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Public Health Applications of Genomics

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April 18, 2012



Financial Disclosures

No financial interests that would influence the content of this presentation

Today's talk

- Translation research to understand Public Health applications of genomics needed.
- Principles of public health
- Social and behavioral research methods
- Examples of priority areas and translation research
- Take home messages

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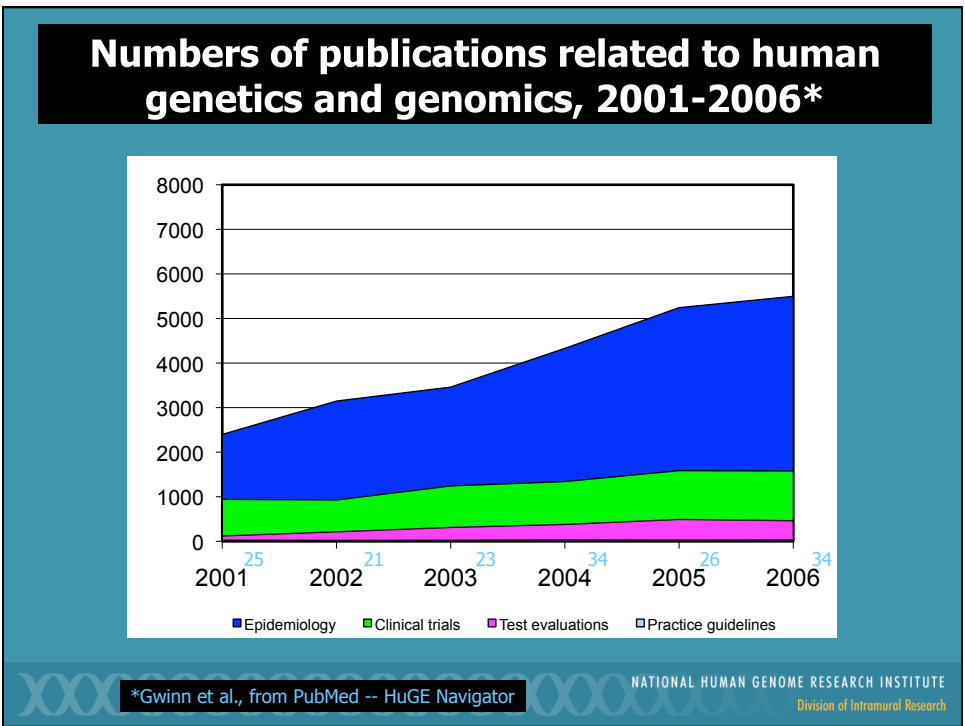
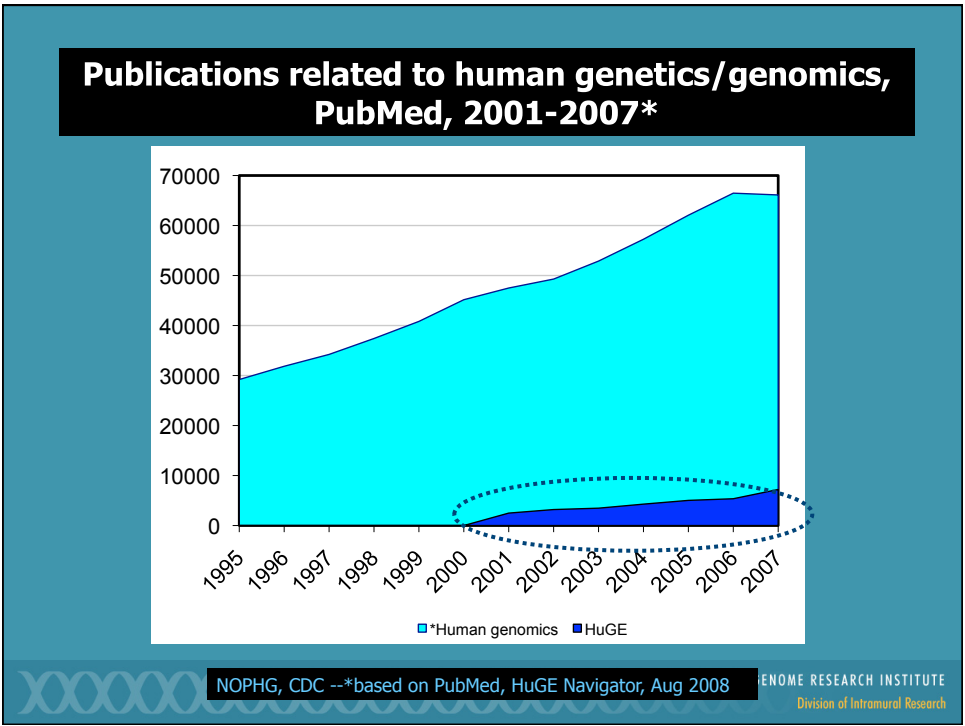
Genomic discovery



Hokusai Great Wave



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Challenge [^] Assumed Path to Translation

Trailblazing

- **Stage 5: Consider existing health challenges/unmet needs**
- **Stage 5: Anticipate how discovery could address challenges**
- **Stage 1:** Basic Research
- **Stage 2:** "Treatment" Development
- **Stage 3/4:** Efficacy/Effectiveness


T1 From Gene Discovery to Health Application	T2 From Health Application to Evidence-based Guideline	T3 From Guideline to Health Practice	T4 From Practice to Health Impact
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Genomic Translation: research agenda


Optimal application

Lost in translation



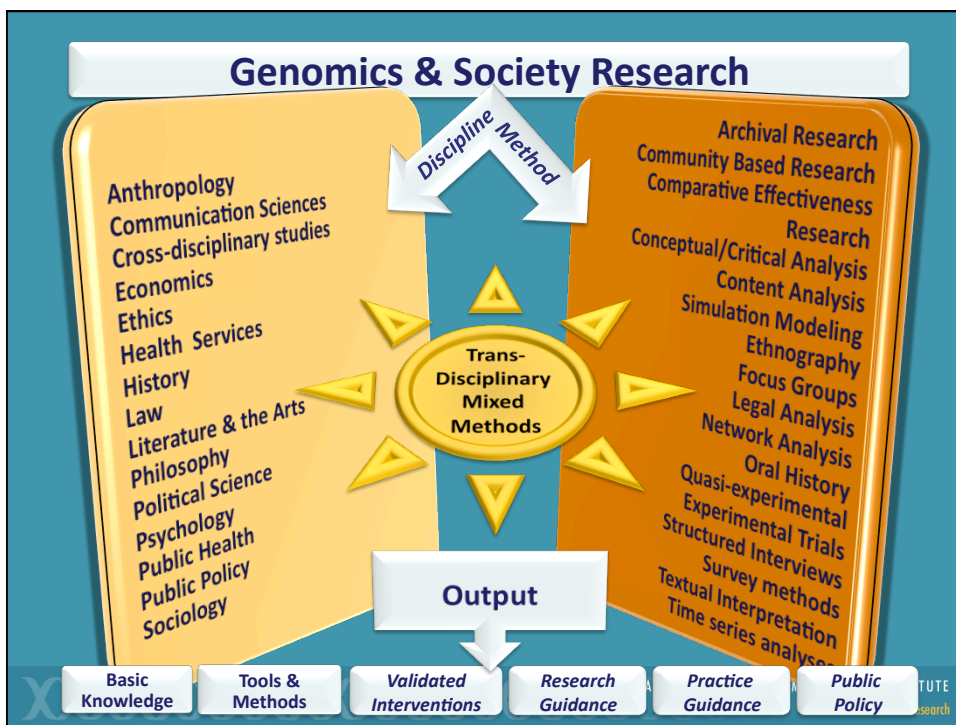
Premature translation





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The image shows a screenshot of the Pathway Genomics website and a snippet of a Washington Post article. The website header includes the logo and tagline "YOUR FUTURE. Only Better!". Below the header is a navigation menu with links for HOME, HOW IT WORKS, MORE INFO, PRODUCTS, PARTNERS, and ABOUT US. The main content area features a large image of a family (a man, a woman, and a child) with the text "Your Personal DNA Report". Below this image is a testimonial: "Our DNA results provided us peace-of-mind. We've already taken action to reduce our risks!". In the foreground, there is an image of the Pathway Genomics DNA test kit, which is a small black box with a blue circular component. To the right of the website screenshot is a snippet of a Washington Post article titled "Walgreens won't sell genetic test over FDA objections" by Rob Stein. The article discusses the FDA's objections to the test and Walgreens' decision to not sell it.



