NATIONAL HUMAN GENOME RESEARCH INSTITUTE Division of Intramural Research

Public Health Applications of Genomics

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Social and Behavioral Research Branch
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Financial Disclosures

No financial interests that would influence the content of this presentation

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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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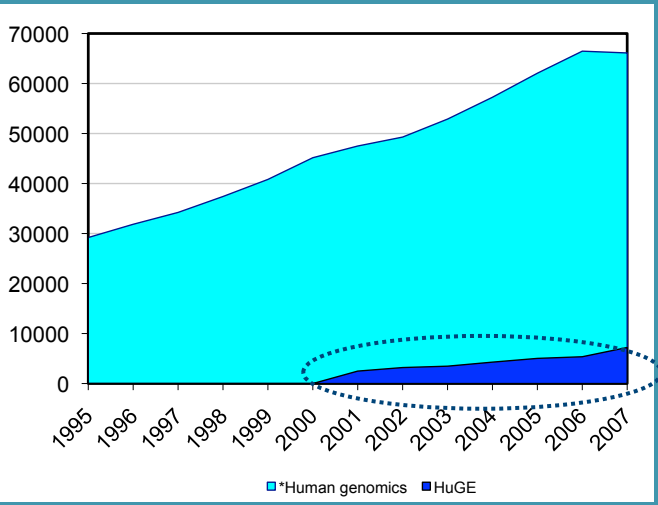
Publications related to human genetics/genomics, PubMed, 2001-2007*



NOPHG, CDC --*based on PubMed, HuGE Navigator, Aug 2008

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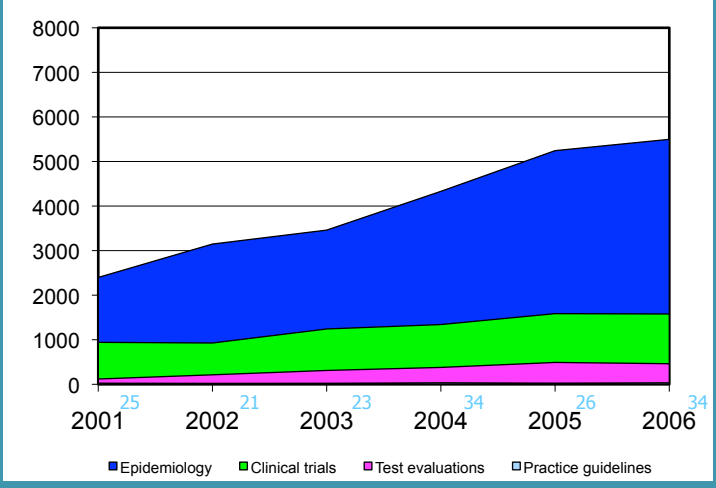
Numbers of publications related to human genetics and genomics, 2001-2006*



*Gwinn et al., from PubMed -- HuGE Navigator

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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	T2	T3	T4
From Gene Discovery to Health Application	From Health Application to Evidence-based Guideline	From Guideline to Health Practice	From Practice to Health Impact

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Genomic Translation: research agenda

Optimal application

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 diseas-
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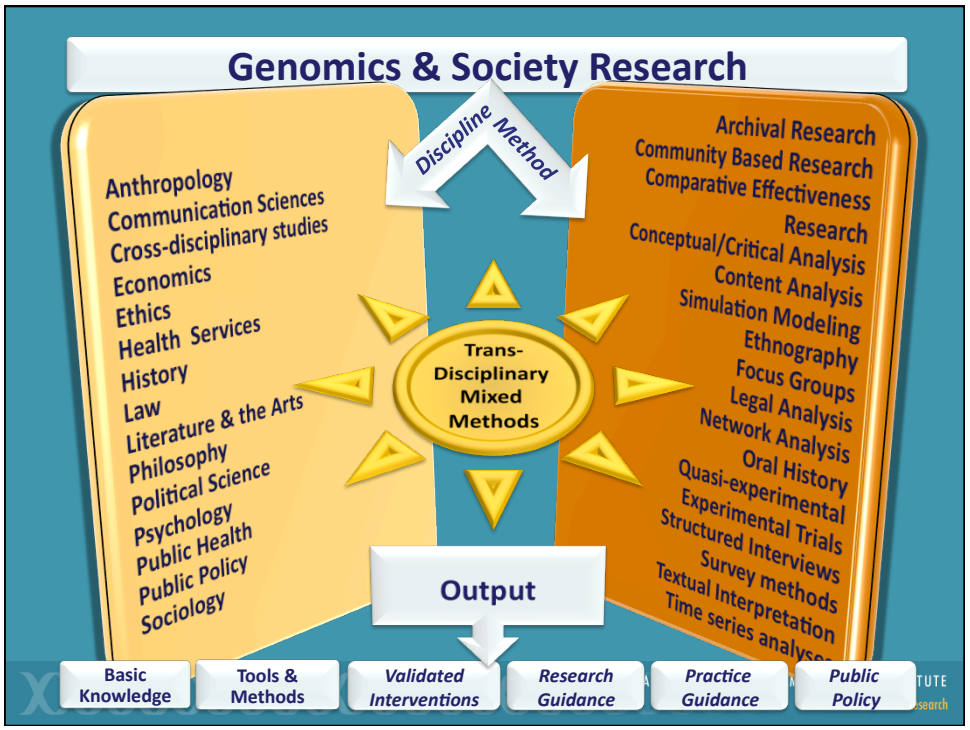
Genomics & Society Research
Discipline
Method
Anthropology
Communication Sciences
Cross-disciplinary studies
Economics
Ethics
Health Services
History
Law
Literature & the Arts
Philosophy
Political Science
Psychology
Public Health
Public Policy
Sociology
Trans-Disciplinary Mixed Methods
Archival Research
Community Based Research
Comparative Effectiveness Research
Conceptual/Critical Analysis
Content Analysis
Simulation Modeling
Ethnography
Focus Groups
Legal Analysis
Network Analysis
Oral History
Quasi-experimental
Experimental Trials
Structured Interviews
Survey methods
Textual Interpretation
Time series analyse
Output
Basic Knowledge
Tools & Methods
Validated Interventions
Research Guidance
Practice Guidance
Public Policy

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

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Intervention Objectives at the Intersection of Genetic Applications

