

Testing Gene × Environment  
Hypotheses Using Longitudinal  
and Randomized Prevention  
Research Designs

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# The State of Georgia and Our Research Participants



# African Americans in the Rural South

- Several million families live in small towns and communities.
- Poverty rates are some of the highest in the United States.
  - 50% are poor
  - another 25% live close to poverty

# Characteristics of the Counties in Which Our Research Is Conducted

- African American population: 49%
  - Living in poverty: 29%, compared to 17% of overall population
  - Mean weekly wage: \$471
  - Median annual household income: \$21,245
  - Adults with less than a high school education: 45%
  - Single-woman-headed families: 48%
  - Unemployment
    - Men, 34%; women, 41%
- Health care
  - 1 hospital per county in 36 counties
  - No hospital in 13 counties

# Community Partnerships

- Community liaisons
- Community ambassadors
- Partnerships with
  - Schools
  - Faith-based organizations
  - Cooperative Extension Service

# Concerns About Collecting Genetic Data: Center Staff

- Tuskegee Syphilis Experiment
- Detection of personal information
- Uncertainty about relevance to research objectives

# Concerns About Collecting Genetic Data: Focus Group Members

- Procedural clarity
- Detection and disclosure of personal information
- Uncertainty about benefits to participants

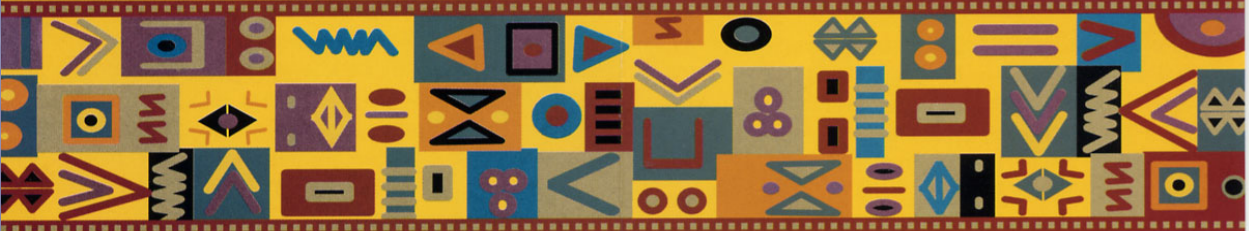


## ***A New Way of Understanding Health and Success in African American Families***

***For more information  
call us toll-free at:***

**1-888-542-3068**

***and ask to speak to our  
genetic information specialist.***



**The Center for Family Research  
1095 College Station Road  
Athens, Georgia 30602**



### **FREQUENTLY ASKED QUESTIONS:**

#### ***Why collect information about genes?***

Information about how genes and life experiences work together to make us who we are has the potential to change our understanding of health and illness. We are particularly interested in health problems that occur frequently among African Americans, like diabetes, hypertension and heart disease. By including a genetic sample with information about attitudes and beliefs, relationships, home and health, we will be able to answer questions about how our experiences may actually protect us from genetic vulnerability to some illnesses!

#### ***What does this have to do with me as an African American?***

In order to understand how genes work, we must study people whose ancestors come from all parts of the world. It is important, then, to include people of all races in genetic studies. If African Americans are to benefit from this research, we must learn first-hand how their genes and life experiences work together to influence their health. We do not want to assume that how it works for people of one race is how it works for all races.

#### ***What will I be asked to do?***

Since genes are in every cell of the body, we can get a sample of your genetic information from your saliva. You will be asked to rinse your mouth with water, and then spit into a small vial called Oragene. When you cap the vial, a seal will be broken and your saliva will mix with the Oragene liquid. The field interviewer will provide instructions and the materials needed. Your participation is completely voluntary.

**F**or many, many years people have wondered what makes us who we are. Is it the way our parents raise us? Is it the experiences that life sends our way? Or is it what we each carry inside the cells of our bodies—the unique genetic blueprint we are born with? Most scientists would agree that it is a mixture of how we are made on the inside (our genes) and what we experience on the outside (our environment) that makes us who we are.



### ***Our Research is Changing***

Over the years, the research conducted at the Center for Family Research has looked at the kinds of families, schools and communities that foster health and success in African American youth. Now we are collecting genetic as well as environmental information from the families who participate in our research. By looking at the connections between how we are made (our genes) and what we experience (our environment), we hope to better understand why some people are able to succeed in difficult situations.

### ***Why This Research is Important***

Scientists have identified all of the genes in the human body. More than 20,000 of them! But many questions remain about how genes work and why they seem to have different effects on our health and behavior under different circumstances. We need to know more about when and how different versions of our genes are affected by the experiences we have—because these experiences (how much stress we experience, whether or not we take good care of our bodies, what kind of relationships we have with friends and family members) influence our health.



Some health problems like hypertension, diabetes and heart disease occur much too frequently in the African American community. The explanation for this may be partially genetic, but it is also related to stress, diet and health care practices. By studying the fit between genes and environment, we may learn how to improve treatments for these illnesses. In fact, we may discover ways in which families and communities actually protect us from developing health problems!

### ***How It Will Help***

This new approach to our research will help us understand how and why certain conditions do or do not develop in African Americans—and what we might do to prevent them. We are looking at genes related to (1) health conditions like hypertension, diabetes, and heart disease, and (2) emotional and behavioral conditions like depression, anxiety, substance abuse, and attention deficit hyperactivity disorder. Our findings will help us develop new ideas about how family life, parenting practices and everyday experiences can encourage health and success in African American children and families.

