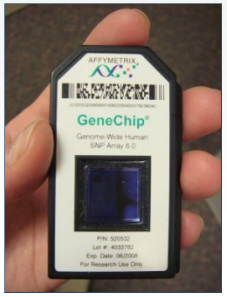
CORIELL INSTITUTE
FOR MEDICAL RESEARCH

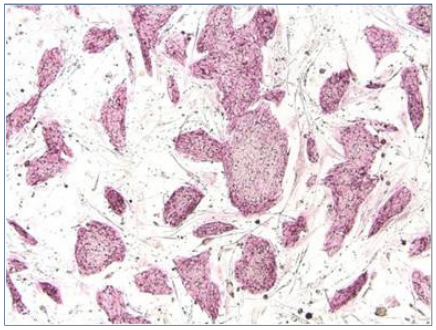
Utility of Genome Information in Clinical Care:
Coriell Personalized Medicine Collaborative®

Michael Christman, Ph.D.
President & CEO, Coriell Institute
July 19, 2011

403 HADDON AVENUE, CAMDEN, NJ 08103 | CORIELL.ORG

Coriell Institute for Medical Research





Coriell Personalized Medicine Collaborative

CPMC Research Study Launched in 2007

CORIELL.ORG

Goals of the CPMC Research Study

- *Study the use of genome-informed medicine in a real-world clinical setting*

- *Determine the best mechanism to provide information to providers and participants/patients*

- *Find correlations in observational data*

www.cpmc.coriell.org

CORIELL.ORG

Dr. Francis Collins

Interview with *Science Magazine*
June 6, 2008

"We desperately need, in this country, ***a large-scale, prospective, population-based cohort study****. And we need to enroll at a minimum half a million people. We would need to have their environmental exposures carefully monitored and recorded, their DNA information recorded, their electronic medical records included, and have them consented for all sorts of other follow-ups."*

CORIELL.ORG

How the CPMC Study works

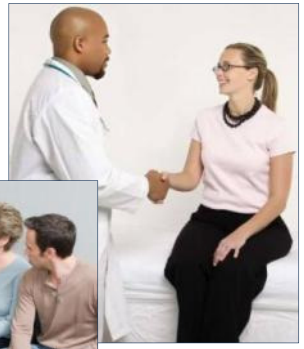
1

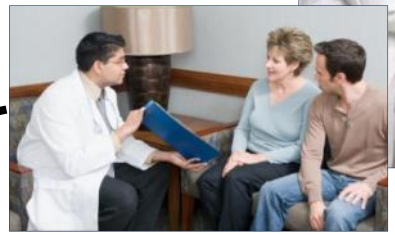
2

CORIELL Personalized Medicine Collaborative

www.cpmc.coriell.org

3





5

4

CORIELL.ORG

Hospital Partners in the CPMC

Coriell Institute for Medical Research

Cooper University Hospital

Fox Chase Cancer Center

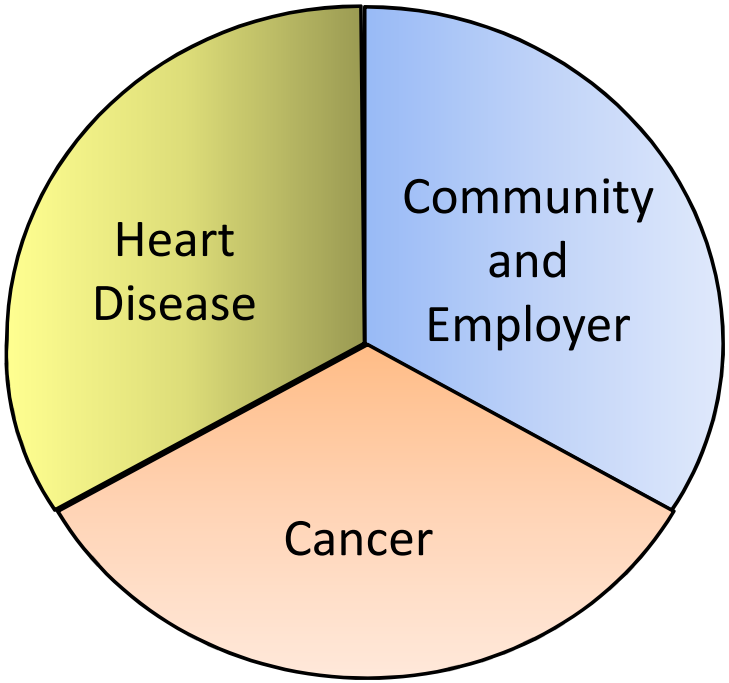
The Ohio State University Medical Center

Helix Health of Connecticut

Virtua Health

CORIELL.ORG

CPMC Recruitment



Eligibility:

- *Be at least 18 years old*
- *Hear informed consent presentation*
- *Have an email address and access to the internet*

Recruitment Mechanisms:

- *Community – based*
- *Cancer Clinic – based*
- *Heart Clinic– based*

CORIELL.ORG

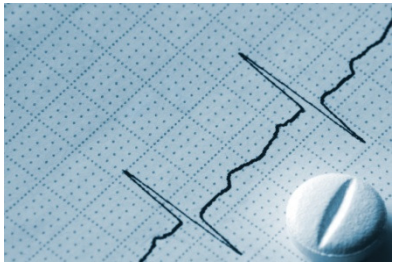
What information do we collect?

All Cohorts:

Demographic Information
Medical History
Medications
Family History
Lifestyle Information
Genetic Knowledge assessment

Cancer Cohorts:

Cancer Registry Data
Cancer-related health records
Prescribing Records



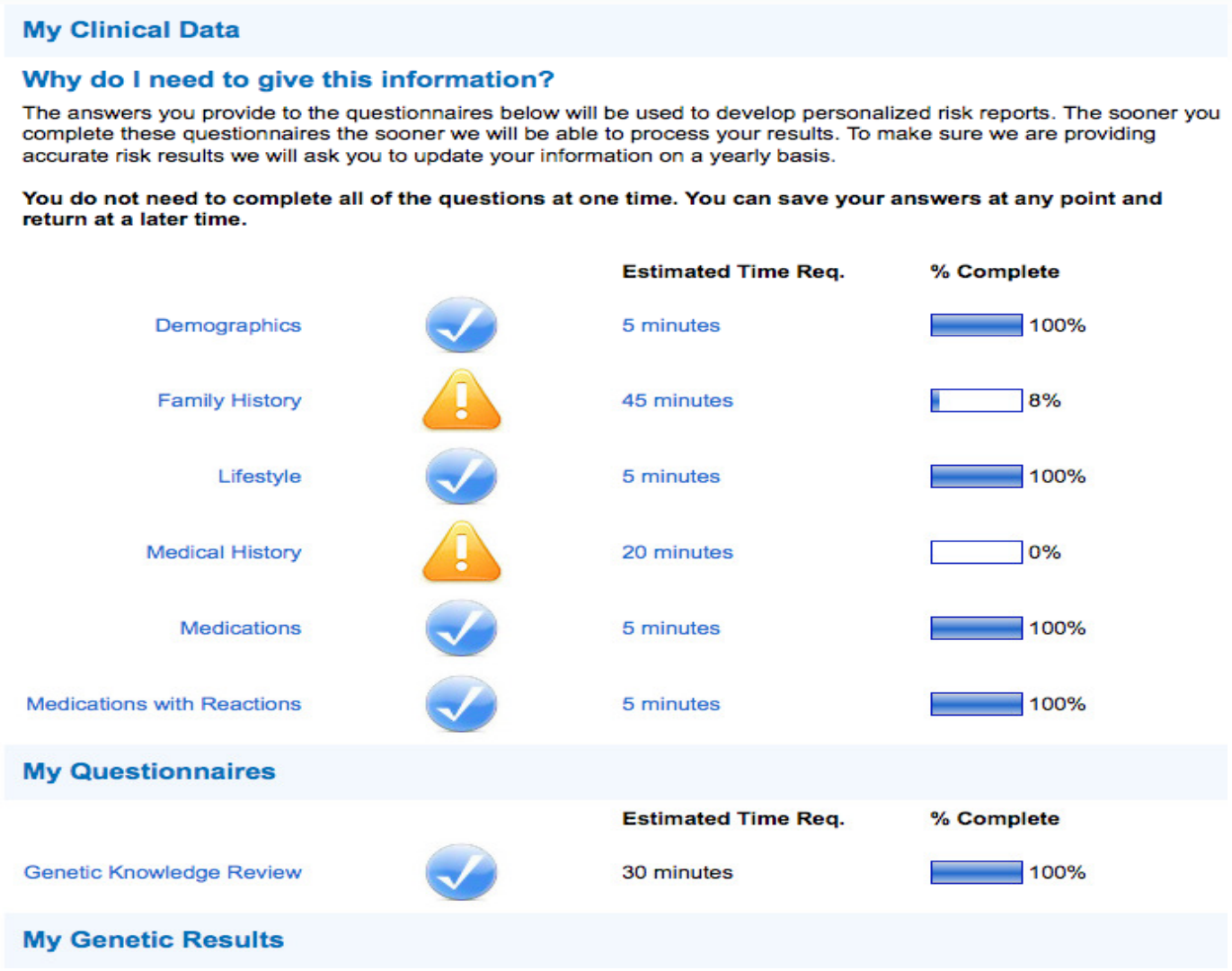
Heart Disease Cohorts:

Electronic Health Records
Prescribing Records

CORIELL.ORG

Detailed:

Family, Medical History, Medication, Lifestyle, and Demographic Information



CORIELL.ORG

The CPMC uses two “GeneChips”

2 million sites of variation

2,000 sites of known relevance to drug action

CORIELL.ORG

Who decides what genetic information is reported?

- *Informed Cohort Oversight Board (ICOB), an external advisory board. Composed of scientists, medical professionals, ethicist, community members.*

- *Vote on whether conditions are potentially actionable.*
- *Meet at least twice a year to approve new conditions.*
- *New results then reported to ALL participants.*

Supported by RNR Foundation

CORIELL.ORG

Informed Cohort Oversight Board (ICOB)

Robert C. Green, MD, MPH
Boston University, MA

Steven A.R. Murphy, MD
The Personalized Medicine Group, CT

Erin O'Shea, PhD
Harvard University, MA

David Pellman, MD
Harvard Medical School, MA

Charles Rotimi, PhD
National Human Genome Research Institute, MD

Reverend Floyd White
Woodland Community Development Corp, NJ

Jennifer Hoheisel, MS
Camden County College, NJ

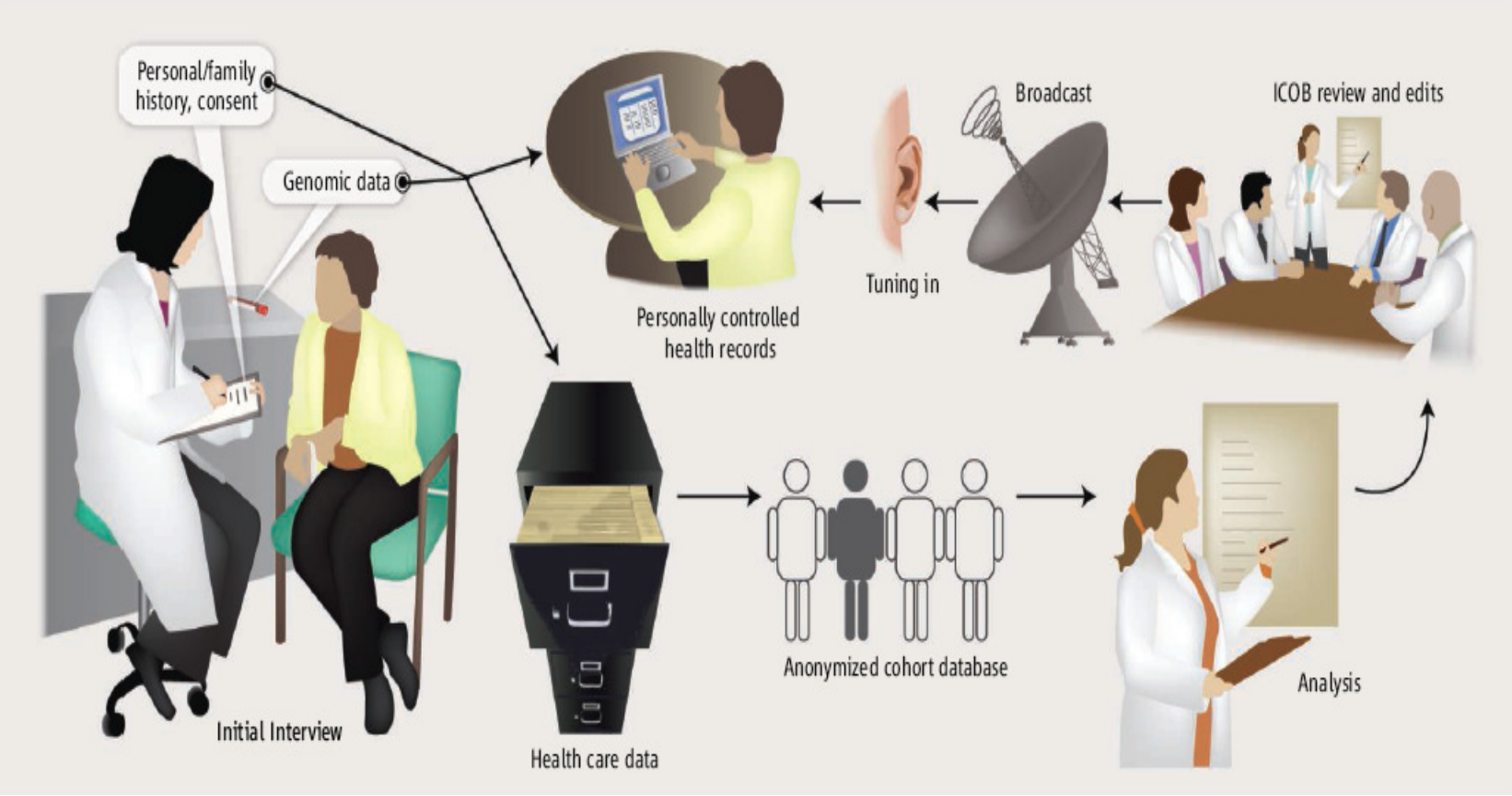
Ellis J. Neufeld, MD, PhD
Children's Hospital Boston, MA

