

Aging Research: A Bird's Eye View

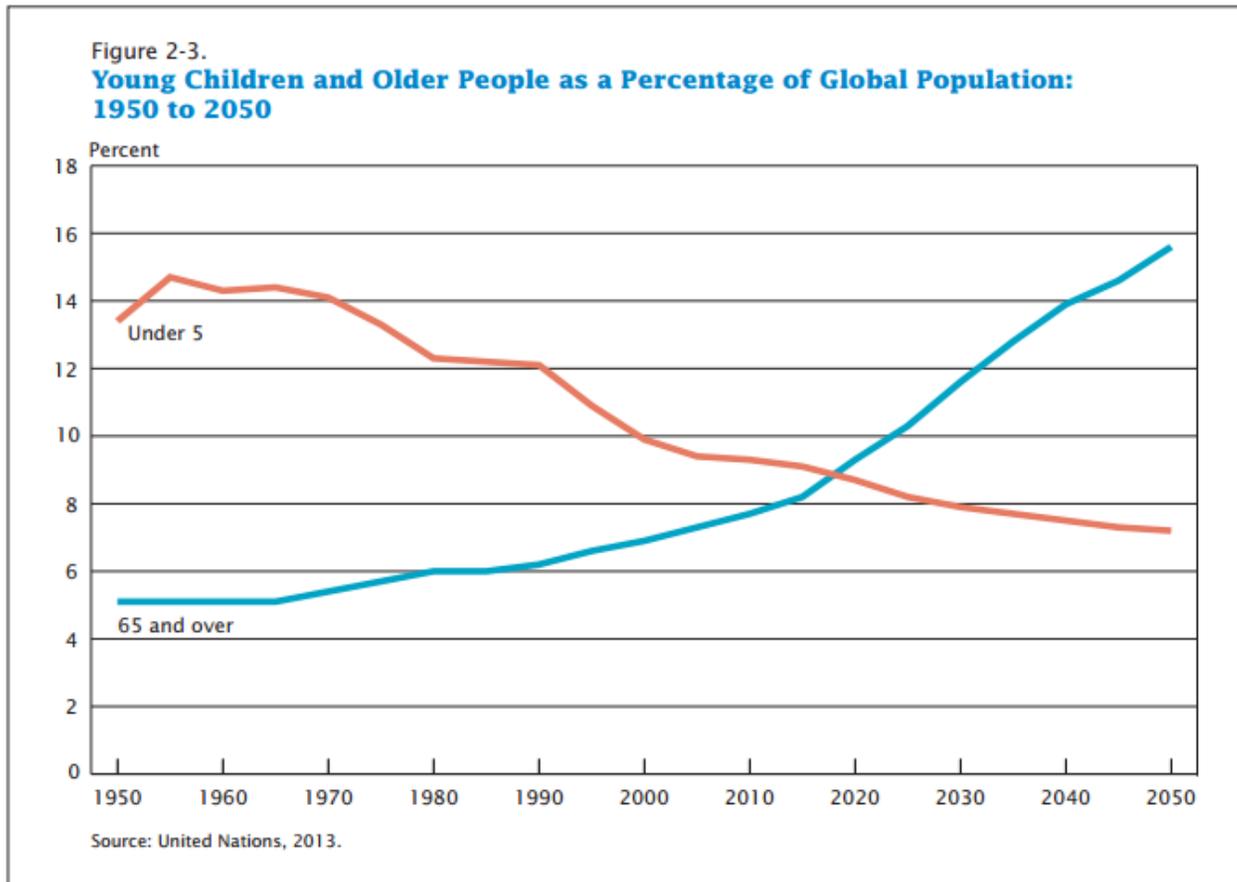
Demystifying Medicine

Richard J. Hodes, M.D.