### ***What will be done with the mouthwash sample?***

Your saliva and Oragene sample will be labeled with an identification number rather than your name. It will be stored and analyzed at the University of Iowa, in Iowa City. When our study is completed, the sample will be destroyed.

### ***Will my genetic information be available to anyone?***

We go to great lengths to keep all of the information that you share with us confidential. This commitment to your privacy will be upheld with your genetic information as well. It will not be shared with any third parties for any reason, including purposes of employment, insurance, paternity or criminal investigation except with your written permission or as may be required by law.

### ***What are the benefits to me and my family?***

The value of participating comes from contributing to a study about African Americans that may reveal information that will help families like yours in the future.

You will not receive any personal genetic information from our researchers because we are not qualified to make medical diagnoses or to provide genetic counseling.

### ***Will I get paid extra for participating in this part of the study?***

You will be paid an additional \$20 for providing the saliva sample.

### ***What if I have questions?***

Please call us toll free (1-888-542-3068) at the Center for Family Research with any questions you may have. Dr. Yvonne Mensa-Wilmot, AIM Project Coordinator, can answer specific questions about the AIM study and our genetic collection procedures.

# The Gene × Environment Initiative: Initial Focus on *5HTT*

- Well-studied human polymorphism
- Two variants: short and long allele
- Short allele effects
  - Lowered serotonin transporter availability
  - Risk for alcohol and heroin dependence in adulthood (Kreck et al., 2005)
- 5-HTTLPR linked to low self-control
  - Children: High activity, short attention span, negative affect
  - Adults: Substance use in community and college samples, disregard for rules, impulsivity, negative affect, aggression

Parenting Moderates the Effects  
of 5-HTTLPR Status on  
Longitudinal Increases in  
Youths' Substance Use

# Hypotheses

- A functional polymorphism (5-HTTLPR) in the promoter region of the serotonin transporter gene *5HTT* will forecast longitudinal increases in the use of alcohol and other substances among adolescents.
- Competence-promoting parenting, which includes high levels of instrumental and emotional support along with racial socialization, will attenuate the link between the 5-HTTLPR polymorphism and longitudinal increases in the use of alcohol and other substances.

# Participants

- African American families ( $N = 298$ )
  - In rural Georgia
  - 41% lived below the poverty threshold
    - 26% lived within 150% of the threshold
- Youths
  - 11 years old when recruited
  - 58% girls, 42% boys
- In-home data collection
  - African American field researchers
  - Computer-based interviews

# Data Collected

- Substance use
  - Youth report
    - At ages 11, 12, 13, and 14 years
    - 91% ( $n = 289$ ) provided data at all assessments
- Parenting
  - Parent report
  - Gathered at first assessment
- DNA
  - Via saliva samples
  - From 85% of youths with complete data ( $n = 253$ )
  - Gathered 2 years after last assessment

# Measures

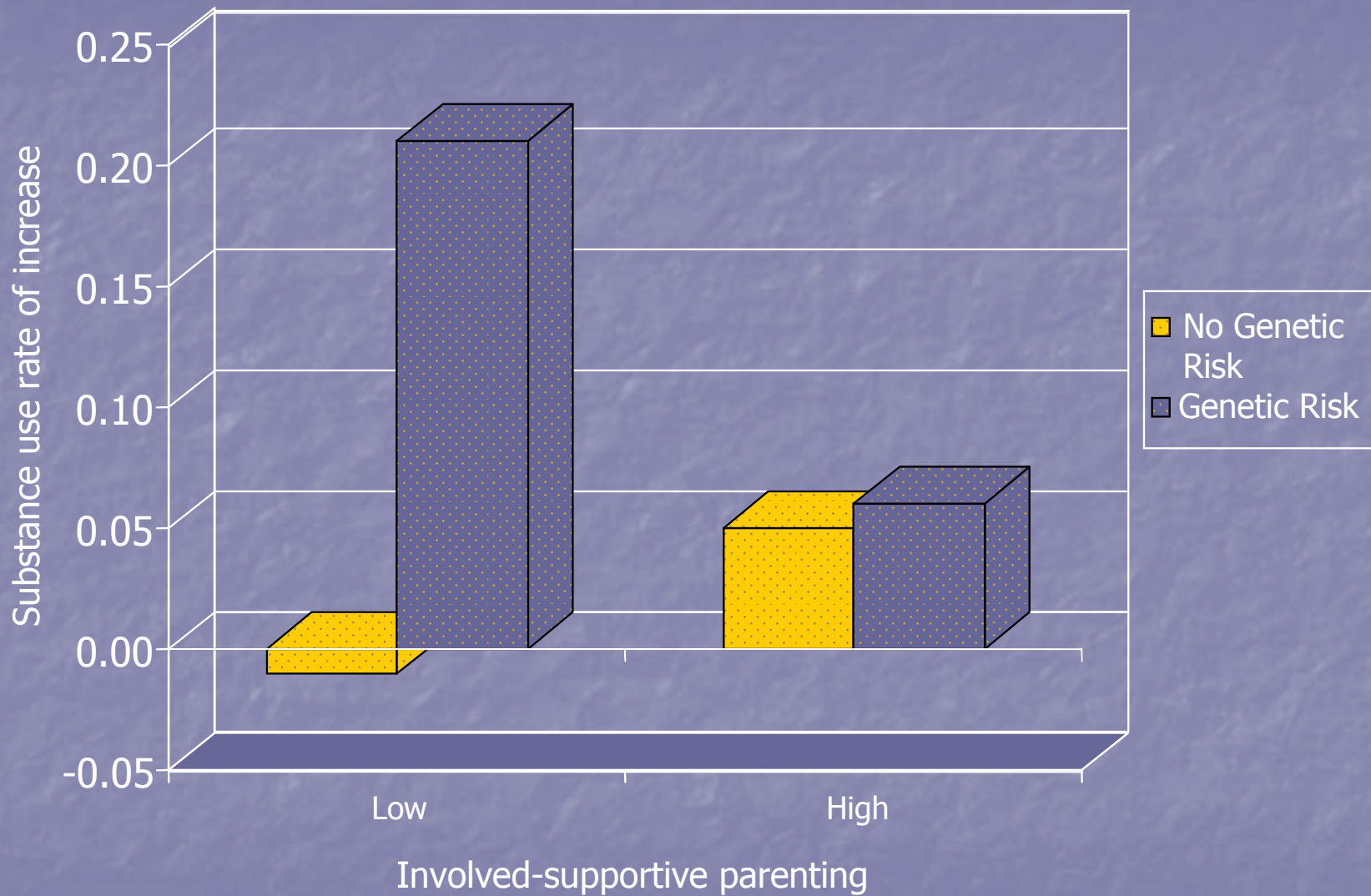
- Substance Use
  - Past-year use of alcohol (including heavy use) cigarettes, marijuana
  - Index created from responses
- Protective Parenting
  - Interaction Behavior Questionnaire,  $\alpha = .84$
  - Racial Socialization Scale,  $\alpha = .84$

