Primary Provider "Just in Time" Education That Supports Screening Healthy Volunteers with Genomics

Inter-Society Coordinating Committee for Practitioner Education in Genomics
Bethesda, MD

Thursday
January 14, 2016
10:45 - 11:20

Michael F. Murray, MD
Director of Clinical Genomics
Genomic Medicine Institute
Geisinger Health System
Forty Fort, PA

No CME Conflicts of Interest

Disclosure: Geisinger has a collaboration with Regeneron Pharmaceutical Company

Problem:

- **Pathogenic Variants in BRCA 1 and 2 result in dramatic increases in Breast and Ovarian Cancer Risk**
- **For over 15 years methods for identifying individuals with this risk have existed**
- **M**
- **Teach… …ropriate testing**

Problem:

- **Pathogenic Variants in BRCA 1 and 2 result in dramatic increases in Breast and Ovarian Cancer Risk**
- **For over 15 years methods for identifying individuals with this risk have existed**
- **Most individuals with this risk are not aware of it**
- **Teach[illegible] appropriate testing**

Problem:

- **Pathogenic Variants in BRCA 1 and 2 result in dramatic increases in Breast and Ovarian Cancer Risk**
- **For over 15 years methods for identifying individuals with this risk have existed**
- **Most individuals with this risk are not aware of it**

Educational Solution:

- **Teach providers to identify risk and order appropriate testing**

Annals of Internal Medicine
Sept 6th 2005

Annals of Internal Medicine | CLINICAL GUIDELINES

Genetic Risk Assessment and *BRCA* Mutation Testing for Breast and Ovarian Cancer Susceptibility: Recommendation Statement

U.S. Preventive Services Task Force*

This statement summarizes the U.S. Preventive Services Task Force (USPSTF) recommendations on genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility, along with the supporting scientific evidence. The complete information on which this statement is based, including evidence tables and references, is included in the evidence synthesis available through the USPSTF Web site (www.preventiveservices.ahrq.gov). The recommendation is also posted on the Web site of the National Guideline Clearinghouse (www.guideline.gov).

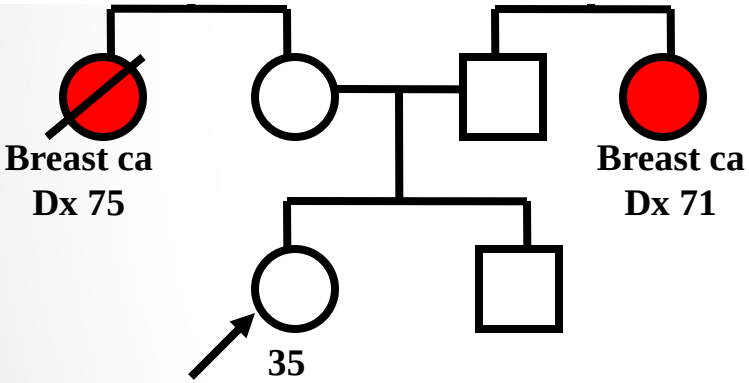
Ann Intern Med. 2005;143:355-361. www.annals.org
For author affiliation, see end of text.

Individuals who wish to cite this recommendation statement should use the following format: U.S. Preventive Services Task Force. Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility. Ann Intern Med. 2005;143:355-61.

*For a list of the members of the U.S. Preventive Services Task Force, see the Appendix.

USPSTF expects this kind of analysis

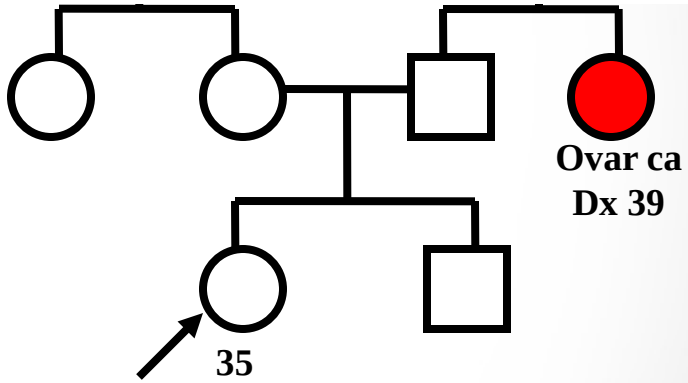
Scenario One – patient concerned



USPSTF screen negative

Should not be referred or tested

Scenario Two – patient not concerned



USPSTF screen positive

Should be referred for possible testing

The New York Times

My Medical Choice

By ANGELINA JOLIE MAY 14, 2013

Loren Capelli

Is it an educational failure that the majority of the estimated 250,000 to 415,000 adult US women with pathogenic variants in BRCA1 or 2 are not aware of it?

