Direct-to-Consumer Genetic Testing for Alzheimer's Risk

Or, what to do when ADC participants bring in their 23andMe results?

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A Brief History of DTC Testing for AD

GENETICS

Once Shunned, Test for Alzheimer's Risk Headed to Market

February 2008

Adding Alzheimer's Risk Option, 23andMe Revives Questions on Utility of DTC Genomics

April 20, 2011

April 2011

Genetic test maker 23andMe stops marketing after FDA warning

Mon Dec 2, 2013 8:35pm EST

December 2013

DAILY NEWS 10 April 2017

23andMe DNA test for Alzheimer's risk approved for sale in US

April 2017

Spit and send: saliva samples are used to assess how likely you are to develop 10 diseases

ZUMA Press, Inc. / Alamy Stock Photo

FDA-approved Genetic Risk Tests (April 2017)

- Alzheimer's disease
  - ***APOE* genotyping**
- Parkinson's disease
- Celiac disease
- Alpha-1 antitrypsin deficiency
  - **Lung, liver disease**
- Early-onset dystonia
  - **Movement disorder**
- Factor XI deficiency
  - **Blood clotting disorder**
- Type 1 Gaucher
- G6PD
  - **Red blood cell condition**
- Hereditary hemochromatosis
  - **Iron overload**
- Hereditary thrombophilia
  - **Blood clotting d/o**

Late-Onset Alzheimer's Disease

Alzheimer's disease is characterized by memory loss, cognitive decline, and personality changes. Late-onset Alzheimer's disease is the most common form of Alzheimer's disease, developing after age 65. Many factors, including genetics, can influence a person's chances of developing the condition. This test includes the most common genetic variant associated with late-onset Alzheimer's disease.

Clark, you have **two copies** of the ε4 variant we tested.

People with this result have an increased risk of developing late-onset Alzheimer's disease. Lifestyle, environment, and other factors can also affect your risk.

https://medical.23andme.org/report-archive/#genetic-health-risk

APOE Genotypes in the General Population

APOE Pair	Percentage
e2/e2	0.5
e2/e3	11
e2/e4	2
e3/e3	61
e3/e4	23
e4/e4	2

Group	Estimated lifetime AD risk
General population	10-15%
e4 heterozygotes	20-30%
e4 homozygotes	40-60%

Raber et al, 2004; Qian et al, 2017

Impact of Personal Genomics (PGen) Study

- NIH-funded longitudinal web survey of >1800 DTC genetic test consumers
  - **23andMe; Pathway Genomics**

- Outcomes at pre-test, 2 wks., 6 mos.
  - **Understanding / decision making**
  - **Motivations / expectations**
  - **Perceived utility**
  - **Behavioral responses**

What disease risks are of interest?
(Roberts et al, *PHG*, 2017)

Disease	Proportion "very interested"
Heart disease	68%
Breast cancer (women only)	67%
Alzheimer's disease	66%
Prostate cancer (men only)	60%
Skin cancer	59%
Diabetes	55%
Colon cancer	53%

Issues to Consider

- Risk communication
- Psychosocial impact
- Behavioral recommendations

Overview of REVEAL Trials

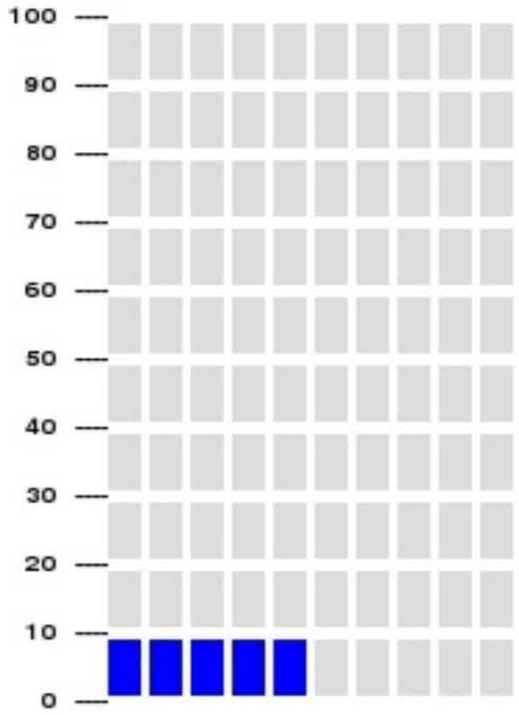
- Series of multi-site randomized clinical trials
  - BU, Brigham & Women's, Duke, Michigan, Penn
- GC-delivered education/counseling protocols
- N = 699 1st-degree relatives of AD patients
- Longitudinal (up to 12 months) psychological, health behavior assessment

Risk Communication

- Address genetic determinism
  - **Fatalism (E4 neither necessary nor sufficient)**
  - **False reassurance in E4-negatives**
- Note implications for family members
  - **Children of E4 homozygotes are ‘obligate carriers’ but may not wish to know**
- If discussing quantitative risks, consider use of visual aids