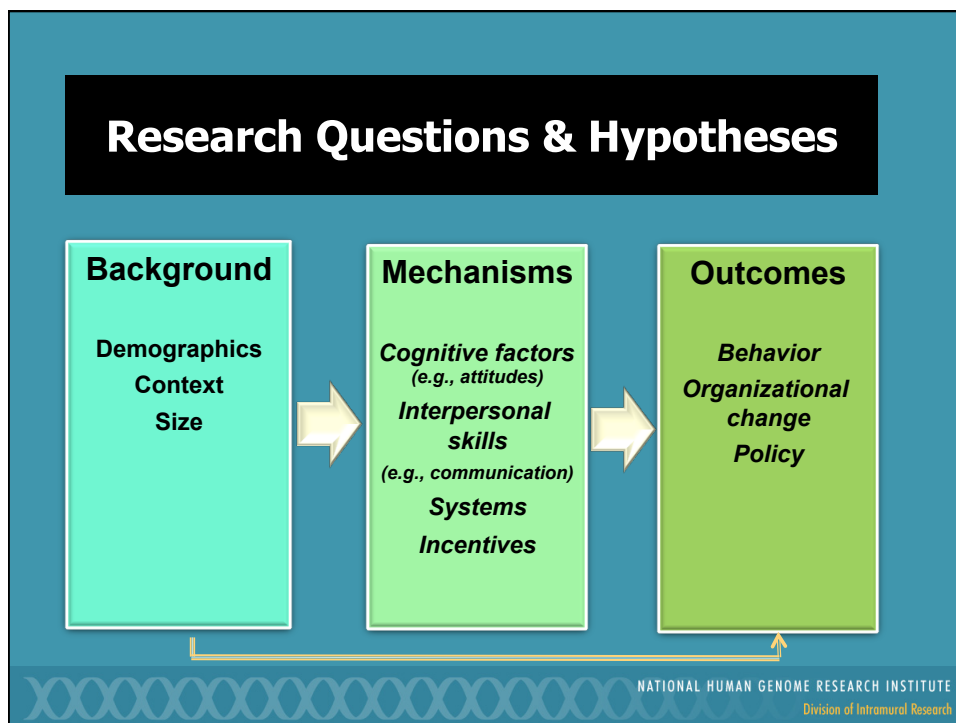
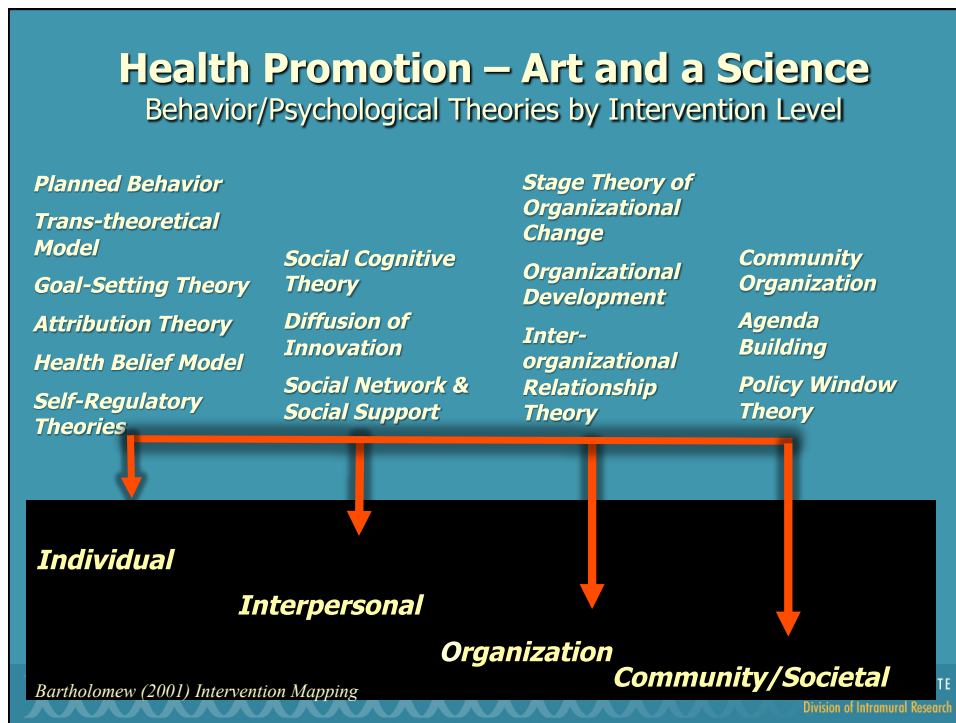
What is an intervention?

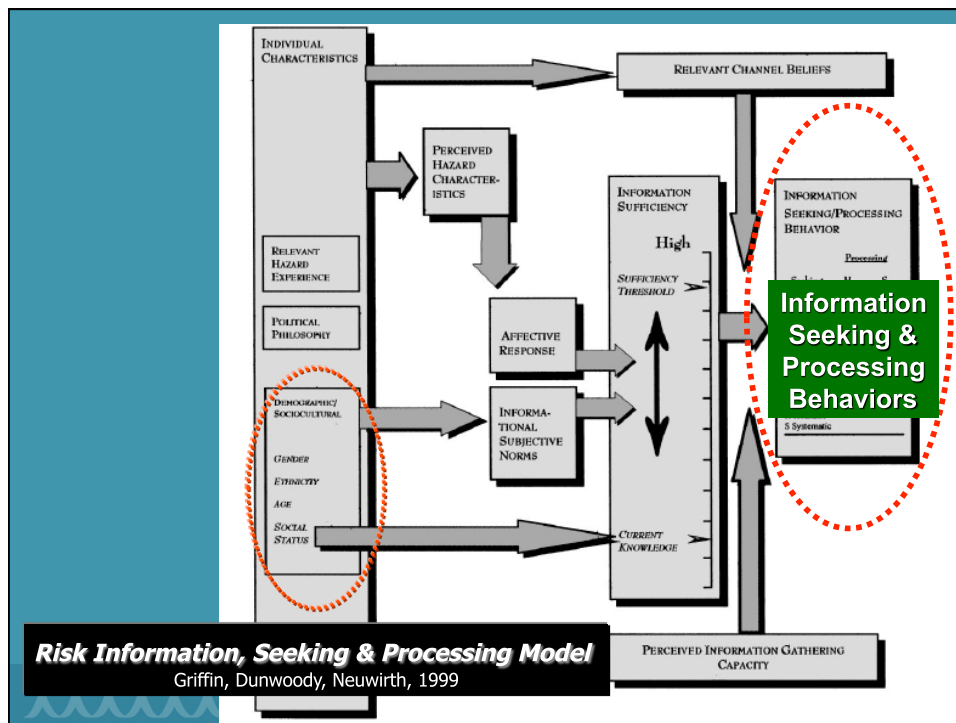
Efforts directed at a target group to influence a desired outcome:

- Informed decision-making
- Individual or group behavior change
- Individual or group attitude change
- Public policy change

Intervention Objectives at the Intersection of Genetic Applications

Primary Prevention	<i>Healthy populations to prevent illness & injury</i>	<i>Susceptibility testing</i>
Secondary Prevention	<i>Early detection, testing, hazard surveillance</i>	<i>Predictive testing of high risk groups, newborn screening</i>
Tertiary	<i>Those with disease conditions & injuries</i>	<i>Assisting those affected – e.g., living with rare conditions</i>





Public Health Applications

Reducing common chronic disease

- Prevention is key
- Decrease risk behaviors
- Public health & primary care
- Genomic information add value?
- Widespread health disparities

Future Health Applications of Genomics Priorities for Communication, Behavioral, and Social Sciences Research

Colleen M. McBride, PhD, Deborah Bowen, PhD, Lawrence C. Brody, PhD,
 Coleste M. Condit, PhD, Robert T. Croyle, PhD, Marta Gwinn, MD,
 Muin J. Khoury, MD, PhD, Laura M. Koehly, PhD, Bruce R. Korf, MD, PhD,
 Theresa M. Marteau, PhD, Kenneth McLeroy, PhD, Kevin Patrick, MD, MS,
 Thomas W. Valente, PhD

Abstract: Despite the quickening momentum of genomic discovery, the communication, behavioral, and social sciences research needed for translating this discovery into public health applications has lagged behind. The National Human Genome Research Institute held a 2-day workshop in October 2008 convening an interdisciplinary group of scientists to recommend forward-looking priorities for translational research. This research agenda would be designed to redress the top three risk factors (tobacco use, poor diet, and physical inactivity) that contribute to the four major chronic diseases (heart disease, type 2 diabetes, lung disease, and many cancers) and account for half of all deaths worldwide. Three priority research areas were identified: (1) improving the public's genetic literacy in order to enhance consumer skills; (2) gauging whether genomic information improves risk communication and adoption of healthier behaviors more than current approaches; and (3) gauging whether genomic information improves risk communication and adoption of healthier behaviors more than current approaches. Multiple directions of genomic discovery, including (1) take an agnostic scientific perspective, research questions asking whether genomic discovery adds value to other health problems. The priorities and themes offer a framework for a variety of stakeholders, including public health practitioners, researchers, and policy makers grappling with how to use the products born of genomics research in preventive medicine.

PLoS Med 2010;5(5):e1000561 © 2010 Published by Elsevier Inc. on behalf of American Society for Preventive Medicine.

Public health research

Real World

Efficacious Intervention

Effectiveness

Efficacy

Reach

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Example: HNPCC Genetic counseling

<u>Current approach</u>	<u>Public Health approach</u>
<ul style="list-style-type: none">❖ High dose:<ul style="list-style-type: none">▪ 2-3 hour sessions❖ Resource intensive<ul style="list-style-type: none">▪ Certified genetic counselor▪ Face to face sessions❖ Demanding to sustain<ul style="list-style-type: none">▪ Few genetic counselors▪ Reimbursement lacking▪ Expensive❖ Highly efficacious<ul style="list-style-type: none">▪ Low reach	<ul style="list-style-type: none">❖ Low dose:<ul style="list-style-type: none">▪ < 1 hour❖ Resource light<ul style="list-style-type: none">▪ Implemented by clinic staff or health educators▪ Telephone, mail, internet❖ Sustainable<ul style="list-style-type: none">▪ Employ existing infrastructure▪ Inexpensive❖ Effectiveness is the goal<ul style="list-style-type: none">▪ Broad reach

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<u>Current approach</u>	<u>Public Health model</u>
• Efficacy = .80	▪ Efficacy = .20
• Reach = .10	▪ Reach = .50
• .80 x .10	▪ .20 x .50
• Effectiveness = .08	▪ Effectiveness = .10

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Table 1. Areas of emphasis for genomic translational research

Priority research areas
Public understanding and use of genomic information
Potential for genomics to improve risk communication and health behavior change
Using genomics and other emerging technologies to identify new behavioral intervention targets and more sensitive intervention outcomes
Crosscutting themes
The need to anticipate directions of genomic discovery
The importance of framing research questions based on the assumption that genomics innovation may or may not add value to either individual or population-level health outcomes
The importance of systems thinking and ecologic or multilevel modeling, and transdisciplinary collaborations

McBride, Bowen, Brody, Condit et al., 2010
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Public Understanding of Genomics

Supposition

Public will be exaggerate genetic contributions to common diseases & downplay behavioral contributors

Contact

The Multiplex Initiative

New Participants

Returning Participants

Health Care Providers | Researchers

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Multiplex Prototype Test

8 health conditions & 15 genes

- **Diabetes**
 - KCNJ11
 - CAPN10
 - PPARg
 - TCF7L2
- **Heart Disease**
 - APOB
 - NOS3
 - CETP
- **High Cholesterol**
 - LIPC
- **Hypertension**
 - AGT
- **Lung cancer**
 - MPO
- **Colon Cancer**
 - MTHFR
- **Skin Cancer**
 - MC1R
- **Osteoporosis**
 - ESR1
 - IL6
 - COL1A1