January 10, 2017

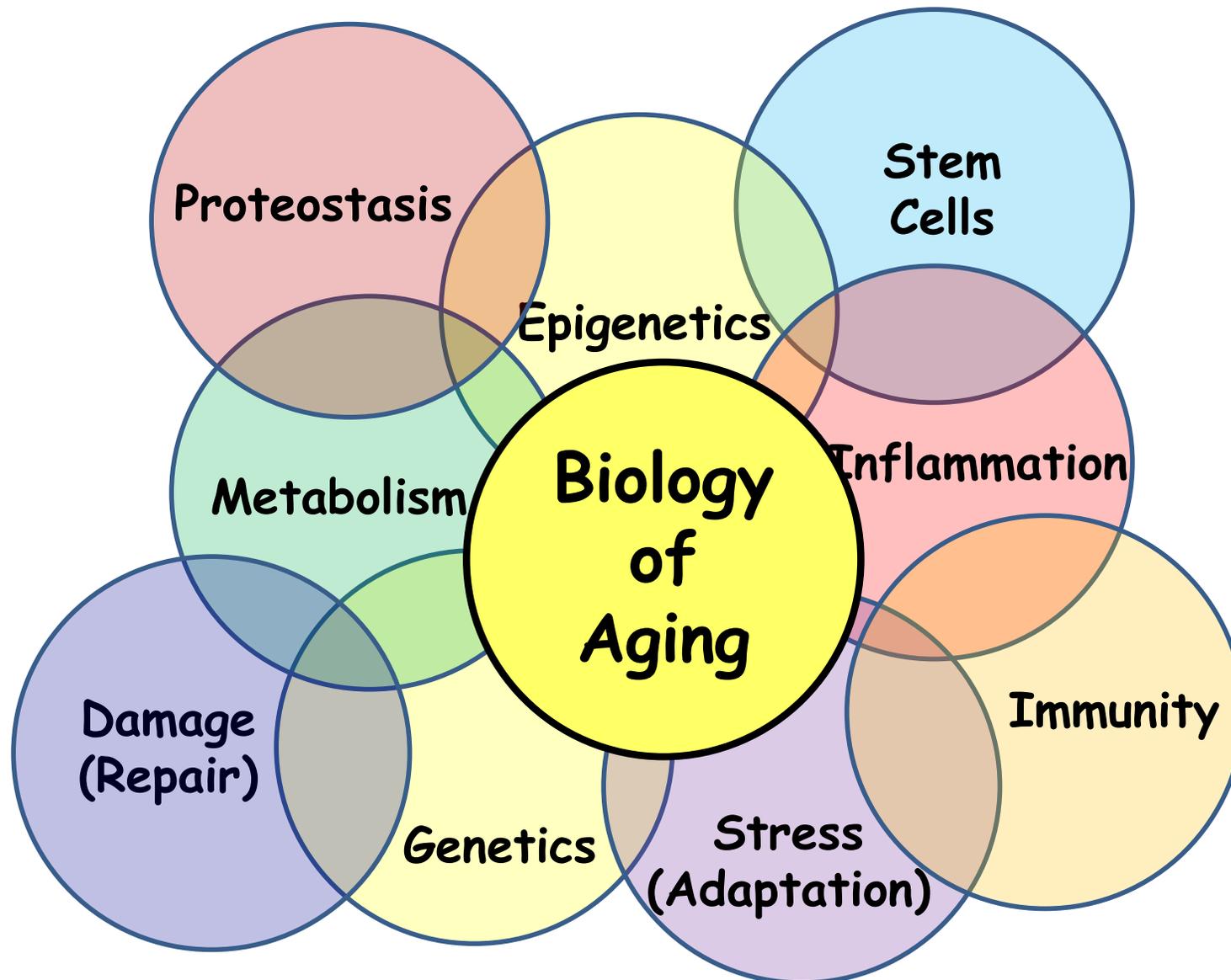


World's Older Population is Growing

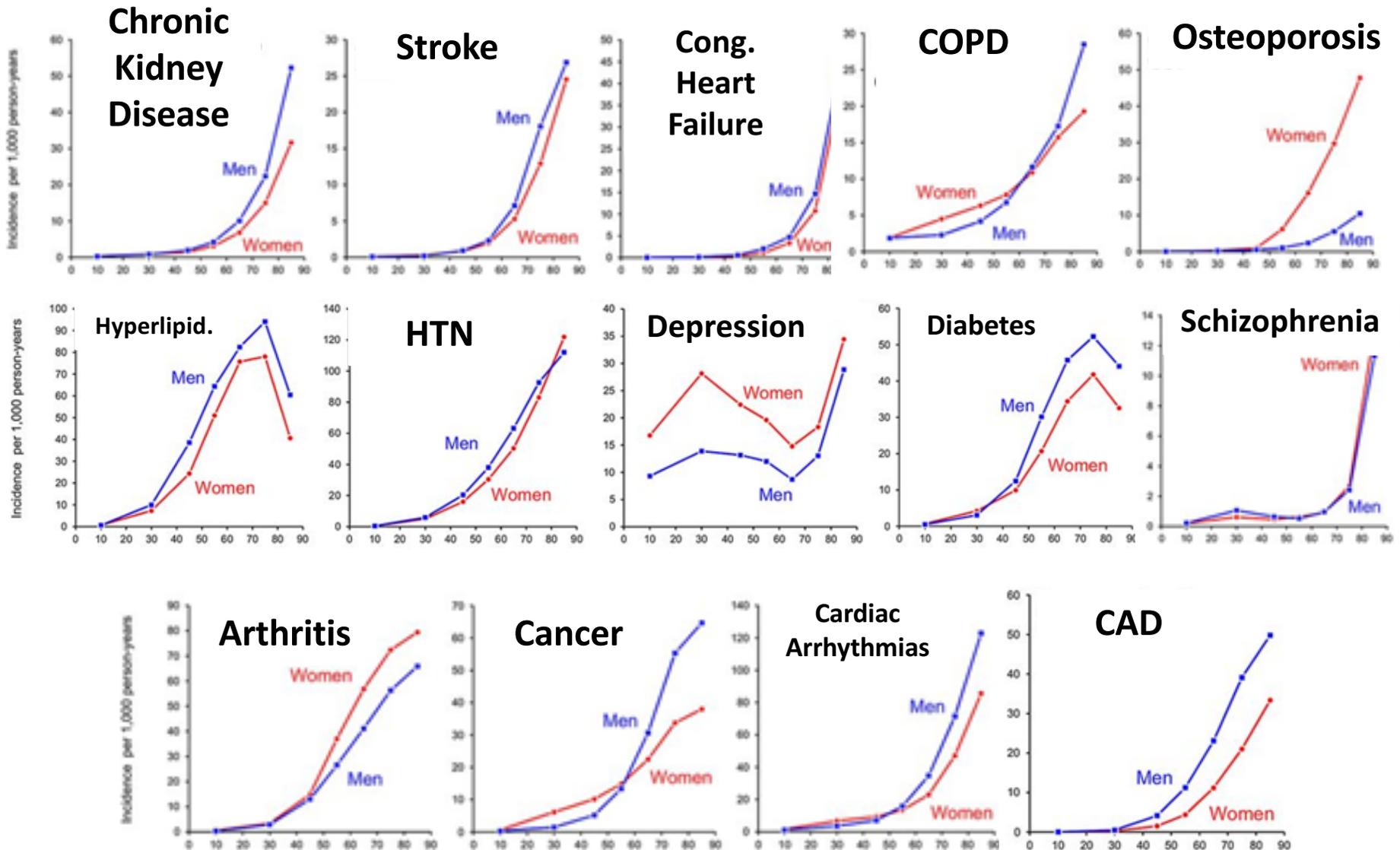


- America's 65-and-over population is projected to nearly double, from 48 mill to 88 mill by 2050
- Global life expectancy is projected to increase by almost eight years, from 68.6 years in 2015 to 76.2 years in 2050
- The global population of people aged 80 and older is expected to more than triple, growing from 126.5 mill to 446.6 mill by 2050

