Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS): Architecture

Citation
Mandl, K. D., I. S. Kohane, D. McFadden, G. M. Weber, M. Natter, J. Mandel, S. Schneeweiss, et al. 2014. “Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS): Architecture.” Journal of the American Medical Informatics Association: JAMIA 21 (4): 615-620. doi:10.1136/amiajnl-2014-002727. http://dx.doi.org/10.1136/amiajnl-2014-002727.

Published Version
doi:10.1136/amiajnl-2014-002727

Permanent link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:12717616

Terms of Use
This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

Share Your Story
The Harvard community has made this article openly available. Please share how this access benefits you. Submit a story.

Accessibility
Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS): Architecture

Kenneth D Mandl,1,2,3,4 Isaac S Kohane,1,2,3,4 Douglas McFadden,2,3 Griffin M Weber,2,5 Marc Natter,1,4 Joshua Mandel,1,4 Sebastian Schneeweiss,6 Sarah Weiler,7 Jeffrey G Klann,7 Jonathan Bickel,1,4,8 William G Adams,9,10 Yaorong Ge,11 Xiaobo Zhou,12 James Perkins,13,14 Keith Marsolo,15 Elmer Bernstein,16 John Showalter,17 Alexander Quarshie,18 Elizabeth Ofili,19 George Hripcsak,20 Shawn N Murphy7,21

ABSTRACT
We describe the architecture of the Patient Centered Outcomes Research Institute (PCORI) funded Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS, http://www.SCILHS.org) clinical data research network, which leverages the $48 billion dollar federal investment in health information technology (IT) to enable a queryable semantic data model across 10 health systems covering more than 8 million patients, plugging universally into the point of care, generating evidence and discovery, and thereby enabling clinician and patient participation in research during the patient encounter. Central to the success of SCILHS is development of innovative ‘apps’ to improve PCOR research methods and capacitate point of care functions such as consent, enrollment, randomization, and outreach for patient-reported outcomes. SCILHS adapts and extends an existing national research network formed on an advanced IT infrastructure built with open source, free, modular components.

INTRODUCTION
The Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS, pronounced ‘skills’) is one of 11 clinical data research networks (CDRNs) funded by the Patient Centered Outcomes Research Institute (PCORI) in 2014. PCORI, a non-governmental organization created under the Patient Affordable Care Act seeks to support comparative effectiveness research at a national scale across both CDRNs and also patient powered research networks (PPRNs).

SCILHS engages patients, clinicians, health systems leadership, and key healthcare stakeholders as collaborators to build on an existing network of hospitals and health systems that have already adopted a common clinical and translational research IT and regulatory framework. SCILHS, comprising 10 health systems (box 1), is a step toward answering the Institute of Medicine’s call for a learning healthcare system (LHS)11,12 to ‘generate and apply the best evidence for the collaborative healthcare choices of each patient and provider; to drive the process of discovery as a natural outgrowth of patient care; and to ensure innovation, quality, safety, and value in health care’. Five

Fifteen years ago, SCILHS informatics leaders began a quest to develop informatics infrastructure and regulatory innovation that would convert the emerging electronic health record (EHR) into a research tool for improving patient outcomes. All of our work and open source toolkits have been supported by grants from the National Institutes of Health, Centers for Disease Control and Prevention, and Office of the National Coordinator of Health Information Technology (ONC). First, we built Indivo,3,4 the first personally controlled health record, which gave patients their data, and apps to make those data useful. Then, i2b2 (Informatics for Integrating Biology and the Bedside)6-7 created an open source analytic platform to the EHR, to fuse and analyze data produced by the delivery system, and identify research cohorts. i2b2’s flexible common semantic data model readily accommodates a variety of clinical data. Our next advance was SHRINE (Shared Health Research Information Network),8-10 a tool enabling investigators to query i2b2 nodes in real time across multiple sites for collaborative population research. i2b2 has been successfully implemented at more than 100 sites across the USA, thereby enabling investigators to use delivery system data to identify patients with specific illnesses and clinical characteristics. A recent PCORI survey of all PCORnet sites revealed that 37% of the existing CDRN nodes and 31% of the PPRN nodes already used i2b2. Finally, we built SMART (Substitutable Medical Applications, Reusable Technologies)—a platform to enable any developer to contribute to an ‘App Store for Health and Research’ compatible with i2b2-SHRINE instances or compliant EHRs.11-13