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

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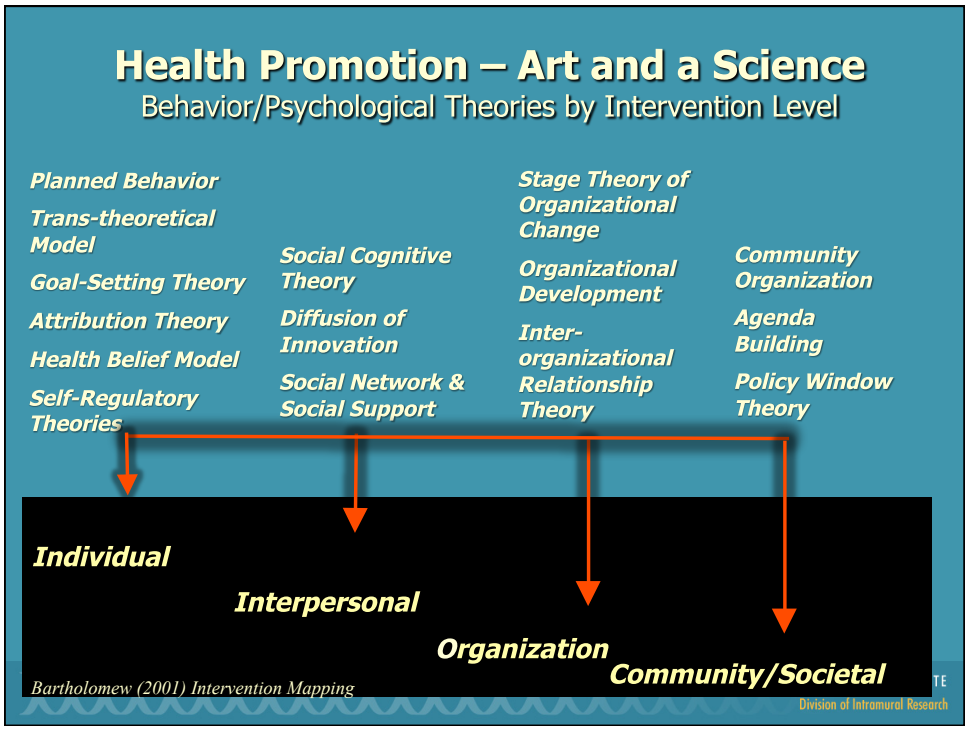
Health Promotion – Art and a Science
Behavior/Psychological Theories by Intervention Level
Planned Behavior
Trans-theoretical Model
Goal-Setting Theory
Attribution Theory
Health Belief Model
Self-Regulatory Theories
Social Cognitive Theory
Diffusion of Innovation
Social Network & Social Support
Stage Theory of Organizational Change
Organizational Development
Inter-organizational Relationship Theory
Community Organization
Agenda Building
Policy Window Theory
Individual
Interpersonal
Organization
Community/Societal
Bartholomew (2001) Intervention Mapping
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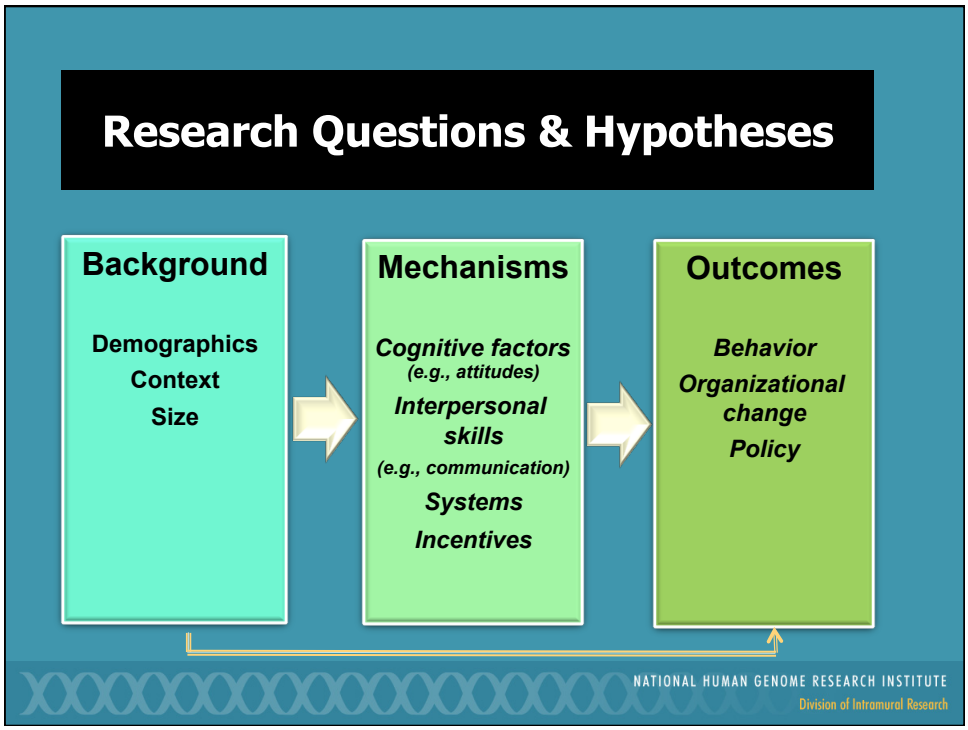
Research Questions & Hypotheses
Background
Demographics
Context
Size
Mechanisms
Cognitive factors
(e.g., attitudes)
Interpersonal skills
(e.g., communication)
Systems
Incentives
Outcomes
Behavior
Organizational change
Policy
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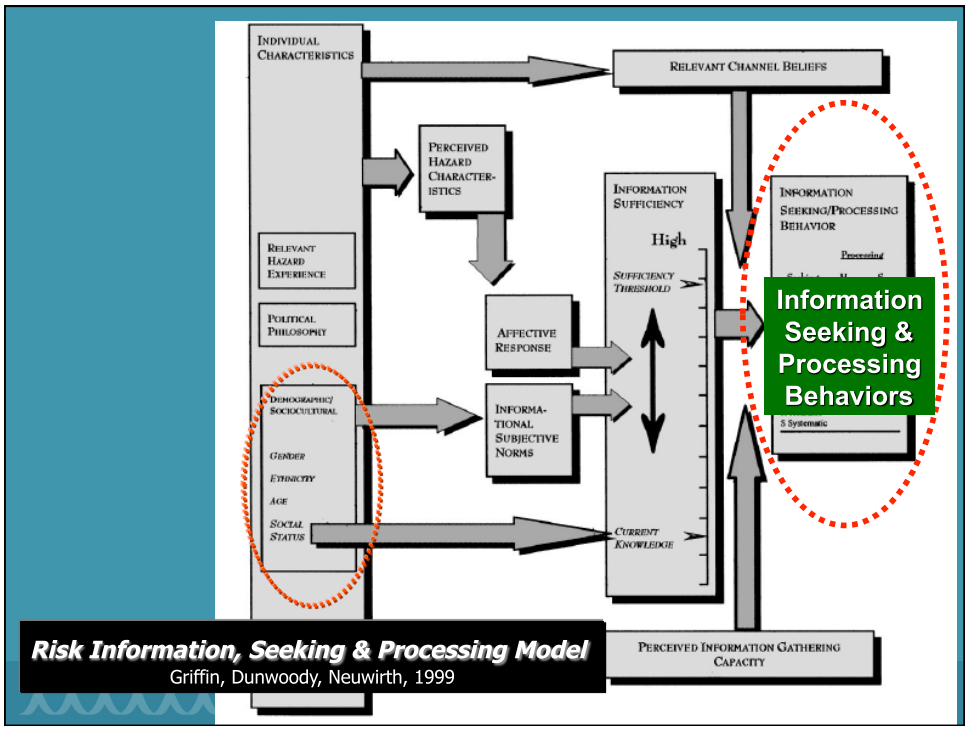
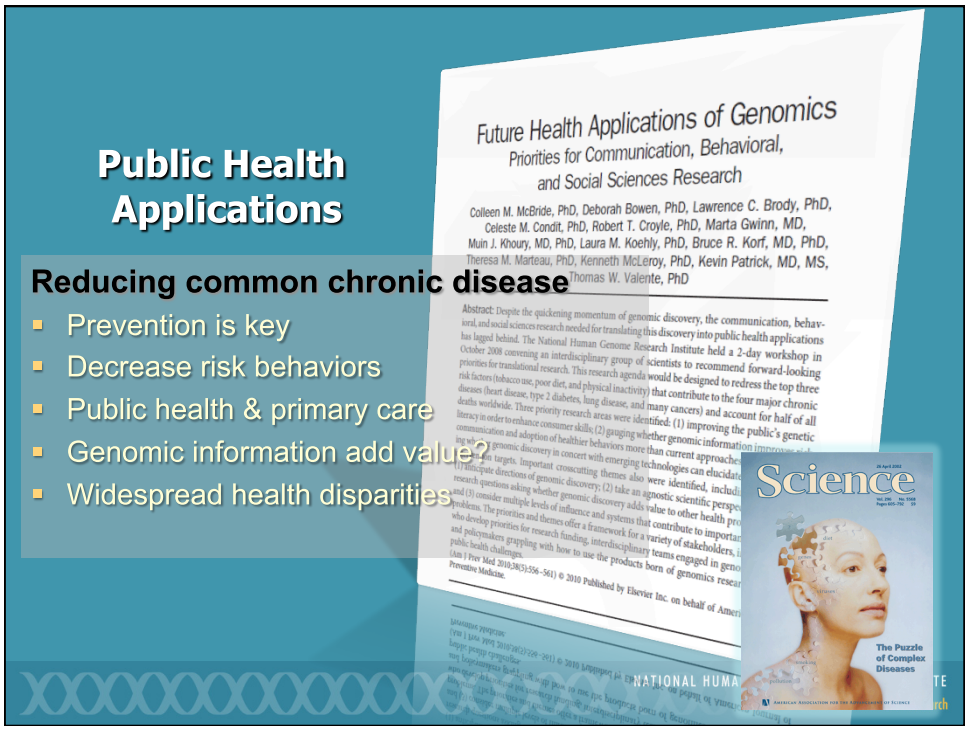

