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Public Health Applications of Genomics

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Financial Disclosures

No financial interests to report that would influence the content of this presentation

Today's talk

- Importance of research to shape translation of genomics for Public Health
- Overview of social and behavioral research approaches
- Principles of public health
- Examples of translation research in priority areas
- Take home messages

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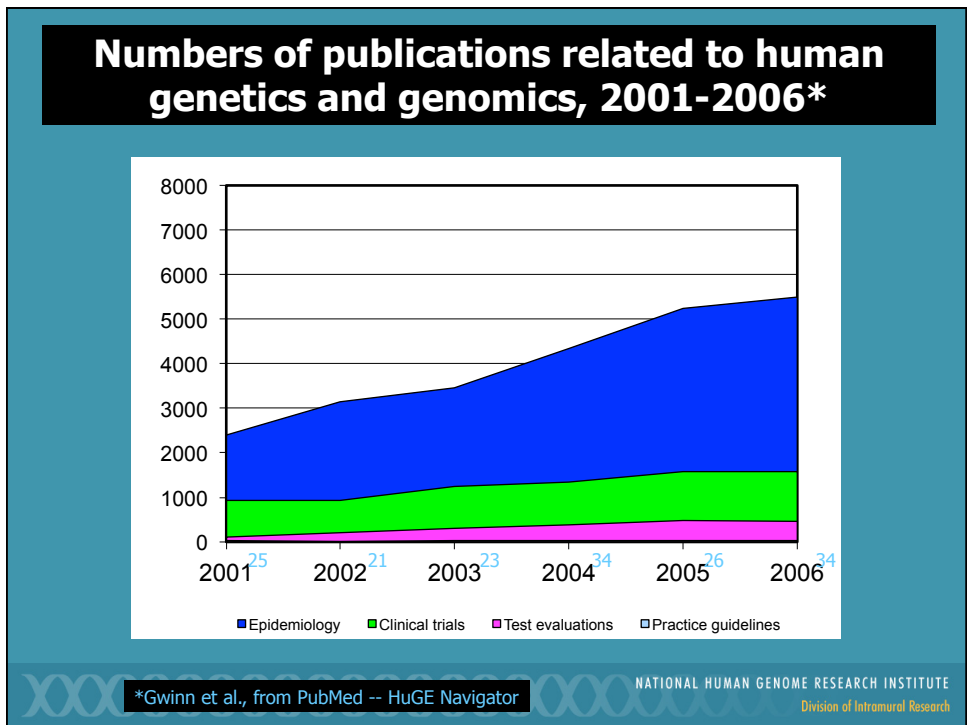
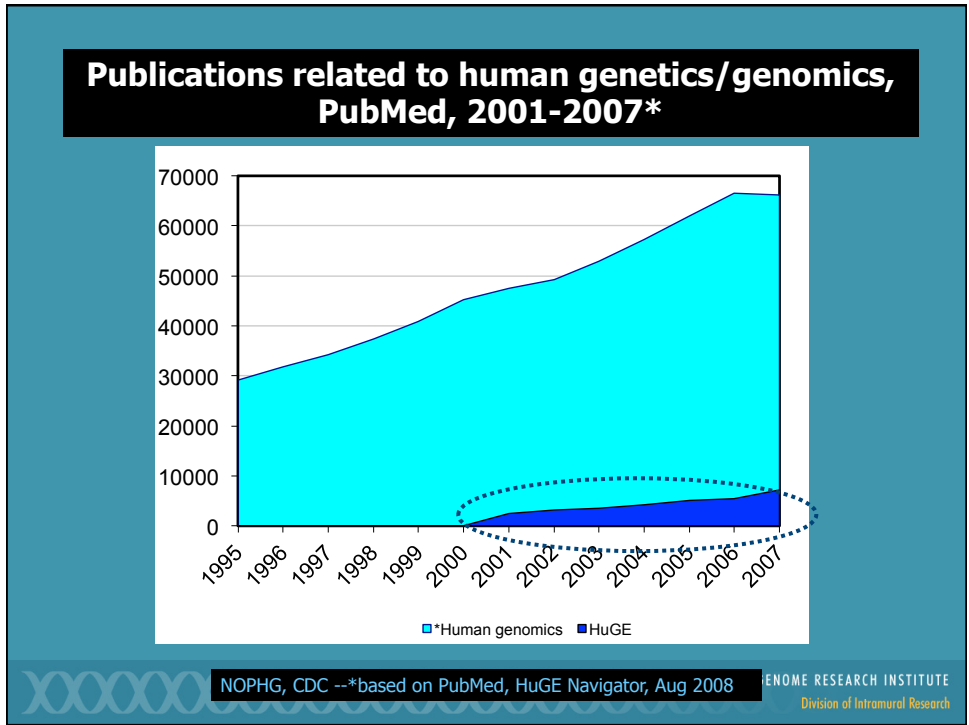
Genomic discovery



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

Lost in translation

Premature translation

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PATHWAY GENOMICS™
 YOUR FUTURE. Only Better!

HOME HOW IT WORKS MORE INFO PRODUCTS PARTNERS ABOUT US

Your Personal DNA Report

"Our DNA results provided us peace-of-mind. We've already taken action to reduce our risks"

The Washington Post
Walgreens won't sell genetic test over FDA objections

BY ROB STEIN

The nation's largest drugstore chain backed out Wednesday of plans to sell a saliva test that promised to scan a customer's DNA to assess his or her risk for breast cancer, heart attacks and a host of other diseases.

Walgreens had planned to offer the Pathway Genomics test at more than 6,000 of its 7,500 stores nationwide beginning Friday, but it reversed course after the Food and Drug Administration questioned whether the test could be sold legally without the agency's authorization.

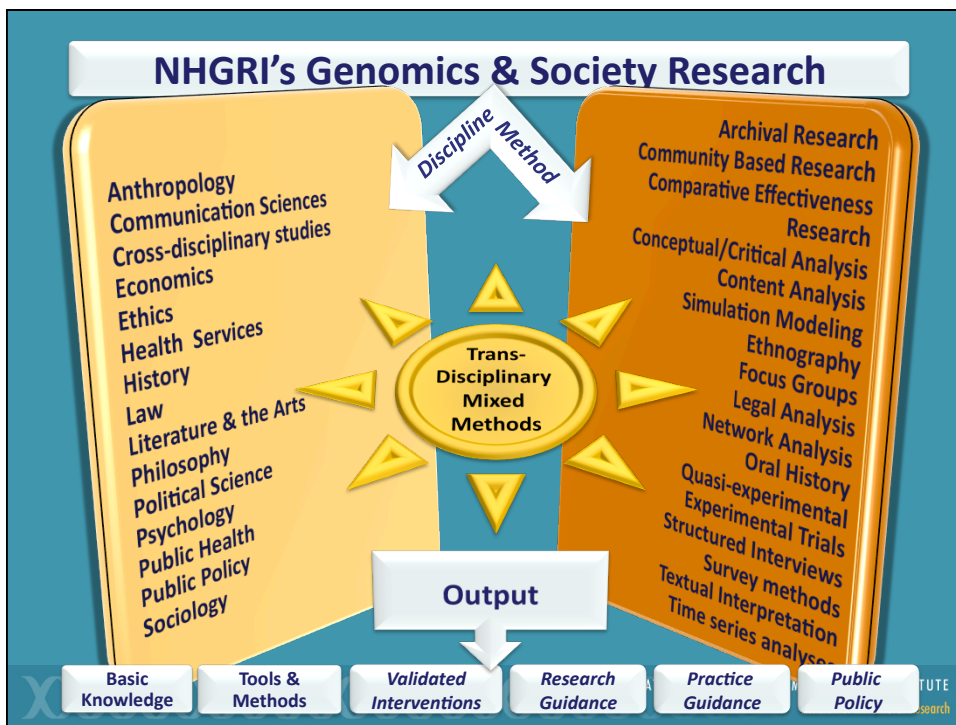
"In light of the FDA contacting Pathway Genomics about its genetic test kit and anticipated ongoing discussions between the two parties, we've elected not to move forward with offering the Pathway product to our customers until we have further clarity on this matter," said Jim Cohn, a Walgreens spokesman.

The Washington Post reported Tuesday about plans by Pathway and Walgreens to start selling the over-the-counter test. Pathway said its Insight test could evaluate a propensity for developing medical conditions such as Alzheimer's disease, diabetes and obesity; the likelihood of parenting a baby with cystic fibrosis, Tay-Sachs disease and other genetic disorders; and the possible reaction to caffeine, cholesterol-lowering drugs, blood thinners and other medications.

Other companies have been selling on the Internet tests that can analyze genes for a person's risk of some diseases, and genetic tests for paternity and ancestry have been widely available in stores. But the plan by Pathway Genomics of San Diego represented the boldest move yet to bring personalized genomic science to the mass market.

It was welcomed by those who hope that deciphering the genetic code will launch a new era in biomedical science. But it raised objections from those who worried that the average consumer would have problems interpreting the results, leading to dangerous complacency about some diseases.