These informatics tools and associated research policy advances have already contributed to transformation in the clinical research enterprise—real-time, collaborative population health research is now enabled across SHRINE member sites distributed nationally—but they have yet to yield substantial improvements in the health of our patients. Now, in establishing PCORnet, PCORI has catalyzed a new national research dialog to answer patient-oriented questions and improve human health. We directly address this challenge via a strategy intended to avoid prior mistakes of large-scale, top-down, costly software infrastructure efforts that...
failed to scale (e.g., caBIG\textsuperscript{14}), instead building SCILHS with open
source, free, modular components\textsuperscript{5} with vibrant user and
software developer communities that have already spread virally
to scale across heterogeneous health systems.

Here, we detail the informatics approaches taken by SCILHS
to identify large cohorts of patients and engage them for
research. Our technology strategy links lockstep to processes for
regulatory innovation, development of robust governance
constructs and policies, and local adoption by hospital leader-
ship and institutional review boards.

THE SIDECAR APPROACH
SCILHS adopts and extends a strategy of establishing a freely
accessible health data ‘sidecar’ warehouse to the EHR, effect-
ively leveraging existing data collected by EHRs during routine
care while avoiding costly, time-consuming EHR integrations
(figure 1). Developed intensively over the past 5 years at
Harvard Medical School, this approach employs vendor agnos-
tic, free, open source, scalable, and interoperable technologies
to produce the only research-based, shared repository of EHR
data that can be queried in real-time. Of already proven value in
the research ecosystem, these components support a cost-
effective and sustainable research network of >8 million
patients.

We consider the heterogeneity of collaborating institutions to
be a key measure of success; via adoption of the sidecar
approach, we enable any institution to join our SCILHS
network. Specifically, a primary goal is inclusion of diverse
populations within our CDRN network, thereby enabling
capture of the genetic, genomic, and socioeconomic variation
that exists beyond insured populations in managed care settings
alone. Further, by freely sharing the processes and software that
have been developed and supported by Harvard, we hope to
catalyze the formation of many other new networks across het-
erogeneous health systems and institutions, and involve new

---

**Box 1 Alphabetical list of Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS) sites**

Beth Israel Deaconess Medical Center  
Boston Children’s Hospital  
Boston Health Net (Boston Medical Center and Community Health Centers)  
Cincinnati Children’s Hospital Medical Center  
Columbia University Medical Center and New York Presbyterian Hospital  
Morehouse School of Medicine/Grady Memorial Hospital (Research Centers in Minority Institutions)  
Partners HealthCare System (includes Massachusetts General and Brigham & Women’s Hospital)  
University Mississippi Medical Center  
The University of Texas Health Science Center at Houston  
Wake Forest Baptist Medical Center

---

 frente a la cirugía de la enfermedad congestiva cardíaca (EC). En esta fase, el estímulo es una presión arterial alta, lo que provoca una reacción de la vía de señales intrínseca de la fibrilación auricular (IC), la cual puede desencadenar la conversión a la FA. Sin embargo, en caso de que la FA persista, se requerirá tratamiento adicional.
partners in improving our core components, common data models, and ontologies.

The sidecar infrastructure is composed of the following:

- **i2b2** (Informatics for Integrating Biology and the Bedside). Data analytic platform employed for EHR data analytics and clinical research at >100 academic medical centers worldwide (NIH funded).

- **SHRINE** (Shared Health Research Informatics Network). Federated query and response system that enables investigators to discover EHR data housed in i2b2 nodes across multiple independent institutions (NIH CTSA funded).

- **SMART Platforms**. First described in the *New England Journal of Medicine*, SMART has programmatic interfaces and applications that transform both EHRs and their sidecars into platforms that run substitutable iPhone-like apps. SMART enables a national scale ‘App Store’ for PCOR for rapid cycle innovation of PCOR methods (ONC funded).

- **Indivo**. The original personally controlled health record links patients to clinical and research settings. Used by hundreds of thousands of employees of Dossia’s founding companies (Wal-Mart, Intel, and AT&T), Indivo was also the initial software codebase for Microsoft’s HealthVault platform (NIH, CDC, and ONC funded).

