Progress and Plans at the NIA

NIH Council of Councils

Richard J. Hodes, M.D.
Director
National Institute on Aging

May 26, 2017

NIH National Institute on Aging

NIA Mission

- Established in 1974 to support and ***conduct research*** on:
  - aging processes
  - age-related diseases
  - special problems and needs of the aged
- ***Train*** and develop research scientists
- ***Provide*** research ***resources***
- ***Disseminate information*** on health and research advances

NIA Divisions:
Portfolio Highlights

Intramural Research Program

- Multi-disciplinary research program focused on:
  - understanding biology and pathophysiology of aging
  - understanding the changes associated with healthy aging
  - developing insight about the pathophysiology of age-related diseases and disability

- Ten scientific laboratories and specialized branches for clinical research and provision of research resources located in Baltimore and Bethesda

Scientific Director: Luigi Ferrucci, M.D., Ph.D.
Ferruccilu@grc.nia.nih.gov
Deputy Director: Michele K. Evans, M.D.
me42v@nih.gov

Baltimore Longitudinal Study of Aging

- Started in 1958 - one of the longest ongoing longitudinal studies of aging in the world
- BLSA answers critical questions about what happens as people get older
- Study findings have helped us understand changes due to normal aging and those due to disease or other causes

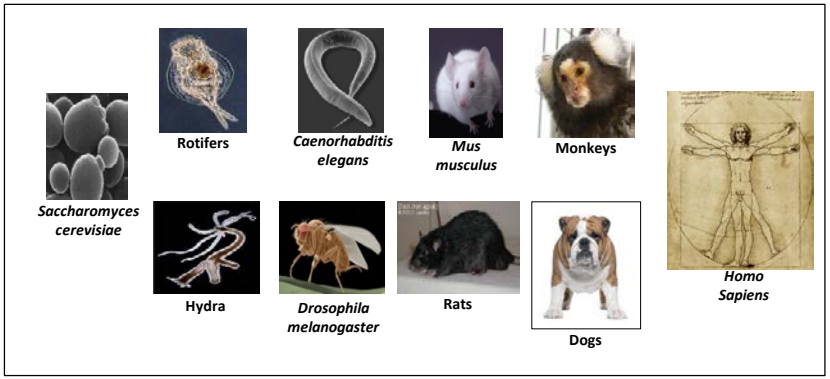
Division of Aging Biology

- **Nathan Shock Centers of Excellence**

- **Genetics and Cell Biology**
  - Genetics
  - Cell Biology
  - Metabolic Regulation

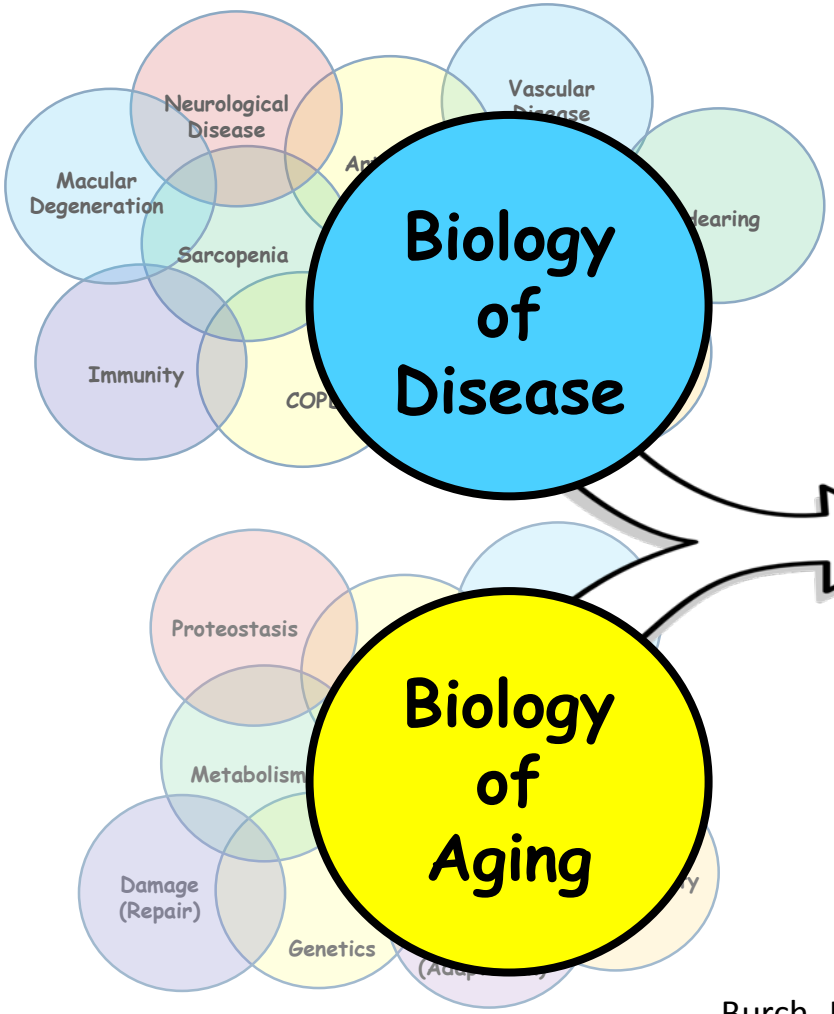
- **Aging Physiology**
  - Stem cells & Regenerative Biology
  - Immunology
  - Endocrinology
  - Musculoskeletal Biology
  - Tissue Physiology

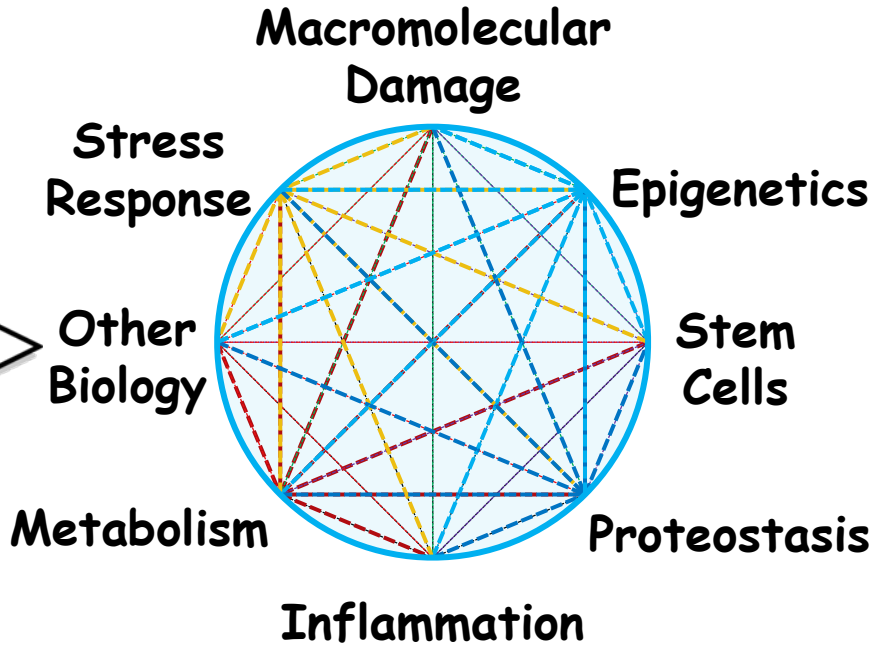
- **Biological Resources**
  - Animal Models
  - Biological Resources



Director: Felipe Sierra, Ph.D.
sierraf@nia.nih.gov
Deputy Director: Ron Kohanski, Ph.D.
kohanskir@nia.nih.gov

"Geroscience" is the Convergence of Two Fields of Study





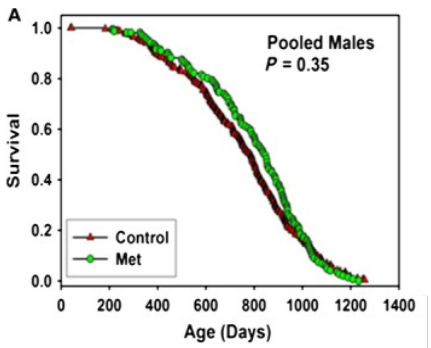
Burch, JB et al. (2014) *J Gerontol A Biol Sci Med Sc*i Jun;69 Suppl 1:S1-3.
Kennedy, BK et al. (2014) Cell Nov 159(4): 709–713.