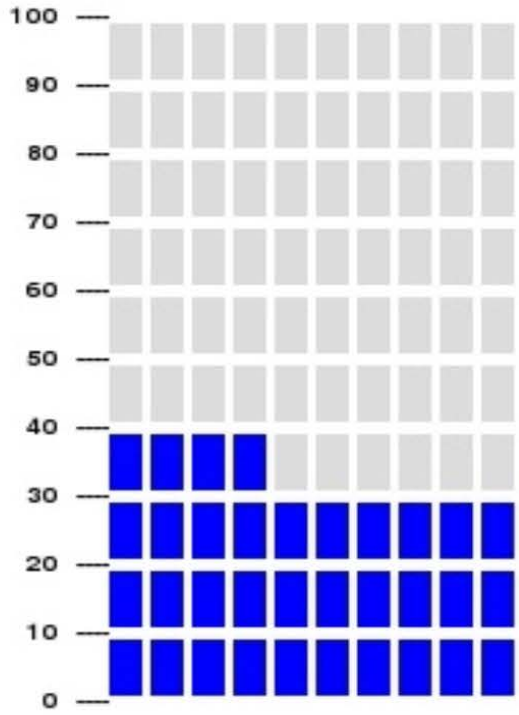
Risk of progressing to dementia of the Alzheimer's type

General Population



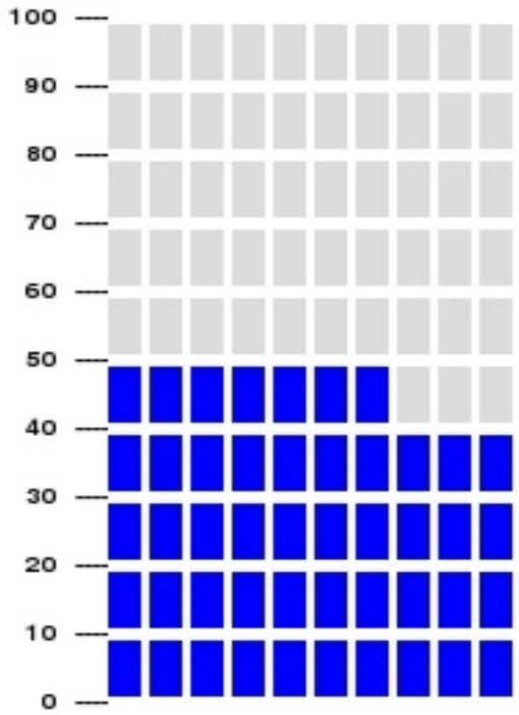
5% risk of progressing to dementia of the AD type in **3 years**

MCI



34% risk of progressing to dementia of the AD type in **3 years**

MCI and *APOE* ! 4 Present



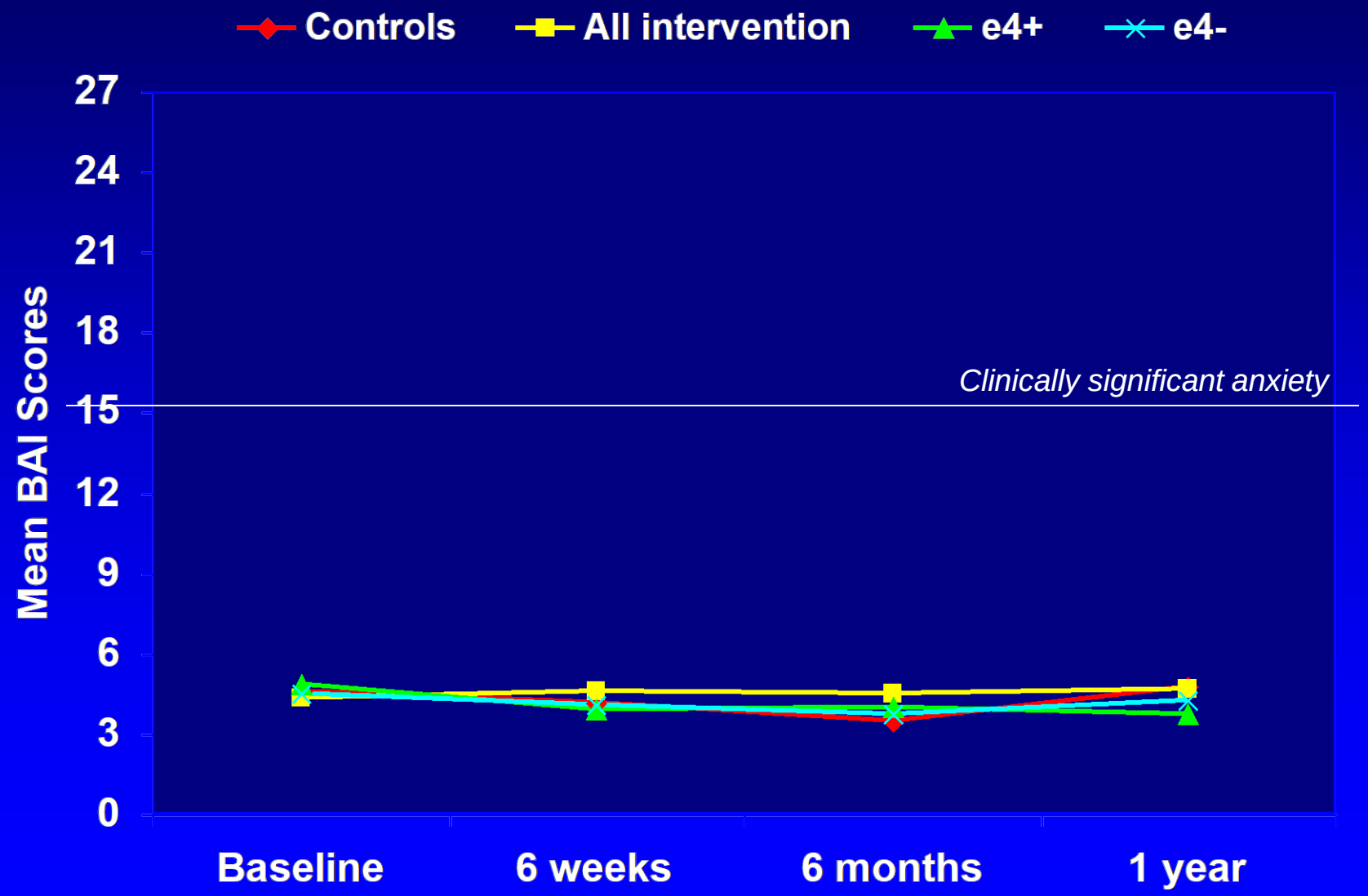
47% risk of progressing to dementia of the AD type in **3 years**