# Genotype Assessment

- DNA obtained using Oragene DNA kits
  - Identified genotype at 5-HTTLPR
  - Genotype distribution
    - 7% homozygous for the short allele (*ss*)
    - 36% heterozygous (*s/*)
    - 57% homozygous for the long allele (*//*)
  - Two groups formed (Hariri et al., 2005)
    - At risk: *ss* + *s/*
    - Not at risk: *//*

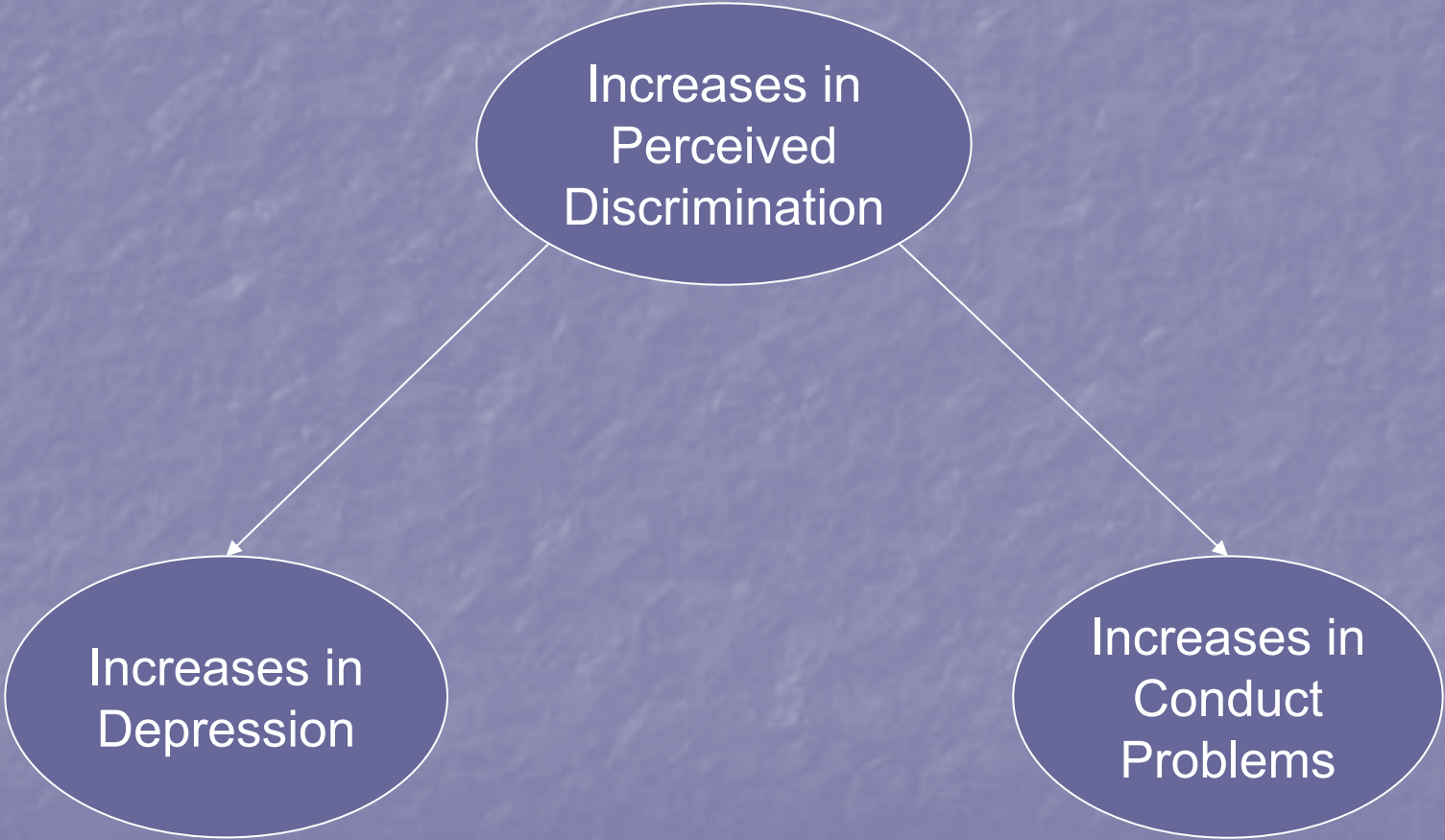
# Results

- Latent growth modeling confirmed Hypothesis 1
  - Genetic risk was positively associated with increases in substance use
    - $\beta = .29, p < .01$
- A significant interaction confirmed Hypothesis 2