Marc Lenburg, PhD
Boston University School of Medicine, MA

Kenneth Offit, MD, MPH
Cornell University, NY

CORIELL.ORG

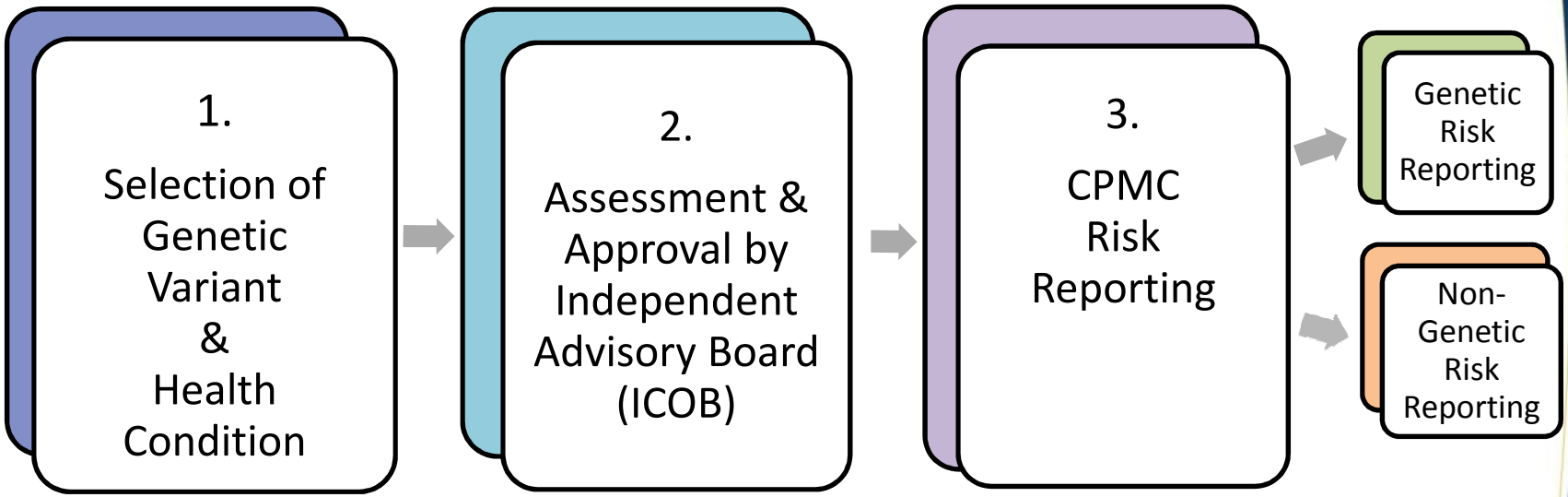
Informed Cohort Concept



Kohane et al., Science 2007

CORIELL.ORG

CPMC Process Overview



Potentially Actionable Conditions Currently Approved to be Reported by the CPMC Study®