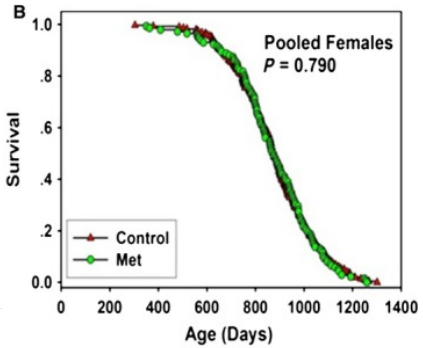
NIH GeroScience Interest Group (GSIG)

Trans-NIH organization of 21 Institutes initiated by NIA to:

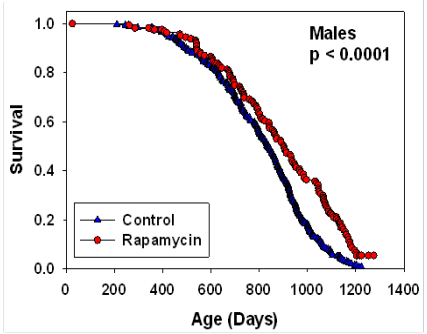
- Raise awareness of the relevant role played by aging biology in the development of diseases and disabilities
- Promote discussion and co-funding of initiatives across the NIH, based on the above
- ***Gero I – 2013 Summit***
- ***Gero II - Disease Drivers of Aging: 2016 Advances in Geroscience Summit- focused on how diseases and associated therapies can accelerate the onset of age-related changes***

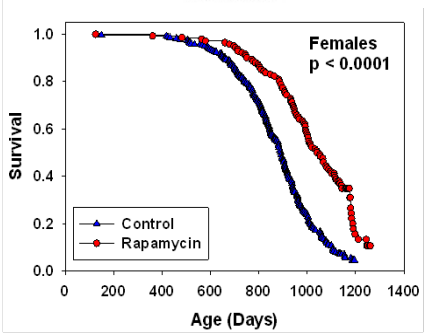
Longer lifespan in mice treated with a combination of rapamycin and metformin



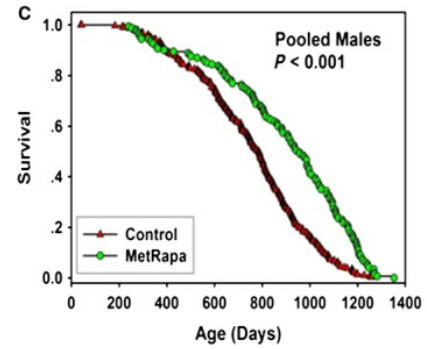


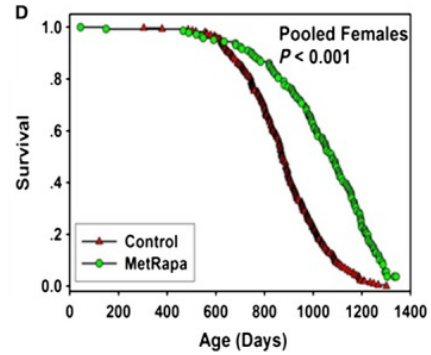
Metformin





Rapamycin

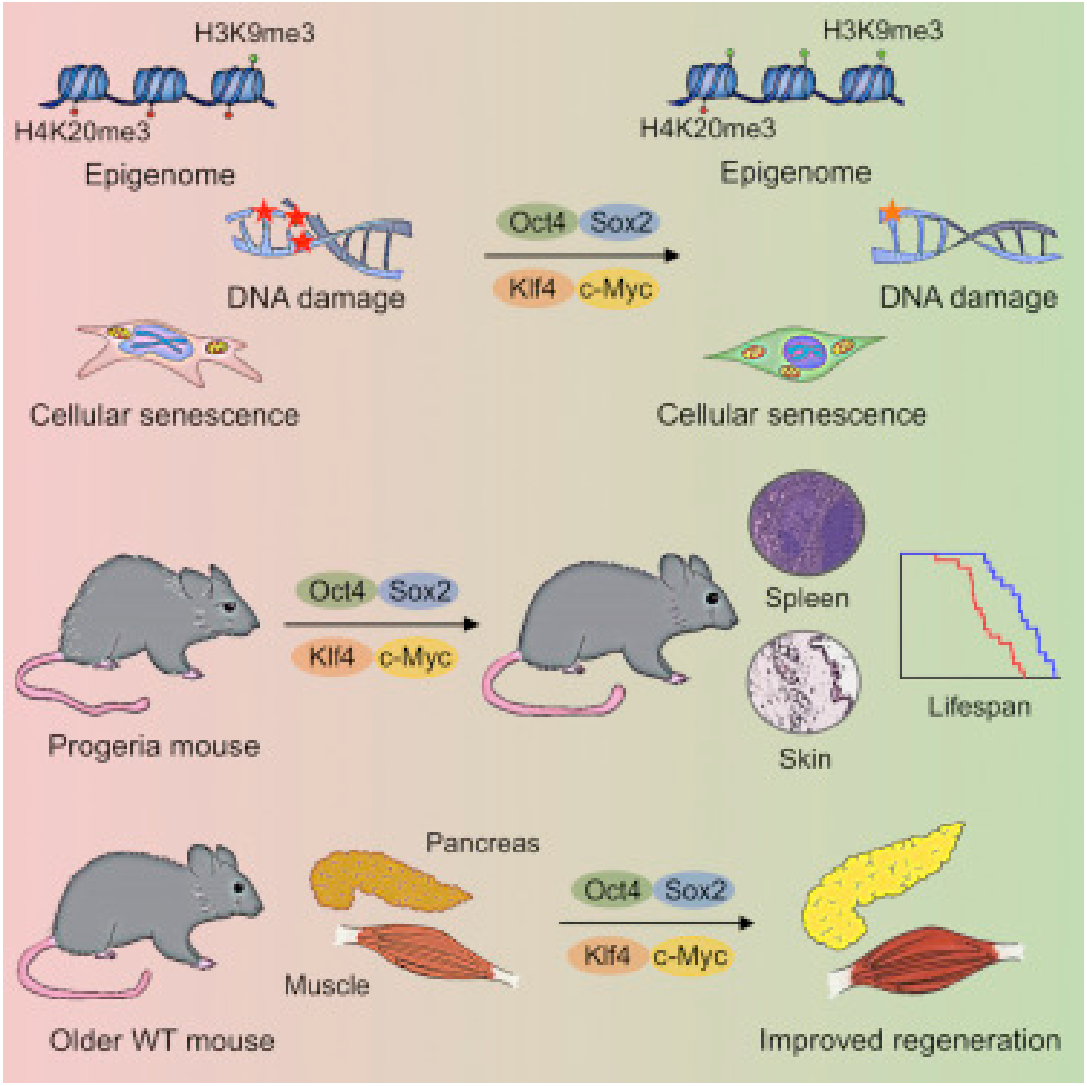




Rapamycin + Metformin

Strong, R. et al. (2016). *Aging Cell* 15: 872-84.
Miller, R.A. et al. (2010). *J Geront A* 66(2):191-201

In Vivo Amelioration of Age-Associated Hallmarks by Partial Reprogramming



Ocampo A. et al. (2016). *Cell* 167 (7): 1719-33.

