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PEDSnet: How A Prototype Pediatric Learning Health System Is Being Expanded Into A National Network

ABSTRACT Except for a few conditions, pediatric disorders are rare diseases. Because of this, no single institution has enough patients to generate adequate sample sizes to produce generalizable knowledge. Aggregating electronic clinical data from millions of children across many pediatric institutions holds the promise of producing sufficiently large data sets to accelerate knowledge discovery. However, without deliberately embedding these data in a pediatric learning health system (defined as a health care organization that is purposefully designed to produce research in routine care settings and implement evidence at the point of care), efforts to act on this new knowledge, reducing the distress and suffering that children experience when sick, will be ineffective. In this article we discuss a prototype pediatric learning health system, ImproveCareNow, for children with inflammatory bowel disease. This prototype is being scaled up to create PEDSnet, a national network that will support the efficient conduct of clinical trials, observational research, and quality improvement across diseases, specialties, and institutions.

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Except for a handful of disorders (such as asthma, attention deficit hyperactivity disorder, autism spectrum disorder, obesity, and acute infections), virtually all childhood conditions are rare diseases. As a result of the infrequent occurrence of pediatric disorders, no single institution has enough patients to generate adequate sample sizes to produce generalizable knowledge. This epidemiological reality has resulted in the reliance on "hand-me-down" results from research done among adults[1] and a sparse pediatric evidence base.

One approach to overcoming these sample-size limitations is to invest in pediatric big data. By *big data*, we refer to large amounts of clinical data obtained from electronic health records (EHRs); patient-generated data sources; and biospecimens aggregated from multiple institutions and thousands, even millions, of children.

Perhaps the most promising approach for de-veloping big data and then using it for research and quality improvement is the formation of a pediatric learning health system. We define a *learning health system* as comprising four essential attributes: an organizational architecture that facilitates formation of communities of patients, families, front-line clinicians, researchers, and health system leaders who collaborate to produce and use pediatric big data; large electronic health and health care data sets (big data); quality improvement for each patient at the point of care brought about by the integration of relevant new knowledge generated through research;[2–5] and observational research and clinical trials done in routine clinical care settings.

We present a model for a pediatric learning health system that purposefully integrates research and quality improvement as part of one system of care. This model takes advantage of pediatric big data; engages a community of stakeholders pursuing a common purpose; and

distributes the work of creating knowledge and know-how across a broad population of patients and families, clinicians, and researchers organized in networks. We illustrate the model by describing a prototype pediatric learning health system called the ImproveCareNow network for children with inflammatory bowel disease and sketch how the prototype is being scaled up to create a national pediatric learning health system called PEDSnet.

The Learning Health System

In today's health system, research is done by scientists, improvement is implemented by quality specialists, patient care is administered by clinicians, and management is handled by health care executives. Patients are relatively passive consumers of these services. Communication across these communities is scant, knowledge is siloed, and diffusion of evidence of best practices to achieve good outcomes into clinical practice is unacceptably slow.[6]

We envision a transformation from the current state to one in which research, improvement, management, and patient care are intentionally integrated. In such a health system, "learning while doing"[7] is the default, thus ensuring that the right care is provided to the right child at the right time, every time.

The learning health system is more than big data and big clinical trials. The system is predicated on the active collaboration of all members of the system, from patients to clinicians to health system leaders, and success is defined by the impact of the system on the health and lives of patients. Each of these four components—engaged communities, big data, quality improvement, and research—should be considered within an overall system design. Clinical research focuses on "what works." Implementation research focuses on "how to make it work."[8] Both are needed as part of the learning health system.

