

The Impact of Disclosing Personal Genome Information: Possible Insights for the Personal Genome Project from the REVEAL Study

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Equity:	None

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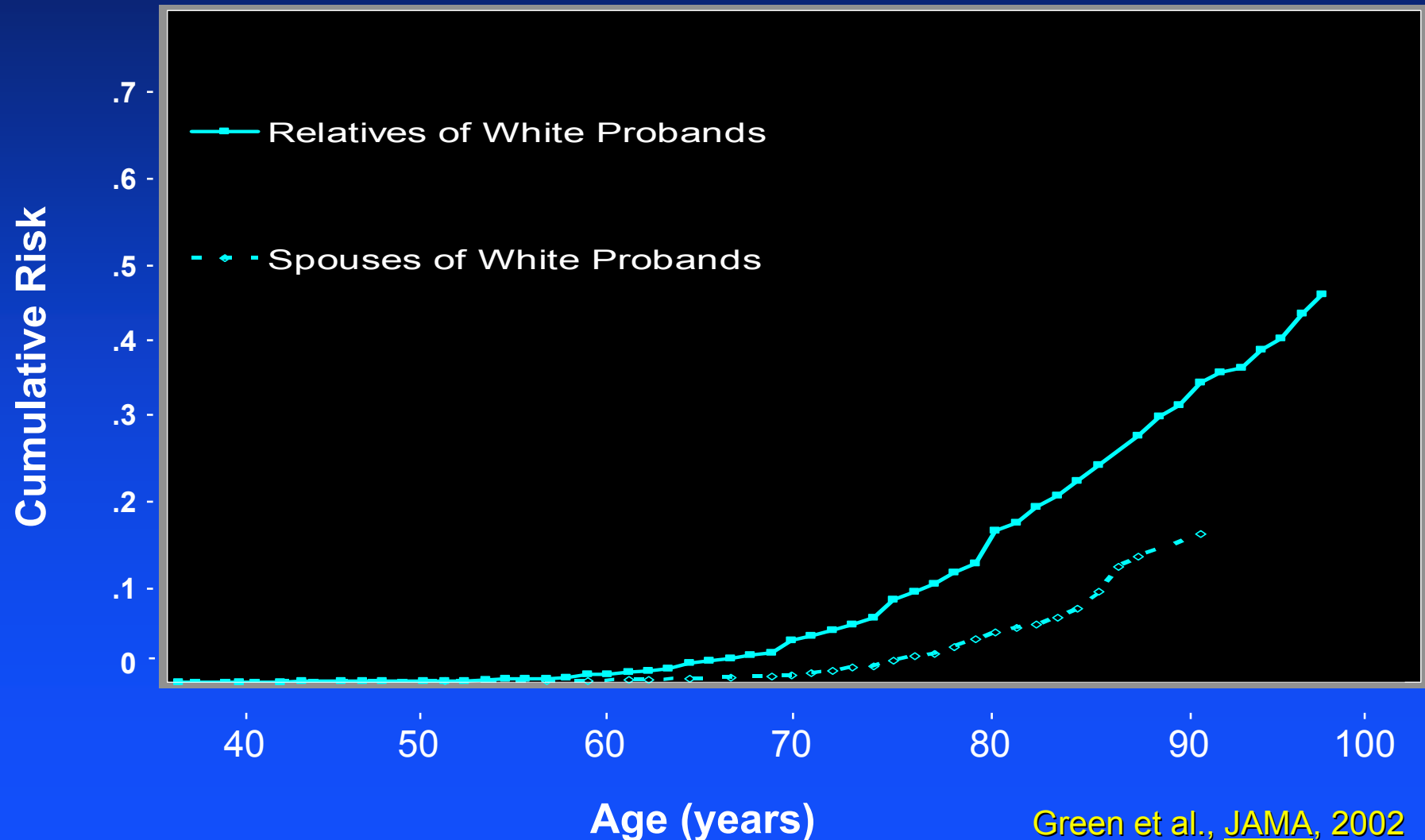
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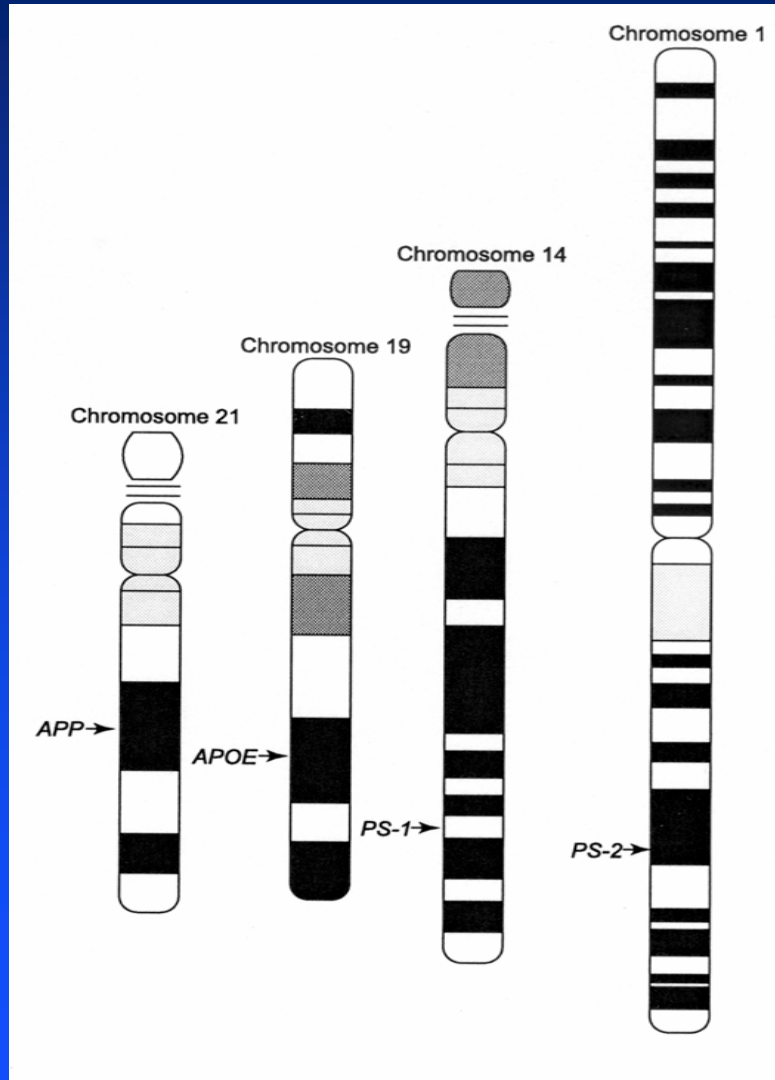


Cumulative Risk of Dementia in First-Degree Relatives of Patients with AD



Gene Markers for Alzheimer's Disease

Rare Mendelian Disease and Common Complex Disease



Deterministic Mutations:

Amyloid Precursor Protein (APP)

Presenilin-1 (PS-1)

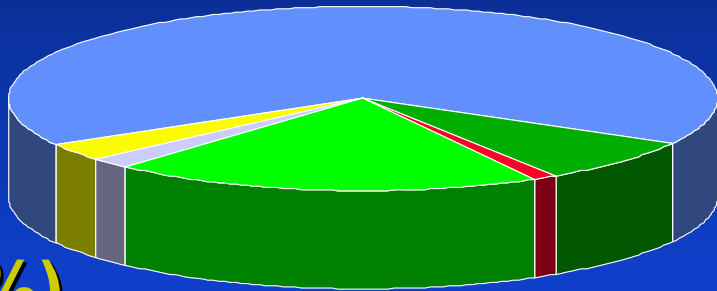
Presenilin-2 (PS-2)

Susceptibility Polymorphism:

Apolipoprotein E (APOE)

APOE Genotypes in the General Population

3/3 (67%)



2/4 (3%)

4/4 (2%)

3/4 (20%)

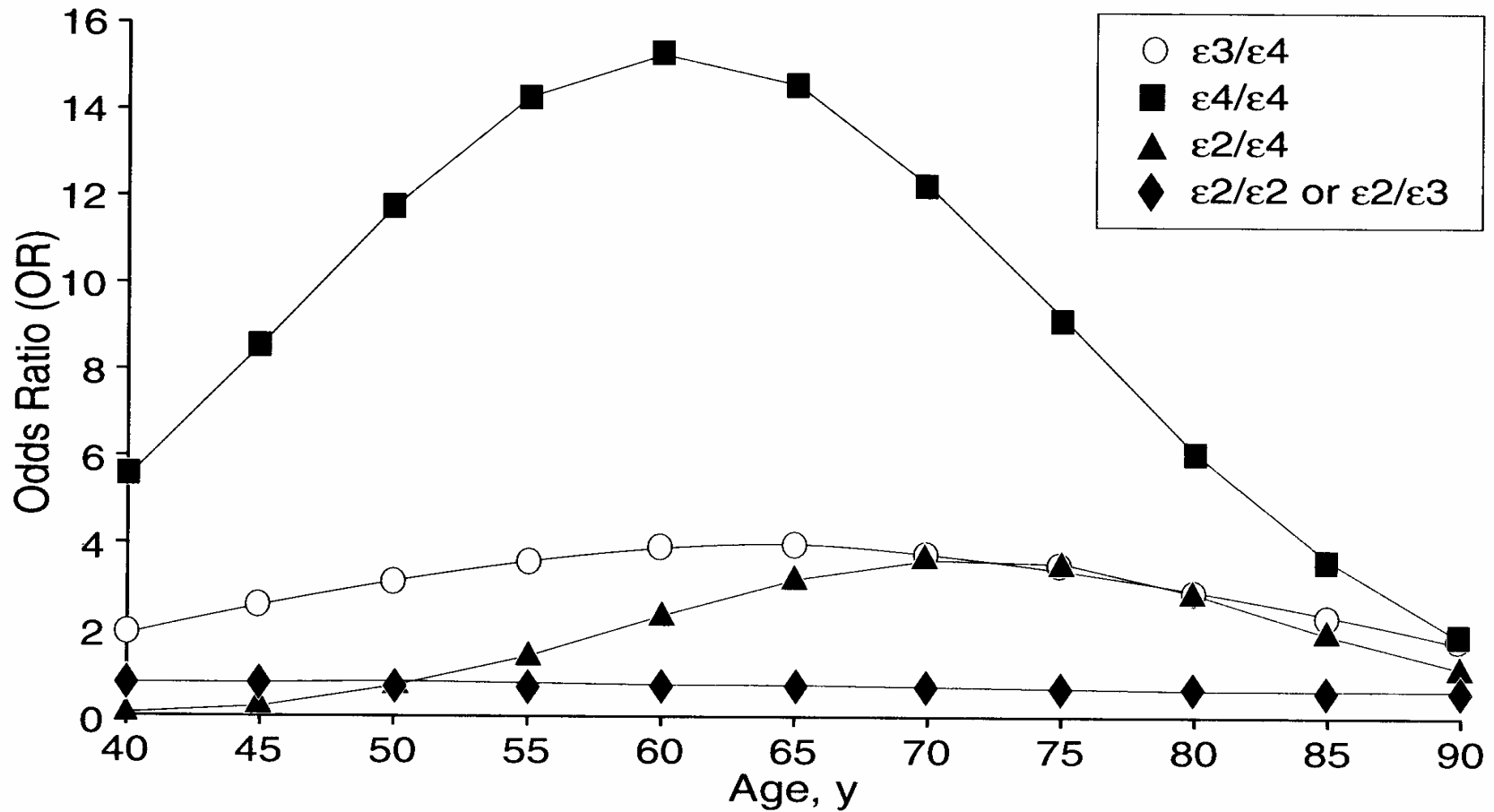
2/3 (8%)

2/2 (1%)

There are six possible combinations of the three APOE forms. These combinations are called genotypes.



Odds of Alzheimer's Disease by APOE and Age



The ACCE Model for Genetic Testing

- Alytic Validity
- Clinical Validity
- Clinical Utility
- Ethical, Legal, Social Issues (ELSI)

APOE and Alzheimer's Disease

A Unique Model for Exploring Clinical Utility and ELSI

- Excellent Analytic Validity
- Well documented Clinical Validity
- No treatments and (no market pressures!)
- Terrifying disease
- People still want to know their risk

“I would like to know if I am going to develop Alzheimer’s disease at some point in my life”

Strongly or Somewhat Agree	50.3%
Undecided	22.0%
Somewhat or Strongly Disagree	27.9%

The REVEAL Study

Is risk information beneficial or toxic?

Empirically measure the benefits and risks of genetic susceptibility testing...



REVEAL Questions

How can we clearly communicate risk information based on genetics?