Individual Characteristics
Relevant Channel Beliefs
Perceived Hazard Characteristics
Information Sufficiency
High
Sufficiency Threshold
Information Seeking/Processing Behavior
Relevant Hazard Experience
Political Philosophy
Affective Response
Informational Subjective Norms
Demographic/ Sociocultural
Gender
Ethnicity
Age
Social Status
Current Knowledge
Perceived Information Gathering Capacity
Information Seeking & Processing Behaviors
Risk Information, Seeking & Processing Model
Griffin, Dunwoody, Neuwirth, 1999


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
Science
The Puzzle of Complex Diseases

Example: HNPCC Genetic counseling

Current approach

- High dose:
  - 2-3 hour sessions
- Resource intensive
  - Certified genetic counselor
  - Face to face sessions
- Demanding to sustain
  - Few genetic counselors
  - Reimbursement lacking
  - Expensive
- Highly efficacious
  - Low reach

Public Health approach

- Low dose:
  - < 1 hour
- Resource light
  - Implemented by clinic staff or health educators
  - Telephone, mail, internet
- Sustainable
  - Employ existing infrastructure
  - Inexpensive
- Effectiveness is the goal
  - Broad reach

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Current approach

- Efficacy = .80
- Reach = .10
- .80 x .10
- Effectiveness = .08

Public Health model

- 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

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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

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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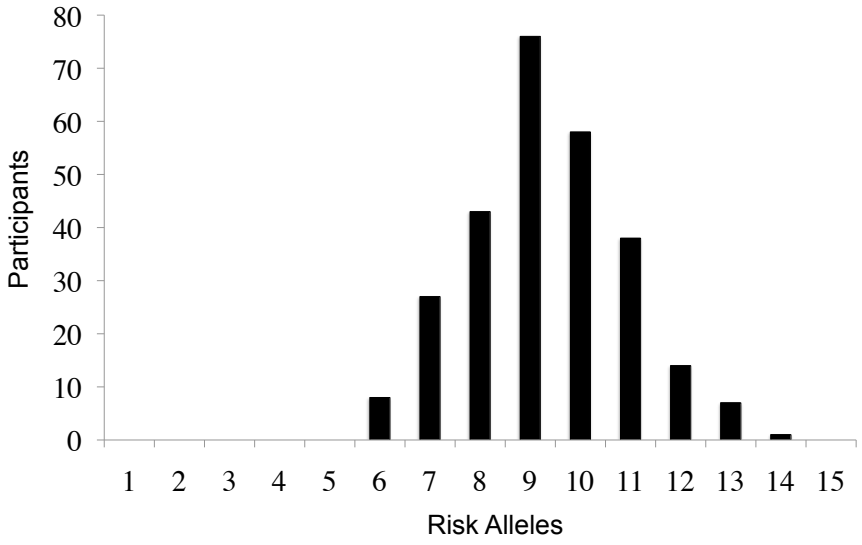
Test Results: Risk Versions

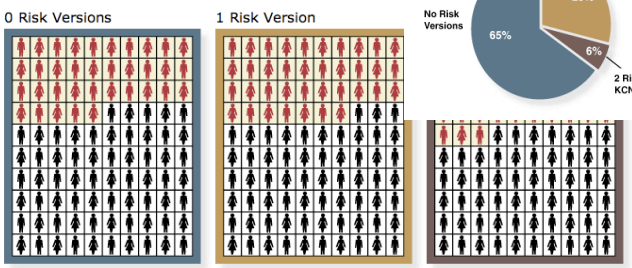


Information About Genes

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.

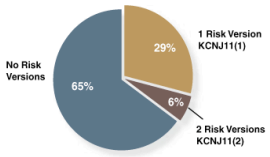
Chance of getting diabetes based on the number of (Out of 100 people. People with diabetes are shown in re



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



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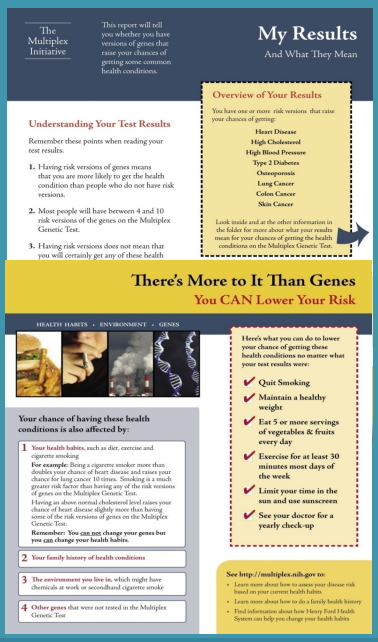
Study Design

- **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



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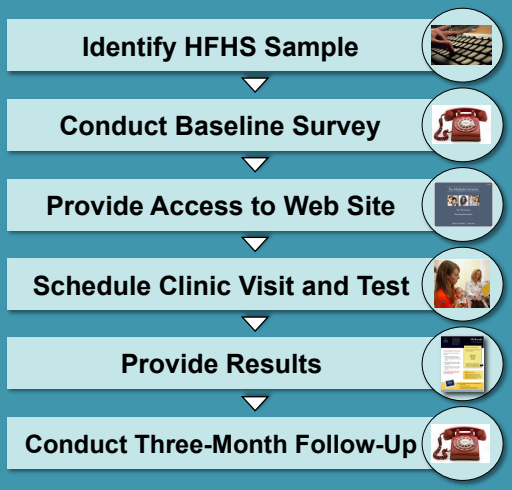
Multiplex Study Flow



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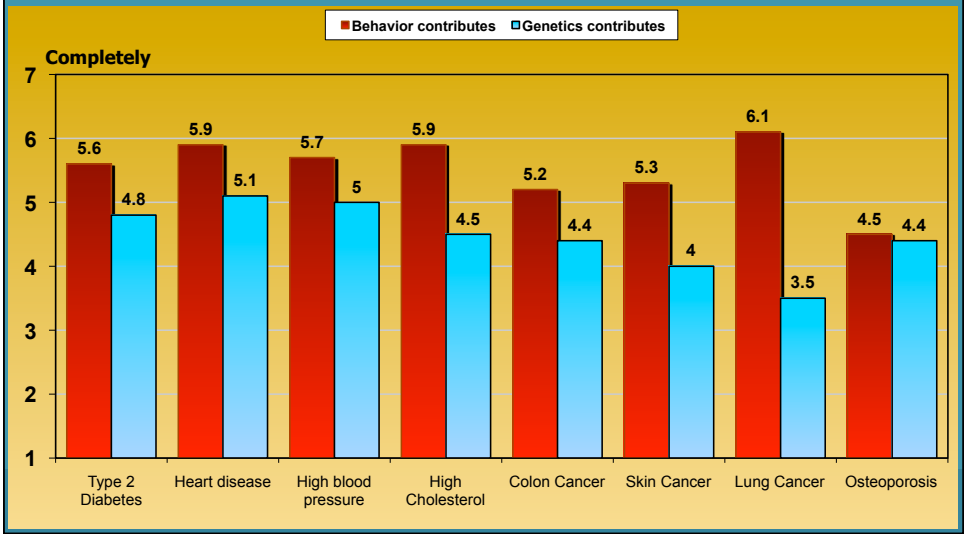
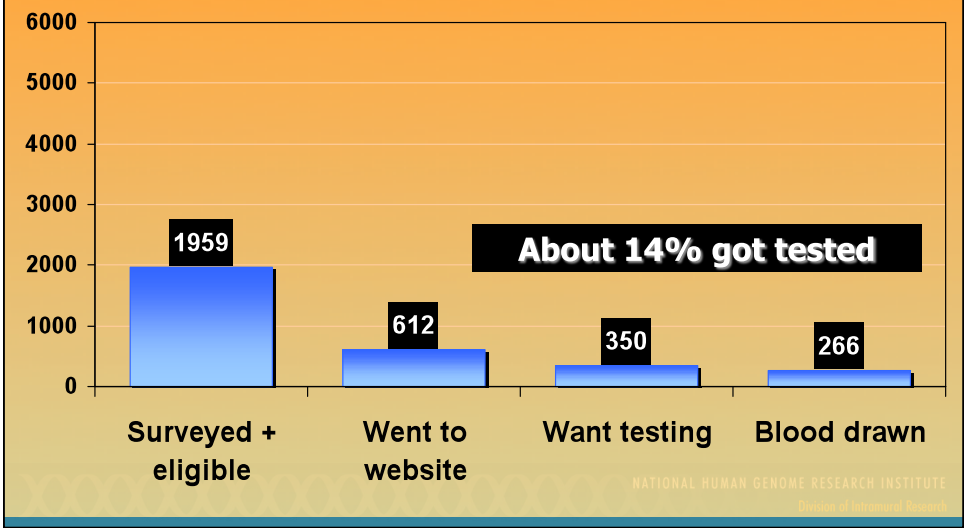
Mean ratings for behavior & genetics as contributors to common health conditions