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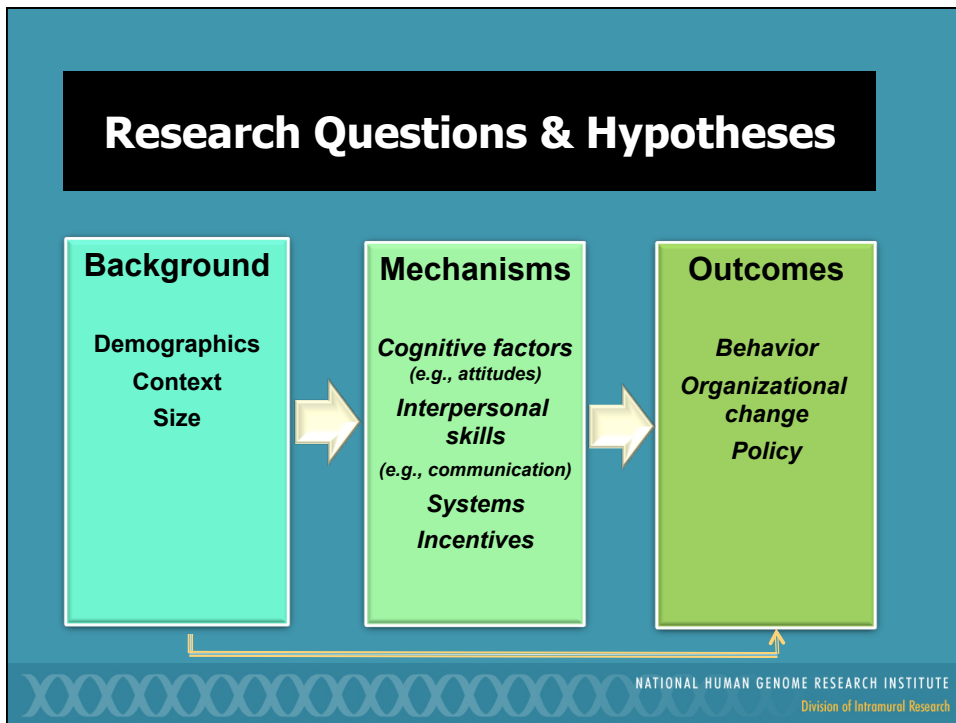
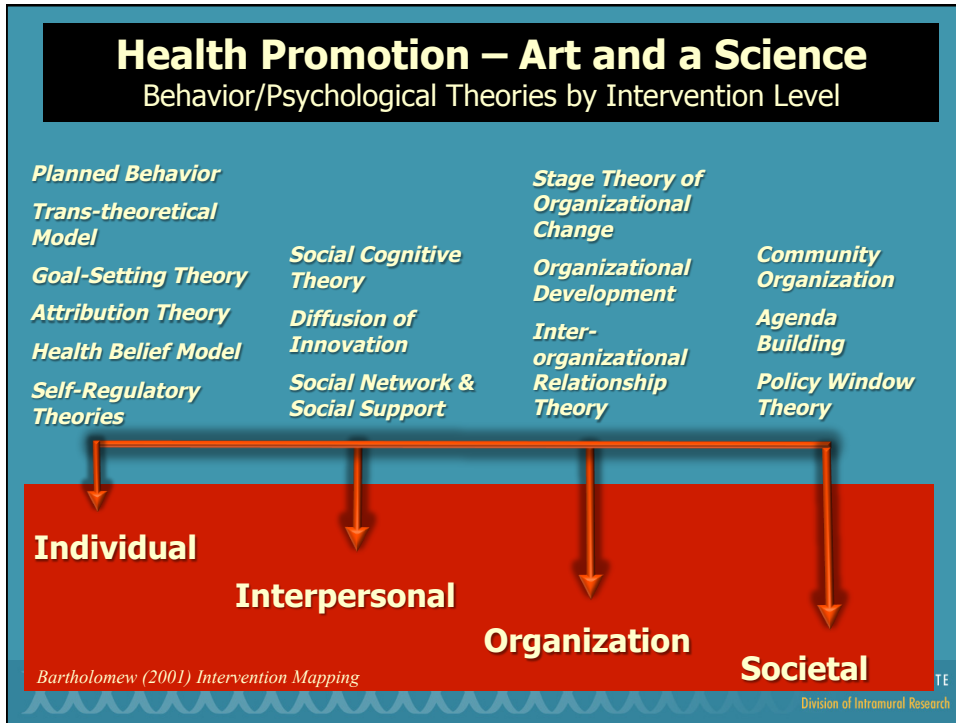
What is an intervention?

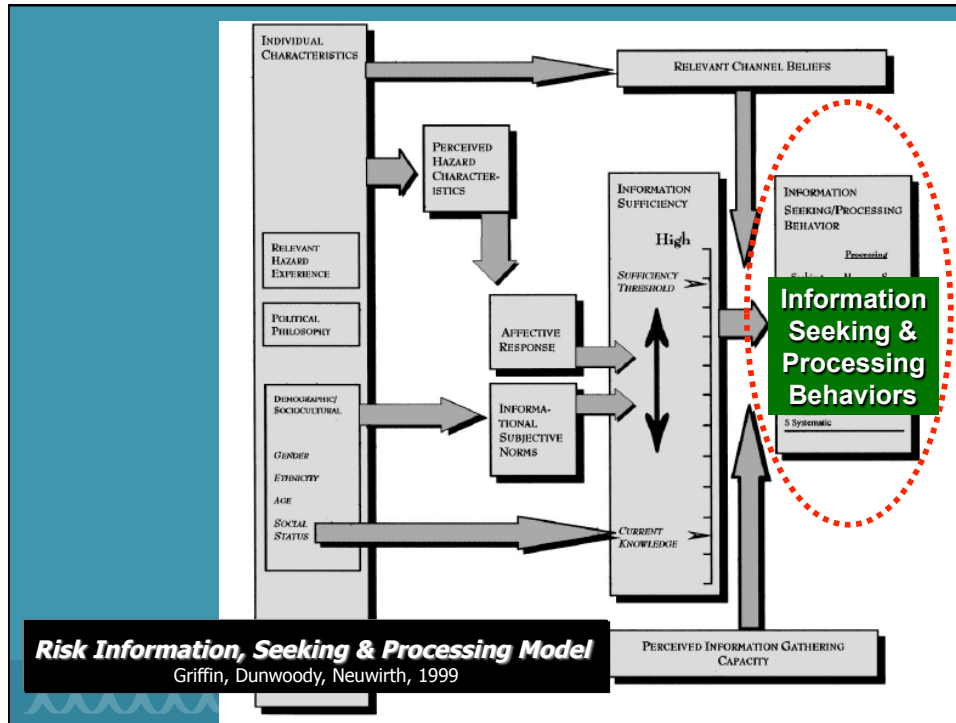
Efforts directed at a target group to influence a desired outcome:

- 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, Celeste M. Condit, PhD, Robert T. Croyle, PhD, Marta Gwinn, MD, Muin J. Khoury, MD, 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 address 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 the communication and adoption of healthier behaviors more than current information approaches; and (3) anticipating directions of genomic discovery that also were identified, including 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 who develop priorities for research funding, interdisciplinary teams engaged in genomic public health challenges.

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Science

The Puzzle of Complex Diseases

Public health applications

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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Clinical Genetic vs. Public Health Applications

Efficacy – Effectiveness Trade-off

<u>Current approach</u>	<u>Public Health model</u>
<ul style="list-style-type: none"> • Efficacy = .80 • Reach = .10 • .80 x .10 • Effectiveness = .08 	<ul style="list-style-type: none"> ▪ Efficacy = .20 ▪ Reach = .50 ▪ .20 x .50 ▪ 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**
 -
 -
 -
 -
- **Heart Disease**
 -
 -
 -
- **High Cholesterol**
 -
- **Hypertension**
 -
- **Lung cancer**
 - MPO
- **Colon Cancer**
 - MTHFR
- **Skin Cancer**
 - MC1R
- **Osteoporosis**
 - ESR1
 - IL6
 - COL1A1

Original Paper

Public Health Genomics

Public Health Genomics
 DOI: 10.1159/000236061

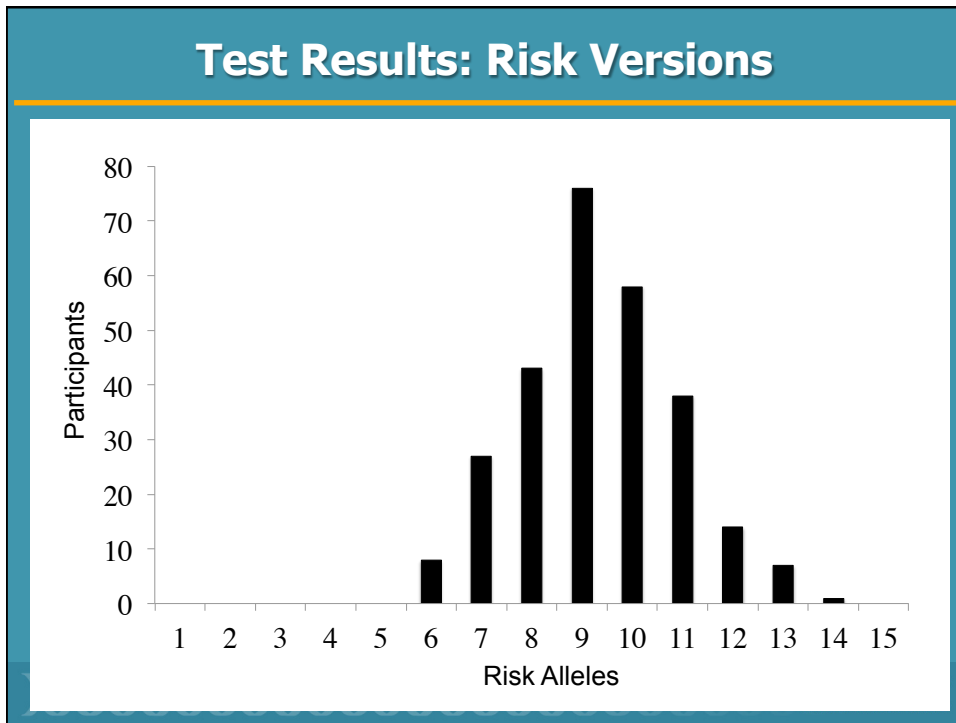
Considerations for Designing a Prototype Genetic Test for Use in Translational Research

