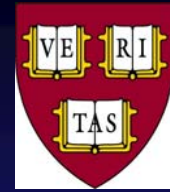


**Harvard/MGH Center on Genomics,  
Vulnerable Populations  
& Health Disparities**



## **Lost in Translation?**

# **Ensuring that New Genetics Research on Addiction gets Translated into Improved Health Outcomes**

**Alexandra E. Shields, Ph.D.**

**Harvard/MGH Center on Genomics, Vulnerable  
Populations & Health Disparities**

**NIDA Congressional Briefing**

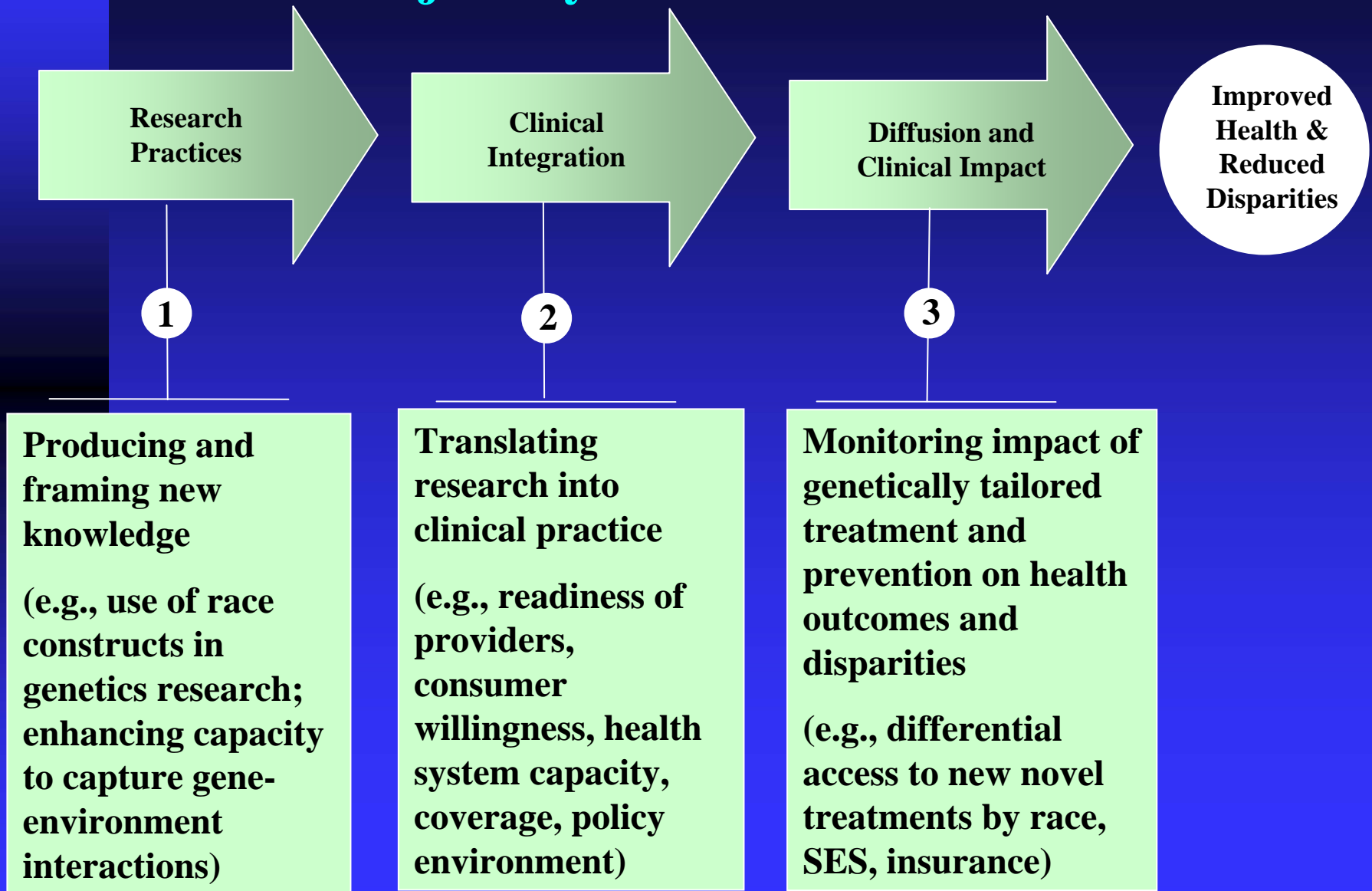
**April 2008**

# NIDA/NCI/RWJF TTURC Initiative

## ■ FORWARD THINKING:

Funders acknowledged the importance of anticipating and addressing challenges that would emerge in translating emerging genomics research on nicotine dependence and response to treatment into clinical practice

