Geisinger’s MyCode Project: Leveraging Genomics and EMR Data to Improve Health

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Captain Nemo at 20,000 Leagues Under the Sea
Regional Demographics

• 2.6 million people in 31 county service area
• Older and poorer relative to national averages
• Most counties officially designated as rural and medically underserved
• Non-transient: <1% annual out-migration rate in most counties
• 96% White European descent
Conduct experiments in re-engineering healthcare to improve patient outcomes and reduce cost of care

**Geisinger Clinic**
- ~1,100 physician group practice
- ~700 advanced practitioners (PAs, CRNs)
- 1/3rd primary care
- 2/3rd specialists
- ~410 residents/fellow
- ~270 medical students

**IP & OP Facilities**
- 2 tertiary/quaternary teaching hospitals
  - Geisinger Medical Center
  - Geisinger Wyoming Valley
- 49 community-based outpatient clinics
- Ambulatory surgery centers
- IP substance abuse treatment center

**Geisinger Health Plan**
- ~450,000 member health plan
- members in 5 states
- Ranked 1st in PA for quality*
- Ranked 3rd in the US*

*US News and World Report
MyCode Project
CONTRIBUTE TO THE FUTURE OF HEALTHCARE

We would like you to take part in MyCode, a project that will involve collection and storage of blood samples and health information from 200,000 patients. Researchers will use your blood to study your genes. This information will help researchers to understand how diseases develop and how we can improve detection and treatment of diseases.

WHAT WILL YOU BE ASKED TO DO?
1) Complete the MyCode consent form.
2) Give us permission to collect up to two tablespoons of your blood. We will only collect the MyCode blood sample when you are already having blood drawn that your doctor ordered.
3) Choose whether your blood can be collected one time only, or whether your blood will be collected up to one time per year for as long as you allow it.
4) Allow us to get information from your electronic health record (EHR) about your health history.

WHAT WE WILL DO WITH THE INFORMATION!
If blood samples and medical information are already available, researchers can study and understand what causes diseases including ways to detect diseases earlier and to improve treatments.

WHY WERE YOU ASKED TO TAKE PART?
We are asking anyone who is 18 years of age or older and is a Geisinger Clinic patient to take part.

WHAT ARE THE BENEFITS/RISKS INVOLVED?
There are few benefits or risks to you. You will not receive money for your help. It will not cost you money to take part. This research will not affect your health. The research may lead to discoveries to help doctors learn about diseases in general. We will take special care to protect your privacy.

WHAT IF YOU DON'T WANT TO BE INVOLVED?
Participation is completely voluntary. Your choice to take part or not take part in the project will not affect your healthcare.

FOR MORE INFORMATION
You can call us at 1.886.910.6486 to ask for more information about MyCode.
MyCode

History:
- MyCode began at the recommendation of the External Scientific Advisory Board in 2006
- High consent rate – 85% to 95%
- Rate limiting factor was number of consenters

Limitations:
- At the time very concerned about “risk”
- Consent stated:
  - Unlikely to get personal results
  - Results will NOT be placed in electronic medical record
Clinic schedule and patient eligibility from EMR → Patient informed consent → Blood draw order placed in EMR

Research samples retrieved and coded → Centrally collected via Geisinger lab courier service → Blood sample collected via clinical phlebotomy

CLIA

Long-term storage and tracking → Sample analysis
Research Data Broker and Clinical Decision Intelligence System (CDIS) Data Warehouse

EHR

Orders
Diagnoses
Lab values
Meds
Procedures
Etc.

CDIS

searchable
exportable

Data Broker

Research data

Investigator

Governing Board

Central Biobank (MyCode)

>50,000 consented participants
>100,000 samples
• Blood, serum, DNA, tissue

TPO

EHR Firewall

Orders
Diagnoses
Lab values
Meds
Procedures

CDIS

Claims
Finance
Ops

Research data

Linkable

>50,000 consented participants
>100,000 samples
• Blood, serum, DNA, tissue
Geisinger Genomic Medicine Implementation Team

Dan Davis, Ph.D. (NIH, Georgetown)
Andrew Faucett, MS, CGC (Emory University)
Brenda Finucane, MS, CGC (Elwynn)
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David Ledbetter, PhD, FACMG (Emory University)
Christa Lese Martin, PhD, FACMG (Emory University)
Michael F. Murray, MD, FACMG (Harvard/Brigham & Women’s)
Erin Rooney Riggs, MS, CGC (Emory University)
Janet Williams, MS, CGC (Intermountain Health)
Marc S. Williams, MD, FACMG (Intermountain Health)
The eMERGE Network

electronic Medical Records & Genomics

A consortium of biorepositories linked to electronic medical records data for conducting genomic studies.
Geisinger Clinic Biobank Inventory