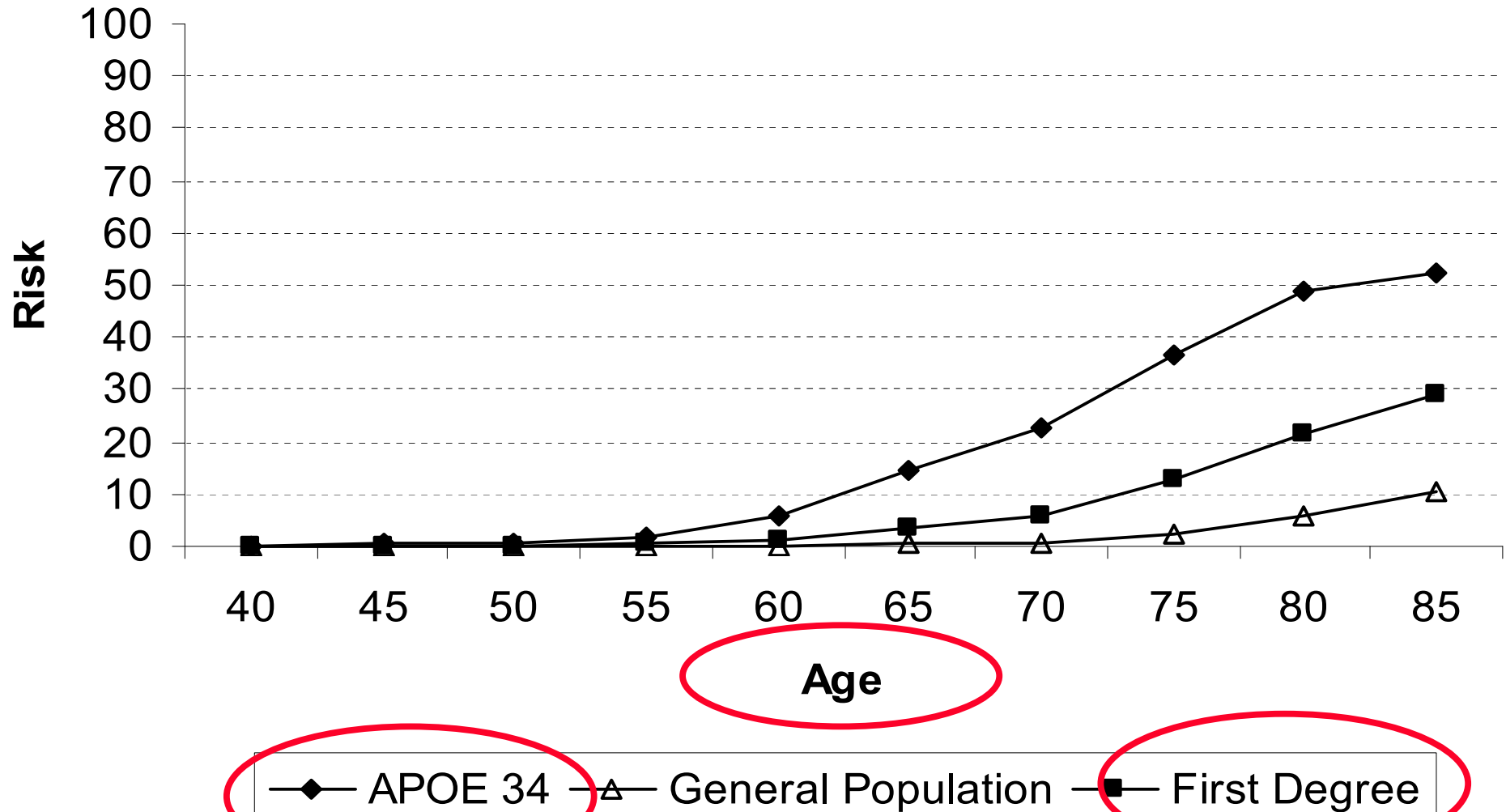
GENE

RISK

Estimating risk curves for first-degree relatives of patients with Alzheimer's disease: The REVEAL study

L. Adrienne Cupples, PhD^{1,2}, Lindsay A. Farrer, PhD¹⁻⁵, A. Dessa Sadovnick, PhD⁶, Norman Relkin, MD, PhD⁷, Peter Whitehouse, MD, PhD⁸, and Robert C. Green, MD, MPH²⁻⁴

Risk of AD by APOE in Women

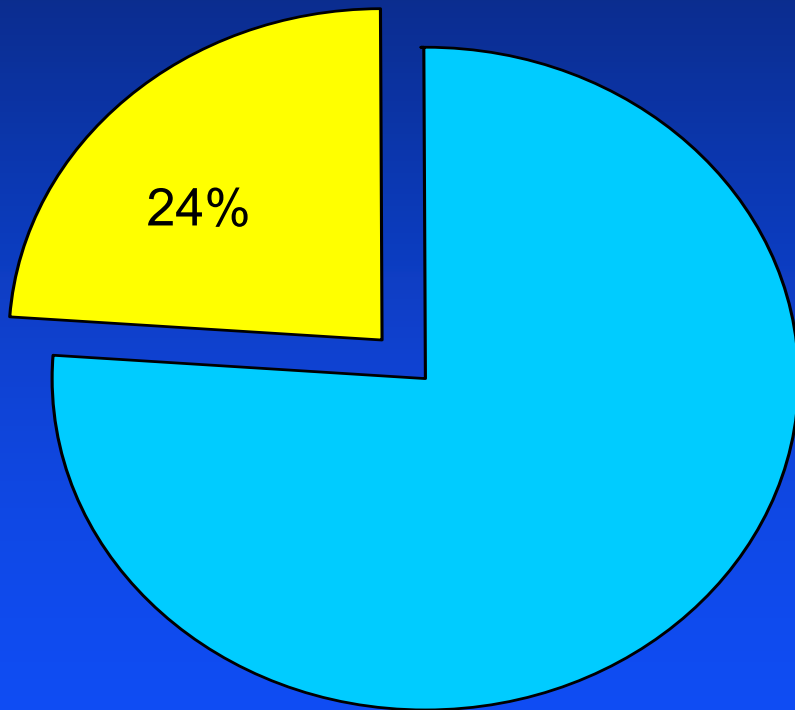


REVEAL Questions

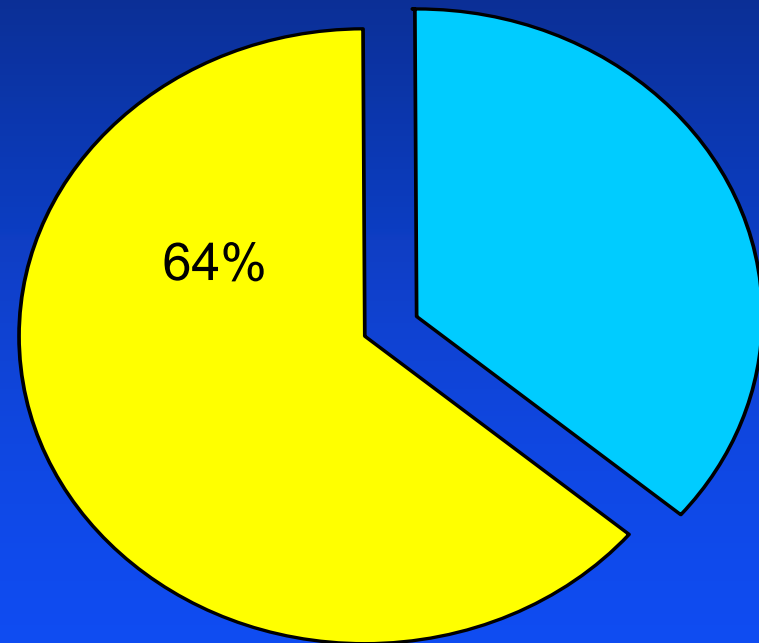
Who wants to know?