Psychological Responses to *APOE* Testing

- Clinically concerning, enduring distress responses in REVEAL were rare
  - **Relief, empowerment more common (even among e4 carriers)**

- Important caveats
  - **Volunteers seeking out this info**
  - **Pre & post-test genetic education / counseling**
  - **Highly vulnerable screened out**

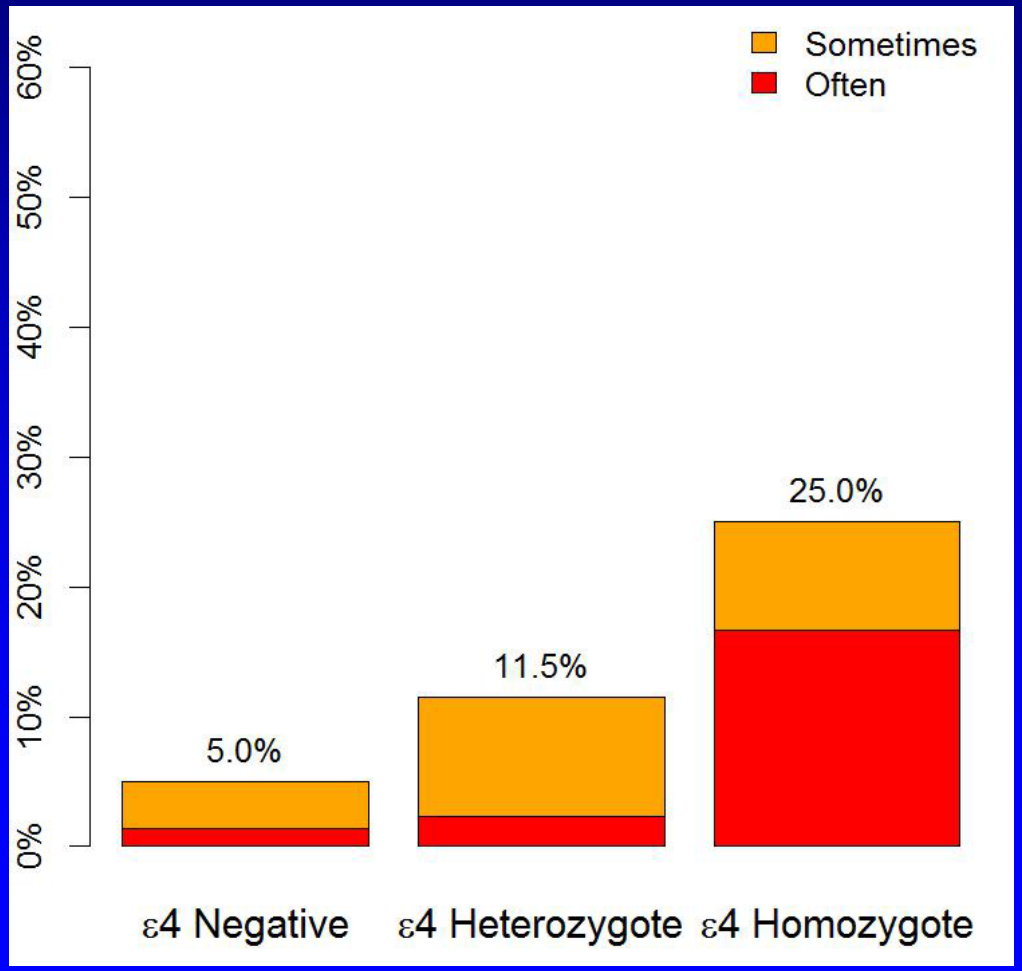
APOE Disclosure: Impact on Clinical Anxiety