Drug Metabolism

CYP2D6

VKORC1

CYP2C9

CYP2C19

UGT1A1

CYP4F2

Complex Disease

Age-related macular degeneration

Breast cancer

Bladder cancer

Chronic obstructive pulmonary disease

Colon cancer

Coronary artery disease

Inflammatory bowel disease

Hemochromatosis

Lupus

Melanoma

Obesity

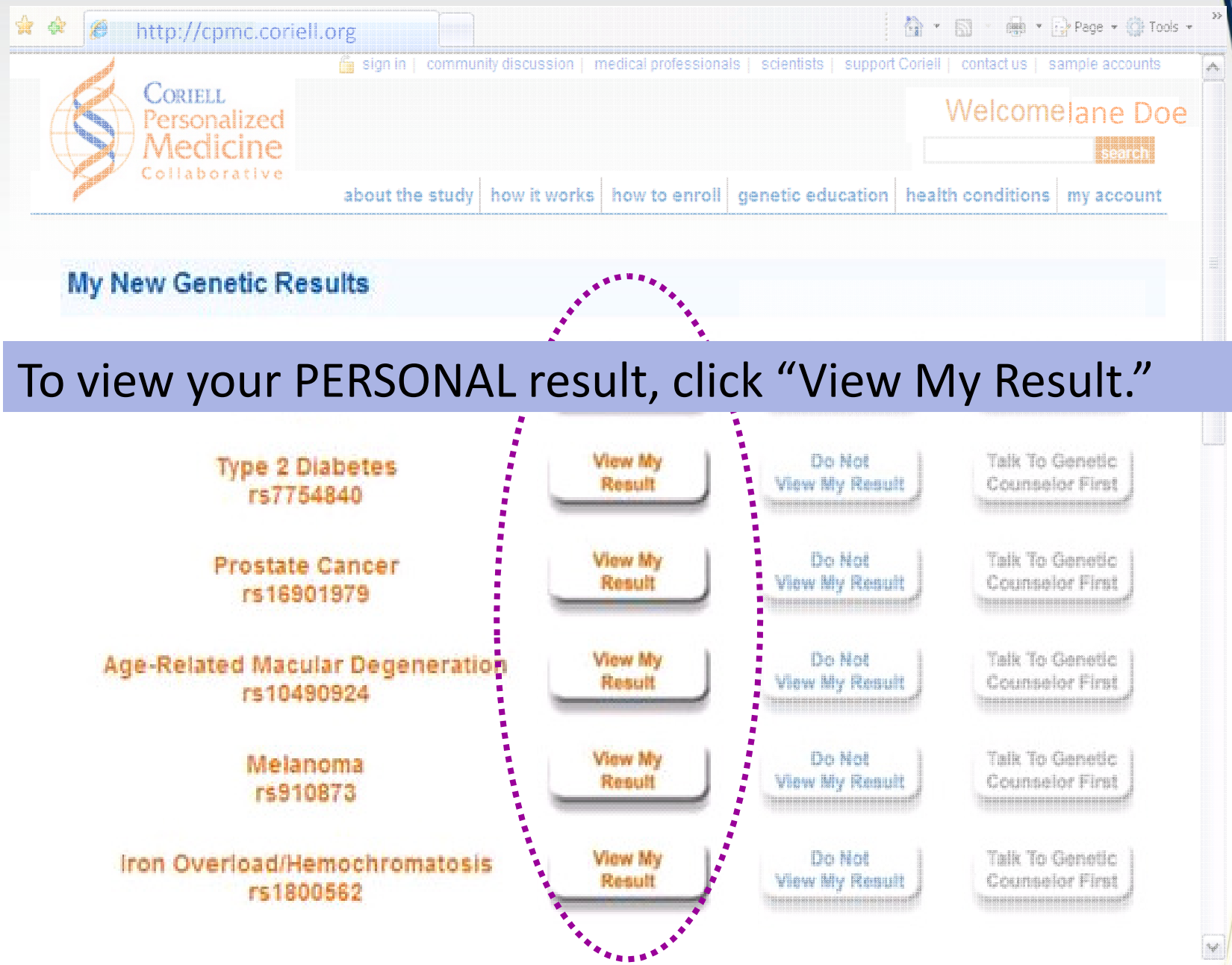
Prostate cancer

Rheumatoid arthritis

Testicular cancer

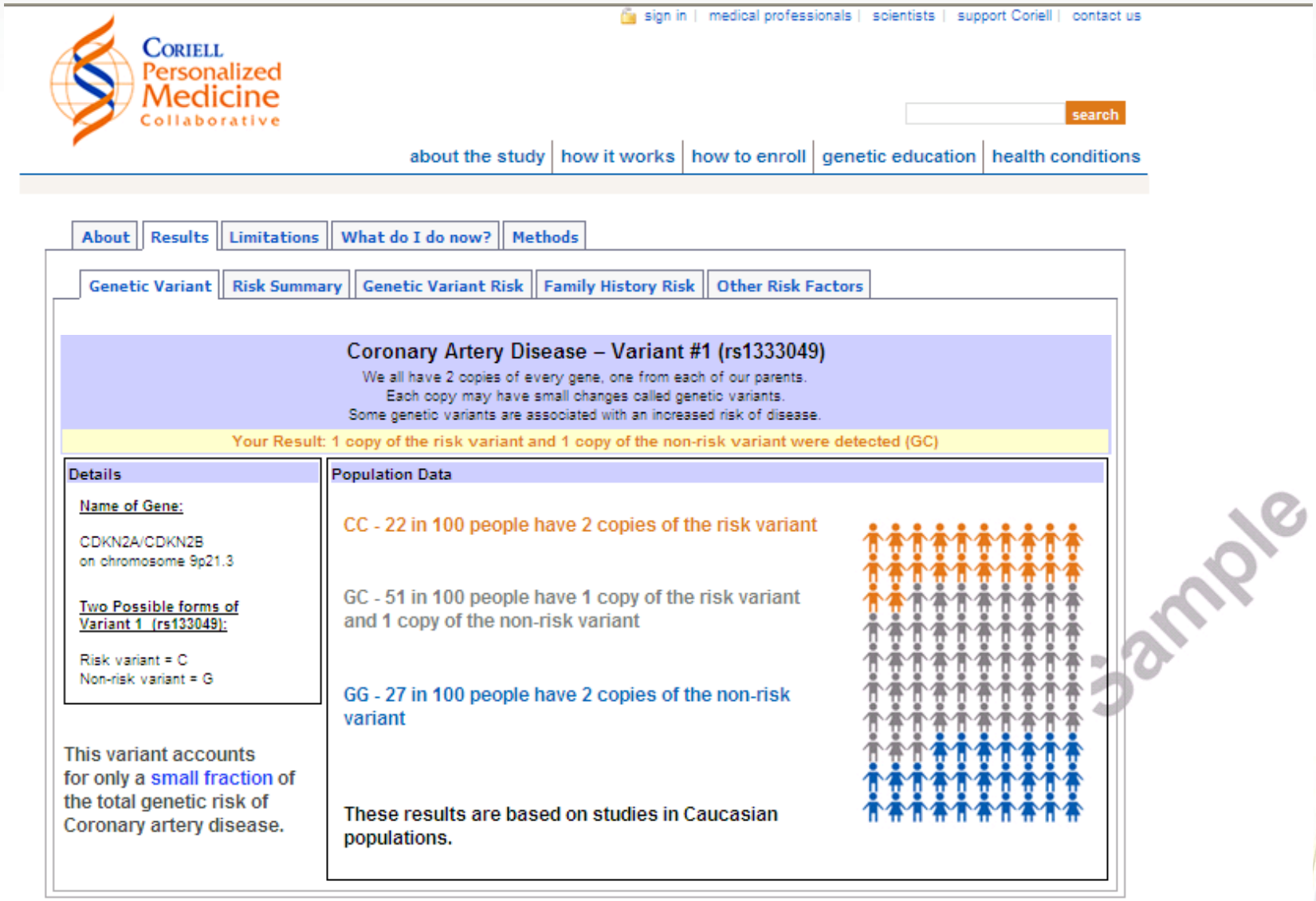
Type 1 diabetes, and Type 2 diabetes

CORIELL.ORG


http://cpmc.coriell.org
sign in | community discussion | medical professionals | scientists | support Coriell | contact us | sample accounts
Coriell Personalized Medicine Collaborative
Welcomelane Doe
search
about the study | how it works | how to enroll | genetic education | health conditions | my account
My New Genetic Results
To view your PERSONAL result, click "View My Result."
Type 2 Diabetes
rs7754840
Prostate Cancer
rs16901979
Age-Related Macular Degeneration
rs10490924
Melanoma
rs910873
Iron Overload/Hemochromatosis
rs1800562
View My Result
Do Not View My Result
Talk To Genetic Counselor First