Persons Agreeing to Participate in REVEAL

Systematically Ascertained



Self Referred



REVEAL Questions

Why do people want to know?

Reasons Associated with Enrollment

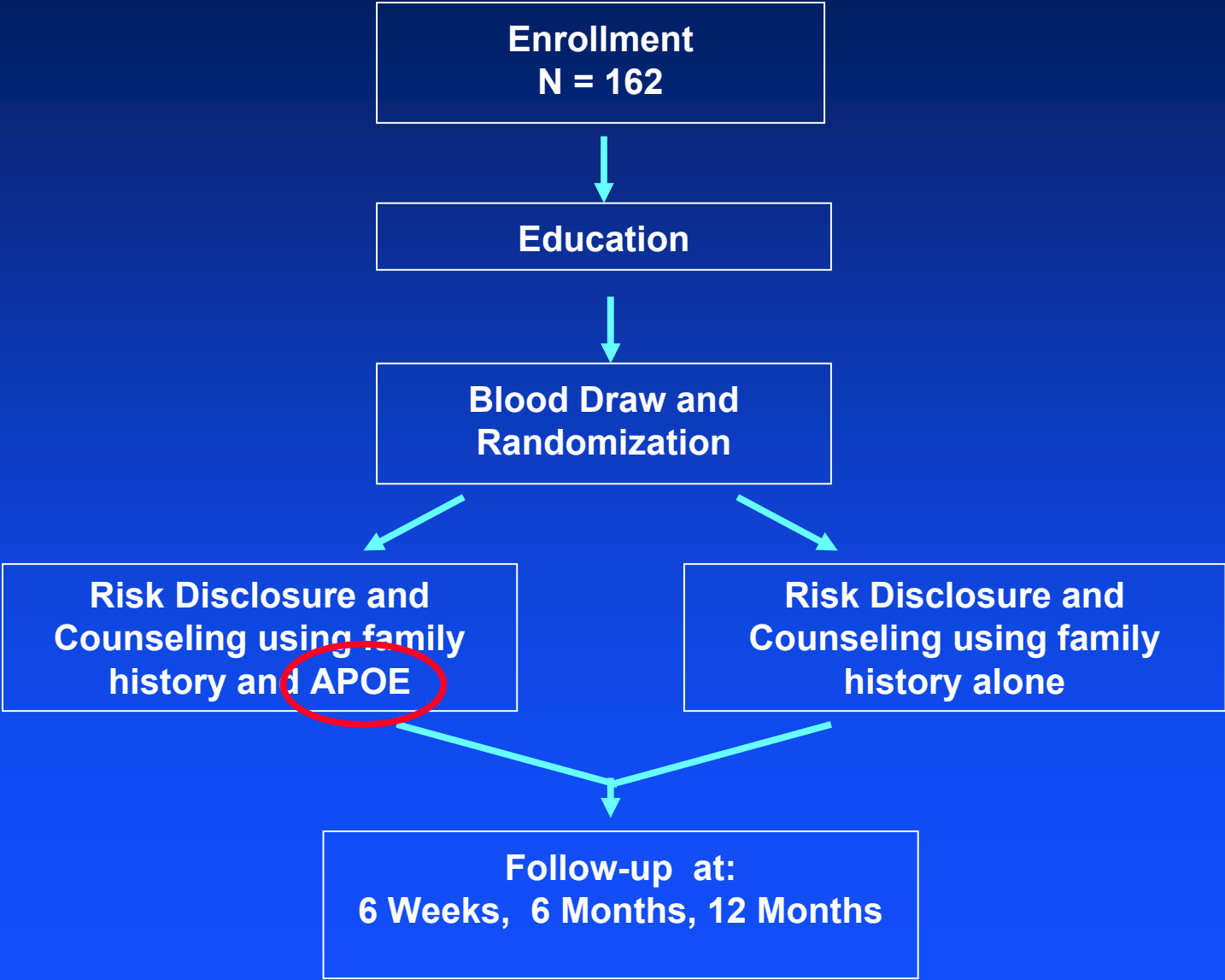
<i>Strongly endorsed reason for seeking testing as predictor of study enrollment</i>	<i>Odds ratio</i>
To prepare family for AD	3.33
To arrange personal affairs	2.62
To arrange long-term care	2.52
To learn information for family planning	2.25