Multiplex Initiative Uptake

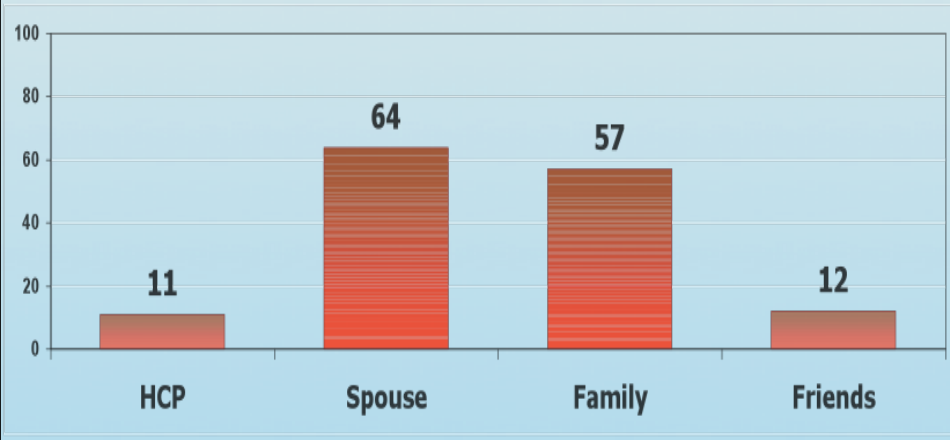


Web usage & decision outcomes

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

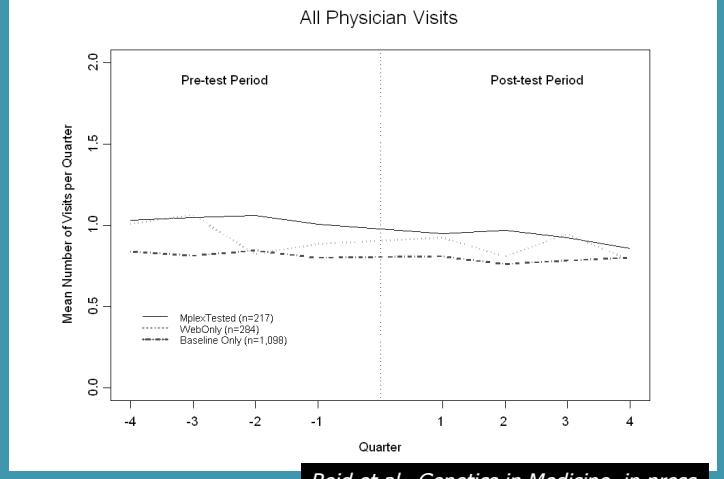
Predictors	Decide to test Odds ratio	Ease of decision Odds ratio
Pages viewed	1.08*	1.04*
Male gender	1.26	0.87
Age	1.03	0.99
Education		
HS or less	0.51*	0.81
Some college	1.04	0.74
Race		
White	1.65	1.00
Black	0.66	0.58
Marital status	0.91	0.96
Family history	1.10	0.94
Genetic self efficacy	1.24*	1.27*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

Results discussed with…



Reid et al., Genetics in Medicine, in press

Health Care Utilization by Test Group



Reid et al., Genetics in Medicine, in press

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Potential to motivate behavior change

Context

Genetic risk communication

↑ Perceived susceptibility
↑ Motivational relevance

↓ Controllability
↓ Confidence to change

MOTIVATION

Likelihood of behavior change

Cognitive capabilities

Motivations

Attitudes, beliefs, affect

Dispositional factors

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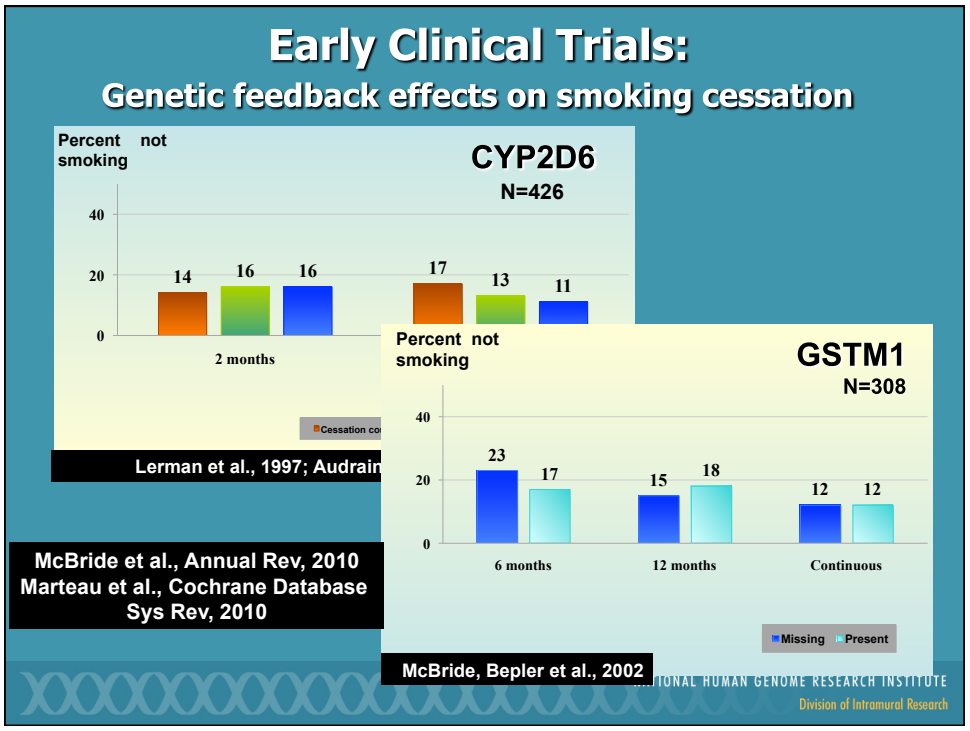
Early Clinical Trials:
Genetic feedback effects on smoking cessation
Percent not smoking
CYP2D6
N=426
40
20
0
14
16
16
17
13
11
2 months
Lerman et al., 1997; Audrain
Percent not smoking
GSTM1
N=308
40
20
0
23
17
15
18
12
12
6 months
12 months
Continuous
Missing
Present
McBride et al., Annual Rev, 2010
Marteau et al., Cochrane Database Sys Rev, 2010
McBride, Bepler et al., 2002
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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?

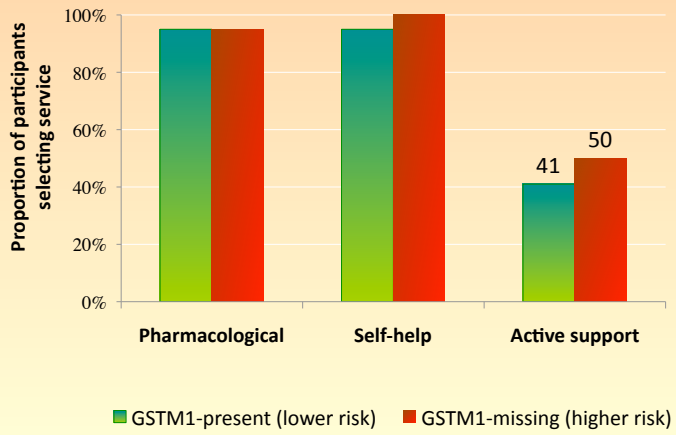
Demographics	Logged on (n = 58)	Did not log on (n = 58)	Sig.
			NS
Female	59%	48%	
Mean Age (yrs)	40.1 (8.3)	36.5 (10.5)	<0.05
Education			
High school or less	28%	36%	NS
Technical degree / some college	50%	41%	
College degree	22%	23%	
Unemployed	14%	14%	NS
Non-Hispanic white	96%	96%	NS
Daily internet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