# Challenges and opportunities throughout the translational trajectory...



# Challenges in Translating Genetics Research on Addiction into Clinical Practice

- Physician Readiness
- Consumer Willingness
- Access to Novel Addiction Treatment and Prevention Strategies
- Future Directions

# These challenges are exacerbated by the characteristics of complex genetic traits

- Complexity of information – multiple genes interacting with other genes and environmental exposures along multiple pathways
- Racial differences in allele frequencies
- Collateral information

# **(1) Primary Care Providers**

# National Survey of Primary Care Physicians in the U.S.

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- National random sample of 2000 PCPs in the U.S. (internal medicine, general medicine, and family practitioners) from the AMA Masterfile.
  - N = 1120 (62% response rate)

# Physician Preparedness

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- Only **5%** of primary care physicians feel very confident in their ability to interpret the results of genetic tests.
- Only **4%** of primary care physicians feel very prepared to counsel patients considering a genetic test.
- Only **60%** have ever ordered or referred a patient for any type of genetic testing.

# Research Questions

- How willing would PCPs be to order a new genetic test to tailor smoking treatment
- Would willingness change according to test characteristics

# Anticipating Physician Response to Complex Genetic Information

## ■ Baseline Scenario:

Assume new smoking cessation research demonstrates to your satisfaction that:

- Among individuals who **[have a particular genotype]**, the nicotine nasal spray yields a clinically meaningful improvement in smoking quit rates over the nicotine patch,
- A **[genetic test]** with acceptable sensitivity, specificity, and predictive value can detect this particular **[genotype]**, and
- This particular **[genotype]** is fairly prevalent in the population.

# Genetic tests face greater barriers to physician adoption

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- Describing a new test to tailor smoking treatment as a genetic test versus a non-genetic test reduced physicians' willingness to offer the new test to their patients who smoked by 11%.
- **This 11% reduction translates into 3.9 million daily smokers (N=35.4 million)\* who would not be offered a new genetic-based treatment for smoking.**

\*56.3 million total current (past month) cigarette smokers, 11% reduction out of total smokers translates into 6.2 million smokers; Results from the 2001 National Household Survey on Drug Abuse, 2002.

# Additional Facts

(based on Lerman's research on pharmacogenetics)

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In addition to predicting treatment outcomes (as described in the Baseline Scenario) now suppose that:

1. This particular [genotype] has been shown to predict an increased risk of becoming addicted to nicotine in the first place,
2. That the prevalence of this particular [genotype] is approximately 43% among white smokers and 53% among African-American smokers
3. This same [genotype] is also associated with an increased risk of alcohol and cocaine, as well as a number of other conditions, such as attention deficit hyperactivity disorder (ADHD) and Tourette's syndrome.

