Genetic Insights Project

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…on behalf of a large and great team

University of Nebraska Medical Center

Nebraska Medicine

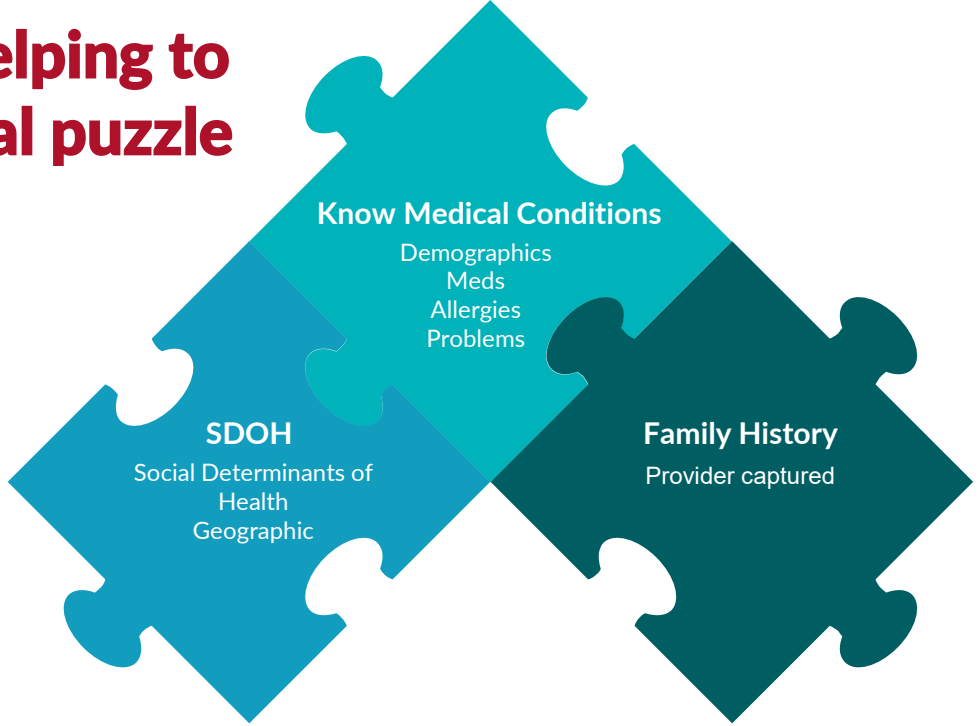
Conflicts of Interest Disclosure

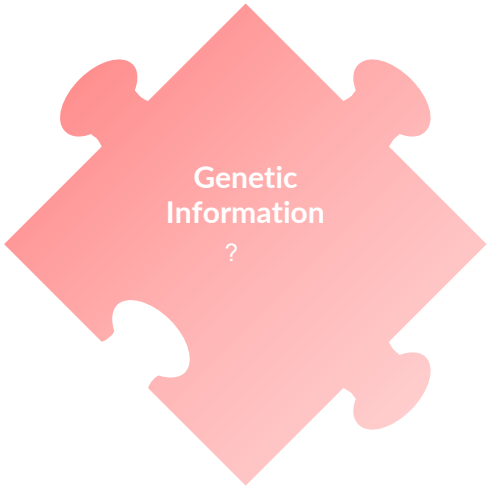
BeiGene – Speaker
CellTrion – Consultant/advisory board participant
Nuvem – Board member
Leiters Health – Consultant/advisory board participant
Astra Zeneca – Consultant/advisory board participant

I have no conflicts of interest related to this content

Precision Medicine - Helping to put together the medical puzzle

- Precision Medicine is prevention, diagnosis and treatment tailored to the genetic contributions to a patient's disease
- Genomic variants can be inherited from a parent (germline) or acquired at some point during a person's lifetime (somatic.)





