Summary of Presentations and Discussion at the First Annual Symposium on the Ethical, Legal, and Social Implications of Learning Health Systems

Background

The purpose of the first annual symposium on the ethical legal and social implications of learning health systems (ELSI-LHS) was to begin establishing a community to engage in ELSI-LHS scholarship and practice. Held in November 2016 at the University of Michigan, the symposium was co-sponsored by the University of Michigan Department of Learning Health Sciences, School of Public Health, the Center for Bioethics and Social Sciences in Medicine, Michigan Institute for Clinical and Health Research, the Brehm Center, and the Healthcare Information and Management Systems Society (HIMSS). The content of the symposium was developed by an interdisciplinary planning committee and applied the framework approach of Responsible Research and Innovation (RRI) to the LHS. Initially defined in the context of the European Commission's Horizon 2020 initiative, RRI strives to ensure "Science with and for Society" by integrating ELSI research with multi-stakeholder engagement, system design, and implementation. The ELSI-LHS symposium brought together experts and leaders in bioethics, social science, medical practice, clinical research, community-academic partnerships, and law with an interdisciplinary group of participants for a daylong session of presentations and dialogue. Speakers included Charles Bosk, Jeffrey Botkin, Kent Key, Scott Kim, Patricia Kingori, John Lantos, Yvonne Lewis, David Magnus, Jerry Menikoff, Todd Rice, Richard Sharp, and Tania Simocelli. The issues and case examples explored in the November symposium, as summarized below, were organized into four sessions according to principles consistent with the RRI framework: (1) Ethics, (2) Engagement, (3) Equity, and (4) Law and Policy in Practice. Each session had a moderator who introduced each session and directed the discussion, and a discussant who provided a brief statement or reflection on the presentation.

Sessions and Presentation Summaries

⊙ Denotes author published in special issue on the ethical, legal, and social implications of learning health systems: Volume 2, Issue 1, *Learning Health Systems*

Session 1*: Ethics*

Moderator: Andrew Shuman
Discussant: Peter Jacobson
Central themes:

- The research/treatment distinction is increasingly fluid
- Transparency and consent are key issues that need to be modernized and articulated for learning health systems

⊙**Scott Kim**: Senior Investigator in the Department of Bioethics at the National Institutes of Health.

Kim spoke on the ethics of pragmatic clinical trials, and noted that the integration of research and clinical procedures would generate valuable, practically useful data. Yet that integration, in his view, would not erase the research/treatment distinction as some learning health system visionaries have imagined; instead, it would "make the ethical distinction more challenging to identify, and push this tension to the highest levels of organization." A key issue, Kim argued, will be the problem of applying

practicable, appropriate, and specific consent procedures in the continuous integration of pragmatic trials and usual clinical operations. Kim further explored approaches to examining ethical issues that arise in standard-of-care randomized control trials.

⊙**Jeffrey Botkin**: Professor of Pediatrics at the University of Utah.

Botkin pointed to potential conflicts in the interests of facilitating valuable research, maintaining transparency, and respecting autonomous decision-making by participants and patients. He argued that transparency and patient engagement will be critical to addressing this tension and to maintaining trust on which the learning health system is said to depend. He proposes the use of a notice-and-opt-out procedure in the place of traditional consent is appropriate when risks are low and institutional safeguards are in place. Botkin's recommendations for respecting patient participants in the learning health system included developing mechanisms to track and honor choice; IRB approval of disclosure information and process, and convenient delivery of layered information on institutional practices that patients can access at their preferred level of detail.

⊙**John Lantos**: Professor of Pediatrics at University of Missouri; founding director of the Children's Mercy Hospital Bioethics Center.

For the author, participation in learning is a moral obligation for both patients and health professionals who are not well served by our current system of research regulation. Lantos describes our deep history of viewing the moral obligations of clinicians and researchers as different, since presumably, researchers don't share the goal—or attending moral authority—of healing the patient. But research, treatment, therapy, research on medical practices, quality improvement, pursuit of knowledge, and learning can be intertwined and overlapping efforts with intertwined and overlapping goals. A key question for Lantos is whether "research" inevitably increases risk compared to standard care that may arbitrarily vary. "If so, extra layers of protection are sensible; if not, extra layers of protection are deceiving, because they suggest that clinical care is safer, and research riskier, than they truly are." In Lantos' view, "we may have an ethical obligation to do something that we are ethically and legally prohibited from doing, that is, studying outcomes in ordinary practice settings in order to improve quality and save lives." Anticipating the themes of the subsequent sessions, Lantos suggested the shift toward learning health systems will require change not only in oversight and research regulation, but also in culture and ethics—beginning with new governance systems that thoroughly engage patients or surrogates in all processes of learning.

Session 2: *Engagement*

Moderator: Joy Downs-Young
Discussant: Gretchen Piatt
Central themes:

- Engagement is not a mechanical process but a complex, fallible, and sensitive human enterprise.
- Learning health systems will need to articulate what it means to engage communities, patients, and other stakeholders, and what they hope to achieve in doing so.