Aging is the Major Risk Factor for Most Chronic Diseases



Disease Prevalence as a Function of Age

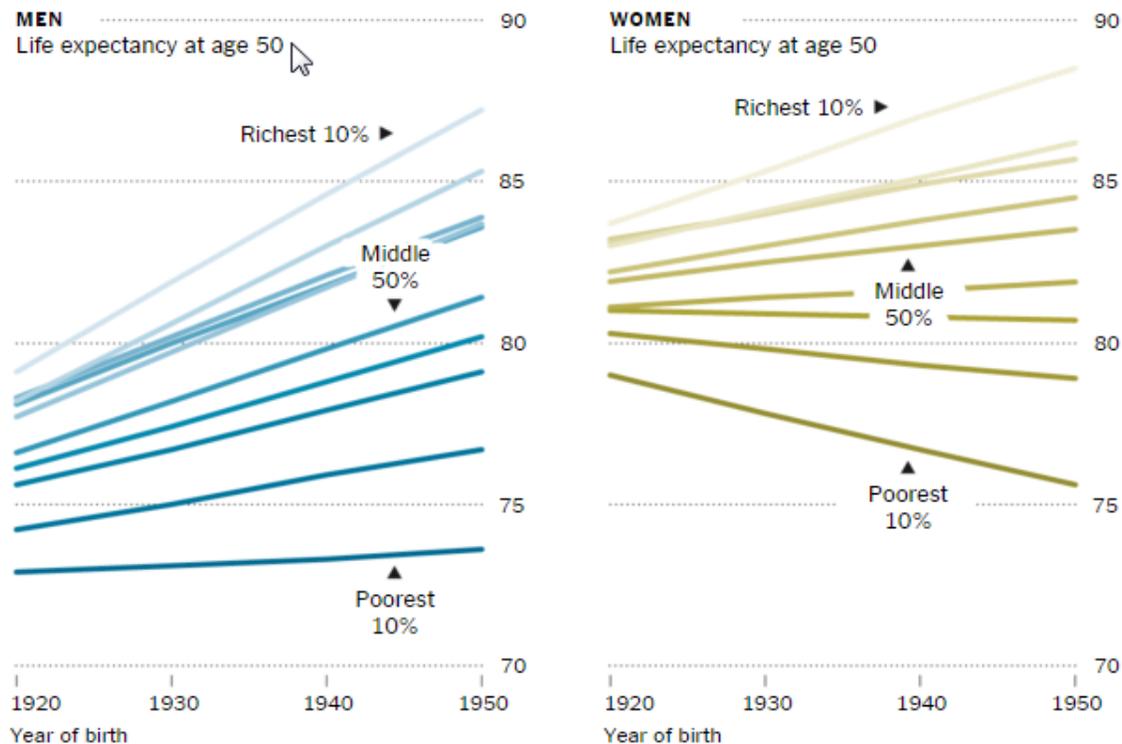


Life expectancy falling for the poor, rising for the rich



An Expanding Longevity Gap

Wealthier Americans tend to live longer than poorer Americans. Despite advances in medicine and education, the difference in life span after age 50 between richest and poorest has more than doubled since the 1970s.