# Average Likelihood by Scenario, by Genetic and Non-Genetic Version of Scenarios

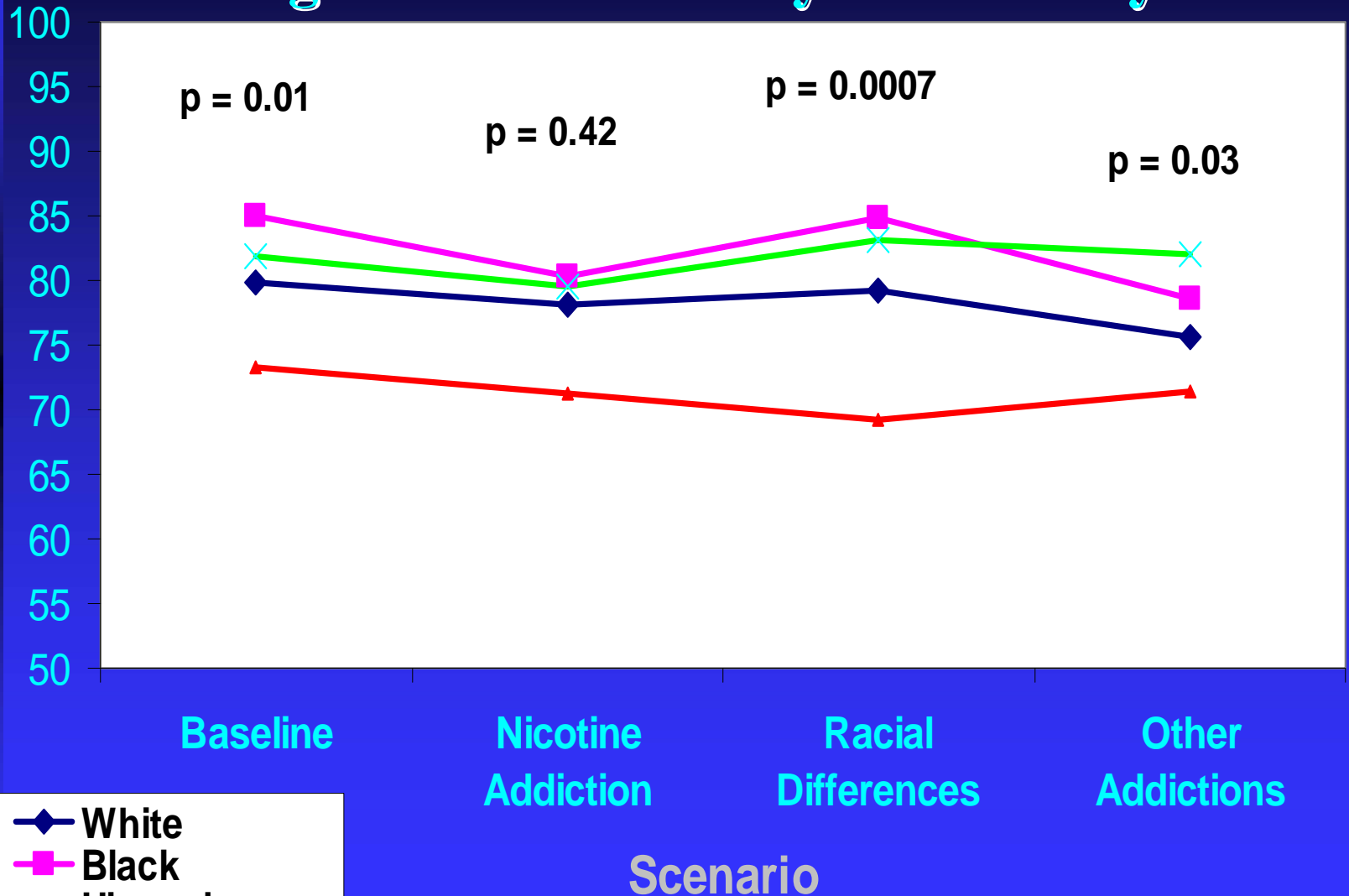
Scenarios	Genetic	Non-Genetic	Significance
Baseline Scenario	69.8%	77.9%	$p < 0.001$
Increased Risk of Nicotine Addiction	69.4%	72.3%	$p < 0.001$
Racial Differences in Allele Frequencies	69.2%	74.5%	$p = 0.005$
Also Predicts Drug Abuse and Psychiatric	71.6%	72.6%	$p < 0.001$

A Comparison of responses of those randomly assigned to receive a version of the survey in which the new test to tailor treatment was described as a genetic versus non-genetic test, based on generalized linear model unadjusted for covariates.

Shields, AE et al. Primary care physicians' willingness to offer a new genetic test to tailor smoking cessation treatment according to test characteristic. *Nicotine & Tobacco Research* (in press)