Original Paper

Public Health Genomics
 DOI: 10.1155/2009/236561

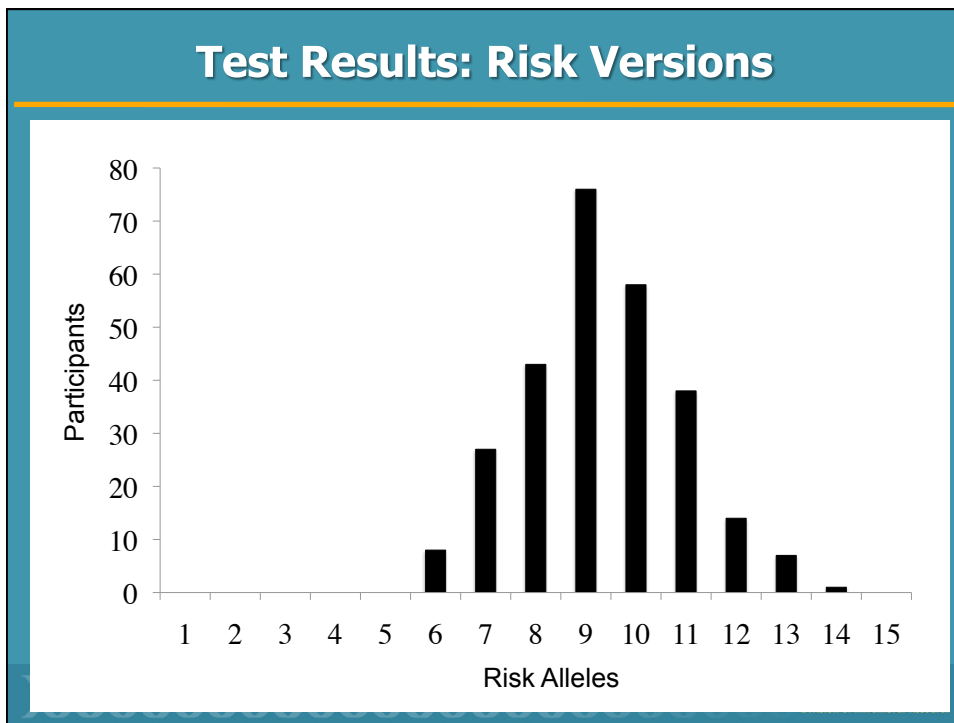
Received March 2, 2009
 Accepted after review May 13, 2009
 Published online September 3, 2009

Considerations for Designing a Prototype Genetic Test for Use in Translational Research

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Information About Genes

What is someone's chance of getting diabetes in th KCNJ11 risk versions?

- People who have **no risk versions** of KCNJ11 will h chance of getting diabetes.
- People who have **1 risk version** of KCNJ11 will hav chance of getting diabetes.
- People who have **2 risk versions** of KCNJ11 will ha chance of getting diabetes.

How common are the risk versions of KCNJ11?

- About 65% of people in the general public have **0 risk versions**.
- About 29% of people in the general public have **1 risk version**.
- About 6% of people in the general public have **2 risk versions**.

Percentage of People With 0, 1, or 2 Risk Versions of KCNJ11 in the General Public

Chance of getting diabetes based on the number of (Out of 100 people. People with diabetes are shown in red)

0 Risk Versions

1 Risk Version

2 Risk Versions

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Study Design

- **NCI-funded Cancer Research Network**
 - Henry Ford Health System clinical recruitment site
 - Group Health Cooperative Survey coordination
- **Sample: Healthy adults**
 - Ages 25-40
 - Without diseases on test battery

The Multiplex Initiative

This report will tell you whether you have versions of genes that raise your chances of getting some common health conditions.

My Results
And What They Mean

Overview of Your Results

You have one or more risk variants that raise your chances of getting:

- Heart Disease
- High Cholesterol
- High Blood Pressure
- Type 2 Diabetes
- Obesity
- Lung Cancer
- Colon Cancer
- Skin Cancer

Look inside and at the other information in the folder for more about what your results mean for your chances of getting the health conditions on the Multiplex Genetic Test.


Understanding Your Test Results

Remember these points when reading your test results:

1. Having risk versions of genes means that you are more likely to get the health conditions than people who do not have risk versions.
2. Most people will have between 4 and 10 risk versions of the genes on the Multiplex Genetic Test.
3. Having risk versions does not mean that you will certainly get any of these health conditions.

There's More to It Than Genes
You CAN Lower Your Risk

HEALTHY HABITS • ENVIRONMENT • GENES



Your chance of having these health conditions is also affected by:

1. Your health habits, such as diet, exercise and cigarette smoking.
For example: Being a cigarette smoker raises your chance of heart disease and raises your chance for cancer 10 times. Smoking is a much greater risk factor than having any of the risk versions of genes on the Multiplex Genetic Test. Having an above normal cholesterol level raises your chance of heart disease slightly more than having some of the risk versions of genes on the Multiplex Genetic Test. **Remember: You can act, change your genes but you can't change your health habits.**
2. Your family history of health conditions.
3. The environment you live in, which might have chemicals at work or secondhand cigarette smoke.
4. Other genes that were not tested on the Multiplex Genetic Test.

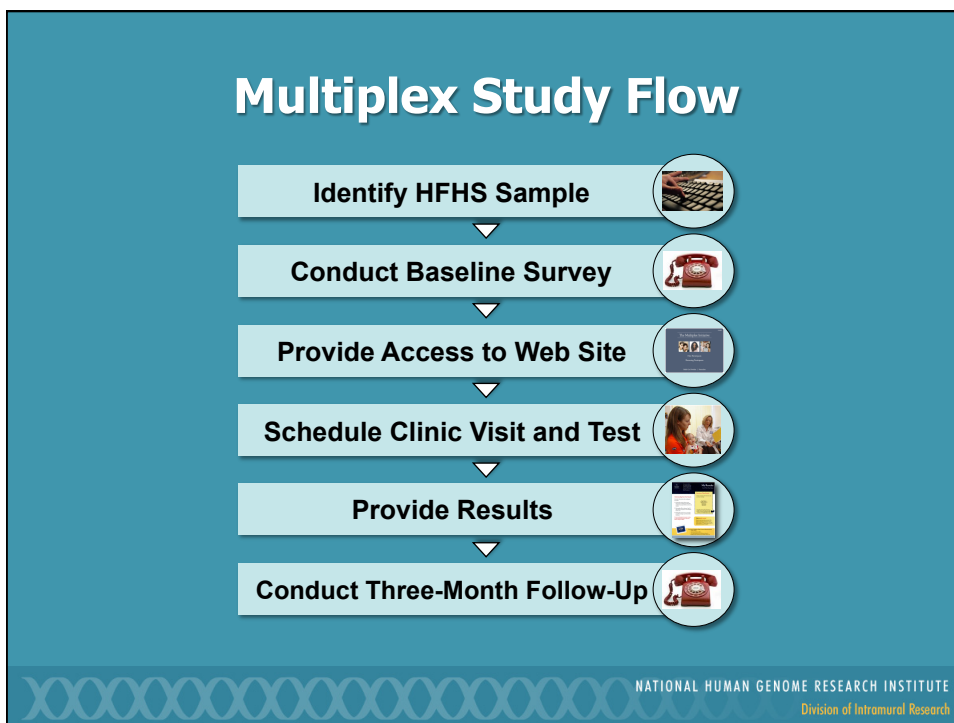
Here's what you can do to lower your chance of getting these health conditions: see matter what your test results were:

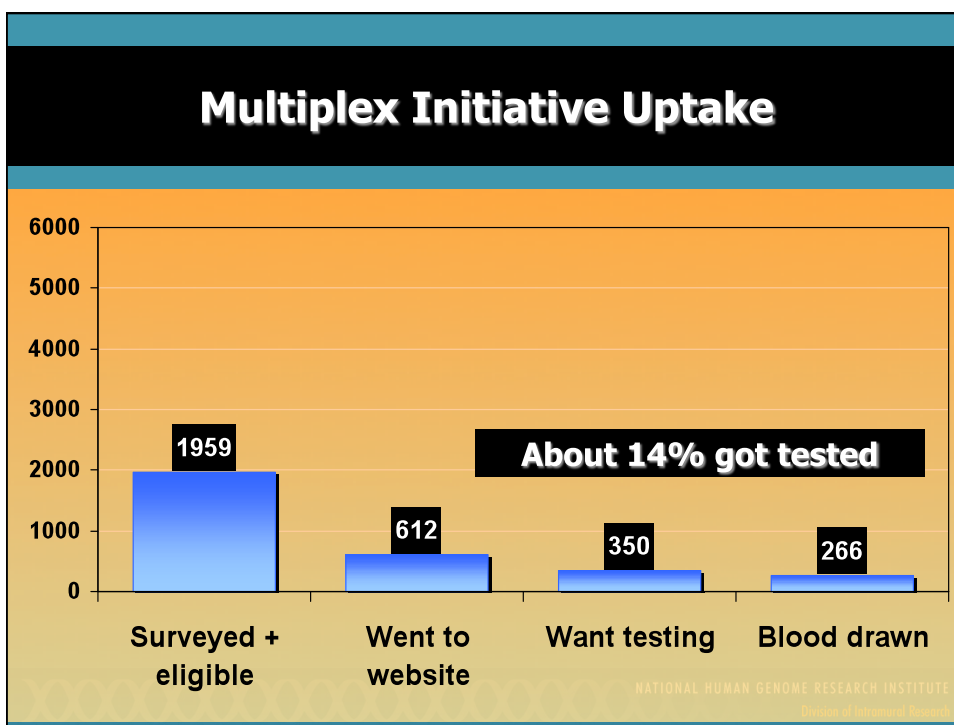
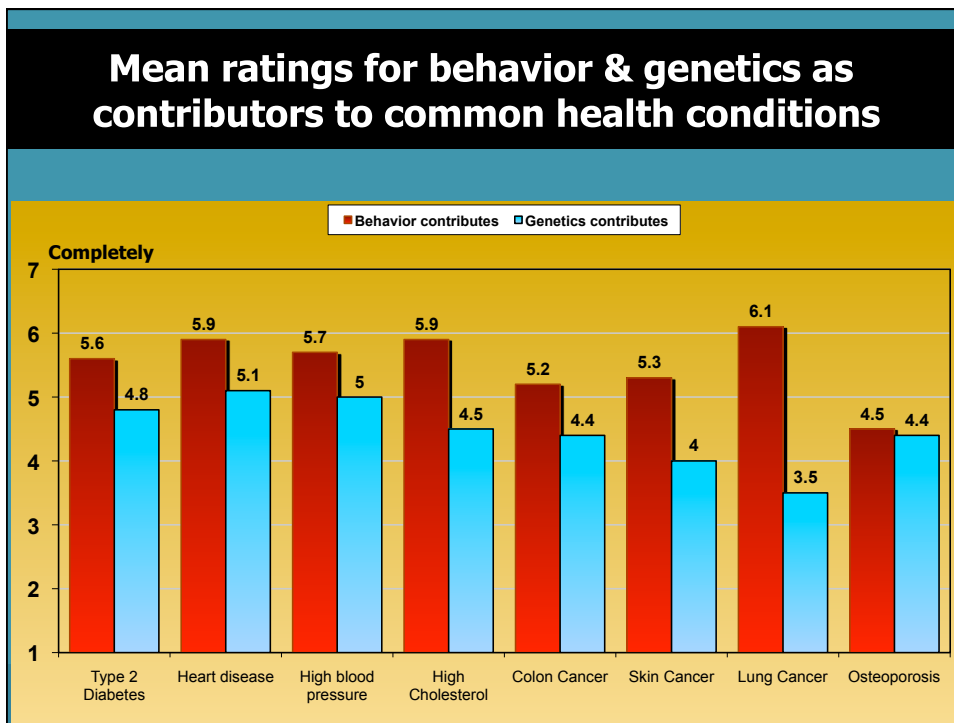
- ✓ Quit Smoking
- ✓ Maintain a healthy weight
- ✓ Eat 5 or more servings of vegetables & fruits every day
- ✓ Exercise for at least 30 minutes most days of the week
- ✓ Limit your time in the sun and use sunscreen
- ✓ See your doctor for a yearly check-up

See <http://multiplex.nhgri.nih.gov> to:

- Learn more about how to assess your disease risk, based on your current health habits.
- Learn more about how to do a family health history.
- Find information about how Henry Ford Health System can help you change your health habits.