Division of Geriatrics and Clinical Gerontology

- Maintaining health and independence in old age
- Improving functional abilities in old age
- Coexisting conditions
- Aging across the life span; exceptionally healthy aging
- Aging mechanisms influencing health span and longevity
- Clinical trials: Prevention and treatment

Director: Evan Hadley, M.D.
ehadley@nih.gov
Deputy Director: Winifred Rossi, M.A.
rossiw@nia.nih.gov

SPRINT Study

Systolic Blood Pressure Intervention Trial

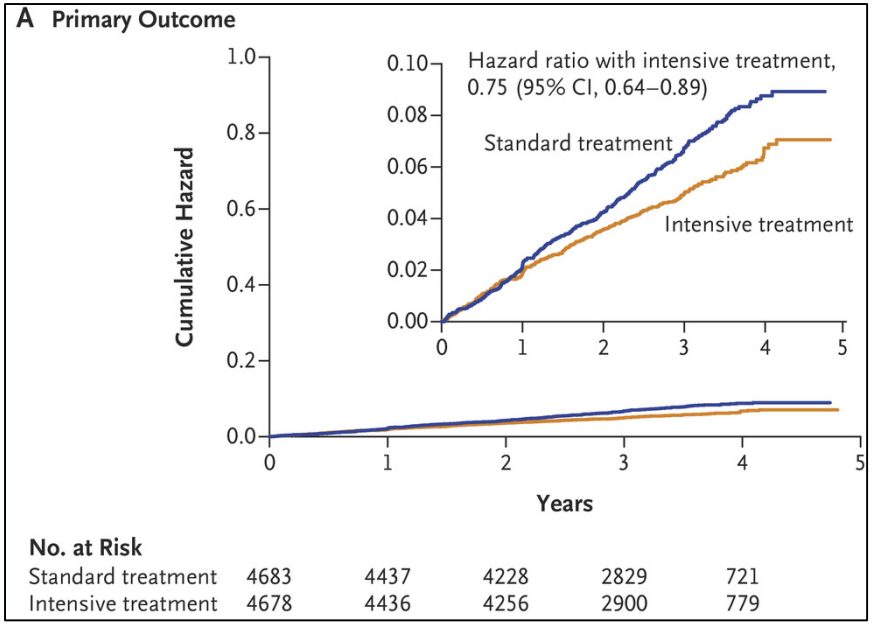
- Participants: 9,361 diverse, non-diabetic participants age 50 and older with high blood pressure

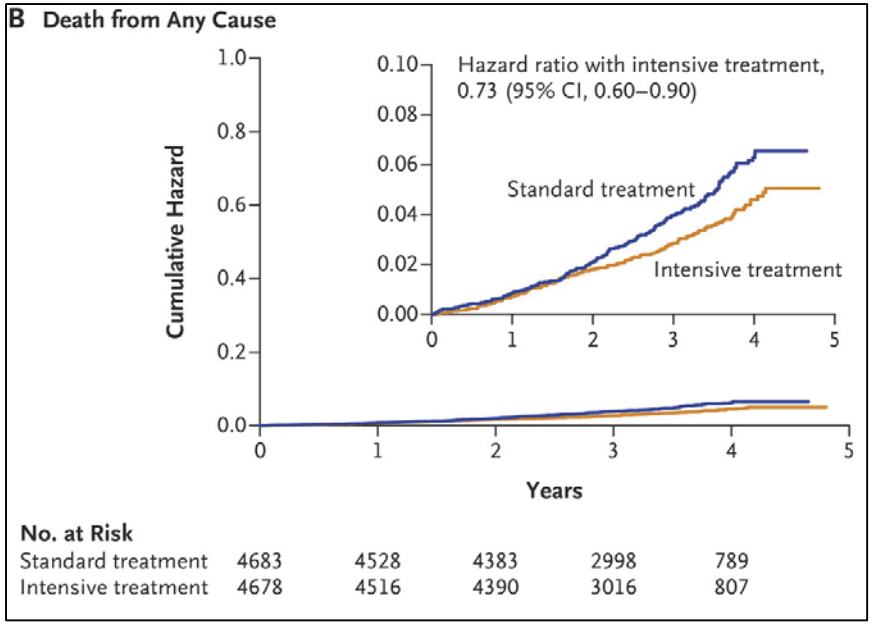
- Intervention: Adjusted the amount/type of blood pressure medication to achieve a target systolic pressure of 120 mm Hg (140 mm Hg is the standard guideline)

- The study was ended early in order to share the significant preliminary findings

NHLBI was the primary funder; NIDDK, NINDS and NIA co-funded the study.

SPRINT Study

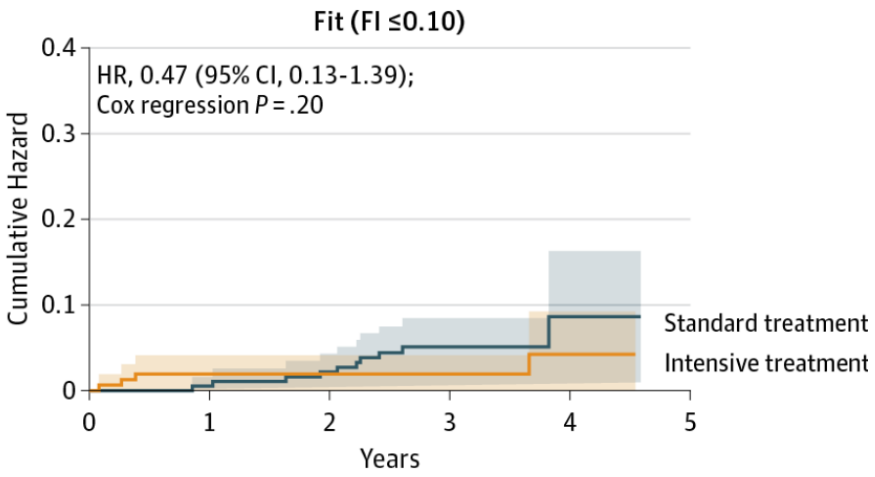


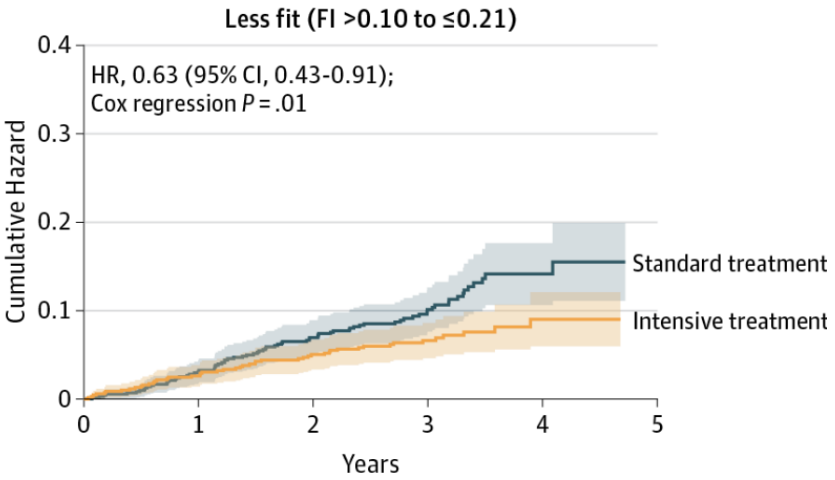


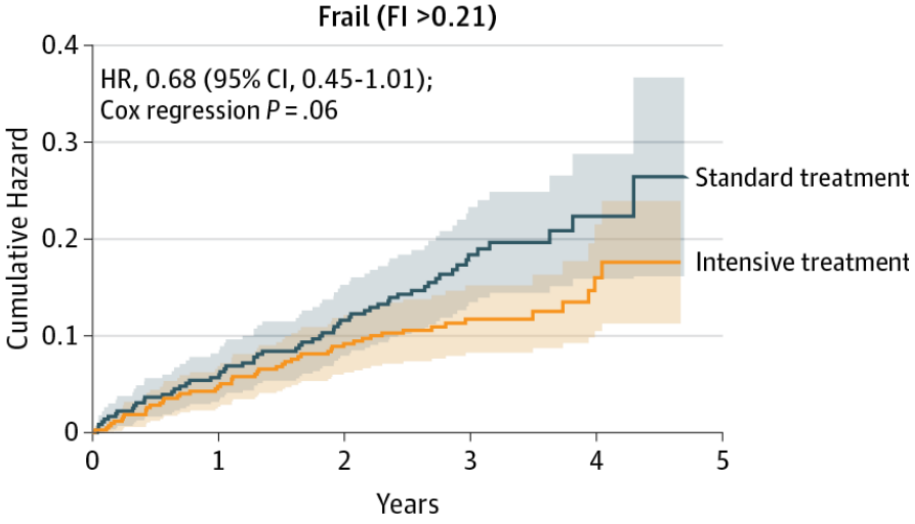
- Outcome: Reduced rates of cardiovascular events and stroke by 25% and the risk of death from any cause by 27%

Wright J et al. (2015) *N Engl J Med;* Nov 26; 373:2103-2116.

