

# **The Future of Evidence Synthesis: Incorporating heterogeneous and patient-specific evidence towards Evidence-based Precision Medicine**

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**Abstract** *As clinical practice becomes more focused on personalized and precision medicine, there are increasing challenges for evidence-based practice, which combines the best research evidence, clinical expertise, and patient values and preferences in order to support clinical decision making. Identifying the best research evidence relevant to a particular patient requires new approaches to evidence synthesis. New technologies are emerging for both the current standard (group-oriented Randomized Controlled Trials) and “beyond the RCT” studies.*

## **Timeliness of the Topic**

Recently there has been an explosion of new technologies for assessing evidence, resulting in a vigorous and fast-moving field at the intersection of evidence-based medicine and precision medicine. Evidence-based precision medicine investigates a key question: how to generate high-quality assessments of the evidence that are customized to specific patients and produced fast enough to be relevant to patient care right now. Current approaches (such as writing systematic reviews) are too slow and labor-intensive, and do not always provide actionable recommendations useful for clinicians dealing with individual patients, or even for clinical guidelines.

## **General Description of the Panel**

Innovation brings new opportunities, but also brings further challenges to the interpretability and comparability of data for evidence syntheses. Using patient-level data and real-world evidence for evidence-based medicine will require a better understanding of the comparability and relative strengths/disadvantages between these “beyond the RCT” studies and the current standard: group-oriented Randomized Controlled Trials. The panel will cover emerging trends in clinical evidence gathering as well as how technology is enabling novel approaches to evidence synthesis tasks that inform precision medicine.

Informaticists and methodologists have been working to co-develop new technologies and new methods for evidence-based precision medicine. Such innovations already have a large impact, including:

- Synthesizing evidence more quickly. Partial automation of certain tasks in systematic reviewing has become feasible. Quicker evidence synthesis, especially for scoping and rapid reviews, is enabled by technologies such as text mining, machine learning, and ontologies. Living reviews can continually update a given research synthesis.
- Maximizing the use of clinical trial data. Prospective meta-analyses, network meta-analyses, use of individual-level data, and umbrella reviews, leverage existing clinical trial data.
- Generating evidence with novel trial design. In technology assisted trials of Parkinson's medication, researchers at SAGE, Pfizer, and IBM are using mobile phones and biosensors to monitor enormous numbers of patients, pinpointing whether and when medication is working for one specific patient.
- Deriving best practices from real-world health records. Learning health systems are becoming reality. Real-world health records can be more quickly aggregated and synthesized. Readmission risk, for example, is being widely studied due to health system incentives.

## Panelists

**Ida Sim, MD, PhD** is a primary care physician, informatics researcher, and entrepreneur. She is a Professor of Medicine at the University of California, San Francisco, where she co-directs Biomedical Informatics at UCSF's Clinical and Translational Sciences Institute. She is Consortium Core Lead with the Mobile Data to Knowledge NIH Center of Excellence. Her current research focuses on the use of mobile apps and sensors to improve health and manage disease for populations and individuals, and to make clinical research faster and less expensive.

**John Ioannidis, MD, DSc** is C.F. Rehnborg Chair in Disease Prevention at Stanford University, Professor of Medicine, Professor of Health Research and Policy, Professor (by courtesy) of Biomedical Data Science, Professor (by courtesy) of Statistics; co-Director, Meta-Research Innovation Center at Stanford; and Director of the PhD program in Epidemiology and Clinical Research.

**Ralph I. Horwitz, MD, MACP**, is Professor of Medicine and Director, Transformative Medicine Institute, Temple University and Harold H. Hines, Jr. Professor Emeritus of Medicine and Epidemiology at Yale University. His work advances the field of population health research and expands translational research into factors and interventions that influence the health of individuals and populations.

**Jonathan C. Silverstein, MD, MS, FACS, FACMI** serves as Chief Research Informatics Officer and Professor of Biomedical Informatics at University of Pittsburgh School of Medicine. He is internationally known for the application of advanced computing architectures to biomedicine and on the design, implementation and evaluation of high-performance collaboration and visualization environments for anatomic education and surgery.

## Moderator

**Jodi Schneider, MA, MSLIS, PhD** is Assistant Professor of Information Sciences at the University of Illinois at Urbana-Champaign. She is a researcher in biomedical knowledge management, focusing on biomedical ontologies, evidence synthesis methodologies, and systematic review automation. She is a co-investigator on the NIH-funded Evidence Based Medicine project headed by Aaron Cohen and Neil Smalheiser which focuses on development of automated tools to assist in the writing of systematic reviews.

## Presentations

In this 90-minute panel, we plan four brief presentations followed by an extensive Q&A session.

Dr. Sim will open the panel with an overview of the emerging trends in evidence-based medicine. She will talk about the emerging availability of participant-level clinical trial data<sup>1</sup> and what that means for evidence synthesis<sup>9</sup> such as living systematic reviews. She will also describe new tech-enabled study designs that are enabling more personalized evidence generation.

Dr. Ioannidis will then discuss the present and future of specific types of evidence-based medicine analyses including network meta-analyses: prospective meta-analysis, individual-level data, networks and umbrella reviews.<sup>6,7</sup>

Dr. Horwitz will discuss evidence generation for individualized decision making, focused on addressing the question “Will a given therapeutic regimen help my patient at a given point in her/his clinical course?”<sup>4, 5</sup>

Dr. Silverstein will introduce and use the learning health systems framework<sup>3</sup> to offer a very applications-focused talk about the secondary use of electronic health records<sup>8</sup> around the full loop of innovations, with examples from clinical/public health, genomics, and sensors.<sup>2</sup> He will describe the potential for personalized analytics: how artificial intelligence can cluster patients into fine-grained subgroups to determine the personalized treatment that may be best for one particular patient.

Finally, Dr. Schneider will lead the Q&A, and facilitate a broad, wide-ranging discussion on the major theme of the panel, which is how future evidence synthesis can support evidence-based *precision* medicine, by incorporating heterogeneous and patient-specific evidence.

## **Anticipated Audience**

The primary audience for this panel will include clinical research informaticians, clinical informaticians, evidence-based medicine researchers, and clinical trial practitioners. The panel will also be of interest to health information and knowledge management industry professionals related to clinical research and translational research and designers and developers of Electronic Health Records and patient registries.

## **Discussion Questions to Enhance Audience Participation**

- What are the major roadblocks to progress towards evidence-based precision medicine?
- What are the first actionable steps along the way?
- What are the major take home messages do you have for CMIOs and clinicians? For researchers in clinical informatics and evidence-based medicine?

## **Learning Objectives**

- Participants will be able to describe evidence-based medicine and evidence synthesis in their own words.
- Participants will demonstrate awareness of emerging trends in clinical evidence gathering and how this could potentially impact evidence-based medicine.
- Participants will demonstrate awareness of how technology is enabling novel approaches to evidence synthesis tasks that inform precision medicine.

## **Statement**

All listed persons have participated in the creation of this proposal and have agreed to participate in the panel presentation.

## **Acknowledgements**

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