C.H. Wade^{a,b} C.M. McBride^b S.L.R. Kardia^c L.C. Brody^a

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Information About Genes

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

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

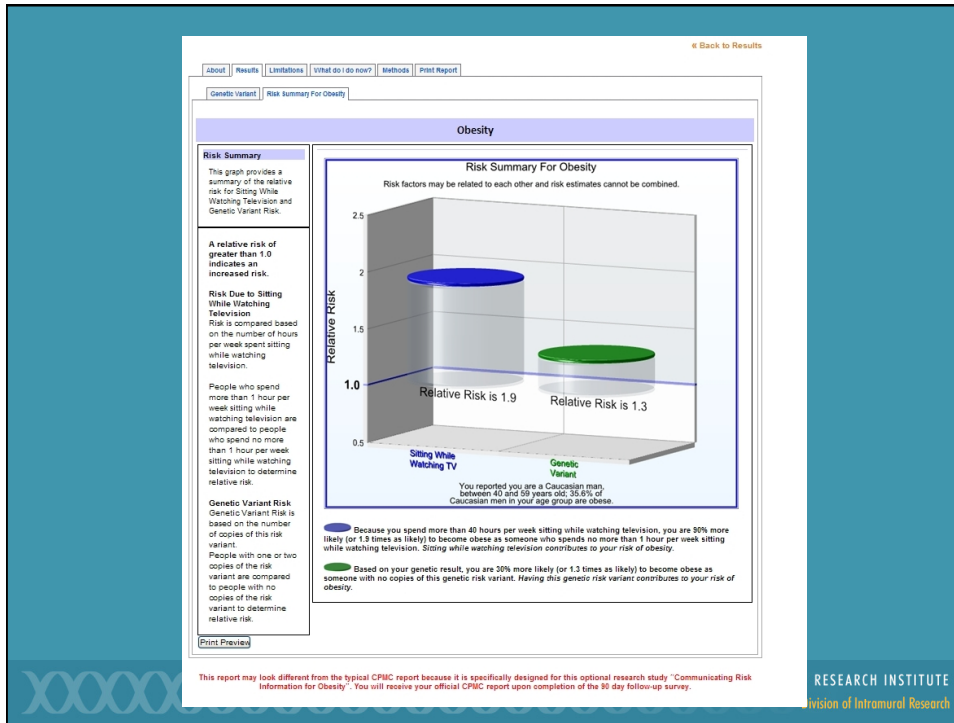
Percentage of People With 0, 1, or 2 Risk Versions of KCNJ11 in the General Public

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

Understanding Your Test Results

Remember these points when reading your test results:

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

Overview of Your Results

You have one or more risk versions 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.

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

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

- Your health habits, such as diet, exercise and cigarette smoking.
For example: Being a cigarette smoker increases your chance for lung 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 not change your genes but you can change your health habits.
- Your family history of health conditions.
- The environment you live in, which might have chemicals or work or secondhand cigarette smoke.
- Other genes that were not tested in the Multiplex Genetic Test.

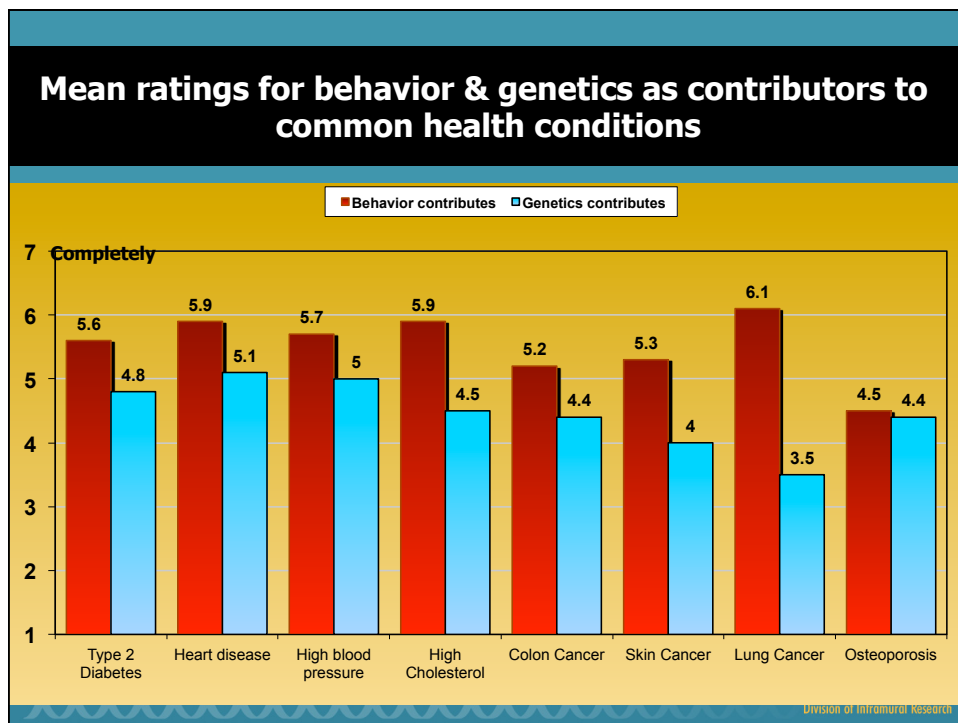
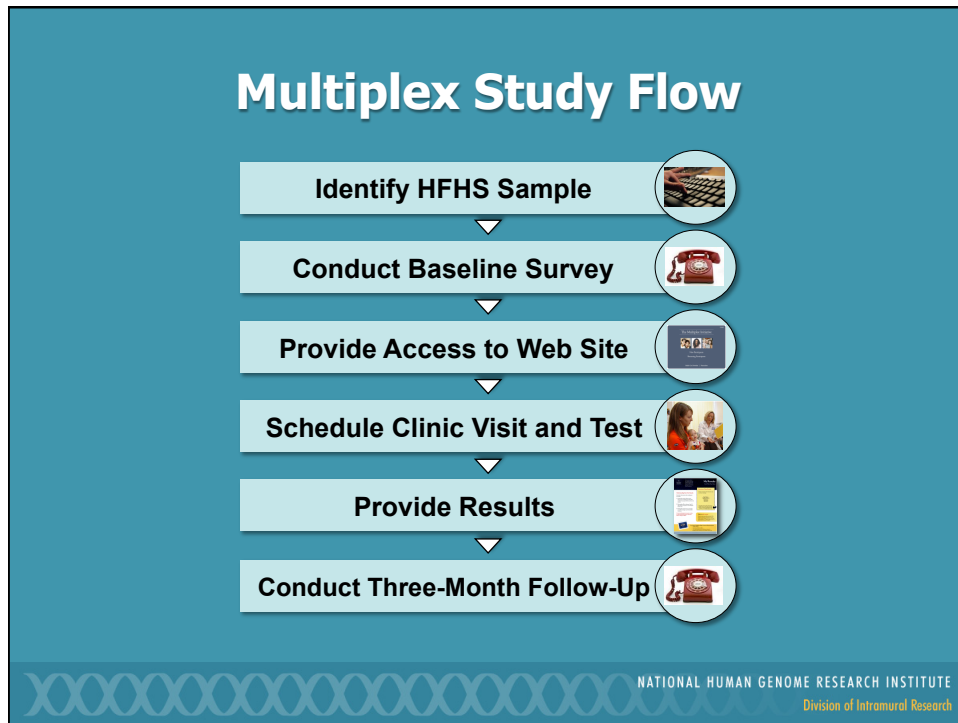
Here's what you can do to lower your chance of getting these health conditions no matter what your test results were:

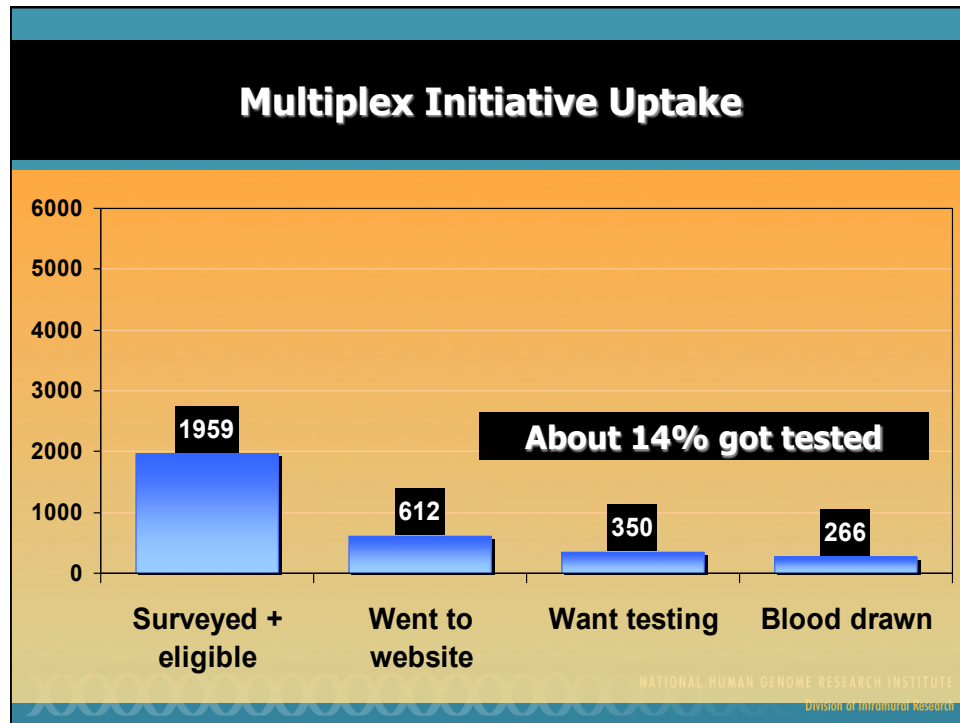
- ✔ Quit Smoking
- ✔ Maintain a healthy weight
- ✔ Eat 5 or more servings of vegetables & fruits every day
- ✔ Exercise for at least 30 minutes most days of the week
- ✔ Limit your time in the sun and use sunscreen
- ✔ See your doctor for a yearly check-up