Precision Medicine Strategy

Diagnosis and treatment

Increased specificity in diagnosis

Improved ability to predict which treatments will work for specific patient

Improved ability to rule out inappropriate treatment

Population health

Identify patients at higher risk of disease - prevention

Identify patients at an earlier state in disease progression - detection

Research

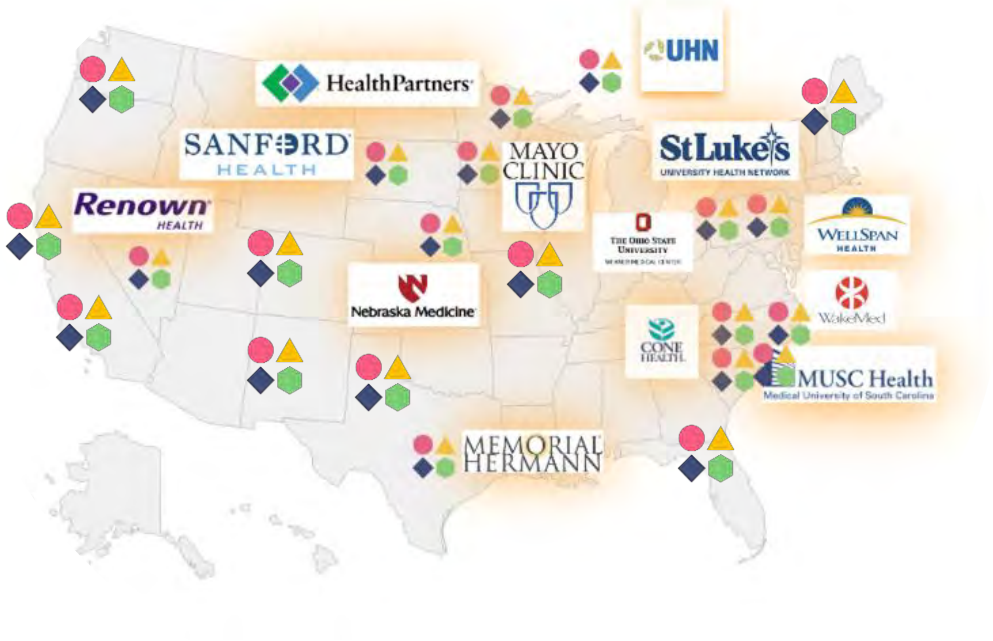
Identify patients for clinical trials and other research

Identify targets for future treatments

Partnership and Program Overview

- Nebraska Medicine, UNMC and Helix have launched a major population genomics initiative.
- Goal is to recruit 100K+ participants over five years.
- The program will provide participants (age 19+) in Nebraska with no-cost genetic (exome) sequencing (i.e. no billing implications).
- Nebraska Medicine is a founding member of the Helix Research Network, a federated learning network of normalized EHR + Genetic information.
- Aims:
  - Improve patient outcomes
  - Expand access to genetic testing (screening), especially in underserved populations
  - Enable access to large data sets for research
  - Form commercial partnerships
  - Improve health outcomes in Nebraska and beyond
  - Partner with a single vendor for germline testing (diagnostic)
  - Become a leader in genetic medicine

Helix Research Network (HRN)



Founded by Helix

15+ institutions (and growing)

Genetic Insights Projects = UNMC/NebMed arm of HRN

What clinical tests are included in the project?