SPRINT Follow-up in Adults 75 years or Older



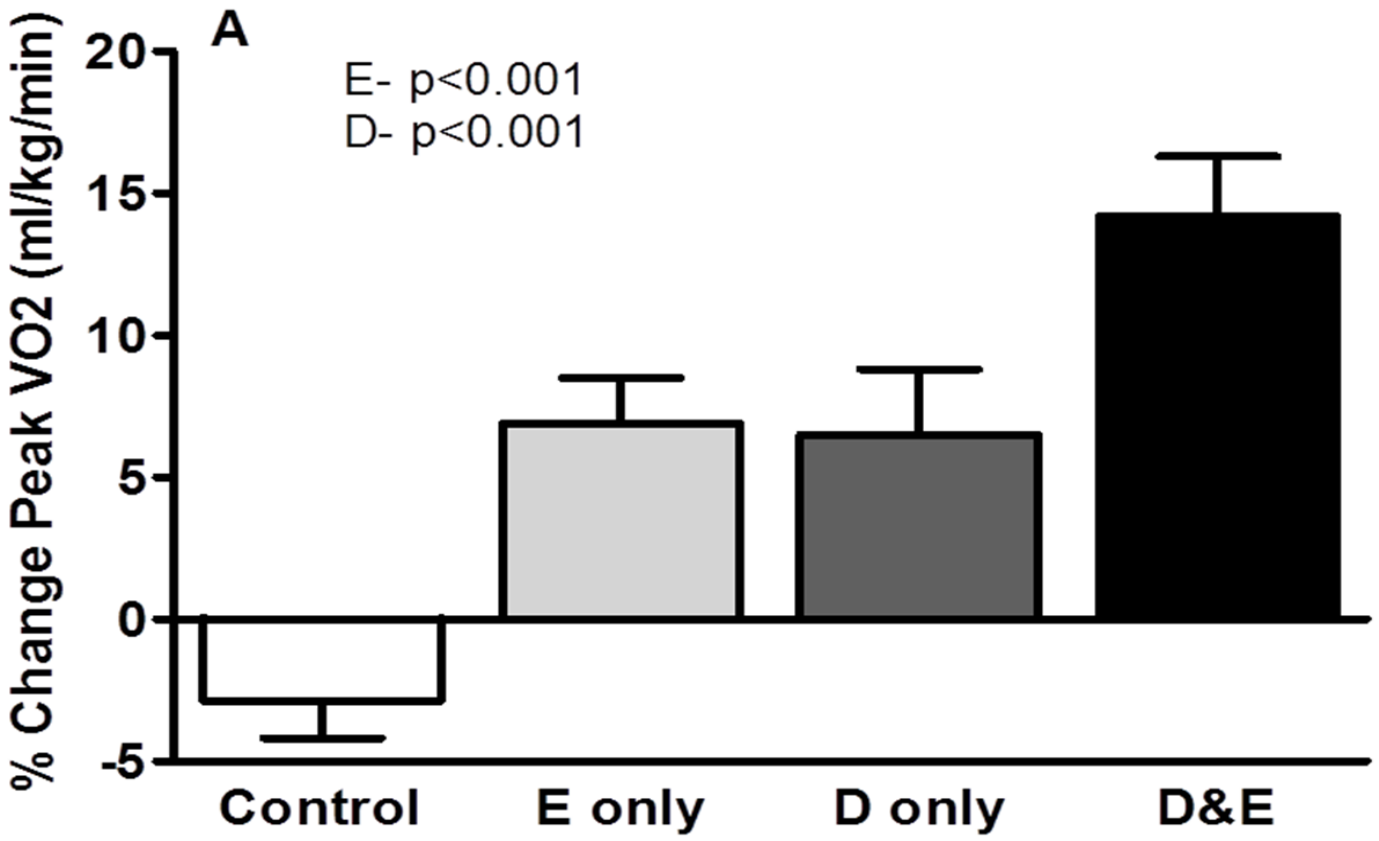




- Cumulative hazard was reduced in participants, even those less fit and frail
- Incident cardiovascular disease was reduced by 33% and mortality (from any cause) was reduced by 32%
- The rate of serious adverse events was not statically different across treatment groups, including among the most frail participants

Williamson, Jeff D., et al. (2016) *JAMA* Epub ahead of print

Diet and/or Exercise to Treat Heart Failure With Preserved Ejection Fraction



Kitzman, D et al. (2016) *JAMA 315*(1):36-46.

Division of Neuroscience

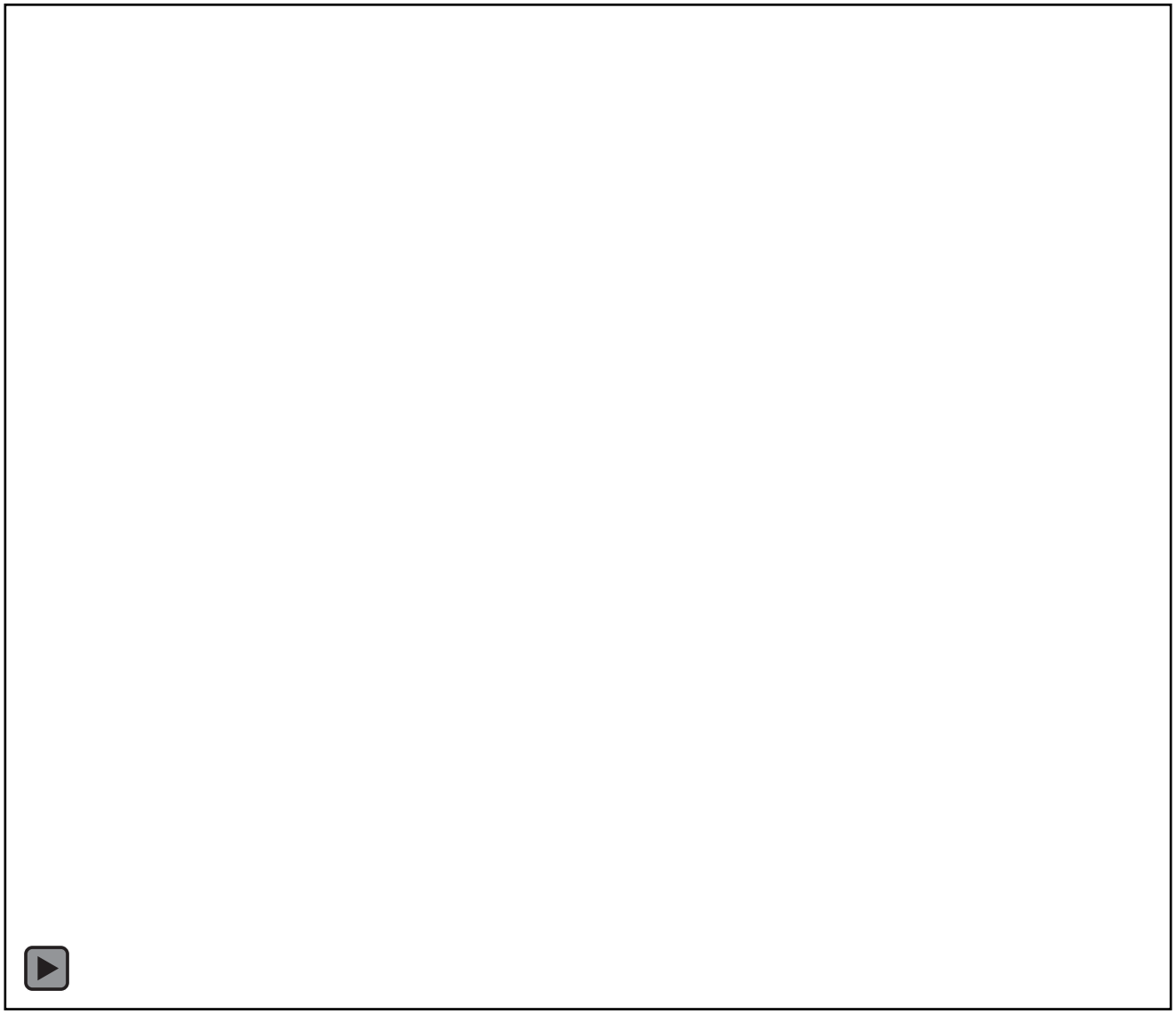
- Basic Neurobiology
- Alzheimer's Disease
- Sensory Processes
- Learning and Memory
- Sleep
- Cognitive Health