[1]1-7 scale

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

Uptake of offered cessation services

Sanderson et al., Cancer Epi, Biomarkers & Prevention, 2009



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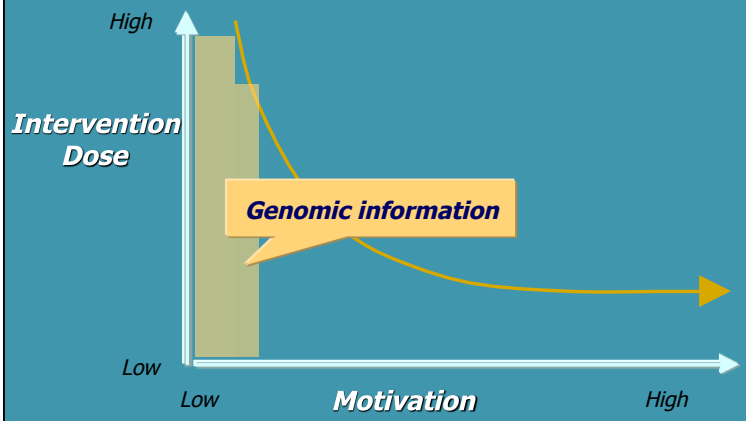
Optimal contexts for genomic information



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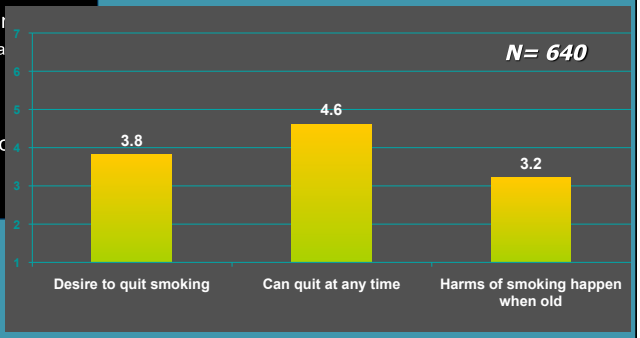
College smokers' responses to genetic risk of lung cancer

Lipkus PI (NCI-funded)

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



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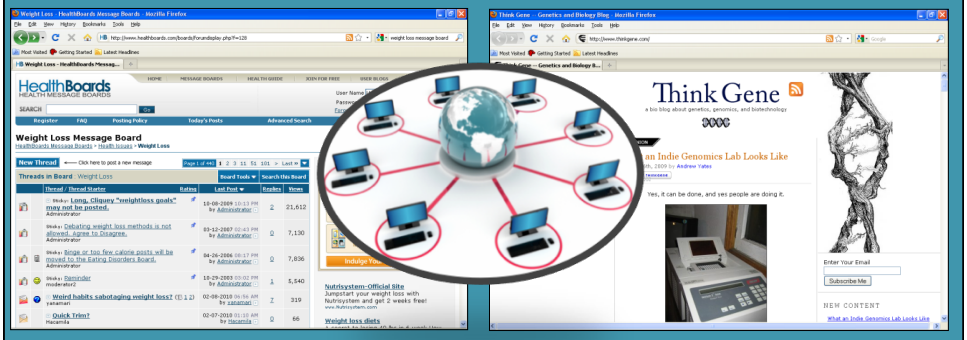
Could social media be a viable tool for engaging target groups in discourse for learning?



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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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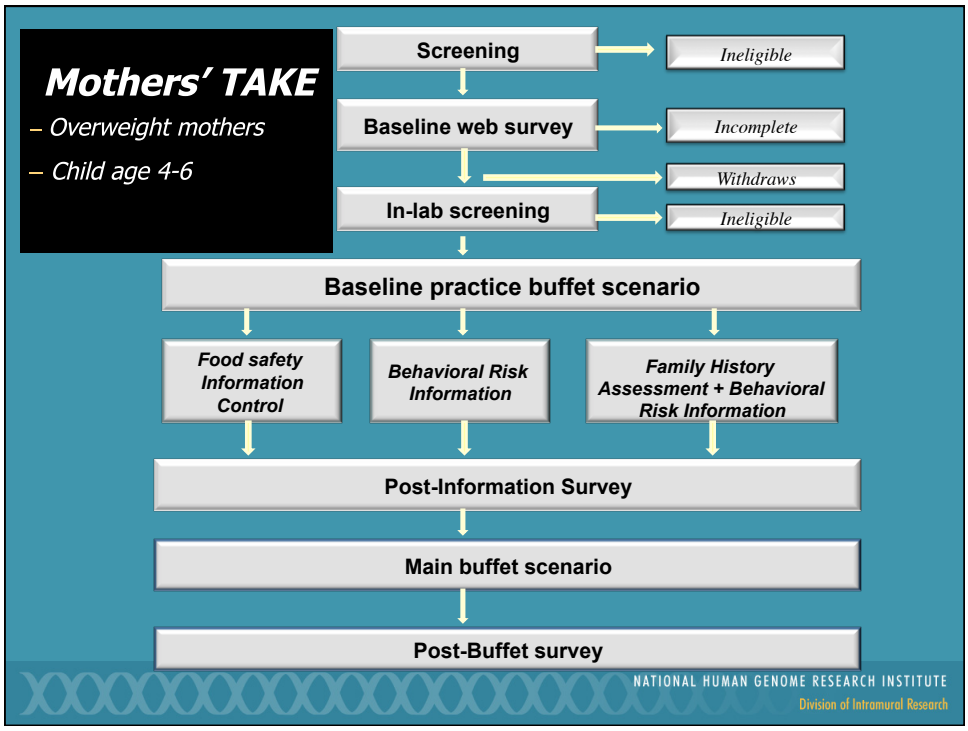
Mothers' TAKE
– Overweight mothers
– Child age 4-6
Screening
Ineligible
Baseline web survey
Incomplete
Withdraws
In-lab screening
Ineligible
Baseline practice buffet scenario
Food safety Information Control
Behavioral Risk Information
Family History Assessment + Behavioral Risk Information
Post-Information Survey
Main buffet scenario
Post-Buffet survey
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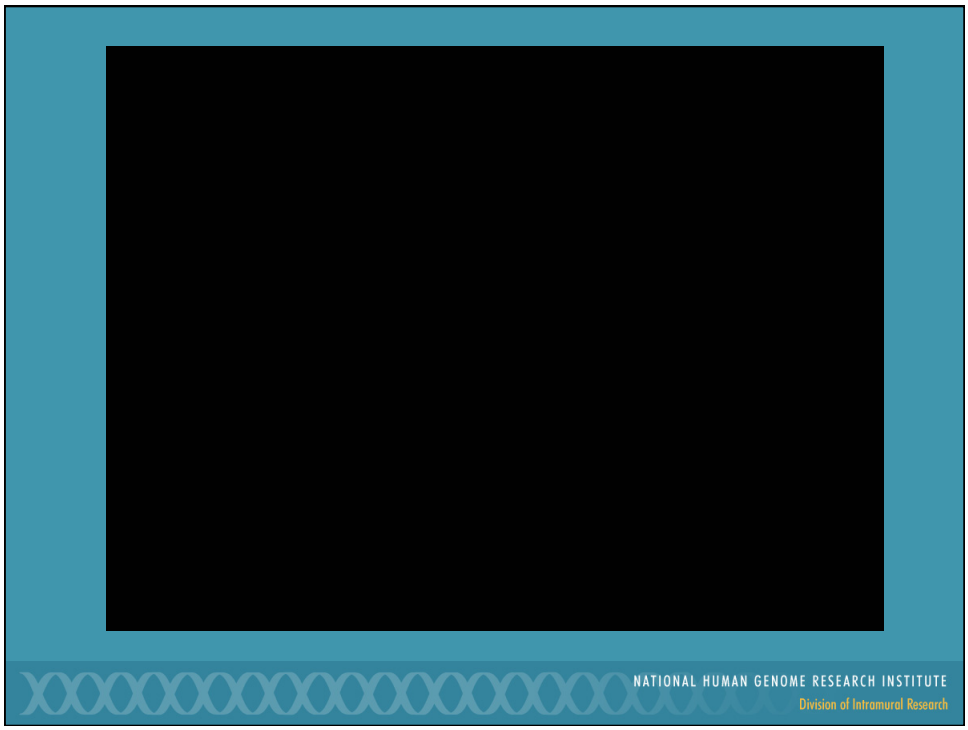
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Virtual Buffet

