Workshop: Our Memory – Alzheimer's Disease & Dementia

Update on Alzheimer's/dementia research and how to reduce one's risk for the disease, the latest on prevention, and why Alzheimer's and dementia are women's health issues

Margaret Gatz, Ph.D.
University of Southern California

Mind, Body, Spirit, Age: Integrating Behavioral and Physical Health
The California Endowment, April 6, 2015

Is it dementia or is it Alzheimer's disease?

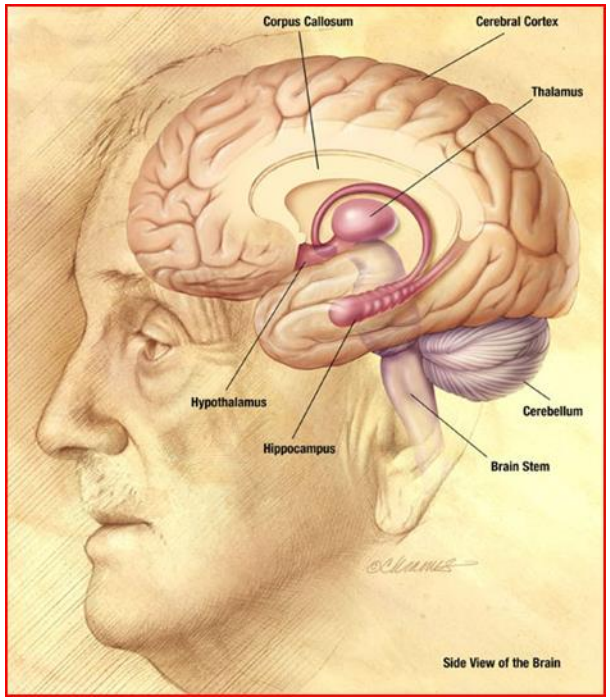
Dementia is a term used to describe a variety of disorders that share these characteristics:

- acquired problem
- generally progressive
- impairment in any of these:
  - memory
  - language
  - visual processing and orientation
  - mood, personality, social skills
  - planning, problem solving

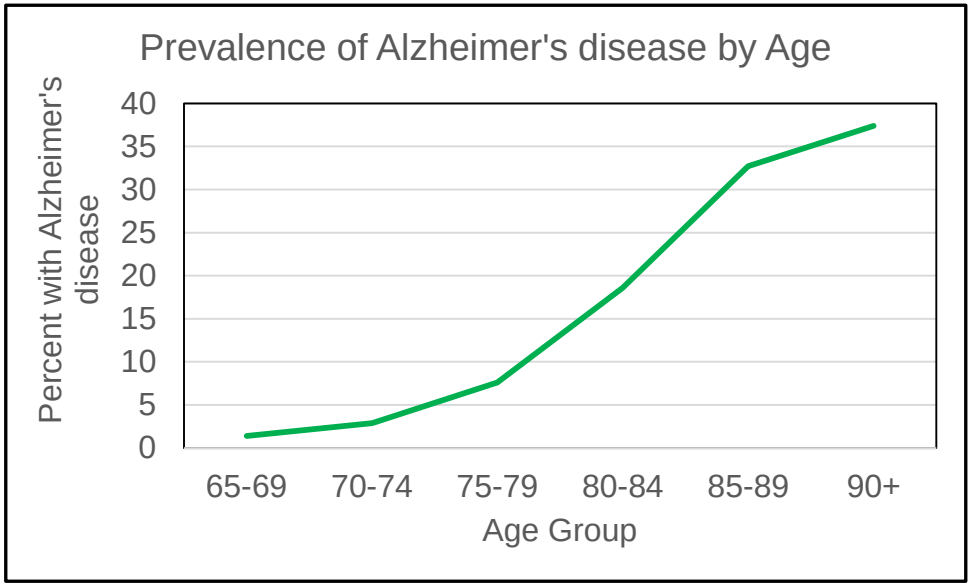
Is it Alzheimer's disease or is it normal aging?

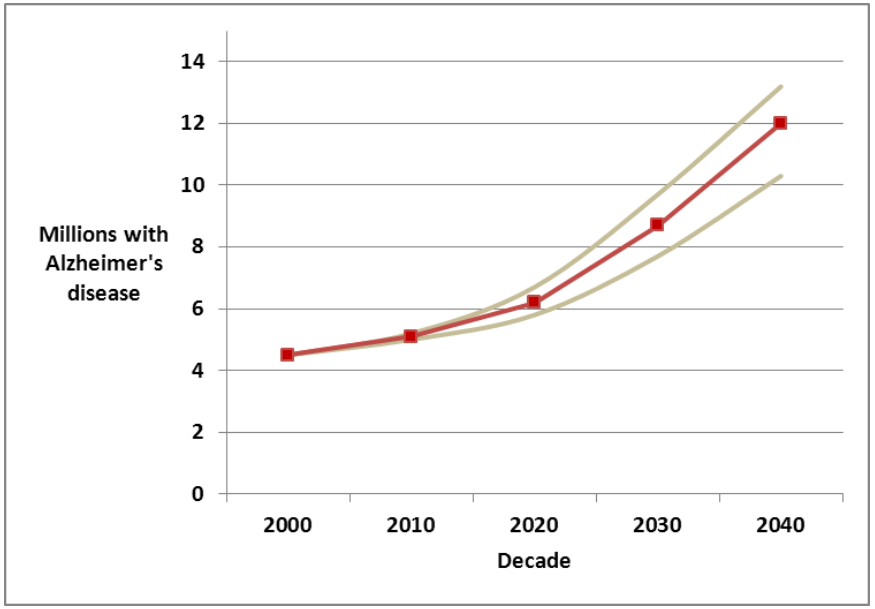
With age it is normal to:

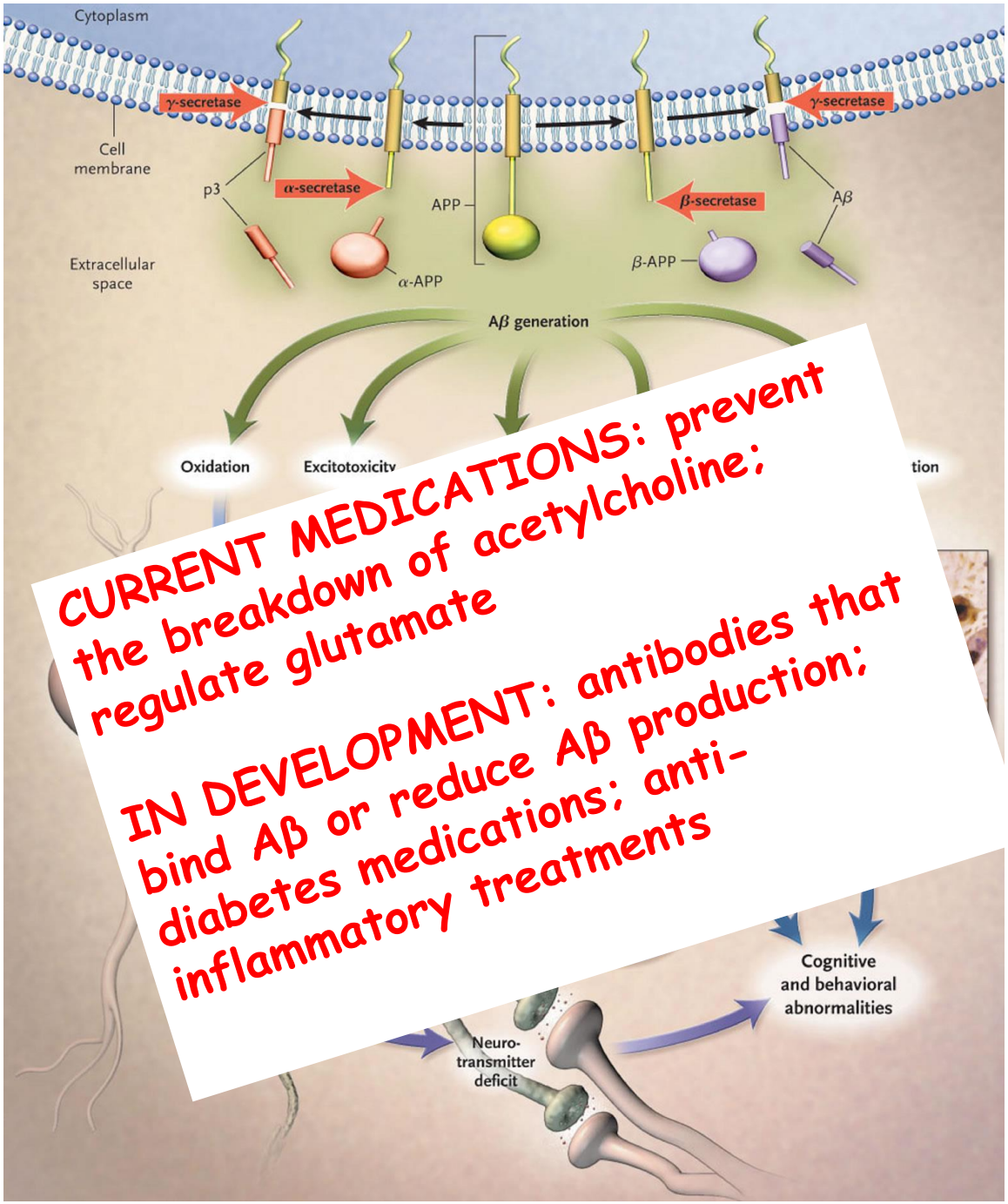
- Experience some memory failures and have to rely on "external memory aids"
- Be less able to attend to several things at once
- Process information more slowly



Rate of dementia increases with age

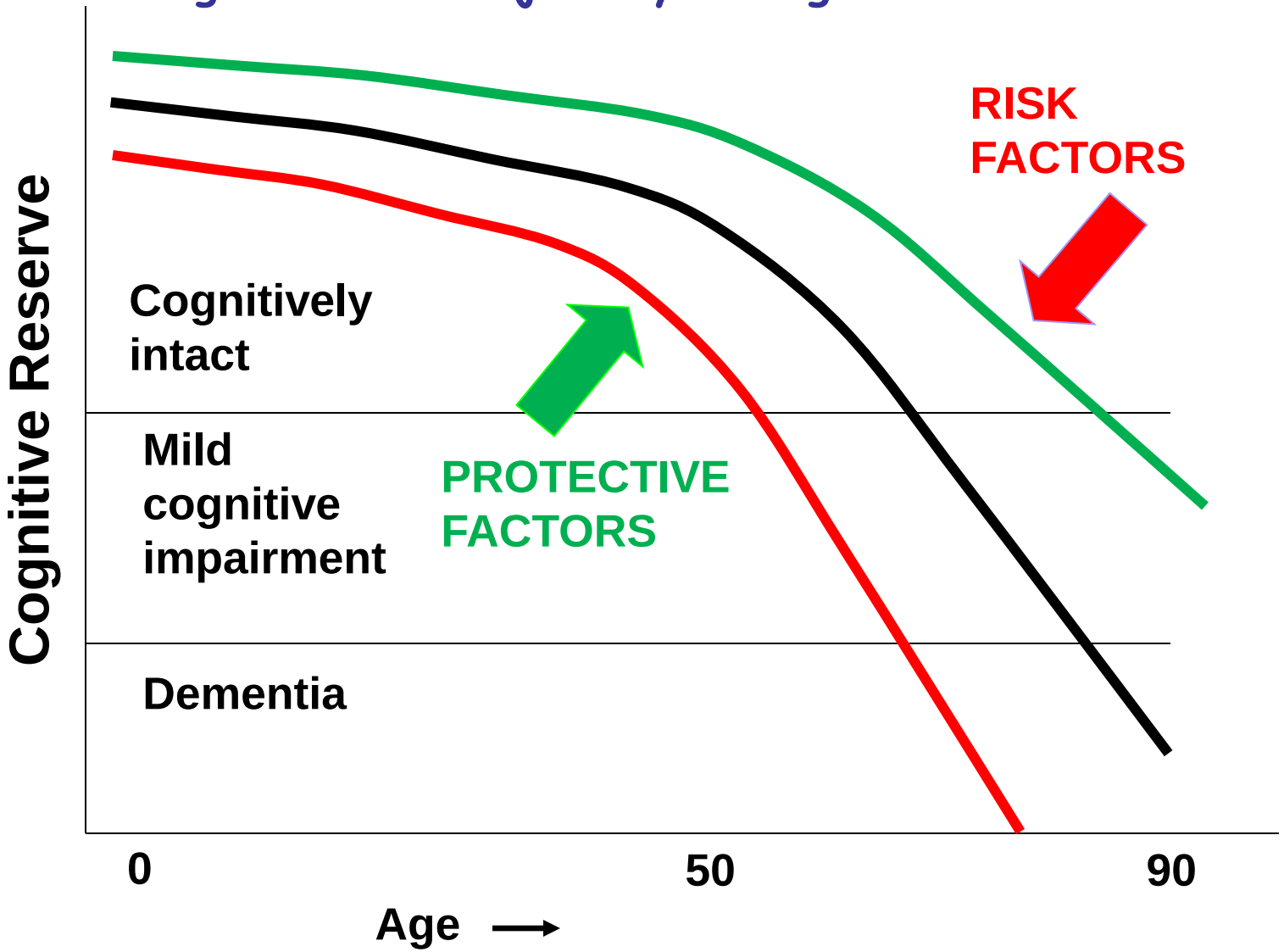






- Inflammation
- Hyperinsulinemia
- Microvascular disease
- Oxidative stress
- Deposition of beta-amyloid (Aβ)
- First noticed in the entorhinal cortex, then the hippocampus
- Neuritic plaques
- Neurofibrillary tangles
- Acetylcholine deficits
- Neuron loss