Women strongly endorsed more reasons for seeking testing than men, $p = .01$

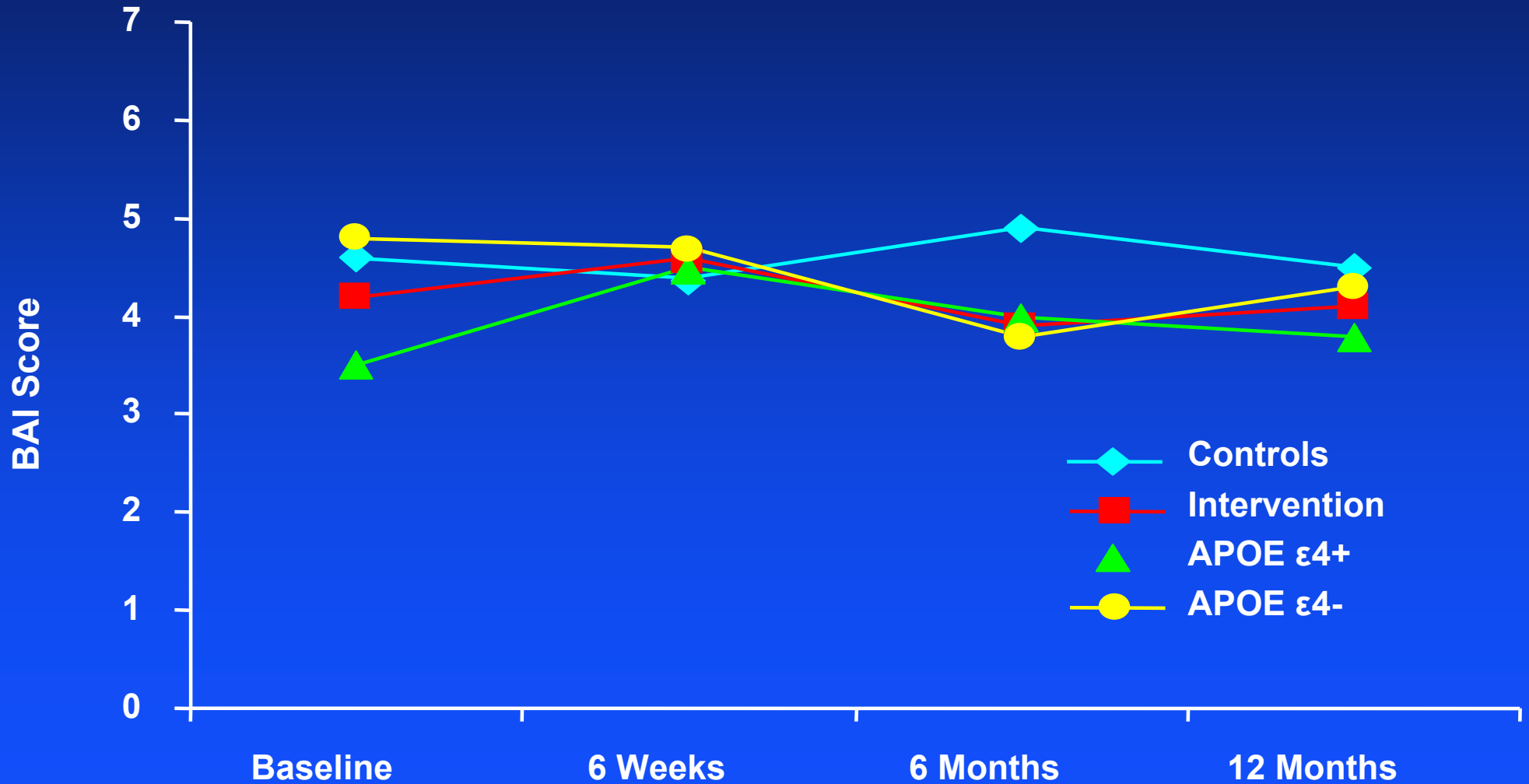
REVEAL Questions

What happens to them when they find out?

