Incorporating genetic data on PCOR studies: building a road map for stakeholder engagement

PCORI-EAIN 2419 Presentation #4

Principle Investigator:
Zohreh Talebizadeh, PhD

Outline

- Overview of the previous PowerPoint presentation (PPT#3)
- Results of the PPT#3 evaluation survey
- Overview of existing resources that include patient genetic data and clinical information:
  - PCORI resources: PCORnet
  - Non-PCORI resources: eMERGE
- Overview of Electronic Medical Records (EMRs)
- Examples of technologies facilitating research:
  - Prometheus, LLC
  - Pathfinder, Inc
- Project website-Update
- What is next? Collecting participants' feedback!

Introduction

- Our overall goals are to:
  - (1) Assess IF it is possible to use genetic information to improve patient health outcomes and
  - (2) If YES, then HOW can this be achieved?

- In the PPT#3, we reviewed additional patient/parent stories, and briefly described examples of research done by our CAB members (Scientists) or from literatures, related to the objective of this Engagement project.

- In the PPT#4:
  - The results of the PPT#3 evaluation survey will be shared.
  - Examples of existing resources that include patient genetic data and clinical information as well as technologies facilitating research will be reviewed.
  - Overall objectives and challenges of Electronic Medical Record (EMR) systems will be reviewed.

PPT#3 Evaluation Survey-Results

32/33 members responded =97%

For the following statements, please indicate to what extent you disagree or agree with "0" indicating "strongly disagree" and "10" indicating "strongly agree". There are no right or wrong answers, it is important that the responses reflect your individual experience and opinions.

1. "The information in the PPT#3 presentation was provided in an easy to understand manner"	**Rating Average**	**Response Count**
	8.97	**32**
answered question		**32**

2. "Additional patient/parent personal stories were informative and provided in an easy to understand manner"	**Rating Average**	**Response Count**
	9.47	**32**
answered question		**32**

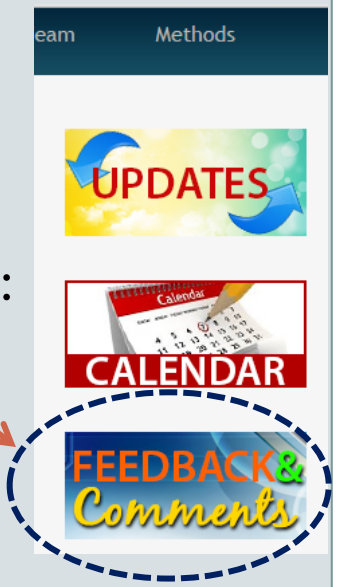
3. "Examples of published epidemiological/patient outcomes studies were informative and provided in an easy to understand manner"	**Rating Average**	**Response Count**
	8.91	**32**
answered question		**32**

4. "Examples of genetic research done by our CAB members (Scientists) were informative and provided in an easy to understand manner"	**Rating Average**	**Response Count**
	9	**32**
answered question		**32**

5. Would you like to schedule a personal meeting and/or call with the PI for further clarification of materials discussed in the PPT #3 presentation?	**Response Percent**	**Response Count**
Yes, I would like to schedule a meeting	**3.1%**	**1**
No, not at this point	**96.9%**	**31**
answered question		**32**

Feedback & Comments

- To see all Feedback & Comments received from our participants please visit the project website:
  - http://genetics-outcomes.net/EAIN/feedback.html



- Feedback & Comments are listed by the following categories:
  - Meeting#1 presentation (PPT#1)
  - Meeting#2 presentation (PPT#2)
  - Meeting#3 presentation (PPT#3)
  - Project website
  - Memorandum of Agreement (MOA)
  - Suggested structure for the meetings
  - Selection of topics to be covered during the course of this project
  - Overall comments/suggestions

PPT#3 Group Discussion

- Our PPT#3 group discussion was held on 5/26/2016 with a number of our local members (n=7).
- Group discussion notes are posted on the website.