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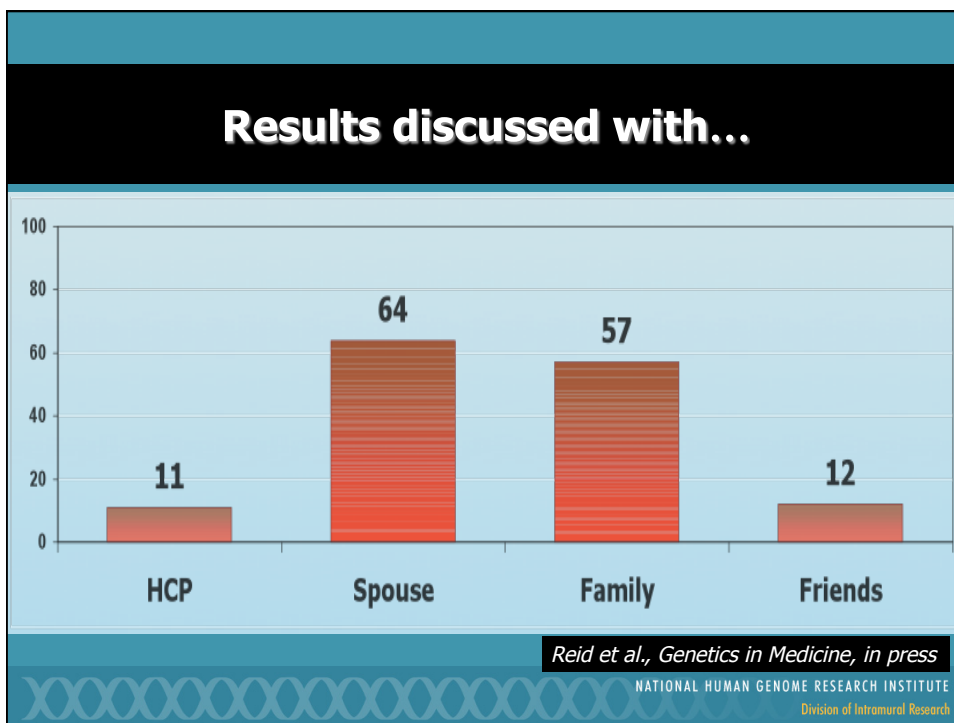


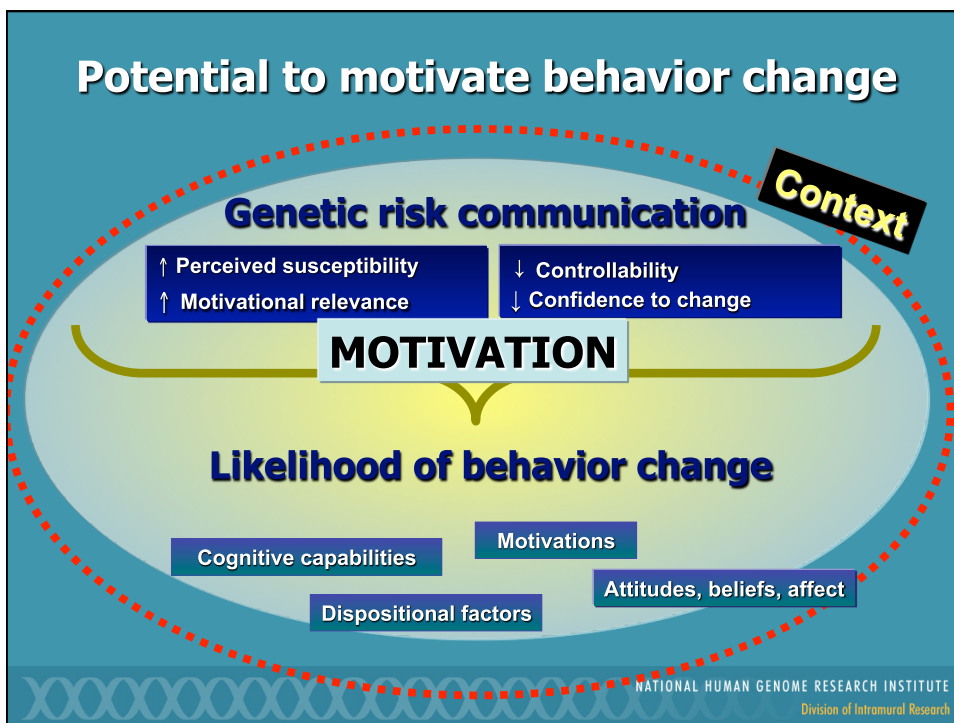
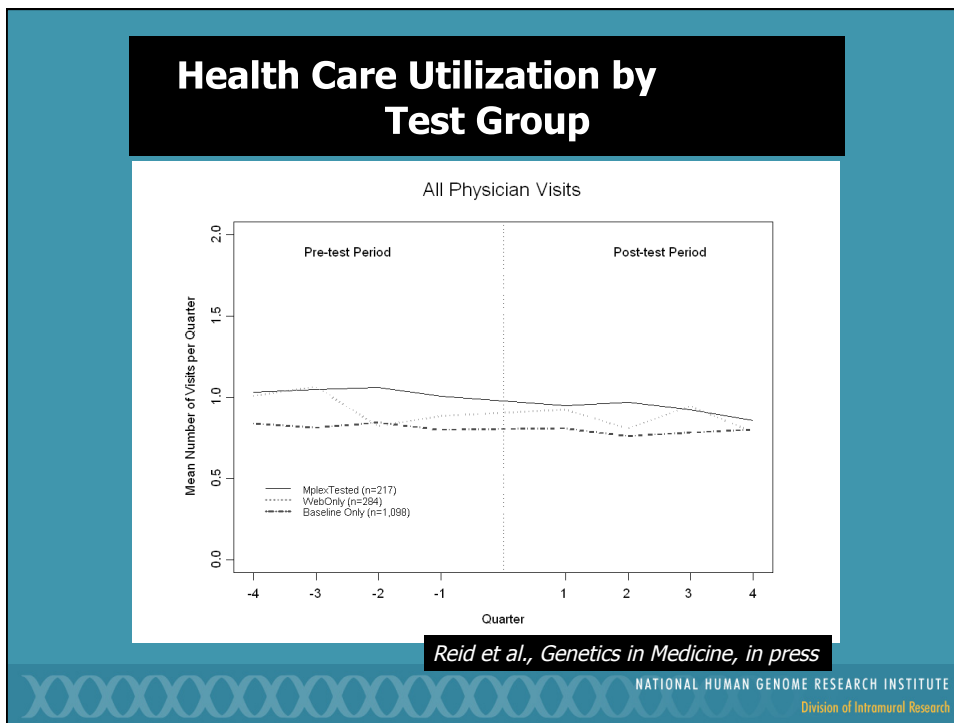
Web usage & decision outcomes

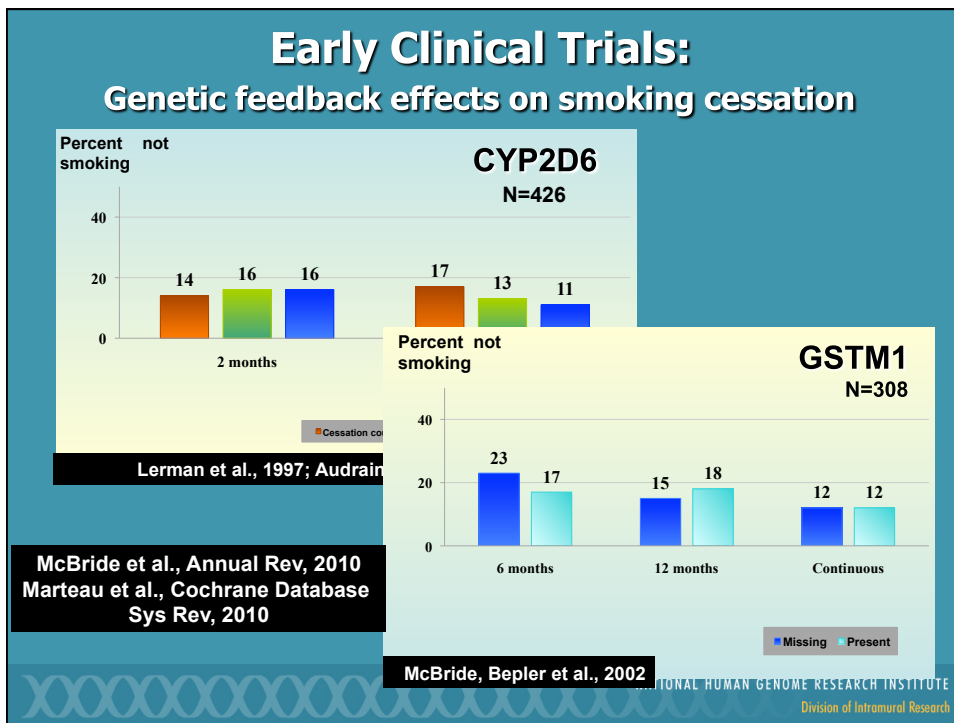
Kaphingst et al., J. of Med Internet Research, 2010

Predictors	Decide to test Odds ratio	Ease of decision Odds ratio
Pages viewed	1.08*	1.04*
Male gender	1.26	0.87
Age	1.03	0.99
Education		
HS or less	0.51*	0.81
Some college	1.04	0.74
Race		
White	1.65	1.00
Black	0.66	0.58
Marital status	0.91	0.96
Family history	1.10	0.94
Genetic self efficacy	1.24*	1.27*
Importance of genetic info	1.24*	1.18*

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Can genetic risk information motivate smokers to quit?