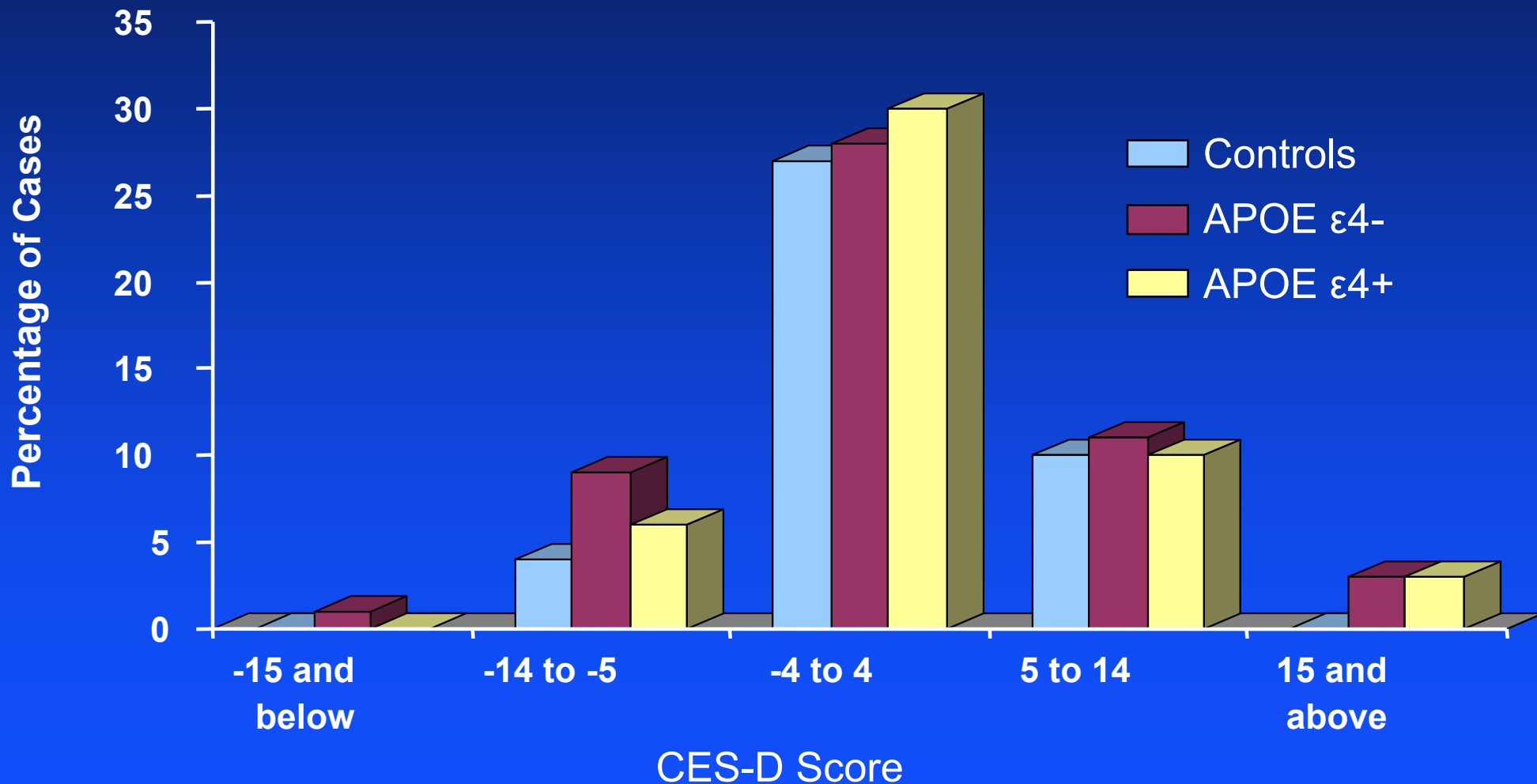
REVEAL I - Randomized Clinical Trial



REVEAL Study: Mean Anxiety Scale Score



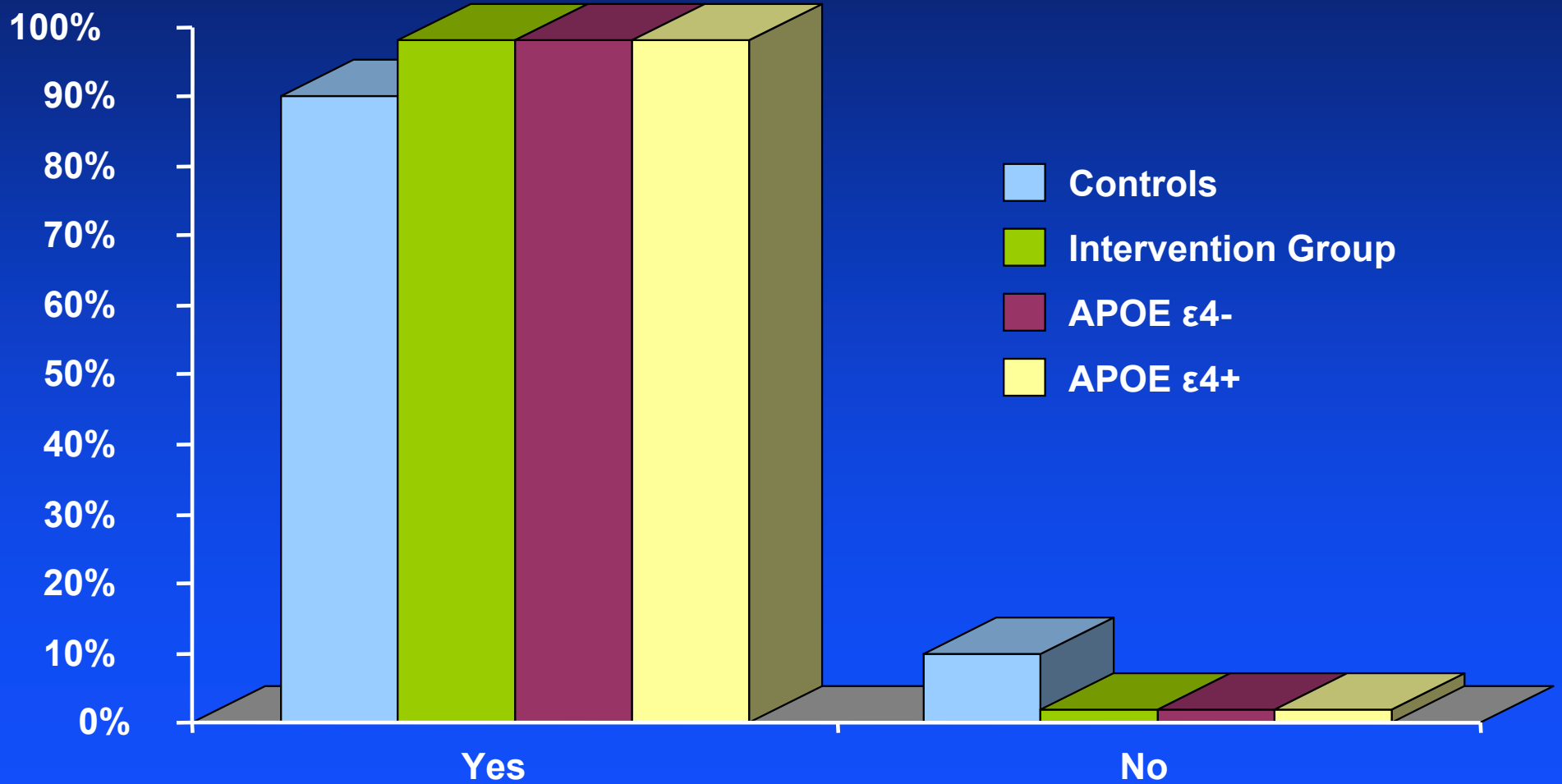
Post-Disclosure Change to Depression Symptoms: 1 year



REVEAL Questions

Are they satisfied with the information?

Would Do Risk Assessment Again...



REVEAL Questions

How should we handle ethnicity?

Risk of Dementia Among White and African American Relatives of Patients With Alzheimer Disease

Comparison of Alzheimer's disease risk factors in white and African American families

D.L. Bachman, MD; R.C. Green, MD, MPH; K.S. Benke, AB; L.A. Cupples, PhD; and L.A. Farrer, PhD; for the MIRAGE Study Group*

Incorporating ethnicity into genetic risk assessment for Alzheimer's disease: the REVEAL study experience

Kurt D. Christensen, MPH¹, J. Scott Roberts, PhD¹, Charmaine D. M. Royal, PhD², Grace-Ann Fasaye, ScM, CGC³, Thomas Obisesan, MD⁴, L. Adrienne Cupples, PhD^{5,6}, Peter J. Whitehouse, MD, PhD⁷, Melissa Barber Butson, ScM, CGC⁷, Erin Linnenbringer, MS, CGC¹, Norman R. Relkin, MD, PhD⁸, Lindsay Farrer, PhD^{5,6,9,10}, Robert Cook-Deegan, MD², and Robert C. Green, MD, MPH^{6,9}

Georgia, U.S.A.

likelihood of carrying APOE $\epsilon 4$ allele.² with AD in both among populations have been less than there is evidence disease, as well as to specific genetic genotype, may vary ethnic groups.²

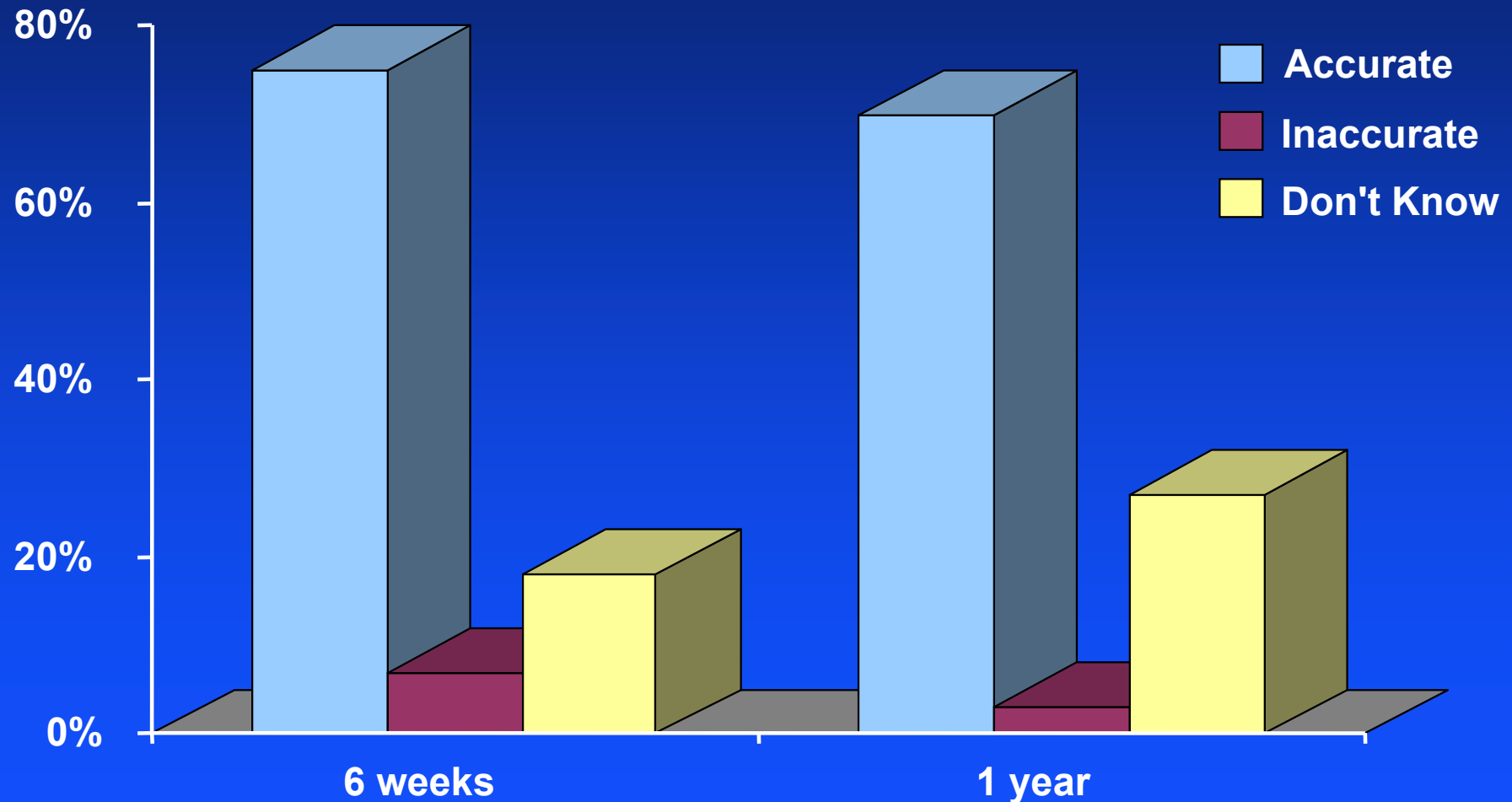
Differences Between African Americans and Whites in Their Attitudes Toward Genetic Testing for Alzheimer's Disease