# Willingness to Offer a New Genetic Test to Tailor Smoking TX also Differs by Race of Physician

Regression-Adjusted Mean Adoption Scores



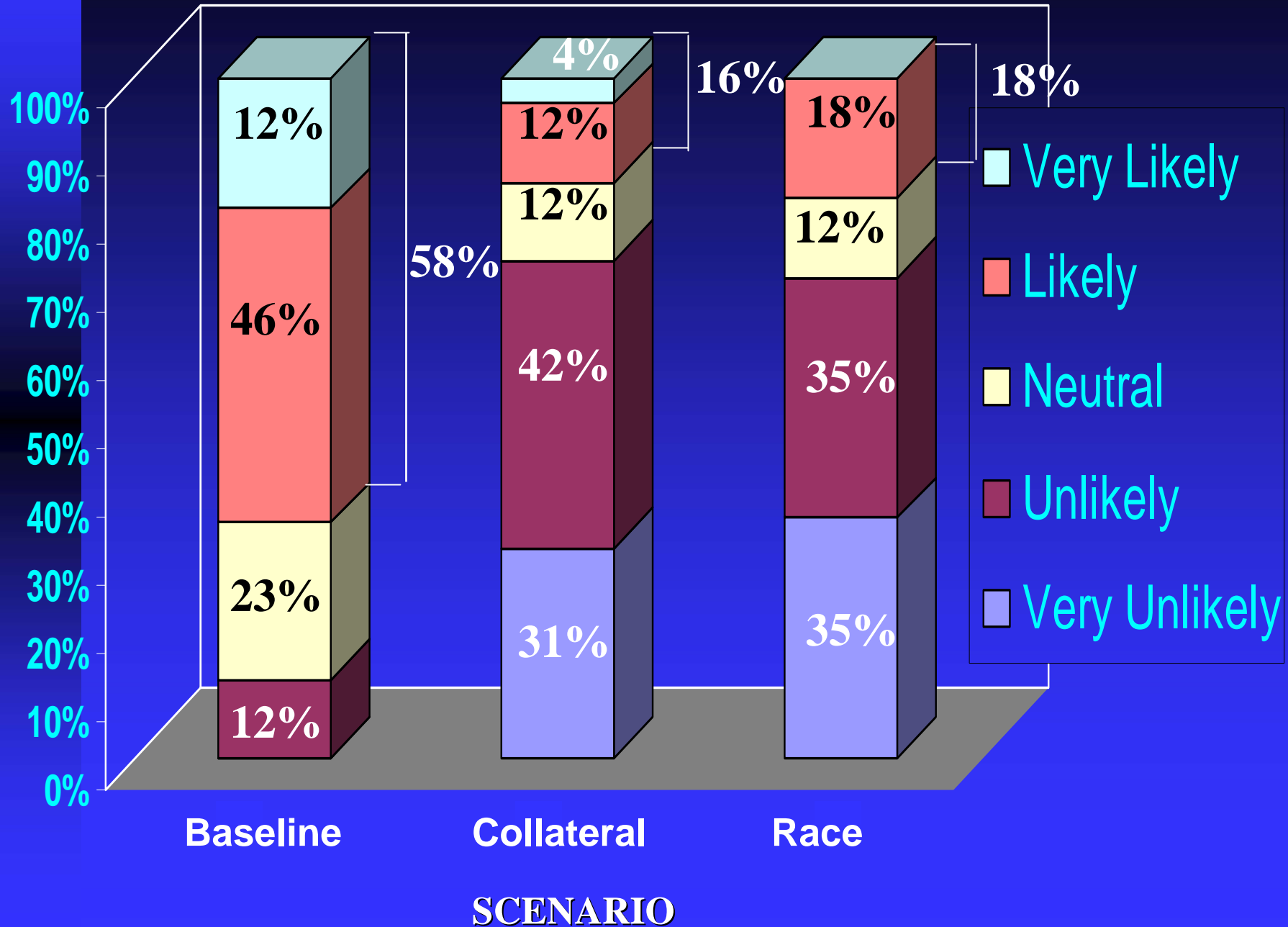
- ◆ White
- Black
- ▲ Hispanic
- × Asian

## **(2) The Patient Perspective**

# Study Goal

- To explore smokers' willingness to undergo genetic testing for tailored smoking treatment