PPT#3 group discussion

Meeting 3 agenda (took place via email on May 9, 2016)

- Overview of the previous PowerPoint (PPT) presentations
- Results of the PPT#2 evaluation survey
- Additional patient/parent personal stories
- Examples of published epidemiological/patient outcomes studies information
- Examples of genetic research done by our CAB members (Scientists outcomes
- Project website-Update
- What is next?

Meeting 3-PowerPoint Presentation (PPT#3)

Meeting 3-Group Discussion

Meeting 3-Evaluation Survey

- If you are interested to participate in upcoming group discussions, please let us know!

Examples: existing resources that include patient genetic data and clinical information

- In this section, we are introducing two existing resources that include clinical information and/or patient genetic data, potentially useful for genetic studies. The purpose of sharing these materials is to familiarize our study participants with some potential avenues on HOW including genetic information may improve patient health outcomes, which is the goal of our Engagement project.

- Please note that
  - These resources were selected for the educational purpose only, but there might be other resources available.

PCORnet

- **Source:** http://www.pcornet.org/
  - **CER**=Comparative Effectiveness Research
  - **PCORnet**= The National Patient-Centered Clinical Research Network

- PCORnet is a large, highly representative, national network, funded by PCORI, for conducting CER.
- To facilitate more efficient CER that could significantly increase the amount of information available to healthcare decision makers and the speed at which it is generated, PCORI has invested more than $250 million in the development of PCORnet.
- It fosters a range of observational and experimental CER by establishing a resource of clinical data gathered in a variety of healthcare settings, including hospitals, doctors' offices and community clinics.
- PCORnet aims to advance the shift in clinical research from investigator-driven to patient-centered studies.

PCORnet (Cont.)

- Data are collected and stored in standardized, interoperable formats under rigorous security protocols, and data sharing across the network uses a variety of methods that ensure confidentiality by preventing patient identification.
- A hallmark of PCORnet is that the patients, clinicians, and healthcare systems that provide the research data housed in each constituent network are actively involved in the governance and use of the data.
- PCORnet is establishing a functional research network of health information that is nationally representative and will significantly reduce the time and effort required to start studies and build the necessary infrastructure to conduct them.
- It will support a range of study designs, including large, simple clinical trials and studies that combine an experimental component, such as a randomized trial, with a complementary observational component.

PCORnet (Cont.)

- PCORnet is made up of two kinds of individual partner networks—Clinical Data Research Networks (CDRNs) and Patient-Powered Research Networks (PPRNs):
  - CDRNs are networks that originate in healthcare systems, such as hospitals, health plans, or practice-based networks, and securely collect health information during the routine course of patient care.
  - PPRNs are operated and governed by patient groups and their partners and are focused on a particular condition or characteristic.
  - A Coordinating Center, led by Harvard Pilgrim Health Care Institute, the Duke Clinical Research Institute, and Genetic Alliance provides technical and logistical support to the data networks.

PCORnet (Cont.)

More details about the concept and overall goal of this initiative can be found here:

- What is PCORnet?
  - Joe Selby, executive director for PCORI, tells viewers what PCORnet is and why it was created.

    (length: 1:50 min)
- Phase I Accomplishments-PCORnet
  - Joe Selby and Rachael Fleurence talk about some of PCORnet's greatest achievements over the past 18 months.

    (length: 3 min)
- Phase II What will success look like?-PCORnet
  - Joe Selby and Rachael Fleurence tell viewers what to expect from Phase II launch of PCORnet.

    (length: 3 min)

eMERGE

- **Source:** https://www.genome.gov/27540473/electronic-medical-records-and-genomics-emerge-network/
  - **eMERGE:** Electronic Medical Records and Genomics Network

- The eMERGE Network is a National Institutes of Health (NIH)-organized and funded consortium of U.S. medical research institutions.
- The Network brings together researchers with a wide range of expertise in genomics, statistics, ethics, informatics, and clinical medicine from leading medical research institutions across the country to conduct research in genomics, including discovery, clinical implementation and public resources.
- eMERGE was announced in September 2007 and began its third phase in September 2015.
- The primary goal of the eMERGE Network is to develop, disseminate, and apply approaches to research that combine biorepositories with electronic medical record (EMR) systems for genomic discovery and genomic medicine implementation research.

eMERGE (Cont.)