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

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

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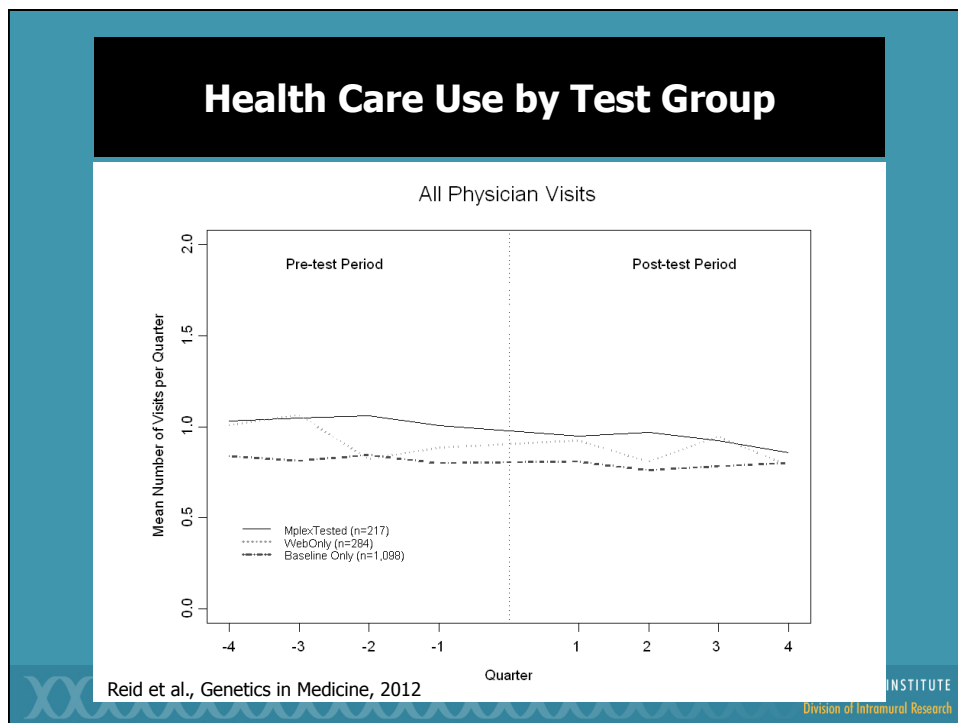
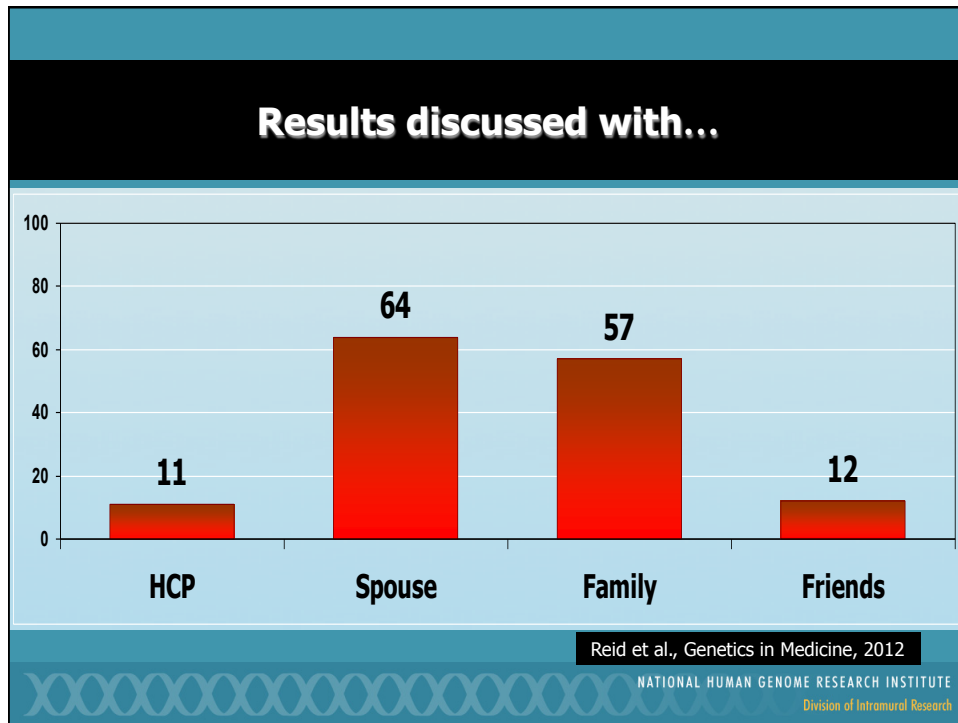


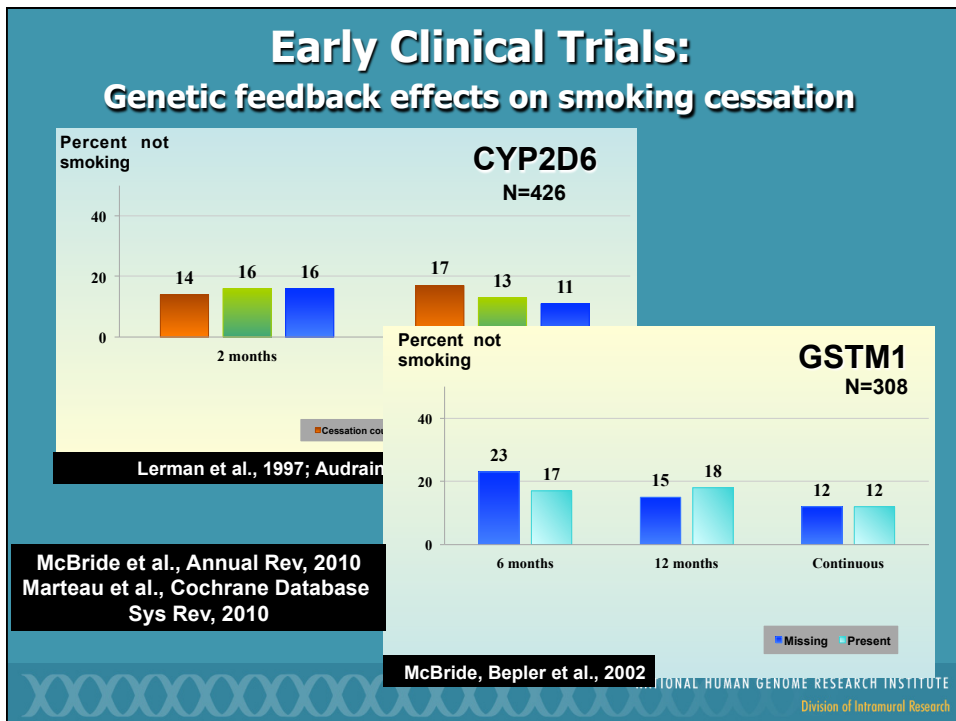
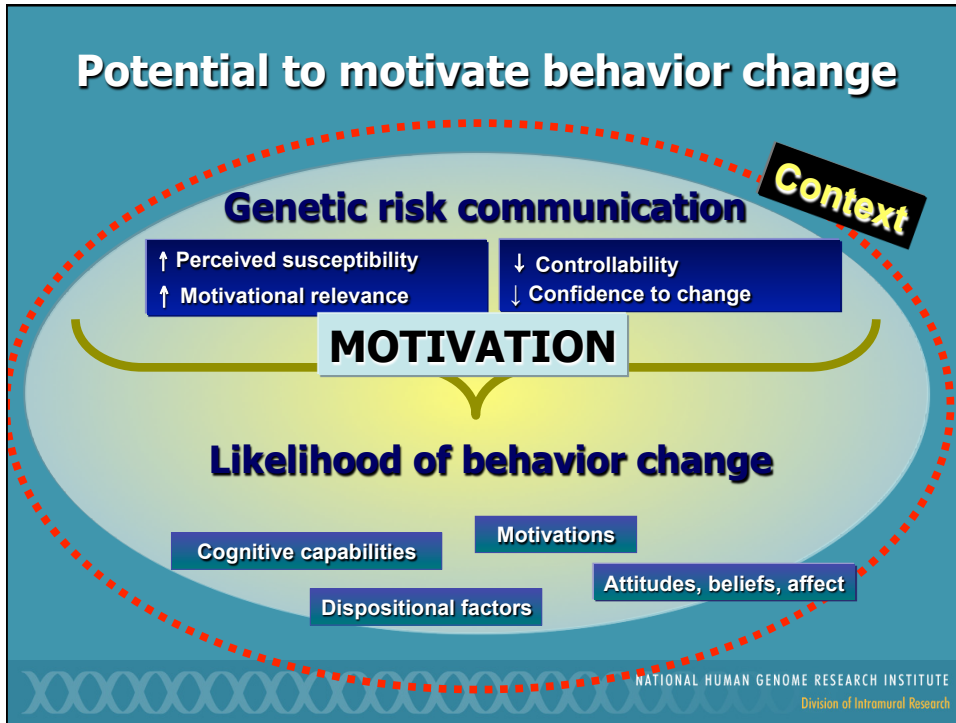
Web usage & decision outcomes

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!