FH

Genes: *LDLR, APOB, PCSK9* and *LDLRAP1*

- Hypercholesterolemia and increased risk for cardiovascular events

HBOC

Genes: *BRCA1* and *BRCA2*

- Significantly increased lifetime risk of breast, ovarian and other cancers

Lynch

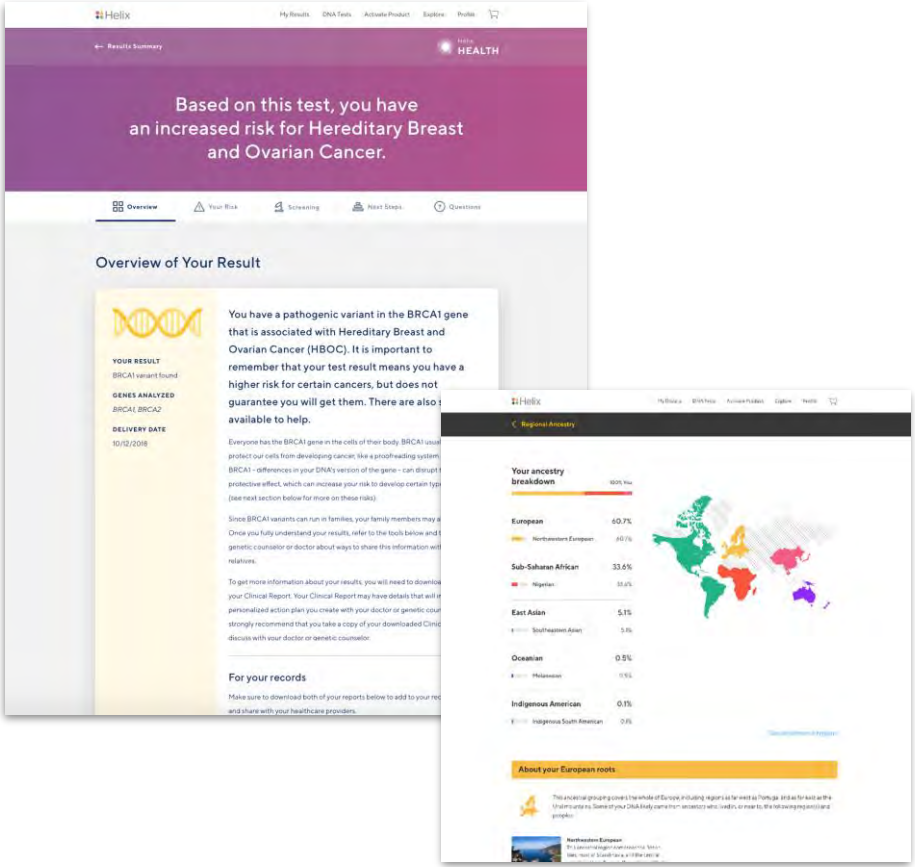
Genes: *MLH1, MSH2, MSH6, PMS2* and *EPCAM*

- Significantly increased lifetime risk of colorectal, endometrial, ovarian and other cancers

1-2% of all patients (1 in 75)* have one of these conditions

* Study from Renown Health/Healthy Nevada Project

External Helix portal: Delivering health, ancestry & trait insights to participants



Helix Health:

A genetic health screen that looks for variants that predispose people to the CDC Tier 1 conditions

Helix Ancestry:

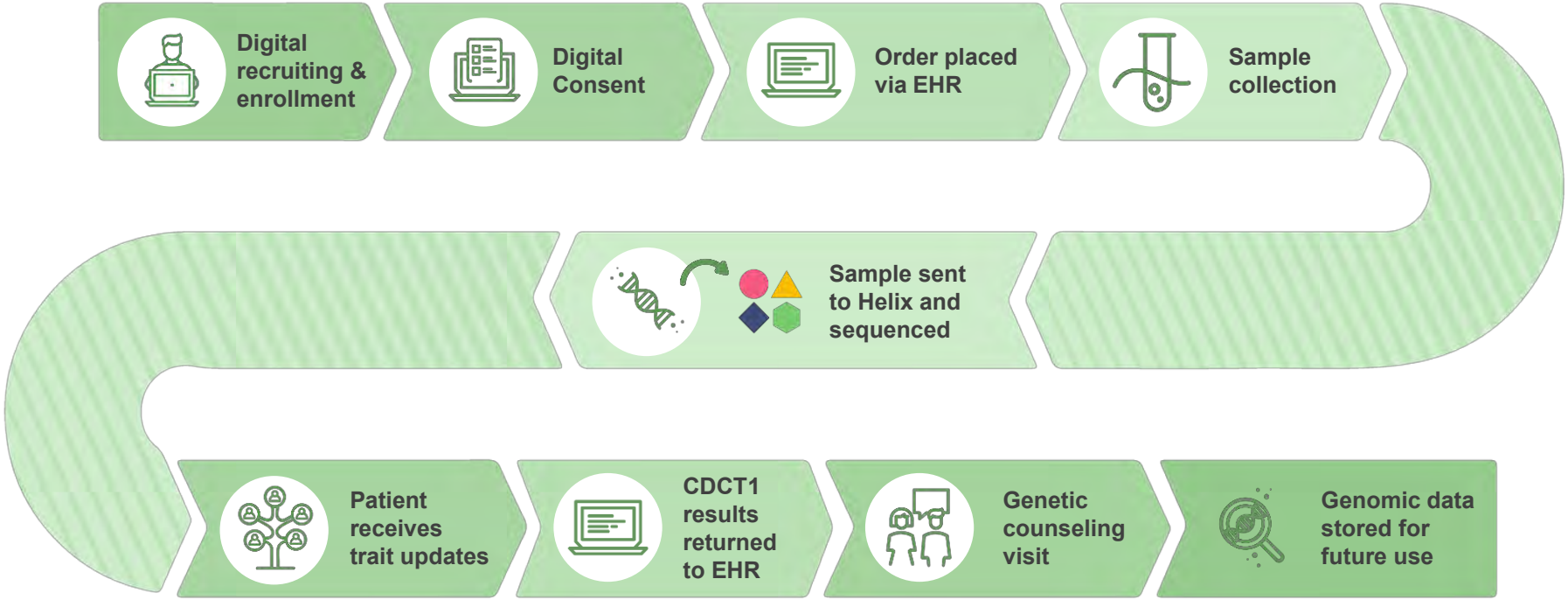
A genetic analysis that helps individuals understand their regional ancestry

Helix Traits:

A genetic analysis that helps individuals understand the traits that affect wellness, appearance & fitness

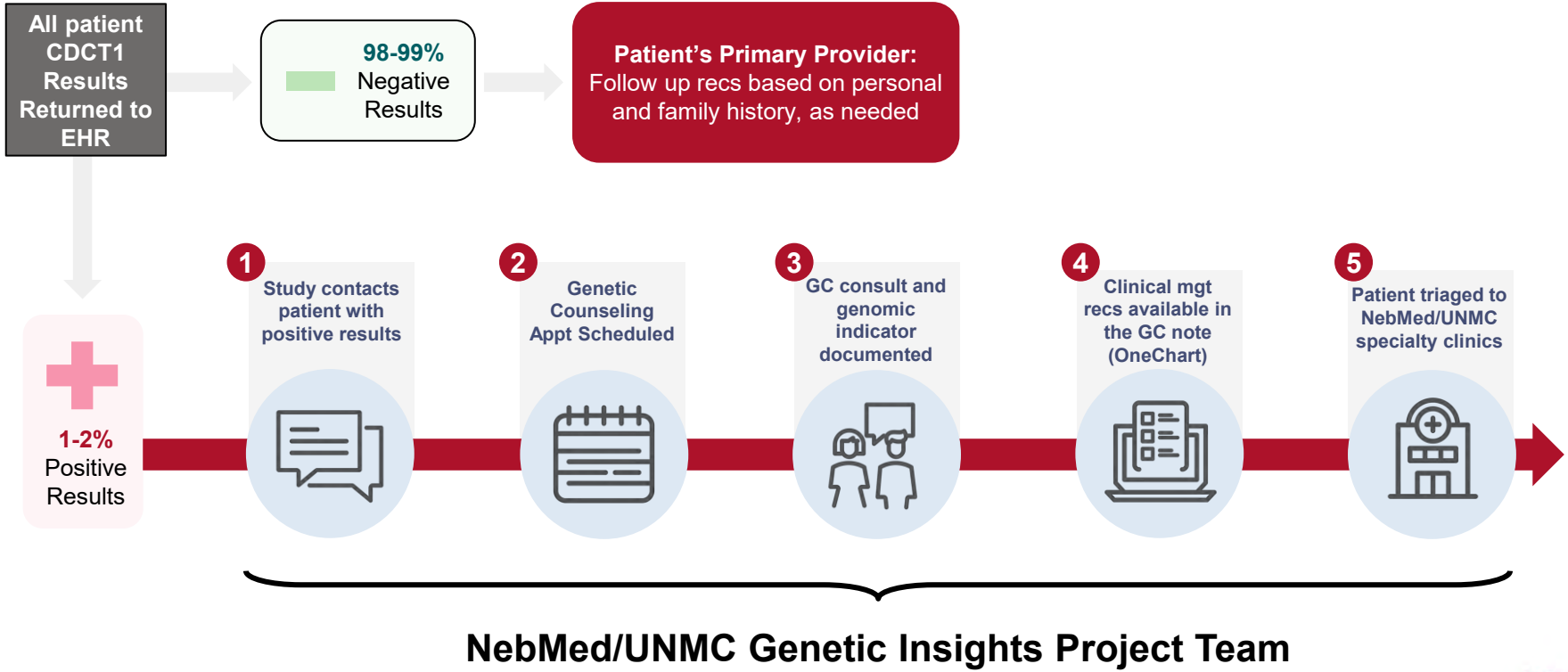
Creating a Helix Health account is optional