Perceived Discrimination and  
the Adjustment of African  
American Youths: A 5-Year  
Longitudinal Study

# Across 5 Years

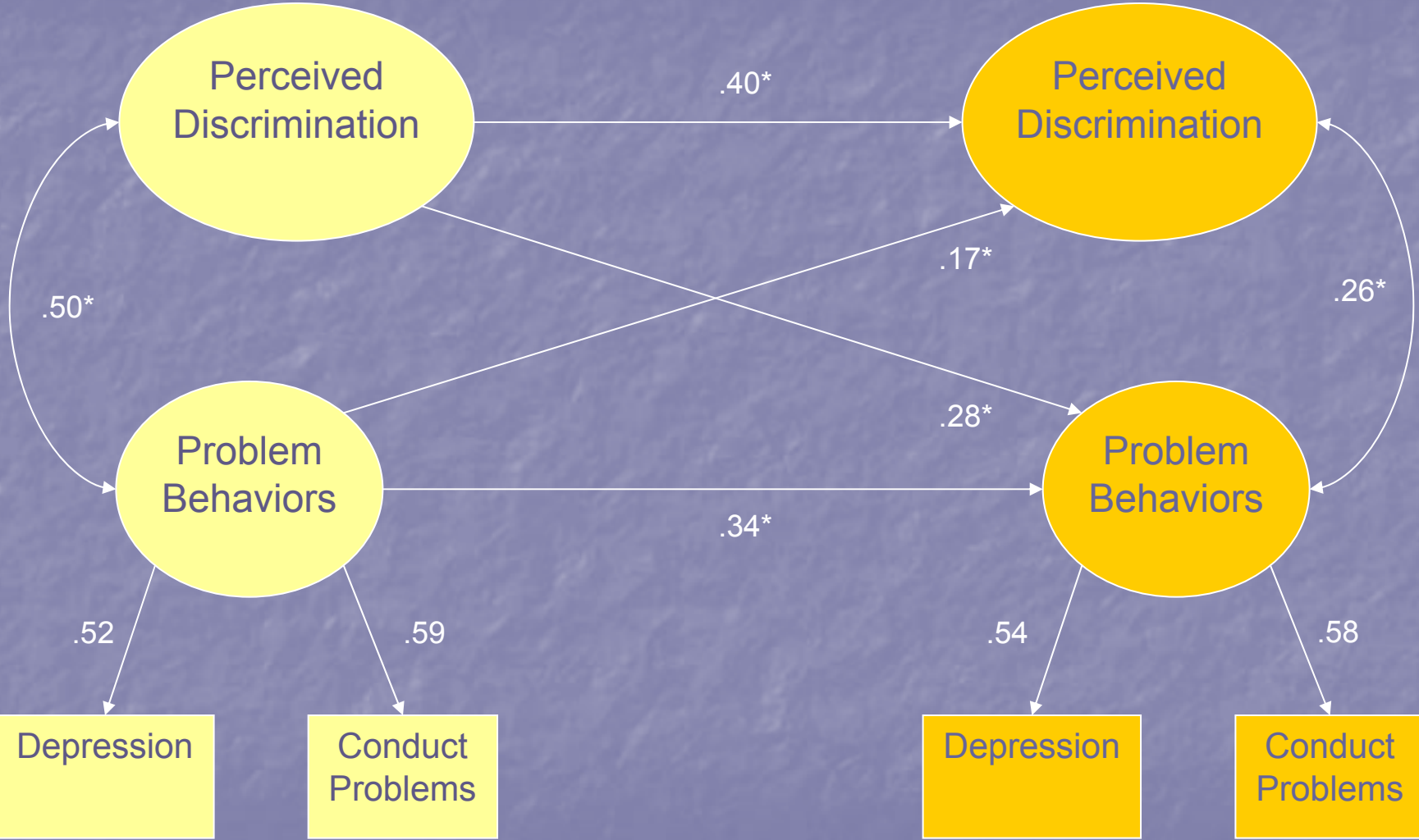


# Measures

- Perceived discrimination
  - Schedule of Racist Events
- Depression
  - Diagnostic Interview Schedule for Children
- Conduct problems
  - Diagnostic Interview Schedule for Children
- Involved-vigilant parenting
  - Scales developed for FACHS