Influence of non-genetic risk and protective factors on age-related trajectory of cognition



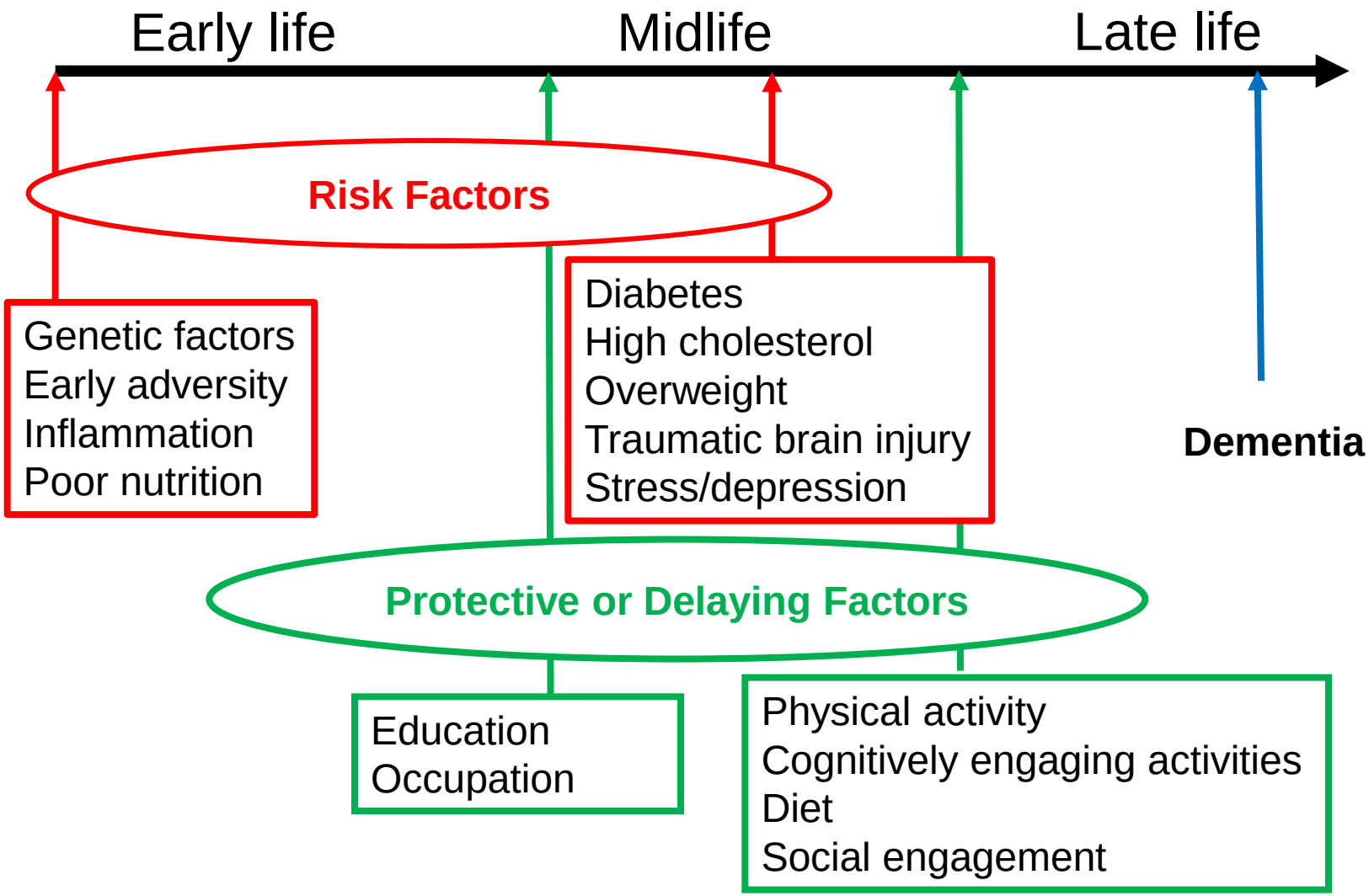
Types of studies that provide evidence about risk and protective factors for dementia

- Longitudinal studies that correlate cognitive performance in old age with lifestyle factors measured earlier
- Epidemiological studies comparing dementia patients to normal controls
- Twin studies
- Randomized clinical trials testing whether cognition is improved (or rate of decline reduced) in those receiving a specific agent

Types of outcomes indicating a protective effect for a lifestyle factor

- Whether likelihood of developing Alzheimer disease (or any dementia) differs for those with and without the factor
- Whether or the rate of cognitive decline over time diverges for those with and without the factor
- Whether biomarkers associated with Alzheimer's disease and other dementias change in association with the factor
    - Hippocampal atrophy
    - Neuritic plaques
    - Brain derived neurotropic factor (BDNF)

Dementia Risk and Protective Factors over the Lifespan



Genes and dementia

Definite linkages (e.g., APP, PS1)

- autosomal dominant
- explain < 5% of Alzheimer disease

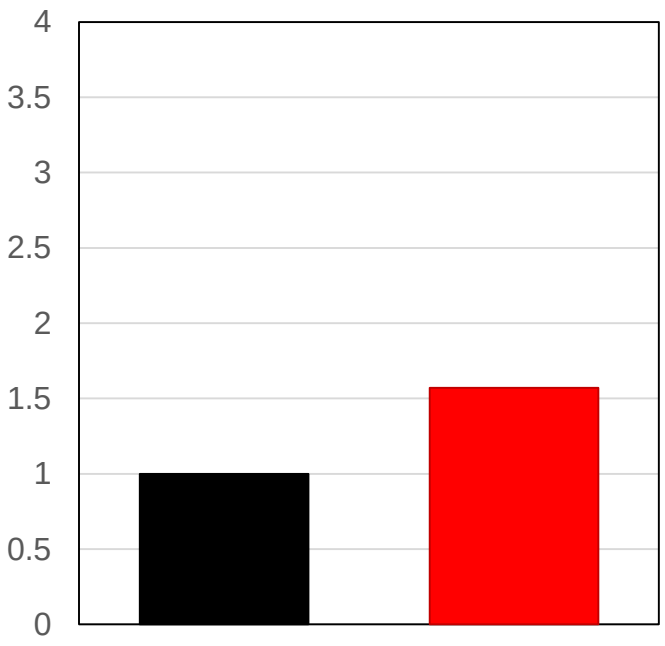
Susceptibility genes (e.g., APOE)