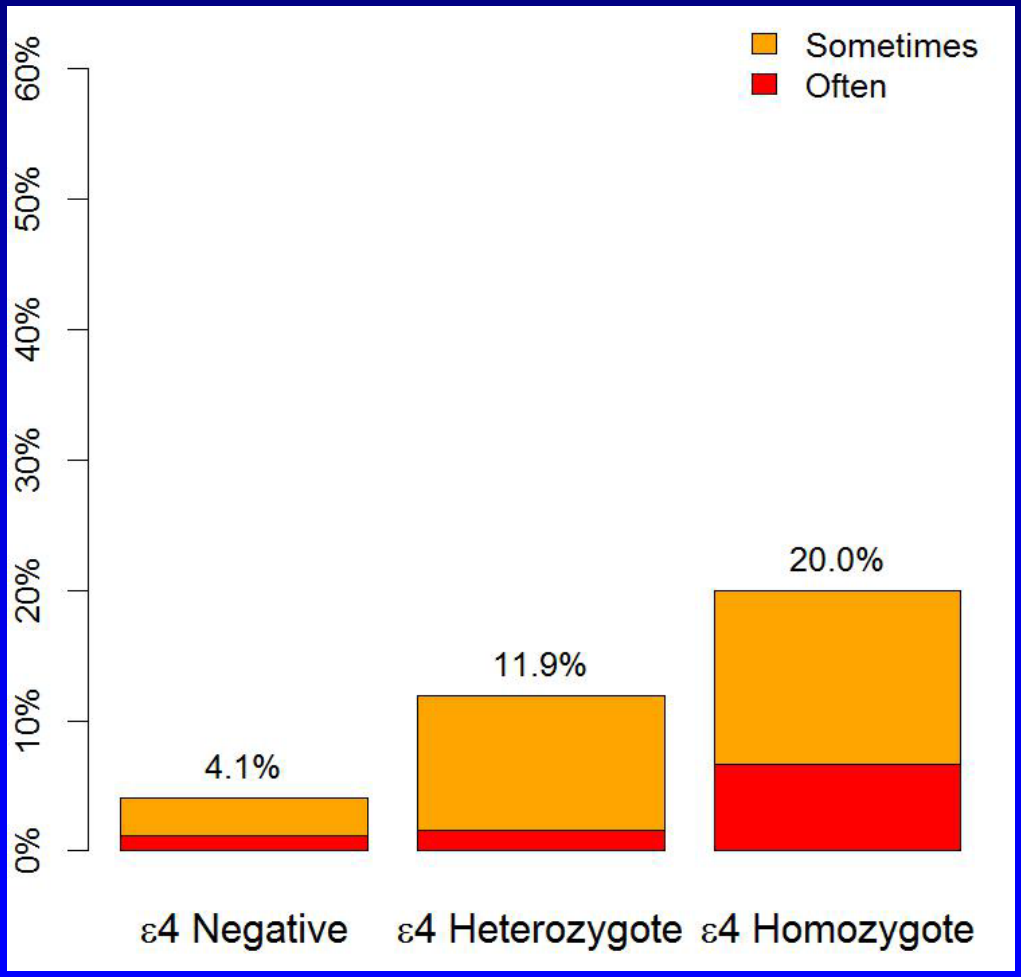
Green, Roberts et al, *NEJM*, 2009

% of DTC-GT Consumers Upset by Any Test Results

2-3 Weeks

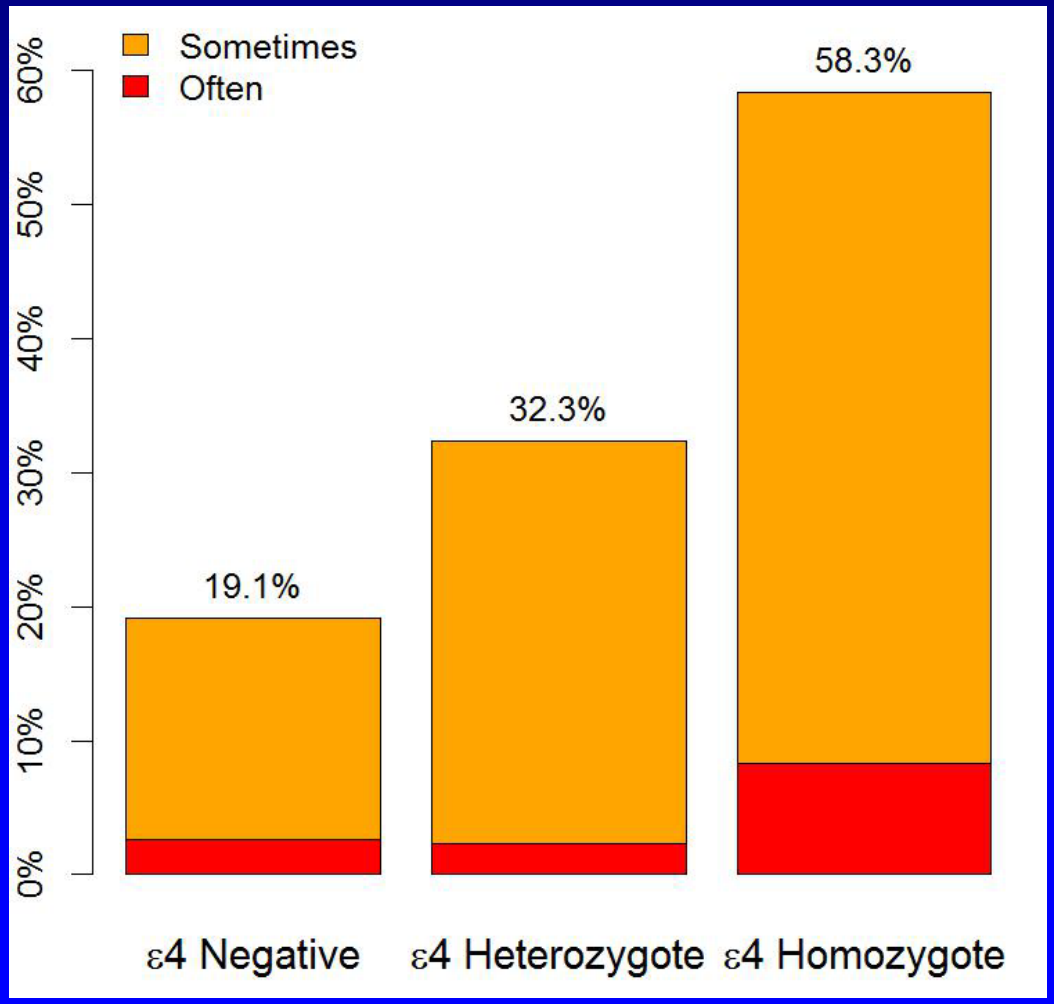


6 Months

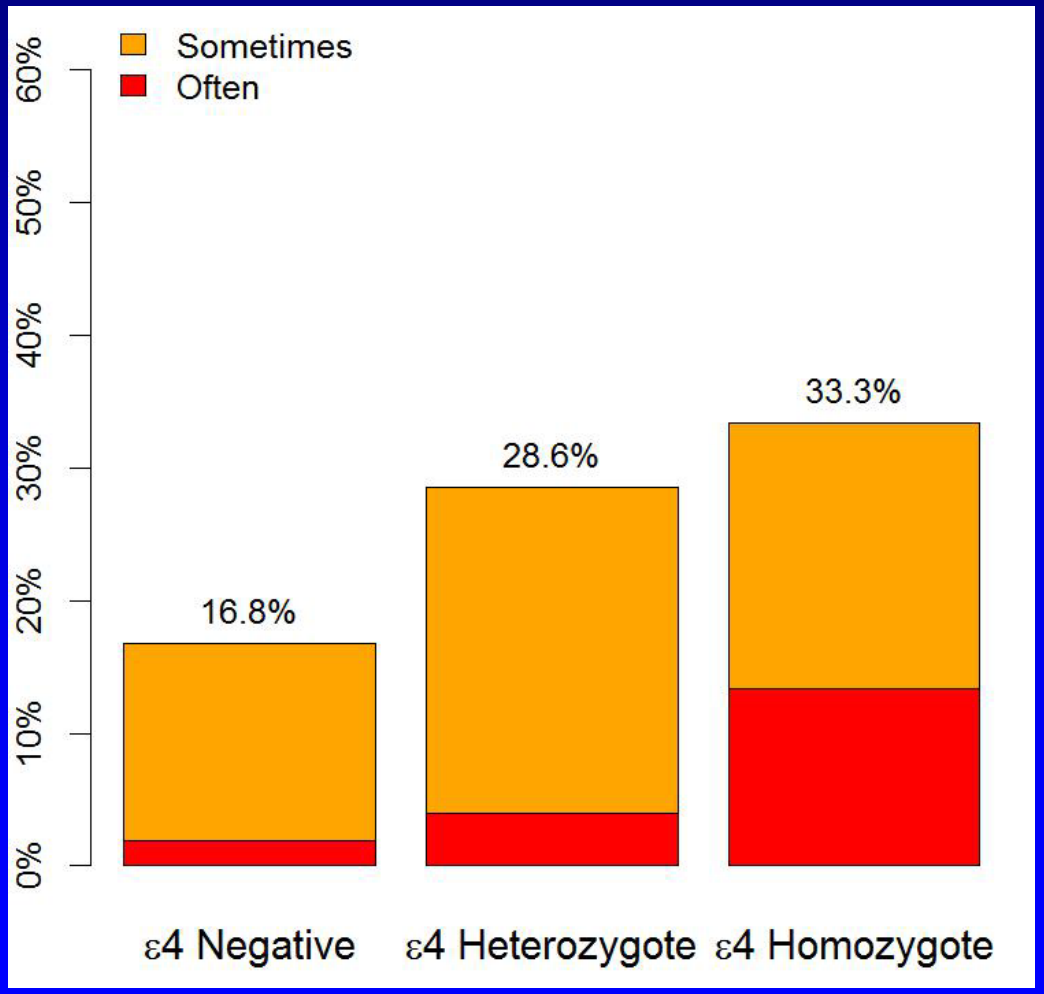


% of DTC-GT Consumers Worried about Risk of Disease