The engine of the learning health system is the learning cycle. The cycle begins with patient-clinician interactions at any location where care is provided. Data from these interactions are routinely captured electronically and combined across patients, time, and settings, allowing for comparative studies. Findings from these comparative studies coupled with existing biomedical research add to the knowledge network—the database of current knowledge that is relevant to improving the health and care of patients and populations. Quality improvement methods, such as previsit planning individualized to each patient, are used to ensure that this evidence is applied to meet the needs of patients. When the learning cycle is fully operational, research influences practice and practice influences research in a virtuous cycle.[5]

A Pediatric Learning Health System Prototype: ImproveCareNow

The concept of the learning health system is typically applied to a single health care organization.[5] In pediatrics and rare diseases, learning must occur among organizations and patients who are dispersed across geography and institutions to create a distributed learning health system. There are few examples of such distributed learning health systems involving more than one organizationally distinct institution. One example of an operational prototype is ImproveCare Now. Established in 2007, ImproveCareNow was launched to advance the quality of care for children with Crohn's disease and ulcerative colitis: severe immunologic diseases referred to as inflammatory bowel disease that result in abdominal pain, diarrhea, bloody stools, weight loss, stunted growth, and fatigue. Children with inflammatory bowel disease endure emergency department visits, colonoscopies, and x-rays, and they risk hospitalization and surgery (such as bowel resection and colectomy). Treatment may require numerous daily pills and regular intravenous infusions of medication. When patients are in remission (no symptoms, feeling well, and fully active), they can lead normal lives.

Since its inception, the network has grown from eight to sixty-six pediatric gastroenterology care centers, now including approximately 35 percent of all US children with inflammatory bowel disease. Without the addition of new drugs to the therapeutic options available to patients and clinicians, ImproveCareNow increased the proportion of patients in remission from 55 percent to 77 percent (Exhibit 1), markedly reducing the burden of suffering. The ImproveCareNow innovations are described in more detail below.

For the first few years of its existence, Improve CareNow involved only clinicians and their care centers. Over the past four years and with funding from a National Institutes of Health Transformative Research grant, ImproveCareNow has worked with the C3N Project (c3nproject.org) to develop infrastructure and methods that are needed to transition from a quality improvement collaborative into a disease-specific learning health system.[9] With funding from the Agency for Healthcare Research and Quality's Enhanced Registry program, ImproveCareNow developed a digital architecture based on EHRs and scientific infrastructure for conducting comparative effectiveness research.

EXHIBIT 1

Percentage Of Pediatric Inflammatory Bowel Disease Patients In Remission, 2007–14
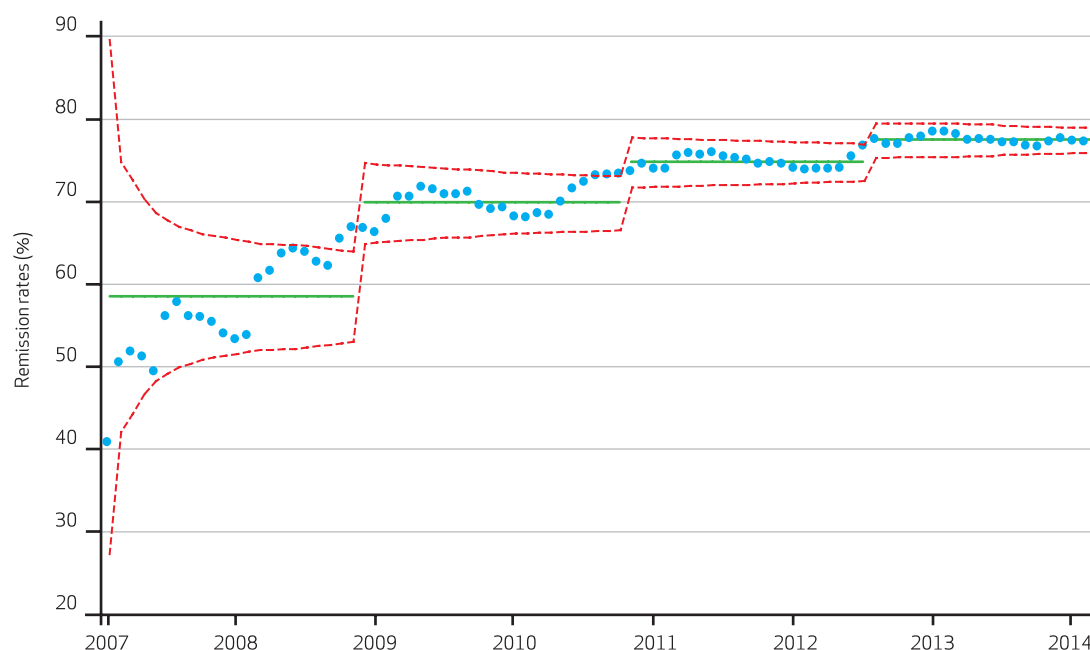
SOURCE Data are from the ImproveCareNow pediatric inflammatory bowel disease registry for 2007–14. NOTES Each blue dot represents the percentage of patients in remission among care centers with more than 75 percent of their patients enrolled in Improve CareNow in a given month. The figure shows the upper and lower confidence limits (dashed red lines in red) and the mean (green solid lines).