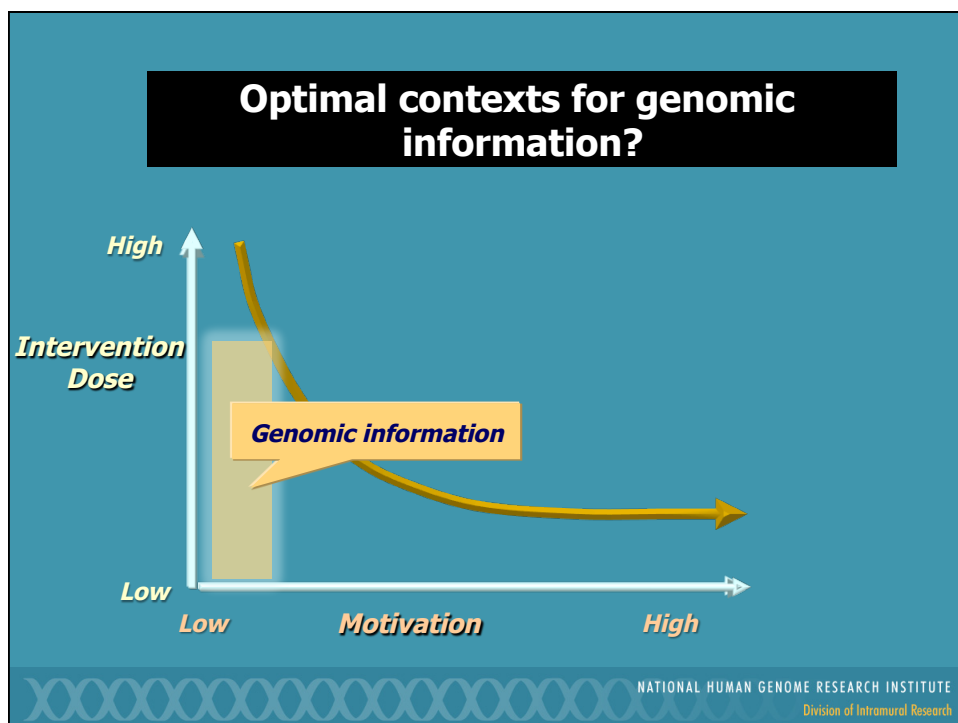
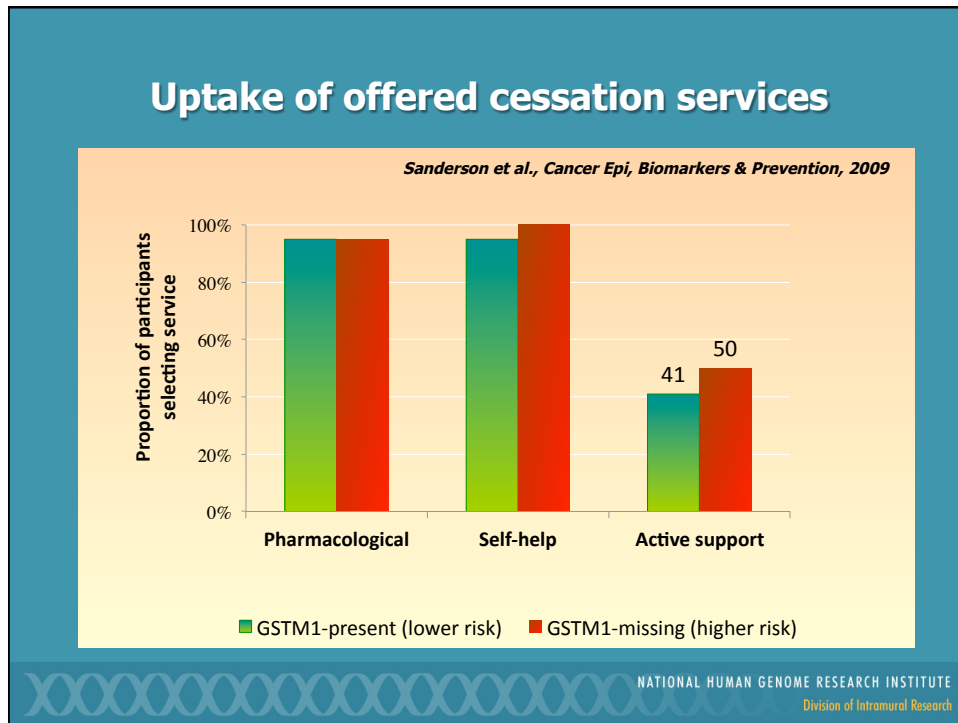
NEXT

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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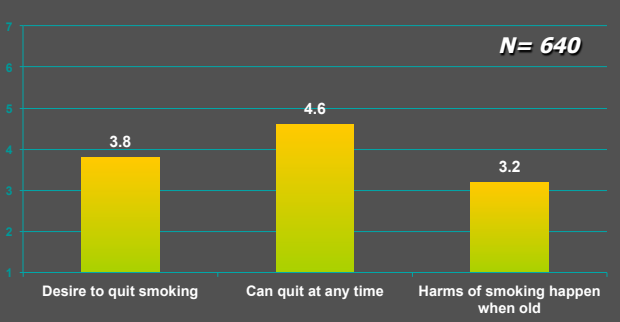


College smokers' responses to genetic risk of lung cancer

Lipkus PI (NCI-funded)



- **Primary Prevention:**
 - College smokers important target group (Patterson, Lerman et al., 2004)
 - Interested in genetic testing and genetic risk (McBride, Lipkus, Jolly, Lyna)
- **Conceptual models**
 - Protection motivation theory (Rogers, 1983)



Statement	Score
Desire to quit smoking	3.8
Can quit at any time	4.6
Harms of smoking happen when old	3.2


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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*, 2011



- **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?

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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

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Immersive Virtual Environment Testing Area



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

Aims

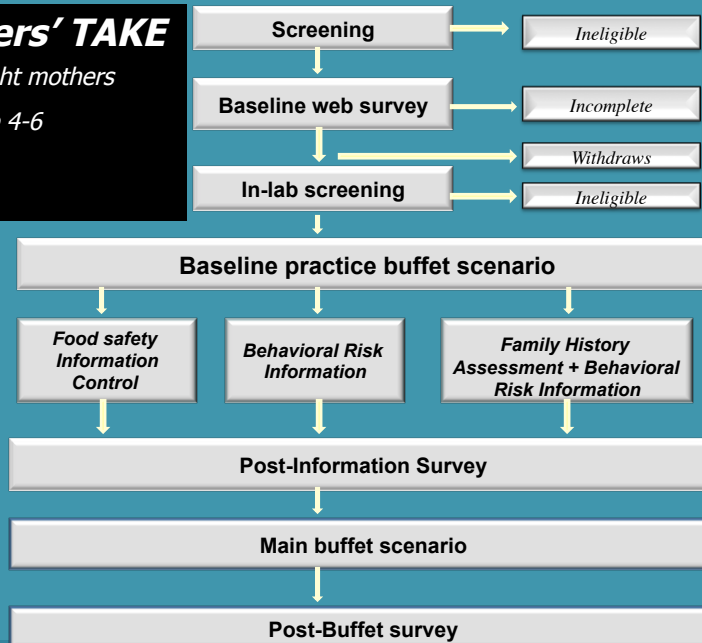
- Explore concerns that genetic risk info for obesity may increase restrictive parenting practices
- Evaluate behavioral effects of providing family history-based obesity risk information about children to parents



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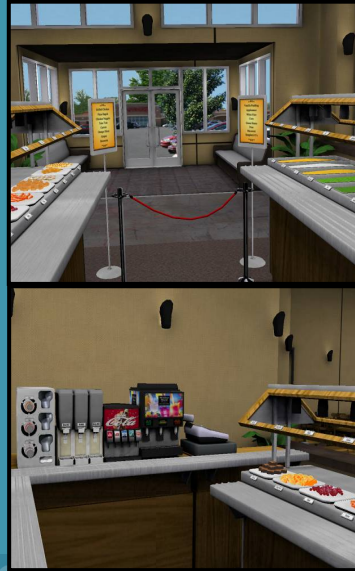
Mothers' TAKE

- Overweight mothers
- Child age 4-6



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Virtual Buffet



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Total Calories by Experimental Arm

	Estimate	SE
Intercept	248.73**	88.83
Pre-calorie	0.67***	0.20
Mother's age	-2.68	1.61
Mother is white	-34.65	18.22
Mother's BMI	2.75	1.80
Beh. Risk arm	-35.48	21.10
Beh + Fam hx arm	-45.26*	21.19
Index child is overweight	15.19	17.80
Index child is male	35.72*	17.32
Family has one child	0.48	20.13

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$; **** $p \leq 0.0001$

McBride, Persky et al., 2012

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Influence of Risk Message on Total Calories for Family Hx Arm

	Estimate	SE
Intercept	176.92	140.27
Pre-calorie	0.73	0.38
Mother's age	-2.66	3.05
Mother is white	21.23	33.29
Mother's BMI	0.75	3.19
Two overweight parents	71.48*	31.97
Index child is overweight	19.38	32.49
Index child is male	23.55	30.47
Family has one child	-23.93	37.91

*p<0.05

McBride, Persky et al., Obesity, 2012

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Is the effect of risk message specific to the family history arm?

Outcome	Food Safety			Beh Risk Info			Beh Risk + Fam Hx		
	Number of overweight biological parents		sig	Number of overweight biological parents		sig	Number of overweight biological parents		sig
	One	Two		One	Two		One	Two	
	n=31	n=42		n=29	n=43		n=22	N=53	
Plated calories	<u>372.20</u>	406.52	0.275	<u>359.50</u>	368.49	0.784	<u>286.9</u>	360.9	0.051
Sweetened beverage	45.2%	47.6%	0.835	48.3%	51.2%	0.810	<u>13.6%</u>	37.7%	0.039

McBride, Persky et al., Obesity, 2012

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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* <small>*Registered annually with MFTPA</small>	1,754	2,420	2,233	868
Duration of Relationship with MFTPA (Years)	11	28 Focus groups 38 Individual interviews 7 Case studies <hr style="border: 1px solid white;"/> 307 Participants		
Distance from MFTPA (Km)	35			

Ayode et al., Am. J. Tropical Medicine & Hygiene, 2012

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Common sense beliefs about the cause of podoconiosis