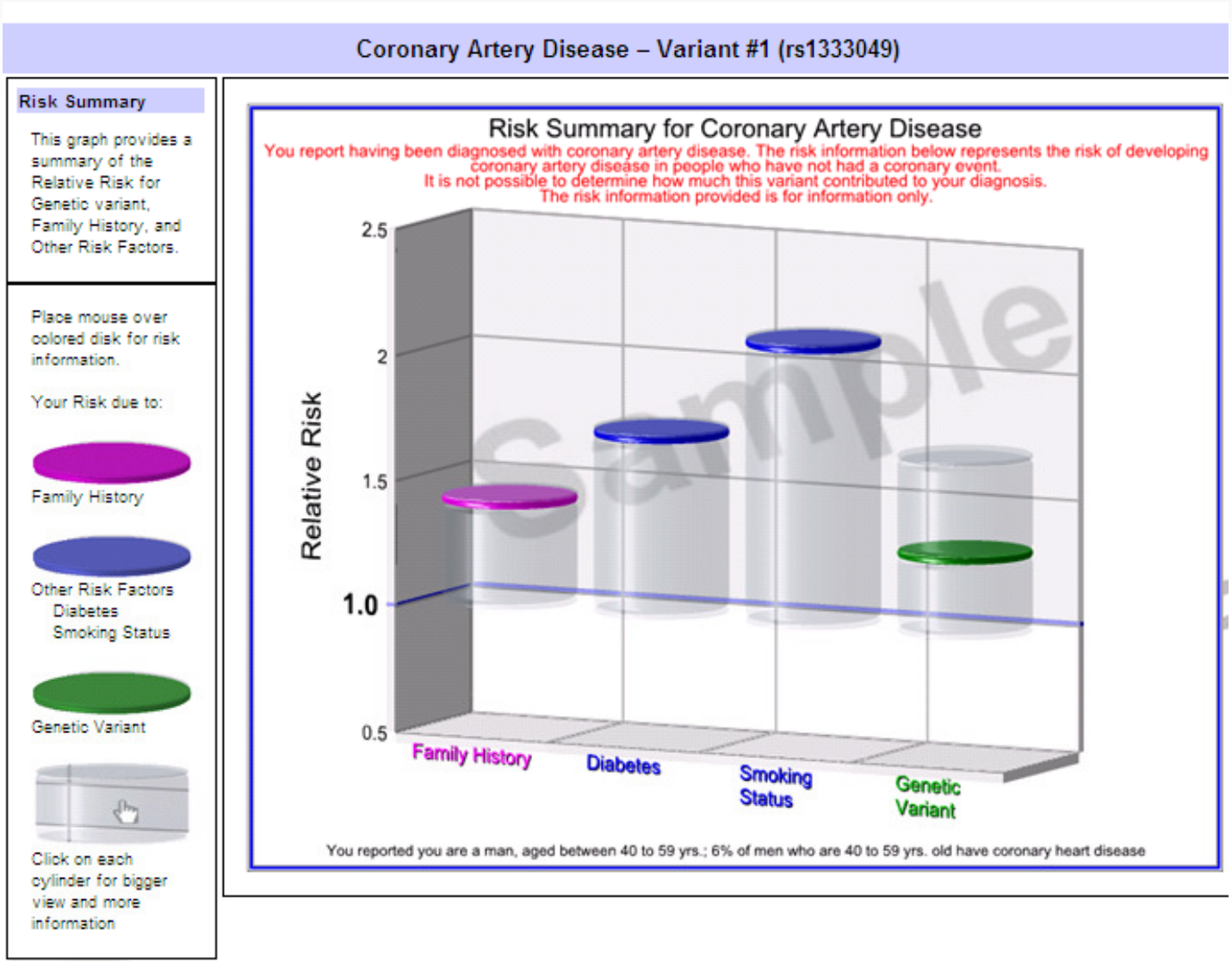
CORIELL.ORG

Demonstrating Variants to CPMC Participants



CORIELL.ORG

Genetic and Non-Genetic Risk Assessments: *Provided via CPMC Online Web Portal*



CORIELL.ORG

Coronary Artery Disease Surveys:
Provided via Portal at 3 and 12 months

CORIELL Personalized Medicine Collaborative

sign in | medical professionals | scientists | support Coriell | contact us

search

about the study | how it works | how to enroll | genetic education | health conditions

how it works

- Informed Consent
- Saliva Collection
- Genetic Testing
- Genetic Results
- Sharing My Results
- Outcomes Research

Outcomes Research

Your Ongoing Participation is Important to Us

The CPMC research study is a longitudinal study that will continue for a minimum of 5 years. This means that we will stay in contact with you as the study goes on to gather more data. Each year, you will be asked to update your medical history, family history and lifestyle information.

In addition, a few months after you view your genetic variant results, we will ask you to provide feedback through the web portal on whether and how you used the information.

Why are we asking so many questions? The goal of the CPMC™ is to understand how you use your personalized genetic information and if you use this knowledge to improve your health. By telling us whether and how you used your genetic results, you will help us achieve this goal.

So, from the CPMC™ team, thanks for your participation in this important project!

CORIELL.ORG

Coronary Artery Disease: Outcome Survey

Respondent Characteristics	N = 472	%
Mean Age 51 years		
Female	315	68.9
Caucasian	433	94.8
Bachelors Degree or higher	328	71.7
Occupation		
Healthcare providers (all)	122	26.7
Life, Physical, Social Scientists	24	5.3
All other Occupations	311	68.1

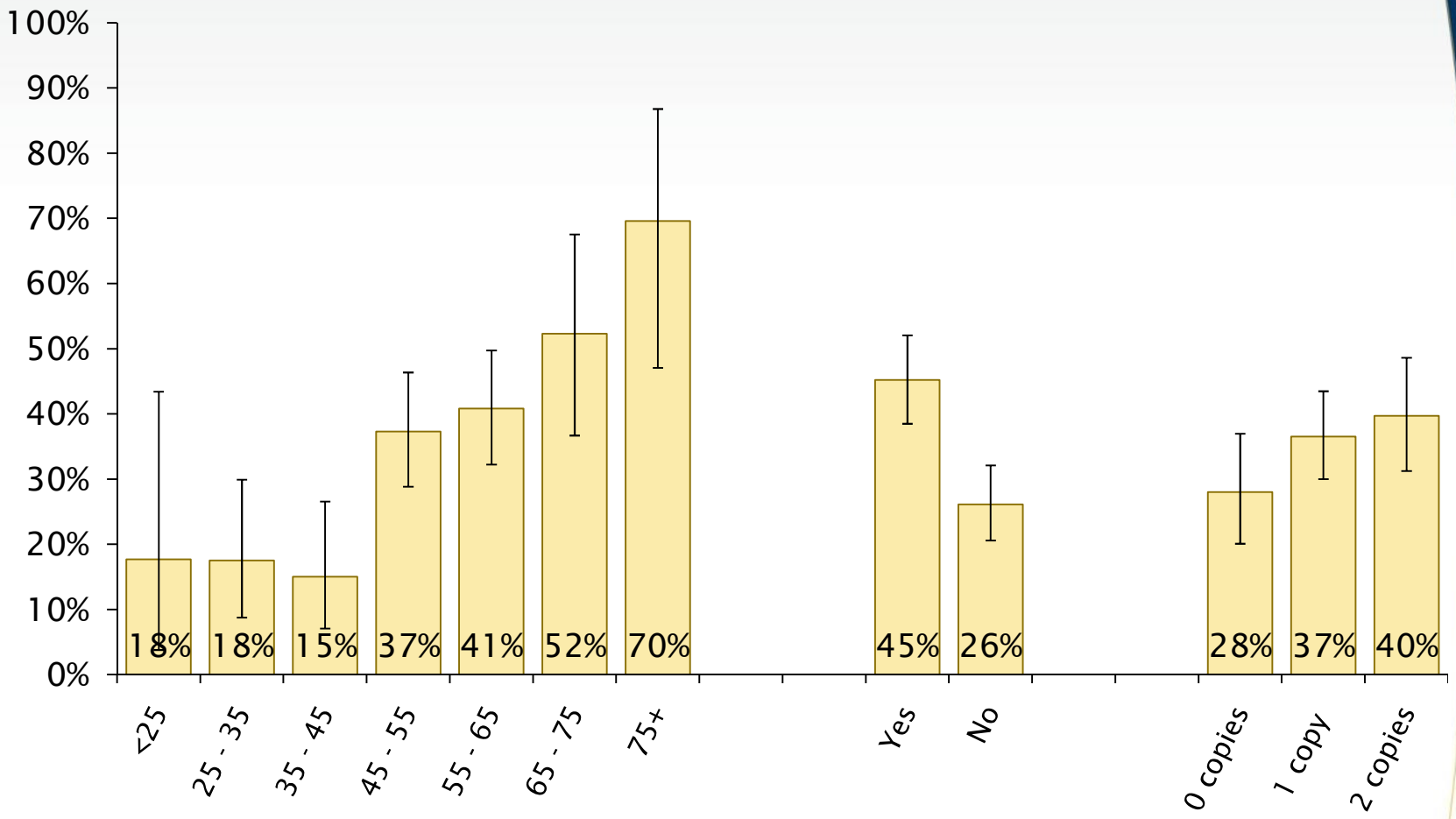
Coronary Artery Disease: Outcome Survey …cont'd:

Distribution of Participants by Number of CAD Risk Factors	N = 430	%
No Risk Factors	55	12.8
One Risk Factors	197	45.8
Two Risk Factors	161	37.4
Three - Four Risk Factors	17	4.0
Participants reporting somewhat/very high perceived risk		
No Risk Factors	1 / 55	1.8
One Risk Factor	63 / 197	32.0
Two Risk Factors	75 / 161	46.6
Three to Four Risk factors	14 / 17	82.4

Outcomes by Risk Group

Tests/Procedures received since receiving CPMC CAD results:		
Electrocardiogram	95	20.8%
Echocardiogram	42	9.2%
Stress Test	31	6.8%
Nuclear Stress Test	17	3.7%
Electron Beam CT	5	1.1%
MRA	4	0.9%
Balloon angioplasty and stent placement	2	0.4%
Other	34	7.4%
Don't Know	2	0.4%
No tests or procedures	296	64.8%

Tests or Procedures by Risk Group



Tests received associated with age and positive family history of CAD. No strong association between genotype and tests received.