- associated with increased risk but are not sufficient for disease
- The ε4 allele is related to elevated risk of Alzheimer disease
- However, even having two copies of ε4 does not mean that AD is inevitable

Early Life Adversity and Alzheimer's disease

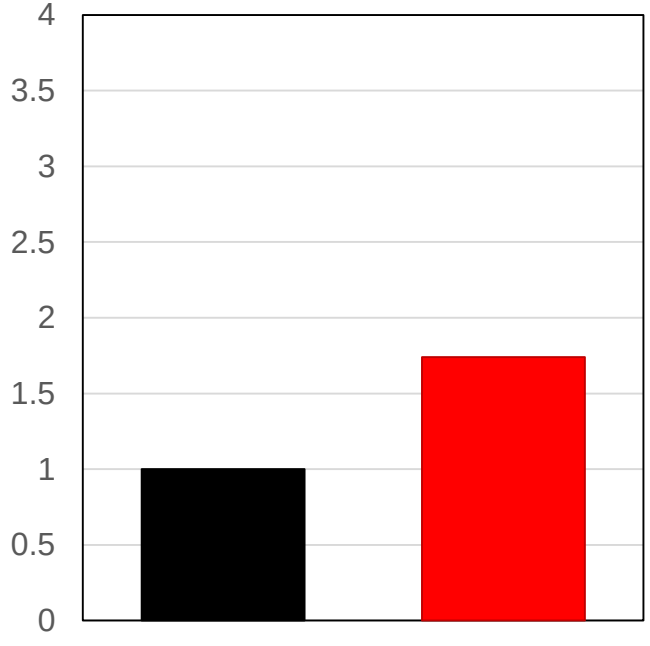
For every one person with normal adult height who develops AD….

On average, one and a half times as many people with short adult stature develop AD



For every one person with normal oral health who develops AD….

On average, 1.75 times as many people with early tooth loss/ periodontal disease develop AD.

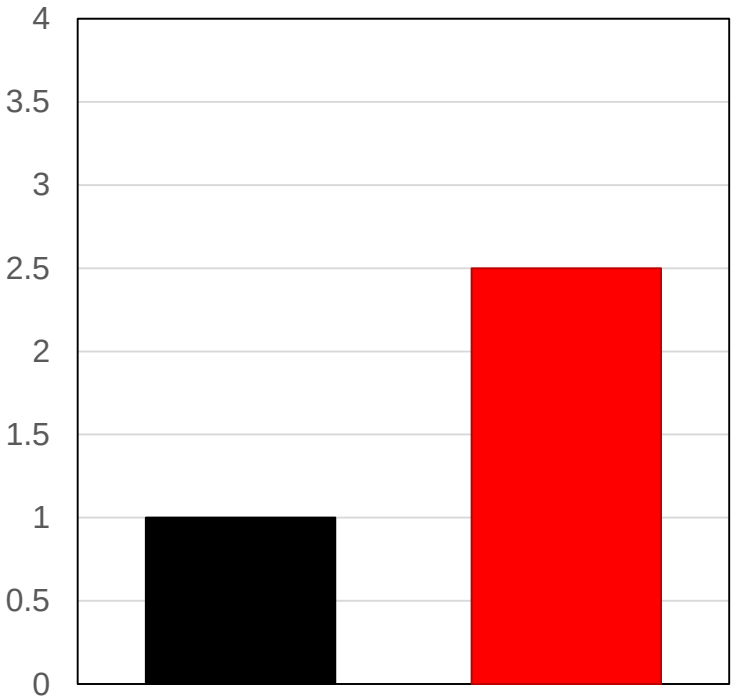


SOURCES: HARMONY: Gatz et al. 2006 University of Washington/GHC AD Patient Registry (ADPR): Moceri et al., 2001; VA Dental Longitudinal Study: Kaye et al. 2010

Diabetes mellitus and Dementia

For every one person without diabetes who develops AD or dementia….

On average, two and a half times as many people with diabetes in midlife develop AD or dementia.

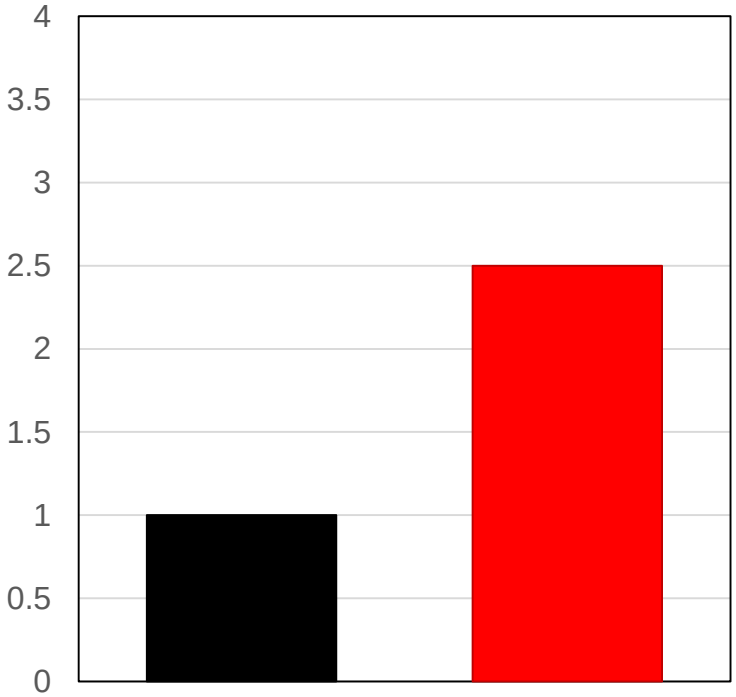


SOURCES: WHICAP (Washington Heights/Hamilton Heights Aging Project): Luchsinger et al 2005;
HAAS (Honolulu Asian Aging Study): Akomolafe et al 2006;Korf et al 2006;
HARMONY: Xu et al 2009

Lipids and Dementia

For every one person with normal range LDL cholesterol in midlife who develops AD or dementia….

On average, two and a half times as many people with elevated LDL cholesterol in midlife develop AD or dementia.