Genetic Insights/Helix Workflow



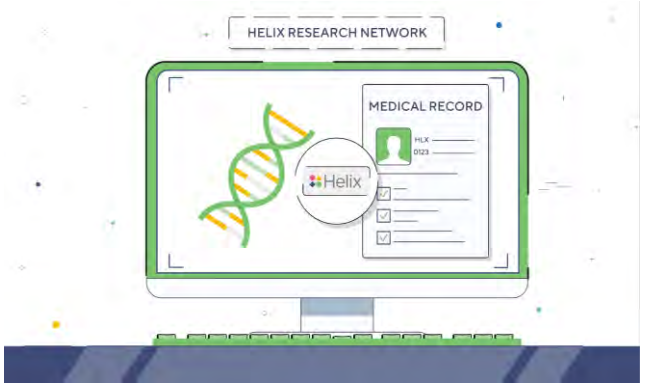
Must Have a Nebraska Medicine One-Chart Patient Portal
Cannot have had a Bone Marrow/Stem Cell Transplant

Post-test workflow



What does the patient consent include?

- ➔ Provide a sample (blood or saliva)
- ➔ Helix will sequence and store the genomic data
- ➔ Receive actionable results (CDC Tier 1) in the EHR and the Helix Health portal
- ➔ Genomic + EHR data will be combined for research
- ➔ Possible future clinical use of the genomic data via provider order (Diagnostic/Therapeutic)
  - ❾ Hereditary Cancer Panel
  - ❾ Cardiomyopathy Panel
  - ❾ Pharmacogenomics



UNMC and Central IRB Involvement

Genetic Insights Project Results

Genetic Insights Project

- ~20,000 Enrolled Participants
- ~13,000 Participants sequenced
- >150 actionable results

Enrolling Patients via:

- My chart messages
- Pre-visit embedded workflow
- Community campaigns

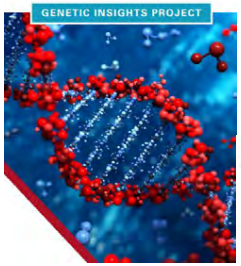
Research:

- Created a database with ~13,000 records
- Part of a larger, multi-system database
- Participated in two additional sub-studies

"It gave me a different view on how important your health is, how it can change, and really listening to your body," she says. "Knowledge is powerful, and this is helping me be more preventive."