Heredity

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

➔

Stigma

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

Not Heredity

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

➔

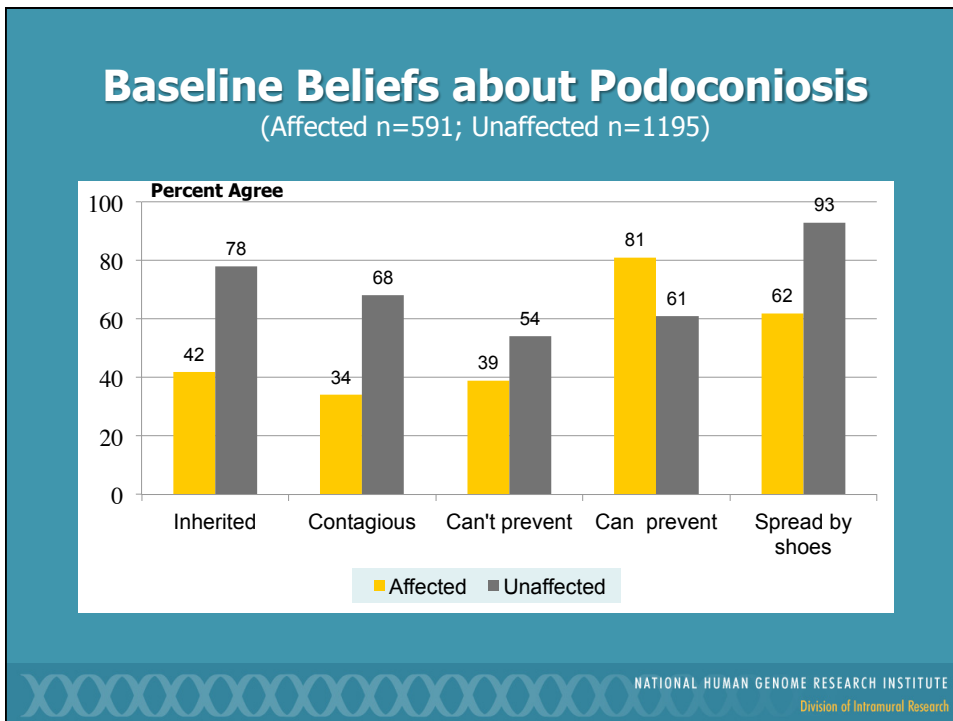
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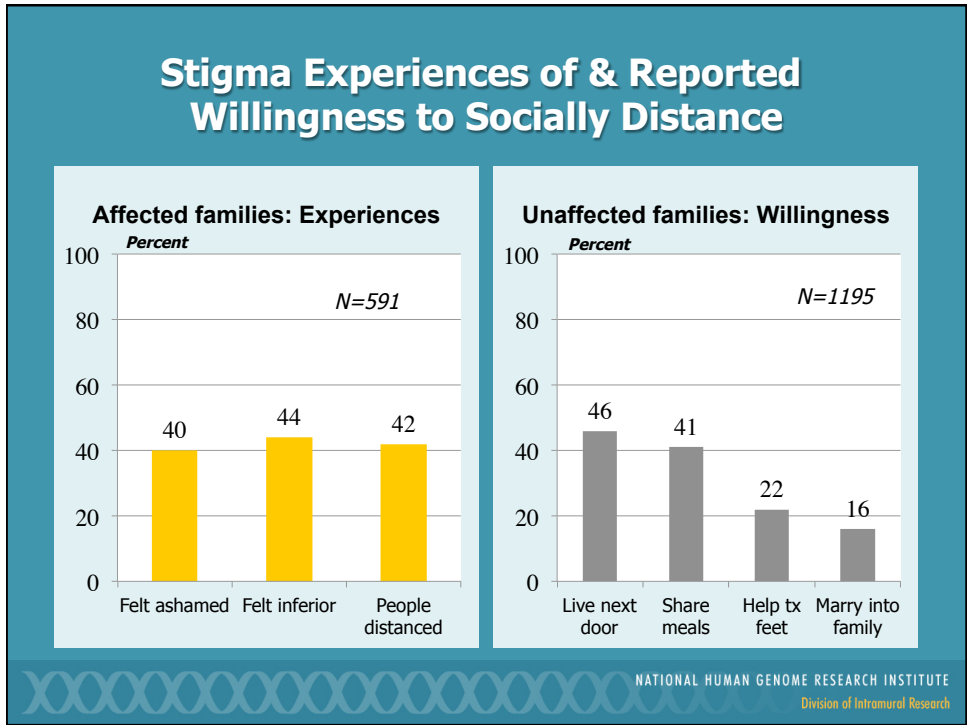
Study Design

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

■ Short term follow-up of educational effect
 ■ Longer term follow-up of primary outcomes (e.g., shoe-wearing in the target audience)





Public Health Campaigns

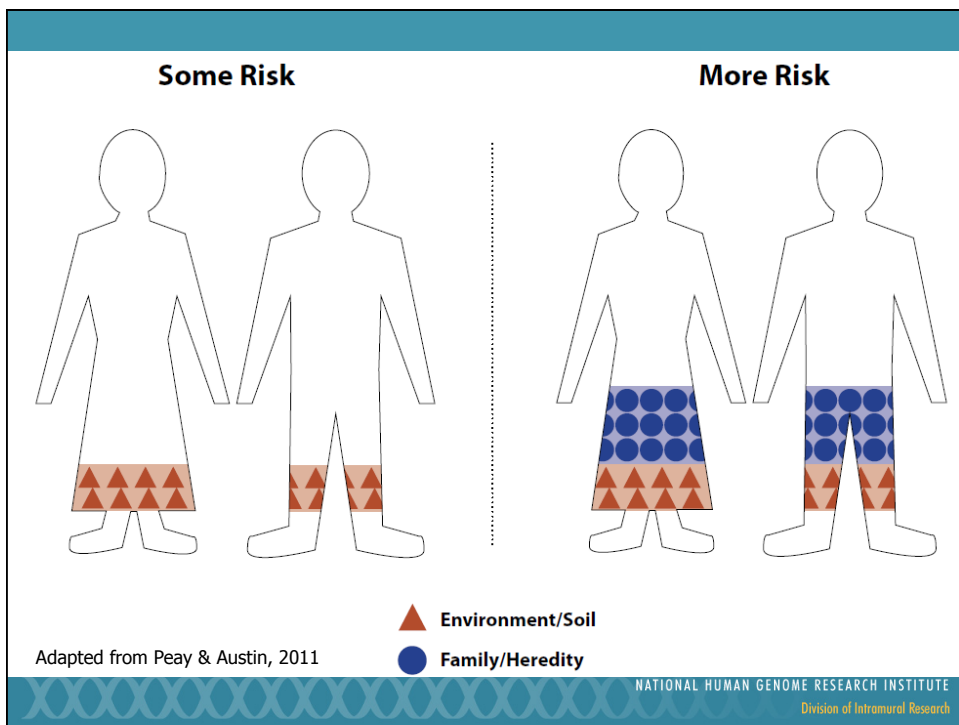
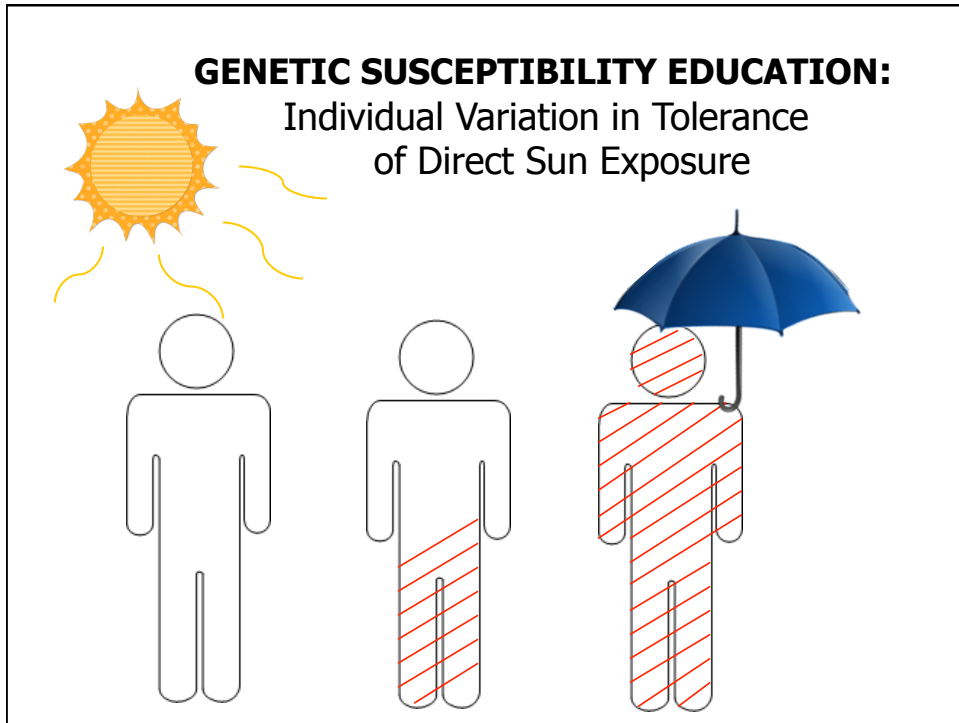
Shoes keep you healthy in the FIELDS