2-3 Weeks



6 Months



Behavioral Recommendations

- Brain health
- Advance planning
- Research participation

Alzheimer's Association Brain Health Campaign

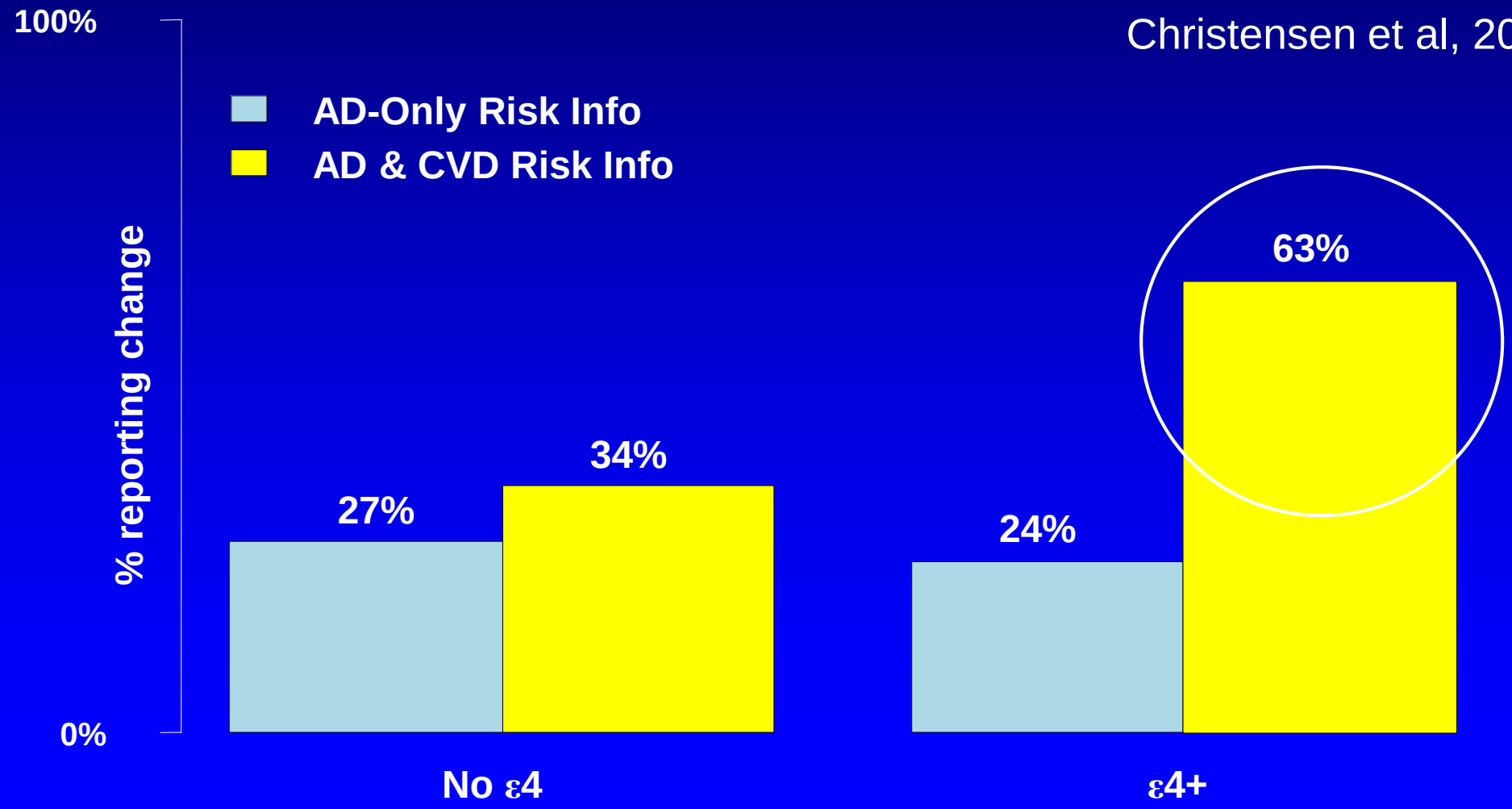
10 Ways to Love Your Brain

Growing evidence indicates that people can reduce their risk of cognitive decline by adopting key lifestyle habits. When possible, combine these habits to achieve maximum benefit for the brain and body. **Start now.** It's never too late or too early to incorporate healthy habits.