Charles Bosk: Professor of Sociology at the University of Pennsylvania.

Bosk opened this session by suggesting an amendment to the National Academy of Medicine's definition of a learning health system as "one in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience." Bosk indicated that they are better described as "mythical beasts that apply best practices when they are known, their best guess when they are not, and their best effort to resolve uncertainty through sound clinical science." Bosk urged that distinctions be drawn between data and information, transmission and communication, and between systems and the people that inhabit them who are uniquely capable of learning. "Bioinformatics removes disease from individuals and places it in populations," said Bosk. "The issue is, do we have a method for recognizing that diseases still happen to people in populations?"

Richard Sharp: Director of the Biomedical Ethics Program at Mayo Clinic.

Sharp spoke about the challenges of scaling up community engagement to the level of big data research, drawing on the case of the Mayo Clinic Biobank, a proto-learning health system comprising ~55,000 participants. These engagement challenges, which are not necessarily resolvable, include problems of scope of permissions, practicability of contact, unknown future uses for data, and potentially shifting preferences for participants over time. Sharp noted patients will not be familiar or invested in distinctions between quality improvement and clinical research, and—echoing Lantos—noted, "If patients are morally important distinctions, we have to clarify for them why they're distinctions that matter." For Sharp, community engagement is best when it is local. But what happens when learning health systems outgrow the local level? (See description of presentation by Tania Simoncelli of the Broad Institute below who grapples with the same question.)

Kent Key: Co-Director of the Healthy Flint Research Coordinating Center; Director of the Office of Community Scholars and Partnerships, Michigan State University, College of Human Medicine.
E. Yvonne Lewis: Co-Director of the Healthy Flint Research Coordinating Center; Founder/CEO of the National Center for African American Health Consciousness.

Both authors drew on their experiences forging academic and community research partnerships in Flint, Michigan. According to Key, Community might be defined to include researchers, clinicians, and insurance providers, as well as patients, families, and caregivers. Engagement in research occurs on a continuum, with "academically driven" or "community-placed" research involving less engagement compared to "community-partnered" or community-based participatory research. But much is at stake in community partnership—from trust and transparency to cultural understanding, effective communication, alignments of expectation and use, and partnership based on shared commitments to health learning. They further develop the concept of a "Continuum of Engagement" as an essential tool for a LHS.

Session 3: *Equity*

Panel Moderator: Dorene Markel
Discussant: Scott Roberts
Central themes:

- System designers and users should be aware of "hardwired" structural inequities that may perpetuate disparities by race, gender, and socioeconomic status.
- Learning health systems hold great potential to reduce health disparities

- Public values should be better reflected in the decision and rule making for learning health systems and related enterprises.

Patricia Kingori: Wellcome Trust Biomedical Society and Ethics Fellow at the Ethox Centre.

Kingori laid out how "categories and ideas in the design of data can exclude groups, include controversial concepts, [and shape] outcomes." Her presentation began with examples and lessons drawn from feminist critique of architecture, observing that public spaces, material culture and infrastructure are built for imagined users, producing structures that are "seemingly inanimate and objective" but that are directed by ethical and political interests which, in turn, "shape people's experiences of those things." Structures that exclude users by design or effect are ubiquitous, whether in parks or bathrooms, gated communities, or planned cities and roadways. Applying this observation to the learning health system means asking who and what may be excluded from seemingly value-free, aggregated data—and which users the data are designed to serve. Categories used in data collection may be ideologically configured. System designers and users should observe carefully as ideas about race, gender, and socioeconomic status may be built into long-lasting system machinery. She argued that equity in the learning health system will depend on data that is transparent and in service of the goals of reducing disparities and providing benefits to all.

⊙**Vence Bonham**: Senior Advisor to the NHGRI Director on Genomics and Health Disparities at the National Human Genome Research Institute.

The author presented a related challenge: that the potential for learning healthcare systems, and especially genomic-based learning healthcare systems, to significantly improve health equity and benefit groups adversely affected by disparities in our country *will be hard*. These issues begin with the fundamental substrate of genomic medicine: genomic research. To illustrate this challenge, Bonham cited a recent study in *Nature* that found less than 4% of samples analyzed in catalogued genome-wide association studies (GWAS) as of 2016 were from individuals of African, Latin American, Hispanic, or indigenous ancestry. Lacunae in genomic databases have made it impossible in some cases to inform medical development based on available data, because for some populations, we simply do not have data available. A learning health system focused on health equity, can benefit individual patient and understand population differences in health outcomes when there is data available. Bonham referenced a current lawsuit in the State of Hawaii against the makers of Clopidogrel, a drug used to prevent heart attack and stroke, for marketing to ancestral populations likely to have an allele known to affect the drug's efficacy. If the data was in the electronic health record and utilized in the learning health system it could benefit the patient and provide new information in population health. To Bonham, this case suggests both the potential benefits and contextual challenges that a genomic-enabled learning health care system can have on population health. He closed with three recommendations: increase ancestral diversity in research, control rising drug costs of precision medicines, and improve the ease and usefulness of implementing precision medicine to allow for non-ethnicity or race-based approaches.