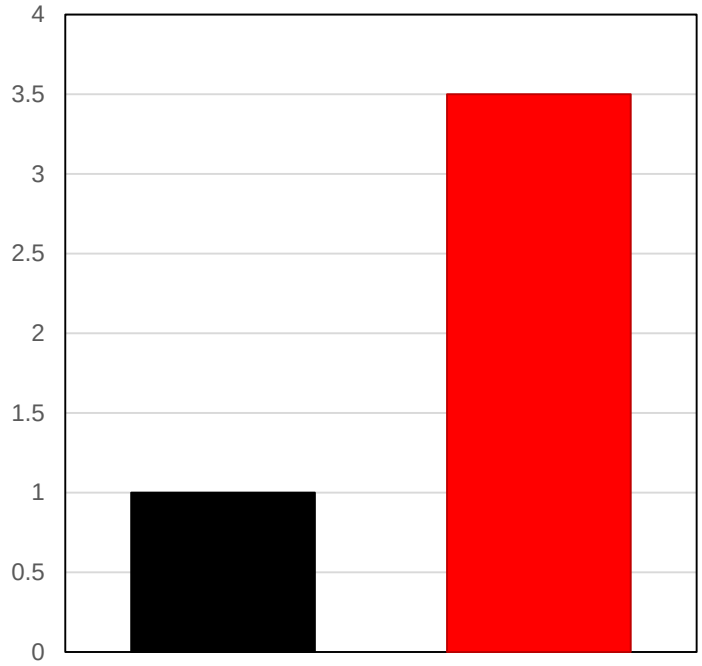


SOURCES: Swedish twin studies: Reynolds et al 2010; FINMONICA: Kivipelto et al 2002

Blood Pressure and Dementia

For every one person with normal midlife blood pressure who develops AD or dementia….

On average, three and a half times as many people with midlife untreated hypertension develop AD or dementia.

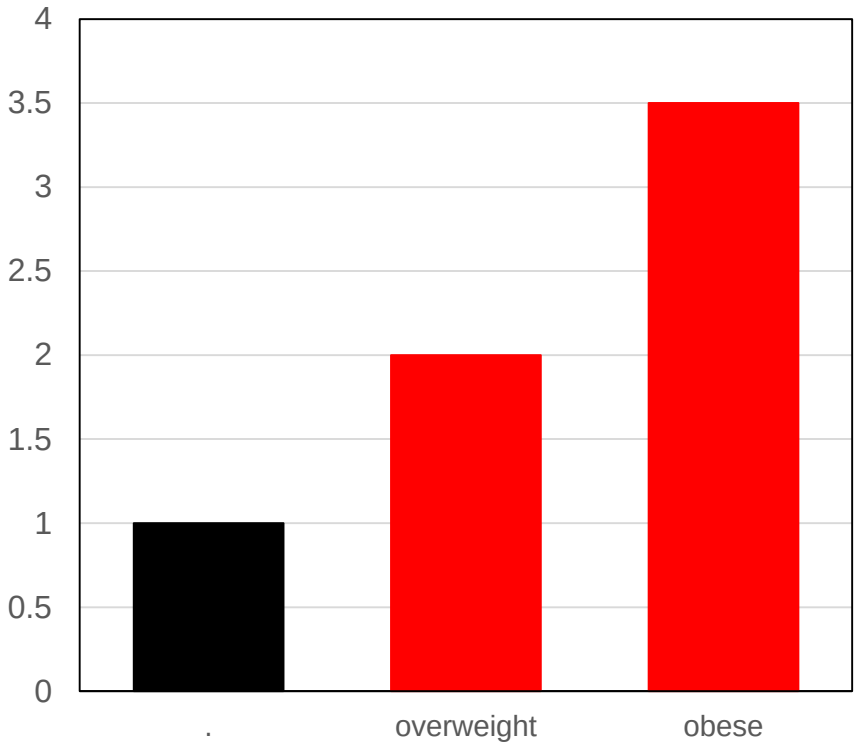


SOURCES: HAAS (Honolulu Asian Aging Study): : Korf et al 2004; Launer et al 2000; FINMONICA (North Karelia Project and the Finnish part of the Multinational Monitoring of Trends and Determinants in Cardiovascular Disease): Kivipelto et al 2002

Midlife Overweight and Obesity and Dementia

For every one person with normal range weight in midlife who develops AD or dementia….

On average, two times as many overweight and three and a half times as many obese people develop AD or dementia.

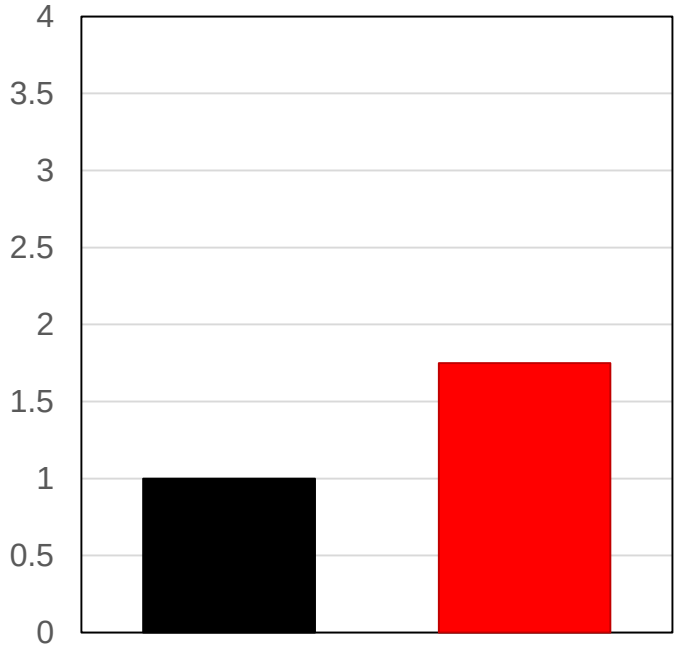


SOURCES: KP (Kaiser Permanente of Northern California): Witmer et al 2000; Swedish twin studies: Xu et al 2011; Dahl et al 2010

Anxiety/Stress Proneness/Neuroticism and Dementia

For every one person with normal range midlife stress or anxiety who develops AD or dementia….