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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			
Distance from MFTPA (Km)	35			

*Registered annually with MFTPA

28 Focus groups
38 Individual interviews
7 Case studies
307 Participants

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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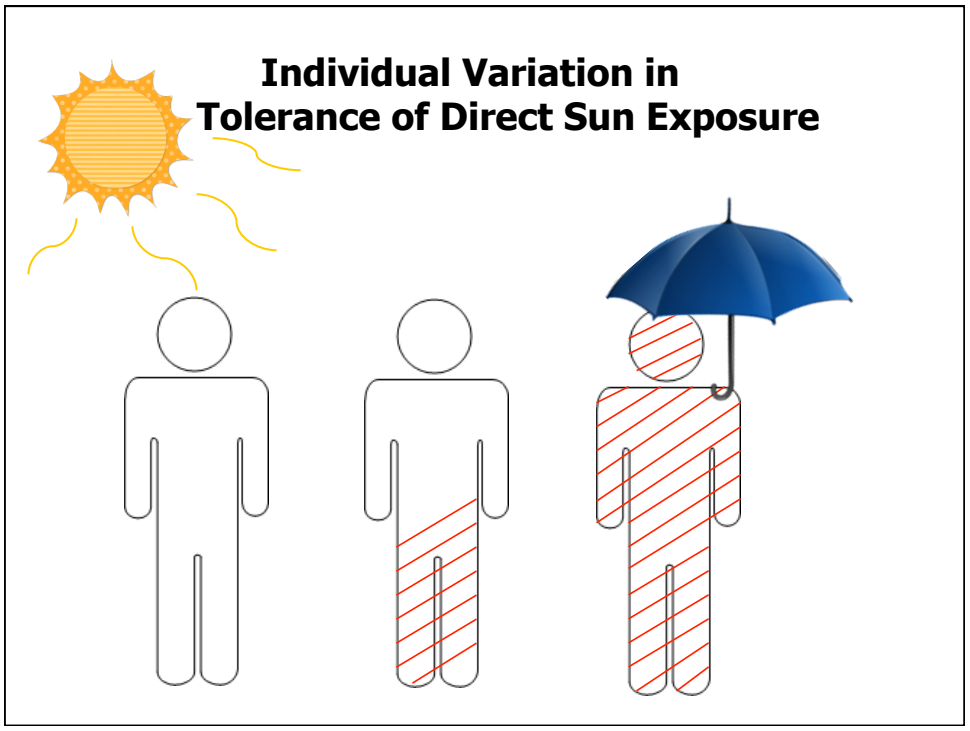
Study Design

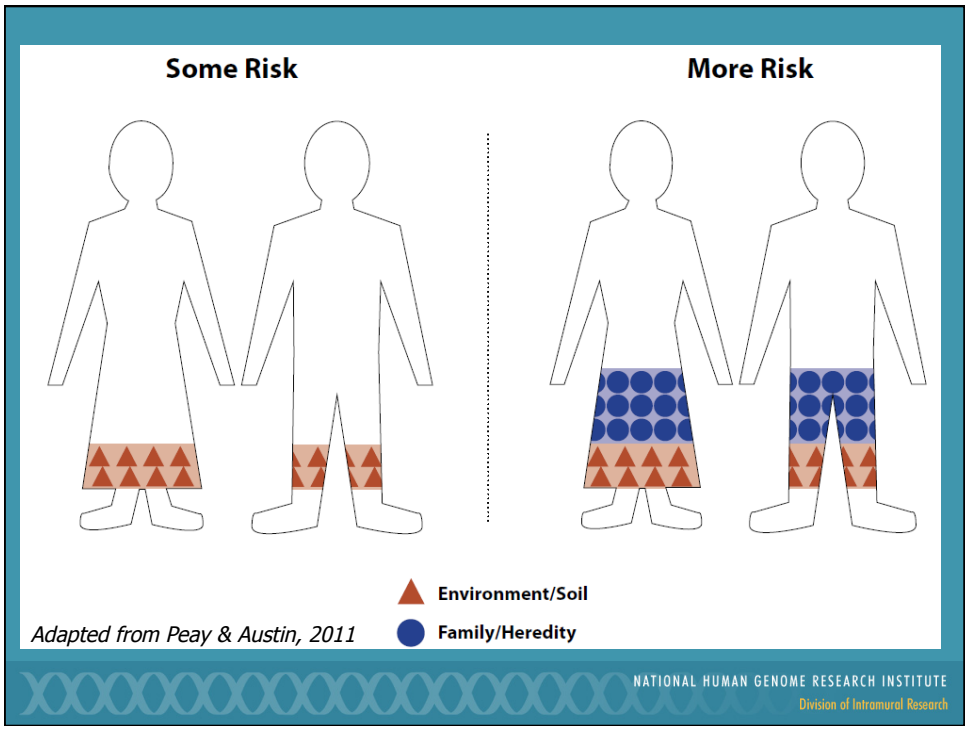
Community Level Interventions Quasi-experimental Design

- **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

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


Individual Variation in
Tolerance of Direct Sun Exposure


Some Risk
More Risk
Environment/Soil
Family/Heredity
Adapted from Peay & Austin, 2011
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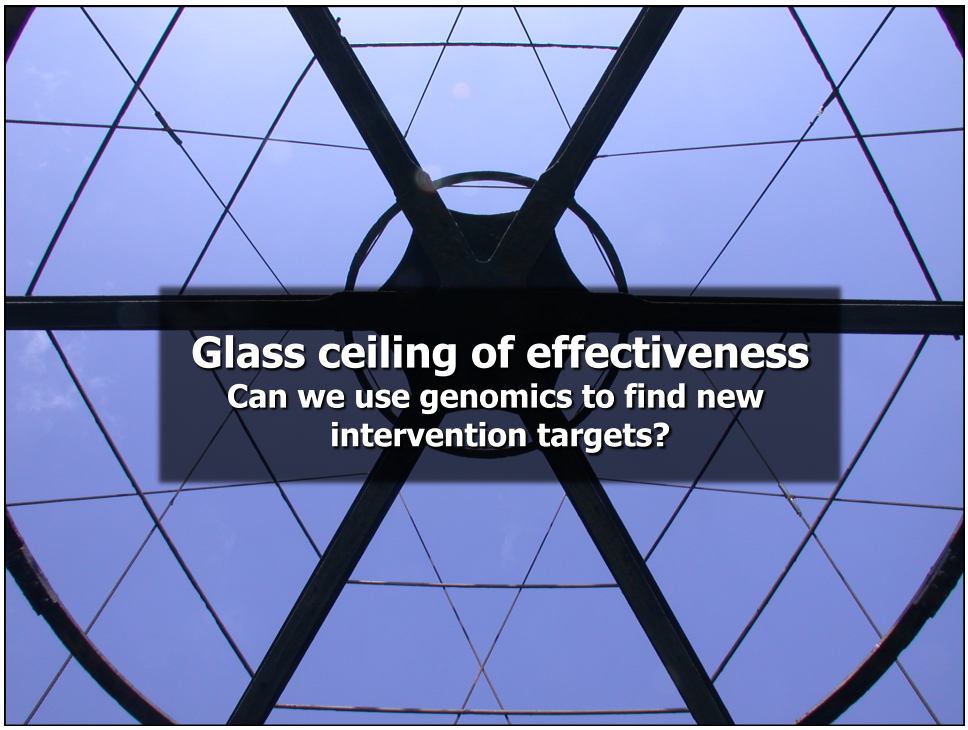
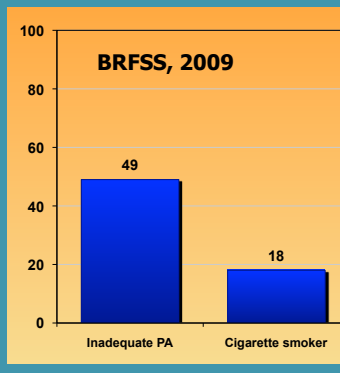


