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# **Bridging the Gap** **from Genomes To Public Health** A Role for Behavioral & Social Sciences

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**Colleen M. McBride, Ph.D.**  
Social & Behavioral Research Branch  
National Human Genome Research Institute



# Today's Talk

- **Potential contribution of genomics to improve public health**
- **Addressing common health conditions**
  - Reducing prevalent behavioral risk factors
  - Reducing disparities in chronic disease outcomes
  - Improving health care delivery at reduced cost
- **Important role for social & behavioral research**
  - Proactive research agenda
  - Frame change
- **Suggestions for next steps**

FEBRUARY 17, 2003

COUNTDOWN TO WAR

# TIME

SPECIAL REPORT

SOLVING  
THE  
MYSTERIES  
OF

# DNA

*The 50th Anniversary:  
Reliving Watson and Crick's  
historic discovery*

*How gene science has  
changed our lives*

*Visions of the future*

**CNN ranked in  
top 25 stories**



www.time.com AOL Keyword: TIME

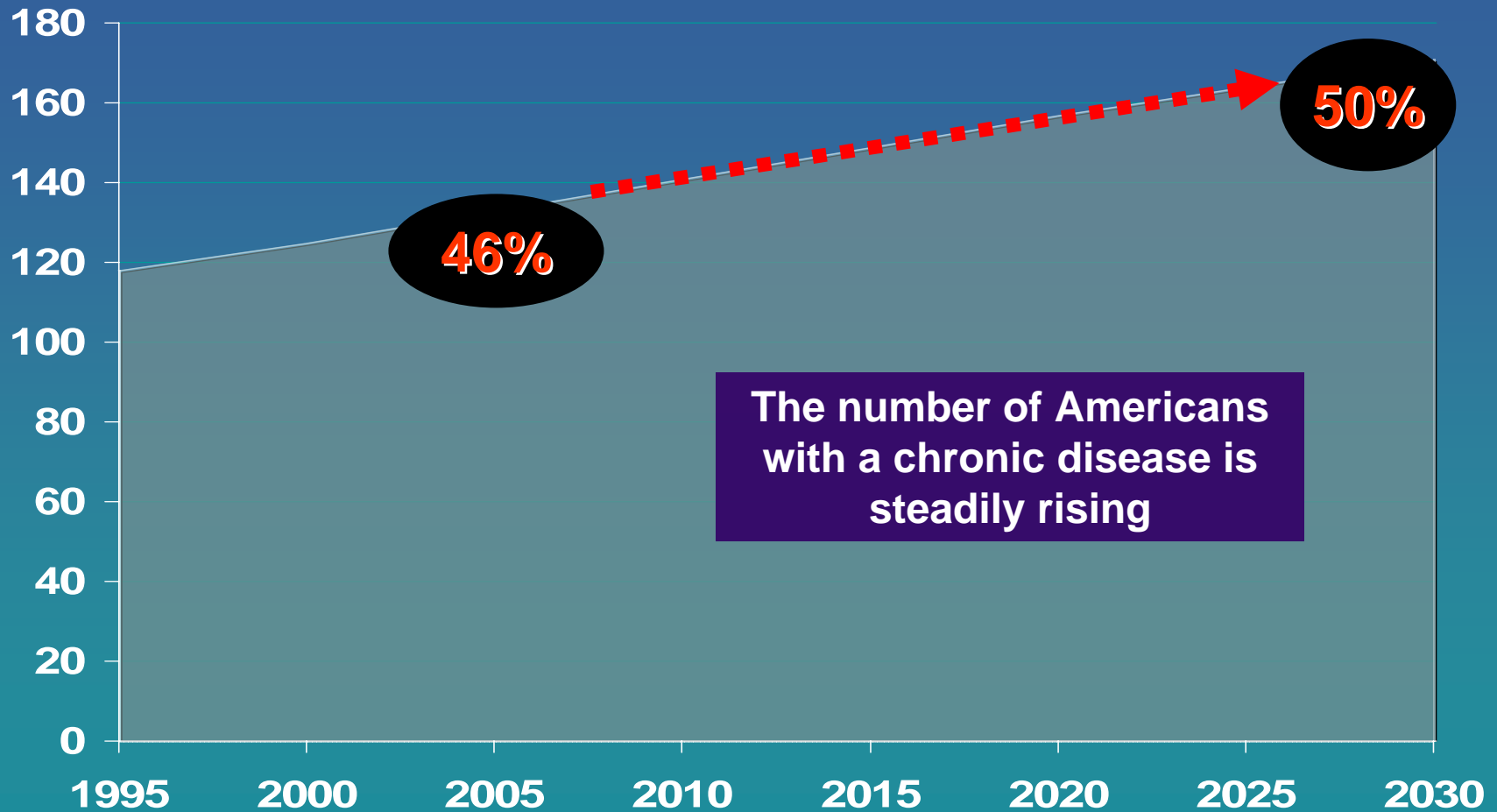
GENOME RESEARCH INSTITUTE  
Division of Intramural Research

PHASE TWO: INTERPRETATION

SEIDMAN The Star-Ledger

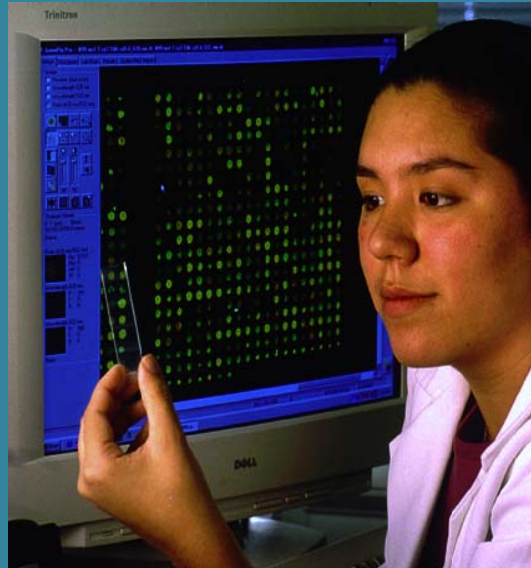


# Public Health Burden = Chronic disease





# Transform Medicine Through Discovery



Predictive ↔ Personalized ↔ Preemptive

# Promise of Genetic Testing & Personalization

## Risk assessment

- ↑ Individual Adherence
  - Prevention recommendations
  - Treatment regimens
- ↑ Health care efficiency
- ↑ Sensitivity of risk stratification at population level

# Challenge for Common Disease



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**Mendelian**  
**1 gene = 1 trait**

- Multiple genes involved
- Usually, small effect per gene
- Common Disease =  
Genes ( $g_1 + g_2 + g_3 \dots$ )  
+ Environment ( $e_1 + e_2 + e_3 \dots$ )
- Pleitropy



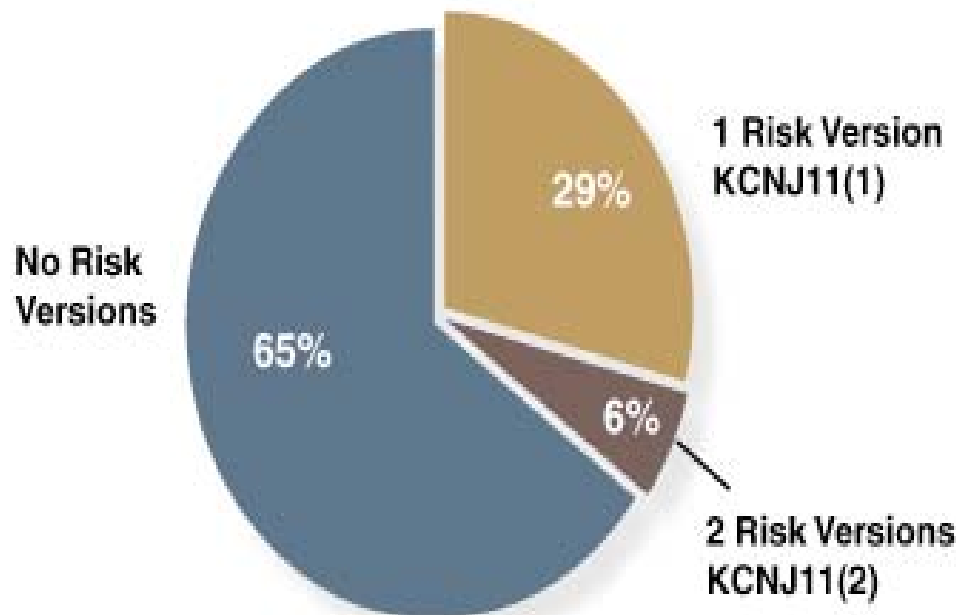
# Common Genetic Variants & Common Conditions

	<u>Marker</u>	<u>Function</u>
<b>Drug Response</b>	Cytochrome P450	Drug metabolism
<b>Colon Cancer</b>	MTHFR	Folate metabolism
<b>Type 2 Diabetes</b>	PPAR gamma KCNJ11	Fat cell development Insulin regulation
<b>Lipid metabolism</b>	OLR1, IL-6	Plaque development Inflammatory response
<b>Osteoporosis</b>	COLIA1, ER-a	Accelerated bone loss Estrogen resistance

## 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

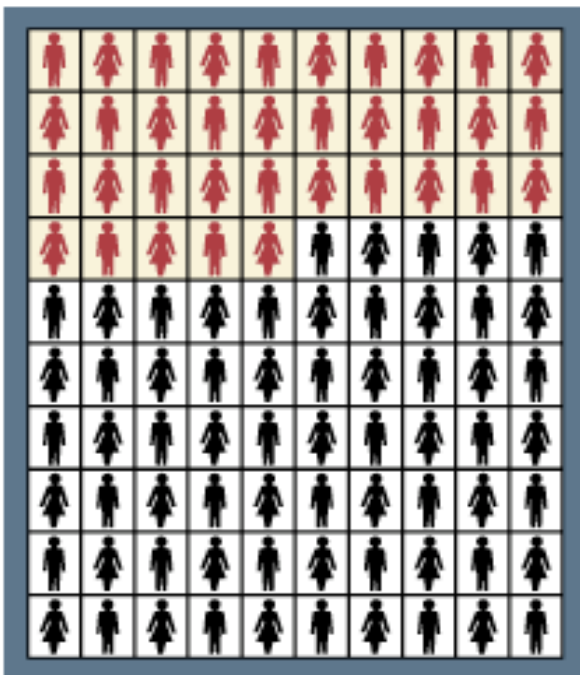


## What is someone's chance of getting diabetes in their lifetime if they have any KCNJ11 risk versions?

- People who have **no risk versions** of KCNJ11 will have, on average, a 35 in 100 chance of getting diabetes.
- People who have **1 risk version** of KCNJ11 will have, on average, a 37 in 100 chance of getting diabetes.
- People who have **2 risk versions** of KCNJ11 will have, on average, a 43 in 100 chance of getting diabetes.