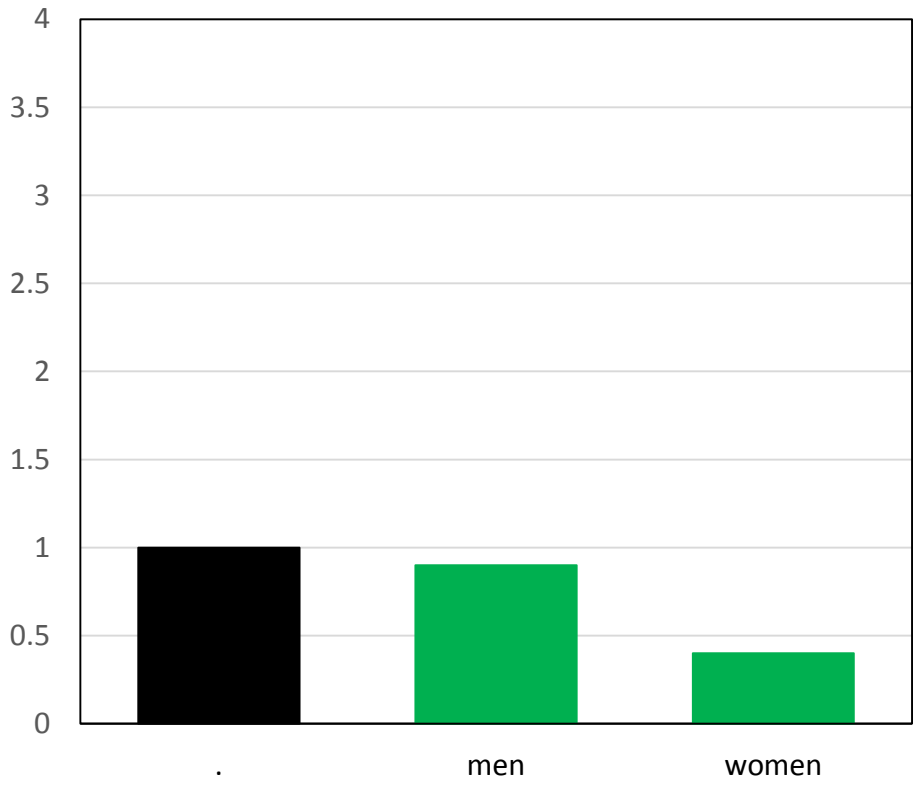
On average, 75% more people with high midlife stress or elevated anxiety develop AD or dementia.



SOURCES: Rush Memory and Aging Project: Wilson et al, 2011; Prospective Population Study of Women in Gothernberg: Johansson et al., 2014; HARMONY: Andel et al., 2012; Crowe et al., 2007;

Leisure Activities and Alzheimer's disease

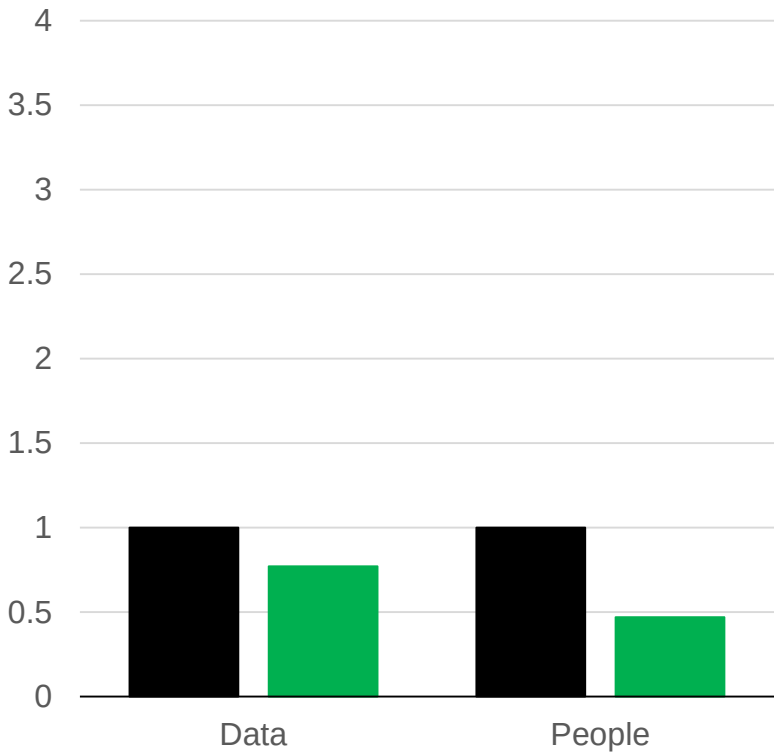
Risk of Alzheimer's disease is, on average nearly halved for those who engaged in more intellectual or cultural leisure activities in mid-life. Risk is lowered more in women than in men



SOURCE: Swedish twin studies: Crowe et al. 2008

Occupational complexity and Dementia

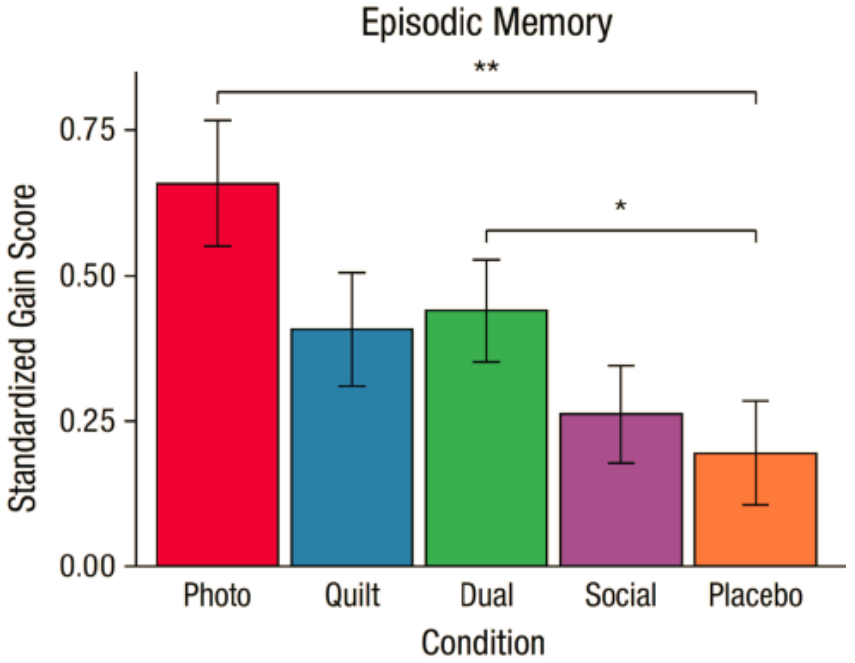
Risk of dementia is, on average, lower by 25% if occupations entailed more complex work with data. Risk is more than halved if occupations entailed more complex work with people.