Director: Eliezer Masliah, M.D.
eliezer.masliah@nih.gov
Acting Deputy Director: Brad Wise, Ph.D.
wiseb@nia.nih.gov

Recent Appropriations History for AD/ADRD Research

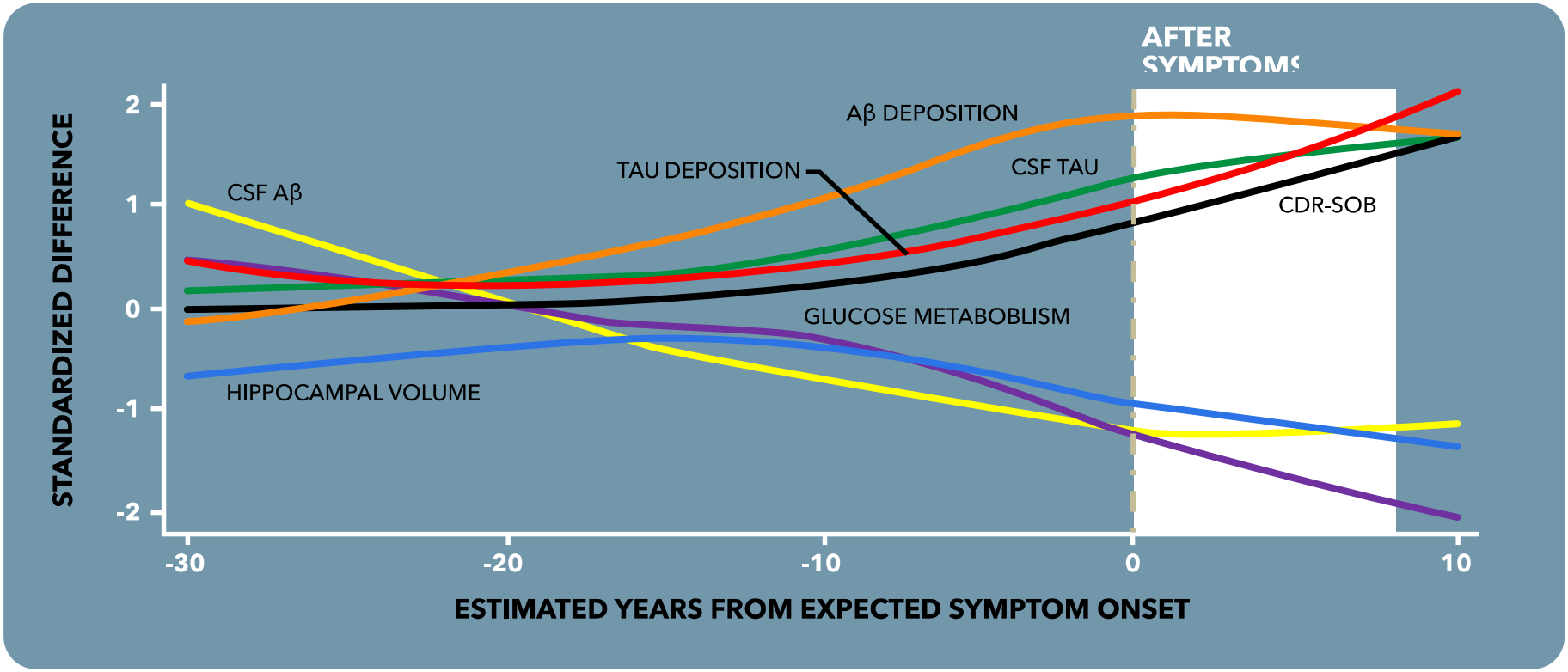
- **FY2012:** Dr. Collins redirected **$50 million** – as part of a Presidential initiative
- **FY2013:** Dr. Collins redirected **$40 million** (from unallocated funds in the NIH budget)
- **FY2014:** NIA received **$100 million** in additional appropriations
- **FY2015:** NIA received **$25 million** in additional appropriations
- **FY2016:** NIA received **$350 million** in additional appropriations
- **FY2017:** NIA received **$400 million** in additional appropriations

Aβ Deposition in Autosomal Dominant AD
Years before Expected Clinical Symptoms



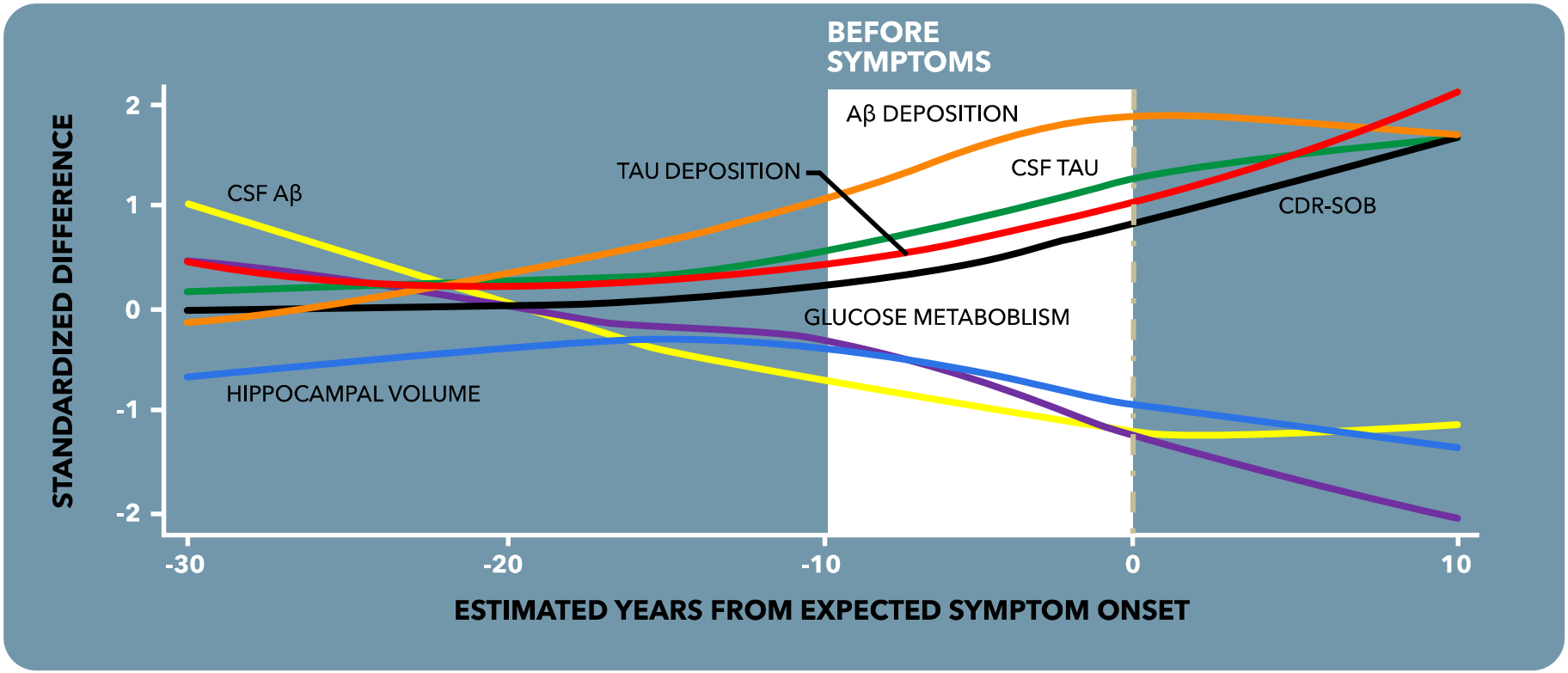
Courtesy of Tammie Benzinger; Bateman, R et al. (2012) N Engl J Med; Aug 30; 367(9):795-804