### Chance of getting diabetes based on the number of risk versions of KCNJ11 (Out of 100 people. People with diabetes are shown in red.)

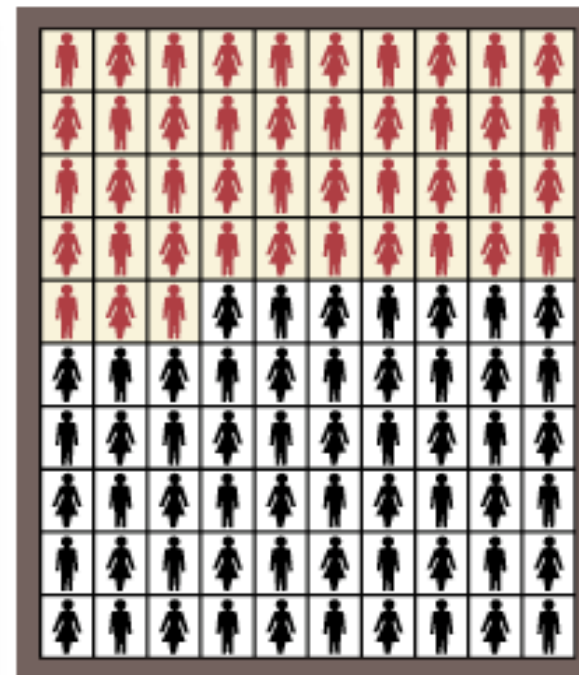
0 Risk Versions



1 Risk Version



2 Risk Versions



# Public Health Challenges

## Operationalizing the "3 P's"



➤ **Reducing Prevalent Risk factors**



➤ **Reducing disparities in chronic disease outcomes**



➤ **Improving health care delivery at reduce cost**

# Reducing Prevalent Risk factors

A stylized DNA double helix is the central focus, rendered in dark red and purple. The rungs are represented by vertical bars in blue, green, orange, and yellow. A clock face is integrated into the structure, showing a time of approximately 10:10. A lit fuse with a starburst effect is attached to the bottom of the clock mechanism.

**Understand challenges to communicating genetic risk information**



# Communication challenges

## Genetics of Common Disease

- Individually confer low risk
- Environment/Behaviors role > genetics

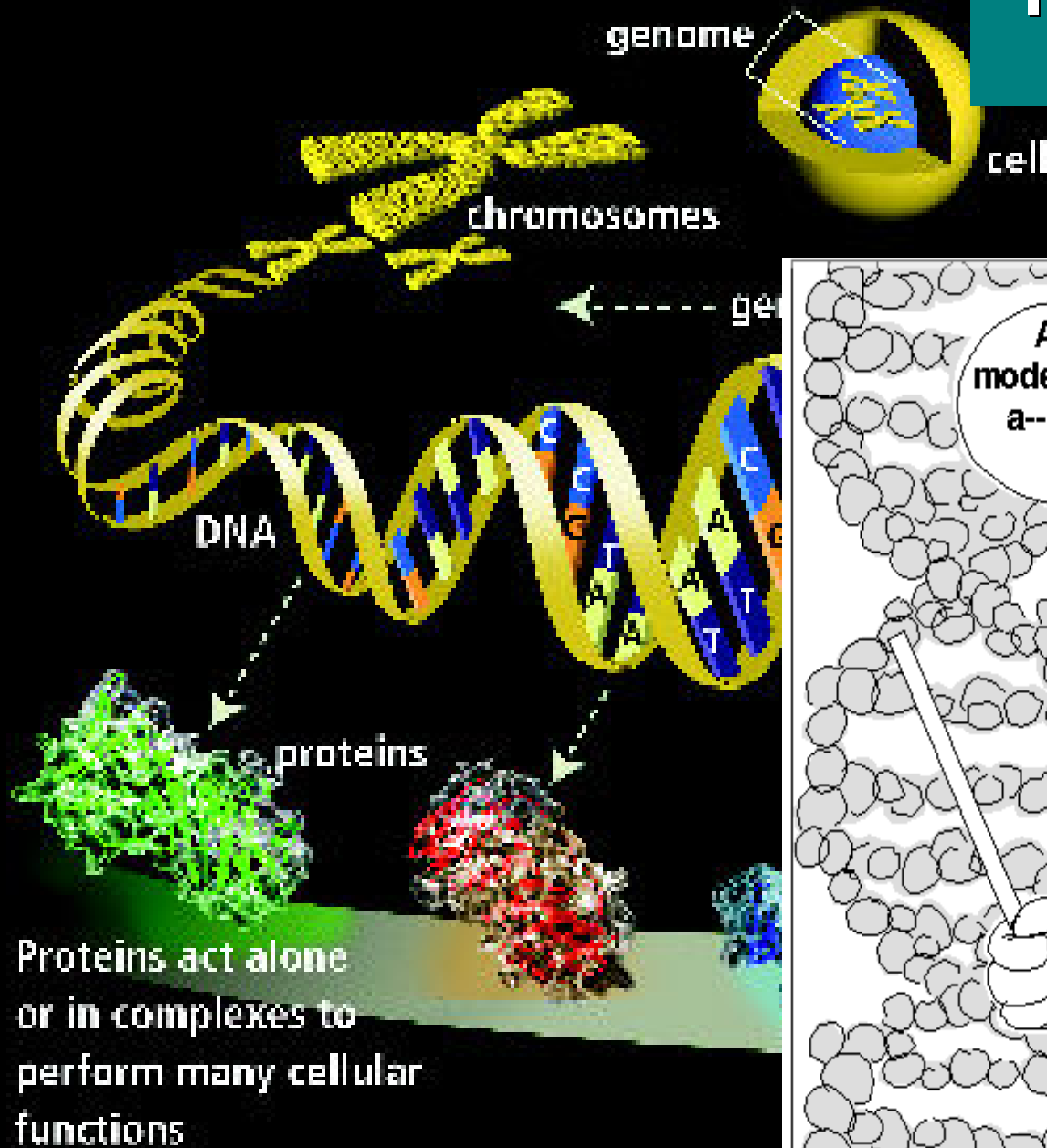
## Informed decision-making

- **Consumer empowerment: General genetics education**
- **Specific to technology/treatment**
  - ✓ What the test *is* going to tell them
  - ✓ What the test *is not* going to tell them

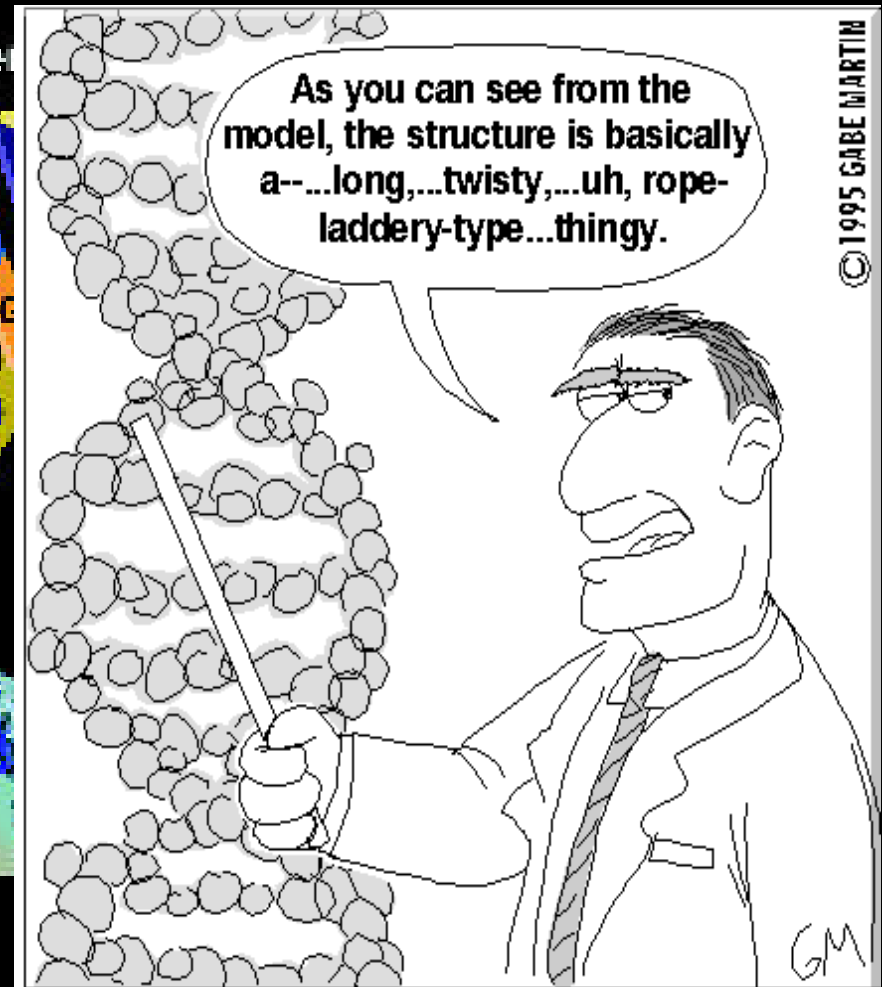
## Conveying feedback to motivate

- ✓ **Avoid fatalism** when results show higher risk
- ✓ **Sustain motivation** when results show average risk