- Simple Answer is no.

Is it an educational failure that the majority of the estimated 250,000 to 415,000 adult US women with pathogenic variants in BRCA1 or 2 are not aware of it?

- 50% of families found to harbor *BRCA1* or *BRCA2* mutations had no history of breast or ovarian cancer that would have triggered clinical attention.

Gabai-Kapara E, et al*. Proc Natl Acad Sci U S A*. 2014.

Genomics Education: past and future

Principle:

- Targeted testing

Education:

- Who to test
- How to test
- What to do with negative
- What to do with positive

Genomics Education: past and future

Principle:

- Targeted testing

Education:

- Who to test
- How to test
- What to do with negative
- What to do with positive

Principle:

- Population is tested

Education:

- What to do with positive

Primary Provider "Just in Time" Education That Supports Screening Healthy Volunteers with Genomics

Describe:

- GenomeFIRST CME Modules
- GenomeFIRST Clinical Guidance

Primary Provider "Just in Time" Education That Supports Screening Healthy Volunteers with Genomics

Describe:

- Geisinger Health System
- MyCode Community Health Initiative
- GenomeFIRST Return of Results Project
- GenomeFIRST CME Modules
- GenomeFIRST Clinical Guidance

Geisinger's GenomeFIRST Program Return of Results

The prompt for the clinical encounter is the DNA variant

GenomeFIRST ™

Our Return of Incidental Findings Flips the Care Model within Geisinger's HealthCare System

- Genotype First – is the use of DNA sequence information as the trigger for clinical evaluation and management.

- Phenotype First – is the use of clinical clues as the trigger for clinical evaluation and management.

Geisinger GenomeFIRST Overview (1 of 2)

Geisinger's MyCode® Biobank is carrying out an unselected recruitment of patient participants from across the healthcare system.

Patients consented for both research and potential return of results.

Samples from approximately 50,000 patient participants have undergone WES for discovery research.

Geisinger GenomeFIRST Overview (2 of 2)

We have initiated a return of secondary findings to participants with pathogenic/likely pathogenic findings in the "Geisinger 76" (i.e. the ACMG 56 plus 20 genes).

Anticipate 1 in 50 patients will receive a result.

Half of the results returned will be linked to just **three conditions.**

GenomicFIRST™ Return of Results

Geisinger Incidental Findings List (The Geisinger 76)

- Focus on 27 conditions (76 genes)
- Builds on the ACMG Incidental Findings List (published 2013)
- Cancer predisposition (e.g. BRCA 1 and BRCA 2 mutations)
- Cardiovascular disease (e.g. Hypertrophic Cardiomyopathy)
- Malignant Hyperthermia (leads to anesthesia complications)
- Hereditary Hemorrhagic Telangiectasia (risk for visceral arteriovenous malformations)
- Ornithine transcarbamylase (OTC) deficiency (hyperammonemia, coma)