SOURCES: HARMONY: Andel et al., 2005; SWEOLD: Andel et al., 2007

Meaningful Engagement and Cognition

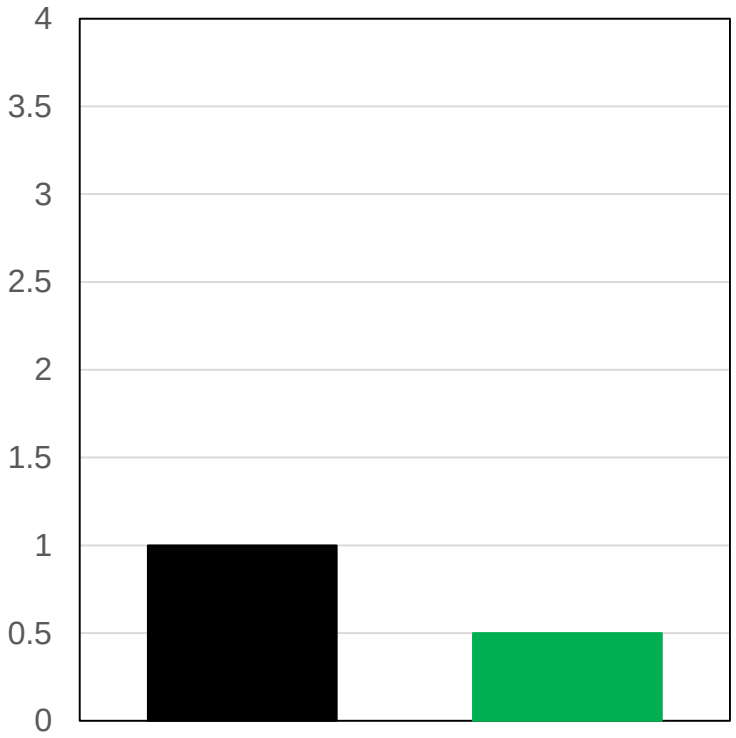
People who report being lonely have an increased risk of developing AD and show lower cognitive function over the lifespan



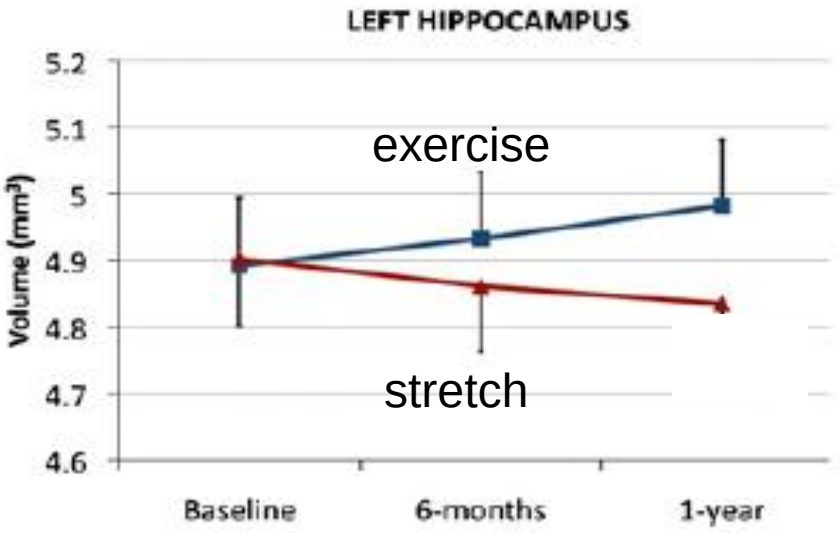
SOURCES: Rush Memory and Aging Project: Wilson et al 207; Lothian Birth Cohort: Gow et al 2007; SYNAPSE Project: Park et al 2013; Experience Corps: Carlson et al 2009

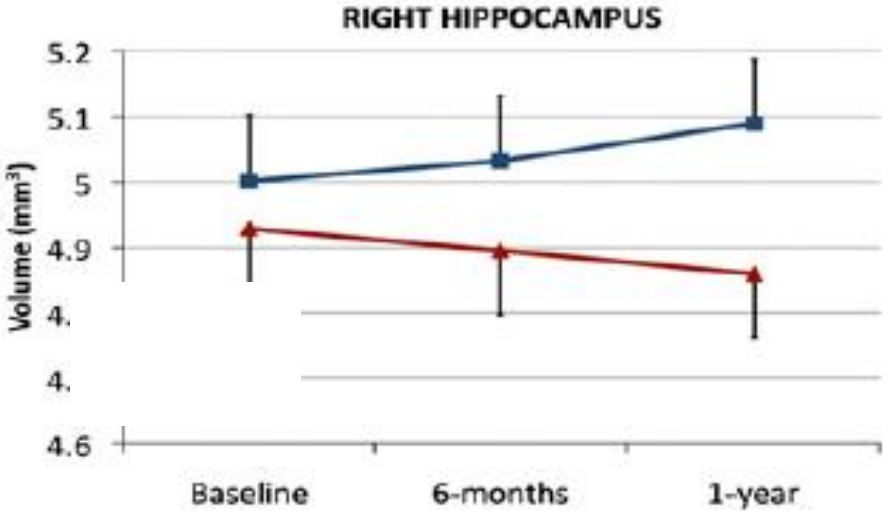
Physical exercise and dementia

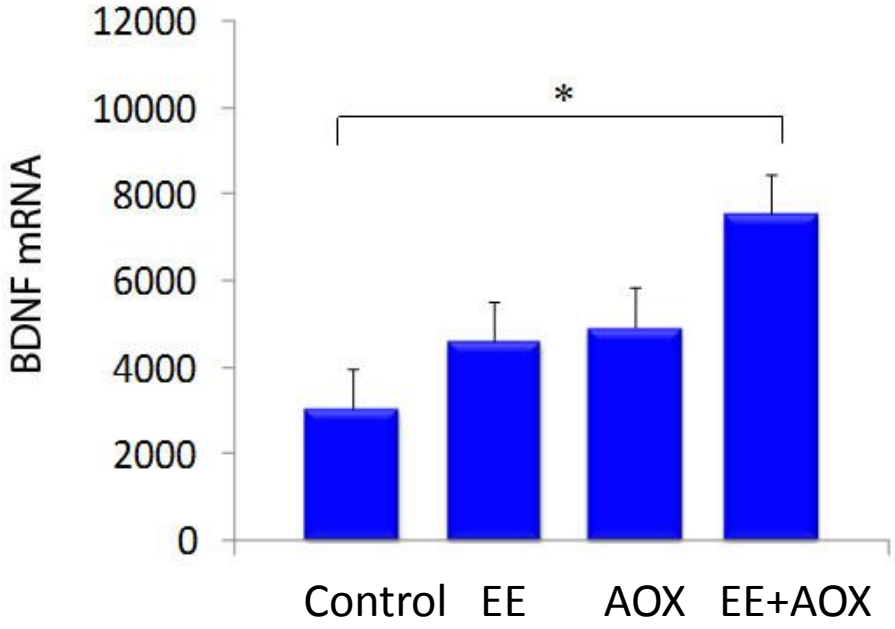
Risk of dementia is, on average, halved if people engaged in moderate exercise in midlife.