# Informed decision-making



Proteins act alone or in complexes to perform many cellular functions

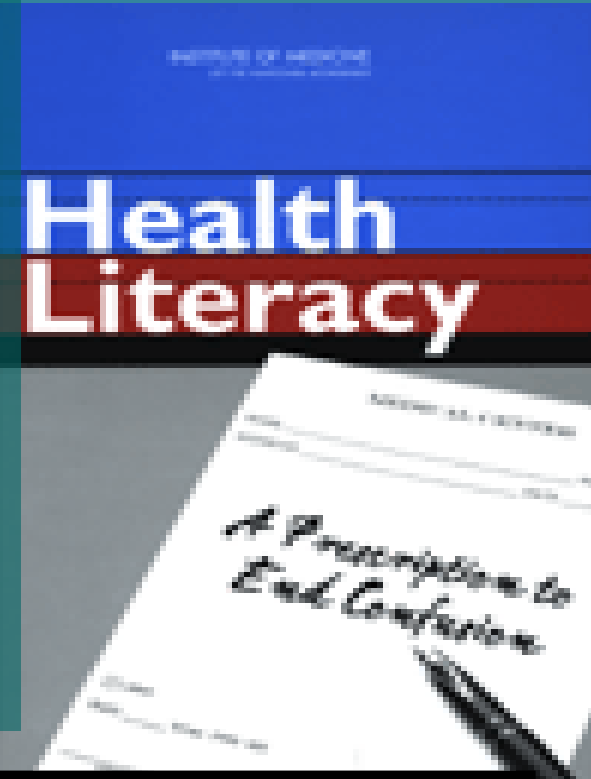


1953: The structure of the DNA molecule is first described.

# IOM Report Calls for National Effort to Improve Health Literacy

WASHINGTON -- **Nearly half of all American adults – 90 million people – have difficulty understanding and using health information...** says a new report from the Institute of Medicine of the National Academies....

....Health literacy is defined as the degree to which individuals have the capacity to obtain, process, and understand basic information and services needed to make appropriate decisions regarding their health.



April 8, 2004 National Academies of Science

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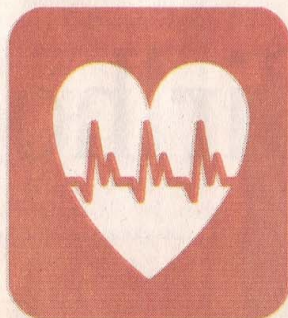
# Literacy Problems Create A Silent Health-Care Epidemic

LITERACY, From F1

obtain and understand basic health information and services needed to make informed decisions. Low health literacy, the institute noted, affects an estimated 90 million Americans, who struggle to understand what a doctor has told them or to comply with treatment recommendations as essential as taking the proper dose of medication. A 1999 report by the American Medical Association found that consent forms and other medical forms are typically written at the graduate school level, although the average American adult reads at the eighth-grade level.

Earlier this month a Chicago-based organization known as the Joint Commission, which accredits the nation's hospitals and clinics, unveiled a list of 35 recommendations to address the problem, which is estimated to cost taxpayers \$58 billion annually. Among the recommendations developed by a panel of experts: adoption of communication techniques proven to be effective with patients, simplification of jargon-laden consent forms, and development of patient-friendly navigation signs, which may include the use of pictures or icons that are also recognizable to non-English speakers.

Low health literacy "is a silent epidemic that threatens the



CARDIOLOGY  
CARDIOLOGÍA

The statistics don't differ much from the literacy assessment conducted a decade earlier. That survey found that many Americans could not determine the difference between two prices using a calculator or were unable to write a brief letter explaining a credit card billing error. Studies of health literacy have found that a surprisingly large number of adults were perplexed by the meaning of the term "orally," didn't know the difference between a teaspoon and tablespoon and were unable to calculate the proper dose of medicine. Low health literacy is more common among elderly or low-income patients and those with a chronic illness, researchers say.

A study published in the *Journal of the American Medical Association* in 1995 found that more than 80 percent of patients treated

at two of the nation's largest public hospitals could not understand instructions written at the fourth-grade level for the preparation of gastrointestinal X-rays known as an upper GI series. A 1999 study of more than 3,200 Medicare recipients found that one in three native-born patients could not answer a question about normal blood sugar readings even after being given a paper to read that listed the correct answer. And a study of 2,500 elderly patients published last year in

such linguistic confusion, said Ronald M. Davis, president-elect of the American Medical Association, who chaired the Joint Commission panel.

"You still have physicians who use medical jargon too much," Davis added, citing the use of "hypertension" instead of "high blood pressure" and "febrile" rather than "fever." Because doctors are rushed, he noted, they tend to lapse into medical jargon because it is what they are used to.

O'Leary said that the Joint Commission's interest in the issue should serve as a signal to hospitals to ramp up their efforts to communicate better with patients. Literacy improvements might be included in future standards hospitals must meet, he said, because they are inextricably linked to patient safety. At the Washington Hospital Center, the largest hospital in the District and health-care provider for many low-income and elderly patients, spokeswoman Paula Faria said administrators are aware of the problem and are examining admission forms and other documents to see whether they are intelligible as well as culturally sensitive. "We want to make sure that people understand what they're reading and, if they can't read, what they're hearing," she said.

Faria said that some departments are using a technique endorsed by the Joint Commission known as "teach back." Instead of asking a patient, "Do you have any questions?" — which will probably elicit little in the way of a useful response and puts the patient on the spot — doctors are taught to ask, "What is the most important thing you learned from our visit today?"

"You never want to put a patient in a situation where they feel like they're dense," Davis said.

Another effort regarded as promising, underwritten by drug manufacturer Pfizer, is called Ask Me 3. Designed by the Partnership for Clear Health Communication, a coalition of national health and literacy



SURGERY  
CIRUGÍA

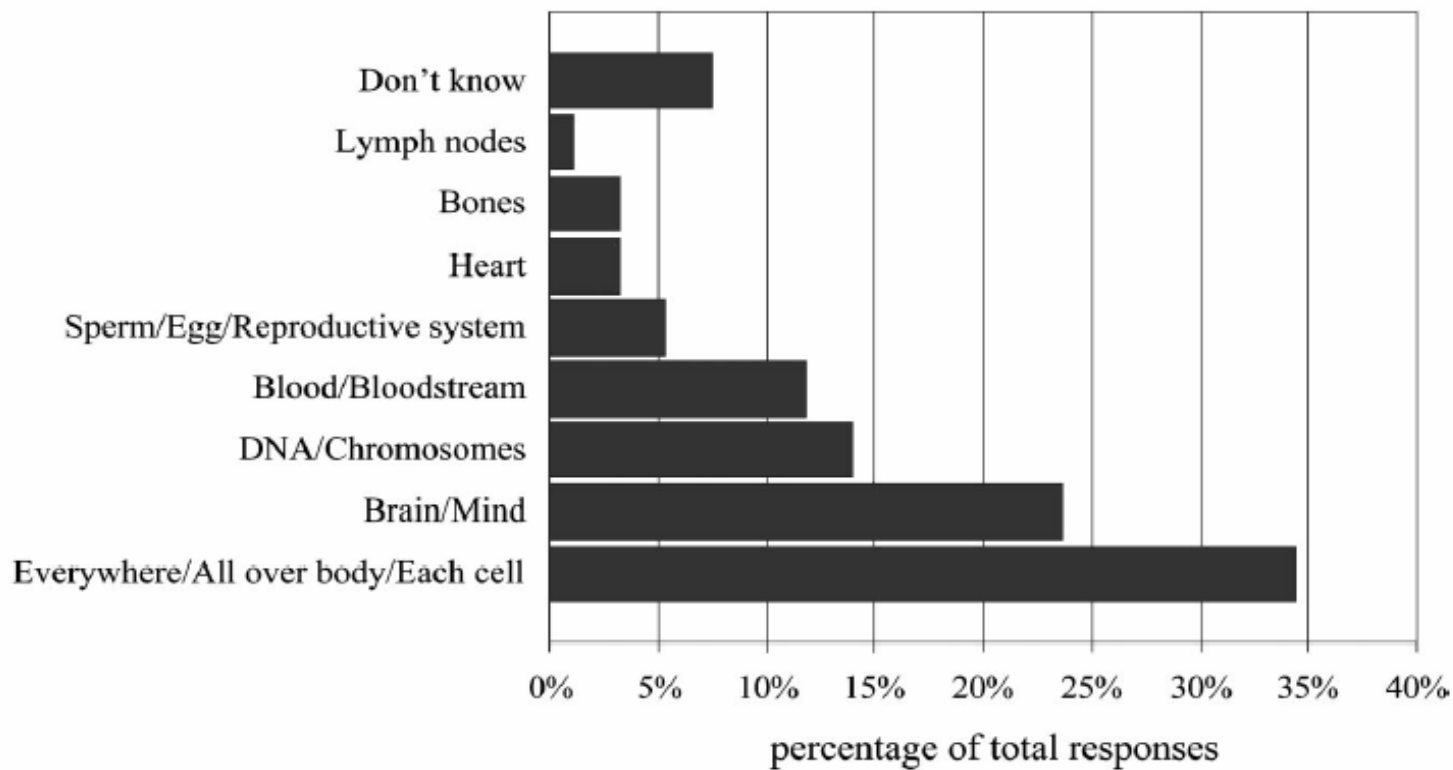


VACCINATIONS  
VACACIONES

**"Interest in healthy literacy comes at a time when Americans are expected to assume ever greater responsibility for their care & are discharged from hospitals sicker and quicker...."**

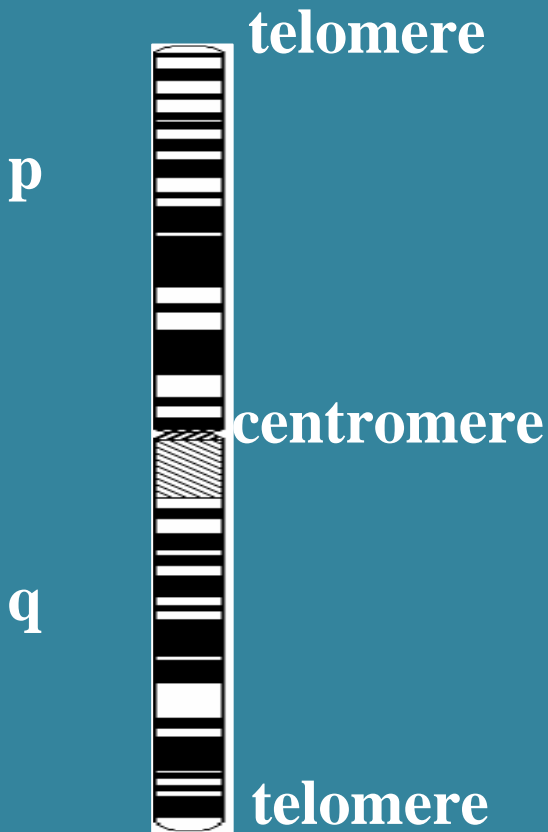
# Public Understanding of Genetics

"Where do you think genes might be located in someone's body?"

