Real World Data and its promise for medicine and research

By Grace-Marie Turner

Better access to data about real world patient experience holds enormous potential to help achieve many of the goals of health reform, including improving the quality and delivery of medical care, reducing costs, and improving safety and outcomes by accelerating the knowledge base upon which the development of new treatments and cures relies.

Capturing data about the actual experience of patients outside of the carefully controlled clinical trial setting – Real World Data – can help fill the knowledge gap between clinical trials and clinical practice. RWD offers a treasure-trove of information that could allow providers, innovators, health plans, researchers, and others in the scientific and medical communities to make faster, more efficient, and less costly advances in medical research and clinical treatment. Life sciences companies can use this data to explore the benefits and risks of treatment options including their effectiveness in patient subpopulations, expedite enrollment in clinical trials, identify new targets for research and development, and transform the value equation in medical care.1

However, there are obstacles that must be removed for the promise and potential of Real World Data to be realized.

While the potential is great, the future of RWD is highly uncertain. Governments and private health care companies who administer government-sponsored health insurance have vast databases of information, primarily medical claims. Most of this information is inaccessible to the researchers who are developing the next generation of treatments and cures, such as pharmaceutical and medical device companies and academics.

Longstanding policies by the Department of Health and Human Services deny access to federal Medicare A, B, D, Medicaid, and other data sets on Prescription Drug Event (PDE) data by entities with commercial interests, yet these are the very entities that we rely on to invest in the expensive process of bringing new treatments to patients. These policies inhibit medical research and ultimately are detrimental to patients whose care could be improved by access to more robust information. In cases where academics are able to request access to the government data, the cost is often prohibitive.

Real World Data has the potential to support a more personalized model of care that can enhance patient outcomes, improve quality of care, facilitate access to appropriate innovative therapies, lower costs, and improve the efficiency of care delivery.
This paper will seek to identify the biggest challenges the industry will face as it moves towards a wide use of real world data, including policy obstacles that must be overcome, the important protection of patient privacy, and the development of systems that allow for real world application of these massive data sets.

The promise

Real World Data (RWD) can provide information on how patients are treated in clinical practice and sometimes the outcomes of the treatments. Real world is contrasted with the much more carefully-controlled realm of controlled clinical trials which provide data on the cause and effect relationship of specific treatment interventions, but which do not provide information about how the interventions are used and work in real world settings. Additionally, clinical trial data may not reflect the diversity of the actual patient population that uses the treatment.

RWD sources can include electronic medical records created by care providers, data used to coordinate and pay for care, payment information collected by private and public plans and programs, and first-hand information from patients on actual experiences. Information derived from RWD can be extremely useful to researchers to learn the effectiveness of treatments and medicines in practice, to develop new treatments and cures, and also produce information on the comparative value of different types of medical and surgical interventions.

Some policymakers misinterpret RWD as Big Data. “Big Data” is an emerging field that seems to have no uniformly accepted definition. In concept, it involves research in which a vast amount of information from multiple large and diverse data sets can be analyzed to gain new insight into products, processes, relationships, and outcomes. It can be used to quickly test new ideas and even shape predictions. Big Data focuses on finding trends and patterns which would be difficult, expensive, and even impossible to find using traditional information-gathering and information-processing methods.

In contrast, the centerpiece of Real World Data involves the narrower realm of information on actual patient contact and eventually, outcomes data. By understanding more about this process of care, researchers can employ advanced analytics to make medical care more targeted, efficient, and effective and thereby reduce unnecessary treatments and expenditures, including hospitalizations. There are a number of reasons why RWD is important to researchers – and to patients and health care providers – to improve quality and efficiency in the health care system and ultimately to improve outcomes. Some advantages:

- Enabling more knowledgeable choices by doctors and patients
- More precise monitoring of medications and other medical treatments
- Supporting systems that pay for value and quality rather than the volume of care delivered
- Better management of care and costs under new payment paradigms
- Better management of targeted patient populations, especially high risk patients
- More clarity for investors in new research and development projects
- More precise design of clinical trials, including gathering information about which subpopulations of patients may benefit the most from specific therapies
• Identifying patients appropriate for inclusion in clinical trials
• Assessment of the value of new and sometimes breakthrough interventions
• Assessment of safety and efficacy as required by regulatory agencies and payers
• Promoting more rapid collection and dissemination of information to improve safety and patient care
• Better understanding of how complex combination of medical interventions may benefit patients apart from the structured clinical trial setting

Congress is paying attention

House Energy and Commerce Committee Chairman Fred Upton and Rep. Diana DeGette are soliciting ideas from a broad range of experts as part of an initiative they are leading: The Path to 21st Century Cures. They are “looking at the full arc of this process – from the discovery of clues in basic science, to streamlining the drug and device development process, to unleashing the power of digital medicine and social media at the treatment delivery phase.”