Clinical, Cognitive, Structural, Metabolic, and Biochemical Changes Years Before AD Symptom Onset



Adapted from Bateman, R et al. (2012) *N Engl J Med*; Aug 30; 367(9):795-804

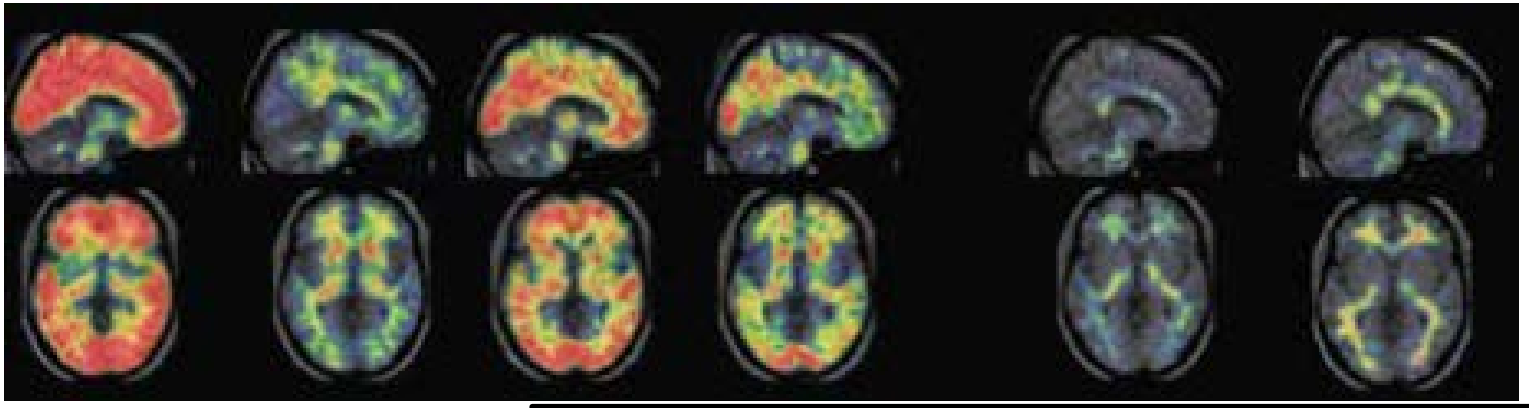
Clinical, Cognitive, Structural, Metabolic, and Biochemical Changes Years Before AD Symptom Onset



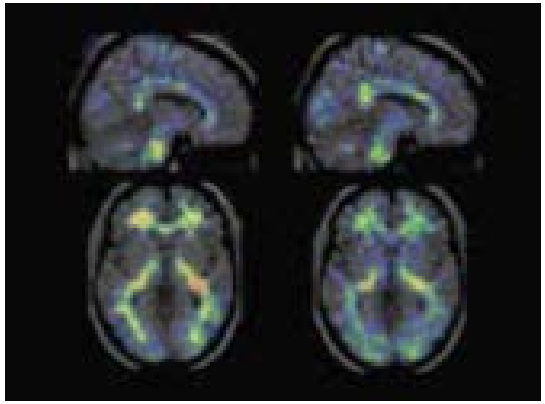
Adapted from Bateman, R et al. (2012) *N Engl J Med*; Aug 30; 367(9):795-804

Amyloid PET Scans in *Presymptomatic* Early-Onset Alzheimer's Disease

Gene Carriers **Non-Carriers**



Age 35-39 Years



Age 25-29 Years

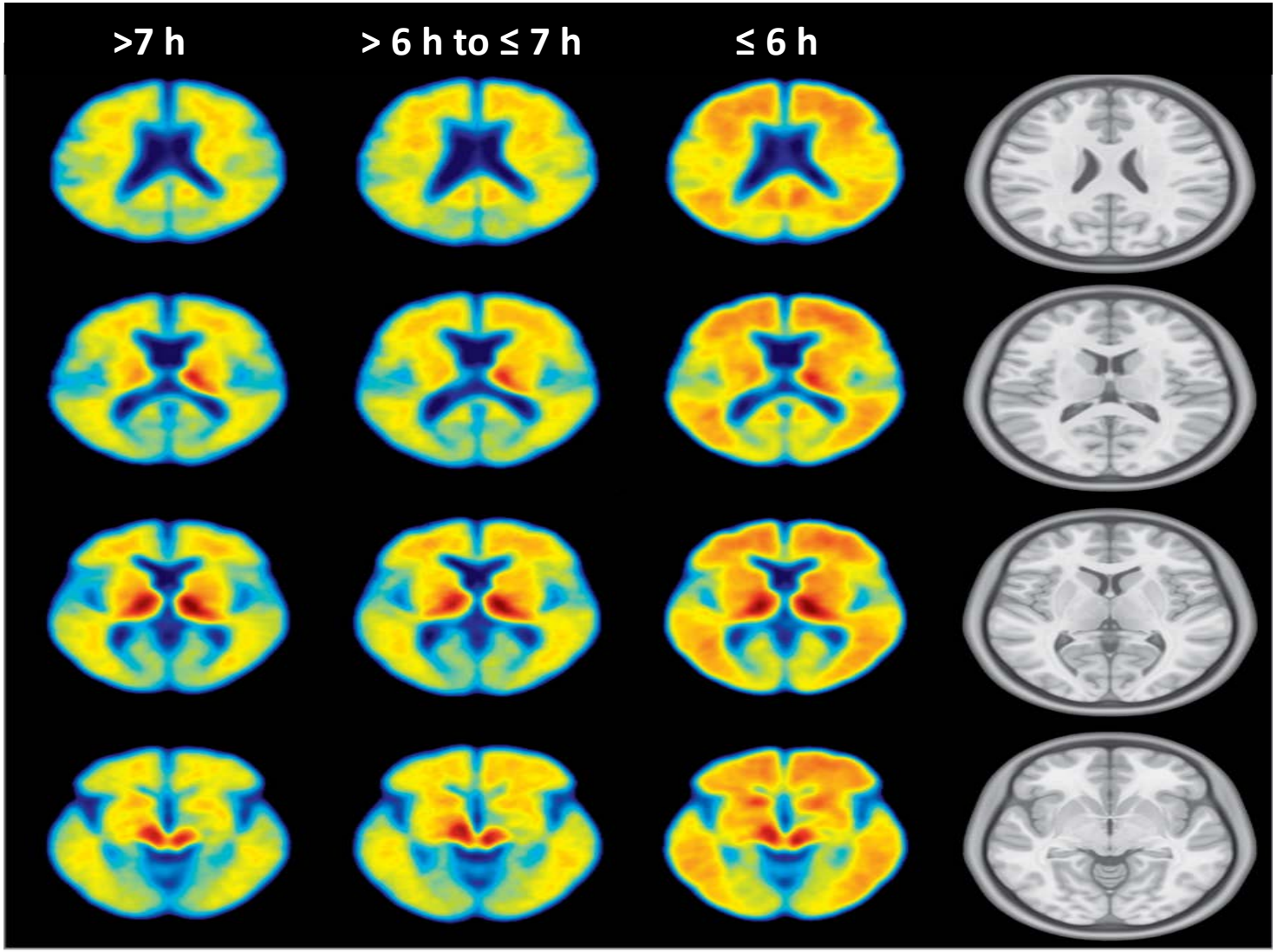
Colombian Kindred

- N = 5000 living individuals from ~ 25 families
- 1500 with the *E280A (Glu280Ala) Presenilin1* mutation
- Autosomal dominant, 100% penetrance
- Median age of MCI = 44 years, dementia = 49 years

Double-blind, placebo-controlled trial for up to 60 months
- crenezumab 300 mg SC every 2 weeks

Fleisher, AS et al. (2012) *Lancet Neurology* 11(12):1057-65.