Return of Results

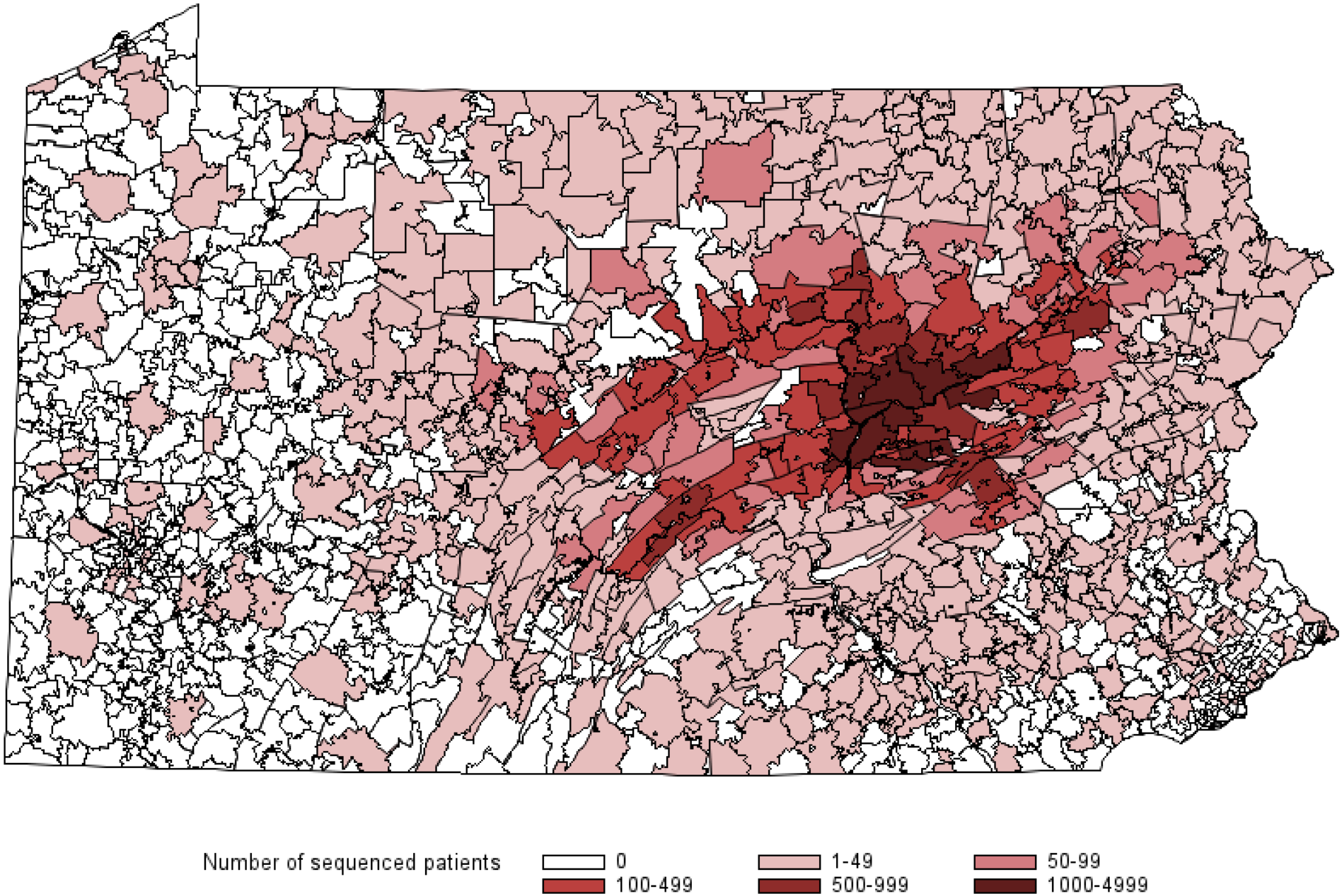
- Patients with genomic findings that warrant return for clinical management will receive that result (initially ~ 2%).
- Infrastructure and decision support to be developed to support patients and providers.

MyCode® Participants

- **Goal Enrollment** **250,000**
- **Current Enrollment** **95,000+**
- **Current WES** **60,000+**
- **Current QC’d Cases** **53,000**

WES = Whole Exome Sequence

Number of sequenced MyCode patients - 10/12/2015



Returnable Results from Other Studies

Study	ClinSeq 2012-2013	Univ Wash 2013	Univ Wash 2015
N	870 *	1000	6500
Demographics	96% EA	50% EA 50% AA	~ 66% EA ~ 33% AA
Gene List	80	114	112
Percent Returnable	2.3%	3.4% EA	~ 2% EA

In Geisinger's GenomeFIRST we anticipate that:

9 genes (BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS2, LDLR, APOB, PCSK9) associated with 3 conditions will drive half of the return of results