- **REDCap (Research Electronic Data Capture)**. Electronic data capture tool with 757 institutional partners, used to survey patients online (NIH CTSA funded).

### DATA MODELS AND ONTOLOGIES

SCILHS will combine EHR data with payer claims to facilitate longitudinal tracking of patients over time and across sites of care. The sidecar approach provides the capability to implement new data models without transforming all of the stored source data—a key element in the scalability and interoperability of our platform (table 1). By enabling well-designed, cross-mapped ontologies that support a PCORnet common data model, this approach incorporates otherwise disparate clinical data sources into an easily-queried system that stores data in a flexible format. Data are stored in i2b2 using an entity–attribute–value model, employing a central i2b2 format. Data are stored in i2b2 using an entity–attribute–value model, employing a central i2b2 format. Data are stored in i2b2 using an entity–attribute–value model, employing a central i2b2 format.

| Table 1 | Approaches to scalability and interoperability |
|---------|-----------------------------------------------|
| **Sidecar approach** | **‘Community-extensible ontologies’** |
| EHR data are managed in a sidecar, readily established at any institution, regardless of EHR vendor product (Epic, etc) | All schemas and ontologies we produce are open source, free, and already widely adopted |
| i2b2 uses a simple data model (Star Schema) greatly simplifying the Extract, Transform, and Load procedure. These ETL procedures are established for all major EHR products SMART platform specifications enable any app developer to create substitutable PCOR apps without knowing details about the underlying hospital systems | Ontologies can be imposed on the data after the fact, enabling a hospital in our network to readily adapt to any ratified PCORI Common Data Model |
| For example, there are existing transpositions between OMOP and i2b2 and PopMedNet can query i2b2 | For example, there are existing transpositions between OMOP and i2b2 and PopMedNet can query i2b2 |

i2b2 employs an ontology-based approach that supports flexible, on-the-fly incorporation of new data elements and coding systems. Terminologies such as ICD, NDC, and LOINC may be pre-loaded as hierarchical concept trees; new or ad-hoc terminologies including patient-reported outcome measures or locally defined data dictionaries readily coexist and may be cross-mapped in i2b2. Concepts may be grouped using simple hierarchies and then optionally re-mapped into other reference coding systems and data models (eg, Observational Medical Outcomes Partnership (OMOP) data model). In this way, i2b2 accommodates diverse real-world coding systems while maintaining a straightforward query interface for its users.

**The SHRINE Adaptor Cell** maps local i2b2 terminologies into a common, standards-based SHRINE ontology. This enables a common shared ontology for federated queries while allowing individual i2b2 instances within institutions to retain local hierarchies and terminologies. The Adaptor transforms a federated SHRINE query into a query that runs on the local i2b2 database. The Adaptor then converts the result of that query back into the common SHRINE message format, using well-maintained standards including RxNorm, ICD9, and LOINC. In addition, SHRINE includes tools for ontology mapping and ontology-based data mining. Simple SHRINE customizations enable use of other query systems, for example the QueryHealth distributed query system (ONC) uses PopMedNet to query i2b2.

### SUCCESS TO DATE

SHRINE and i2b2-based research includes characterization of rare morbidities of common diseases, very rare diseases such as peri-partum cardiomyopathy (discovered in SHRINE and published in *Nature*), detections of drug–drug interactions, and measures of quality and clinical efficacy across self-organized SHRINE networks in Europe, the University of California healthcare systems, and a just-in-time network to study the prevalence of complication rates of type 1 and type 2 diabetes in hospitals across this country. Others have used SHRINE to characterize and track the rising incidence of colorectal cancer and further characterize it, and to identify and optimize practice variation in inflammatory bowel disease and intervene to change that practice. i2b2 and SHRINE have been implemented as the base infrastructure for a variety of enhanced chronic disease registry-based research efforts. The Childhood Arthritis and Rheumatology Research Alliance uses the SHRINE/i2b2 registry framework to federate clinical care data and patient-reported data from 62 academic medical centers in the USA and Canada and is currently piloting consensus treatment protocol trials. The Harvard Inflammatory Bowel Disease (IBD) Longitudinal Data Repository employs the same infrastructure, utilizes i2b2 as its centralized data warehouse for IBD-related quality improvement development at 50 centers.
PATIENT ENGAGEMENT