<table>
<thead>
<tr>
<th>Category</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individual patients</td>
<td>&gt;50,000</td>
</tr>
<tr>
<td>• Primary care</td>
<td>&gt;23,130</td>
</tr>
<tr>
<td>• Specialty clinic</td>
<td>&gt;15,200*</td>
</tr>
<tr>
<td>Blood samples</td>
<td>28,637</td>
</tr>
<tr>
<td>Serum samples</td>
<td>51,716</td>
</tr>
<tr>
<td>DNA samples</td>
<td>21,314</td>
</tr>
<tr>
<td>Tissue samples</td>
<td>6,059</td>
</tr>
<tr>
<td>Total samples</td>
<td>&gt;112,000</td>
</tr>
</tbody>
</table>

* >70% from Adult Obesity, Cardiac Cath and Vasc. Surgery
# Common Conditions in the MyCode® Primary Care Cohort (16,714 total patients)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>4,323</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>402</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>410</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1,463</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>9,454</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>1,217</td>
</tr>
<tr>
<td>BMI &gt;40</td>
<td>1,814</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>3,853</td>
</tr>
<tr>
<td>Asthma</td>
<td>1,999</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1,726</td>
</tr>
</tbody>
</table>

*2 or more office visits with diagnosis code or problem list entry; data as of 1-1-2011
Why Change MyCode™

- National discussion about the duty to return research results
  - Engage research participants
  - Geisinger is a health system – patient benefit a priority

- Cost of Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) dropping rapidly
  - Results available for many participants

- Set the national biobank standard and become attractive to research partners
  - Bring benefits of WGS and WES to Geisinger Community
Focus Group Participation

- 6 focus groups held
- Bariatric surgery group and Primary Care Clinics in Bloomsburg and Kulpmont
- 93 participants – 57% F, 43% M
  - 22% Age 71 & >
  - 65% Age 51 – 70
  - 13% Age 18 – 50
  - (Ages match biobank participants)
- 49.5% GHS patients for 20+ years
- 85% receive majority of care at GHS
Overall Positive View of Health Care Research

• Participants were highly supportive of medical research
• They took pride that such research was being conducted in their own local area
• Support was expressed regardless of whether the benefits are short-term or “for our children and grandchildren.”
• Almost all participants were willing to participate in a study based on this description:
  • “donating [blood] for future studies [to] help . . . advance the science of medicine for families in your region . . . . to make advances in medicine through research studies that will lay the groundwork for understanding how genes affect health and the risk of disease”
Types of Results Discussed in Focus Groups

- Pharmacogenomics (genetic variation that impacts medication dosage and choice)
- Recessive Carrier (risk for serious disease, information for children and grandchildren)
- Increased Risk for Preventable or Treatable condition
- Increased Risk for NON Preventable or Treatable condition
- Genetic changes that we currently do not understand
Wanted ALL results

Results should be returned to healthcare provider and participant (most preferred same time)

Geisinger should develop educational materials and expert support system

Results should be put in EMR!
MyCode™ Consent & Protocol Changes

- Research may include WGS or WES
- Geisinger will return results that are medically actionable
- Geisinger will NOT return results that are NOT medically actionable
- Geisinger Oversight Committee will decide what to return
- Expansion of research partners (including industry)
- Will share research data with national databases to improve ability to interpret results
- Blood draw at consent / Online consent
- Commitment to regular communication
MyCode Consent Changes

• Original MyCode consent
  – 5 pages plus Signature page
  – 4 check boxes

• Current MyCode Consent
  – 4 pages plus Signature page
  – 1 check box for re-contact

• MyCode Consent after recent discussion with IRB
  – 3.5 pages plus Signature
  – No check box (majority agreed to re-contact)
Next Steps

- Converting MyCode™ biobank to CLIA
  - Currently collecting two samples (one in CLIA)

- Mike Murray, MD developing process for return of research results and oversight committee

- Launch online consenting through MyGeisinger, Advancing Healthcare Tab
Geisinger Genomic Sequencing Study
Objective: Improve our ability to predict and prevent disease, optimize treatments based on genetic information for each individual