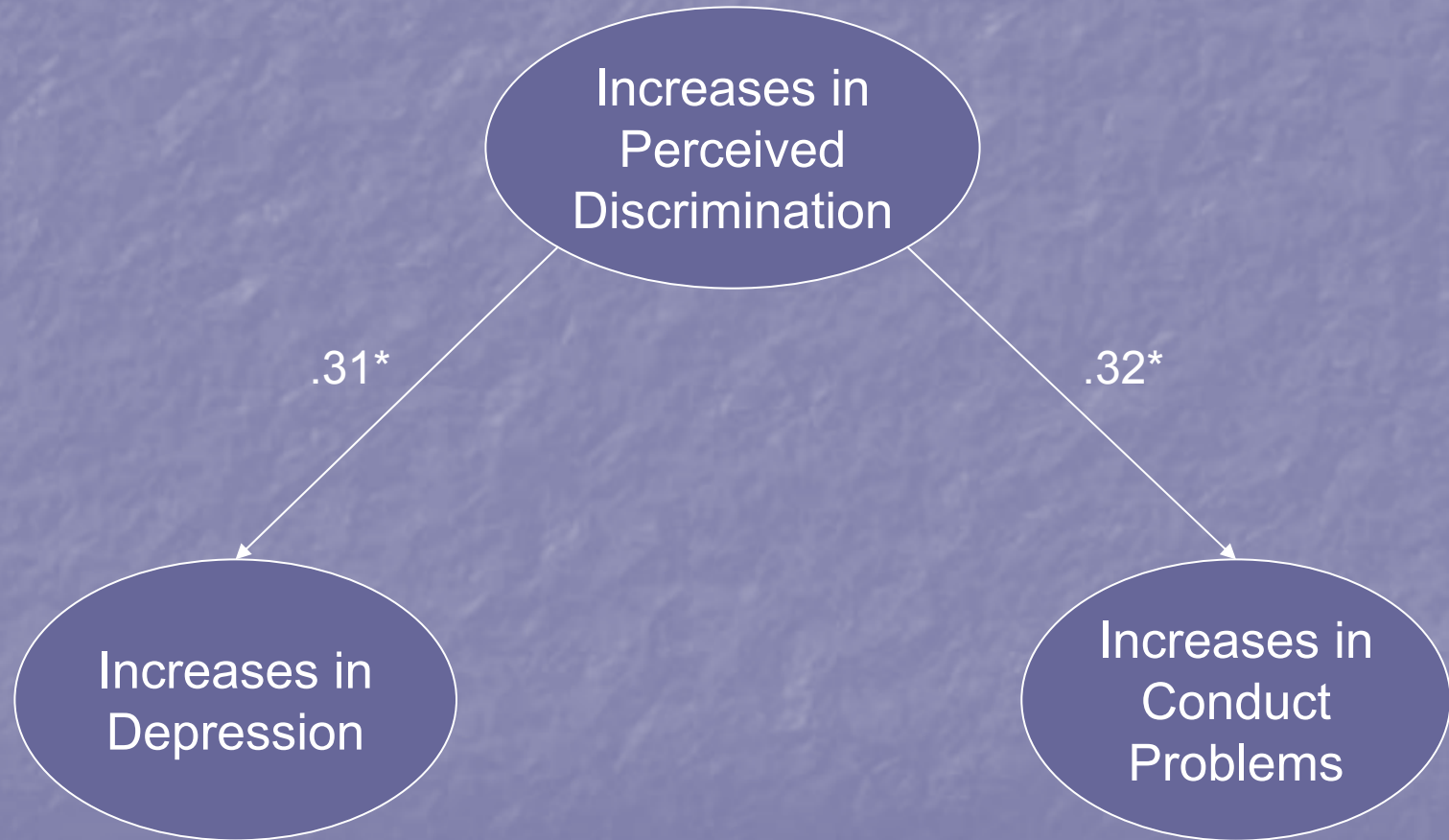
Wave 1

Wave 2



\*  $p < .05$

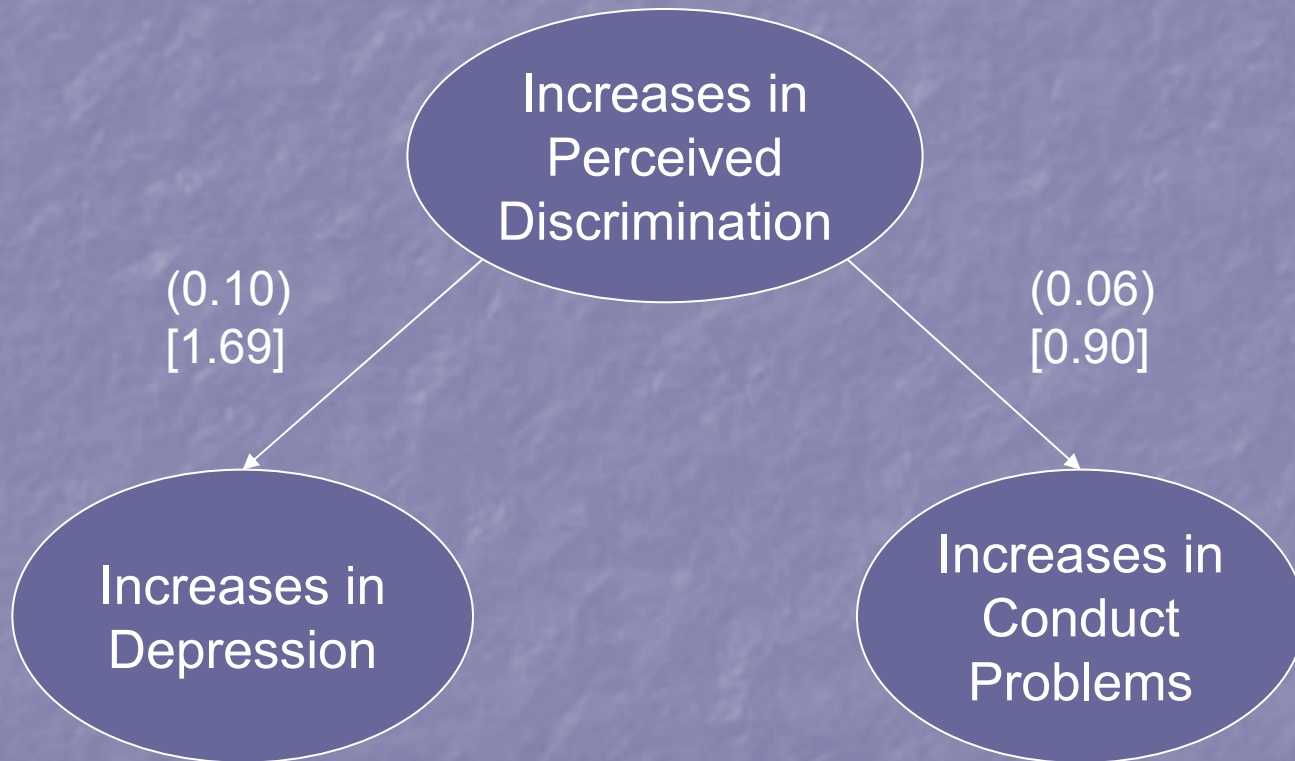
# Across 5 Years



\*  $p < .05$

# Parenting Moderates Contributions of Perceived Discrimination

Across 5 Years



Involved-vigilant parenting levels: (high), [low]