GENOMIC CONDITION	POPULATION PREVALENCE	CLINICAL RISK	DISEASE-ALTERING INTERVENTION
Hereditary Breast and Ovarian Cancer Syndrome	~1 in 400	Early-onset Breast, Ovarian, and Prostate Cancers	Targeted screening with prophylactic medical and surgical intervention
Lynch Syndrome	~1 in 400	Early-onset Colon and Uterine Cancers	Targeted screening and management of pre-cancerous changes
Familial Hypercholesterolemia	~1 in 200	Early-onset Coronary Artery Disease and Stroke	Targeted screening and aggressive medical management
TOTAL	~1 in 100	Multiple Cancers and Cardiovascular Diseases	Life-saving screening and intervention before development of disease

Predicted Clinical Volume for Return of Results

Patients Identified	MyCode Participants		
	100,000	250,000	500,000
Participants with pathogenic variants from Geisinger 76	2,000	5,000	10,000
** Relatives identified with same variant	6,000	15,000	30,000
Total	8,000	20,000	40,000

**Estimated average 3 per participant with variant, and 3 who will test negative for risk variant

Genomics Education: past and future

Principle:

- Targeted testing

Education:

- Who to test
- How to test
- What to do with negative
- What to do with positive

Principle:

- Population is tested

Education:

- What to do with positive

Supporting tools in Return of Results

- Provider and patient support for all results returned

- Provider support include:
  - [1] “Just in Time” Continuing Medical Education
  - [2] condition specific standardized phenotyping
  - [3] opportunity to consult clinical genomics and other specialists

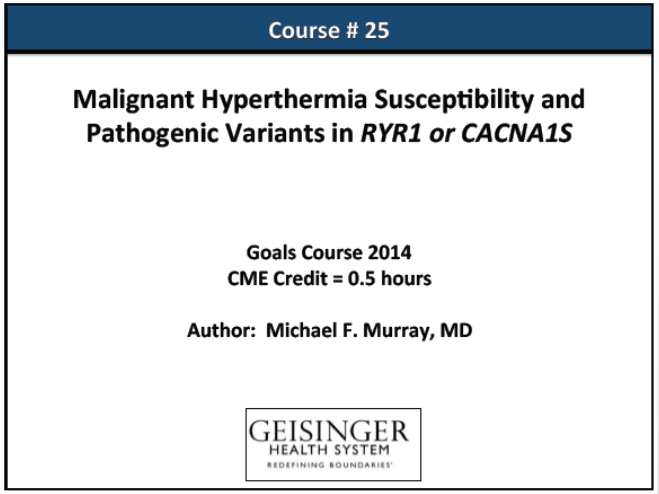
  - Patient support plan which includes opportunities to have queries answered and for counseling

Provider Education in Return of Results

- Over 1000 practitioners are the immediate target audience
- They are motivated by desire to manage their patient
- Principles:
  - Start with the result
  - Don’t try to create 1000+ Genetics Experts
  - Offer Repetitive Opportunities to Learn Content
  - Motivate by offering CME Credit
  - Make it available to External Audience

GenomeFIRST™ CME for Practitioners

- The educational modules
  - 30 free-standing CME modules (30 minute duration)
  - Electronically hosted on internal website
  - Pre- and post-test evaluation
- Providers receiving medically actionable clinical result will receive a hyperlink to condition specific module
- Participation is optional



Course #9
Genomics Learning Objectives

Describe clinical features common to individuals with a pathogenic germline variant in *RET*

Describe management considerations for patients with a pathogenic germline variant in *RET*