- **eMERGE Phase I (September 2007 - July 2011)** included five study investigator sites and an administrative coordinating center within one of these sites.
- Each site participating in the consortium led studies on the relationship between genetic variation and at least two common traits among the network participants, using the technique of genome-wide association analysis.
- Such studies involve testing hundreds of thousands of genetic variants called single nucleotide polymorphisms (SNPs) throughout the genome in people with and without a condition of interest.
- eMERGE Phase I sought to answer the question of whether EMR systems and biorepositories can serve as resources for such complex genome-wide association studies (GWAS) of disease susceptibility and therapeutic outcomes.

eMERGE (Cont.)

- **eMERGE Phase II (August 2011 - July 2015)** expanded the network to include nine study investigator sites (including two pediatric sites) and a coordinating center.
- In addition to the continuation of GWAS studies for genomic variant discovery, the consortium sought to explore the best avenues to incorporate genetics variants into EMR for use in clinical care, to improve genetic risk assessment, prevention, diagnosis, and treatment, as well as accessibility of genomic medicine.
- eMERGE Phase II continued to develop algorithms for electronic phenotyping and to identify genomic variants associated with those phenotypes.
- eMERGE Phase II conducted two sets of clinical implementation pilot studies: 1) site specific pilots, and 2) the eMERGE network pharmacogenomics (eMERGE PGx) project, which sequenced 84 pharmacogenomics candidate genes in over 9,000 participants.
- Consent, education, regulation and consultation - important issues related to the use of genomic data in clinical care - were also addressed.

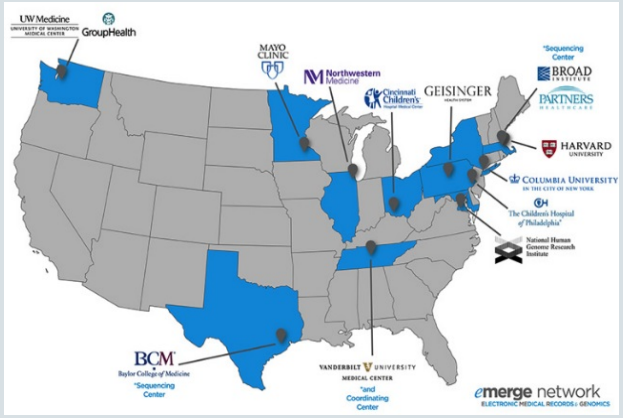
eMERGE (Cont.)

- **eMERGE Phase III (September 2015 - May 2019)** consists of nine study sites, two central sequencing and genotyping facilities, and a coordinating center.
- eMERGE III aims to continue to develop and validate electronic phenotyping algorithms for large-scale, high-throughput genomics research; to discover genetic variants related to complex traits; to disseminate results and lessons learned to the scientific community; and to deliver state-of-the-art genomic knowledge, methods, and approaches to clinical decision support and clinical care.
- More specifically, eMERGE Phase III aims to: 1) sequence and assess the phenotypic implication of rare variants in ~100 clinically relevant genes presumed to affect gene function in about 25,000 individuals; 2) assess the phenotypic implications of these variants, 3) integrate genetic variants into EMRs for clinical care; and 4) create community resources.
- Work on the eMERGE PGx project from eMERGE II will also continue in eMERGE III.
- In addition, eMERGE III will continue to assess health impact, cost effectiveness, and ethical, legal and social implications of reporting genetic variants on a broader population scale for patients, clinicians and healthcare institutions.

eMERGE (Cont.)