David Magnus: Director of the Stanford Center for Biomedical Ethics.

Magnus presented findings from two studies of public attitudes toward consent and research on medical practices (ROMP) comparing treatments already in use. He found great discrepancies in the attitudes of patients and IRB members toward randomization vs. observational medical record review, the question of who should obtain consent, and the acceptability of broad consent or opt out with

notification. Patients were found to prefer consent conversations with physicians, to be less likely to hold randomization to a higher consent standard, and to be more willing to accept less elaborate consent approaches. Magnus' second main point, based on studies of public attitudes on electronic health records and biobanking, is that while our regulatory system is framed on issues of autonomy and risk, public attitudes center on trust and trustworthiness. Notably, all groups expressed some mistrust, but African American groups in particular brought up historical discrimination and abuse.

The problem of trust arose again during the *panel discussion*. Genetic epidemiologist Sharon Kardia (a symposium planner) posed a concern from the floor: that mistrust in consent processes can create another disparity in data and its use, which can push researchers into the complex position of trying to manufacture trust among people who may not benefit. Focusing on investigator and institutional responsibility, accountability and upstream engagement, noted Magnus, will be important for engendering trust in the best way possible: by being trustworthy.

Session 4: *Law and Policy in Practice*

Moderator: Kayte Spector-Bagdady
Discussant: Raymond J. Hutchinson
Central themes:

- Ethical, legal, and social implications of learning health systems challenge boundaries that guide healthcare systems in practice today.
- Gray areas of risk, the overlap of quality improvement and research, the limits of inclusivity in data and systems structure and use, and the bounds of acceptability of specific and broad learning health system practices for IRBs and patients

Jerry Menikoff: Director of the HHS Office for Human Research Protections.

The author dealt primarily with the theme of risk—diverging from and contending with Magnus's approach. Menikoff's case example was the SUPPORT study, a large randomized controlled trial with premature babies who received varying levels of oxygen in the neonatology intensive care unit, albeit the ranges of oxygen were all within the professed "standard of care" at the time. Menikoff argued that changing a person's care from one version of "standard care" to another can sometimes involve more than minimal risk, and questioned the appropriateness of risk disclosure to parents in the trial. Menikoff analyzed randomization scenarios involving treatments presumed to be equally good with no suspected differences; research is likely most needed, said Menikoff, to compare treatments with suspected differences.

Tania Simoncelli: Executive Director of the *Count Me In* Initiative at the Broad Institute of MIT and Harvard.

The author spoke of the need to better integrate medical data with tumor and germline data to advance cancer research and develop precision treatments. Because patients are not being offered opportunities to participate in research, said Simoncelli, "we're failing to systematically learn from the experiences of patients." The Metastatic Breast Cancer Project of the Broad Institute and the Dana Farber Cancer Institute has engaged more than 2,900 research participants through social media and partnerships with breast cancer advocacy groups in less than one year. A major challenge for scaling this project, she said, lies in collecting and abstracting medical records in this process: electronic health records were not

designed to optimize shareability; standardized, machine-readable data can be too limited for cancer research; and while patients have a legal right to obtain and share their complete medical record under the HIPAA Privacy Rule, the data are rarely returned in a form and format that is useful and cleaning and structuring data on the back end remains a challenge. What are the elements of the health record that we want to see standardized and more readily accessible? Simoncelli asked whether we might leverage this legal right of access HIPAA access to liberate more medical data for research. She also raised some ethical, practical, and regulatory issues related to return of results, which will continue to arise as patients increasingly request results "as part of the quid pro quo of participating in research."

Todd Rice: Medical Director of the IRB at Vanderbilt and a physician-scientist in its ICU.

Rice described three studies conducted to use the ICU as a learning healthcare system. The studies addressed three unknowns: whether chlorhexidine bathing cloths reduced healthcare-associated infections, which of two IV fluids to use in routine patient care, and whether a video scope facilitated the process of intubation. These studies required collaboration across the healthcare environment, including nursing, bioinformatics, pharmacy, and regulators; and careful navigation around consent, data collection, and study design. While the first studies used cluster randomization, the intubation trial used an individual randomized design. In two cases (the intubation and IV fluid studies), physicians could override randomization in favor of personal choice, which they rarely did. Whether or not these studies presented minimal risk to patients, Rice acknowledged, is still debated. The video scope study compared two devices that might be selected arbitrarily, and were found to have no impact on ease or speed of intubation. Chlorhexidine bathing cloths were found to have no effect on infection and are therefore no longer being used in the ICU. The IV fluids study, by contrast, with results forthcoming, will track potential impacts on incidences of death, dialysis, and renal dysfunction. Such a scenario captures what is at stake in both the means and ends of the learning in the healthcare system.