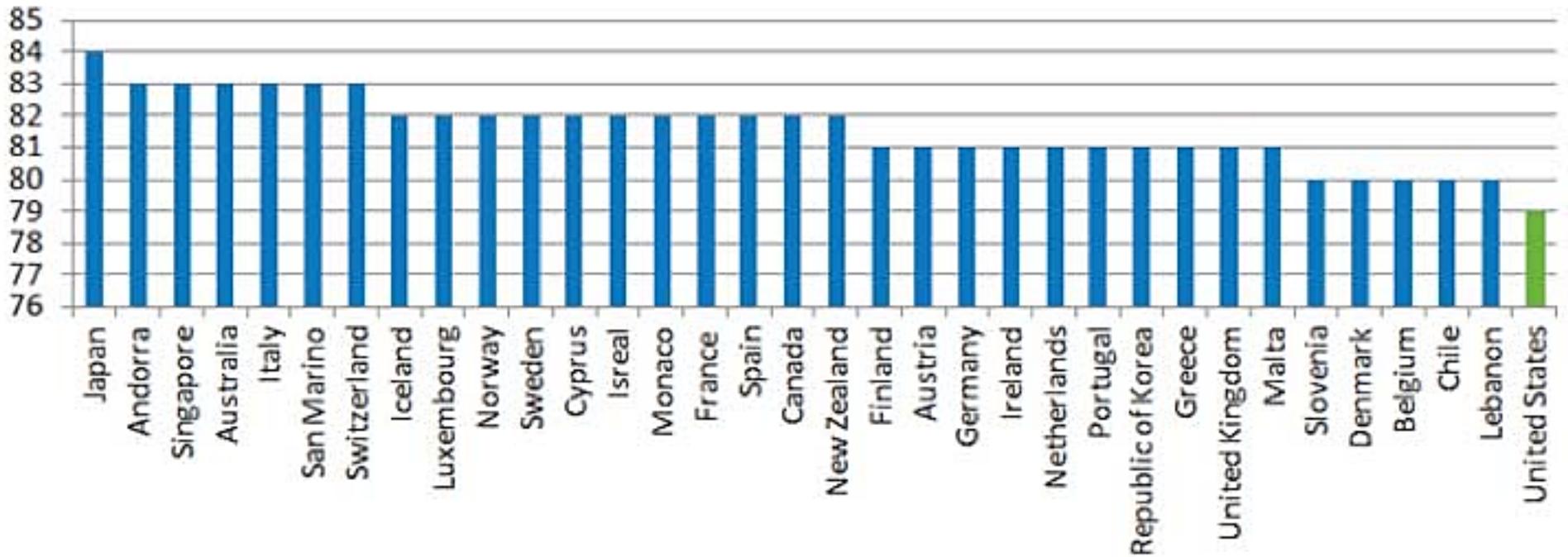


Sources: Brookings Institution; U. of Michigan Health and Retirement Study

By The New York Times

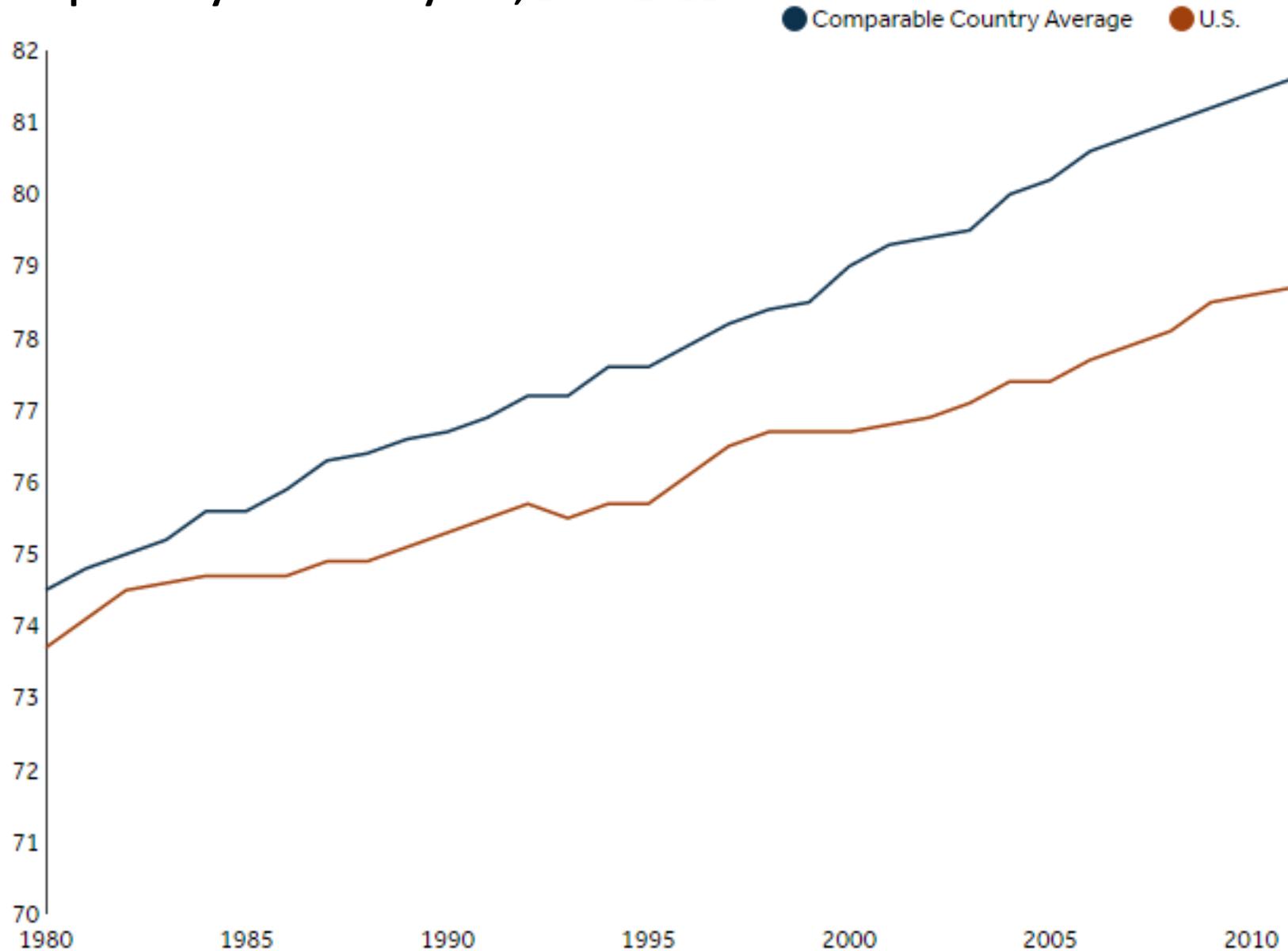
From NIA
Health and
Retirement
Study data