The health systems that have joined SCILHS reflect the American demographic—an essential requirement for reaching statistically valid, clinically meaningful, and patient-centric conclusions about therapies across the diverse spectrum of all healthcare consumers. In order to achieve the comprehensive, patient-centered outcomes infrastructure called for by PCORI, we introduce a new, patient-centric platform (mySCILHS) based on the Indivo system and incorporating the REDCap electronic data capture tool.

mySCILHS will support the Blue Button REST API for standards-based interactions with PPRNs and other patient-selected tools. This API exposes up-to-date, structured clinical summary data for each participating patient. Via a consumer-friendly workflow based on web standards including OAuth2, patients can authorize third-party apps and services, including PPRNs, to access their clinical data.

ANTICIPATED WORKFLOW

Figure 2 shows the workflow from an initial query through the analytic phase in a comparative effectiveness study. Each node in the network maintains an instance of i2b2 containing claims and de-identified electronic medical record data. SCILHS is a true peer-to-peer network, meaning that any SHRINE-based node can initiate a query, using a common ontology, that aggregates results from all participating sites. After the initial query, the investigator can automatically pass the query to each site where duly authorized local site investigators may review individual subject data for study eligibility using i2b2 SMART apps (figure 3). The final patient list is transmitted to the mySCILHS

Figure 2  The Scalable Collaborative Infrastructure for a Learning Healthcare System (SCILHS) data workflow. We present here a general workflow. There will be important variations depending on the nature of the study, whether in-person consent is required, and whether patient identifiers are needed. Shared Health Research Information Network (SHRINE) architecture implemented as a modular framework. Using a mapper toolkit, each site exposes a common queryable data model, implemented in the ontology (ONT) cell. The ONT cell manages the vocabulary of the data model and is one of several cells in the i2b2 architecture, including the broadcaster-aggregator cell (AGG, broadcasts the query across all i2b2 nodes in the SHRINE peer-to-peer network and aggregates the results), the Identity Management Cell (IM, used for authentication), the Clinical Research Chart (CRC, manages the clinical data), the Workplace Cell (WORK, manages the workflow), and the Substitutable Medical Applications, Reusable Technologies (SMART) Cell (manages the SMART API). We implement the following workflow. A query from a Patient Centered Outcomes Research Institute (PCORI) approved study is translated to a SHRINE central node query either manually, or by a PCORNet adaptor, the specifications for which are still to be determined. The SHRINE Central Node broadcasts the query across the true peer-to-peer network (ARROW 1). i2b2 nodes containing coded data are queried at each site to identify appropriate patients returning obfuscated, aggregate patient counts (ARROW 2). Patient identifiable data remains at each site where investigators can use SMART Apps to review records prior to aggregation (ARROW 3). Also, see figure 3. The patient list is passed to mySCILHS for outreach to patients via apps, survey, or telephony (ARROW 4). Patient generated data are imported into i2b2 via simple input formats (CSV, for example) and placed into the i2b2 data model in a flexible schema that allows these to become first-class queryable data objects (ARROW 5). The adjudicated patient data (reviewed by investigators using SMART Apps and confirmed as valid) from each site, including patient-reported data can be added (ARROW 6) to a research data mart in one of several analytic data models (including the PCORI Common Data Model) with a level of identifiers appropriate to the level of consent obtained. Additional, outside data such as Centers for Medicare and Medicaid claims can be added in this step.

PATIENT ENGAGEMENT

The health systems that have joined SCILHS reflect the American demographic—an essential requirement for reaching statistically valid, clinically meaningful, and patient-centric conclusions about therapies across the diverse spectrum of all healthcare consumers. In order to achieve the comprehensive, patient-centered outcomes infrastructure called for by PCORI, we introduce a new, patient-centric platform (mySCILHS) based on the Indivo system and incorporating the REDCap electronic data capture tool.

mySCILHS will support the Blue Button REST API for standards-based interactions with PPRNs and other patient-selected tools. This API exposes up-to-date, structured clinical summary data for each participating patient. Via a consumer-friendly workflow based on web standards including OAuth2, patients can authorize third-party apps and services, including PPRNs, to access their clinical data.