- (+) Lynch Patient

https://www.nebraskamed.com/health/patient-stories/cancer-care/a-patients-empowering-experience-with-genetic-screening



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CDC Tier 1 Results Breakdown

TOTAL RESULTS DELIVERED

12,293

TOTAL NEGATIVE	TOTAL POSITIVES
12,118	175

- Lynch Syndrome (Ls)
- Familial Hypercholesterolemia (Fh)
- Hereditary Breast & Ovarian Cancer Syndrome (Hboc)

LYNCH SYNDROME (LS)

45 0.4% of all results delivered

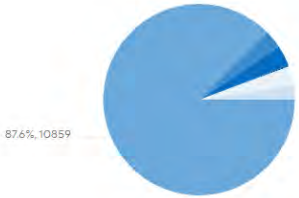
FAMILIAL HYPERCHOLESTEROLEMIA (FH)

48 0.4% of all results delivered

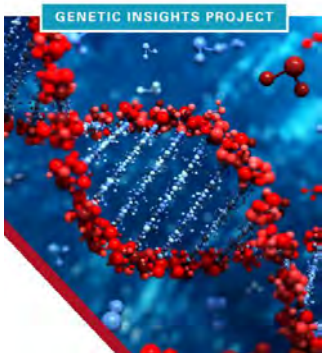
HEREDITARY BREAST & OVARIAN CANCER SYNDROME (HBOC)

82 0.7% of all results delivered

Race & Ethnicity



- **Asian** 2.4%, 293
- **Other Race** 3.5%, 439
- **Black Or African American** 3.3%, 411
- **Unknown** 3.1%, 385
- **Native Hawaiian Or Other Pacific Islander** 0.1%, 15
- **White** 87.6%, 1085



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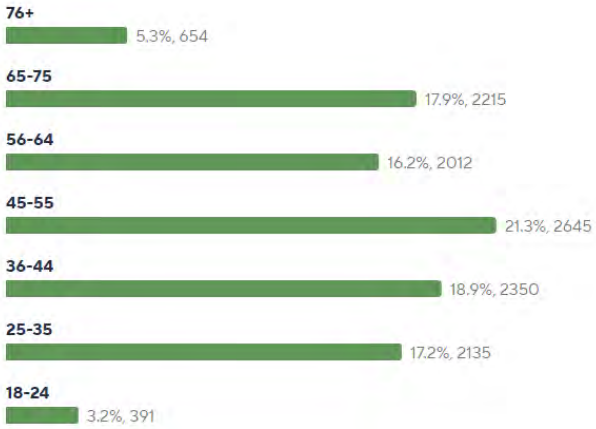
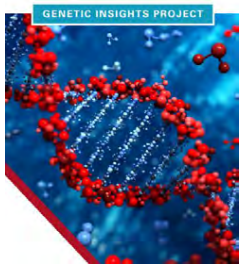
Age Range



Sex at Birth

- **Female** 74.0%, 9174
- **Male** 26.0%, 3228



Research and the Genetic Insights Project

The goal:

Broadly accessible and useful data

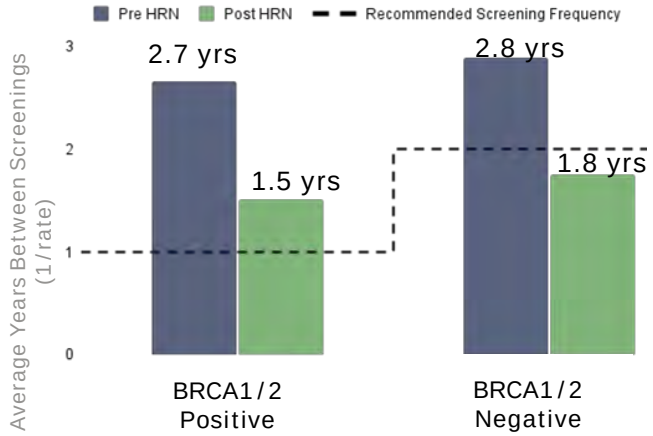
Available to faculty investigators

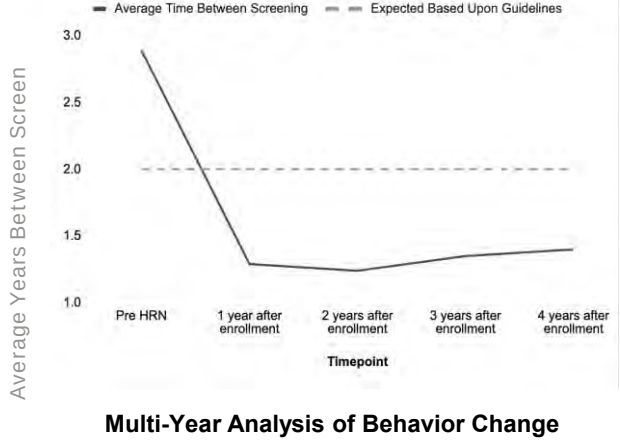
Utilized by many with appropriate safeguards and oversight

Genetic screenings results in early detection of disease risk

Improved compliance with guideline driven activities result in primary prevention / early detection of serious disease

10	Regionally Diverse Systems	>200 K	CDCT1 Results Returned	>2,500	Positive Results Returned	>900	Positive BRCA1/2





Multi-Year Analysis of Behavior Change

Takeaways

- Proactive approach identifies underlying risk
- Increased mammograms even with negative population
- Personalized approach drives longitudinal durability

Increased adverse events from clopidogrel in poor metabolizers

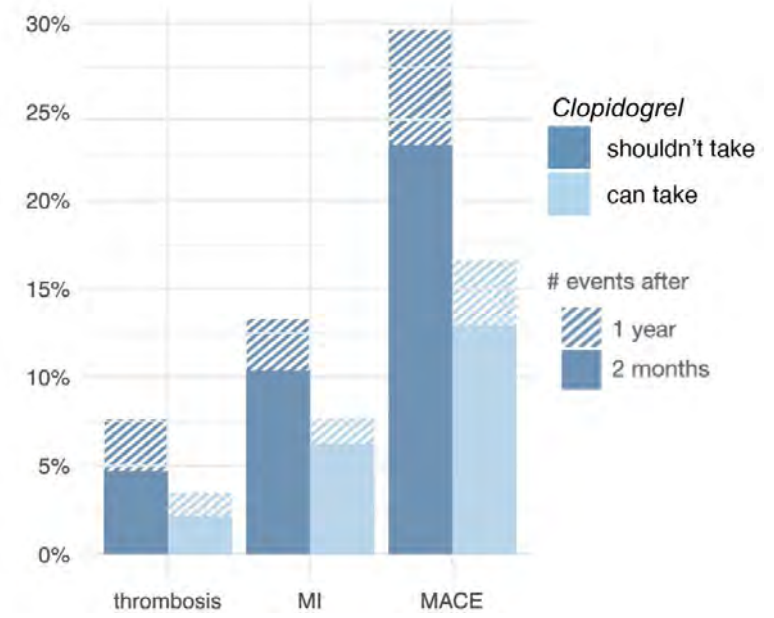
HRN Network
>100k individuals

3.8k clopidogrel users

Compiled events following initiation of clopidogrel prescription

29% mismatch between recommended dosage based CYP2C19 genotype and that given

Adverse events enriched 2x in Poor or Intermediate Metabolizers



Scalable system-wide CYP2C19 pharmacogenomic testing reveals 38% excess incidence of adverse events in metabolizers receiving inappropriate prescriptions

Natalie Telis, Douglas Stoller, Christopher N. Chapman, C. Anwar A. Chahal, Daniel P. Judge, Douglas A. Olson, Joseph J. Grzymski, Teresa Kruisselbrink, Nicole L. Washington, Elizabeth T. Cirulli

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What's Next

- Continue expanding outside of Nebraska Medicine
- Growth of saliva testing
- Growth of at home testing
- Community events and partnerships across the state

Questions?

For additional information or to participate:
https://www.nebraskamed.com/genetic-insights-project
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Thank you for your time

University of Nebraska Medical Center

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