In a white paper submitted to the committee, Pfizer Chairman and CEO Ian Read said that “Ensuring access to real world data captured in [electronic medical records], medical claims databases or registries is vital to nearly all stakeholders and can provide crucial information by elucidating unmet needs in our current system and information about the efficiency of healthcare delivery, and helping to demonstrate value, efficacy, and safety.”

The digital era will provide an explosion of new ways to collect data from mobile communications devices and biosensors, including remote patient monitoring to better understand their response to treatment and provide timely interventions. “A combined and coordinated application of these new technologies could ultimately control the increasing burden of healthcare, speed up development of new therapeutic drugs and increase the quality and value of patient-centered healthcare data allowing for a deeper understanding of patients’ disease and well being,” according to Moncef Slaoui, chairman of global research and development and vaccines at GlaxoSmithKline.

Read and Slaoui are among the many industry leaders responding to the Energy and Commerce Committee’s request for information on what is needed to “ensure we are taking full advantage of the advances this country has made in science and technology and use these resources to keep America as the innovation capital of the world.”

“Releasing more of the data housed in government datasets to qualified researchers, and connecting it across multiple sources could dramatically improve the innovation cycle,” Read wrote to the Committee, “as unlocking and analyzing data will enable better decision making between patients and physicians and innovation in care delivery and new treatments.”

Senate Finance Committee leaders also are seeking ideas to improve data transparency. Chairman Ron Wyden and ranking member Charles Grassley say the volume of health care data is growing exponentially but that policies and strategies to harness the data are lagging. They are soliciting ideas from stakeholders on what data should be made publicly available, how the data should be presented to the public, and what reforms are needed to facilitate access and usability of the data.
The value of collaboration

In an information age, pharmaceutical and device companies, academic institutions, and healthcare providers are among those who need resources outside their research laboratories to advance medical progress, including developing the next generation of treatments and cures.

Companies in the health sector see the value not only of greater access to real world data but also to data partnerships where they can work together to speed research and development. For example, Merck began a collaboration in 2012 with researchers from the Regenstrief Institute at the University of Indiana to fund collaborations among researchers from a variety of fields – clinical and basic sciences, computational biology, computer science, and global and public health.

An important data source for the project is the Indiana Network of Patient Care (INPC), an 18-year-old health information exchange that provides clinical information from 80 hospitals, public health departments, laboratories, imaging centers, and some physician practices. The INPC has more than 4.5 billion pieces of clinical data for more than 13 million patients. This is uniquely valuable for observational research, providing clinical and claims data as well as discharge reports, clinical notes, and medication orders. They will investigate how Patient A responded to a treatment regimen vs Patient B, what were the characteristics of the patients and their conditions, and how outcomes differed based upon such criteria as drug adherence.

Collaborative efforts also are underway in Europe with the Innovative Medicines Initiative. Launched in 2008, this is the biggest private partnership in Europe to enable pharmaceutical and biotech companies and academic researchers to work together in addressing specific problems, such as pharmacovigilance, biomarkers, and diabetes. Other companies are developing their own collaborations on RWD. AstraZeneca and HealthCore, for example, are collaborating on studies designed to determine how to most effectively and economically treat disease. The collaboration includes observational studies of comparative effectiveness and the efficacy of medicines in several disease areas.

Pfizer collaborated with Humana to address pain inefficiencies associated with opioid abuse to identify high risk patients, and the companies jointly developed a predictive model. They are now working together on evaluating an intervention that leverages the predictive model to identify and appropriately manage patients at risk for opioid abuse.

Claims data and transparency

Several health plans are joining together to create a payment database to make health care pricing information available to the public at no charge. United Healthcare, Aetna, and Humana are working with the Health Care Cost Institute (HCCI), a non-profit group established in 2011. Professor Stephen Parente of the University of Minnesota’s Carlton School of Management is chair of HCCI’s board. The project is slated to go live in 2015 and will include
claims data from commercial Medicare Advantage plans and Medicaid. There are challenges in the effort since these competing health plans are not accustomed to sharing information and to having information that can be integrated across their different platforms. Nonetheless, other health plans are considering joining the endeavor, showing the energy behind collecting and disseminating huge data resources.

The demand for cost transparency is being spurred by a number of developments, including the move to higher-deductible health plans in which consumers have a greater incentive to shop for the best value in health services.

As a result, a number of states also are starting to make claims data available. The National Conference of State Legislatures in 2013 assessed state efforts at making pricing information accessible to consumers. Massachusetts and New Hampshire got “A”s but most states got “F”s. These failing grades have motivated many states to pass legislation requiring hospitals and other medical providers to post prices they’ve negotiated with insurers for a long list of services.