ANTICIPATED WORKFLOW

Figure 2 shows the workflow from an initial query through the analytic phase in a comparative effectiveness study. Each node in the network maintains an instance of i2b2 containing claims and de-identified electronic medical record data. SCILHS is a true peer-to-peer network, meaning that any SHRINE-based node can initiate a query, using a common ontology, that aggregates results from all participating sites. After the initial query, the investigator can automatically pass the query to each site where duly authorized local site investigators may review individual subject data for study eligibility using i2b2 SMART apps (figure 3). The final patient list is transmitted to the mySCILHS...
patient-facing software. The mySCILHS research contact management module links de-identified i2b2 records to patient demographics and contact information. Patients are engaged by web survey, telephony, or SMART apps; patient-reported data are returned to i2b2 and are then transferred into a secure comparative effectiveness (CE) study environment for analyses. In the CE environment, further transformations may occur, supporting many other analytic tools and processes. We anticipate that PCORnet-level queries, which may launch against the full complement of 11 CDRNs and 18 PPRNs, will be initiated at the PCORnet adapter. We anticipate that natural language processing (NLP) of provider notes will play an important role for adding complete longitudinal coded data to the hospital-based record. Early findings demonstrate that NLP of hospital-based EHR notes provides quite complete longitudinal data even when compared with Centers for Medicare and Medicaid Services claims data (personal communication, Katherine Liao, Brigham and Women’s Hospital, 2014). Using NLP on hospital and clinic notes will complement our strategy of concatenating EHR data with external sources such as claims and pharmacy data.

IMPLEMENTING AND SCALING
SCILHS includes 10 legally and financially independent institutions whose CEO or equivalent senior institutional official has committed to active participation in governance, policy development, data sharing, and sustainability planning. Each member has pledged to invest additional personnel and resources to ensure the network meets local patient and clinical stakeholder needs. By harmonizing informatics infrastructure, data models, regulatory processes and policies, and patient participation within and across member institutions, we anticipate that SCILHS will achieve and remain a successful model for inter-institutional PCOR. Utilizing the innovative SCILHS sidecar IT approach to EHR access, we minimize local informatics burden, further enabling a sustainable and adaptable PCOR infrastructure.