YVONNE G. HIPPS,¹ J. SCOTT ROBERTS,² LINDSAY A. FARRER,³ and ROBERT C. GREEN³

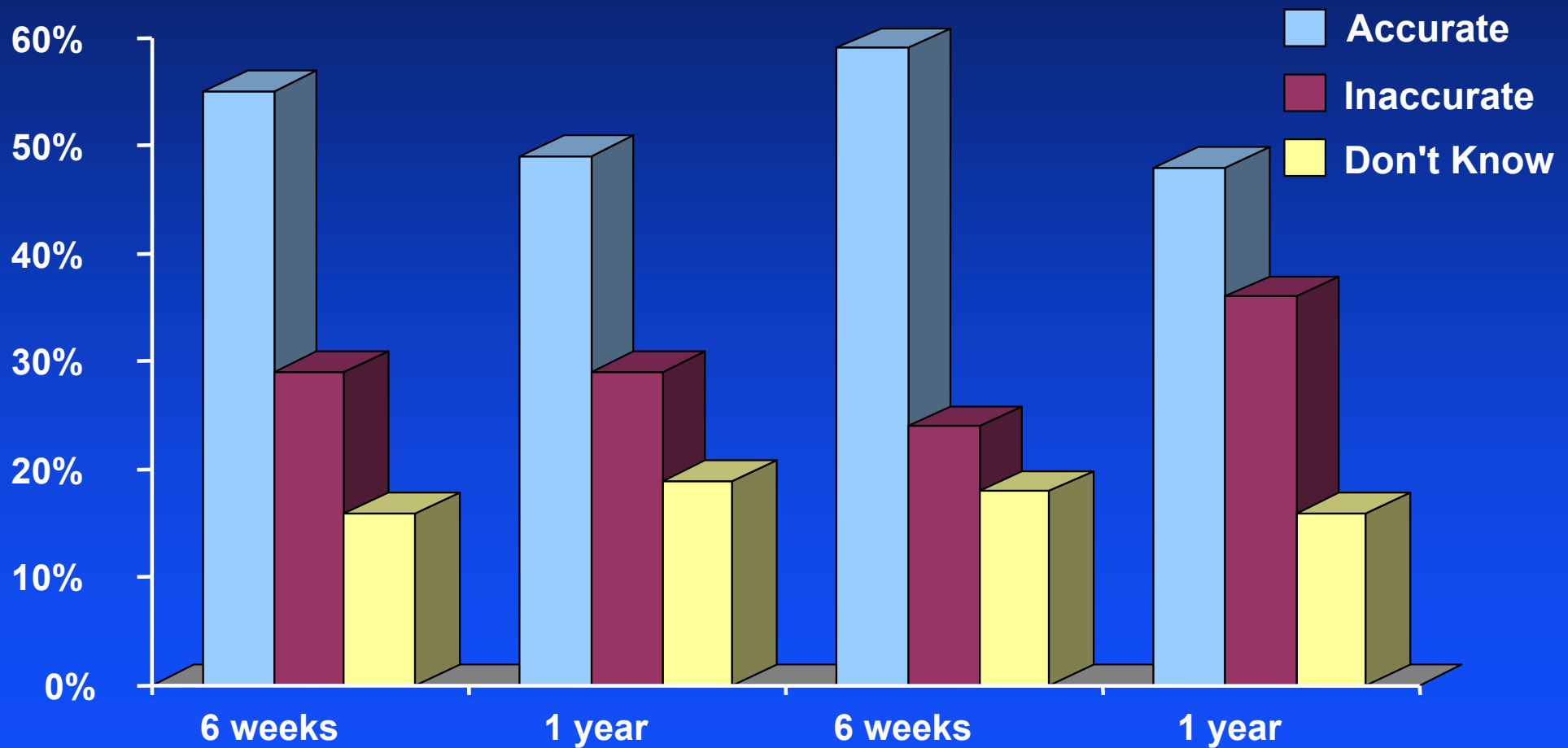
REVEAL Questions

Can they recall the information?

Recall of Disclosure Information APOE Status (positive or negative)