Public Awareness
The Behavior – Intervention Disconnect



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

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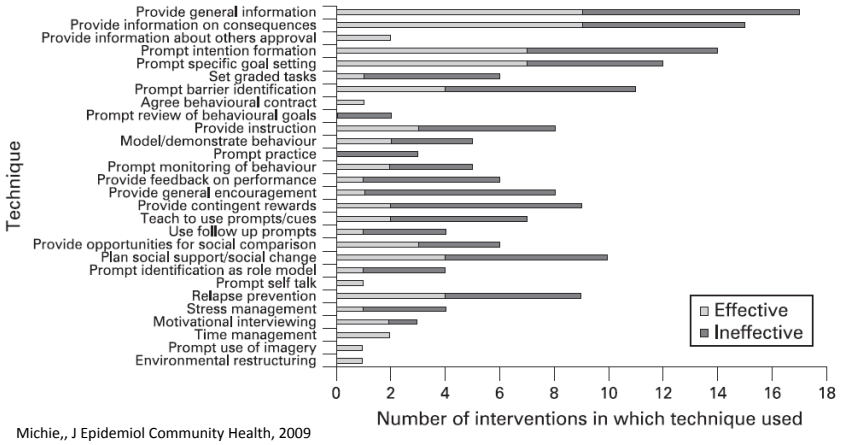
Low-income groups & behavior change interventions:
Intervention effectiveness



Michie,, J Epidemiol Community Health, 2009

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Smoking Relapse

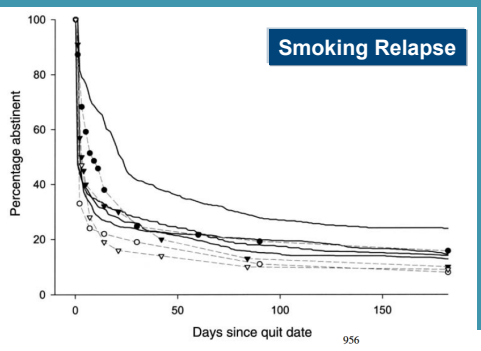

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Figure 1 True survival curves (solid lines) and line-graph relapse curves (dotted lines) in self-quitters (o in control groups (solid circles and triangles) from studies in Table 1.

TATE ET AL

Weight Regain

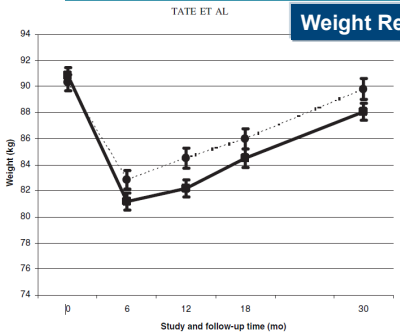


FIGURE 1. Weight by randomized group. ●, Standard behavior treatment group ($n = 66$); ■, high physical activity group ($n = 75$). Time effect, $P < 0.001$; treatment × time interaction, $P = 0.21$ (repeated-measures ANOVA).

Randomized controlled trial of four commercial weight loss programs in the UK

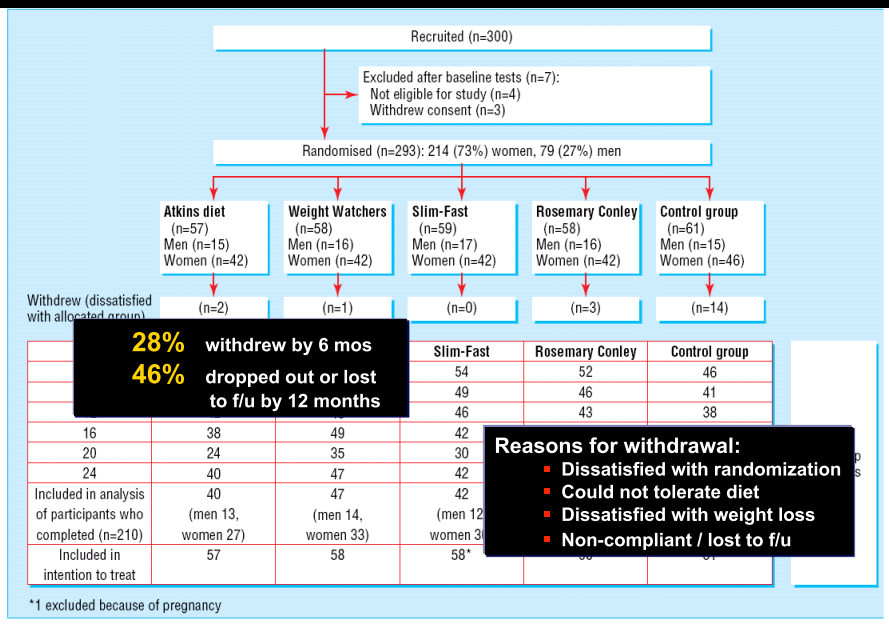
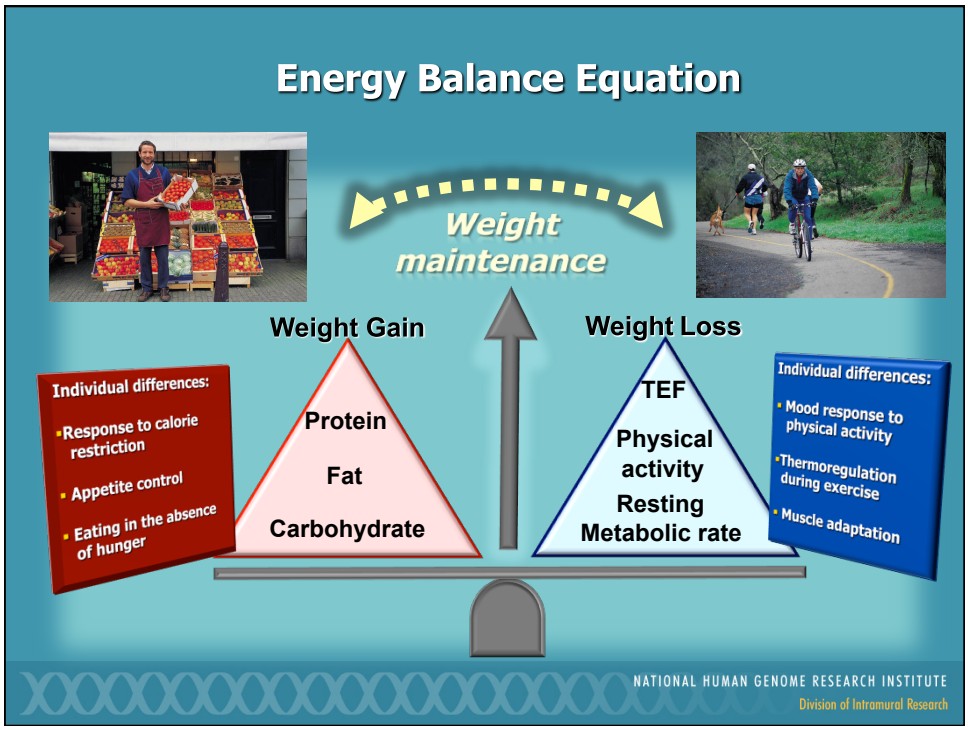
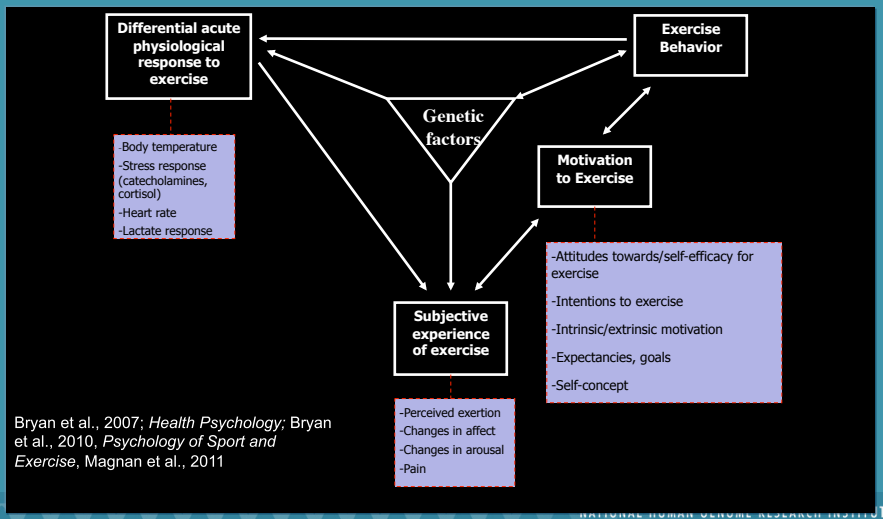


