A CLINICAL IMPERATIVE: Genomics, Population Health, and Precision Health

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Geisinger and Precision Health

Our genomes are the bedrock of lifelong care. Universal sequencing will become a routine part of public health and medicine, to improve individual health and well-being while rationalizing expenditures in healthcare over the lifespan.

To do this, we strive to demonstrate the clinical utility and personal value of genomic information at the individual and community level....

Geisinger is an ideal “healthcare laboratory” for implementation of genomic precision health.

Not just someday, but today.
USING GENOMICS TO INFORM PATIENT CARE:
Genomics and Precision Health at Geisinger National

**Population Screening**
- Genome we’re born with as **bedrock of lifelong health**
- Clinically relevant information for patients and their families

**Pharmacogenomics**
- Testing genes known to influence **drug metabolism and therapeutic response**

**Diagnostic Testing**
- Finding underlying genes/variants to understand patient’s clinical presentation and phenotype and guide management

**Molecular Oncology**
- Testing for specific **somatic mutations to inform therapeutic options** for individual patients
USING GENOMICS TO IMPACT PATIENT CARE:
The Evolution of Genomic Precision Health at Geisinger

### mycode

**2007**
- ~225,000 participants consented
- ~92,000 (~140,000) *research exomes*
- ~65,000 eligible for clinical report on clinically actionable findings
- ~1100 patients with results reported

**2014**

### Population Health Screening in Routine Care

**2018**
- Launched in July 2018 as part of routine clinical care
- >500 patients consented to date
- >300 *clinical exomes* completed
- 7 positive findings to date

### Geisinger National Precision Health

**2018**
- Outward-looking business unit
- End-to-end solutions for health systems to launch genomic precision health programs
- Genomic/clinical data consortium
As of February 2019

- 3 conditions account for ~50% of cases (Breast/Ovarian cancer, FH, Lynch syndrome)

- In total, results have engaged >300 different PCPs and specialists from at least 14 medical specialties since 2015

As of February 2019
Initial Impact of Population Genomic Screening

- **1048 patients** with clinical reporting of results since 2015
- **350 with >12 months since clinical report** of a CDC Tier I genomic finding
  - Breast and Ovarian Cancer (HBOC)
  - Familial Hypercholesterolemia
  - Lynch Syndrome
- **87% had no known genetic dx** prior to exome screening, and only 50% had relevant **personal and/or family history** to raise suspicion
- **14% received new clinical dx** since (and because of) clinical exome report
- **36% increase** in risk management engagement since clinical exome report

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USING GENOMICS TO IMPACT PATIENT CARE:

The Evolution of Genomic Precision Health at Geisinger

2007 - 2014

Population Health Screening in Routine Care

2018

Geisinger National Precision Health

2018
Clinical Implementation of Genomic Precision Health

Clinical whole exome sequencing now offered as part of routine clinical care in a growing set of clinics

- ~2% positive screen yield to date

Keys to implementing such a program:

- Broad acceptance by Geisinger patients and providers
- Driven by commitment to improve clinical care without adding burdens
- Focus on anticipatory and preventive care
- Potential to rationalize costs of healthcare
Primary Care Clinical Model

Testing offered to all adults by Primary Care Physician

PCP will discuss information about the test, get verbal consent to do testing, and order the test.

- Blood sample collected
- Sample shipped to the clinical sequencing lab
- Genomic data are analyzed
- Report sent to PCP and entered into EHR
- Automated referral to Genetic Counselor to discuss results and recommendations

If positive result
Overview of Geisinger Genomic Screening Programs

- **Whole Exome Sequencing**, but reporting results on <100 genes thus far; commitment to *iterative, ongoing updates*

- **Clinical urgency** argues for initial *clinical testing*, not research-based

- **Clinically actionable findings** in ~2-3% of unselected population of patients; automated referral to *genetic counseling*

- Clinically actionable findings will engage many medical specialties, not just medical genetics

- **Family cascade testing** can impact first-degree relatives (*50% risk*) and second-degree relatives (*25% risk*)
Impact on Families: Challenge of Healthcare Hand-off

54-year-old male with no personal history of cancer; father had died of lung cancer in his 70’s

Found to have a **likely pathogenic BRCA2 mutation** by screening:

*Indicates increased risk of breast and ovarian cancer, as well as other cancers, including lung, prostate cancers*

Genetic counseling and workup:

– History of nocturia → PSA testing, urology referral
– No children
– Brother and sister informed, but **not Geisinger patients**
So, why does this work at Geisinger?

• We were determined to make it easy, **not burdensome**
• We committed to **engaging the community** and our primary care physicians from the very beginning
• We committed to helping our doctors and being viewed as **enabling partners**, not competitors
• We committed to fitting into **existing care paths** and workflows
So, why does this work at Geisinger?

And, if it works at Geisinger, can it be implemented at other health systems?
THE GOAL:
Genomic Precision Health on a National Scale

A Partnership of ‘First-Adopters’ for Implementation of Precision Health

Like-minded partners committed to the vision of genome-based population health screening to improve patients’ health and healthcare over the lifespan

• Offer clinical genomic sequencing as part of routine clinical care today

• Combine and share data to accelerate research and improve healthcare tomorrow
Facing Hurdles: Common Points of Failure

- Burden to **move information to action** is on patients and their providers.
- Inadequate solutions for integration into the broad healthcare ecosystem as **people move** and switch providers/hospitals/systems.
- Insufficient respect for **current provider workflows**.
- Lack of structured **involvement of genetic counselors** misses potential value for patients and providers.
- Lack of attention to scale and/or **solutions to achieve scale**.
- Lack of attention to genetic diversity and **disparities in minority populations**.
Facing Hurdles and Avoiding Common Points of Failure

So, where to start?
Genomics in Medicine

• Any two genomes will differ at **millions** of positions among the 3 billion base pairs that comprise the human genome

• Any two **exomes will differ at ~35,000 positions** in the coding regions of the estimated 20,000 genes that encode proteins

• Great variability among populations worldwide (much of which has not yet been detected or catalogued)

• So, which or how many of those variants ‘matter’ clinically in any given individual? **What can we act on today?**
COMPLEXITY OF GENETIC DISEASE:

Genomics in Medicine

- **3,600 genes** with known phenotype-causing mutation(s)
  
  The ‘Clinical Genome’ or ‘Mendelome’...

- More genes and variant reclassification over time

  Iterative reevaluation and updated clinical reports

- Mendelian conditions are the most straightforward place to start **broad clinical implementation**

  Predictable and clinically relevant today?

  Which genes, which variants?

  What does “actionable” mean?
End-to-End Integrated Solutions for Population Genomic Screening

From concept design to clinical care...

- Engagement and Concept
- Project Design and Implementation
- Project Management
- Ongoing Data Management, Updates, and Analysis

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COMPLEXITY OF GENETIC DISEASE:

Genomics in Medicine

3,600 genes with known phenotype-causing mutation(s)

Complex disease and Polygenic Scores

- Heart disease, cancer, diabetes, neurodevelopment, neurodegeneration, obesity, neuropsychiatric conditions
- Other large-scale ‘omics (RNA, protein, microbiome, epigenetics)
- Environment and ZIP Code...

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ONGOING CHALLENGES: Genomics and Precision Health

- How and when to move beyond ‘just’ Mendelian disease?
- How to incorporate risk into routine care at large scale?
- How to predict (and act on) individual penetrance/expressivity?
- How to define the value proposition?
- How to ensure access and validity for different populations?
- How to align and motivate stakeholders across the ecosystem?
- How to capture and integrate the impact of ZIP codes?
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