- More details about the concept and overall goal of this initiative can be found here (YouTube):
  - NHGRI's Electronic Medical Records and Genomics (eMERGE) Network - Dan Roden (length: 15 min)

Network Members



Electronic Medical Records (EMRs)

- **Source:** https://www.healthit.gov/patients-families/basics-health-it

- An electronic medical record (EMR) is a digital version of a paper chart that contains all of a patient's medical history from one practice. It contains primarily the notes and information collected by and for the clinicians in that office. An EMR is mostly used by providers for diagnosis and treatment. An EMR contains the standard medical and clinical data gathered in one provider's office.

- An electronic health record (EHR) goes beyond the data collected in the provider's office and include a more comprehensive patient history. An EHR is built to share information with other health care providers, such as laboratories and specialists. It contains information from all the clinicians involved in the patient's care and authorized clinicians can access the information they need, to provide care to that patient.

EMRs (Cont.)

- For example, EHRs are designed to contain and share information from all providers involved in a patient's care. EHR data can be created, managed, and consulted by authorized providers and staff from across more than one health care organization. Unlike EMRs, EHRs also allow a patient's health record to move with them—to other health care providers, specialists, hospitals, nursing homes, and even across states.

- A personal health record (PHR) contains the same types of information as a EHR—diagnoses, medications, immunizations, family medical history, and contact information for providers—but it is designed to be set up and accessed by patients themselves.

EMRs (Cont.)

- Benefits of Electronic Medical Records
  - An EMR is more beneficial than paper records because it allows providers to:
    - **Track** data over time
    - **Identify** patients who are due for preventive visits and screenings
    - **Monitor** how patients measure up to certain parameters, such as vaccinations and blood pressure readings
    - **Improve** overall quality of care in a practice
- The information stored in EMRs is not easily shared with providers outside of a practice. A patient's record might even have to be printed out and delivered by mail to specialists and other members of the care team.

EMRs (Cont.)

- More details about the concept and overall goal of the Health IT can be found here (YouTube):
  - Health IT for You: Giving You Access to Your Medical Records When and Where They're Needed (length: 3 min)
  - The Future of Health Care: Electronic Health Records (length: 3:30 min)
  - A Patient Perspective: How Technology Has Transformed My Health and Care (length: 14:25 min)
  - Opportunities and challenges related to the use of EHR data for research (length: 28:57 min)

- Related perspectives from two of our CAB members can be seen here (YouTube):
  - CMH Medical Information Technology Expert-Dr. Laura Fitzmaurice (length: 1:30 min)
  - The Envirome: Where Precision Medicine Meets Public Health | Dr. Mark Hoffman | TEDxUMK (length: 17 min)
    - **Description:** Scientists have the ability to look through many different lenses to understand the human body & disease. Scientists and engineers have created the microbiome, the connectome, genome, and the proteome. Dr. Hoffman offers a solution to improve health care delivery by combining "-omic" information with electronic health records. By using a patient's personalized health records, health care providers can provide more effective care resulting in better outcomes.

Examples: technologies facilitating research (Prometheus, LLC)

Leon Rozenblit, JD, PhD
CEO, Prometheus

- Prometheus is a leading provider of research informatics solutions and data management services. Leon Rozenblit, JD, PhD is President/CEO at Prometheus founded in 1999. Privately held, Prometheus began as a consultancy out of Yale University and has been funded by successful customer projects since.

- The company's primary mission is to accelerate the quest for knowledge by designing adaptable informatics systems that promote dynamic scientific collaborations and by delivering effective data management services with those systems. Over the last 17 years, the Prometheus research team has successfully completed over 40 consulting engagements, extending its user community to over 20 leading research institutions across North America.

Prometheus, LLC (Cont.)

- The Prometheus research team has employed innovative software tools to build, maintain, and manage customized systems for multidisciplinary research projects. They enable clients to acquire, centralize, utilize, share, and preserve their research data in a manner that lowers costs, increases efficiency and ensures data integrity. Prometheus is a recognized leader in informatics, particularly autism research.

- Their clients include leading academic researchers and funding organizations with ambitious goals and admirable missions. Research programs and institutions, such as the Simons Foundation, Yale University Child Study Center, the Marcus Autism Center, Autism Speaks, and the National Database for Autism Research achieve their aims by using Prometheus' cost effective services to keep heterogeneous data clean, secure, organized, and readily accessible.