Learning As A Community

ImproveCareNow has implemented a model for engaging participants called actor-oriented collaboration.[10] The actor-oriented architecture for collaboration allows people and institutions with shared values and a common purpose to self-organize for projects that address problems of mutual interest. ImproveCareNow depends on the voluntary participation of care centers, clinicians, and patients. The network facilitates collaboration by providing resources, such as web-based collaboration spaces, project management, learning activities, and communication resources that make it easier for geographically disparate people to work together.

The relentless focus on improving rates of clinical remission for children with inflammatory bowel disease is the common purpose that galvanizes the ImproveCareNow community. The consistent message that "you can make a difference" is communicated through transparent sharing of outcomes data, best practices, and personal narratives. Sharing occurs during monthly teleconference and semiannual, in-person learning sessions and via ImproveCare Now's newsletter, blog, and social media platforms. This is coupled with a credo of "steal shamelessly and share seamlessly" to spread good ideas to all care centers in the network.

These messages motivate contributions.

In ImproveCareNow, patients have collaborated with scientists to develop chronic care innovations. Among their ideas were better use of new technology that enables self-monitoring of symptoms and use of treatments to improve shared decision making between patients and doctors. More recently, ten-year-old children have worked with their parents to create instructional videos illustrating how to insert feeding tubes through their own noses and into their stomachs for nutritional therapy. Parents and clinicians teach (and co-teach) modules at learning sessions that address how to make changes in care delivery, how to form a parent mentoring group, how to incorporate parents into care centers' quality improvement teams, and how to develop an elevator pitch for ImproveCareNow.

Parents have organized to raise money and produce materials for families with newly diagnosed children. They lead online discussion forums, community events such as inflammatory bowel disease education days, and design mobile tracking tools to supplement existing clinical data with patient-reported data to understand the effectiveness of nonpharmaceutical interventions such as probiotics.

To facilitate collaboration among patients and clinicians, ImproveCareNow runs monthly team

calls, semiannual learning sessions attended by teams from each participating center, online communities for parents (www.smartpatients.com/ibd), a digital bulletin board for sharing ideas and tools (www.improvecarenowexchange.org), and a database that clinicians can query.

Digital Architecture

A second characteristic of a learning health system that ImproveCareNow has implemented is facilitated data entry from EHRs. A learning health system relies on data from EHRs and patient registries to foster collaborative improvement, research, data sharing, and innovation.[11–13] This "data in once/used many times" mantra has been the vision of leading thinkers in informatics.[14] Clinicians entered data into the EHR via structured templates and received monthly reports on the quality of their data. Best practices for achieving the highest-quality data are shared during learning sessions.

Although learning health system thought leaders have advocated for a distributed data network in which source data remain with data owners until the data are needed for a specific purpose,[15,16] ImproveCareNow has pursued a centralized approach. This is because many care centers do not have the informatics resources to support such a distributed model or the local capability to undertake near real-time reporting to support care management and improvement activities. A distributed model makes sense if data are combined across health care organizations within the network for one research study at a time. The distributed model becomes more cumbersome, however, when demands for data require near-real-time access, as is the case for ImproveCareNow.