CORIELL.ORG

Members: Pharmacogenomics Advisory Group (PAG)

Marialice Bennett, BS, RPh
Ohio State University, OH

Art Caplan, Ph.D.
University of Pennsylvania, PA

Michael D. Ezekowitz, MBChB, DPhil, FRCP, FACC
Thomas Jefferson University, PA

David A. Flockhart MD, Ph.D.
Indiana University School of Medicine, IN

Andrew Godwin, Ph.D.
Fox Chase Cancer Center, PA

Amalia M. Issa, Ph.D., MPH
College of Pharmacy, University of Houston Methodist Hospital Research Inst., TX

Teri Klein, Ph.D.
Stanford University, CA

Calvin H. Knowlton, Ph.D.
RevolutionCare, Inc., NJ

Howard L. McLeod, Pharm.D
University of North Carolina, NC

Michael F. Murray, MD
Brigham and Women's Hospital, MA

Steven A.R. Murphy, MD
The Personalized Medicine Group, CT

Michael Phillips, Ph.D.
Pharmacogenomics Centre, Quebec

Wolfgang Sadée, Ph.D.
Ohio State University College of Medicine, OH

Issam Zineh, PharmD, MPH
US Food and Drug Administration, MD

CORIELL.ORG

Strength of Evidence Code

Table 1. PGx gene haplotype category assignments based on strength of evidenc for drug interaction phenotype

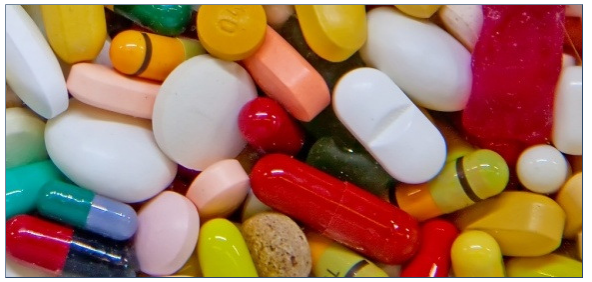
Evidence type	Evidence code	Category type
In vivo clinical outcome for reference drug	1	include
In vivo PK/PD for reference drug	2	include
In vitro enzyme activity for reference drug	3	include
In vitro enzyme activity with probe substrate plus mutation type (n, sb, se, ca)	4n or 4scd or 4se or 4ae	include
In vivo clinical outcome with another drug plus mutation type (n, sb, se, ca)	5n or 5scd or 5se or 5ae	include
In vivo PK/PD for another drug plus mutation type (n, sb, se, ca)	6n or 6scd or 6se or 6ae	include
In vitro enzyme activity with another drug plus mutation type (n, sb, se, ca)	7n or 7scd or 7se or 7ae	include
In vitro enzyme activity with probe substrate only	8	exclude
In vivo clinical outcome with another drug only	9	exclude
In vivo PK/PD for another drug only	10	exclude
In vitro enzyme functional (protein stability or enzyme activity with another drug) only	11	exclude
In vitro or in vivo data does not support functional role	12	exclude
No *in vitro* or *in vivo* data	13	exclude
Genotype frequency data suggestive of "private mutation". A private mutation is defined as a genetic variant found in a single individual or single family without being observed in reference populations.	14	exclude

PK=pharmacokinetic;
PD=pharmacodynamic;
n=null mutation;
scd=mutation located in known important substrate-binding or catalytic domain;
se=mutation leading to splicing error;
ae=mutation leading to altered gene expression.

- *Review in vivo PK/PD evidence or in vitro functional analysis supporting effect on protein function (e.g. enzymatic activity, plasma concentrations, etc.), if available.*
- *Review clinical outcome data supporting drug metabolizing phenotype, including adverse events or reduced efficacy.*

CORIELL.ORG

American Pharmacists Association



CORIELL
Personalized
Medicine
Collaborative

CORIELL.ORG

Minority Participation and Outreach

United States Senator Robert Menendez

Senator Menendez delivers remarks at the Coriell Institute for Medical Research to encourage New Jerseyans to participate in this groundbreaking genome research project which aims to benefit individuals suffering from diseases.

CORIELL.ORG

Potential CPMC Study Outcomes

- *Participant Behavior*
- *Physician Behavior*
- *Adverse Drug Reactions*
- *Pharmacogenomic Efficacy*
- *Clinical Outcomes*

CORIELL Personalized Medicine Collaborative

CORIELL.ORG

CPMC Partnerships and Collaborations

Baseline Genetic Knowledge:
Survey Results

- *15 Questions*
- *2,189 participants completed survey*
- *Mean of 76% correct answers*
- *ANOVA model adjusted for multiple participant*
- *Characteristics shows:*
  - *—Age inversely associated with correct responses ($p<0.001$)*
  - *—No association between income and correct responses ($p=0.74$)*

CORIELL.ORG

Ancillary Studies

CPMC Participant Behavior Upon Receiving Genome Info (Barbara Bernhardt and Reed Peyritz at Penn)

- ***Assess motivations to participate*** *in the CPMC and perceptions of the utility of personalized medicine*

  Recruit potential "early adopters" to complete an anonymous survey from among those who sign up to attend a CPMC enrollment event