5-HTTLPR Status Moderates  
the Link Between Perceived  
Discrimination and  
Longitudinal Increases in  
Youths' Antisocial Behavior

# Hypotheses

- Perceived discrimination will forecast longitudinal increases in antisocial behavior among male youths.
- A functional polymorphism (5-HTTLPR) in the promoter region of the serotonin transporter gene (5-HTT) will potentiate the link between the 5-HTTLPR polymorphism and longitudinal increases in male youths' antisocial behavior.

# Participants

- African American families ( $N = 461$ )
  - In rural Georgia
  - 67% lived within 150% of the poverty threshold
- Youths
  - 11 years old at Wave 1
  - 58% female, 42% male

# Data Collection

- Gathered in families' homes
  - African American field researchers
  - Audio computer-assisted self-interviews (ACASI)
- Antisocial behavior
  - Youth report
  - Yearly, at ages 11 through 16
  - 86% provided data at all assessments
- Perceived discrimination
  - Youth report
  - Wave 1 data used in analyses
- DNA
  - Via saliva samples
  - Gathered at last assessment

# Measures

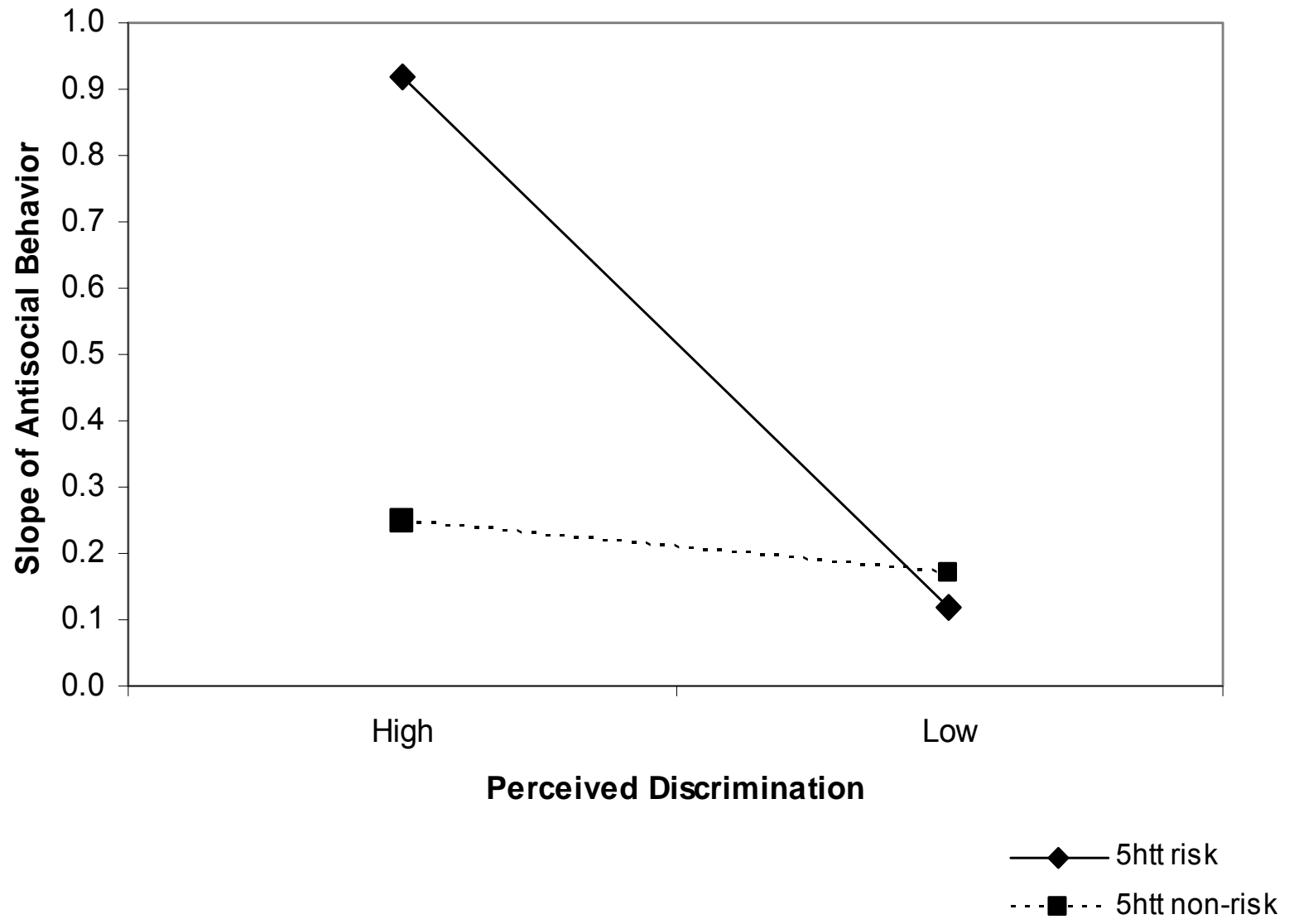
- Past-year antisocial behavior
  - 14-item checklist from the National Youth Survey (Elliott, Ageton, & Huizinga, 1985)
- Perceived discrimination
  - Schedule of Racist Events (Landrine & Klonoff, 1996)
    - $\alpha = .82$ , with present sample