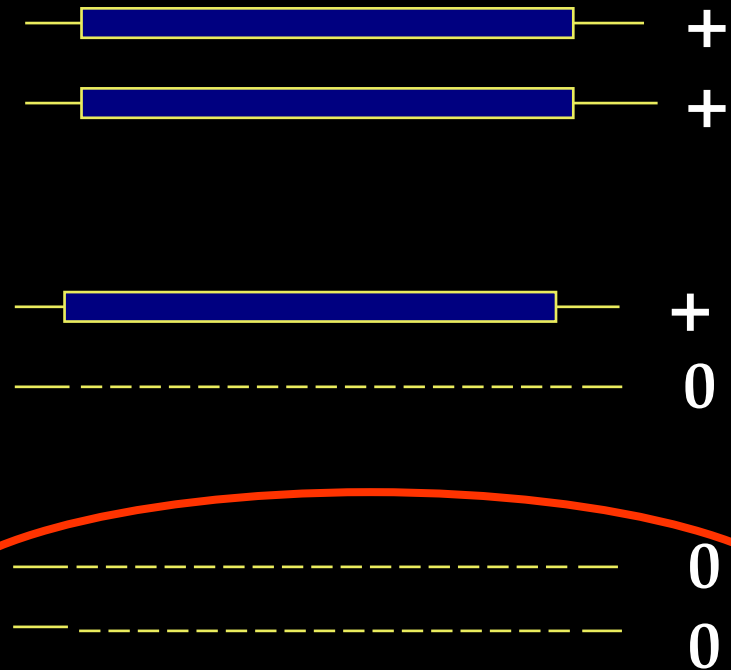




## Chromosome 1p13.3

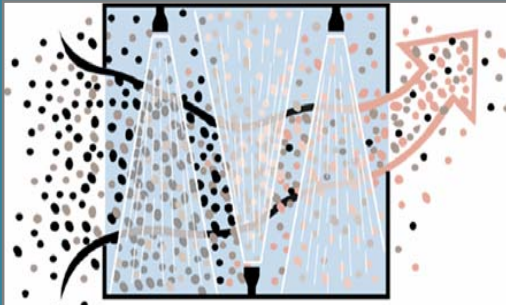


## GSTM1

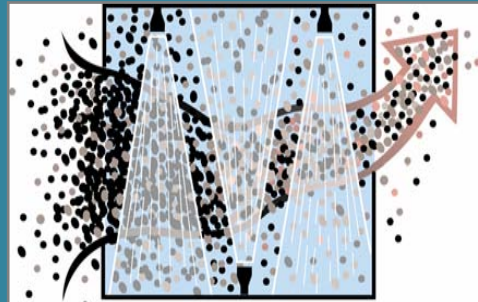


50% population has 0/0 genotype

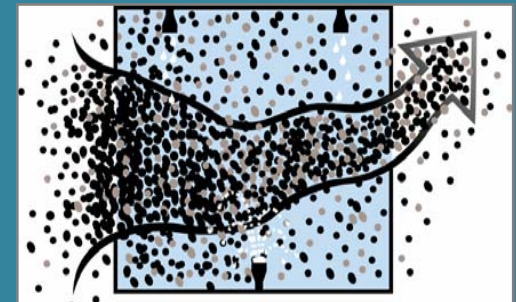
# What is understanding?



“Your body works like a chemical wash - each cell uses enzymes like strong detergents to clean up most chemicals”



“Your result shows that you have the enzyme to help you clean up some of the chemicals in cigarette smoke.”



“Your result shows that you do not have the enzyme. The harmful chemicals coming into your body may not be getting cleaned up very well.”

Percent

100

64

48

38

50

0

Accurate recall

Accurate interpretation

Accurate comprehension

# Accuracy of understanding by test result

GSTM1 is:	Inaccurate recall	Inaccurate interpretation	Inaccurate comprehension
➤ Missing	56 <sup>***</sup>	65 <sup>*</sup>	79
Present	26	49	54

\*\*\* p<.001; \* p<.05

Welcome to the  
**FAMILY RISK AND LUNG CANCER STUDY**

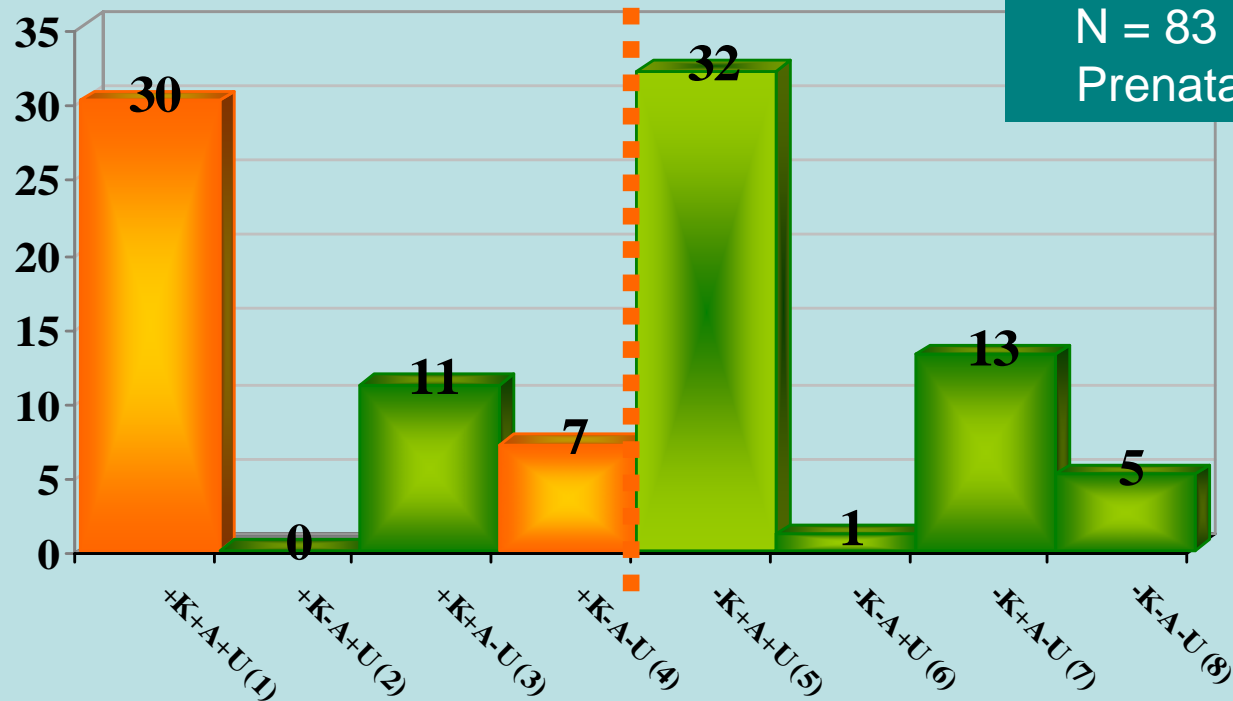
Thank you for Participating!

**Behavioral outcomes**  
Objective observation of how  
individuals engage with  
information



NEXT

# Measuring Informed Choice



Rowe, Fisher, Quinlivan, Roy Aus N Z Ob/Gyn, 2006

Marteau et al., Pt. Educ & Counseling, 2002



# Behavioral Adherence

## Primary & Secondary Prevention

- Guidelines well established
- Behavioral risk factors well established (smoking, poor diet, inactivity)
- Evidence-based interventions

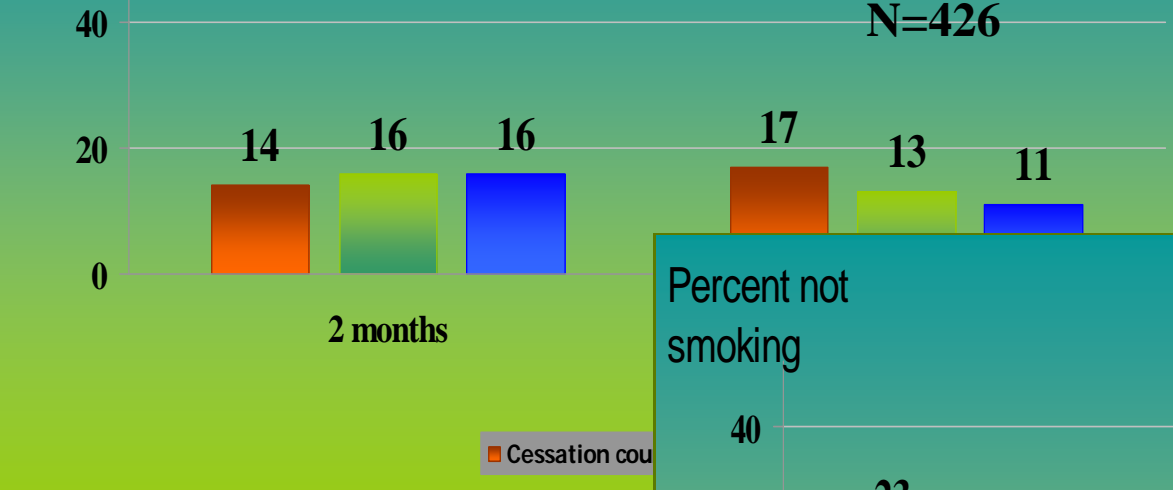
**Know what to do....challenge is how to get people to do it!**