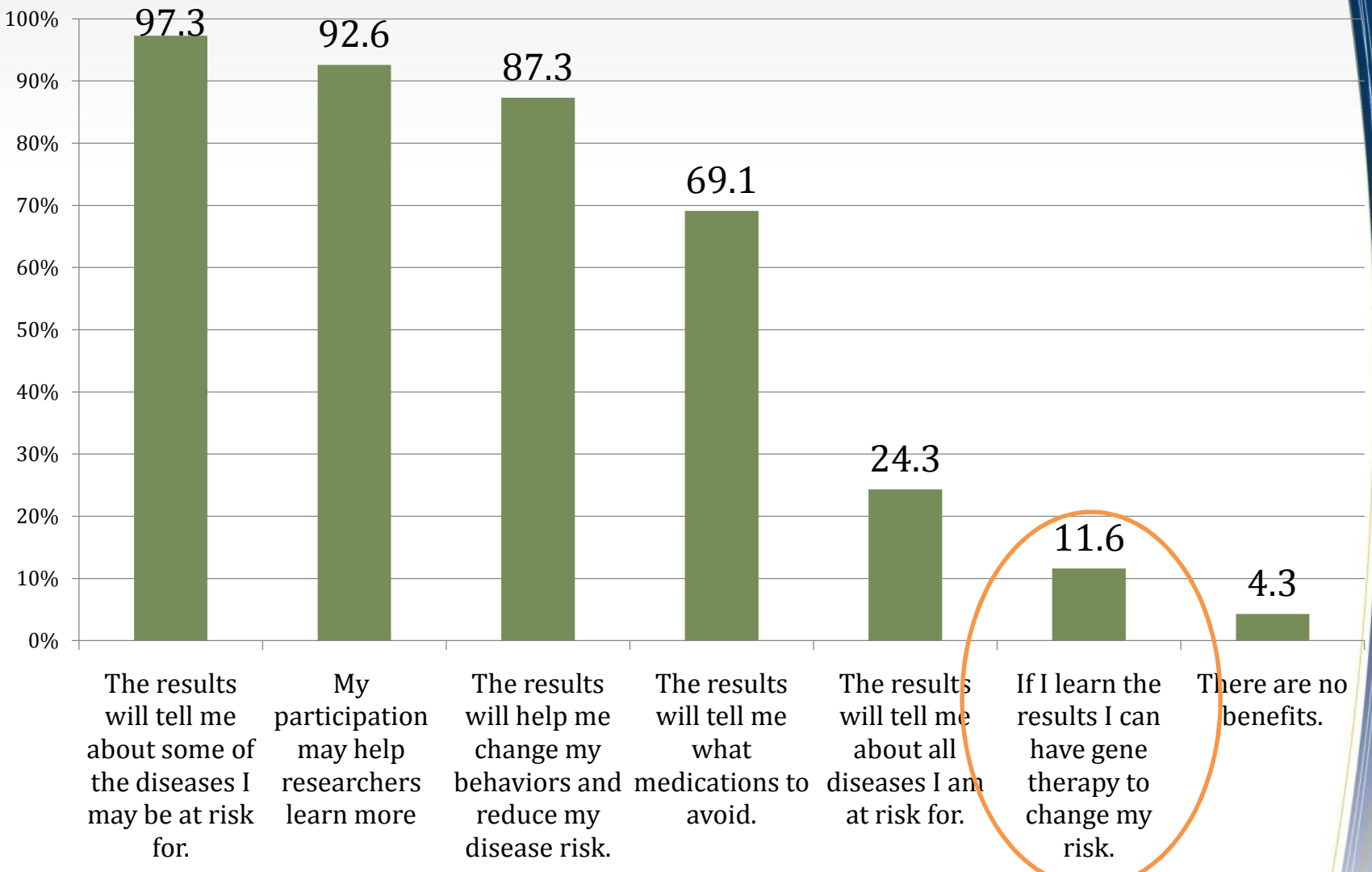
- ***Explore participant understanding*** *of personalized genomic disease risk results, intended and actual use of information and educational needs of individuals receiving results*

  Interview with CPMC participants (n=60)

- ***Develop possibly recommendations*** *for the ethical offering of personalized genomic disease risk assessment*

CORIELL.ORG

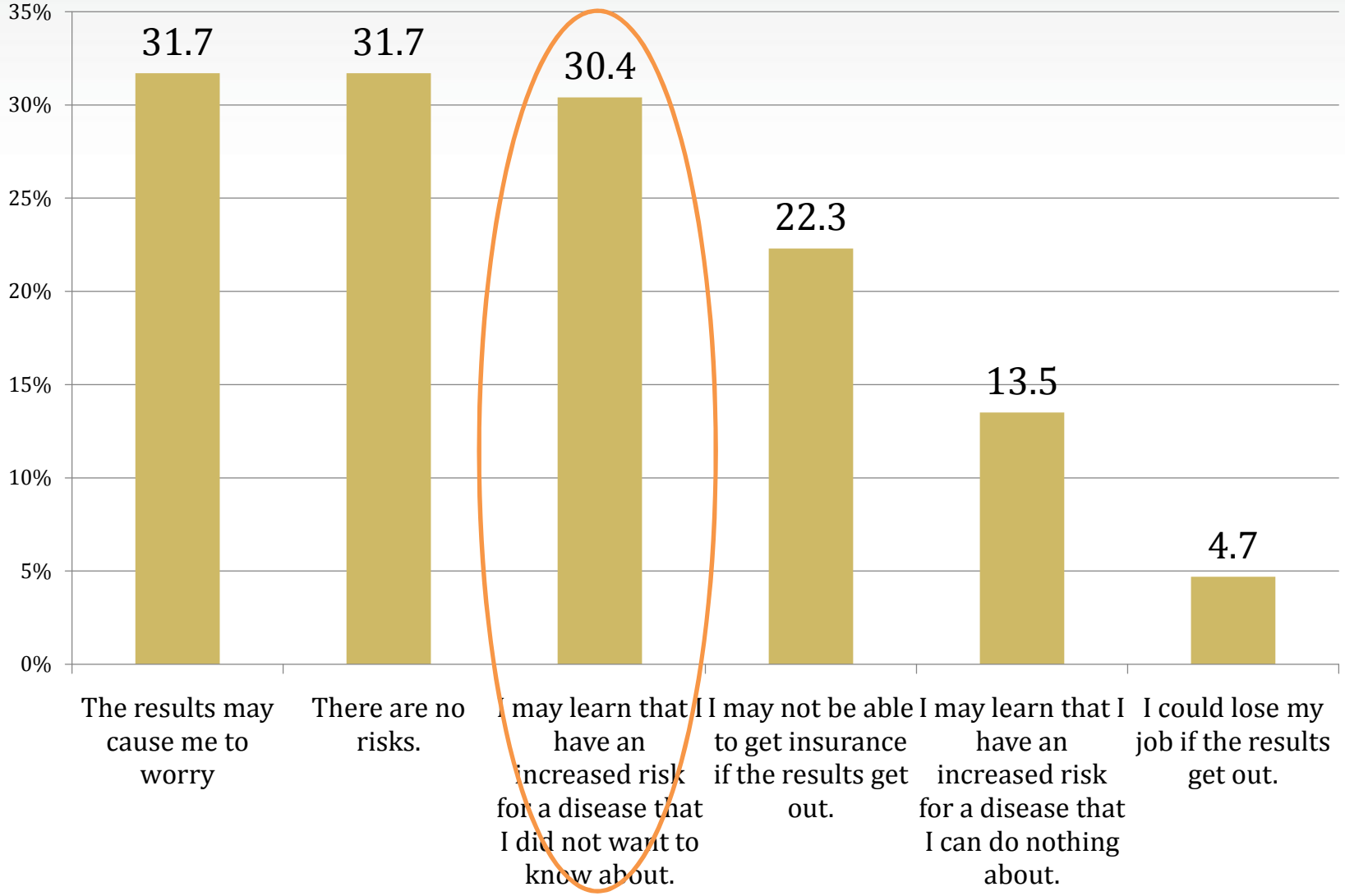
Perceptions of Benefits of CPMC



% agreeing or strongly agreeing

CORIELL.ORG

Perceptions of Risks of CPMC



% agreeing or strongly agreeing

CORIELL.ORG

CPMC at OSUMC

- Patient Participants (n=1800)
  - *–Congestive heart failure patients*
  - *–Hypertensive patients*

- Physician Participants (n=30)
  - –Cardiologists
  - –Primary care physicians

CORIELL.ORG

CPMC at OSUMC

- *Study Design (patients)*

  Patients will be identified through enrolled physicians

  Patients who consent will complete MFLQ and baseline assessment (risk perception, numeracy assessment, etc)

  Patients will be randomized to in person genetic counseling or no counseling (participants in no GC arm will have access to CPMC genetic counselors for urgent questions)