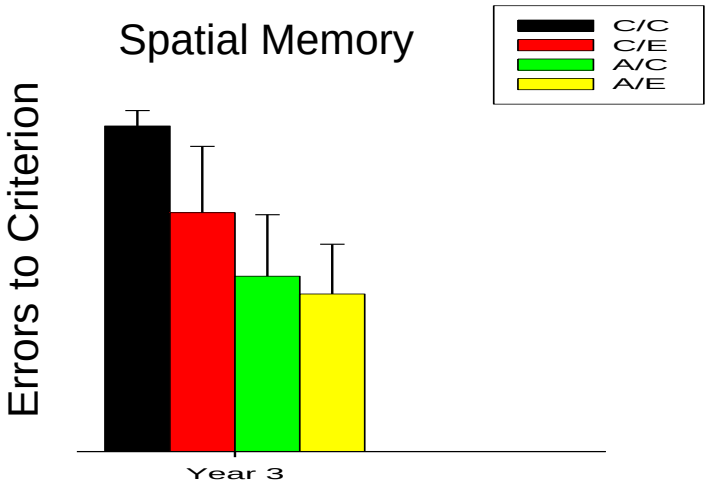


SOURCES: Hamer & Chida 2008 meta-analysis; HARMONY Andel et al 2008; Cleveland Clinic: Smith et al 2014





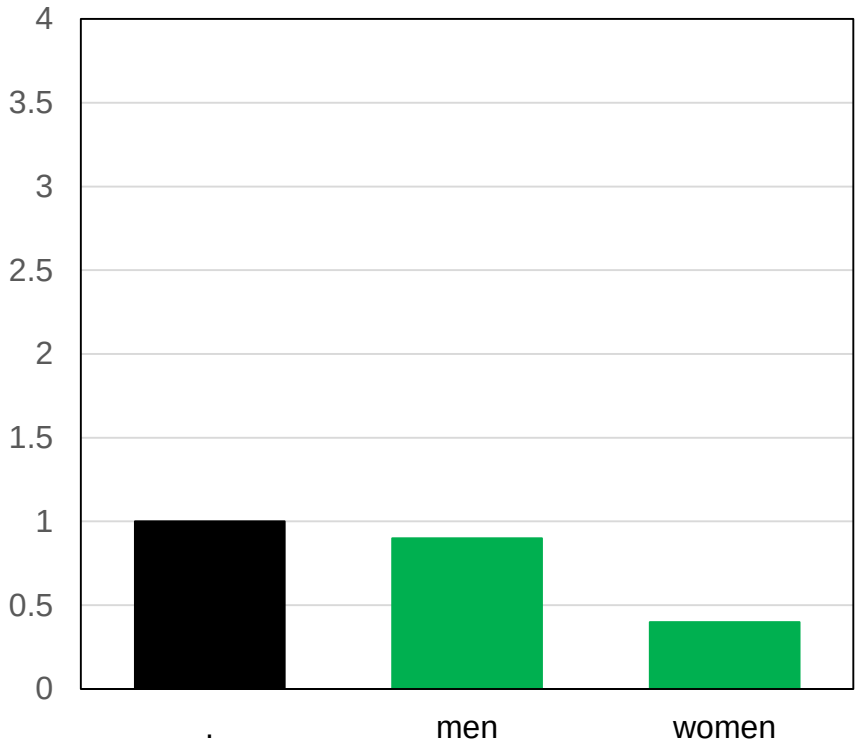




SOURCES: Erickson et al 2011; Fahnestock, Cotman, et al 2010

Diet and Dementia

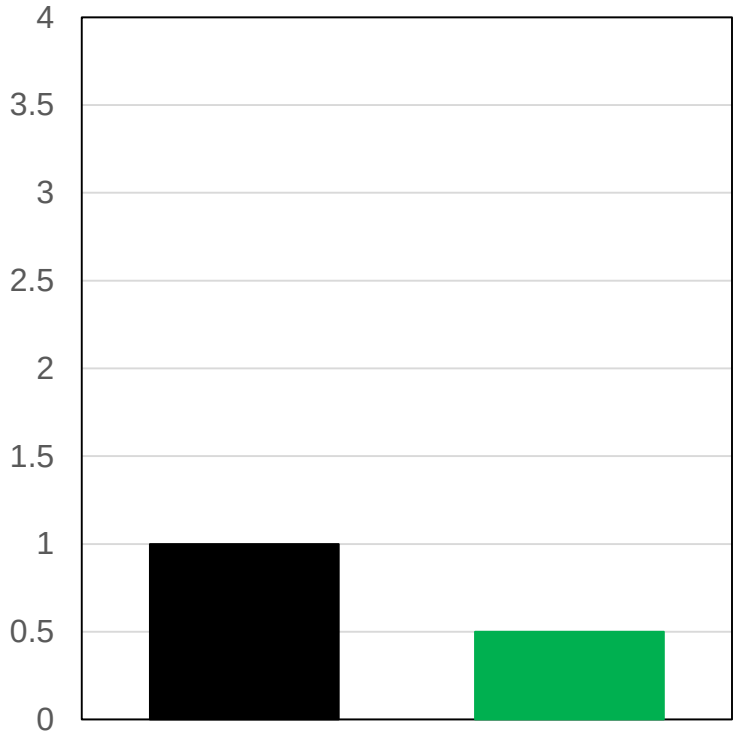
Risk of dementia is, on average, halved if people had a high proportion of fruits/vegetables in the diet at midlife, or eat fish at least 1/week, or follow a Mediterranean diet.



SOURCES: HARMONY: Hughes et al., 2010; CHAP: Morris et al., 2009; WHICAP: Gu & Scarmeas, 2011

Estrogen/Hormone replacement and Dementia

Risk of dementia is, on average, reduced by 40 – 70% in women using HRT for 3 years or more



SOURCES: Cache County Study: Zandi et al., 2002

Implications

- Alzheimer's disease risk is strongly influenced genetically
- Non-genetic influences on risk of dementia and AD include early and midlife exposures
- The strongest evidence across different reviews for potentially modifiable risk and protective factors currently points to diabetes and other vascular risk factors and to physical exercise
- The same interventions that show effects on cognition in non-demented adults may not be effective in preventing or treating dementia

Memory skills or sense of "cognitive vitality" may be aided by behavioral strategies

- Learning something new
- Challenging yourself
- Using memory tricks and mnemonics
- Organizing yourself, e.g., always putting things in the same place, keeping lists
- Writing down information

References

- Alzheimer's Association website http://www.alz.org/
- Alzheimer's Disease Education and Referral Center http://www.nia.nih.gov/
- Guy McKhann and Marilyn Albert, ***Keep Your Brain Young***. John Wiley & Sons, 2002.

MY EMAIL: gatz@usc.edu