- Partnership between Geisinger Health System and Regeneron
- 5 – 10 Year Genomic Sequencing Study
- 100,000 Study Participants
Why Collaborate with pharma – true scientific partner

**Geisinger Resources**
- Unique community partnership, trust
- Stable population (three generation families)
- High recruit rate for MyCode
- Strong research expertise in improving healthcare
- Research financial resources for return-of-results

**Regeneron Resources**
- Strong scientific team
- State-of-the-art DNA sequencing facility
- Strong financial resources for sequencing costs
- Focus on new drug development
Collaboration Operational Elements

1. Expand MyCode biobank
   - REGN funds the addition of 100,000 new patients and their samples (blood, serum, DNA) over 5 years

2. Clinical data mining and modeling
   - REGN funds a team of GHS data analysts and programmers to create a research database using GHS clinical data and to develop and validate “phenotyping algorithms”

3. Genomic analysis
   - REGN performs next generation DNA sequence analysis (minimum 25K whole exome sequences)
   - Other genomic analyses, e.g. high density genotype analysis?
<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Phase</th>
<th>Number of Qualifying Patients</th>
<th>Number Consented in MyCode / Other Biobank</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANGPTL3</td>
<td>Finalized</td>
<td>139</td>
<td>8</td>
</tr>
<tr>
<td>Extreme Lipids</td>
<td>Finalized</td>
<td>8,328</td>
<td>480</td>
</tr>
<tr>
<td>Metabolic Healthy Obese</td>
<td>Finalized</td>
<td>15,142</td>
<td>1,828</td>
</tr>
<tr>
<td>Acute Pancreatitis</td>
<td>Feasibility</td>
<td>208</td>
<td>51</td>
</tr>
<tr>
<td>Catheter Cohort</td>
<td>Refinement</td>
<td>~7,000</td>
<td>~7,000</td>
</tr>
<tr>
<td>Elderly (85+)</td>
<td>Feasibility</td>
<td>21,719</td>
<td>1,445</td>
</tr>
<tr>
<td>Bariatric Surgery</td>
<td>Proposal under development</td>
<td>~3,500</td>
<td>~3,500</td>
</tr>
<tr>
<td>Age-Related Macular Degeneration</td>
<td>Proposal under development</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatric Phenotypes</td>
<td>To be proposed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>Proposal under development</td>
<td>21,016</td>
<td>3,247</td>
</tr>
<tr>
<td>Sudden Cardiac Death</td>
<td>Prospective study</td>
<td>Recruiting future</td>
<td></td>
</tr>
</tbody>
</table>
# Geisinger Wellderly Cohort

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of Patients (MyCode)*</th>
<th>Female N (%)</th>
<th>Smoking Status</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>N (%)</td>
<td>Current</td>
<td>Past</td>
</tr>
<tr>
<td>85-89+</td>
<td>12,351 (947)</td>
<td>7,827 (63.4%)</td>
<td>387 (4.6%)</td>
<td>2,686 (31.7%)</td>
</tr>
<tr>
<td>90-94</td>
<td>5,013 (306)</td>
<td>3,519 (70.2%)</td>
<td>102 (3.1%)</td>
<td>837 (25.2%)</td>
</tr>
<tr>
<td>95-99</td>
<td>1,070 (39)</td>
<td>825 (77.1%)</td>
<td>13 (1.9%)</td>
<td>139 (20.5%)</td>
</tr>
<tr>
<td>100+</td>
<td>124 (2)</td>
<td>108 (87.1%)</td>
<td>0</td>
<td>9 (12.2%)</td>
</tr>
</tbody>
</table>

* Alive as of 5/9/14
Is It Safe To Participate

- **Geisinger Protections**
  - Geisinger is an expert on privacy protection
  - Samples and records assigned coded ID numbers
  - Only Geisinger employees have access to ID codes
  - All researchers agree not to attempt to re-identify participants
  - Regeneron agreed to follow Geisinger’s vigorous privacy standards

- **National Protections**
  - GINA – Genetic Information Non-discrimination Act
  - Affordable Care Act
Benefits of Participation

- Long-term goal to improve health and well-being for generations to come based on individual genetic information
  - our patients want to help others

- Learn their results
  - Participants with clinically actionable findings – 3-5%
  - Share results with family – children, grandchildren (6-8 per participant result)
American College of Medical Genetics and Genomics

ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing

Robert Green, Jonathan Berg, Wayne Grody, Sarah Kalia, Bruce Korf, Christa Martin, Amy McGuire, Robert Nussbaum, Julianne O’ Daniel, Kelly Ormond, Heidi Rehm, Michael Watson, Marc Williams, Leslie Biesecker

We thank the following individuals for their review and comments on drafts of this paper, many of which were adopted by the Working Group.