Review basics of autosomal dominant inheritance

Understand the concepts of penetrance and variable expressivity

Understand the concept of pleiotropy

Understand the importance of identifying at-risk family members

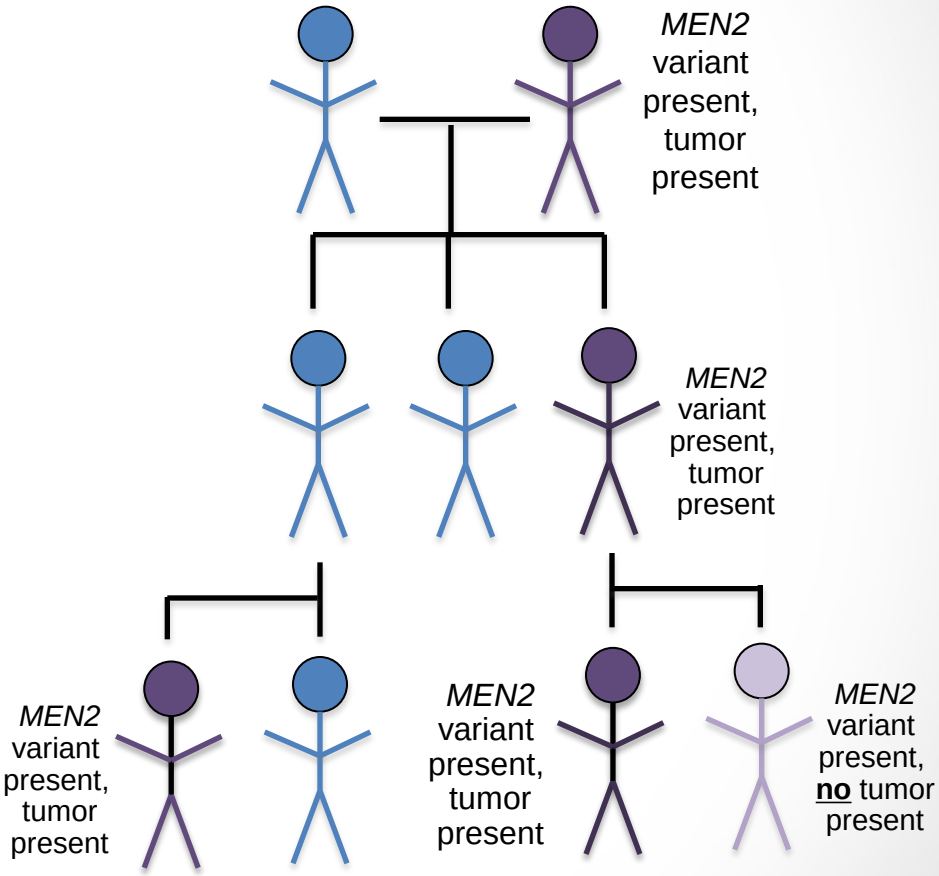
RECOMMENDED REVIEW
MEN2

Marquard and Eng, 2015.
http://www.ncbi.nlm.nih.gov/books/NBK1257

MEN2 Penetrance (1 of 2)

Penetrance = an individual carrying a particular variant of a gene (genotype) also expresses an associated trait (phenotype, shown as shaded dark purple).

Penetrance of MEN2 is high – nearly all individuals with pathogenic variants will develop medullary thyroid cancer without prophylactic thyroidectomy



DNA is not a Diagnosis (1 of 2)

Clinical Follow-Up

- **In your patient-** A "likely pathogenic" DNA variant identified through genomic sequencing warrants clinical follow-up in the patient, similar to incidental findings on radiology studies
- **In family members-** A "likely pathogenic" DNA variant warrants follow-up in the patient's family

New Diagnosis or Unifying Diagnosis

- DNA findings alone do not constitute a diagnosis
- However, in the clinical context of other supportive findings, these DNA findings can lead to a new diagnosis or a unifying diagnosis

DNA is not a Diagnosis (2 of 2)

Problem Listing

•When DNA findings do not lead to a diagnosis, the DNA variant should be listed on the patient's EHR "problem list" to allow re-evaluation should relevant clinical signs or symptoms develop in the future