U.S. ranks 34th in life expectancy at birth



Source: America's Health Rankings, APHA, 2014

Total life expectancy at birth in years, 1980-2011



Source: Kaiser Family Foundation analysis of 2013 OECD data: "OECD Health Data: Health expenditure and financing: Health expenditure indicators." OECD Health Statistics (database). doi: 10.1787/data-00349-en (Accessed on June 25, 2014). Note: Comparable countries are defined as those with above median GDP and above median GDP per capita in at least one of the past ten years.

Leading Causes of Death, Adults 65+ Years, 2014

Rank	Cause of Death
1	Heart disease
2	Cancer
3	Chronic lower respiratory diseases
4	Stroke
5	Alzheimer's disease
6	Diabetes
7	Accidents (unintentional injuries)
8	Influenza and pneumonia
9	Kidney disease
10	Septicemia

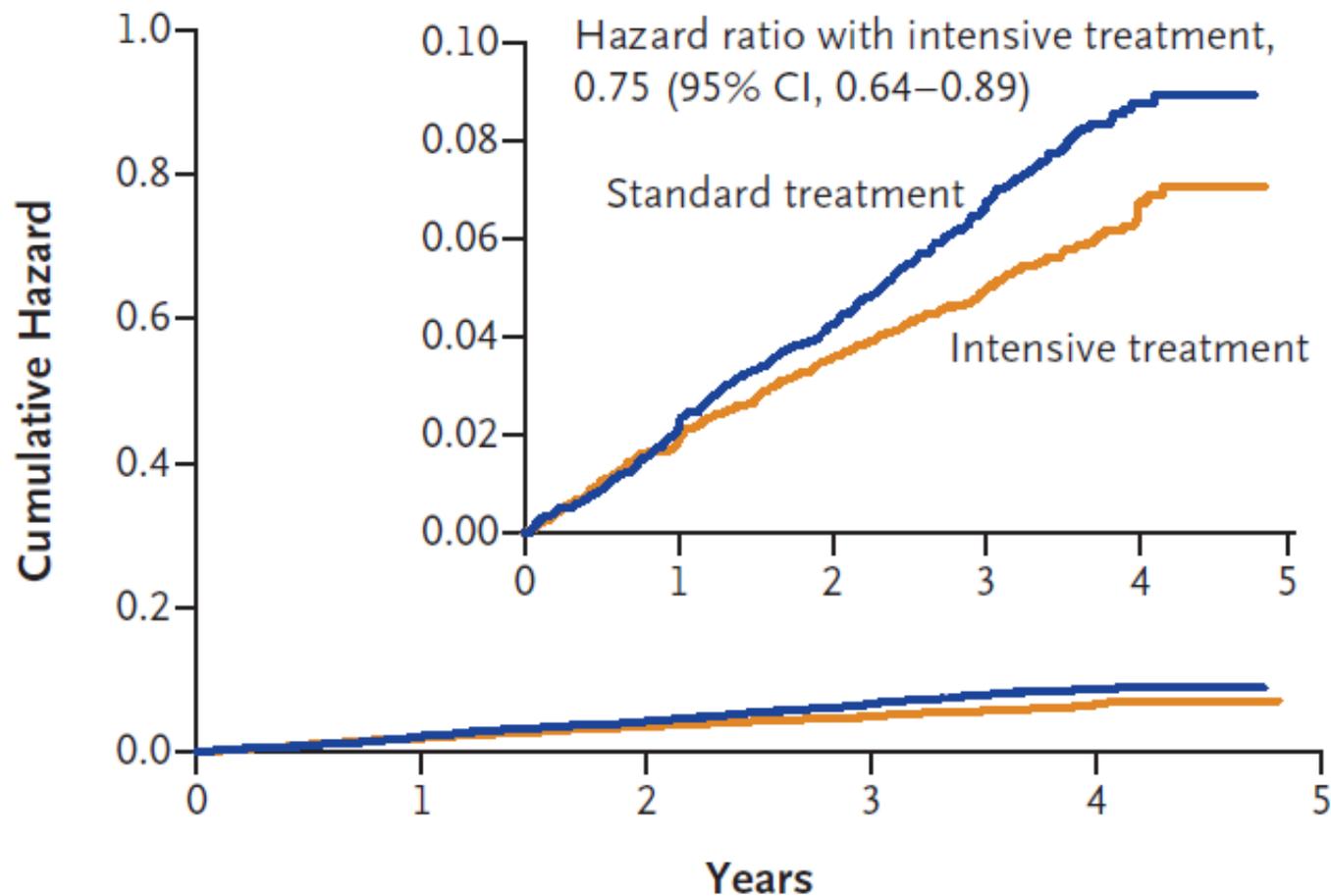
SOURCE: CDC/NCHS,. Public-use 2014 Mortality File. Deaths: Final data for 2014. National vital statistics reports . Available from:
http://www.cdc.gov/nchs/data/dvs/lcwk3_2014.pdf