Author affiliations
1Children’s Hospital Informatics Program at Harvard–MIT Health Sciences and Technology, Boston, Massachusetts, USA
2Center for Biomedical Informatics, Harvard Medical School, Boston, Massachusetts, USA
3Harvard Catalyst, Harvard Medical School, Boston, Massachusetts, USA
4Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA
5Biomedical Research Informatics Core, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA
6Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women’s Hospital, Boston, Massachusetts, USA
7Laboratory of Computer Science, Massachusetts General Hospital, Boston, Massachusetts, USA
8Information Services Department, Boston Children’s Hospital, Boston, Massachusetts, USA
9Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
10Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
11Boston University Clinical and Translational Sciences Institute, Boston, Massachusetts, USA
12College of Computing and Informatics, University of North Carolina at Charlotte, Charlotte, North Carolina, USA
13Department of Radiology, Center for Bioinformatics & Systems Biology, Wake Forest University Health Sciences, Winston-Salem, North Carolina, USA
14Clark Atlanta University, Atlanta, Georgia, USA
15Research Centers in Minority Institutions Translational Research Network, Data Coordinating Center, Jackson State University, Jackson, Mississippi, USA
16Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, USA
17Division of Biomedical Informatics, Biomedical Informatics and Department of Internal Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, USA
18University of Mississippi Medical Center, Jackson, Mississippi, USA
19Department of Internal Medicine, Community Health and Preventive Medicine and Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
20Department of Internal Medicine, Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
21Partners HealthCare Systems, Information Systems, Charlestown, Massachusetts, USA
22Harvard Catalyst, Harvard Medical School, Boston, Massachusetts, USA
23Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA
24Division of Pharmacoepidemiology, Department of Medicine, Brigham and Women’s Hospital, Boston, Massachusetts, USA
25Laboratory of Computer Science, Massachusetts General Hospital, Boston, Massachusetts, USA
26Information Services Department, Boston Children’s Hospital, Boston, Massachusetts, USA
27Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
28Boston University Clinical and Translational Sciences Institute, Boston, Massachusetts, USA
29College of Computing and Informatics, University of North Carolina at Charlotte, Charlotte, North Carolina, USA
30Department of Radiology, Center for Bioinformatics & Systems Biology, Wake Forest University Health Sciences, Winston-Salem, North Carolina, USA
31Clark Atlanta University, Atlanta, Georgia, USA
32Research Centers in Minority Institutions Translational Research Network, Data Coordinating Center, Jackson State University, Jackson, Mississippi, USA
33Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, USA
34Division of Biomedical Informatics, Biomedical Informatics and Department of Internal Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, USA
35University of Mississippi Medical Center, Jackson, Mississippi, USA
36Department of Internal Medicine, Community Health and Preventive Medicine and Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
37Department of Internal Medicine, Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
38Department of Biomedical Informatics, Columbia University, New York, New York, USA
39Partners HealthCare Systems, Information Systems, Charlestown, Massachusetts, USA
40Harvard Catalyst, Harvard Medical School, Boston, Massachusetts, USA
41Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA
42Division of Pharmacoepidemiology, Department of Medicine, Brigham and Women’s Hospital, Boston, Massachusetts, USA
43Laboratory of Computer Science, Massachusetts General Hospital, Boston, Massachusetts, USA
44Information Services Department, Boston Children’s Hospital, Boston, Massachusetts, USA
45Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
46Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
47Boston University Clinical and Translational Sciences Institute, Boston, Massachusetts, USA
48College of Computing and Informatics, University of North Carolina at Charlotte, Charlotte, North Carolina, USA
49Department of Radiology, Center for Bioinformatics & Systems Biology, Wake Forest University Health Sciences, Winston-Salem, North Carolina, USA
50Clark Atlanta University, Atlanta, Georgia, USA
51Research Centers in Minority Institutions Translational Research Network, Data Coordinating Center, Jackson State University, Jackson, Mississippi, USA
52Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, USA
53Division of Biomedical Informatics, Biomedical Informatics and Department of Internal Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, USA
54University of Mississippi Medical Center, Jackson, Mississippi, USA
55Department of Internal Medicine, Community Health and Preventive Medicine and Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
56Department of Internal Medicine, Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
57Department of Biomedical Informatics, Columbia University, New York, New York, USA
58Partners HealthCare Systems, Information Systems, Charlestown, Massachusetts, USA
59Harvard Catalyst, Harvard Medical School, Boston, Massachusetts, USA
60Department of Pediatrics, Harvard Medical School, Boston, Massachusetts, USA
61Division of Pharmacoepidemiology, Department of Medicine, Brigham and Women’s Hospital, Boston, Massachusetts, USA
62Laboratory of Computer Science, Massachusetts General Hospital, Boston, Massachusetts, USA
63Information Services Department, Boston Children’s Hospital, Boston, Massachusetts, USA
64Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
65Boston University School of Medicine/Boston Medical Center, Boston, Massachusetts, USA
66Boston University Clinical and Translational Sciences Institute, Boston, Massachusetts, USA
67College of Computing and Informatics, University of North Carolina at Charlotte, Charlotte, North Carolina, USA
68Department of Radiology, Center for Bioinformatics & Systems Biology, Wake Forest University Health Sciences, Winston-Salem, North Carolina, USA
69Clark Atlanta University, Atlanta, Georgia, USA
70Research Centers in Minority Institutions Translational Research Network, Data Coordinating Center, Jackson State University, Jackson, Mississippi, USA
71Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio, USA
72Division of Biomedical Informatics, Biomedical Informatics and Department of Internal Medicine, The University of Texas Health Science Center at Houston, Houston, Texas, USA
73University of Mississippi Medical Center, Jackson, Mississippi, USA
74Department of Internal Medicine, Community Health and Preventive Medicine and Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
75Department of Internal Medicine, Clinical Research Center, Morehouse School of Medicine, Atlanta, Georgia, USA
76Department of Biomedical Informatics, Columbia University, New York, New York, USA
77Partners HealthCare Systems, Information Systems, Charlestown, Massachusetts, USA

Acknowledgements We acknowledge the invaluable contributions of the many SCILHS investigators, leaders, and supporters and specifically call out those most involved in designing the network in the early phases: Barbara Bierer, Susan Edgeman-Levitan, Jonathan Finkelstein, Allaina Goldfine, Jennifer Haas, John Halama, Manny Hernandez, John Hutton, Ann Kilbanski, David Ludwig, Joshua Metlay, Mary Mullen, Lee Marshall Nadler, Andrew Nierenberg, Harry Orf, Patricia O’Rourke, Eric Peraksilis, Lee Schwamm, Daniel Solomon, Herman Taylor, Patrick Taylor, Aaron Waxman, Laura Weisel, and James Wilson.