http://www.alz.org/brain-health/10_ways-to-love-your-brain.asp

Self-Reported Exercise Changes in REVEAL 3

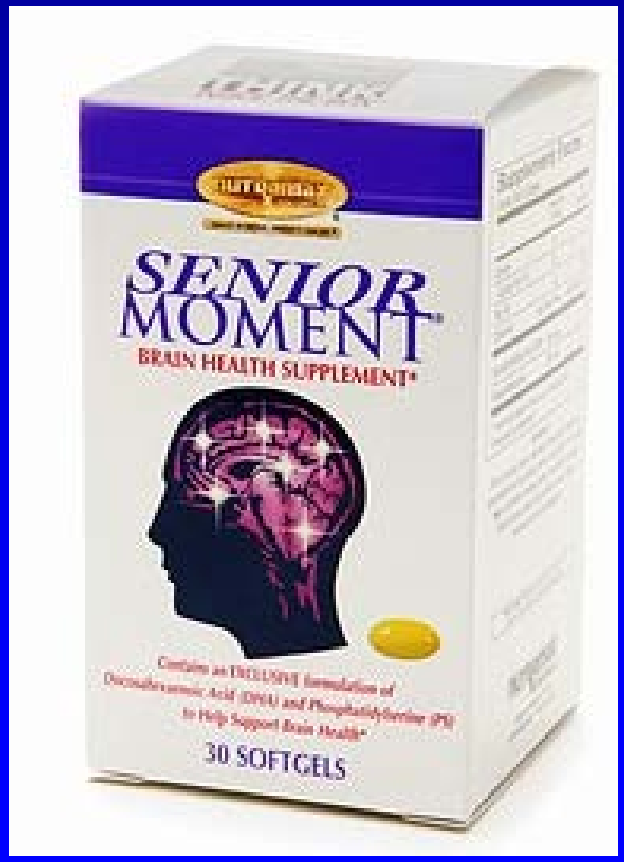
Christensen et al, 2016



Supplement Use in REVEAL 2

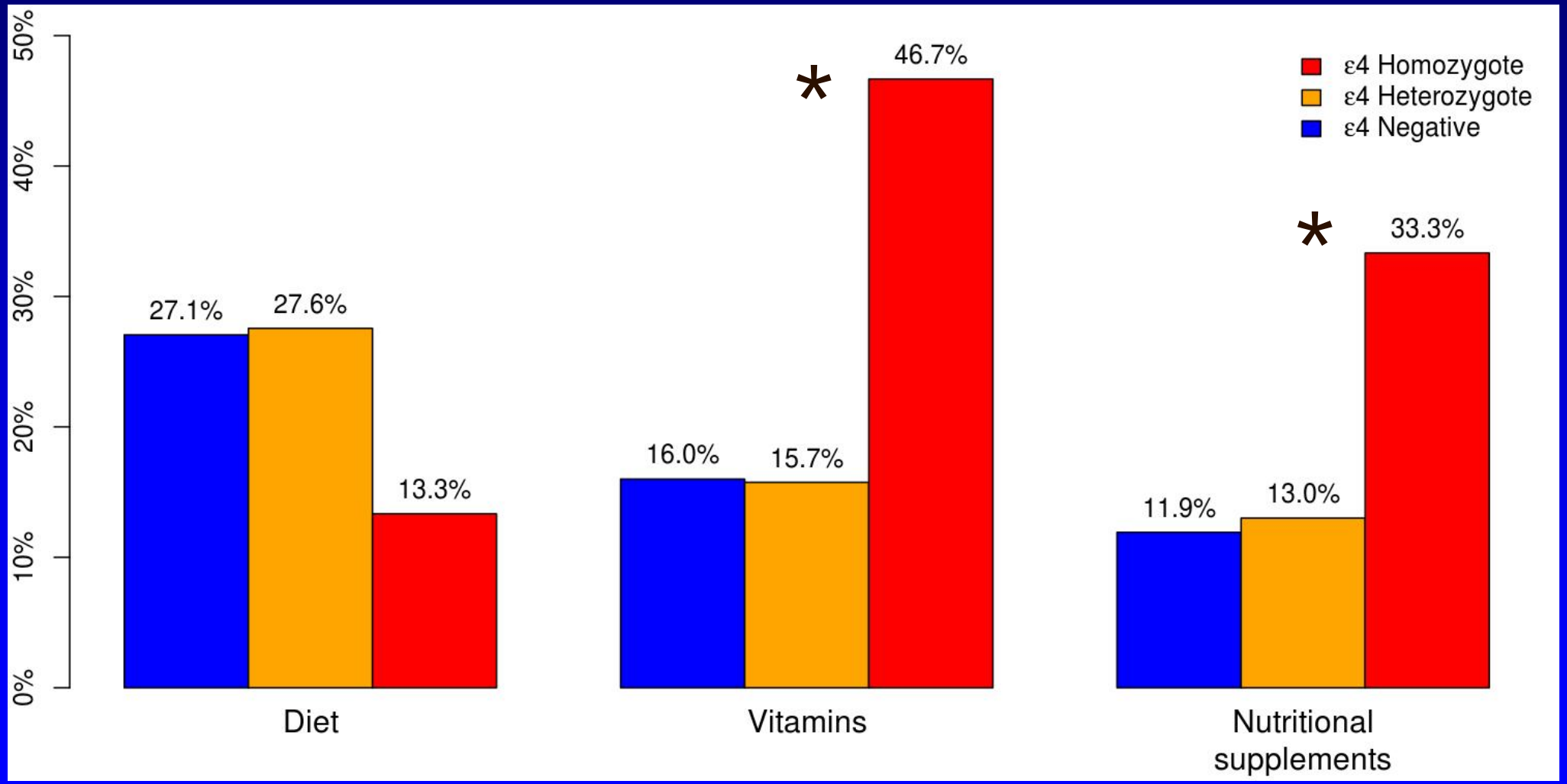
E4+ participants 4.6X more likely to report use than E4-