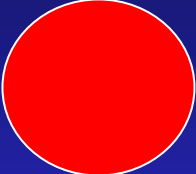
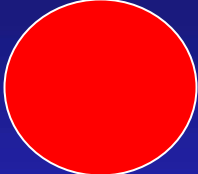
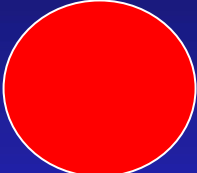
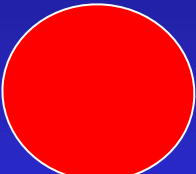
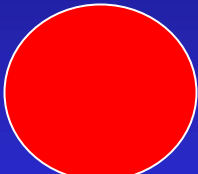
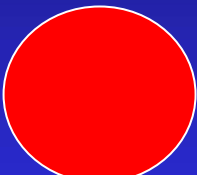
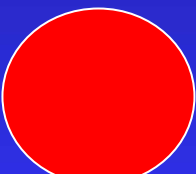
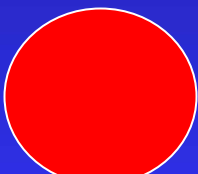
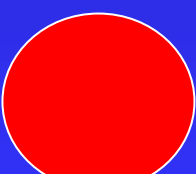
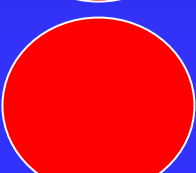
# Smoker Likelihood of Test Adoption



# Lay beliefs about the role of genetics in addiction

- 12 focus groups and 12 one-on-one interviews with black and white adults, smokers and non-smokers, all with less than a college education
- Rural Alabama and Baltimore
- N=112 adults

# “Dot Exercise”: The Role of Genetic Factors in Nicotine Dependence

Social	Environment	Genetic
		
		
		
		
		

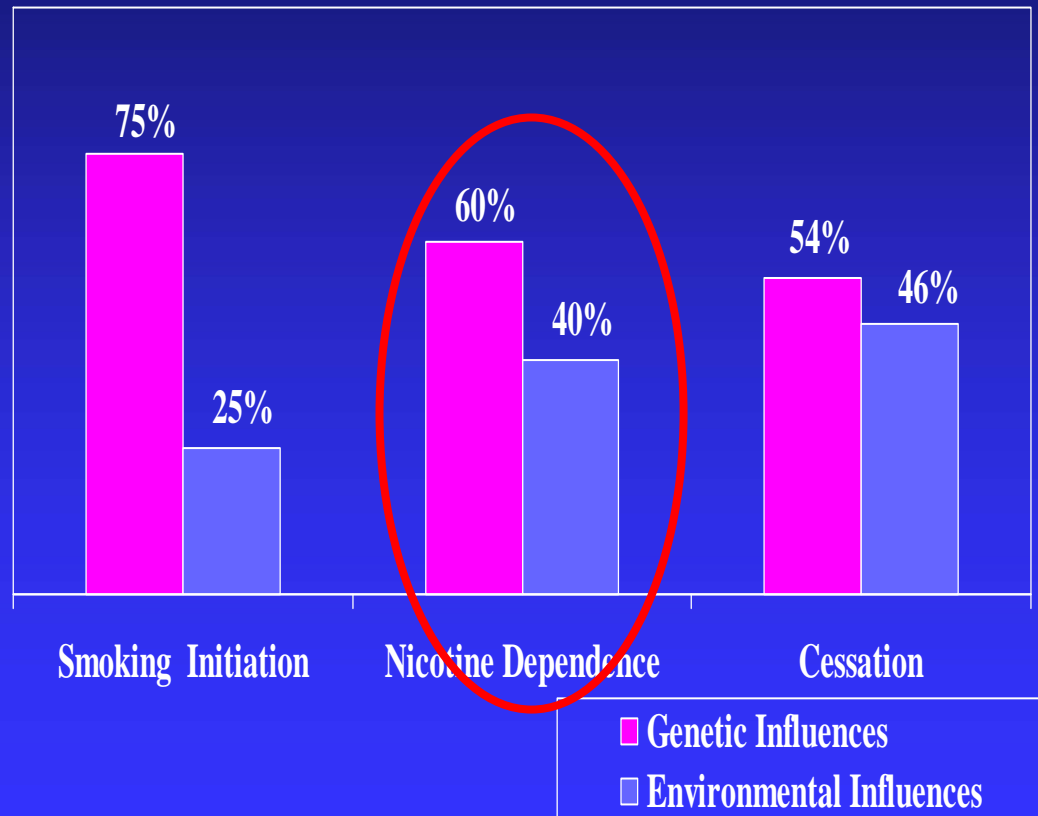
# Consumer beliefs re: the role of genetics in nicotine dependence

	Black Participants		White Participants	
	NS	S	NS	S
Genetic	21%	<b>11%</b>	24%	<b>25%</b>
Environmental	33%	36%	37%	32%
Social	46%	53%	40%	43%

# Tobacco Dependence is Heritable



## Contribution of genetic factors



*Maes et al., 2004, Xian et al., 2003*

# Impact of consumer beliefs on willingness to undergo genetic testing to be matched to optimal smoking cessation treatment

- I already said that I don't believe genetics has anything to do with it, so why would I ever agree to get tested?