Quality Improvement

To make optimal use of its data, ImproveCare Now has developed software applications that enhance chronic care management. A variety of reports that contrast a given health center to its peers are provided monthly. Care centers also have the ability to access the database and generate reports more frequently. Daily reports are made available for each patient, and these are used to improve care at the individual level with decision support and previsit planning. For example, the patient reports include recommendations for appropriate dosing of medications and recommended laboratory evaluations before a visit with a patient.

A learning health system must also reduce the interval between the discovery of new knowledge and its impact on patients. ImproveCareNow

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adapts standardized processes and tools for chronic illness care, such as reviewing the entire population of patients each month to identify if there are patients who missed needed care, learning from variations in performance, and sharing knowledge about how to implement changes to help care centers rapidly integrate new information into patient care.[17] More reliable previsit planning and regular population review make it easier for physicians to adjust treatments to individual patient needs. The big increases in remission rates observed in the ImproveCareNow patient population (Exhibit 1) were associated with adoption of standardized and reliable care delivery processes such as previsit planning and population management.

Rapid Research

The data collected for ImproveCareNow have been used for chronic care improvement since 2007. It was unclear whether these data could also be used to rapidly generate new knowledge that would be generalizable to all children with inflammatory bowel disease. Thus, Improve CareNow recently tested the feasibility and validity of using its registry data for comparative effectiveness research. The study contrasted the effects of anti-tumor necrosis factor α (anti-TNFα) therapy versus conventional care for moderate-to-severe pediatric Crohn's disease patients. This topic was of high priority for clinicians because the cost of anti-TNFα is in the range of tens of thousands of dollars per year, and the long-term direct and indirect costs are substantial.[18] Administration of anti-TNFα has been associated with serious infections, hepatic T-cell lymphomas, systemic lupus, and blood disorders.[19] Nonetheless, in studies done on adults, anti-TNFα had been shown to be highly

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effective for reducing or eliminating the symptoms of Crohn's disease.[20,21] These same comparative studies had not been done in children because of practical (time and cost) and ethical (withholding an effective treatment) challenges. The availability of the ImproveCareNow database, with over 4,000 Crohn's disease patients at the end of 2012 helped overcome these obstacles.

Using the ImproveCareNow data, analyses were done over the course of a few months to estimate the treatment effect for anti-TNFα (intervention group) compared with usual care (control group).[22] The results were remarkably consistent with those of studies that evaluated treatment efficacy among children receiving anti-TNFα but lacked a control group, and comparative controlled clinical trials done among adults.[21,23] They expand the evidence base by providing new information on the comparative effectiveness of anti-TNFα for children managed in routine pediatric gastroenterology settings. The study demonstrated that prospectively collected data from ImproveCareNow could be used to rapidly answer important clinical questions that cannot be addressed with controlled trials because of practical or ethical challenges. Moreover, the study's methodology offers advantages relative to conventional clinical trials in terms of time, cost, recruitment, and the capacity to forgo the use of placebo.

From Prototype To National Pediatric Learning Health System

ImproveCareNow has been a remarkable prototype for learning. It has shown the way forward in the domains of technology, governance, implementation science, comparative effectiveness research, and community engagement. To achieve our vision of a national pediatric learning health system, however, we recognized the need to scale up the ImproveCareNow prototype to large pediatric health care organizations, other disease-specific communities, and national

data partners to create a network-based platform that could support quality improvement and research across all pediatric specialties, diseases, and regions.

This vision is becoming a reality. Recently, with funding from the Patient-Centered Outcomes Research Institute, we established PEDSnet. The purpose of PEDSnet is to create a community of patients, families, clinicians, scientists, and health care system leaders who work together in a distributed learning health system that is dedicated to discovering and implementing new ways of providing the best care and ensuring the best outcomes most efficiently. The governance, regulatory, informatics, social, and scientific infrastructure that PEDSnet is developing will enable research on acute, behavioral, surgical, and chronic medical conditions in pediatrics.