Fig 1 Flow of participants through the BBC diet trials

Truby et al, BMJ, 2006



A Transdisciplinary Model Integrating Genetic, Physiological, and Psychological Correlates of Voluntary Exercise



Bryan et al., 2007; *Health Psychology;* Bryan et al., 2010, *Psychology of Sport and Exercise*, Magnan et al., 2011

International Journal of Obesity (2003) 27, 1028–1036
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www.nature.com/ijo

PAPER

Difficulty in losing weight by behavioral intervention for women with Trp64Arg polymorphism of the β_3-adrenergic receptor gene

K Shiwaku[1]*, A Nogi[1], E Anuurad[1], K Kitajima[1], B Enkhmaa[1], K Shimono[1] and Y Yamane[1]

[1]Department of Environmental Medicine, Shimane Medical University, Izumo City, Shimane, Japan

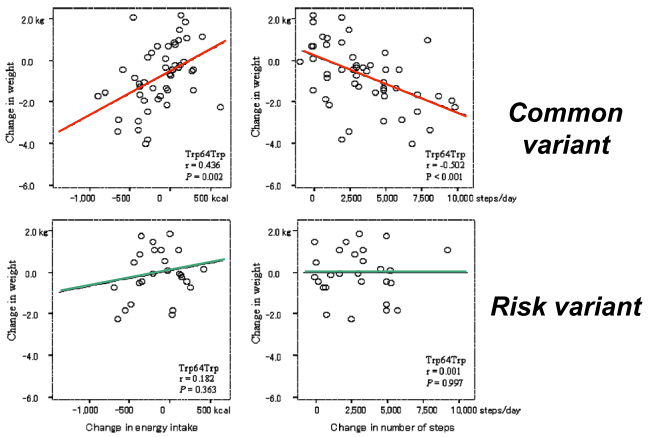
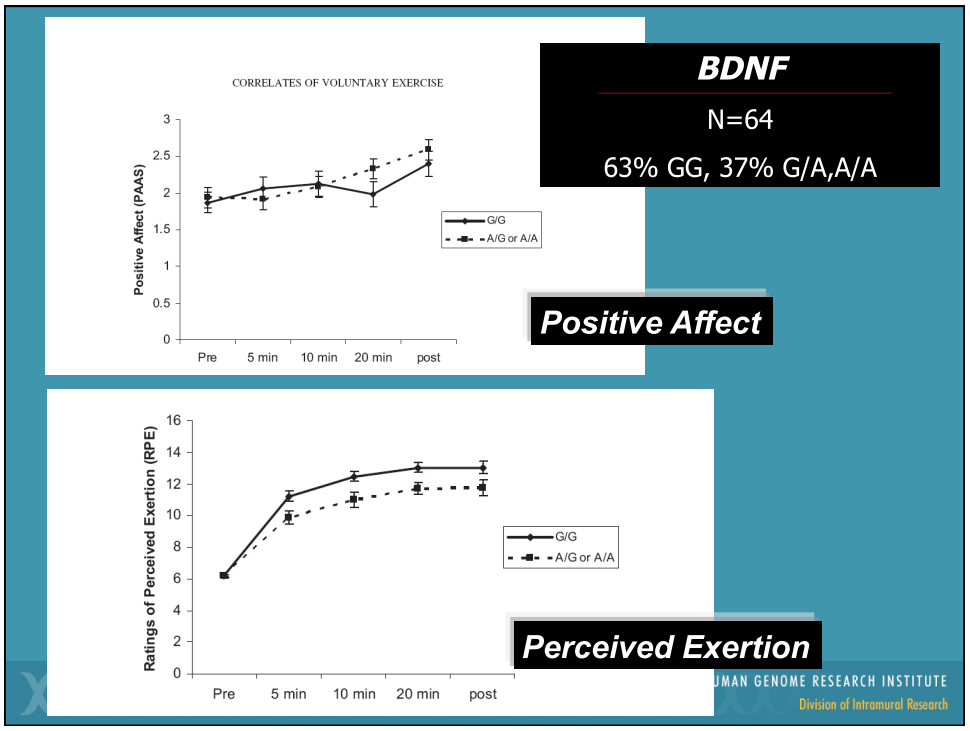


Figure 1 Correlation between weight loss and changes in energy intake or number of steps Pearson's correlation coefficients associated with weight loss and *P* values were expressed.


CORRELATES OF VOLUNTARY EXERCISE
Positive Affect (PAAS)
3
2.5
2
1.5
1
0.5
0
Pre
5 min
10 min
20 min
post
G/G
A/G or A/A
BDNF
N=64
63% GG, 37% G/A,A/A
Positive Affect
Ratings of Perceived Exertion (RPE)
16
14
12
10
8
6
4
2
0
Pre
5 min
10 min
20 min
post
G/G
A/G or A/A
Perceived Exertion
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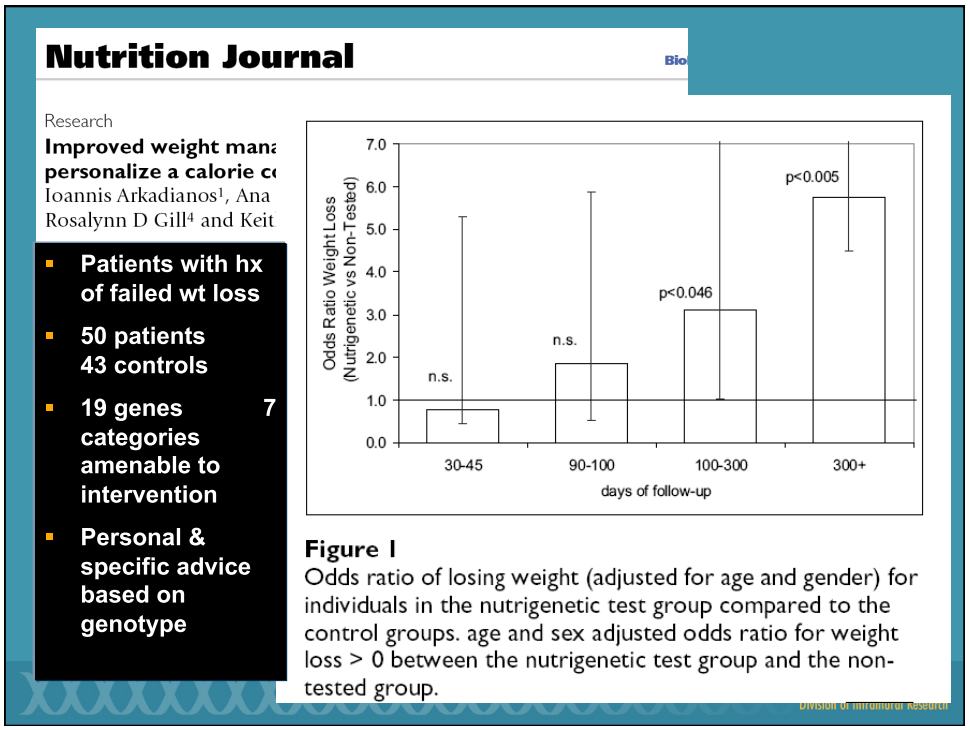
Nutrition Journal
Research
Improved weight mana
personalize a calorie c
Ioannis Arkadianos[1], Ana
Rosalynn D Gill[4] and Keit
Patients with hx of failed wt loss
50 patients 43 controls
19 genes 7 categories amenable to intervention
Personal & specific advice based on genotype
Odds Ratio Weight Loss (Nutrigenetic vs Non-Tested)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
n.s.
n.s.
p<0.046
p<0.005
30-45
90-100
100-300
300+
days of follow-up
Figure 1
Odds ratio of losing weight (adjusted for age and gender) for individuals in the nutrigenetic test group compared to the control groups. age and sex adjusted odds ratio for weight loss > 0 between the nutrigenetic test group and the non-tested group.

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

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