# Challenges communicating complex genetic information to lower literacy adults

## Ex. Lay understandings of *heritability*

- I know alcohol is inherited because I've heard of fetal alcohol syndrome, and I know cocaine is inherited because I've heard of crack babies, but I've never heard of a baby being born hooked on cigarettes, so I don't think [smoking] has anything to do with what you inherit from your parents or with genes or any of that stuff.

# Patient concerns about privacy and genetic discrimination

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- Nearly a quarter (22 %) of Americans with a known genetic condition in the family report being refused health insurance coverage, whether they were symptomatic or not
- 15% of people at risk for developing a genetic condition report having been asked questions about genetic diseases on job applications
- 13% report that they or a family member had been fired or denied a job due to a genetic condition in the family.

Source: National Survey by Hudson et al, 1995. *Science*.

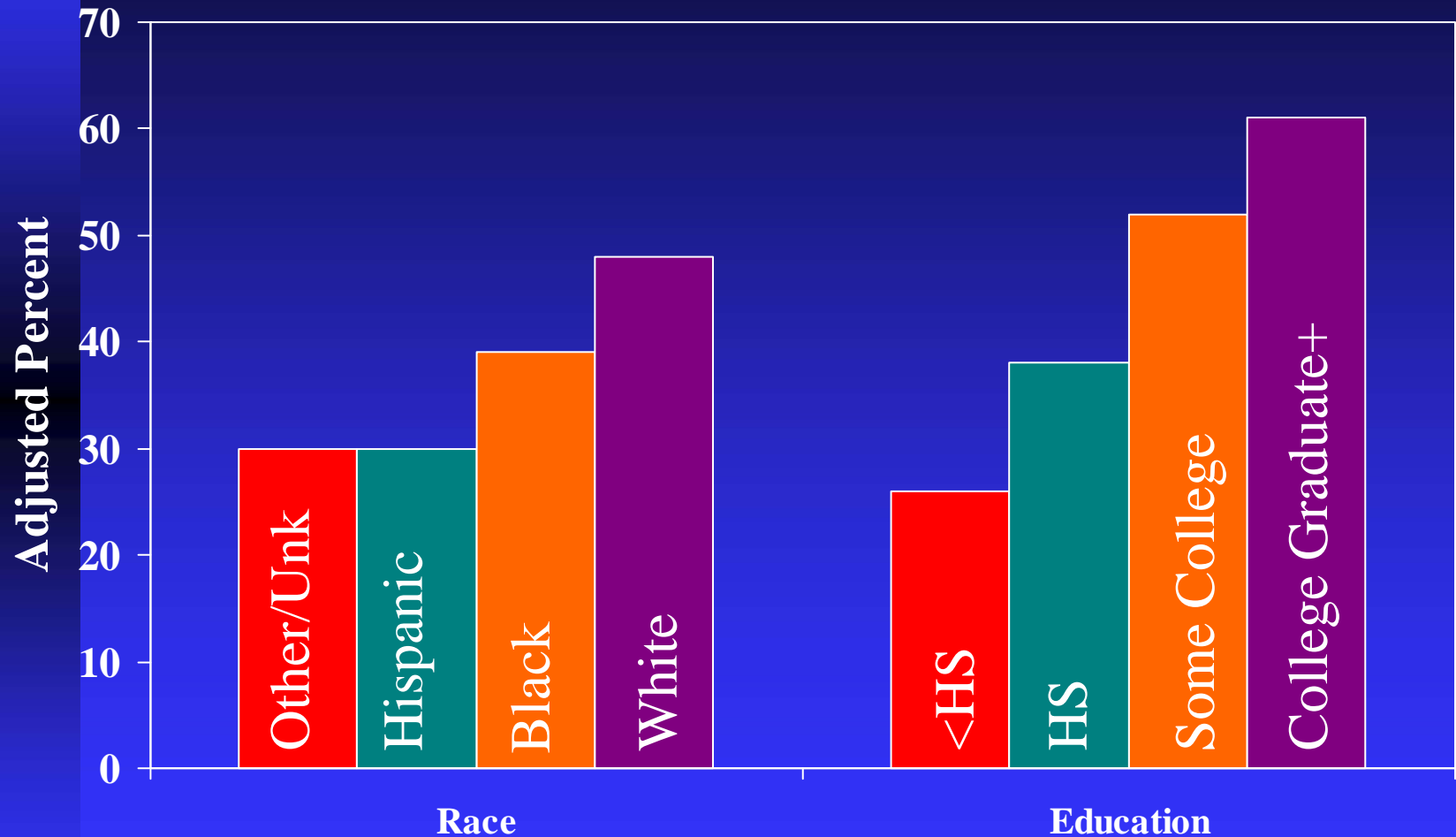
# Genetic Information Nondiscrimination Act (GINA)