PEDSnet is a network currently composed of eight of the nation's largest pediatric academic health centers: Children's Hospital of Philadelphia, Cincinnati Children's Hospital Medical Center, Children's Hospital Colorado, Nemours Children's Health System, Nationwide Children's Hospital, St. Louis Children's Hospital, Seattle Children's Hospital, and Boston Children's Hospital. Each year these institutions care for over two million children.[24]

In addition to developing data, regulatory, scientific, and governance infrastructures across children's hospitals, we are explicitly linking PEDSnet to three disease-specific networks—ImproveCareNow (pediatric inflammatory bowel disease), the National Pediatric Cardiology Quality Improvement Collaborative (complex congenital heart disease), and a newly formed Healthy Weight network (childhood obesity).

PEDSnet And Pediatric Big Data

To create a pediatric big-data resource that is comprehensive in scope, PEDSnet has partnered with two national data partners, ExpressScripts and IMS Health. Over the next two years PEDSnet will link administrative data from these data partners to the clinical data from pediatric academic medical centers to provide retail pharmacy (dispensed medications) and health insurance claims (health care use and costs) for patients.

Once these linkages are complete, PEDSnet will be the most comprehensive pediatric big-data project in the United States and will support the conduct of efficient clinical trials and large-scale observational research. PEDSnet is part of the larger National Patient-Centered Clinical Research Network, or PCORnet (www.pcornet.org), which includes ten other institutional net-

works like PEDSNet and a total of eighteen patient-powered, disease-specific networks including ImproveCareNow. When fully functional, PCORnet will include tens of millions of Americans, improving the capacity to rapidly learn what works for which patients.

As a demonstration project on the validity of using pediatric big data derived from EHRs, PEDSnet combined data from six of the eight institutions to accrue a data set containing information on 1.4 million children ages 2–17.[25] The study demonstrated the feasibility of sharing EHR-derived data for assessing obesity in large populations of children. The time and effort required to retrieve the data were nominal, yet the scale of the EHR-derived data was significant: The sample from six pediatric institutions produced 6,000 body mass index assessments per month of age for most of childhood. Not only were these results consistent with national estimates obtained by the Centers for Disease Control and Prevention, the study also demonstrated associations between obesity and comorbidities such as diabetes, hypertension, dyslipidemia, liver disease, and sleep apnea, and rare diseases such as leukemia.

Another key technology barrier to forming pediatric big data is the lack of standardized definitions and descriptions of clinical observations for pediatric care and child health.[26] Without a common terminology, institutions may define the same clinical concept differently in EHRs. This makes combining data across research studies challenging because different definitions are used for the same underlying concepts. To address this need in pediatrics, PEDSnet and the National Institute of Child Health and Human Development have launched a pediatric research terminology initiative that is linking pediatric terms to existing standard terminologies.[26]

Conclusions

Creating big data in the absence of purposefully designed systems that can produce new knowledge (via research) and apply that knowledge at the point of care (via quality improvement) is unlikely to substantively improve the health and lives of patients. There exists a critical need to develop a national strategy for rapidly improving children's health care. Such a strategy should weave quality improvement and research together into the fabric of the health system. Institu-

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tions must learn how to trust one another as they share data, patients, and the burden of the research regulatory infrastructure. Designing and developing such an infrastructure will also require forward thinking regarding its sustainability, so that it becomes a resource not only today but also for future generations.

Knowledge production followed by passive diffusion is the status quo and is not serving anyone well. Learning health systems are needed to build communities of patients, clinicians, researchers, and health system leaders dedicated to the common purpose of improving the health and lives of children. These new systems of care will generate big-data resources and enable novel types of research. However, by engaging all stakeholders in the knowledge production process, we increase the likelihood that the most important research questions (such as those that can have substantive impacts on the health and lives of patients) are asked and answered. Lastly, the learning health system is continuously improving clinical operations and driving new knowledge into the point of care when and where it is needed. The combination of research and quality improvement can greatly shorten the time from knowledge acquisition to patient impact.

The success of the ImproveCareNow learning health system for pediatric inflammatory bowel disease has paved the way for PEDSnet to spread the learning health system to other diseases, specialties, and health care organizations. If successful, PEDSnet will become a national network of hospitals, clinics, care centers, patient communities, and other data partners that collaborate to create a resource that can help us reach our aspiration of providing care for every child in the nation within the context of a learning health system. ■

NOTES

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