Collaborators SCILHS Network.

Contributors The authors all: made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and drafted the work or revised it critically for important intellectual content; and gave final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the
accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding  This work was supported by the National Institutes of Health: National Library of Medicine RO1LM011185 and U54 LM008748; National Institute of General Medical Sciences RO1GM104303; National Center for Advancing Translational Sciences 1KL2TR001100, UL1TR000454; National Institute on Minority Health and Health Disparities U54 MD007588; the Office of the National Coordinator of Health Information Technology SHARP Program Contract 90TR0001; and by Contract CDRN-1306-04068 from the Patient Centered Outcomes Research Institute (PCORI).

Competing interests  SS is consultant to WHISCO, LLC and to Aetion, Inc., a software manufacturer in which he also owns shares.

Provenance and peer review  Commissioned; internally peer reviewed.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 3.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/3.0/

REFERENCES

1. Etheredge LM. A rapid-learning health system. Health Aff (Millwood) 2007;26: w107–18.

2. Olsen L, Aisner D, McGinnis M. The learning healthcare system: workshop summary. roundtable on evidence-based medicine. Washington, DC: Institute of Medicine of the National Academies, 2007.

3. Mandl KD, Sztolovitz P, Kohane IS. Public standards and patients’ control: how to keep electronic medical records accessible but private. BMJ 2001;322:283–7.

4. Mandl KD, Kohane IS. Tectonic shifts in the health information economy. N Engl J Med 2008;358:1732–7.

5. Murphy SN, Weber G, Mendis M, et al. Serving the enterprise and beyond with informatics for integrating biology and the bedside (i2b2). J Am Med Inform Assoc 2010;17:124–30.

6. Goryachev S, Sordo M, Zeng QT. A suite of natural language processing tools developed for the i2b2 project. AMIA Annu Symp Proc 2006:931.

7. Murphy SN, Gainer V, Mendis M, et al. Strategies for maintaining patient privacy in i2b2. J Am Med Inform Assoc 2011;18(Suppl 1):i103–i08.

8. McMurry AJ, Gilbert CA, Reis BY, et al. A self-scaling, distributed information architecture for public health, research, and clinical care. J Am Med Inform Assoc 2007;14:527–33.

9. Weber GM, Murphy SN, McMurry AJ, et al. The Shared Health Research Information Network (SHRINE): a prototype federated query tool for clinical data repositories. J Am Med Inform Assoc 2009;16:624–30.

10. McMurry AJ, Murphy SN, MacFadden D, et al. SHRINE: Enabling nationally scalable multi-site disease studies. PLoS ONE 2013;8:e55811.

11. Mandl KD, Mandel JC, Murphy SN, et al. The SMART Platform: early experience enabling substitutable applications for electronic health records. J Am Med Inform Assoc 2012;19:597–603.

12. Mandl KD, Kohane IS. No small change for the health information economy. N Engl J Med 2009;360:1278–81.

13. Boil W, Mandel J, Jonikas M, et al. Scalable decision support at the point of care: a substitutable electronic health record app for monitoring medication adherence. Interact J Med Res 2013;2:e13.

14. Board of Scientific Advisors Ad Hoc Working Group. An assessment of the impact of the NC1 cancer biomedical informatics grid (cabig®). 2011. http://deainfo.nci.nih.gov/advisoryboards/iso0311/cabigFinalReport.pdf (accessed Mar 2014).

15. Kohane IS, Churchill SE, Murphy SN. A translational engine at the national scale: informatics for integrating biology and the bedside. J Am Med Inform Assoc 2012;19:181–5.

16. Addia R, Sayal A, Zabak S, et al. Indio x: developing a fully substitutable personally controlled health record platform. AMIA Annu Symp Proc 2010;2010:6–10.

17. Halakma JD, Mandl KD, Tang PC. Early experiences with personal health records. J Am Med Assoc 2008;15:1–7.

18. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.

