in these registries can ultimately lead to more competent healthcare delivery and better outcomes.⁴

How Do Patient Registries Protect Patients' Privacy?

A concern among many patients when participating in a registry is whether their personal information will be revealed to those who are using the data. How personal information is protected is governed in several ways.

First, for an institution to receive U.S. Department of Health and Human Services (HHS) support for research involving human subjects, it must designate at least one international review board (IRB) registered with the HHS Office for Human Research Protections (OHRP). (Protection of human subjects arose from the Belmont Report in the 1970s to be sure all human research follows the same code, which is known as the "common rule" that is under the jurisdiction of the HHS.) An IRB, also known as an independent ethics committee or ethical review board, is a committee that has been formally designated to approve, monitor and review biomedical and behavioral research involving humans. The board often conducts some form of risk-benefit analysis in an attempt to determine whether or not research should be done, with its No. 1 priority to protect human subjects from physical or psychological harm. There is no federal IRB; typically, each institution has its own IRB, which is known as an "internal" IRB. However, it is also possible for an institution to designate an already registered IRB operated by another organization (an "external" IRB) after establishing a written agreement with that organization. Also, to receive support by HHS for research involving human subjects, the institution must have received a federalwide assurance by OHRP that commits to HHS that the institution will comply with the requirements in the HHS Protection of Human Subjects regulations.⁹

Second, all information in a registry is protected by the HIPAA Privacy Rule. HIPAA provides federal protections for individually identifiable health information held by covered entities and their business associates. It also gives patients an array of rights with respect to that information, while at the same time balancing those rights so that the disclosure of health information needed for patient care and other important purposes is permitted.¹⁰

Last, all patients in a registry are assigned a random code, and all personal identifying information for each of those patients is removed and replaced with that code, which is the only identifying item that is ever used when accessing the data. The registry manager is the only person who has access to the personal data if it is contained in the registry database. In addition, representatives of organizations who are providing patient data to the

registry can only input and retrieve their own organization's data. (Registries typically work with healthcare organizations or doctors' offices that designate one or more individuals to enter their patients' data into the registry.) Should they wish to access other organizations' data, they would have to formally request it and, if approved, the data still would only include the code; no patients' identifying information in that data would be available.

When patients decide to enroll in a registry, they often are given different options. An example of this is USIDNET. Each patient participating in the USIDNET registry is provided with four options when enrolling. Under option one, the patient's identity is not stored in the registry and, therefore, it is not accessible by the registry administrator, so that administrator will not be able to determine which information is the patient's. Instead, a code number is assigned to the patient's information, and only the patient's doctor knows it. In addition, the patient's doctor is the facilitator of all communication between the registry and the patient. Under option two, the patient's name, date of birth and mailing and/or email address are recorded by the registry administrator. However, that personal information is kept in a separate database from the patient's medical information that contains an assigned code number. Therefore, investigators reviewing the patient's medical information do not have access to the patient's identifying information. Patients under this second option also have two other options: 1) to have all communication between the registry and the patient go through the patient's doctor (unless the patient has moved or has ended contact with his or her doctor); or 2) to allow the registry staff to directly inform the patient about research results based on information gathered on the patient's disease. The doctor would also receive the information.⁵

What is particularly important for patients to understand is that registries are considered "minimal risk" because they are merely sharing information about human subjects; they are not actually testing medical procedures or products on human subjects.

Succeeding with Patient Registries

Due to the growth in the number of patient registries, in December 2012, the Registry of Patient Registries (RoPR) was established by AHRQ. Known as a "metaregistry," the goal of RoPR is to create a one-stop shop where physicians, patients and researchers can find lists of individuals who have made themselves available for observational medical studies. In essence, the database would serve patients and physicians looking for specific disease registries, researchers

investigating a particular disease, and drug developers. The metaregistry also could be used to monitor outcomes and study best practices. RoPR has particular potential for rare diseases about which little is known by aggregating data and information, speeding up research on the diseases and ensuring that research projects are not redundant.³

But, the benefits of patient registries to patients and healthcare providers depend upon patients' participation because these registries must contain enough data to be useful. Some of the benefits of sufficient data include helping to determine the causes of disease, the best therapies, how to prevent adverse events and how patients can be provided better quality of care. Patient registries can be found through an Internet search, through patients' healthcare providers or by contacting patient organizations. ■

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Editor's note: There are several registries abroad for immunodeficiencies, including the ASCIA Primary Immunodeficiency Disease Register of Australia and New Zealand (www.immunodeficiency.org.au), European Society for Immunodeficiencies Database (www.esid.org/research-database), Latin America Group for Primary Immunodeficiencies (www.lagid.lsuhs.edu) and the French National Reference Center of Primary Immunodeficiencies.

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