FOCUSfactor

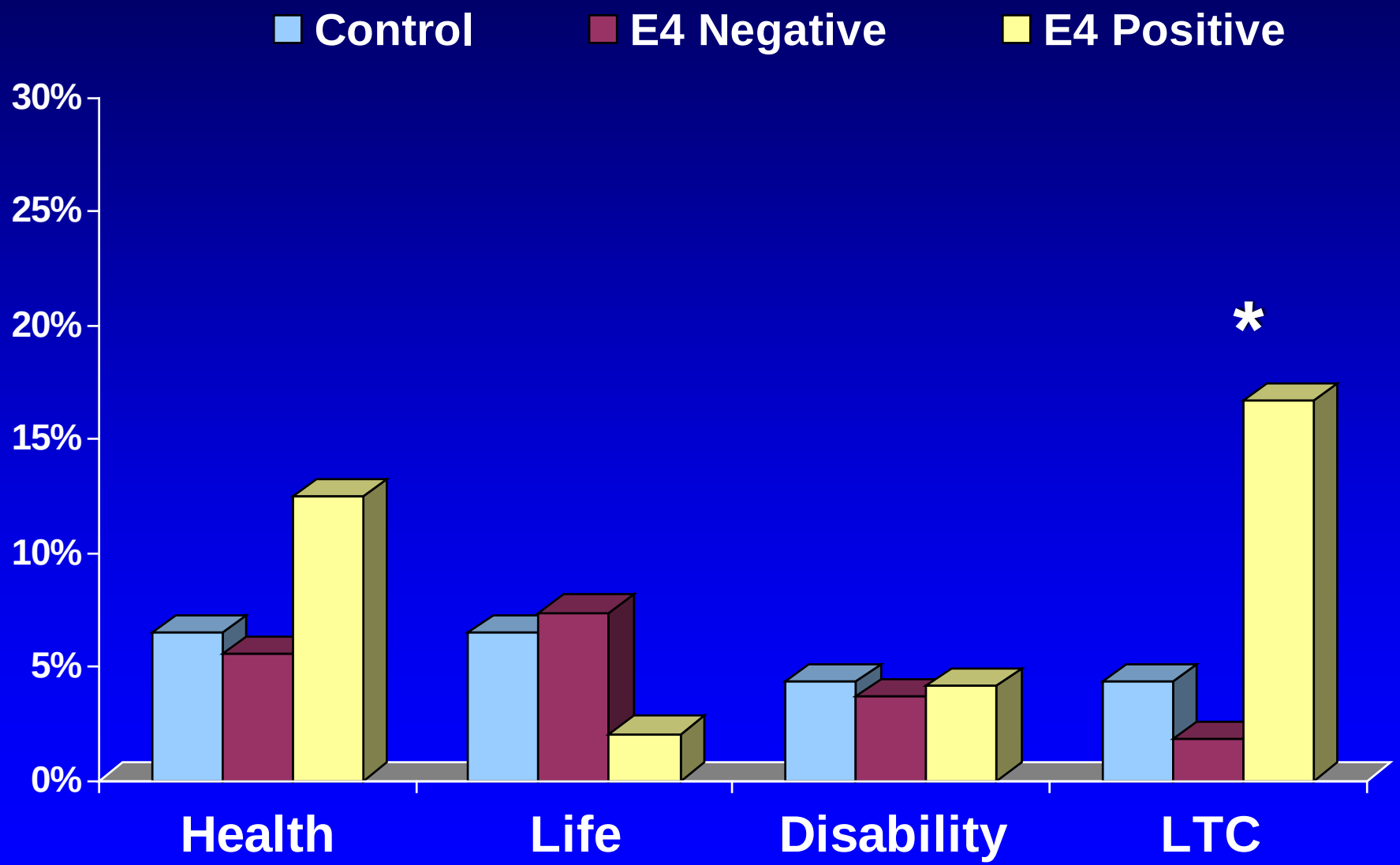


Vernarelli et al, 2010

Self-Reported Health Behavior Changes Among DTC-GT Consumers



Insurance Changes Reported at 12 Mo F/U in REVEAL



Zick, Mathews, Roberts et al., *Health Affairs*, 2005

Genetic Information Nondiscrimination Act (GINA)

- Federal law enacted in 2008
- Prohibits genetic info use by health insurers, employers
  - **Hiring, firing, coverage decisions; setting premiums**
- Does not apply to LTC, disability, life insurance

President George W. Bush signs H.R. 493, the Genetic Information Nondiscrimination Act of 2008, Wednesday, May 21, 2008, in the Oval Office. White House photo by Eric Draper.

Can you help advance Alzheimer's research?

See if you may qualify for the Generation Study.

Get Started

Right now, the Generation Study is looking for people **ages 60 to 75 who have normal memory and thinking ability** but may have a higher risk of developing the disease based on their genetic background.

Our study is investigating medications that could advance doctors' understanding of how to potentially prevent the onset of Alzheimer's disease. By joining this study, you could help impact the future

If you're interested in learning more, **click here to take our simple, no-commitment questionnaire** to see if you may be eligible.

Website: Generationstudy.com

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