# Genetic feedback effects on smoking cessation

Percent not smoking

**CYP2D6**

N=426

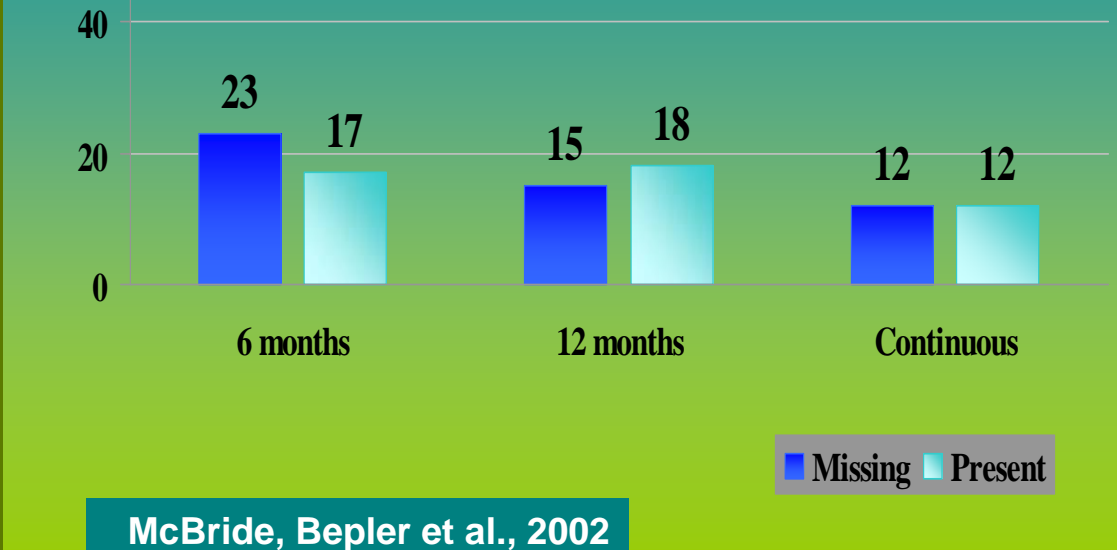


Lerman et al., 1997; Audrain

Percent not smoking

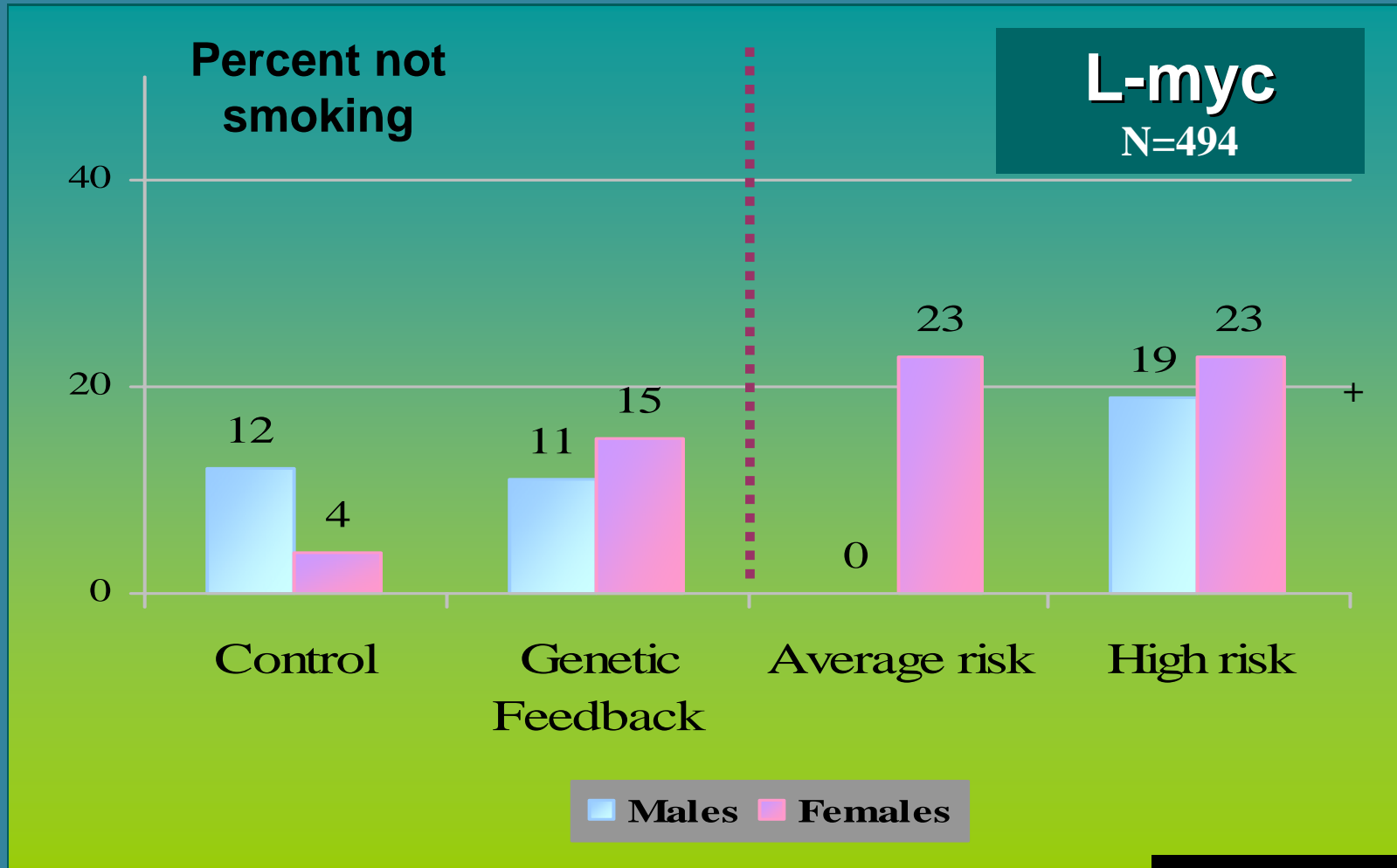
**GSTM1**

N=308



McBride, Bepler et al., 2002

# Genetic feedback effects on smoking cessation



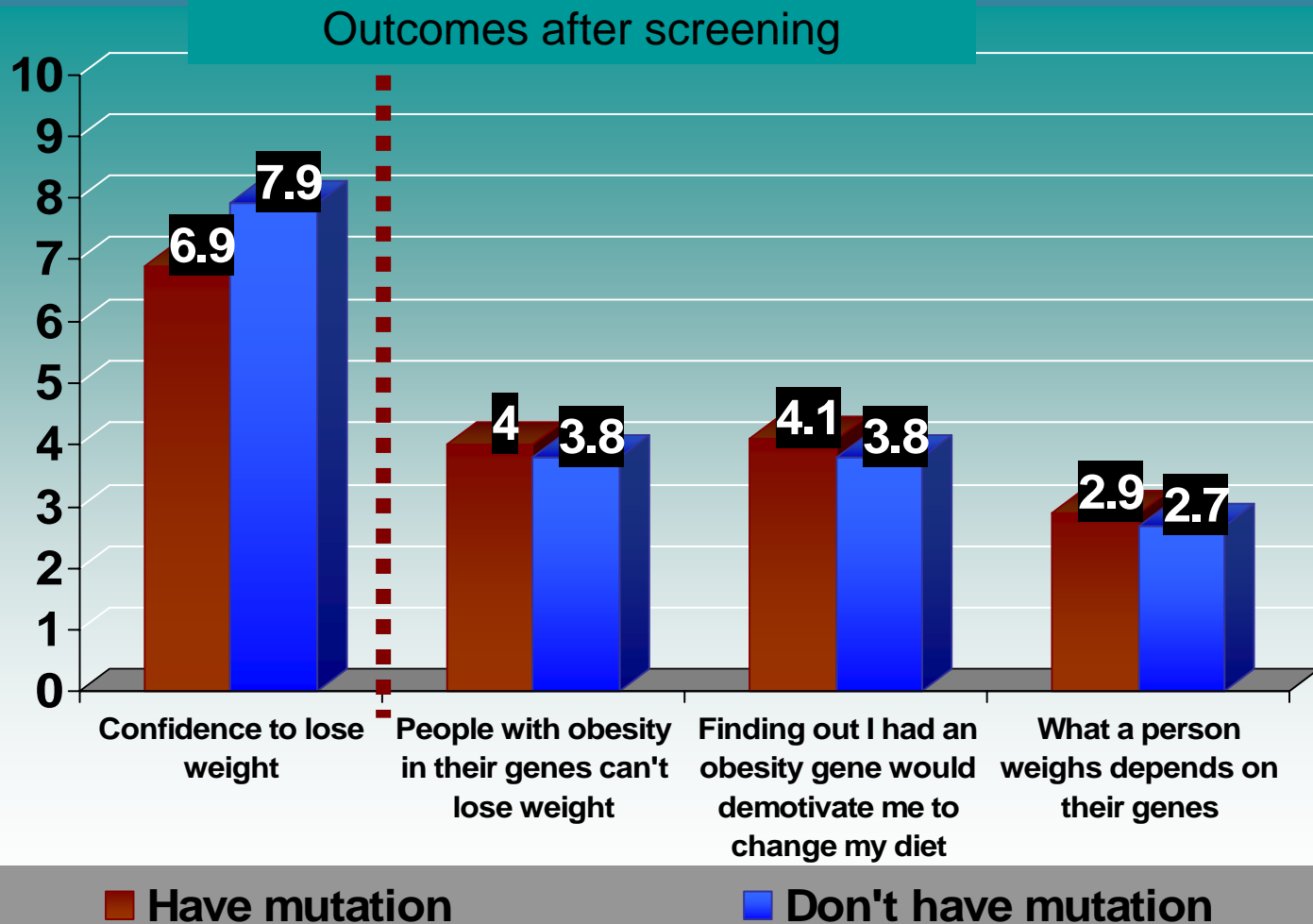
Ito et al., 2006

NATIONAL HUMAN GENOME RESEARCH INSTITUTE

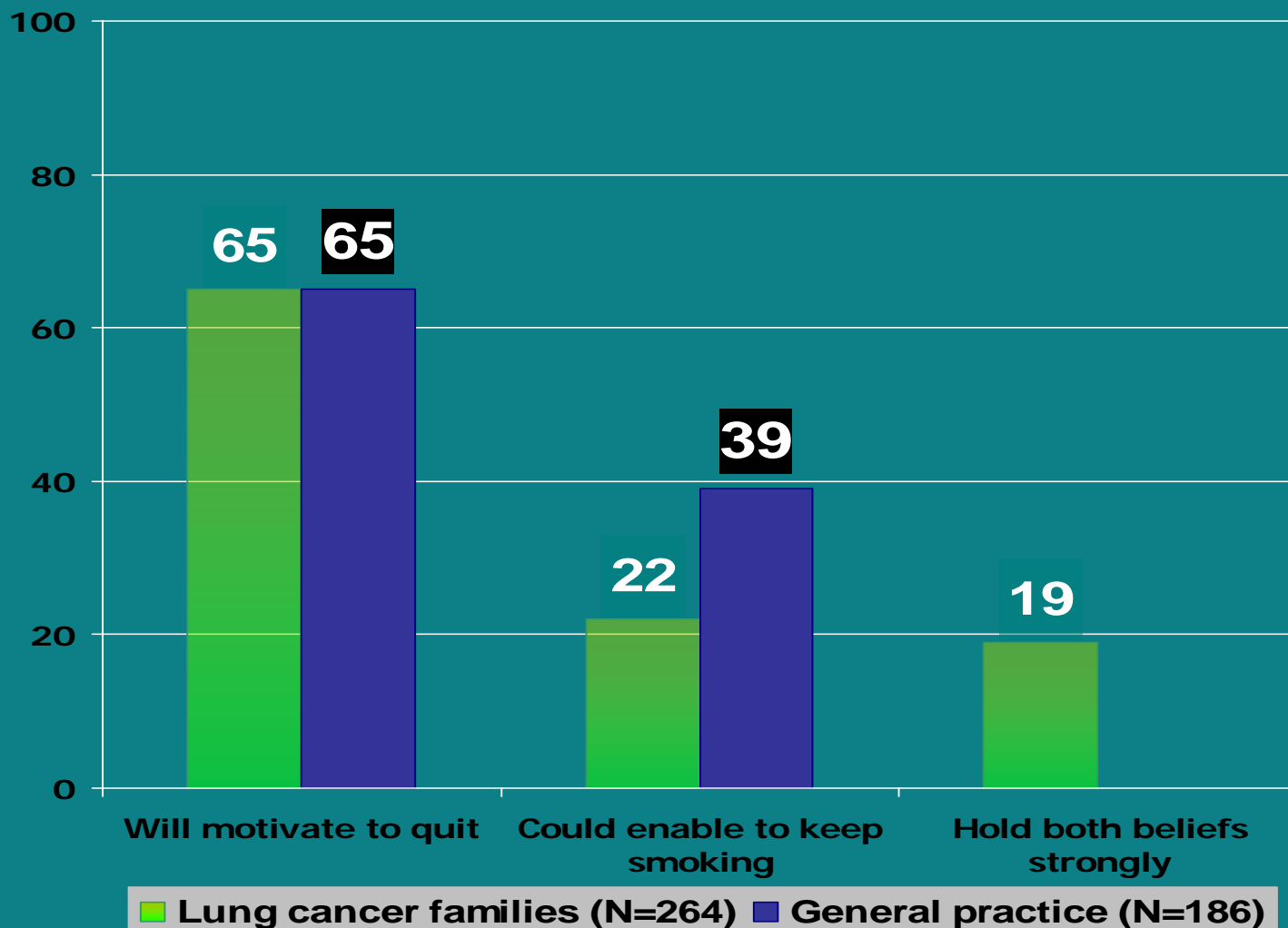
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# Confidence & Attitudes about Weight Management by Mutation Status

Obese Women (N=30)



# Motives for hypothetical genetic testing among smokers



McBride & colleagues, unpublished

Sanderson & Wardle, 2005



# Factors associated with interest in susceptibility testing for lung cancer

	Odds Ratio	Confidence ratio
Age	1.0	.94 – 1.0
Child of patient	.92	.34 – 2.5
Sibling of patient	.49	.11 – 2.2
Level of desire to quit	1.9	.77- 4.9