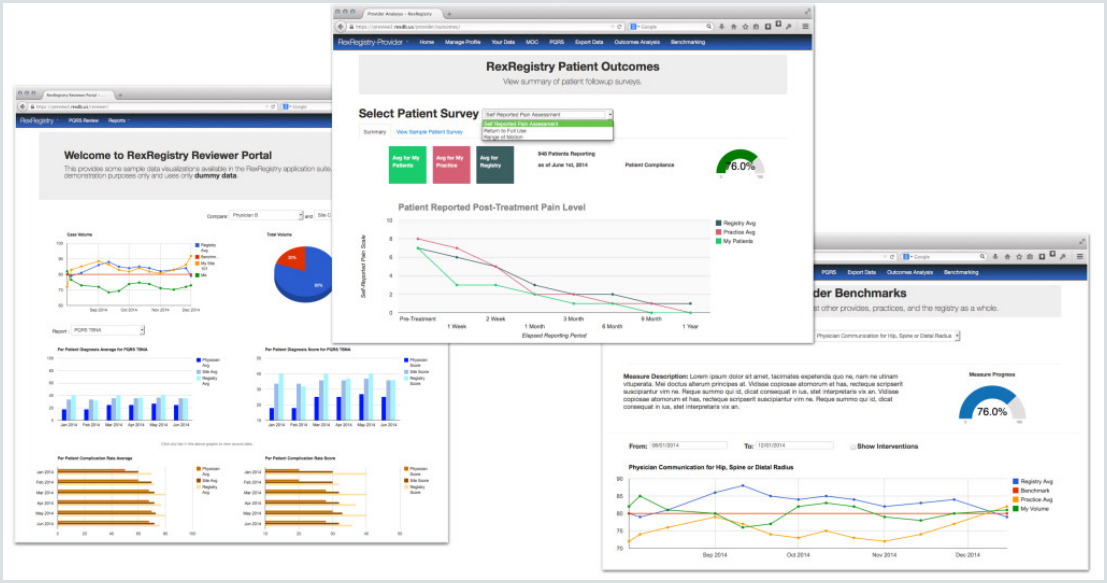
Prometheus, LLC (Cont.)

- **What Problems Does Prometheus Solve?**
  - Prometheus developed several platforms, including RexRegistry (see a brief description below).
  - Information about other platforms can be found at: http://www.prometheusresearch.com/

- RexRegistry platform has been uniquely tailored to support the rapidly evolving needs of patient outcomes and quality research for professional organizations, medical associations and societies. This platform provides users with project management know-how and the cross-functional expertise to help them answer the questions they haven't thought of yet.

Prometheus, LLC (Cont.)

- This figure shows overall RexRegistry configuration.



- Here is a link for a short video taken at the 25th APS Annual Convention describing a project done by Prometheus: https://www.youtube.com/watch?v=KbUNx6OHp7A (length: 1:50 min)

Examples: technologies facilitating research (Pathfinder Health Innovations, Inc.)

Jeff Blackwood
CEO, PathfinderHI

- The following is a description provided by Mr. Jeff Blackwood, our CAB member, about one of Pathfinder's ongoing work.
  - Pathfinder is an outcomes measurement tool. Pathfinder Health Innovations was originally designed as a data collection tool for applied behavior analysis (ABA) therapy, specifically for work with individuals with autism.
  - ABA is a very data-intensive therapy process, often requiring hundreds of data points per therapy session. Traditionally, ABA was performed with three-ring binders, pencils and graph paper.
  - Pathfinder recreated the primary data collection methodologies in software, allowing us to eliminate paper from the therapy process and providing therapists with the ease of using electronic data to review patient progress.
  - From the start, we saw the transition of therapy data from paper to electronic format as beneficial to the research community, allowing rapid access to normalized data across a large geographically disperse population with the ability to rapidly filter for chosen research variables.
  - Where autism studies had previously used 10-30 subjects, now researchers can access information on over 4,000 individuals at the same time.