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- GINA passed in the House in April 2007 as H.R. 493.
- On March 5, 2008 GINA passed again in the House as H.R. 1424, part of the Paul Wellstone Mental Health and Addiction Equity Act
- GINA is currently on hold in the Senate
- Despite original support for the Act, the White House recently released a Statement of Administration Policy on H.R.1424 stating, “While the Administration strongly supports passage of legislation... the Administration has both substantive and process objections to the rule.”

**(3) Access to Genetically-Tailored  
Treatment and the Impact of  
Genomic Medicine on Health  
Disparities**

# Racial/SES Differences in Exposure: Have you ever heard of genetic testing for cancer risk? (NHIS 2000)



\*Percent adjusted for age, sex, region, health insurance, healthcare use, cancer history, and propensity towards preventive health

# Minority patients likely to face greater challenges in accessing quality genetics services

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- Over-represented among low-literacy patients; implications for informed consent.
- More likely to be served in settings with less skilled personnel, lower quality care (Bach, NEJM, 2004).
- Poorer access to health services in general, due to health insurance issues, residential segregation.

# Minority Serving Physicians Experience Referring Patients for a Genetic Test

	Ever Referred to Genetics Center or Counselor N=943	Ever Referred to Specialist N=941	Ever Referred to a Clinical Trial N=934	Any Site of Care N=945
	OR (95% CI)			
<b>High Minority</b>	<b>0.73</b> (0.45-1.18)	<b>0.63</b> (0.40-1.00)	<b>0.46</b> <b>(0.22- 0.96)*</b>	<b>0.60</b> <b>(0.36-0.99)*</b>
<b>High Medicaid</b>	<b>0.58</b> <b>(0.37-0.92)*</b>	<b>0.64</b> (0.41-1.01)	<b>1.04</b> (0.58-1.89)	<b>0.49</b> <b>(0.30-0.80)**</b>

•p<0.05, \*\* p<0.01, †p<0.001

•Note: Also included in model but not shown: physician age, self reported race, region, practice setting (independent practice versus those practicing in a health maintenance organization, hospital-based practice, community health center or other setting), experience with genetic education.

# Minority Serving Physicians Experience Ordering a Genetic Test

	Breast Cancer N=938	Colon Cancer N=938	Sickle Cell N=936	Huntington's Disease N=940	Any Genetic Test N=944
	OR (CI 95%)				
<b>High Minority</b>	<b>0.42</b> (0.23-0.79)**	<b>0.39</b> (0.19- 0.80)**	0.74 (0.45-1.21)	<b>0.21</b> (0.08-0.53)†	0.67 (0.42-1.07)
<b>High Medicaid</b>	1.15 (0.68-1.96)	1.59 (0.87-2.92)	0.82 (0.51-1.31)	1.25 (0.67-2.34)	0.96 (0.61-1.51)

•p<0.05, \*\* p<0.01, †p<0.001

•Note: Also included in model but not shown: physician age, self reported race, region, practice setting (independent practice versus those practicing in a health maintenance organization, hospital-based practice, community health center or other setting), experience with genetic education.