Clinical Research at NIH

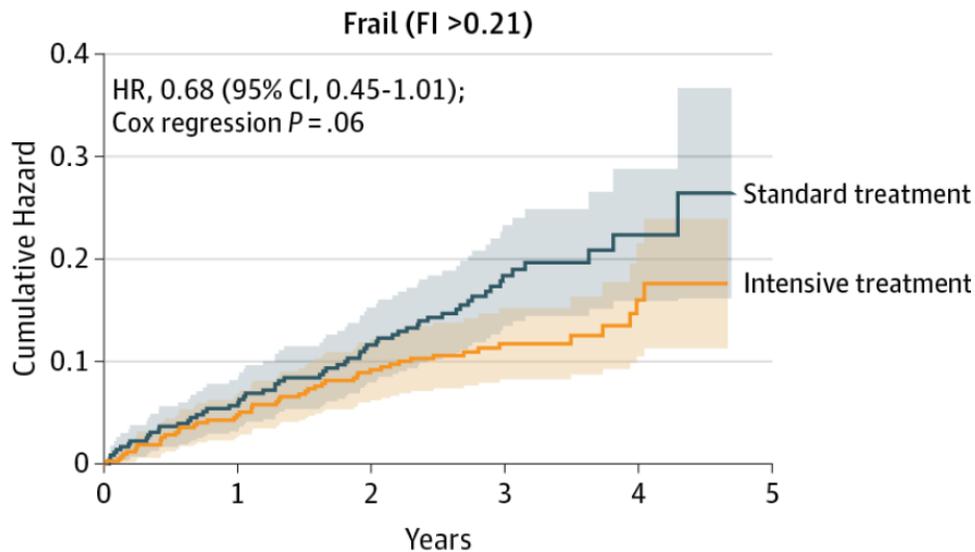
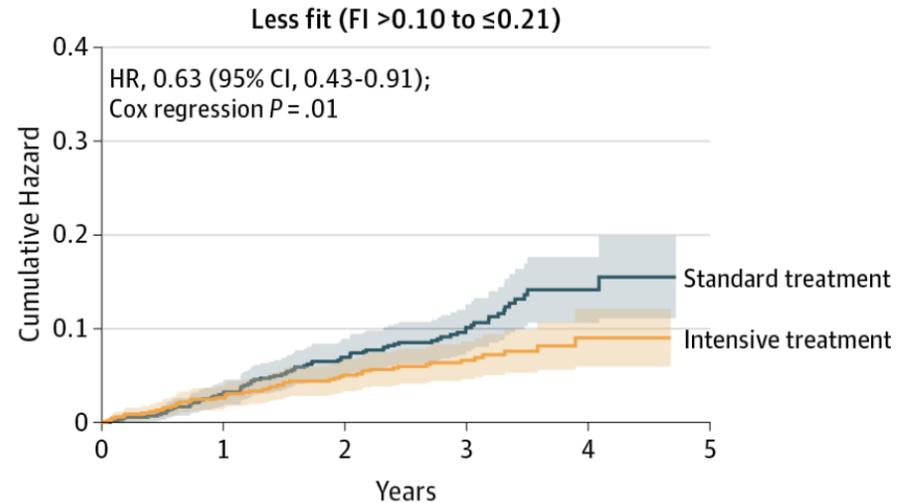
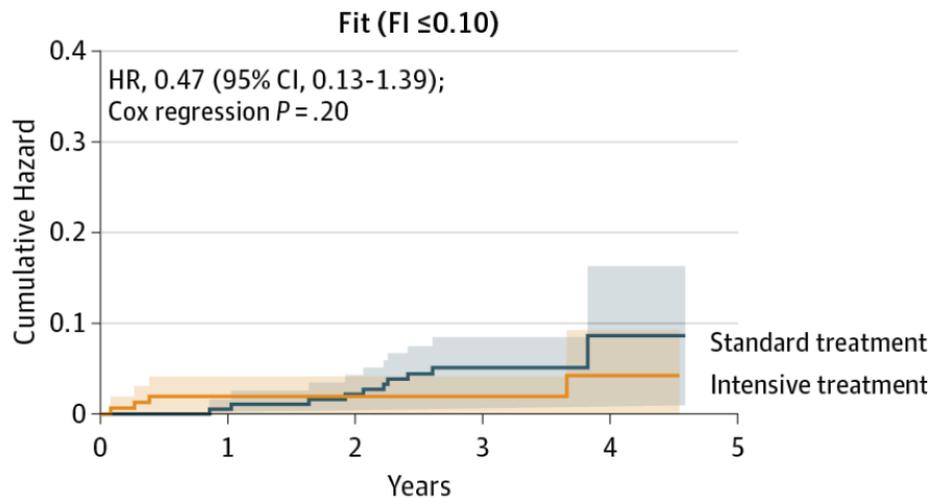
- Advances our understanding of many conditions that contribute to these causes of death
- Diverse clinical trials include:
 - SPRINT study
 - Smoking Cessation Programs
 - UFOV Training
 - Diabetes Intervention
 - AD Trials