Pathfinder, Inc. (Cont.)

- An example of how Pathfinder can be used in research is currently being explored with the Cleveland Clinic's Lerner School for Autism. Cleveland Clinic has been a Pathfinder customer since 2012, and has amassed a data repository of millions of observations for their patient population.
- Pathfinder connected Cleveland Clinic with a genetic testing company called Lineagen, which believes that they have identified specific biomarkers for a sub-type of autism.
- If genetic samples are obtained from Cleveland Clinic's population of 100 patients, it may be determined that 25 of these patients tested positive for the targeted biomarkers.
- Given that we have 3+ years of clinical data on these individuals, can we use these data to identify differences in behavior and skill acquisition patterns of the positive group versus the larger population? And in doing so, can we use those data to develop therapy methodologies more conducive to helping those individuals with the genetic markers?
- In essence, the combination of genetic information combined with historical therapy data could be used to identify a sub-type of autism, resulting in more personalized, effective therapy for those individuals.

Pathfinder, Inc. (Cont.)

- Pathfinder is dedicated to working with the research community to provide access to in depth, easy-to-use outcome measures across a broad population of individuals with autism.
- For more information about Pathfinder, please visit:
  - http://pathfinderhi.com/
- Additional links- YouTube video:
  - An Overview of Pathfinder (length: 1:22 min)
  - Autism Therapy Software by ABPathfinder (length: 2:00 min)

Project Website-Update

- The project website has been updated, including addition of the "Patient Stories" section and Agendas for the remaining presentations (under Methods tab).
- Please visit the website for more information. http://genetics-outcomes.net/EAIN

Methods

Develop Partnerships [Community Advisory Board (CAB) Formation]. Using the principles of community engaged research; our project team will develop and formalize relationships with twenty two stakeholders who will be engaged in every aspects of the project development process. These stakeholders will comprise the members of a formalized genetic concept Community Advisory Board (CAB). Seven of the CAB members have already been recruited by the research team members and engaged from the inception of the project through the application preparation and submission. Additional fifteen CAB members have been recruited at the beginning of the project by the research team members.

Members of the Research Team

Members of the Community Advisory Board-CAB

CAB Meetings. The CAB will convene six meetings at Children's Mercy Hospital or other locations suggested by the stakeholders during the twelve month project period and will work closely with the research team to develop the strategic direction of this engagement/ educational program. CAB members will be strongly encouraged to attend a minimum of 80% of all meetings in person, by telephone or video conference. The specific tasks and activities of each meeting are described below:

Meeting's Agenda (Tentative)

Meeting 1 (click for agenda)

Meeting 2 (click for agenda)

Meeting 3 (click for agenda)

Meeting 4 (click for agenda)

Meeting 5 (click for agenda)

Meeting 6 (click for agenda)

Patient Stories

In this section a number of our patient/parent representatives share their personal stories and why they are interested in genetic information. Some stories have more details to help us grasp the level of health complexity that some patients are dealing with, a long journey they have gone through to find an answer, and how they expect genetic information to help them with better managing health outcomes.

Please note that our Engagement project is not focused on any specific disease. We would be happy to add more patient stories, please feel free to send us your story!

Patient Story 1: Seth Bittker
Patient story 2: Kristen Worden
Patient Story 3: DeeJo Miller
Patient Story 4: Sheryl Chadwick
Patient story 5: Mary Anne Hammond

The following videos provide more information on Precision Medicine Initiative and patient stories.

Personal Genomics: Use of personal genomics in predictive and precision medicine
https://www.youtube.com/watch?v=pSzk-yf6BVU (length: 54 min)

What Is Next? Collecting Participants' Feedback!

- **Survey:** PPT#4 evaluation survey will be sent out to get an overall assessment from all participants about this presentation. Please respond to the survey at your earliest convenience.

- All collected feedback, comments, questions and responses will be summarized and posted on the project website
  - (http://genetics-outcomes.net/EAIN/) and
  - shared in our next presentation (PPT #5).