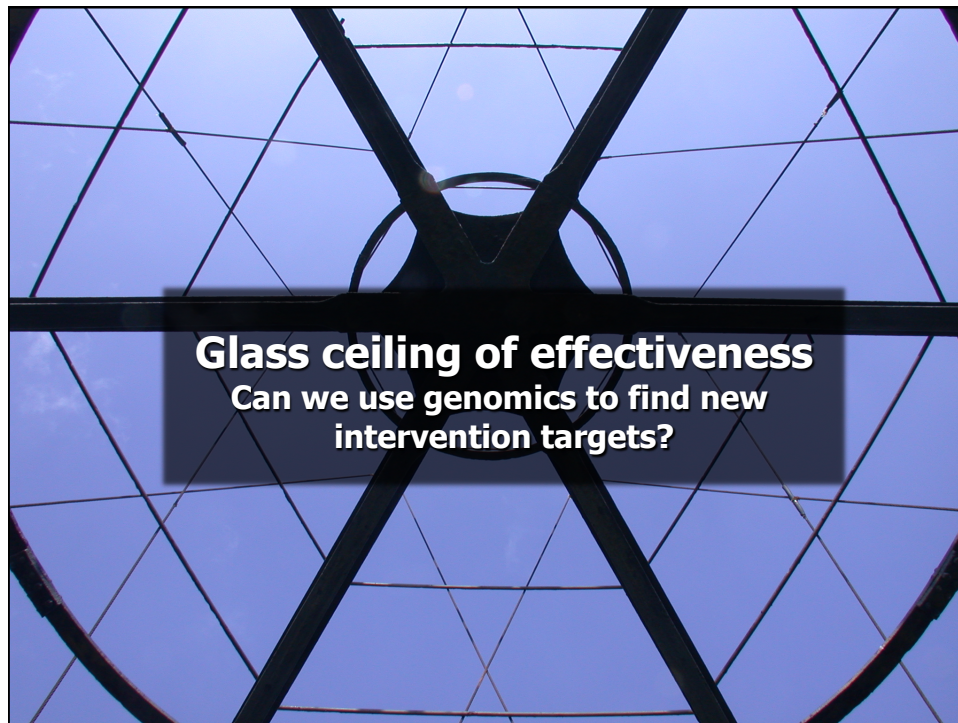
Shoes keep you healthy while you work

Shoes are for PLAY

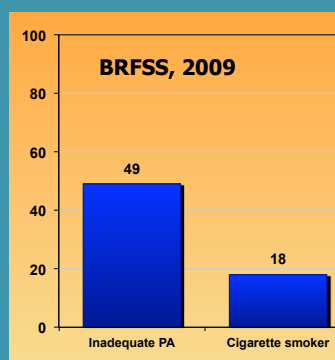
Shoes are for CHORES

Division of Intramural Research





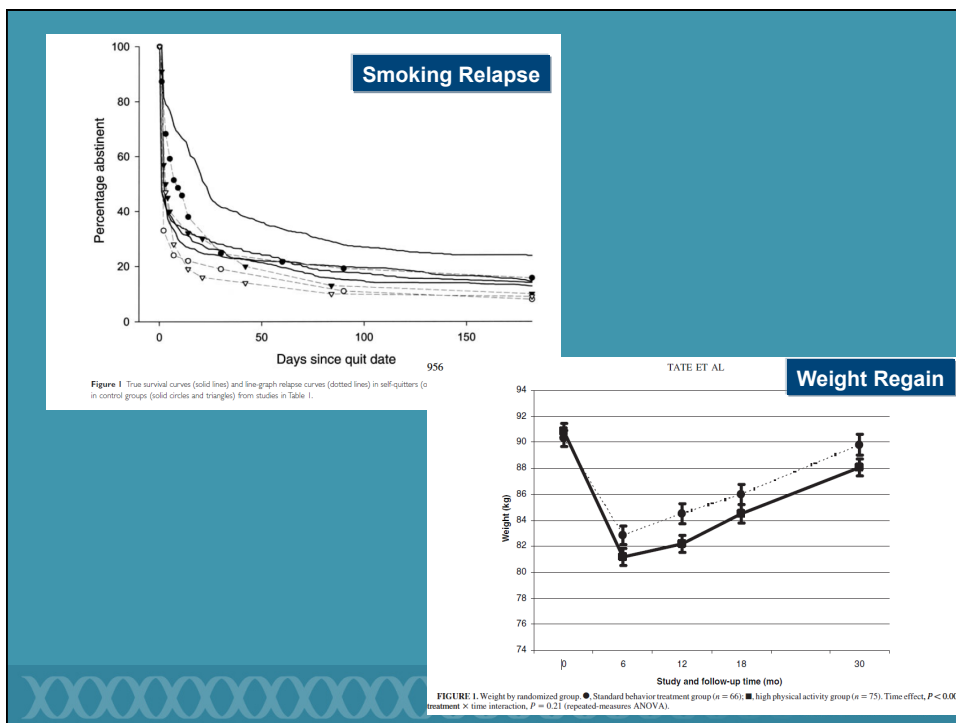
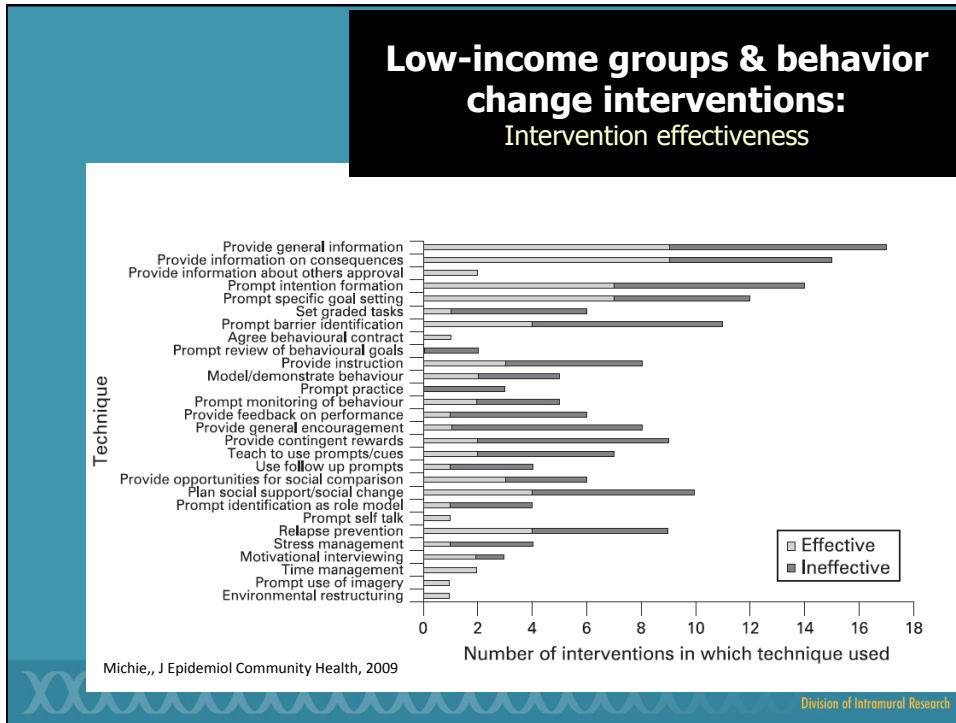
Public Awareness The Behavior – Intervention Disconnect