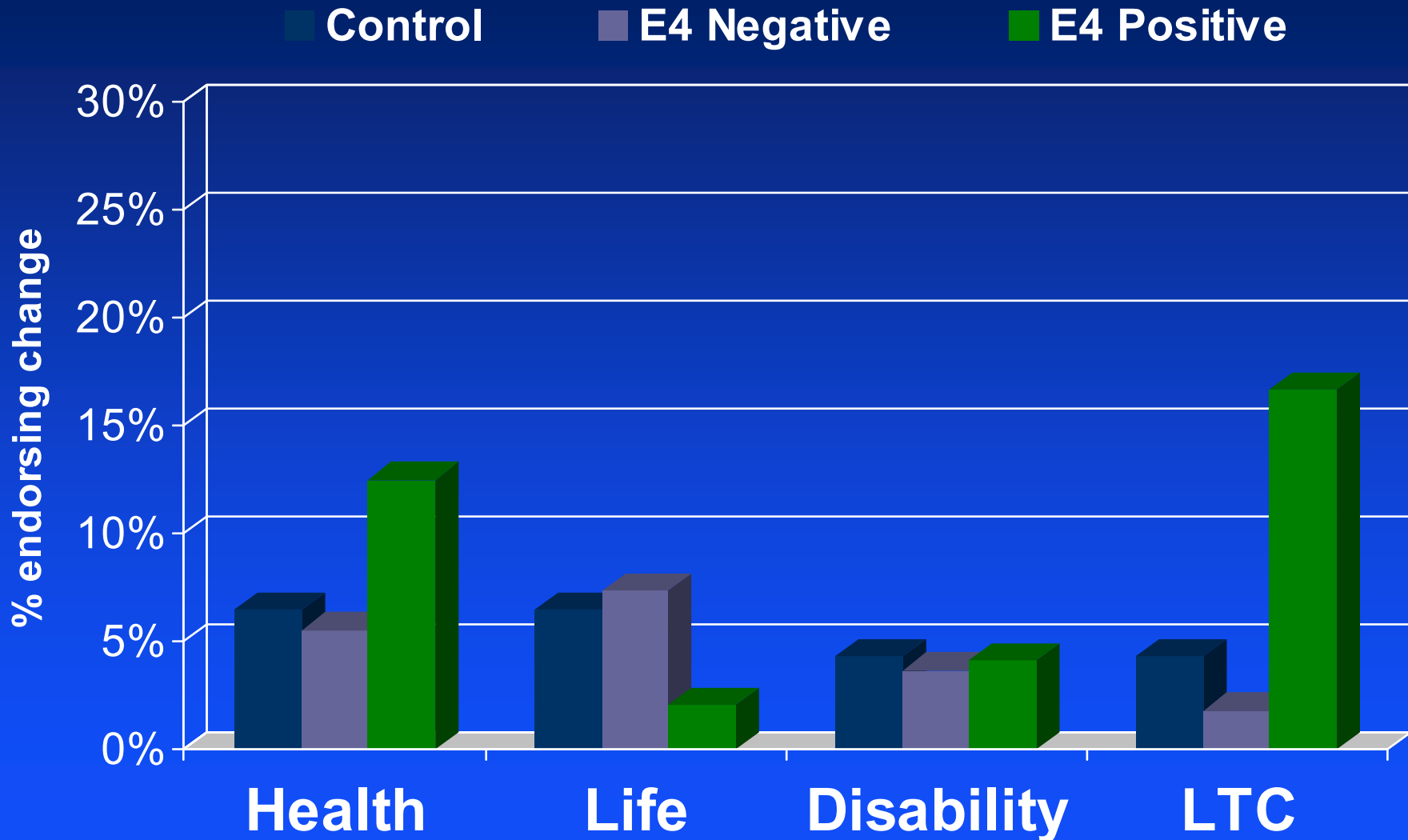
Recall of Risk Information: Lifetime Risk Figures within 5 Points



REVEAL Questions

Does the information change their behavior
(insurance purchasing)?

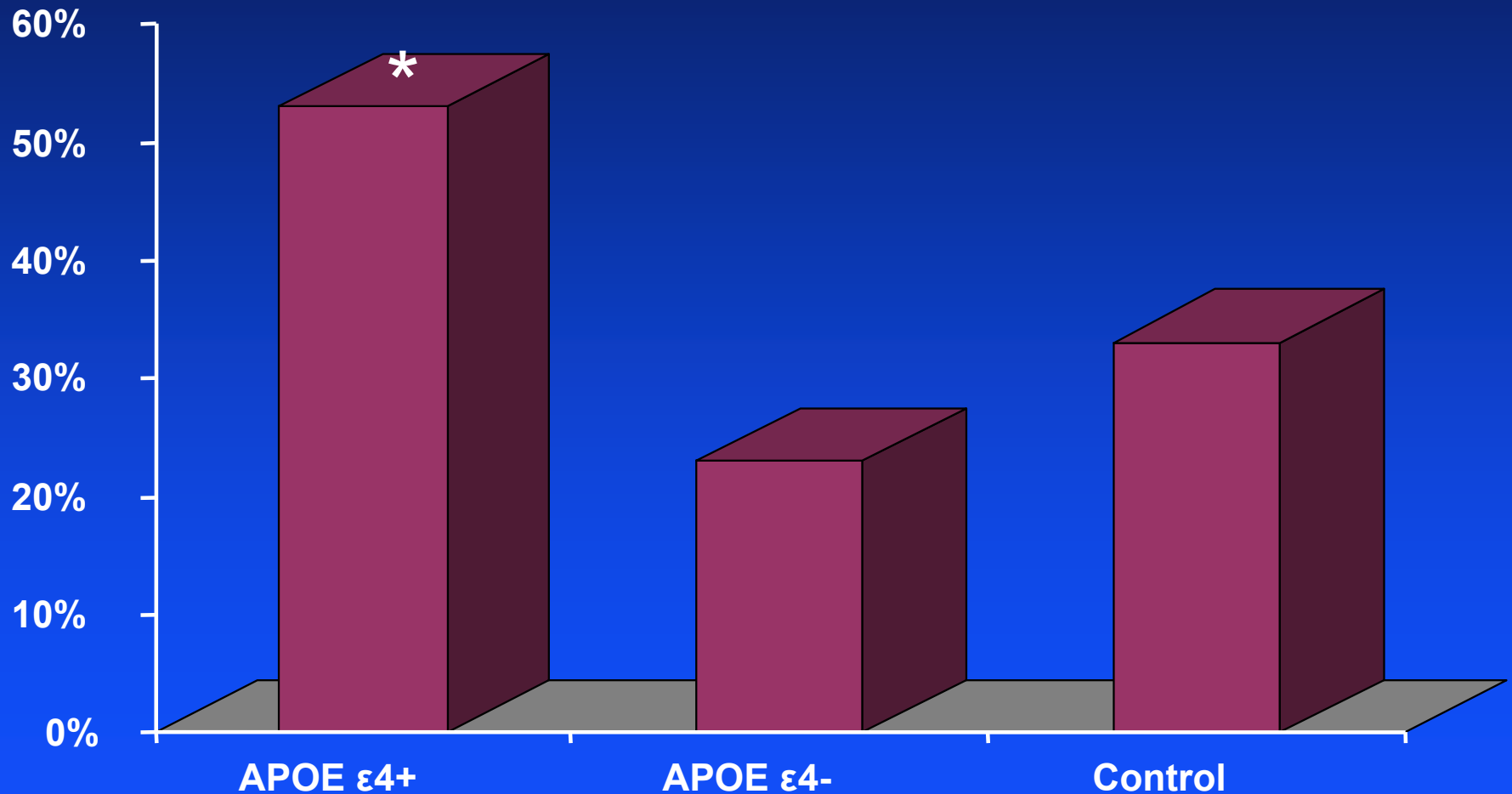
Insurance Changes 1 Year After APOE Disclosure



REVEAL Questions

Does the information change their behavior
(health behavior)?

Health Behavior Changes at 1 Year (Vitamins, Exercise, Medications)



Stay Tuned for These Analyses from REVEAL

- What will people pay for genetic risk information?
- Who will people tell about their genetic results?
- What happens to these parameters with telephone disclosure or on-line disclosure with minimal GC involvement?
- What happens when non-family members seek and receive genetic risk information
- What happens when participants receive risk information about a disease they did not expect to learn about?