# Results

- Perceived discrimination was positively associated with increases in (slope of) antisocial behavior
  - $\beta = .63, p < .05$
- Genetic risk was positively associated with increases in substance use
  - $\beta = .40, p < .05$

# Results

- A significant perceived discrimination  $\times$  genetic interaction also emerged.
  - $\beta = 1.05, p < .01$
  - The link between perceived discrimination and the slope of youths' antisocial behavior was stronger for youths with genetic risk.
- Gendered analyses
  - Data were reanalyzed separately by youth gender.
  - Results emerged for male, but not for female, youths.



Prevention Effects Moderate the  
Association of 5-HTTLPR Status  
with Youths' Risk Behavior  
Initiation

# Using Randomized Prevention Trials to test $G \times E$ Hypotheses

- Environmental effects are identified.
- Threats to internal validity that can be taken for environmental effects are eliminated.
  - Maturation
  - Repeated testing
  - Regression to the mean
  - Gene-environment correlations

# The Strong African American Families (SAAF) Program

- Based on longitudinal, epidemiological studies of rural African American families and youths
- 7-session family-based preventive intervention
- Established efficacy

# SAAF Trial Participants

- Rural African American families ( $N = 641$ )
  - Mothers
  - 11-year-old youths
- Randomly assigned to
  - SAAF preventive intervention program
  - Control condition

# Hypothesis

- Youths with *ss* or *s/* genotypes who are randomly assigned to the control condition will evince greater risk behavior initiation across 29 months than will:
  - Youths with *ss* or *s/* genotypes assigned to the SAAF preventive intervention condition
  - Youths with *//* genotypes assigned to either condition

# Data Collection

- Pretest
- Posttest, 8 months after pretest
- Long-term follow-up, 29 months after pretest
- At all assessments
  - Mothers and youths were interviewed at home
  - Data on risk behavior initiation were gathered

# Measuring Risk Behavior Initiation

- Youth report
  - Alcohol use
    - Beer, wine, wine coolers, whiskey, gin, other liquor
    - Binge drinking (3+ drinks on one occasion)
  - Marijuana use
  - Sexual intercourse
- Dichotomous scoring
  - 1 if *yes*, 0 if *no*
- Summed to form risk behavior initiation index

# Genotype Distribution

- 6% *SS*
- 35% *sI*
- 59% *//*

# Plan of Analysis

- Intent-to-treat design
  - Included all families with pretest, posttest, and long-term follow-up data
  - No families excluded based on number of SAAF sessions attended
  - Prevented self-selection bias
- Latent growth modeling tested for individual effects of genotype and group assignment.
- Planned group comparisons tested the moderational hypothesis.

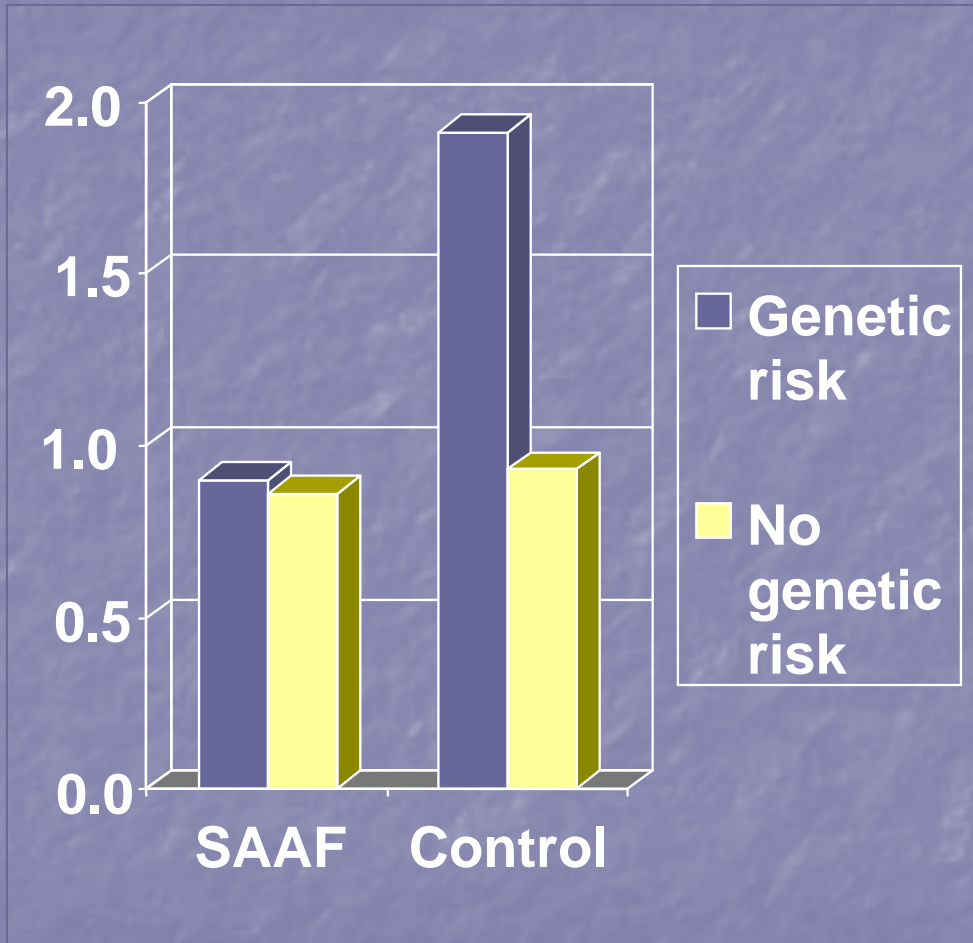
# Results: Latent Growth Modeling

- From pretest to long-term follow-up:
  - Genetic risk was positively associated with risk behavior initiation.
    - $\beta = .19, p < .05$
  - Assignment to the SAAF group was negatively associated with risk behavior initiation.
    - $\beta = -.15, p < .05$