  Follow up assessment of risk perception, understanding of results, satisfaction, information seeking, etc

  Analysis of impact of genetic counseling in genomic testing

CORIELL.ORG

CPMC at OSUMC

- *Exploratory Aims (Pharmacogenomics)*

  To determine if genetic data are effective at differentiating congestive heart failure (CHF) responders from non-responders

  To compare disease progression/negative outcomes between CHF responders and non-responders

  To determine if genetic data are effective at predicting which newly diagnosed hypertensive patients will require modifications and/or additions to their initial treatment

CORIELL.ORG

Observational Data Can Be Useful

CORIELL.ORG

Exploring Best Practices:
Guiding the ethical, legal and responsible implementation of personalized medicine

- *Study participants control information*
- *Genetic counseling offered*
- *Report quantitative non-genetic risk*
- *Web portal provides two way communication with participants*
- *ICOB provides dynamic reassessment of genomic data*
- *Report on only "potentially actionable" conditions*
- *Seek expert advice on actionability (ICOB, PAG)*

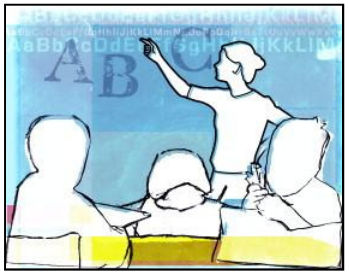
CORIELL.ORG

Big Picture:
Ethical, Legal and Social Issues

- *Ensuring genetic privacy*

- *Reducing anxiety associated with genetic prognosis*

- *Updating medical record technology*

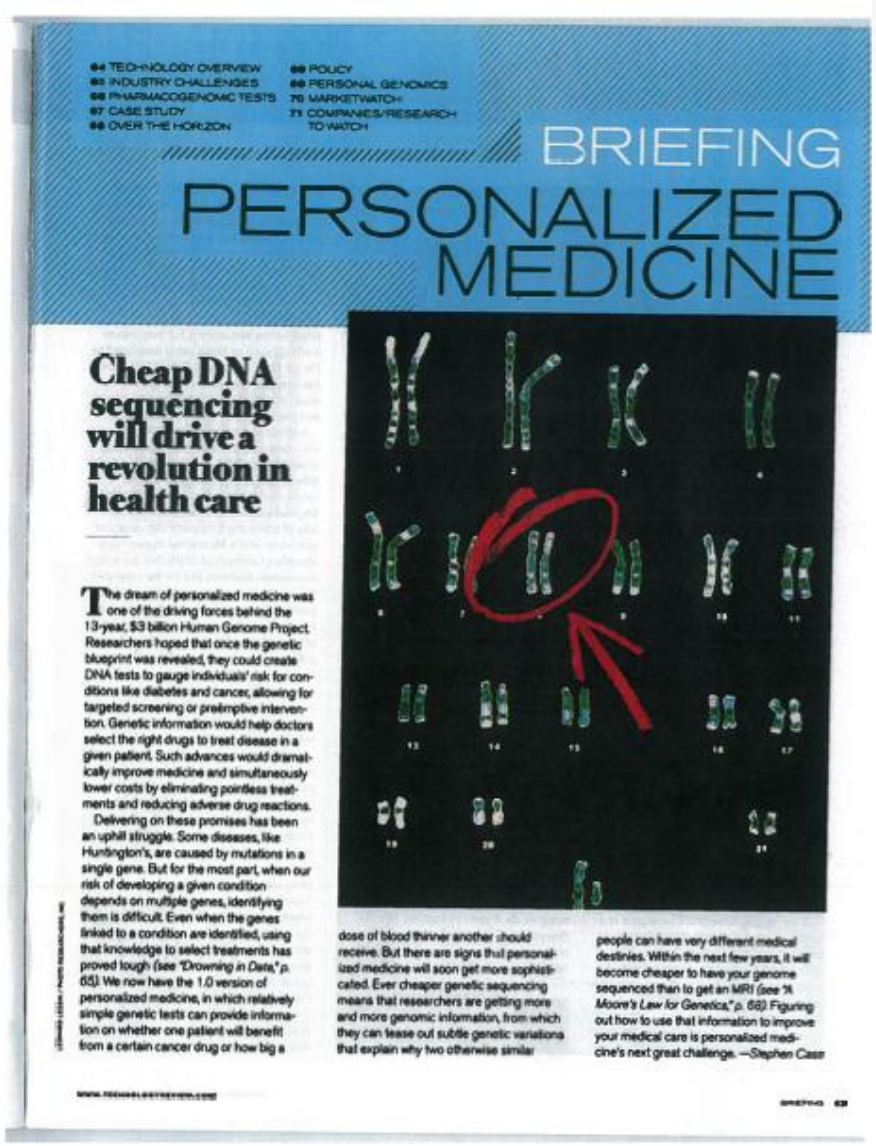


- *Educating the community, doctors, nurses, pharmacists, and genetic counselors*

- *Payors likely to drive clinical adoption*

CORIELL.ORG

MIT Technology Review 2010



64 TECHNOLOGY OVERVIEW
65 INDUSTRY CHALLENGES
66 PHARMACOGENOMIC TESTS
67 CASE STUDY
68 OVER THE HORIZON
69 POLICY
69 PERSONAL GENOMICS
70 MARKETWATCH
71 COMPANIES/RESEARCH TO WATCH

BRIEFING

PERSONALIZED MEDICINE

Cheap DNA sequencing will drive a revolution in health care

The dream of personalized medicine was one of the driving forces behind the 13-year, $3 billion Human Genome Project. Researchers hoped that once the genetic blueprint was revealed, they could create DNA tests to gauge individuals' risk for conditions like diabetes and cancer, allowing for targeted screening or preemptive intervention. Genetic information would help doctors select the right drugs to treat disease in a given patient. Such advances would dramatically improve medicine and simultaneously lower costs by eliminating pointless treatments and reducing adverse drug reactions.

Delivering on these promises has been an uphill struggle. Some diseases, like Huntington's, are caused by mutations in a single gene. But for the most part, when our risk of developing a given condition depends on multiple genes, identifying them is difficult. Even when the genes linked to a condition are identified, using that knowledge to select treatments has proved tough (see "Drowning in Data," p. 65). We now have the 1.0 version of personalized medicine, in which relatively simple genetic tests can provide information on whether one patient will benefit from a certain cancer drug or how big a dose of blood thinner another should receive. But there are signs that personalized medicine will soon get more sophisticated. Ever cheaper genetic sequencing means that researchers are getting more and more genomic information, from which they can tease out subtle genetic variations that explain why two otherwise similar people can have very different medical destinies. Within the next few years, it will become cheaper to have your genome sequenced than to get an MRI (see "A Moore's Law for Genetics," p. 66). Figuring out how to use that information to improve your medical care is personalized medicine's next great challenge. —Stephen Cass

Top 10 "Research To Watch"

April 2010

CORIELL.ORG

CORIELL INSTITUTE

FOR MEDICAL RESEARCH

CORIELL
Personalized
Medicine
Collaborative

http://cpmc.coriell.org
cpmc@coriell.org

403 HADDON AVENUE, CAMDEN, NJ 08103 | CORIELL.ORG