19. Obeid JS, McGraw CA, Minor BL, et al. Procurement of shared data instruments for Research Electronic Data Capture (REDCap). J Biomed Inform 2013;46:259–65.

20. Nadkarni PM, Brandt C. Data extraction and ad hoc query of an entity-attribute-value database. J Am Med Inform Assoc 1998;5:511–27.

21. Johnson SB, Friedman C. Integrating data from natural language processing into a clinical information system. Proc AMIA Annu Fall Symp 1996;537–41.

22. Kimball R. The data warehouse toolkit: Practical techniques for building dimensional data warehouses. New York: John Wiley & Sons, 1996.

23. OMOP (Observational Medical Outcomes Partnership) Common Data Model to i2b2 (Informatics for Integrating Bench to Bedside) Transformation Process. 2011. http://omop.fnih.org/sites/default/files/OMOP%20Version%202%20Transform%20Nov%202011.pdf (accessed Mar 2014).

24. Klinn JG, Murphy SN. Computing health quality measures using Informatics for Integrating Biology and the Bedside. J Med Internet Res 2013;15:e75.

25. Klann JG, Buck MD, Brown J, et al. Query Health: Standards-based, cross-platform population health surveillance. J Am Med Inform Assoc 2014;21:650–6.

26. Kohane IS, McMurry A, Weber G, et al. The co-morbidity burden of children and young adults with autism spectrum disorders. PLoS ONE 2012;7:e33224.

27. Patten BS, Rana S, Shahu S, et al. Cardiac angiogenic imbalance leads to peripartum cardiomyopathy. Nature 2012;485:333–8.

28. Tatonetti NP, Denny JC, Murphy SN, et al. Detecting drug interactions from adverse-event reports: interaction between paroxetine and pravastatin increases blood glucose levels. Clin Pharmacol Ther 2011;90:133–42.

29. Mikcad R. Harnessing the power of SHRINE to identify new cancer trends: Colorectal cancer rising under age 50. Presentation at 2012 National SHRINE Conference. 2012. https://cbmi.med.harvard.edu/shrine2012/presentations/shrine_mikcad.pdf.

30. Crandall WV, Margolis PA, Kappelman MD, et al. Improved outcomes in a quality improvement collaborative for pediatric inflammatory bowel disease. Pediatrics 2012;129:e1030–41.

31. Natter MD, Quan J, Ortiz DM, et al. An i2b2-based, generalizable, open source, self-scaling chronic disease registry. J Am Med Inform Assoc 2013;20:172–9.

32. Ringold S, Beukelman T, Nigrovic PA, et al. Race, ethnicity, and disease outcomes in juvenile idiopathic arthritis: a cross-sectional analysis of the Childhood Arthritis and Rheumatology Research Alliance (CARA) Registry. J Rheumatol 2013;40:936–42.

33. Wallace CA, Ilowite NT. Comparative effectiveness research in pediatric rheumatic diseases: leveraging CARA for improved child health. Seattle, WA: Seattle Children’s Hospital, NAAMS/NH, 2010.

34. Devitt EM, Kimura Y, Beukelman T, et al. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. Arthritis Care Res 2012;64:1001–10.

35. Huber AM, Giannini EH, Bowyer SL, et al. Protocols for the initial treatment of moderately severe juvenile dermatomyositis: results of a Children’s Arthritis and Rheumatology Research Alliance Consensus Conference. Arthritis Care Res 2010;62:219–25.

36. Li SC, Torko KS, Pope E, et al. Development of consensus treatment plans for juvenile localized scleroderm: a roadmap toward comparative effectiveness studies in juvenile localized scleroderma. Arthritis Care Res 2012;64:1175–85.

37. Mina R, von Scheven E, Airdin SP, et al. Consensus treatment plans for induction therapy of newly diagnosed proliferative lupus nephritis in juvenile systemic lupus erythematosus. Arthritis Care Res 2012;64:375–83.

38. Crandall WV, Kappelman MD, Colletti RB, et al. ImproveCareNow: the development of a pediatric inflammatory bowel disease improvement process. Inflamm Bowel Dis 2011;17:450–7.

39. Uzuner O. Second i2b2 workshop on natural language processing challenges for clinical records. AMIA Annu Symp Proc 2008:1252–3.