<i>ProMo</i>	<b>5.5</b>	<b>2.2 - 13.7</b>
<i>NegMo</i>	<b>3.2</b>	<b>1.1 - 9.4</b>
Female gender	1.2	.51 – 2.9
High education	2.6	.76 – 9.0

N=264 Relatives

NATIONAL

TUTE

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# Reducing disparities in chronic disease outcomes

**Representative Evidence Base**



**Reach of Benefits**

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# Risks/Benefits of Genetic Risk Counseling

## Meta-Analysis of Genetic Counseling for Familial Cancer

- 25 Studies
- N's -- 59-578
- Familial cancer clinics
- 21 Breast cancer
- 4 Colon or combined
- 8 USA
- 10 UK, 4 Australian, 3 other

- White, high risk, educated, female
- Accuracy of perceived risk improves
- Cancer-worry, anxiety, depression, distress, to normal range
- Few assess behavioral outcomes
- No measures of informed choice

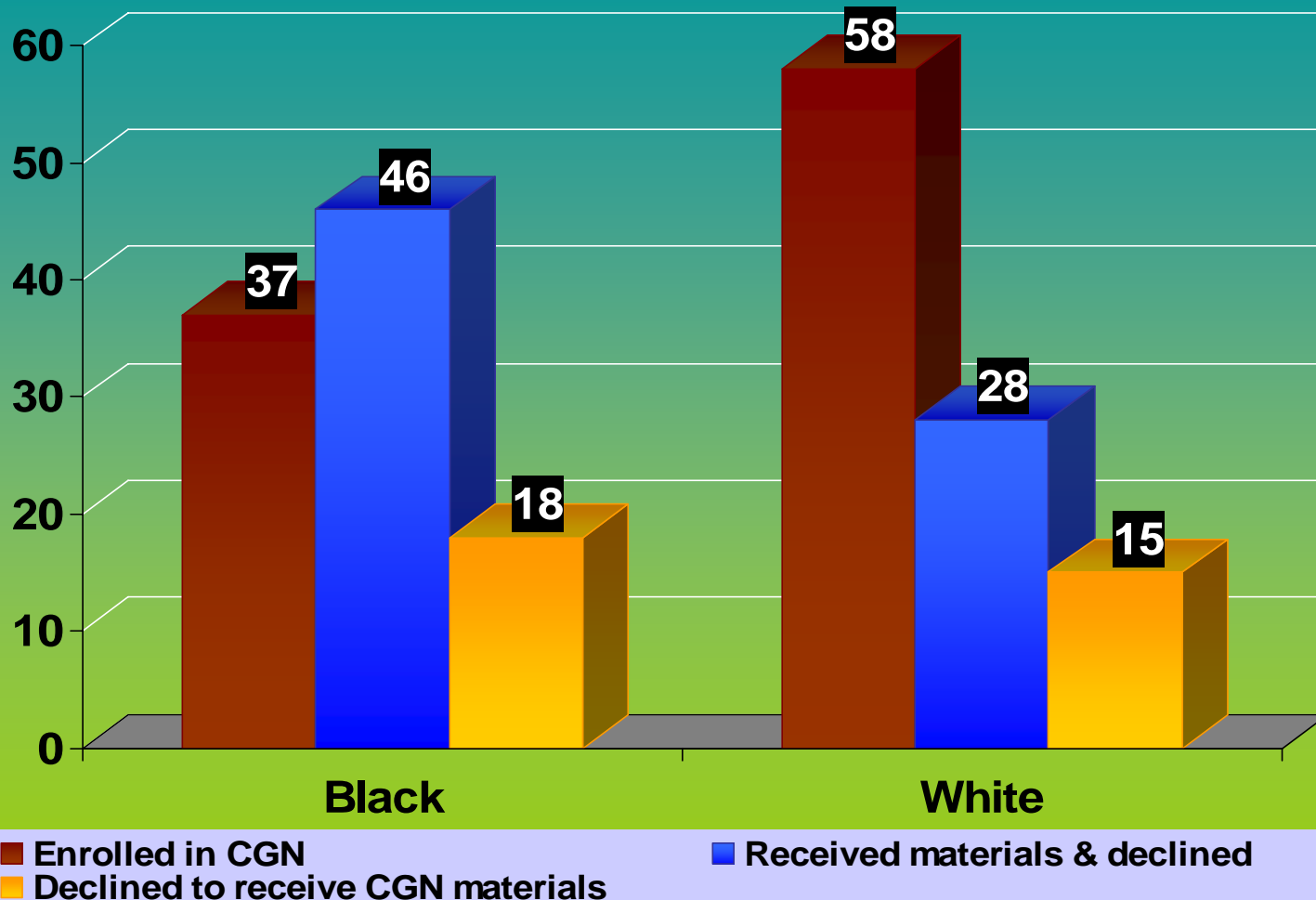
# Population-based centers & family registries