Welcome to the
 FAMILY RISK AND LUNG CANCER STUDY

Thank you for Participating!

NEXT

Which smokers visited the website to consider genetic testing?

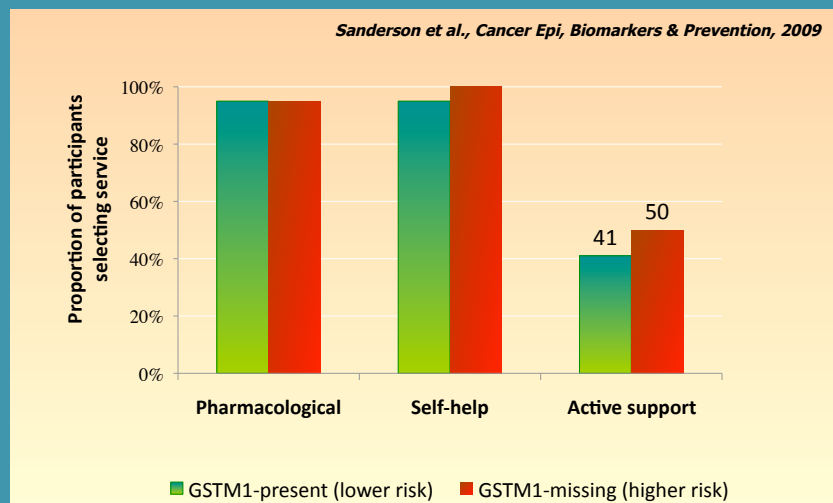
<i>Demographics</i>	Logged on (n = 58)	Did not log on (n = 58)	Sig.
Female	59%	48%	NS
Mean Age (yrs)	40.1 (8.3)	36.5 (10.5)	<0.05
Education			
High school or less	28%	36%	NS
Technical degree / some college	50%	41%	
College degree	22%	23%	
Unemployed	14%	14%	NS
Non-Hispanic white	96%	96%	NS
Daily internet use	85%	62%	<0.05
Aware of cancer genetic testing	61%	42%	<0.05
Motivation to quit smoking¹	6.3 (1.1)	5.6 (1.7)	<0.01
Closeness to patient ¹	5.5 (1.1)	5.2 (1.1)	NS

¹1-7 scale

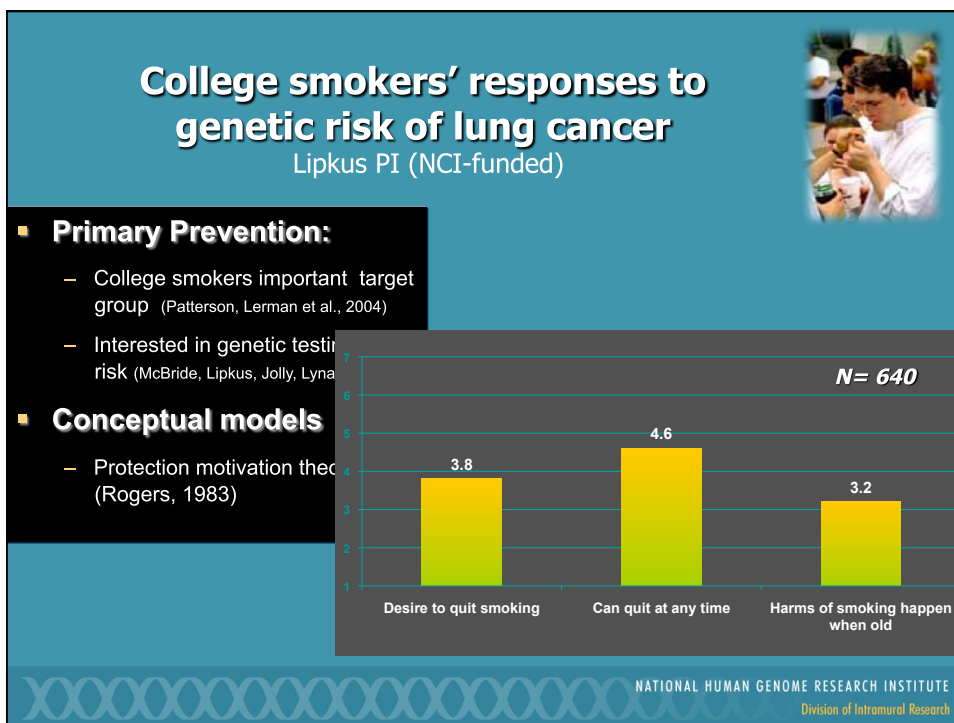
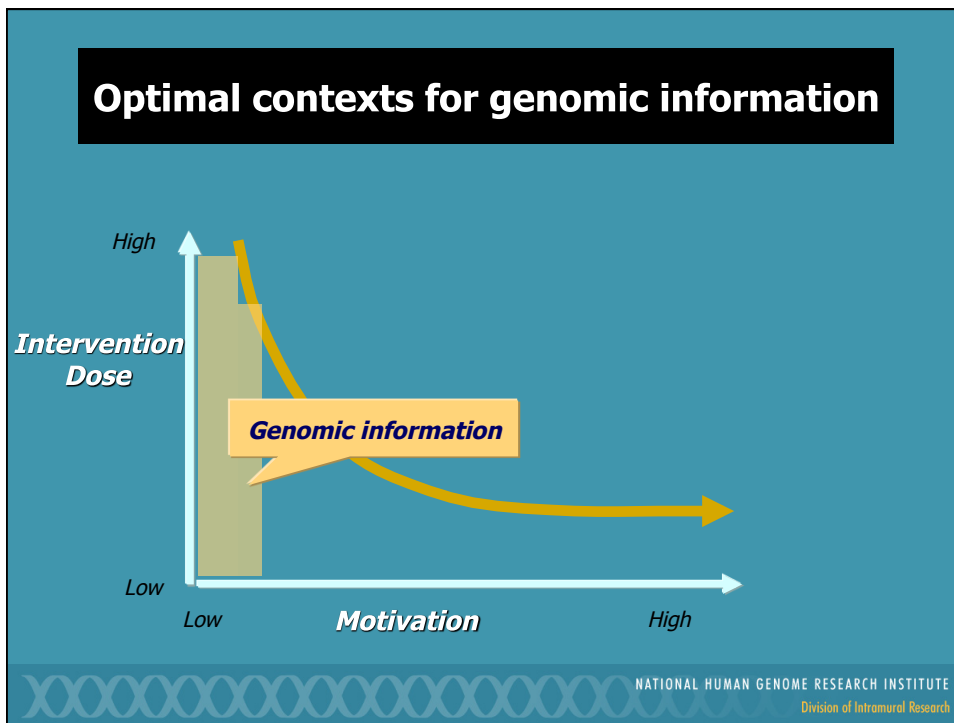
O'Neill et al., *Genetics in Medicine*, 2008

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Uptake of offered cessation services



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■ **Primary Prevention:**

- College smokers important target group (Patterson, Lerman et al., 2004)
- Interested in genetic testing and risk (McBride, Lipkus, Jolly, Lyna)

■ **Conceptual models**

- Protection motivation theory (Rogers, 1983)



Use genomic information to counteract backfiring public health messages

Another major theme reported by 32% of participants related to media reports of speed and ease of lung repair after individuals quit smoking, e.g. "Possibly lung cancer, but I'm not too worried about that. On a scale of 1 to 10, I'm a 2 on that worry. It (smoking) helps with school stress and they say that once you quit your lungs will repair within 2 years, or something. So I figure I can quit after graduate school and my lungs will be great by the time I'm 25".

33 structured interviews

Docherty et al., *Journal of Community Genetics*, in press

Leverage points for genetic risk communications

- **Young smokers do not understand association between susceptibility & exposure**
- **Underestimate potential for addiction**

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Could social media be a viable tool for engaging target groups in discourse for learning?

The collage features a screenshot of a 'Weight Loss Message Board' with several posts, a 'Think Gene' website banner, and a central graphic of a globe connected to several computer monitors by red lines, symbolizing global connectivity and digital communication.

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How might genetic risk information affect parenting practices?
 Wade, Wilfond, McBride, Genet Med, 2010

your child's risk estimate
 100 Children with 0 overweight parents
 100 Children with 1 overweight parent
 Your child is in this group.

your child's risk estimate
 100 Children with 0 overweight parents
 100 Children with 2 overweight parents
 Your child is in this group.

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Challenges for Research on Clinical Integration of Genomics

- Changing nature of genomic technology
 - Future situations difficult to envision, predict
 - Concepts & contexts complicated, technical, unfamiliar
- IVETA useful tool:
 - Improves upon hypothetical scenarios
 - Enables rigorous behavioral outcomes
 - Avoids practical challenges of food preparation