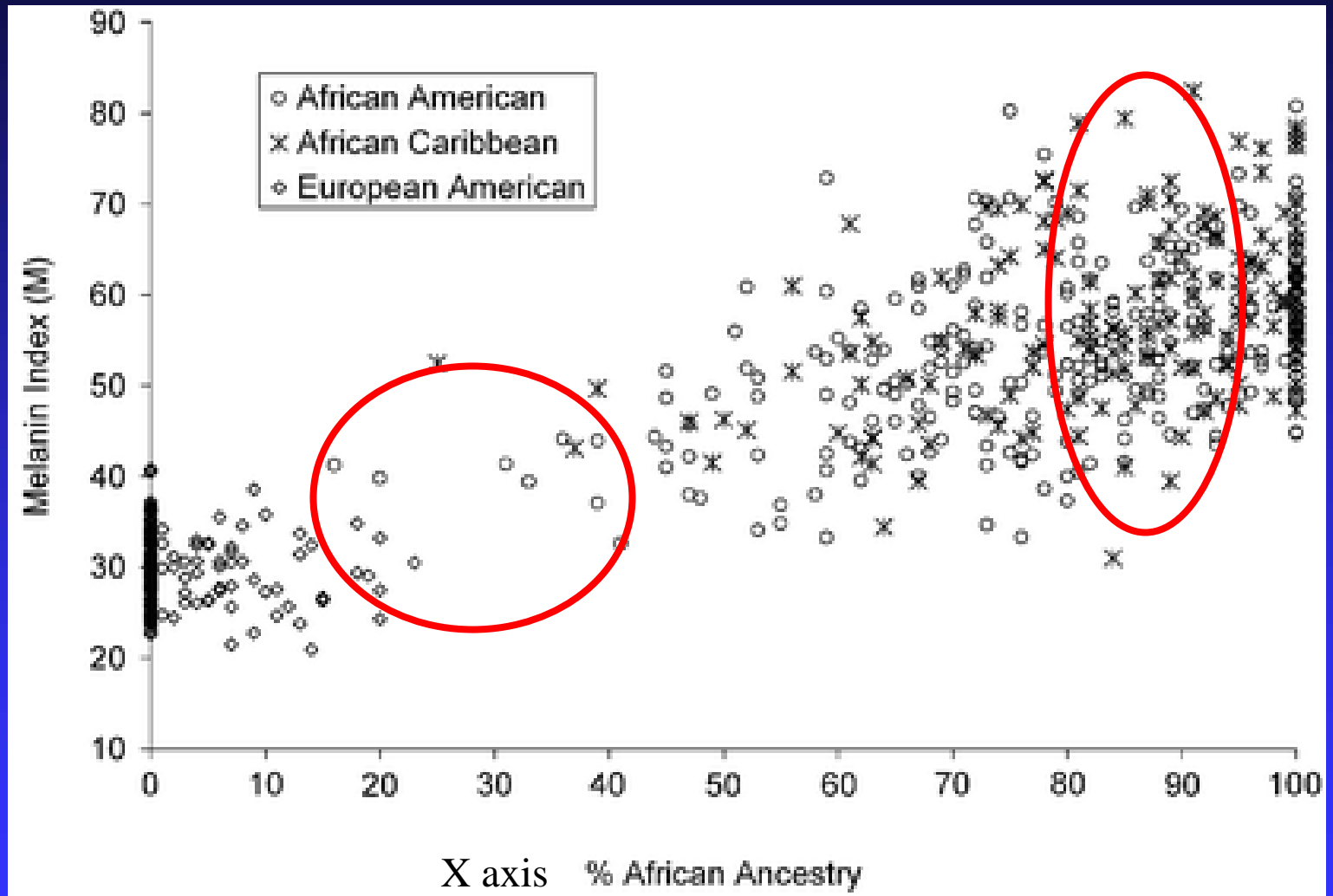
## (4) Future Research

- Communicating complex information about the genetics of addiction to low literacy adults in a culturally competent way
- Preparing PCPs to use novel pharmacogenetic treatment strategies for addiction
- Building capacity to monitor the diffusion and impact of new pharmacogenetic treatment strategies throughout the health care system

# Acknowledgements

- NIDA/NCI Support of TTURC
- Robert Wood Johnson Foundation
- NHGRI
- Caryn Lerman, Doug Levy, Eric Campbell, Elyes Park, Richard Kwong, Emily Youatt, Brian Clarrige and Center for Survey Research at UMASS Boston, Susan Kleiman, Chanita Hughes

# (1) Self-Identified Race versus AIMs



Source: Shriver et al. (2003). *Human Genetics*, 112, 387-399.