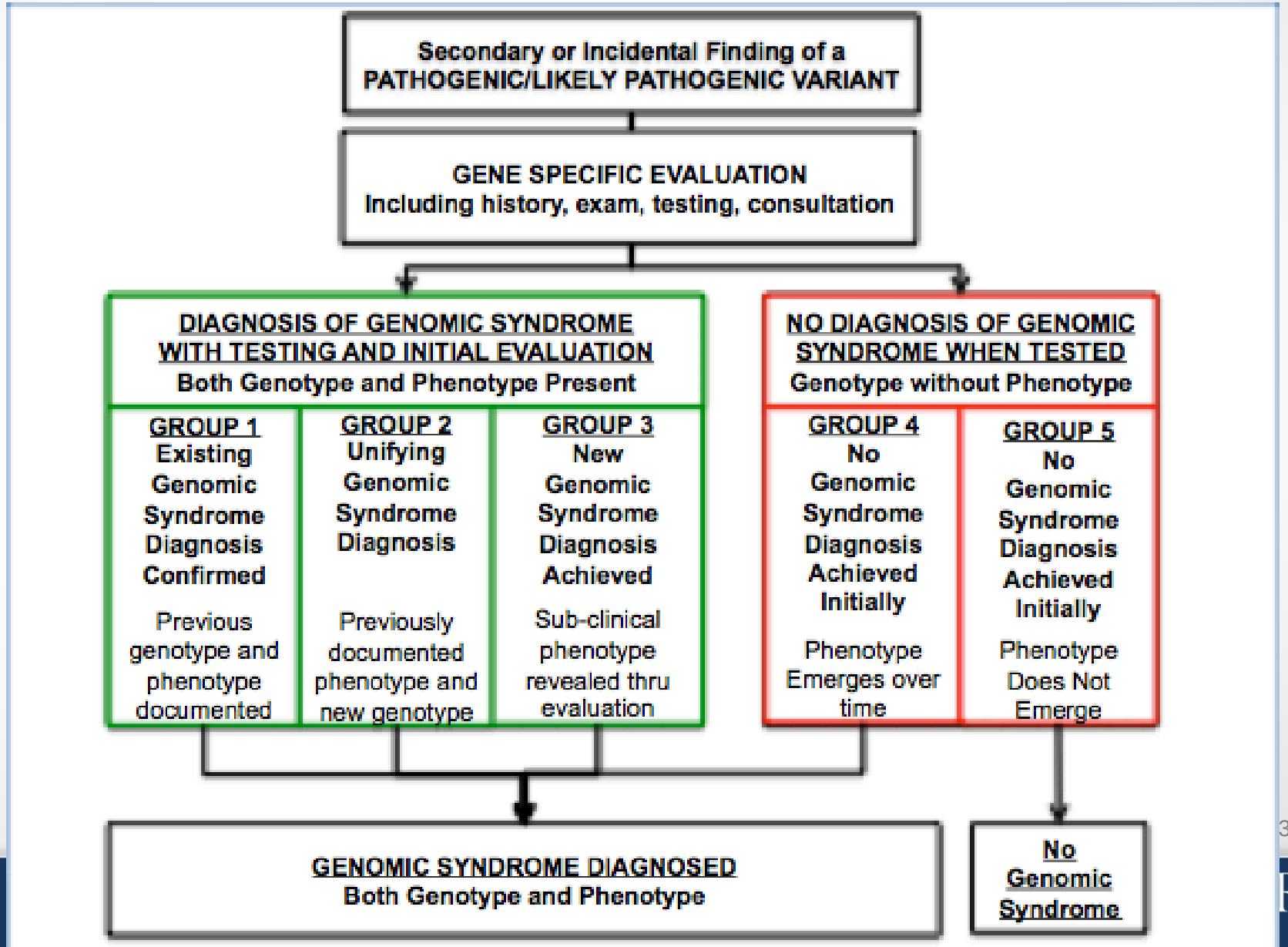
Available Tools

•The GenomeFIRST™ team has developed a list of relevant signs and symptoms for each of the 27 conditions in our return of results program

•The GenomeFIRST™ team has developed explanatory letters for patients and doctors to share with those outside the family or the clinical care team