## Research Goals



**Minority recruitment major challenge**

# Minority recruitment to Cancer Genetics Network





# Minority Populations

## **African Americans = Whites**

- > Risk > Interest in Testing (Hughes et al, 2005; Satia et al., 2006)
- > Accuracy of test > Interest (Higgs et al., 2003)
- See similar risks & benefits to genetic testing (e.g., Higgs et al, 2003)
  - Endorse genetics for use to improve health
  - Divided in concerns about how genetics might be used (Satia et al., 2006)
- ↑Education ↑awareness, knowledge & interest (Satia et al., 2006)

## **African Americans ≠ Whites**

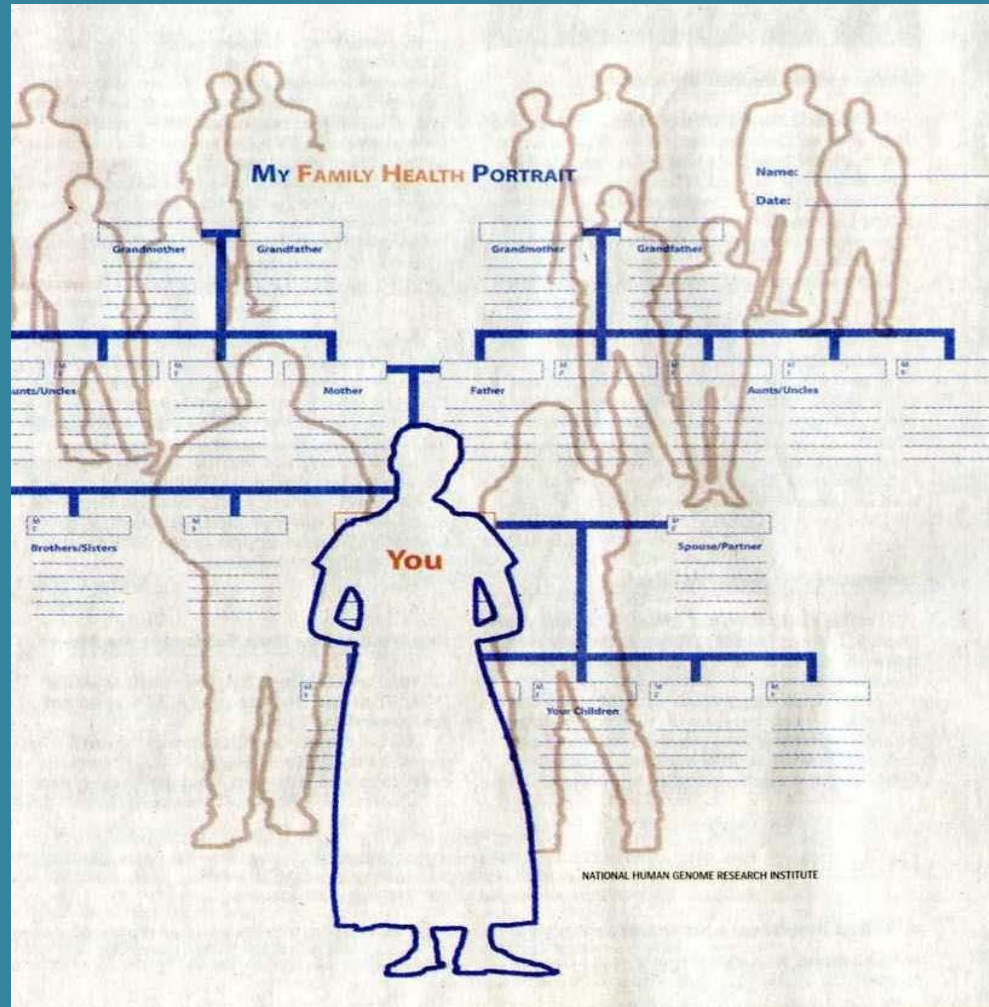
- Preferences regarding confidentiality of genetic information (Sterling et al., 2006)
  - Some different social concerns (Bates et al., 2005)
- Receipt of risk assessment & referral to genetic services (Armstrong et al., 2005)
- Seeking BRCA1/2 counseling when eligible & HCP referred (Hughes-Halbert et al., 2005; Armstrong et al., 2005)



# Improving Health Care Delivery at Reduced Cost

Considering how to achieve clinical  
integration as technologies develop

# Clinical Tools



## Tracing Your Health Roots

*Plant a Health Family Tree Now, and It Could Bear Fruit for Generations*

By ALISON BUCKHOLTZ  
Special to *The Washington Post*

When Deborah Goldstock Ringel was pregnant with her first child, death was on her calendar. A “death brunch,” to be specific.

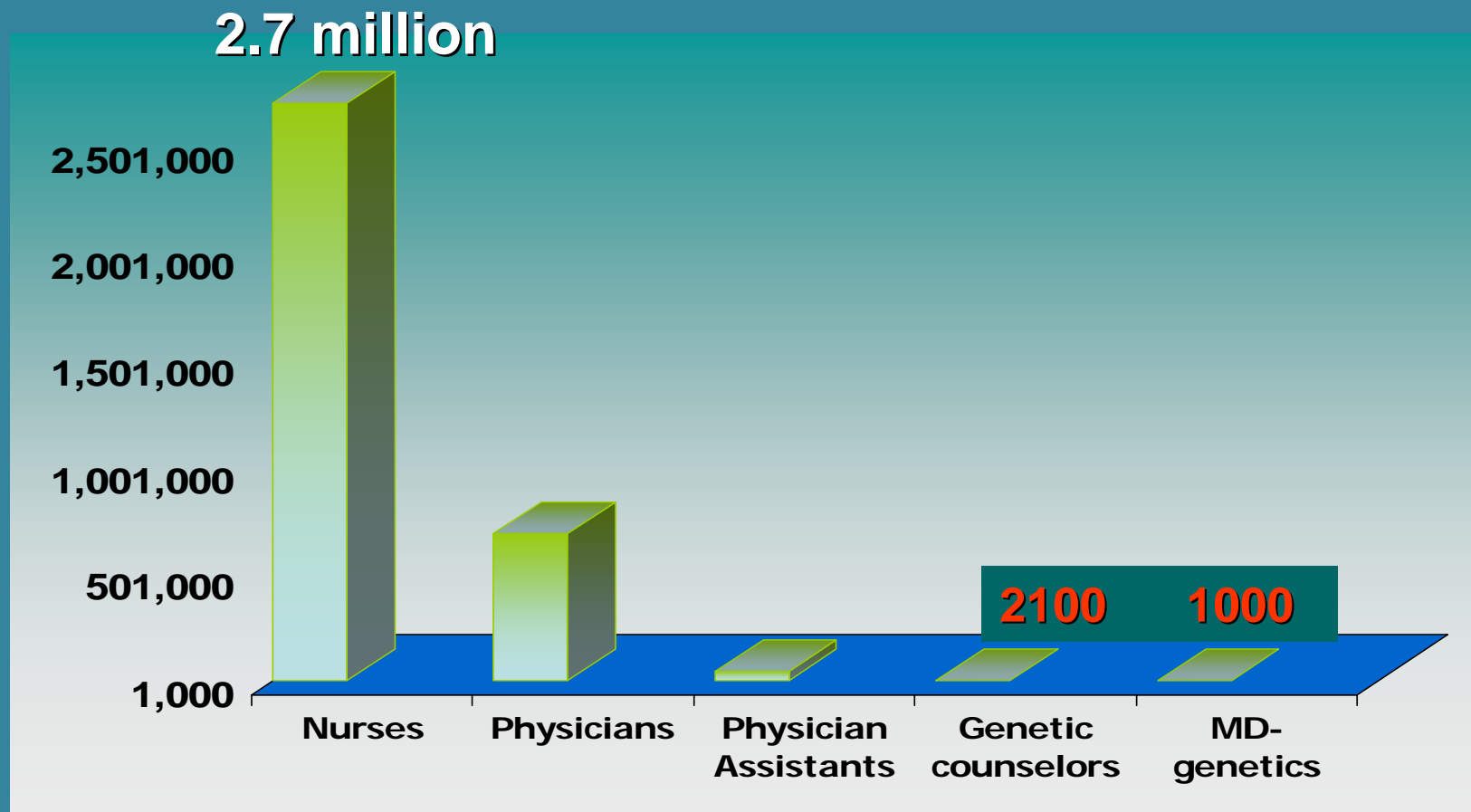
That’s what she termed the meal at which she gathered relatives to ask if anyone had inherited medical conditions that might put her growing family at risk. Ringel, now a mother of three, spent most of her first pregnancy believing that nothing more serious than acne plagued her DNA. But an offhand comment to her father rattled the bones in her ancestors’ closet.

“I spoke to my dad after a [doctor’s] appointment, and told him that I filled out a form which asked about family medical conditions, such as heart disease and high blood pressure,” Ringel remembered. She mentioned to her father that her checklist was completely clean, and then got a shock: “[My father] told me that both of his grandmothers died young from high blood pressure, and his grandfather had diabetes. I realized that I simply didn’t know what medical conditions were in my family.”