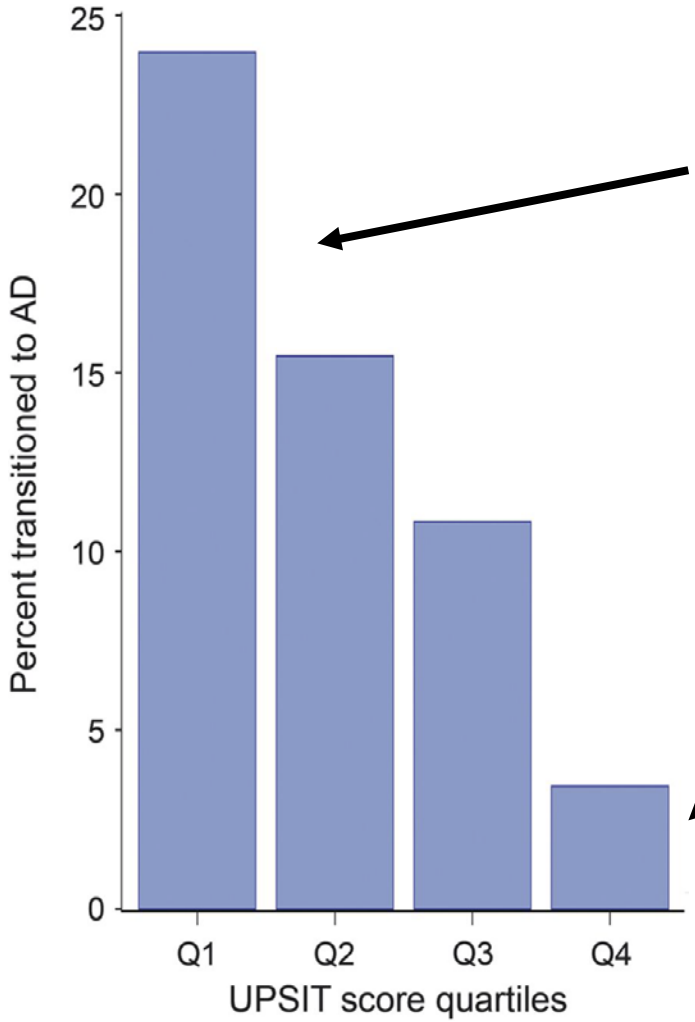
Relationship between sleep and amyloid load



Mean PET PiB images show increased amyloid burden in those subjects who report sleeping less than 6 hours nightly

Spira, A et al. (2013) *JAMA Neurology* 70(12): 1537-1543.

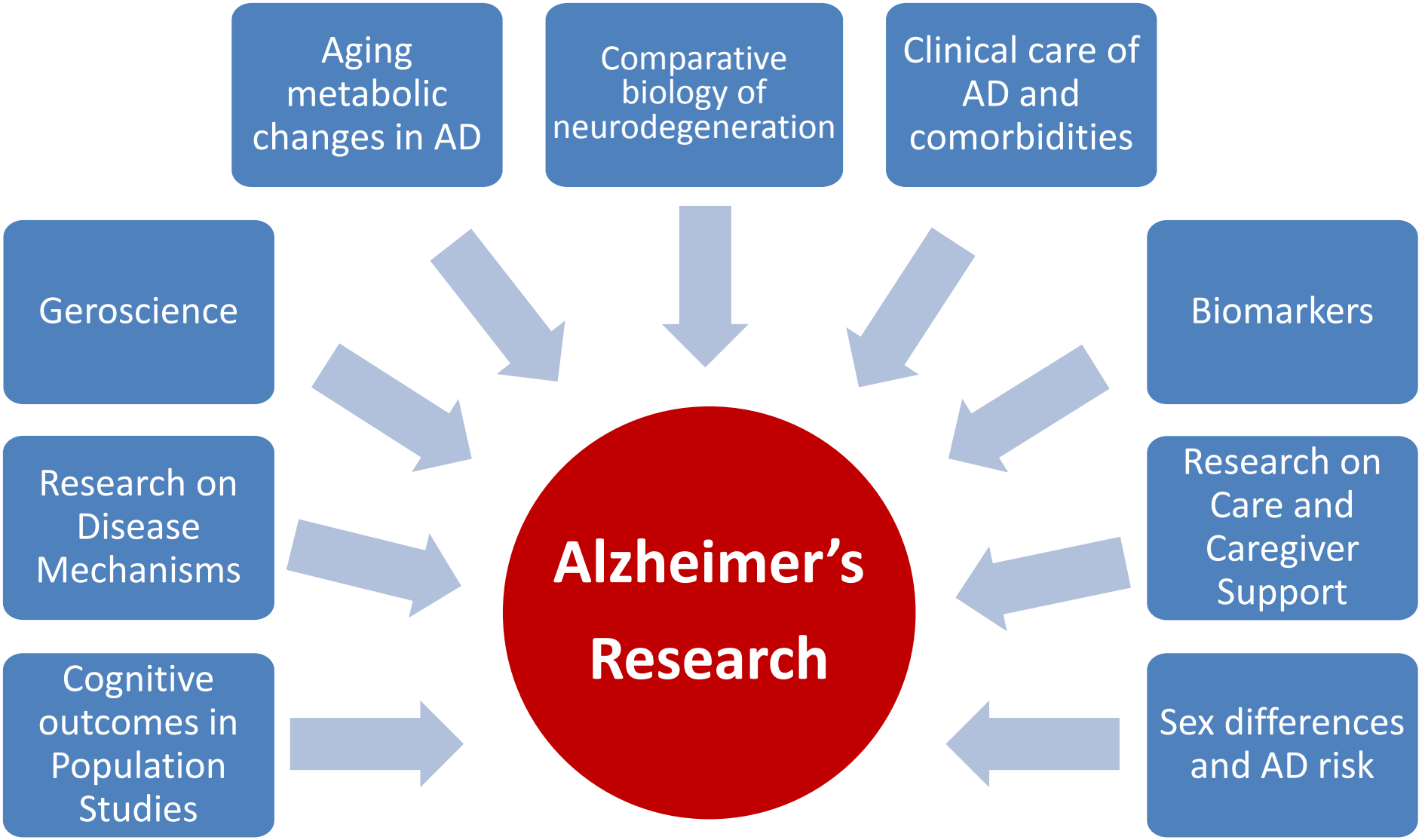
Decreased smell identifies risk for Alzheimer's Disease



Almost 25% of patients with low University of Pennsylvania Smell Identification Test (UPSIT) scores transitioned to AD compared to less than 5% of patients who scored the highest

Devanand, D et al. (2015) *Neurology* 84(2):182-189.