Persky, Kaphingst, Condit & McBride, 2007

Immersive Virtual Environment Testing Area



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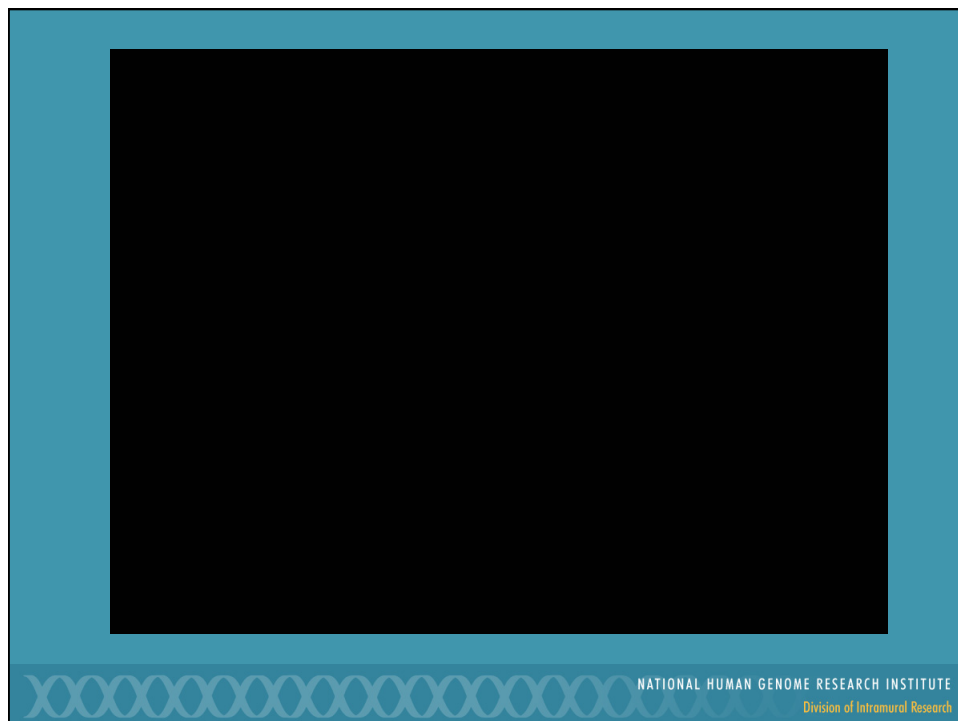
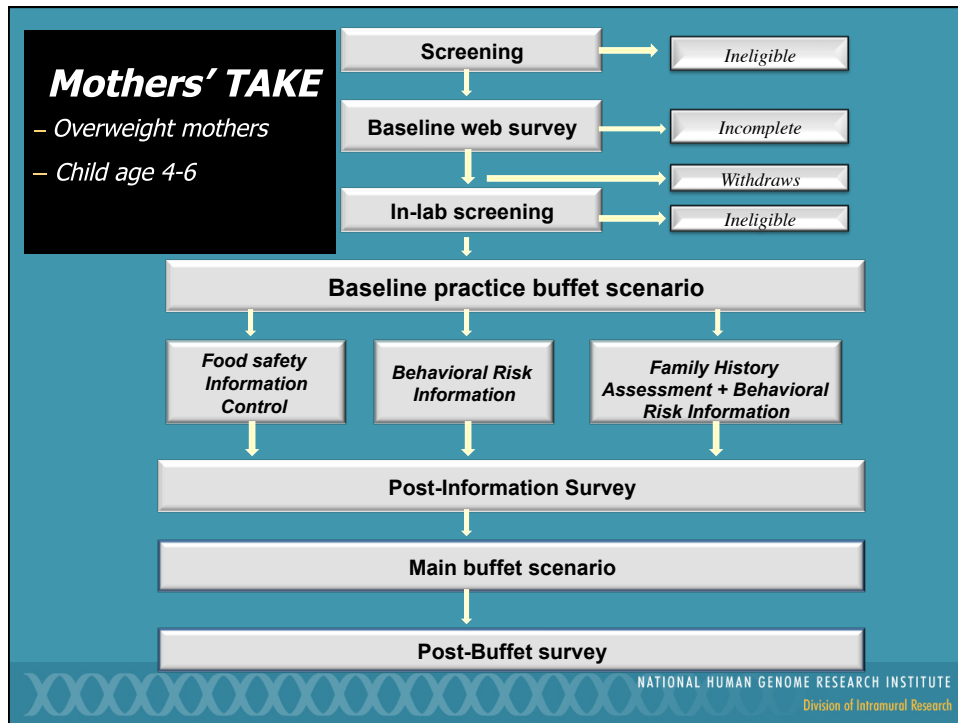
Mothers' TAKE: Virtual Reality Assessment of Mothers' Behavioral Responses to Children's Genomic Risk

Aims

- Explore concerns that genetic risk info for obesity may increase restrictive parenting practices
- Evaluate behavioral effects of providing family history-based obesity risk information about children to parents



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Virtual Buffet



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Preliminary Findings - Realism

1-7 scale

Question	Mean	SD
How realistic did you feel the buffet scenario was?	5.6	1.3
Was the food that ended up on your plate the amount you intended to select?	6.3	1.1

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Promoting Global Public Health?



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Promoting footwear among genetically high-risk children

- Podoconiosis - non-filarial elephantiasis
- Inflammatory lymphatic response to soil irritants
- Clusters in families in Highland Ethiopia.
- Preventable with consistent footwear > inconsistent adherence
- 50% of population < age 15
- Inadequate public health infrastructure
- Targeting shoes to high risk



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The Characteristics of Study Sites

	Site 1	Site 2	Site 3	Site 4
Number of Cases*	1,754	2,420	2,233	868
Duration of Relationship with MFTPA (Years)	11	28 Focus groups 38 Individual interviews 7 Case studies <hr/> 307 Participants		
Distance from MFTPA (Km)	35			

*Registered annually with MFTPA

Ayode et al., Am. J. Tropical Medicine & Hygiene, in press

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Common sense beliefs about the cause of podoconiosis

Heredity

- ↓perceived importance of preventive behaviors
- ↑ interpersonal stigmatizing behavior

Not Heredity

- Endorsed importance of wearing shoes for prevention
- More empathetic to patients
- Fear of contagion → social distance (stigma)

Stigma

- ❖ Social distancing
- ❖ Partner selection
- ❖ Self stigma

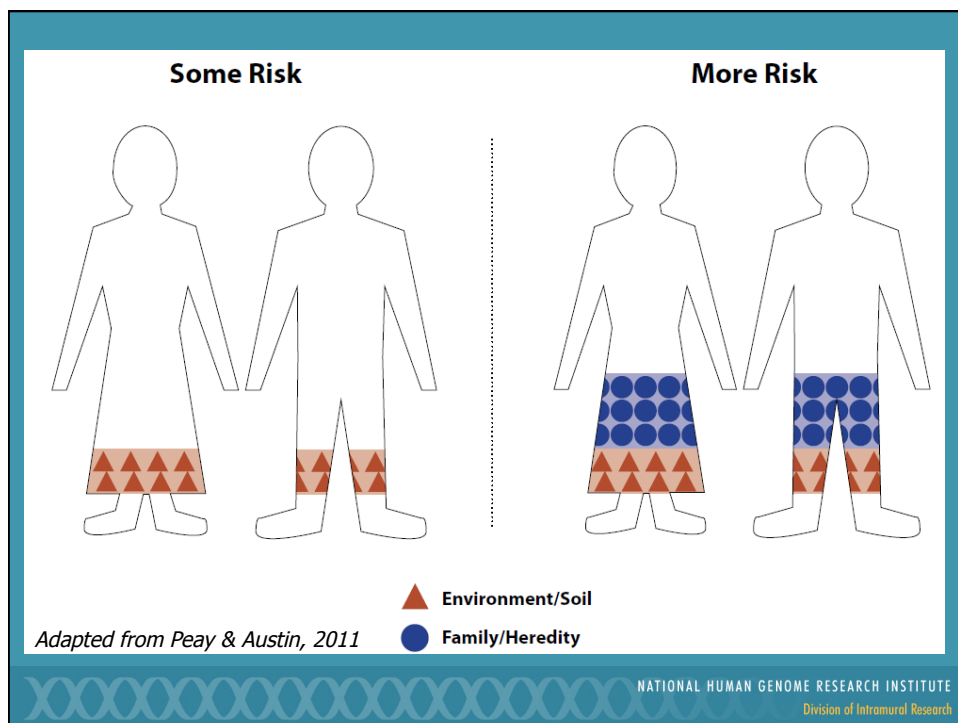
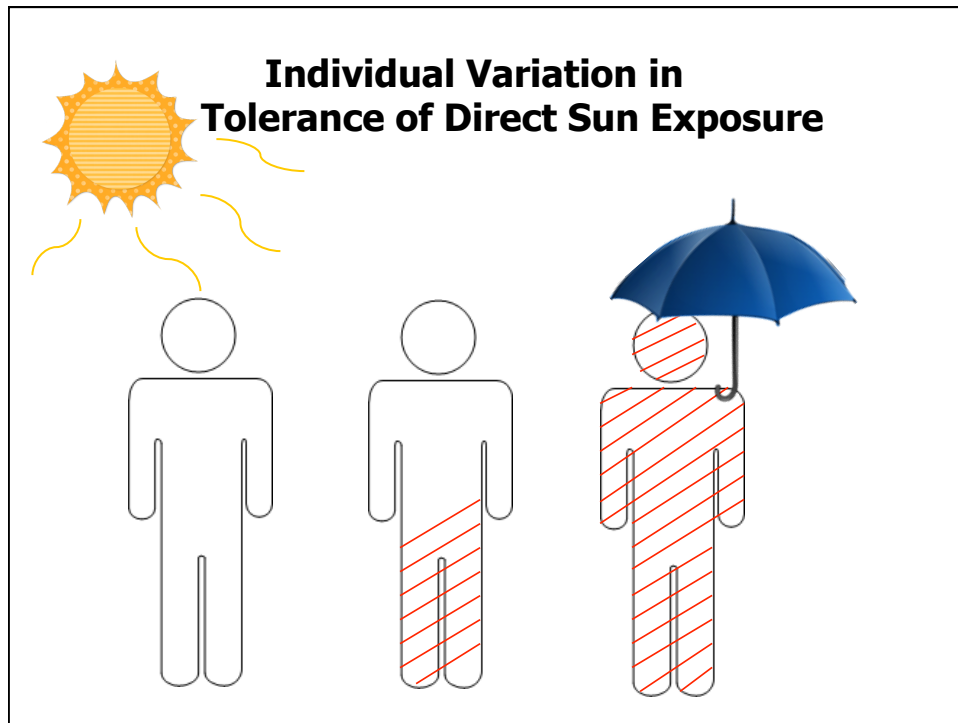
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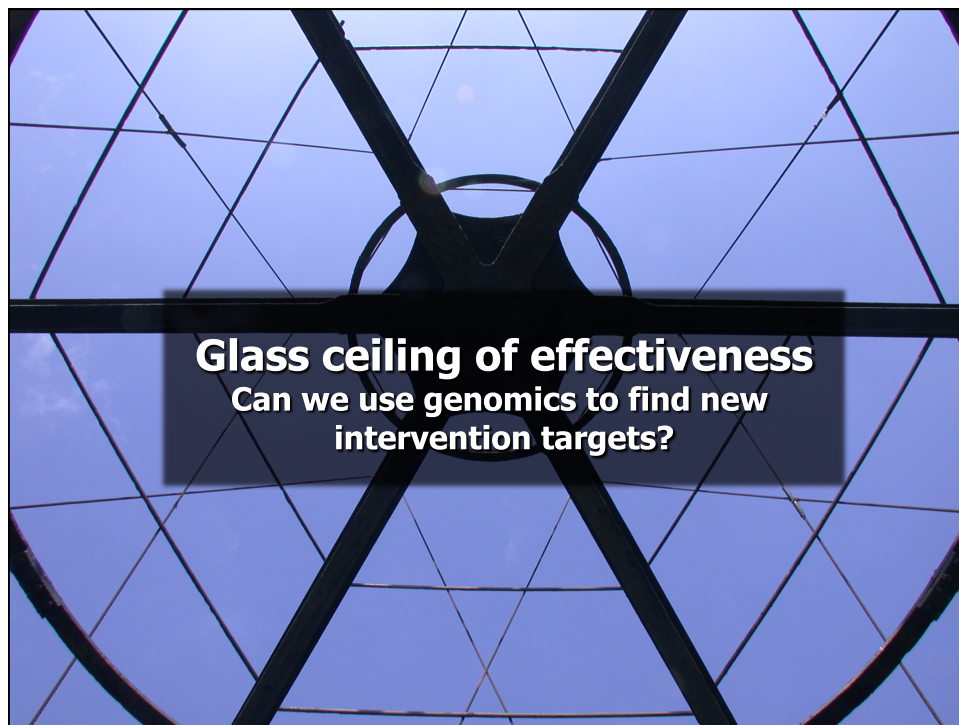
Study Design