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



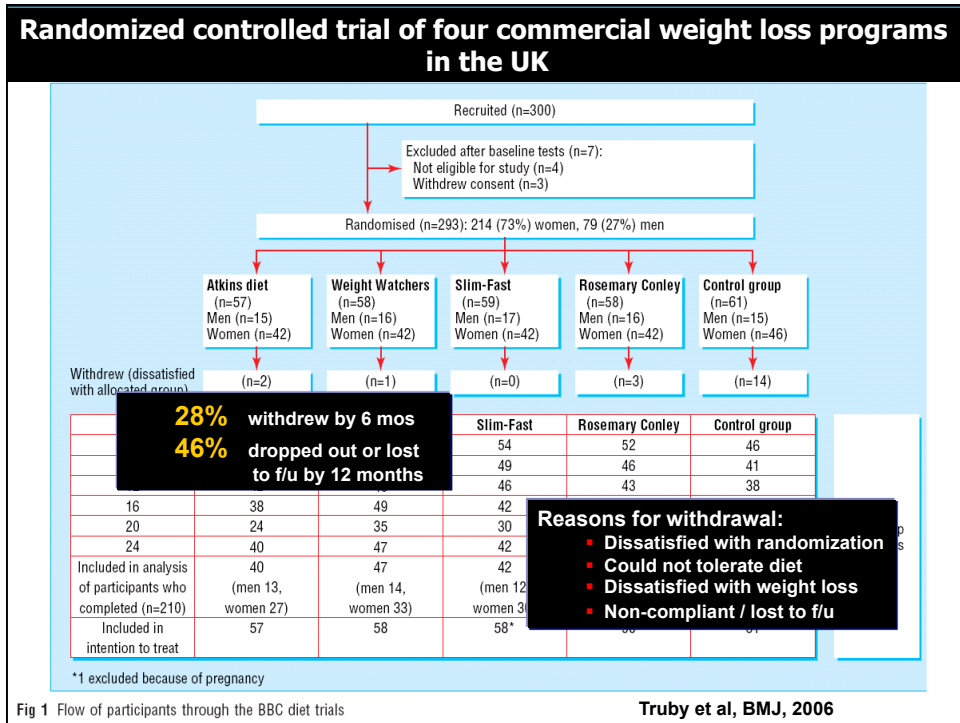
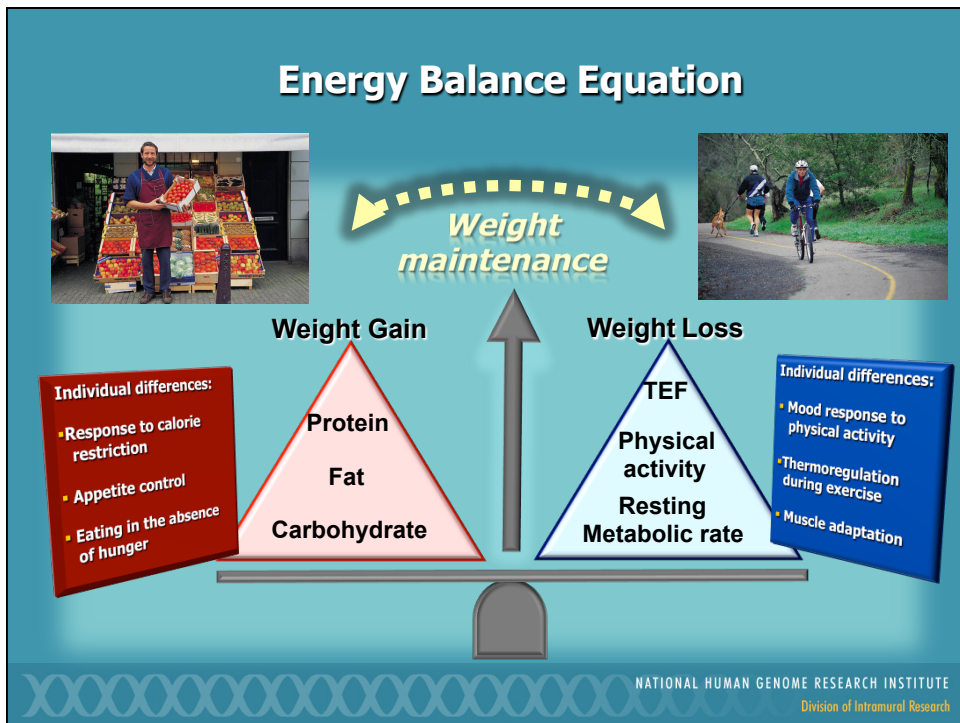
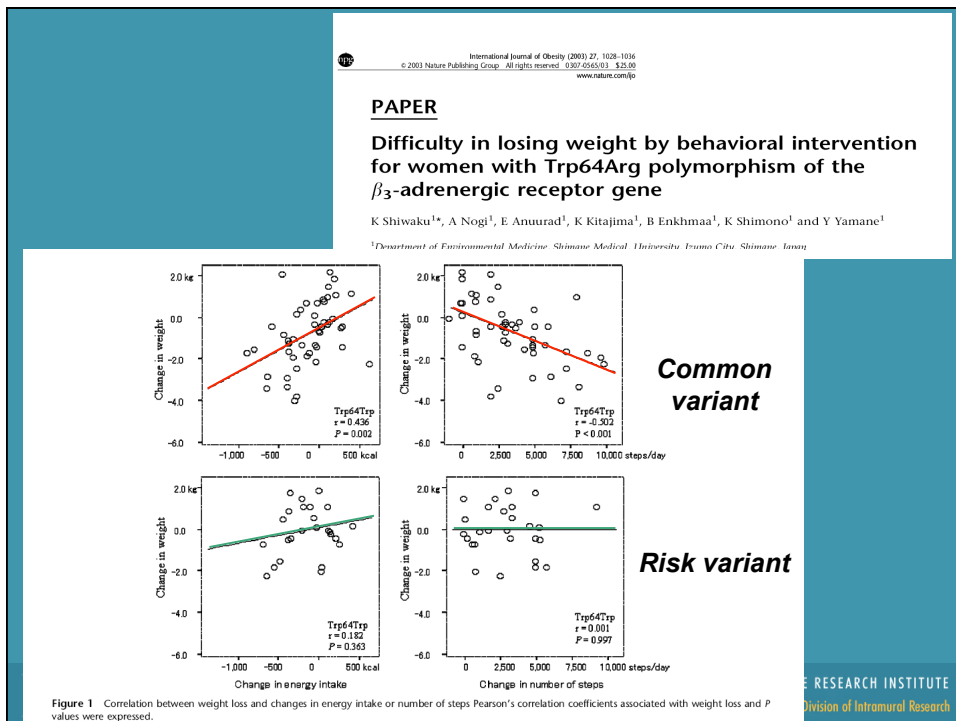
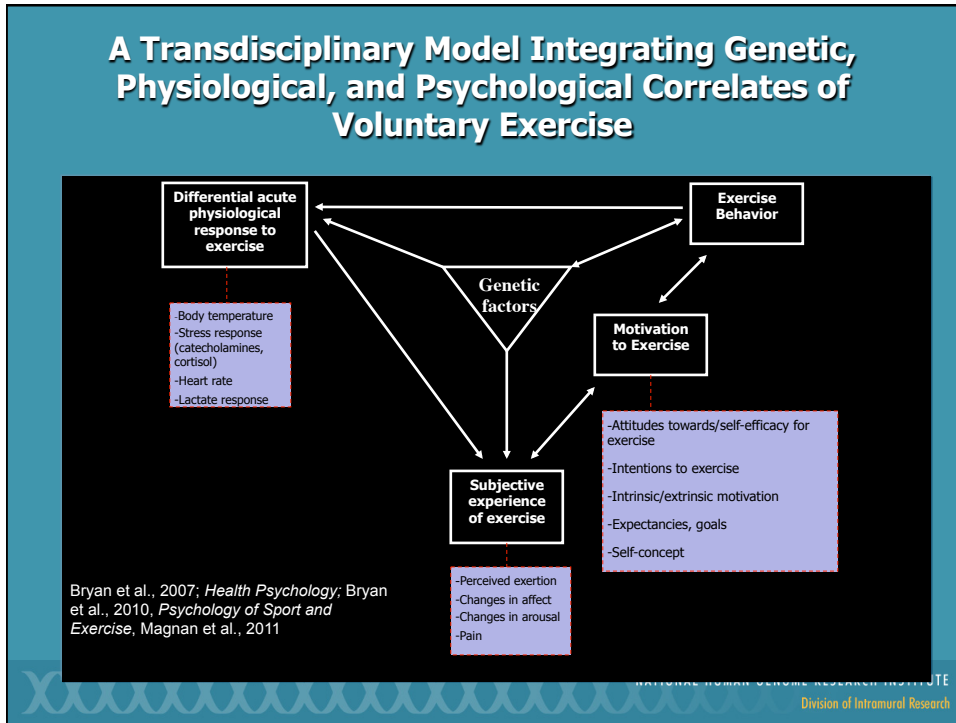
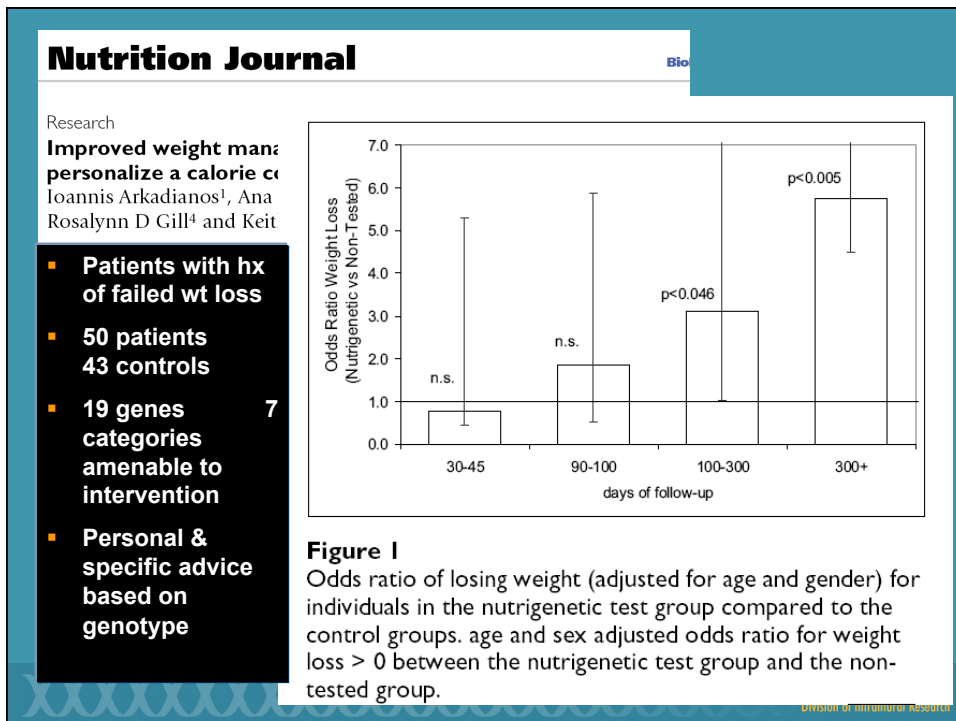
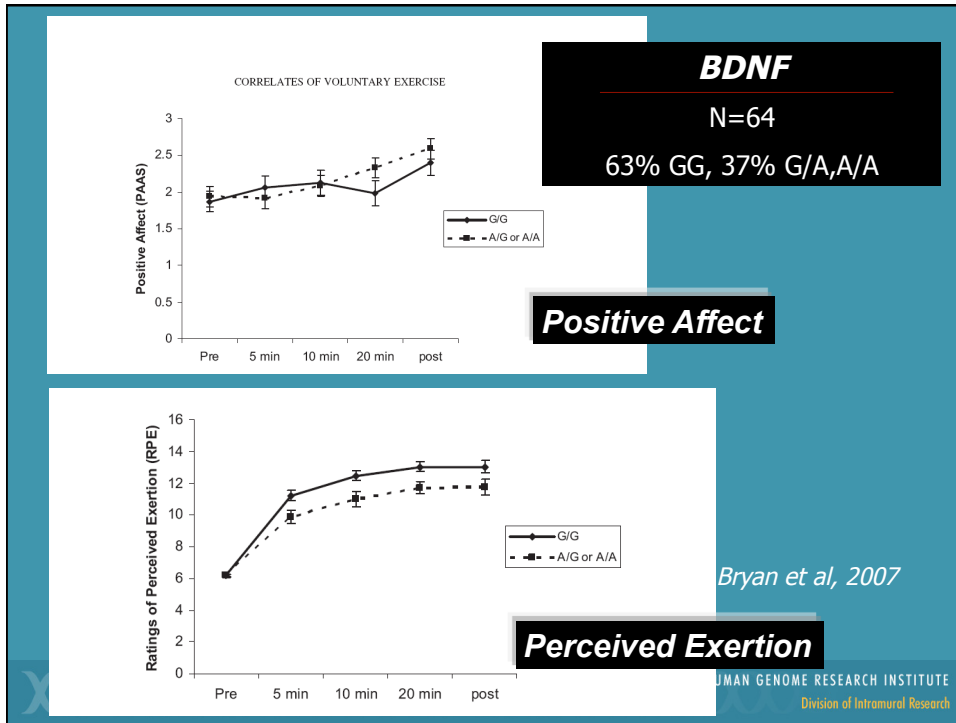


Fig 1 Flow of participants through the BBC diet trials







Take home messages

- Translation research is important
- Many possible avenues for genomics to improve public health
- Conceptual models to guide research questions critical
- Full armamentarium of methods
 - to anticipate and test potential applications of genomics
- Research inherently interdisciplinary

Contact Information

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