As her due date neared, Ringel, a lawyer who lives in Cleveland Park, vowed to press her relatives hard on questions about their health. Coincidentally, Ringel’s husband was elbow-deep in genealogical research at the same time, and the two combined their efforts to create a health family

See *TREE*, Page F4

# Clinical work force





# Clinical Integration

## Counseling

- Tobacco cessation
- Physical activity
- Lap/shoulder belt
- Bike/motorcycle helmet use
- Problem drinking
- Driving while intoxicated
- Limit fat & cholesterol
- Adequate calcium intake
- STD prevention
- Contraception
- Smoke detector
- Safe storage of firearms
- Visits to dental providers
- Floss

## Screening

- Blood pressure
- Pap test
- Mammogram
- CBE
- Height & Weight
- Total blood cho
- FOBT
- Sigmoidoscopy
- Problem drinkin
- Rubella serolog
- Vision screening
- Asses for hearing impairment

## Chemoprevention

- Multivitamin use
- Hormone prophylaxis

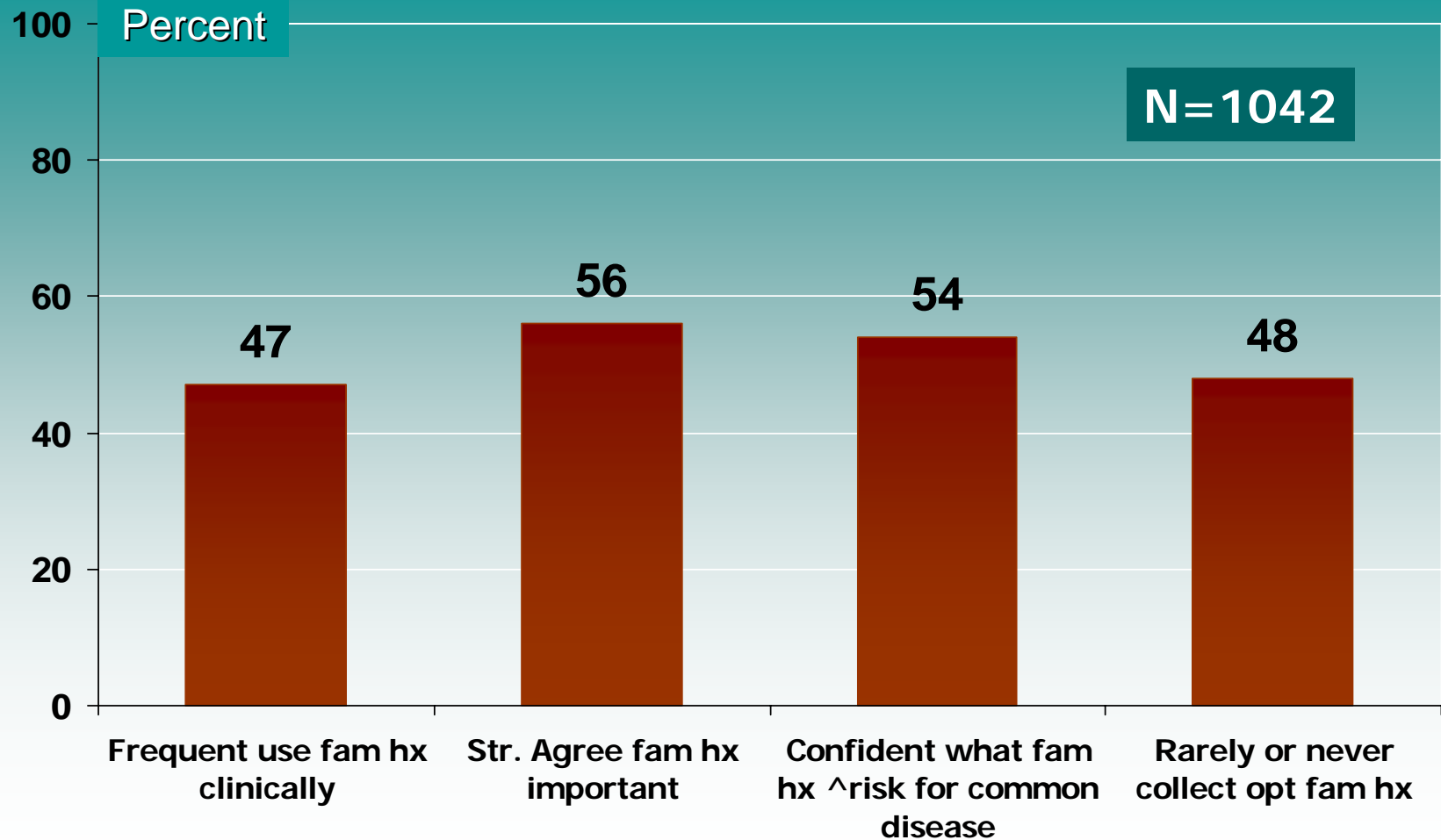
- **Family history taking**
- **Counseling re: genetic testing & interpretation of results**
- **Arranging referral**

**Total hours per day**

**7.4**



# Family Physicians' Views of Family History Assessment



# The best time to beat cancer is before you ever get it.

When it comes to breaking the cycle of inherited cancer, knowledge is power and hope.



Could you have inherited a risk for cancer?



➤ Are you at risk?  
Take a quick quiz.



Should you be tested if you've

Could you pass a risk for cancer



## You don't have to specialize in oncology to prevent cancer.

Discover the risks. Understand the options.

- Order a GENETIC TESTING KIT
- Mutation Prevalence Tables



Inherited Cancer



There are patients in your practice who may have up to a 100%<sup>26</sup> chance of developing hereditary cancer. Find out how to identify and manage these high-risk patients.

Learn about genetic testing for hereditary breast and ovarian cancer.



Learn about genetic testing for hereditary melanoma.



Learn about genetic testing for hereditary colorectal cancer.



➤ Information for Patients

Hereditary Cancers

Genetic Testing

Reimbursement/Privacy

Resources

About Myriad

# Factors influencing (in)appropriate provider referral to BRCA1/2 testing

(White et al.)



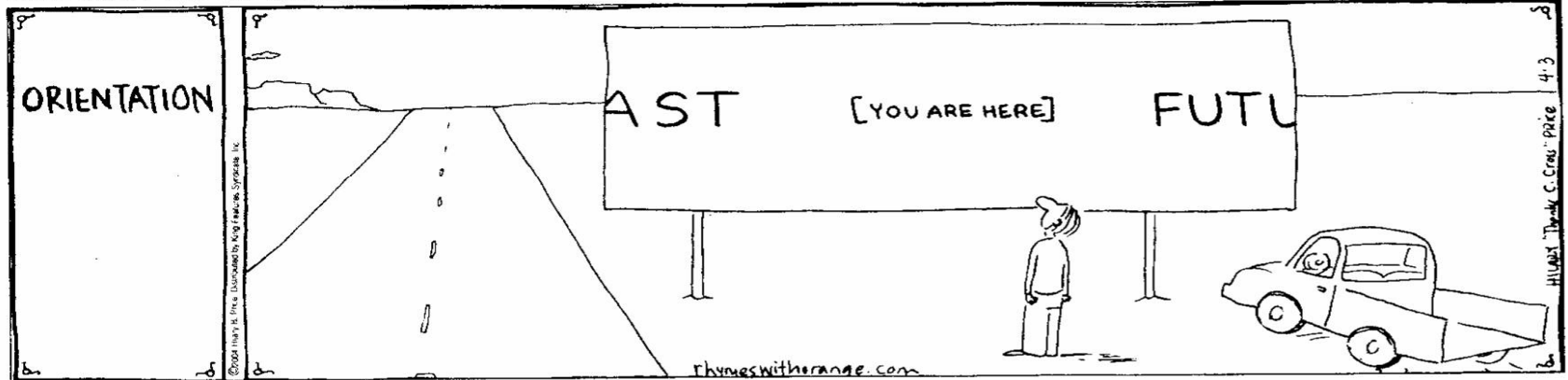
## Terry presents:

- White vs. black
- High affect vs. Not high affect
- Insured vs. insurance not mentioned

- **N= 294 family physicians (42% of those sampled)**
- **No effect of any factors**
  - 8% appropriately referred
  - 50% genetic counseling
  - 23% genetic counseling + genetic testing
- **50% believed not referring would damage relationship with Terry**

# Where does this leave us?

**RHYMES WITH ORANGE** HILARY PRICE



## Translators...

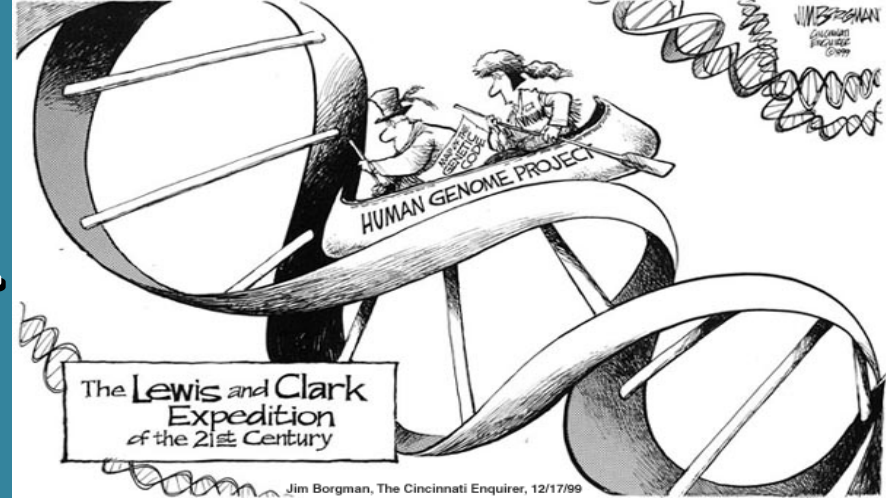
- Bench science sets priorities
- Interpret & disseminate discoveries
- Passive role

## Trail-blazers...

- Actively participate in directing research priorities
- Anticipate clinical & behavioral challenges



# Trail-blazing....



## ➤ “Upstream” research needed now!

- Maximize potential for public health benefit & access

## ➤ Shape genomic discovery by understanding:

- How different groups respond to offer of susceptibility testing & feedback
- How risk assessment will affect health behaviors & health care use
- How susceptibility testing can be used to increase health care efficiencies without increasing disparities



# “Value” of life

Abortion, Disability Eugenics

# Perpetuating Disparities

Access to benefits

## How can genomics reduce health disparities?

Highlighting commonalities across genomes

Genetic determinism

Rights of

employers &

insurers



## Genomics to Health

How can

genomic

creat

efficienci

in heal

ca

delivery

Which genomic applications are cost effective?

Rights and duties of family members

Stress & Coping

Stigma

## Psychological

## Distress

Insurance discrimination

## Privacy and consent

How do we use genomics to reduce prevalent risk factors?

# Immediate Challenges to take on.....

- ❖ Attracting social, behavioral, public health scientists to the field
- ❖ Openness to returning test results in the context of research protocols
- ❖ Test prototypes for research
- ❖ Increasing rigor of science in social & behavioral science related to genomics
- ❖ Journals & scientific meetings with the above focus