Other states are going further and creating all-payer claims databases (APCD) that require commercial insurers, self-funded large employer plans, Medicaid, and other health care payment programs within their borders to make their claims data available to the government. So far, 19 states have created APCDs, and at least 21 others are considering laws to create them. Privacy protections are, of course, crucial, but government can help facilitate a better-functioning market by making clear and accurate information from its own data sources more widely available. These state databases may or may not be available to commercial entities, however, and they also don’t capture patient experiences. They are all built around claims data which only captures utilization and not necessarily utility of health care services. The Patient-Centered Outcomes Research Institute (PCORI) is providing funds to several patient organizations to develop databases that also capture patient experiences in certain disease areas. PCORI is spending $100 million to create the National Patient-Centered Clinical Research Network. PCORNet is designed to create a real world data resource for comparative effectiveness research collected from health care systems and patient networks. The goal is to “advance the shift in clinical research from investigator-driven to patient-centered studies.”

**The demonstrated need for data and analytics**

While RWD holds great promise, and some exciting collaborations are underway, the field is still in its infancy. The President’s Council of Advisors on Science and Technology (PCAST) has cited the nation’s inadequate health data infrastructure as a barrier to improvement in the quality of American health care. PCAST says that our antiquated fee-for-service payment system must be replaced with payment models that reward value rather than volume to improve the quality of care. And these new payment models will depend upon metrics, especially outcomes measurements. They specifically cite the need to increase access to health data and analytics.

RWD is equally important to protect patients from harm. The example of Vioxx is a case in point. The drug was approved by the FDA in 1999 and marketed by Merck & Co. to treat arthritis and other conditions causing
chronic and acute pain. Worldwide, more than 80 million people were prescribed the drug at some time.

The drug was withdrawn from the market in 2004, however, because of evidence of an increased risk of heart attack and stroke associated with long-term, high-dosage use. It became clear that the drug could be dangerous to patients with serious heart disease.

Collection of real world data would have highlighted this danger much earlier, likely eliciting a Black Box warning for patients with heart disease. Instead, all patients were denied the drug, even those who said it provided better pain management than any competing products.

A more robust collection of information can assure patients are receiving the right drug, even the right dosage, and help providers learn how to better target treatments.

**Pharmacy data and Medicare Part D**

Prescribing data are among the most valuable and reliable resources for researchers because of the strong predictive relationship between prescription drug use and medical diagnoses. Accurate pharmacy claims data also are widely available because of the established third-party payment system in the United States.

Automated outpatient pharmacy data provide a rich vein of information that research has shown to provide a stable measure of health status. A groundbreaking study by Von Korff and colleagues at Puget Sound Group Health Cooperative created a measure of chronic disease status using automatic outpatient pharmacy data. They found that the pharmacy data provided a stable and valid indication of a patient’s health status. The data was predictive regarding health care visits and hospitalizations. Such tools are cost-effective ways to do screening and to anticipate the need for interventions. Others have since replicated the findings. This method of assessing risk also has been replicated for pediatric patients.

The Centers for Medicare and Medicaid Services proposed a rule on January 10, 2014, [CMS-4159-P] about whether or not commercial enterprises would finally be able to have access to Medicare Part D prescription drug data for research. There is no question that this data could be invaluable to researchers and thereby to clinicians and patients. The Healthcare Leadership Council (HLC) and the National Pharmaceutical Council were among those offering detailed comments, arguing that, “In an aligned, high functioning healthcare system, everyone should be able to benefit financially from effective use of data to improve quality and efficiency in the healthcare system…Patient level information is needed to achieve the very care transformation CMS seeks.”

The Affordable Care Act relies heavily on commercial enterprises to implement the law, especially private health plans offered through the exchanges and private Medicaid managed care companies that are offering coverage through the optional expansion. But these entities are barred from accessing the valuable information that could help guide the efficiency authors of the law sought to create. The Healthcare Leadership Council observed that “…any notion that commercial interests is limited and discrete is outdated.”
CMS finalized its Medicare Part D rule in May, 2014, and concluded that the Part D information still may not be used for commercial purposes, although it left the door open for reconsideration of its decision. “Commenters stated that the challenging of quantifying greater efficiency and evidence of improvement as part of the overall health reform requires more access to the unique data sets in federal data, and that the current restriction on the use of these data for commercial purposes will grow increasingly challenging in the future as Medicare employs more value-based payment incentives, and as Medicare data are included in broader multi-payer sets, such as those being established by the Patient-Centered Outcomes Research Institute,” the CMS rule notes.16

The quality and efficiency of health care delivery would be enhanced if the companies actually creating and delivering new medical treatments were to have access to comprehensive Real World Data. This information would allow them to identify effective interventions to better manage care for high-risk patients, do a better job of avoiding hospital readmissions, identify factors that would improve medication adherence, and develop new diagnostics to better target therapies to patients who are most likely to benefit.