Community Level Interventions Quasi-experimental Design

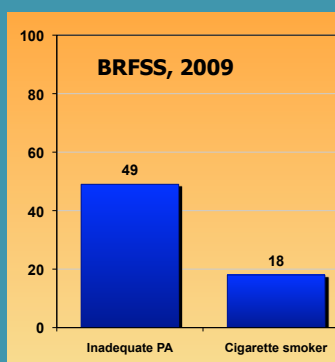
Baseline assessment – assignment to condition					
Comparison Group		Standardized health education		Standardized health education + genetics education	
Affected households -- free shoes from MFTPA	Unaffected households -- measured only	Affected households -- free shoes from MFTPA	Unaffected households -- public education campaign	Affected households -- free shoes from MFTPA -- public education campaign + genetic susceptibility modules	Unaffected households -- public education campaign + genetic susceptibility module
<ul style="list-style-type: none"> Short term follow-up of educational effect Longer term follow-up of primary outcomes (e.g., shoe-wearing in the target audience) 					





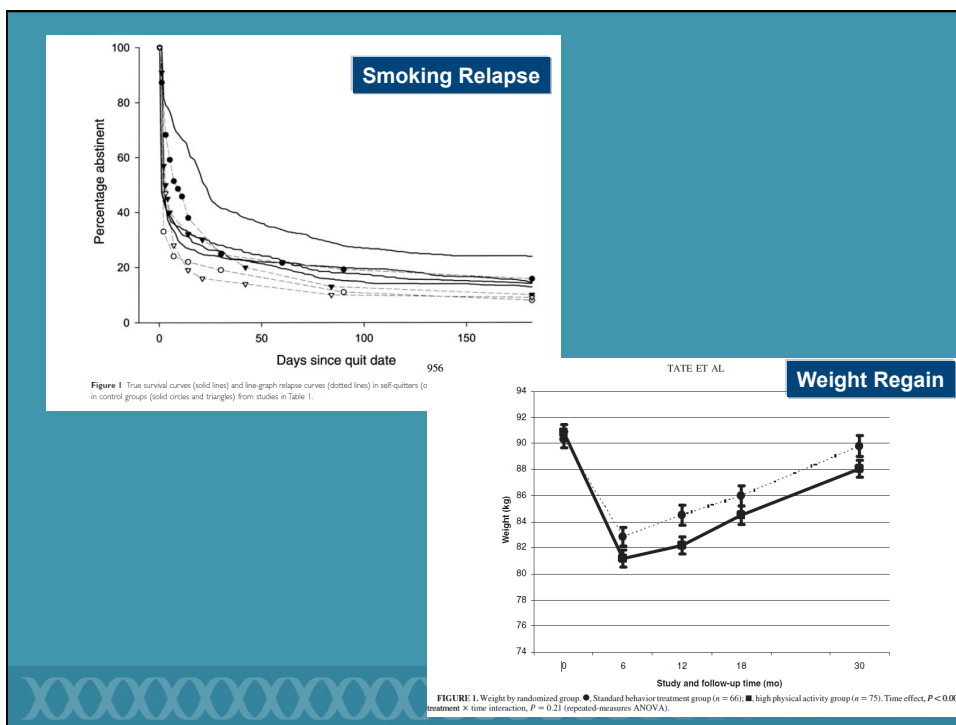
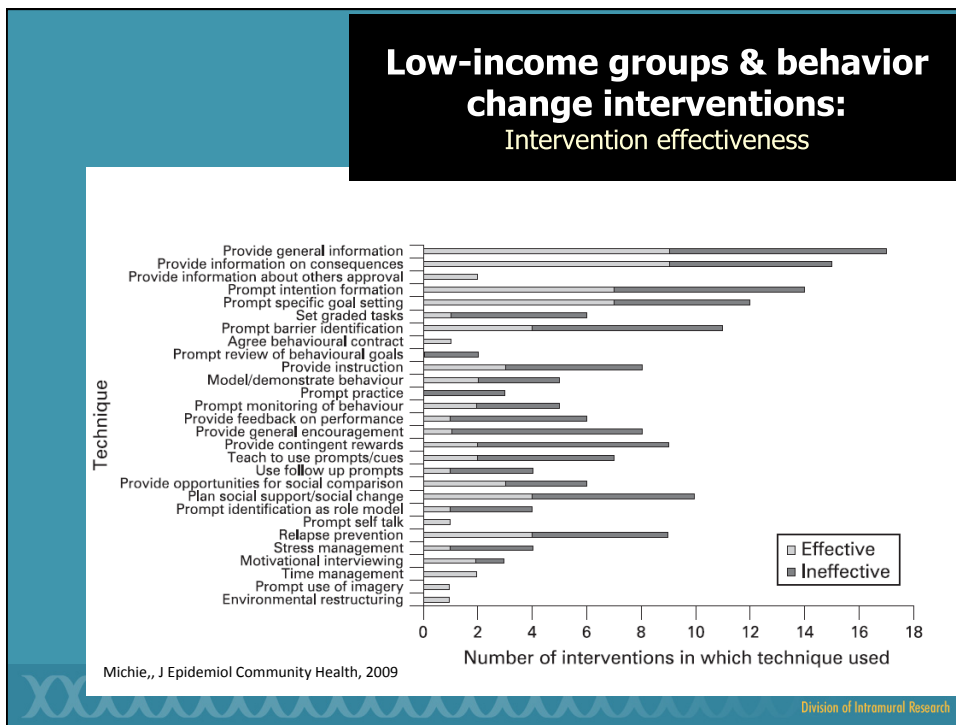


Public Awareness The Behavior – Intervention Disconnect



CLINICAL SIGNIFICANCE

- Over the last 18 years, obesity has increased from 28% to 36%; regular physical activity has decreased from 53% to 43%; and eating 5 or more fruits and vegetables a day has decreased from 42% to 26% among adults aged 40-74 years.
 - Adherence to all 5 healthy habits has gone from 15% to 8% ($P < .05$).
 - Adherence to healthy habits is no more likely in people with cardiovascular disease, hypertension, diabetes, or hypercholesterolemia.
- King et al., AJPM 2009 -- NHANES*