Diversity of AD Research



Research Planning and Initiatives

Concept Approvals:
https://www.nia.nih.gov/research/initiatives/approved-concepts

General FOAs:
https://www.nia.nih.gov/research/funding

Alzheimer's Disease FOAs:
http://www.nia.nih.gov/AD-FOAs

Division of Behavioral and Social Research

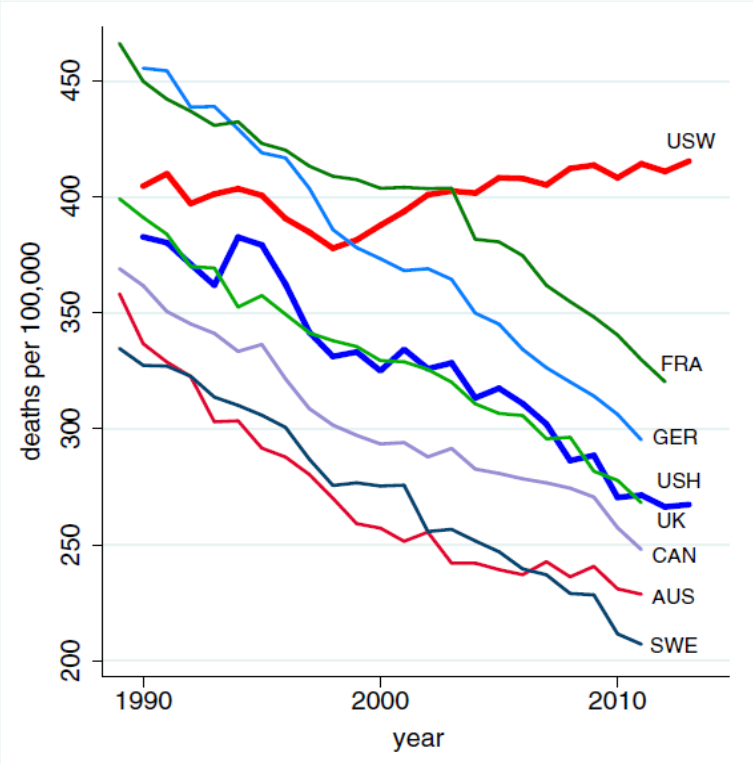
- Reversibility of early-established risk factors
- Regional and international differences in health and longevity
- Social neuroscience of aging
- Longitudinal Studies
- Centers programs
- Interventions

c/o Gerontology Society of Iowa

Director: John Haaga, Ph.D.
HaagaJ@mail.nih.gov
Deputy Director: Dana Plude, Ph.D.
Dana.plude@mail.nih.gov

Midlife Morbidity/Mortality Trends

- From 1970-2013, mortality rates for those aged 45–54 have decreased by 44%
- However, all-cause mortality of <u>middle-aged white non-Hispanic men and women</u> *increased* in the United States between 1999-2013 – this trend is unique to the US
- Increases in drug and alcohol poisonings, suicide, and chronic liver diseases and cirrhosis may be contributing

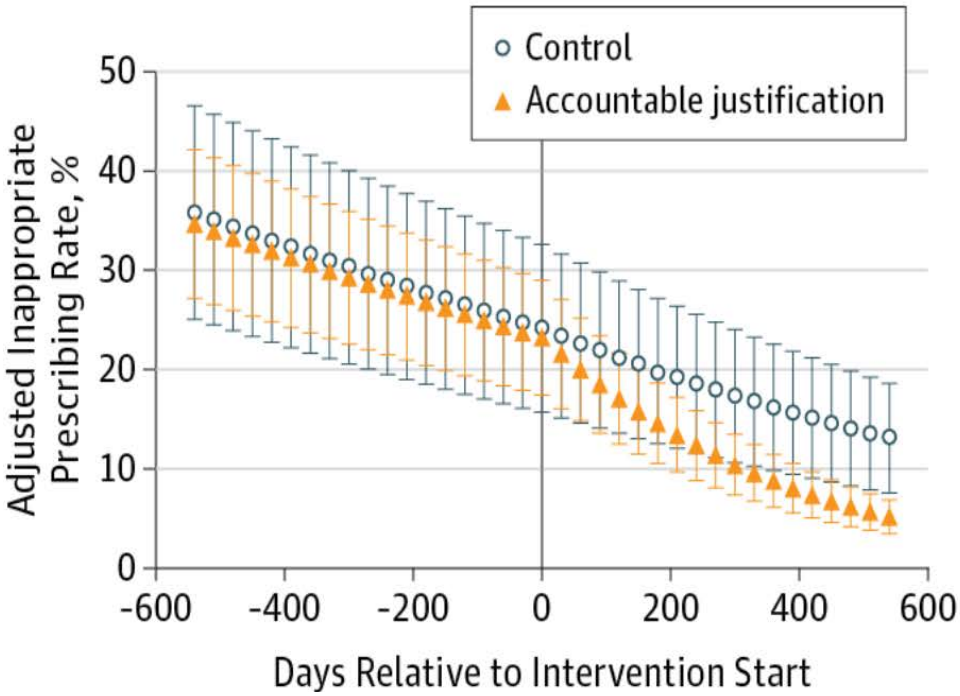


All-cause mortality, ages 45–54

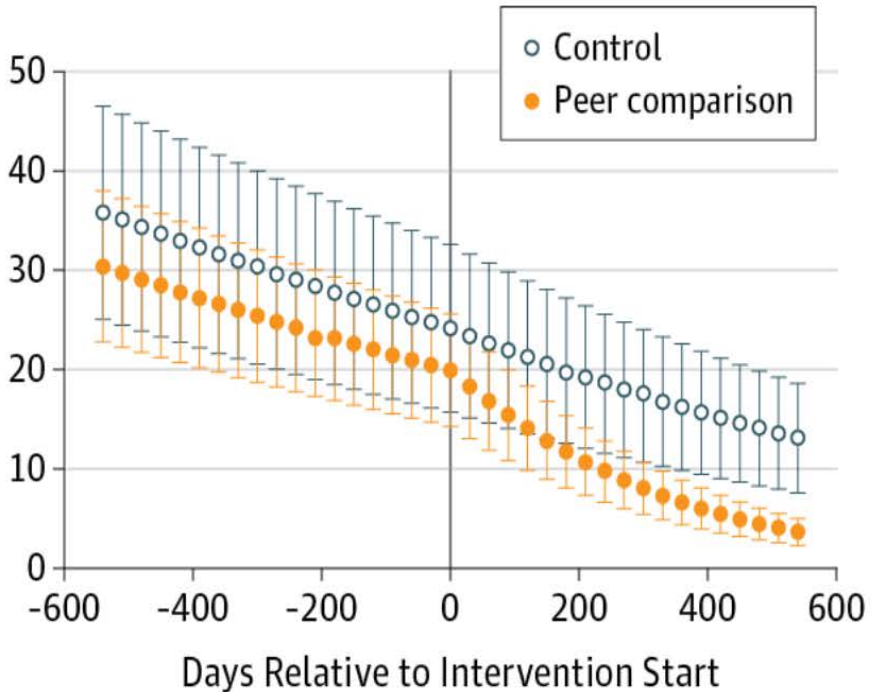
Case A and A Deaton. (2015) *PNAS* 112(49):15078-83.

Improving Inappropriate Antibiotic Prescribing

Accountable justification



Peer comparison



Both behavioral interventions resulted in lower rates of inappropriate antibiotic prescribing

Meeker, D. et al. (2016) *JAMA* 315(6):562-570.

Caregiver Success: REACH

- Major Goal: Improve caregiver quality of life
- Outcome: Significant improvement in quality of life contributors: depression, support, self-care, burden, difficult patient behaviors
- Status:
  - VA and multiple states have translated the program
  - REACH VA being pilot tested with several Tribal Nations sites through the IHS and ACL/AOA
  - REACH VA is also being modified to help caregivers of veterans with TBI and spinal cord injury
  - There are racial and ethnic differences in the intervention delivery, such that black caregivers receive less intervention contact than other groups

Impact of the REACH II and REACH VA on Healthcare Costs

- Major Goal: Examine healthcare costs associated with caregiver participation in REACH II or REACH VA
- Outcomes:
    - Neither REACH II or REACH VA were associated with additional healthcare costs for caregivers or recipient
    - No increase in VA or Medicare expenditures for caregivers and recipients in both interventions
    - There was a significantly lower (33.6%) total VA cost with REACH VA
    - Behavioral interventions such as REACH II and REACH VA can support caregivers without additional healthcare costs, and may even reduce costs

Nichols, LO et al. (2017) *J Am Geriatr Soc.* [Epub ahead of print]

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