Privacy protection and security

There would, of course, need to be contractual agreements that protect the use of sensitive data. All researchers should be subject to the same rules for data access and data protection if access to Personal Health Information Medicare data were to be allowed. These criteria would include: A strong design of the research project, expertise and experience of the researcher, and strong agreements concerning handling and use of the data, especially pertaining to confidentiality and protection of the data.

Some organizations are experimenting with private “clouds” to collect electronic medical record information and store it securely. Private companies also are developing sophisticated cryptographic methods that place security tags on data and assign specific access rights to specific users.17 These security tools, first developed to support national intelligence agencies, can “place different levels of security on different types of data, from demographic information to highly sensitive health data.”

The importance of protection of patient privacy cannot be overstated, but advanced information technologies have the potential to both gather the information and offer multiple levels of protection. Receiving patients’ consent to have their medical information anonymously aggregated into these massive data bases can support patients’ desire to help others with similar conditions and illnesses. Guidelines, of course, are needed to develop viable consent forms and mechanisms.

At the same time, technological advances are especially needed to speed the collection of this data in the clinical setting so as not to further burden physicians, nurses, and other medical practitioners with mountains of forms and reporting requirements.

Challenges to RWD

Companies in the health care industry face a number of challenges as they move toward a wide use of real world data, including:

- Collection of data: Collecting RWD efficiently and effectively to improve clinical practice and development of new medical treatments.
• **Electronic Medical Records:** Developing electronic medical record standards that contain useful information to enable analysts access the information across platforms

• **Harmonization:** Combining data generated across different sites of care that can be aggregated in order to be useful to researchers. Volumes of data are being collected but inconsistent coding and analysis standards hinder the optimal use of RWD for decision making.

• **Privacy:** Addressing the very real issue of protection of patient privacy

• **Cost:** Overcoming the high (and often inhibitive) initial costs of purchasing the data

• **Accessibility:** Changing policies to make information available. Even if the data were not prohibitively expensive, commercial interests, such as pharmaceutical researchers, are banned to having access to Medicare data, as explained in the previous section. This blocks those on the front lines of medical research from having access to a rich vein of RWD that could lead to new and better treatments, and at lower costs than current research tools and techniques allow.

Most RWD data sets are claims data which may or may not demonstrate cause and effect relationships of certain interventions or innovative therapies. In addition, claims data do not capture valuable information about patient experiences that can be combined with claims data to provide a meaningful picture of the impact of such endeavors on quality of life and patient satisfaction. As noted earlier, the Patient-Centered Outcomes Research Institute is commissioning studies and work with patient groups to collect patient experience data in certain prevalent disease areas, but much more work needs to be done.

Building these capabilities is a long and expensive process, but it is crucial to future success in research. The first step is access to existing payment data including Medicare. Next will be patient-approved use of information from electronic medical records, and then collecting useable data from patient experience with built-in privacy protections.

**Conclusion**

The 21st century may well be defined as the century of medical discoveries. Advancing this vision requires building on the extraordinary opportunities to collect, capture, and analyze information so that we can build a rapid learning health care system. Real world data is a vital component of that progress.

Real world data has the potential to complement clinical trial evidence by providing information that can dramatically improve current standards of care. It also can provide evidence to enhance safety and outcomes. But there are challenges: The quality of the data may be uneven and difficult to harmonize and therefore analyze. Patient privacy must be protected. And policy obstacles abound in providing access to the data.

Information is key to the next generation of medical discoveries, and real world data is key to unlocking clues that will enable better decision making between patients and physicians to improve care delivery and outcomes. The time has come to unleash a new generation of information-based improvements in the quality and efficiency of health care through effective use of Real World Data.
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ENDNOTES


8 Pasquale, M. “Dr. Margaret K. Pasquale and Team Identify High-Risk Factors Predicting Opioid Abuse.” http://www.ajmc.com/ajmc-tv/interviews/Margaret-K-Pasquale-PhD-Identifies-Factors-in-High-Risk-Opioid-Use

9 Vestal, C. “Can claims data crack the health care cost riddle?” USA Today, June 17, 2014.

10 PCORnet: The National Patient-Centered Clinical Research Network is designed to “foster a range of observational and experimental CER by establishing a resource of clinical data gathered in ‘real-time’ and in ‘real-world’ settings, such as clinics. Data will be collected and stored in standardized, interoperable formats under rigorous security protocols, and data sharing across the network will be accomplished using a variety of methods that ensure confidentiality by preventing patient identification.” Full description available at: http://www.pcori.org/funding-opportunities/pcornet-national-patient-centered-clinical-research-network/