Margaret Adam, Jeffrey Botkin, Wendy Chung, David Dimmock, Christine Eng, Madhuri Hegde, Gail Jarvik, Stephen Kingsmore, Michael Murray, Katherine Nathanson, Sharon Plon, Reed Pyeritz, Cheryl Reid, V. Reid Sutton, Benjamin Wilfond.

The final version of this paper and its recommendations do not necessarily reflect the views of these individuals.
ABSTRACT

• The ACMG appointed a Working Group on Incidental Findings in Clinical Exome and Genome Sequencing to make recommendations about responsible management of incidental findings when patients undergo exome or genome sequencing.
• This Working Group conducted a year-long consensus process, including review by outside experts, and produced recommendations that have been approved by the ACMG Board.
• Specific and detailed recommendations, and the background and rationale for these recommendations, are described herein.
• **We recommend that laboratories performing clinical sequencing seek and report mutations of the specified classes or types in the genes listed here.**
• This evaluation and reporting should be performed for all clinical germline (constitutional) exome and genome sequencing, including the ‘normal’ of tumor-normal subtractive analyses in all subjects, irrespective of age, but excluding fetal samples.
• We recognize that there are insufficient data on clinical utility to fully support these recommendations and we encourage the creation of an ongoing process for updating these recommendations at least annually as further data are collected.

Initially recommended reporting 56 disease genes, largely dominant disorders with high penetrance.
### Most Common Conditions Expected in the Return of Results from the Geisinger 75

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>INCIDENCE</th>
<th>GENES</th>
<th>CLINICAL Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant Hyperthermia</td>
<td>1 in 300</td>
<td>RYR1 and CACNA1S</td>
<td>Fatal complications of anesthesia</td>
</tr>
<tr>
<td>HBOC</td>
<td>1 in 500</td>
<td>BRCA1 and BRCA2</td>
<td>Early Breast or Ovarian Cancer</td>
</tr>
<tr>
<td>Hypertrophic Cardiomyopathy</td>
<td>1 in 500</td>
<td>Multiple genes on list</td>
<td>Cardiac Arrest Heart Transplant</td>
</tr>
<tr>
<td>Polycystic Kidney Disease</td>
<td>1 in 500</td>
<td>PKD1 and PKD2</td>
<td>Kidney Failure Kidney Transplant</td>
</tr>
</tbody>
</table>
MyCode Community Health Initiative: An Ethics Advisory Committee

- Best practice in biobank governance: independent oversight, consultation and advice for evolving issues and questions

- 8 members
  - 4 with expertise in genomics and ethics
  - 4 individuals, preferably patients, drawn from the Geisinger community

- An evolving agenda
  - Questions for guiding and driving participant-focused research
  - Issues related to the familial implications for return of results
  - Changes in consent practices
  - Strategies for participant and community engagement
MyCode Community Health Initiative: An Ethics Advisory Committee

- **Kevin T. FitzGerald, SJ, PhD, chair**
  Jesuit priest, PhDs in molecular genetics and bioethics, Georgetown faculty in oncology and bioethics, former member of the Secretary’s Advisory Committee on Genetics, Health & Society (SACGHS)

- **Reed Tuckson, MD**
  Physician, former executive with UnitedHealth Group, and former senior vice president at the AMA; former Chair of SACGHS, prominent in the AAMC, ACCME, and ACGME; board member, National Patient Safety Foundation

- **Sylvia Mann Au, MS, CGC**
  Certified genetic counselor, State Genetics Coordinator for Hawaii Department of Health, and member of SACGHS

- **Kyle Brothers, MD, PhD**
  Pediatrician with research interests in childhood obesity, genomic research and clinical use of genomic data; trained at Vanderbilt, now on faculty at University of Louisville, lead publication of eMERGE paper on consent for children
Summary

- High value, integrated healthcare system provides ideal “learning healthcare laboratory” to perform experiments to improve patient outcomes and reduce total cost of care.

- Genomics data, available from birth (or prenatally) may allow personalized health guidance in the form of prevention and optimized treatment through the lifespan.

- Lessons learned from a unique model system will be tested in other demographic areas and healthcare systems.