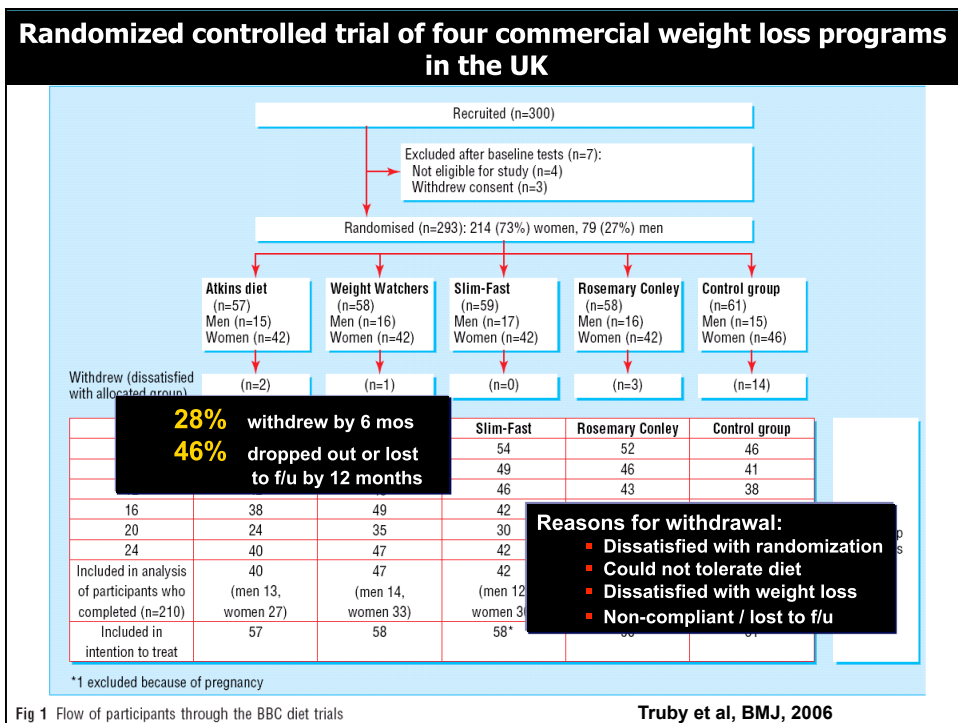
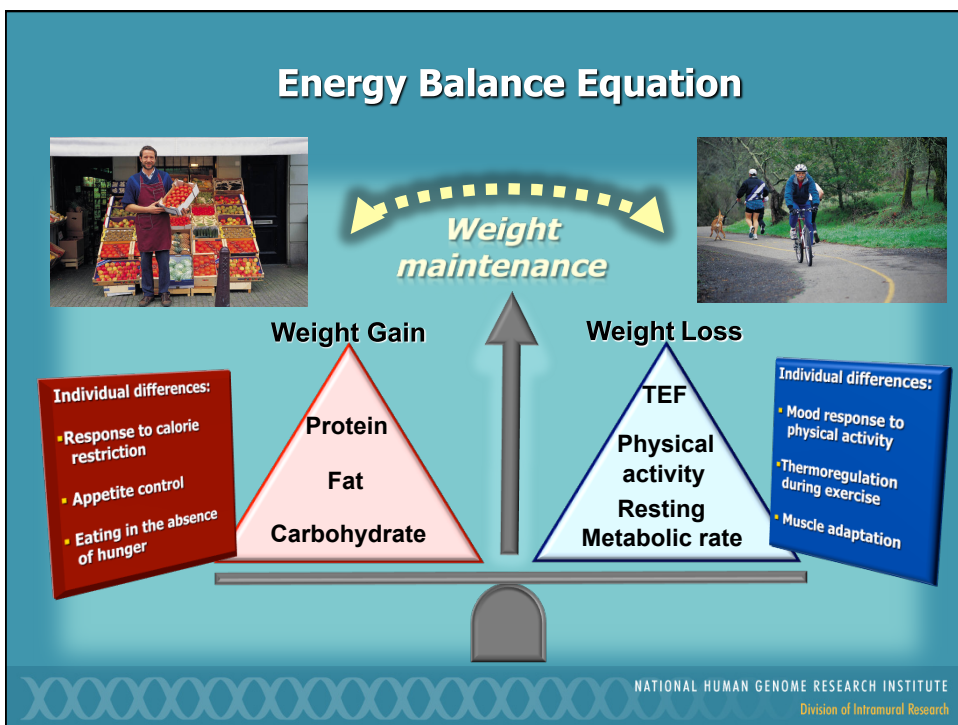
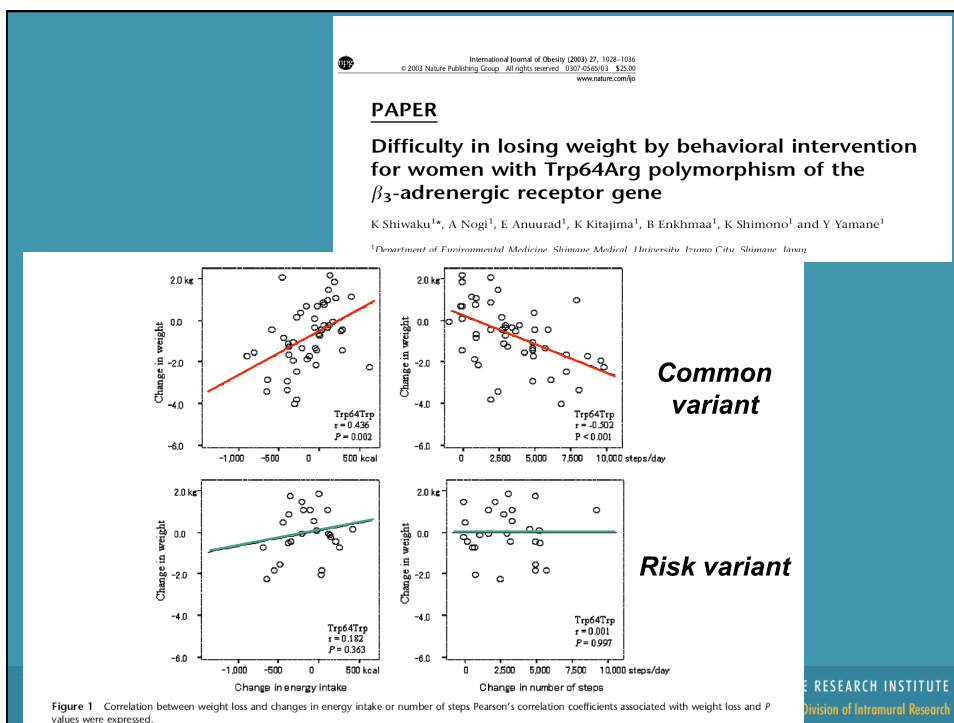
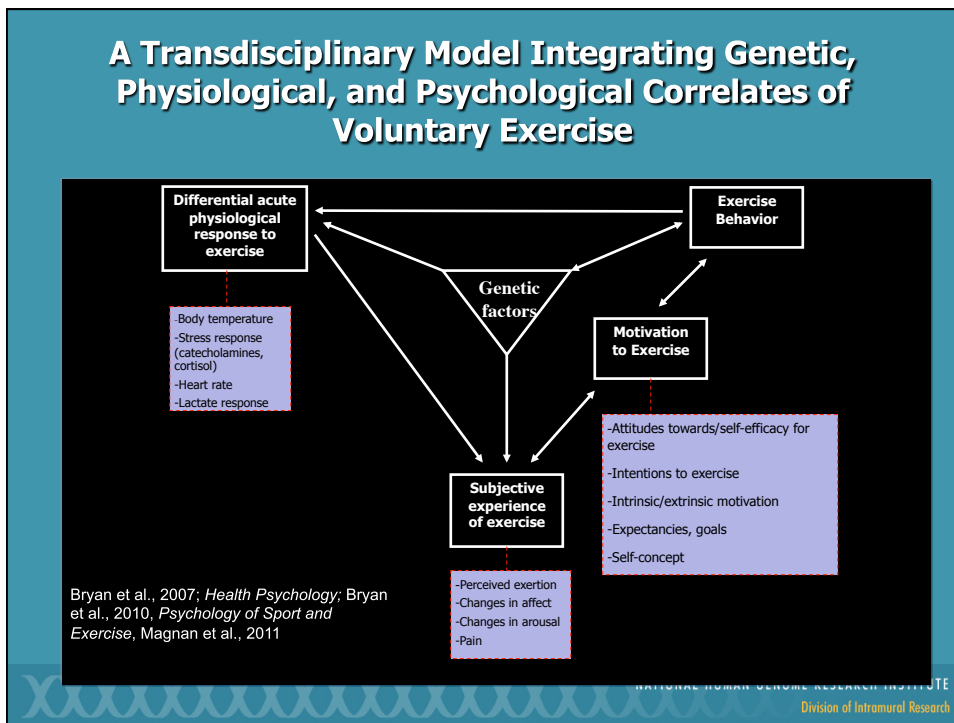
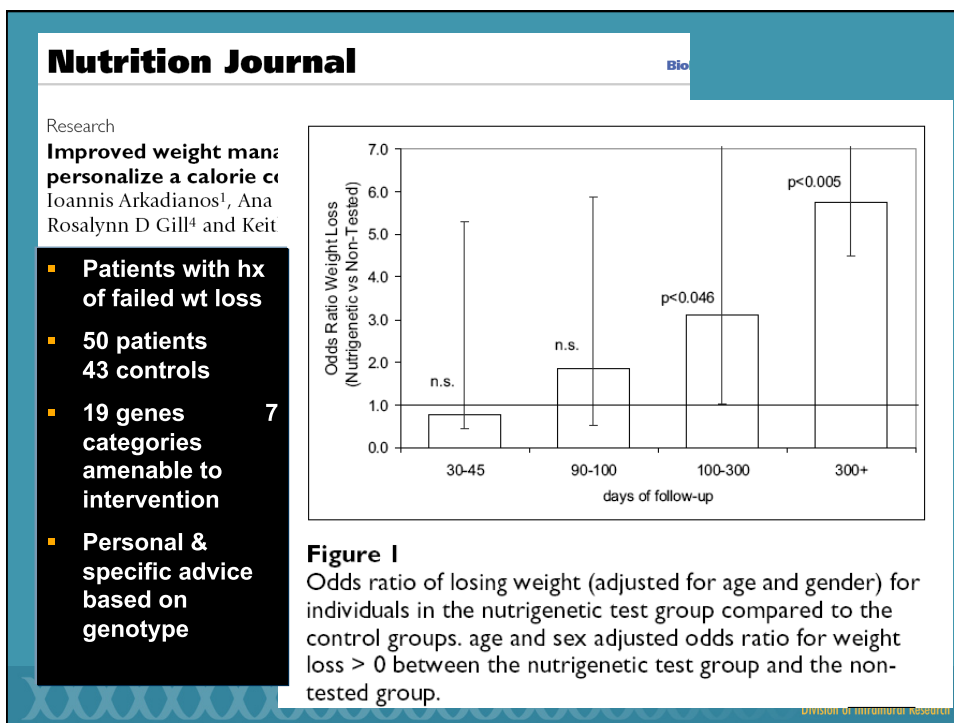
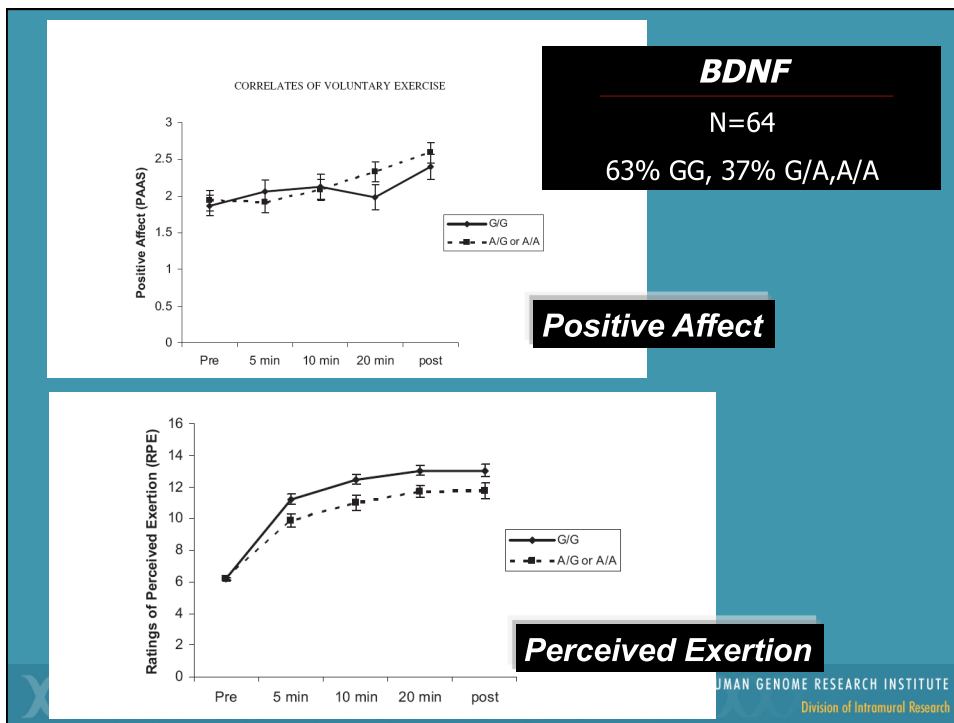


Fig 1 Flow of participants through the BBC diet trials







Take home messages

- Translation research is important
- Many ways that genomics may improve public health
- Conceptual models critical
- Full armamentarium of methods
 - to anticipate and test potential applications of genomics
- Research inherently interdisciplinary

Contact Information

Social and Behavioral Research Branch

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