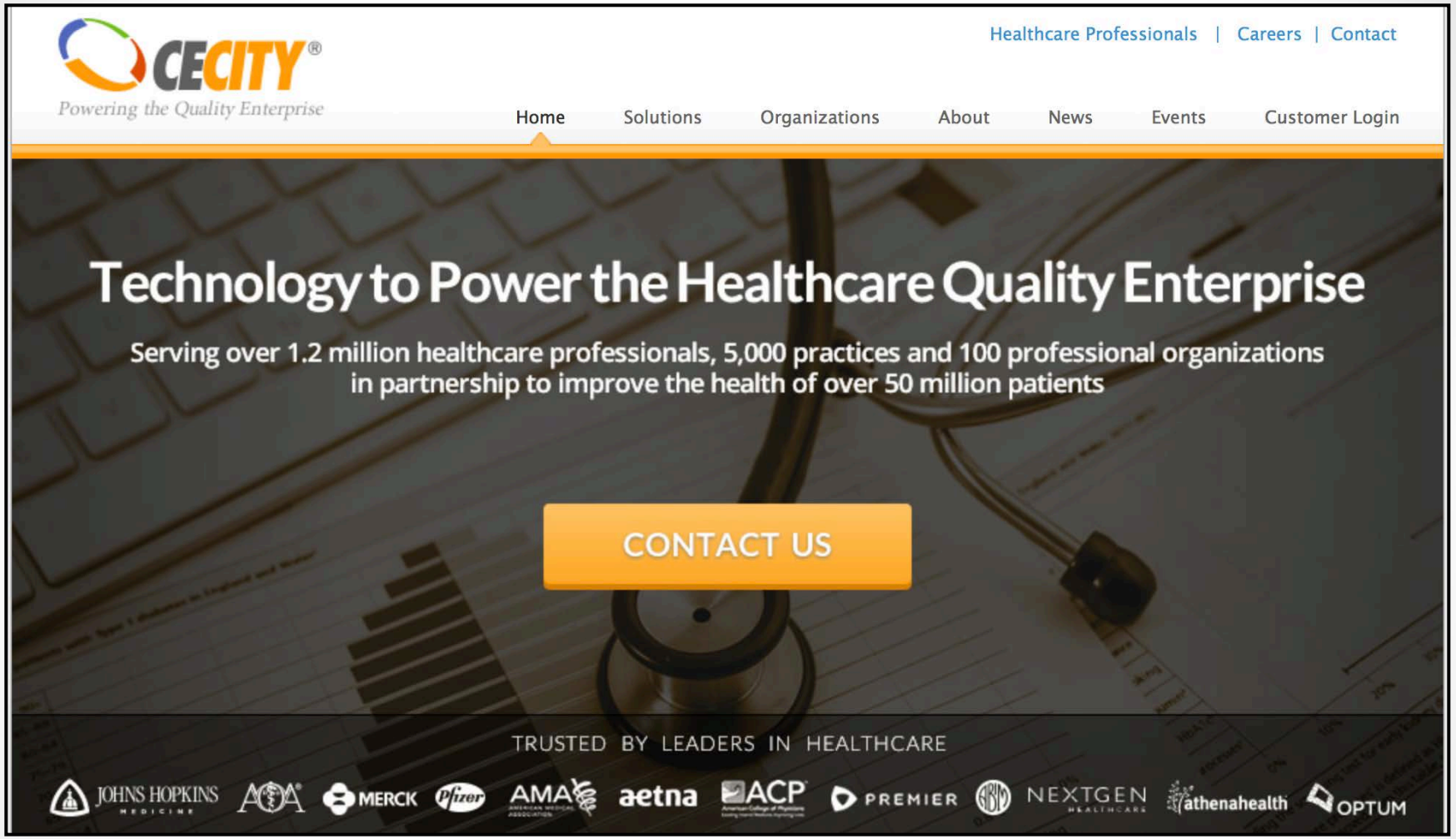
In Geisinger's GenomeFIRST we anticipate that:

Patients receiving secondary results will fall into one of five diagnostic groups.



Home of GenomeFIRST ™

PRECISION HEALTH CENTER in Forty Fort PA


CECITY®
Powering the Quality Enterprise
Healthcare Professionals | Careers | Contact
Home
Solutions
Organizations
About
News
Events
Customer Login
Technology to Power the Healthcare Quality Enterprise
Serving over 1.2 million healthcare professionals, 5,000 practices and 100 professional organizations in partnership to improve the health of over 50 million patients
CONTACT US
TRUSTED BY LEADERS IN HEALTHCARE
JOHNS HOPKINS MEDICINE
MERCK
Pfizer
AMA
aetna
ACP
PREMIER
NEXTGEN HEALTHCARE
athenahealth
OPTUM

15 Positive Results Delivered

	Pathogenic variant identified	Laboratory confirmed P/PL	Clinical Report Generated and Entered into EHR	Report Pending
HBOC (BRCA1/2)	57	11	11	46
Familial Hypercholesterolemia (FH)	52	1	1	51
Lynch	42	2	2	40
Other	9	0	0	9
Final Revised Report (non-pathogenic final)	1	0	1	0
Totals	161	14	15	146

Thank you.