# Results: Planned Group Comparison Test of the Moderational Hypothesis

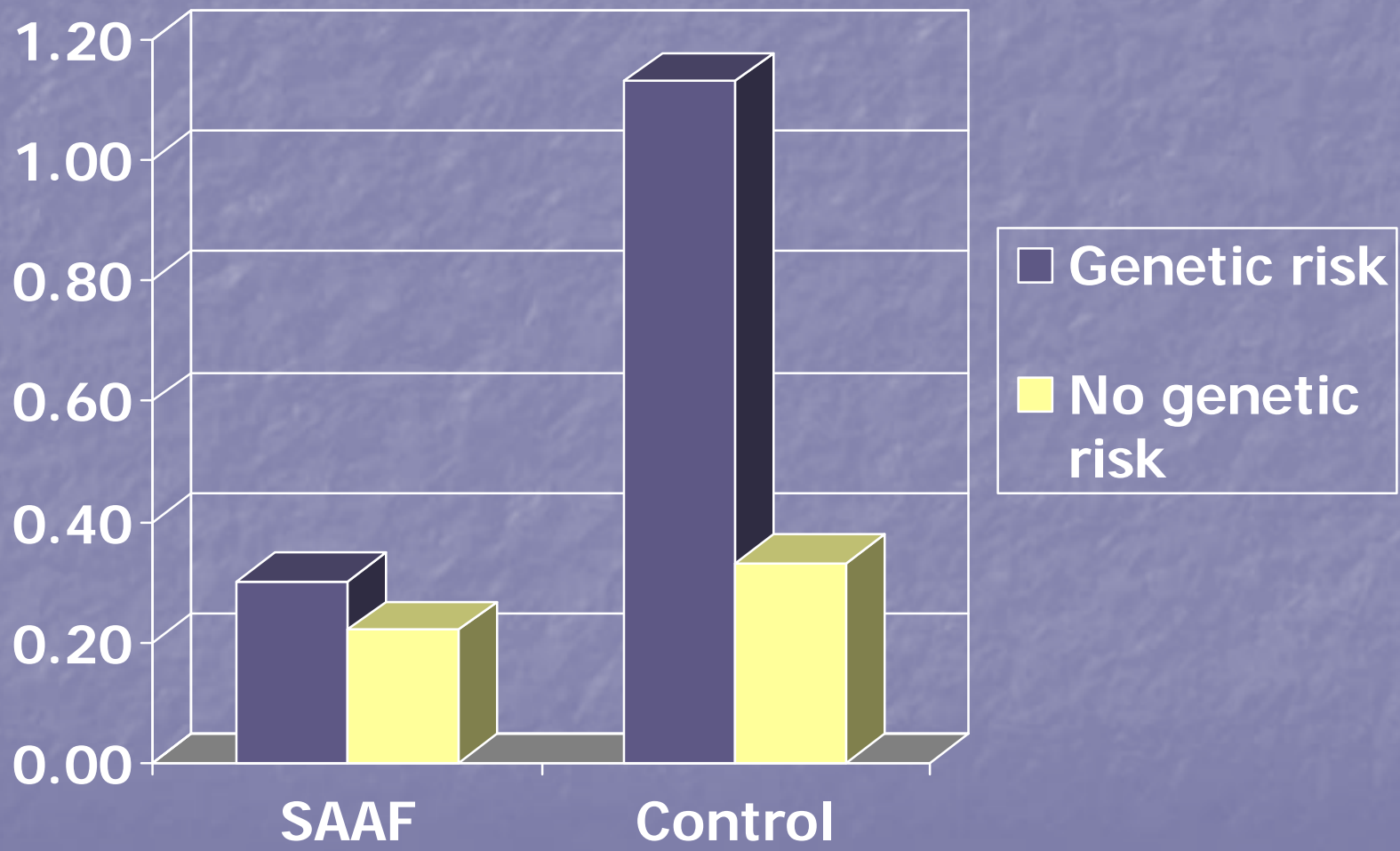
- Four groups were formed
  - SAAF, with genetic risk ( $n = 105$ )
  - SAAF, without genetic risk ( $n = 153$ )
  - Control, with genetic risk ( $n = 78$ )
  - Control, without genetic risk ( $n = 104$ )
- Equivalence tests showed no group differences at pretest on any demographic or study variables.

# Results: Test of the Moderational Hypothesis



- $F(1,430) = 8.41$
- $p < .004$
- Confirmed moderational hypothesis

# Change in mean frequency of past-month risk behaviors across 29 months, ages 11 to 14 years



# Future Directions

- Biology and the environment
  - G×E interactions
    - With different genes
    - At different stages of development
  - Allostatic load
    - A biological measure
      - Reflects wear and tear on the body caused by repeatedly drawing on resources to meet environmental demands

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