SPRINT Study

Systolic Blood Pressure Intervention Trial Primary Outcome

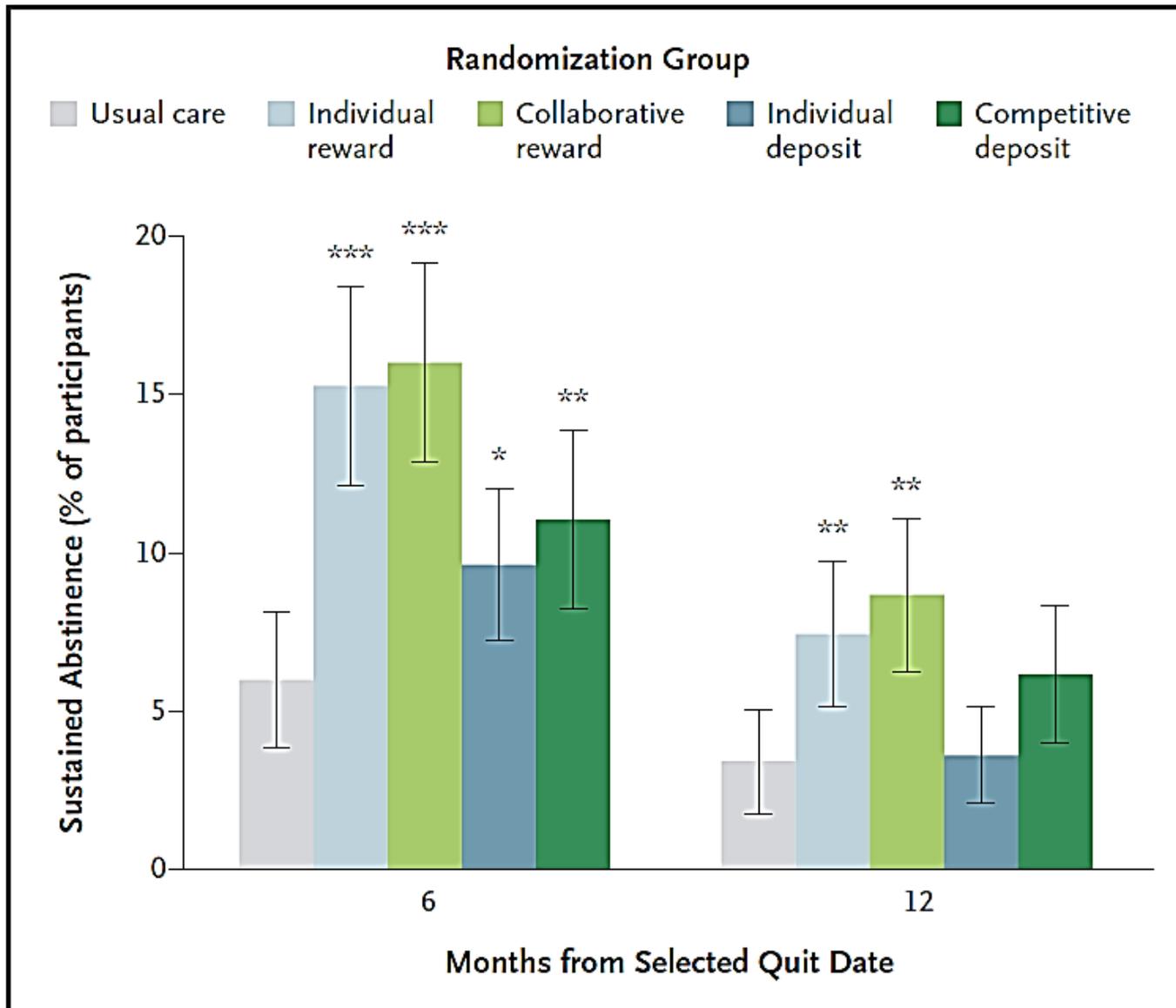


SPRINT Follow-up in Adults 75 years or Older

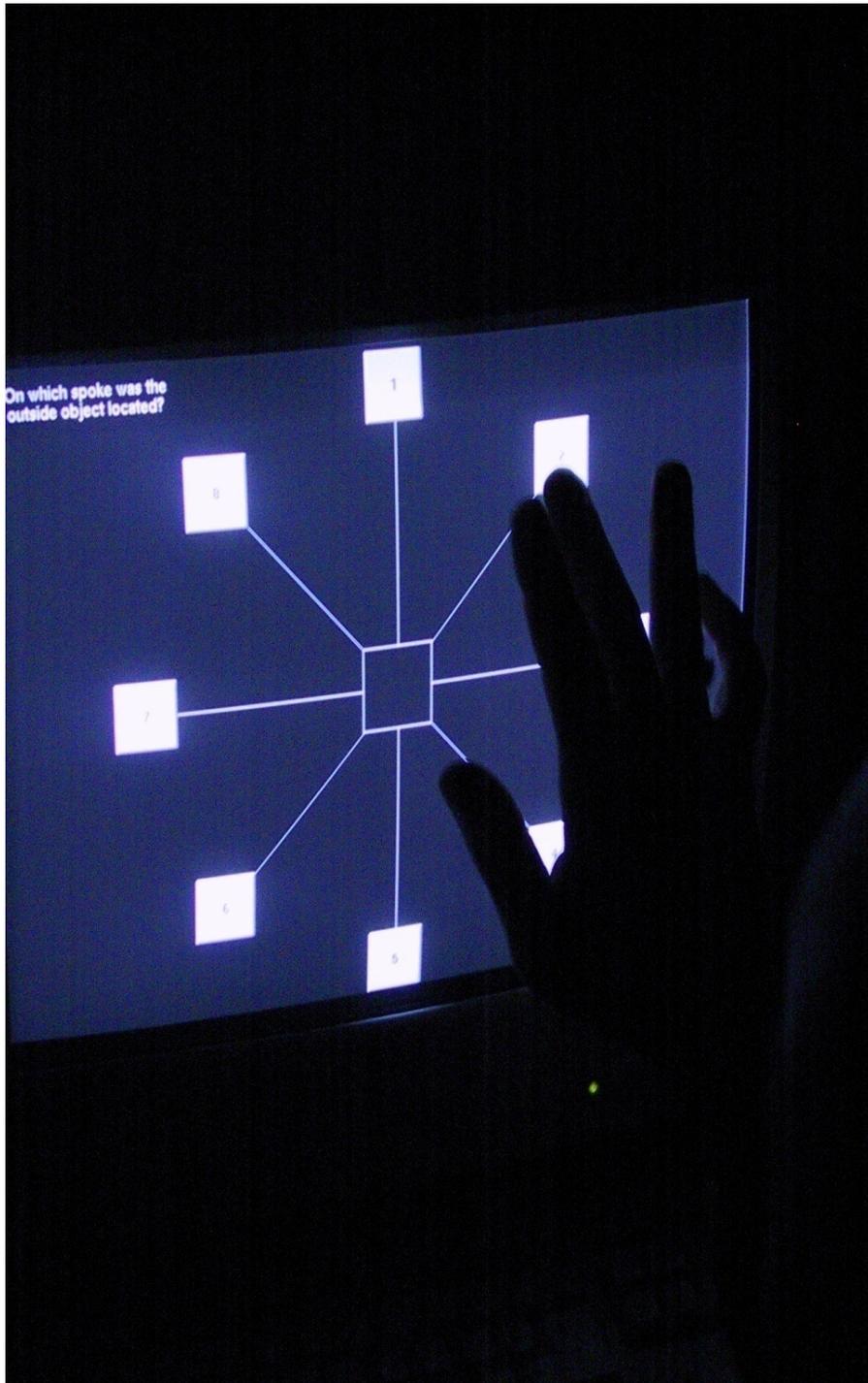


- Cumulative hazard was reduced in participants, even those less fit and frail
- Incident cardiovascular disease was reduced by 33% and mortality (from any cause) was reduced by 32%
- The rate of serious adverse events was not statically different across treatment groups, including among the most frail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

Randomized Trial of Financial-Incentive Programs for Smoking Cessation



“Reward” and “Commitment” participants quit more often than treatment as usual



Useful Field of View

Area from which one can extract visual information at a glance without head or eye movements. Visual impairment, difficulties in dividing attention or ignoring distracting information, and slower processing speed could all contribute to reductions in UFOV.

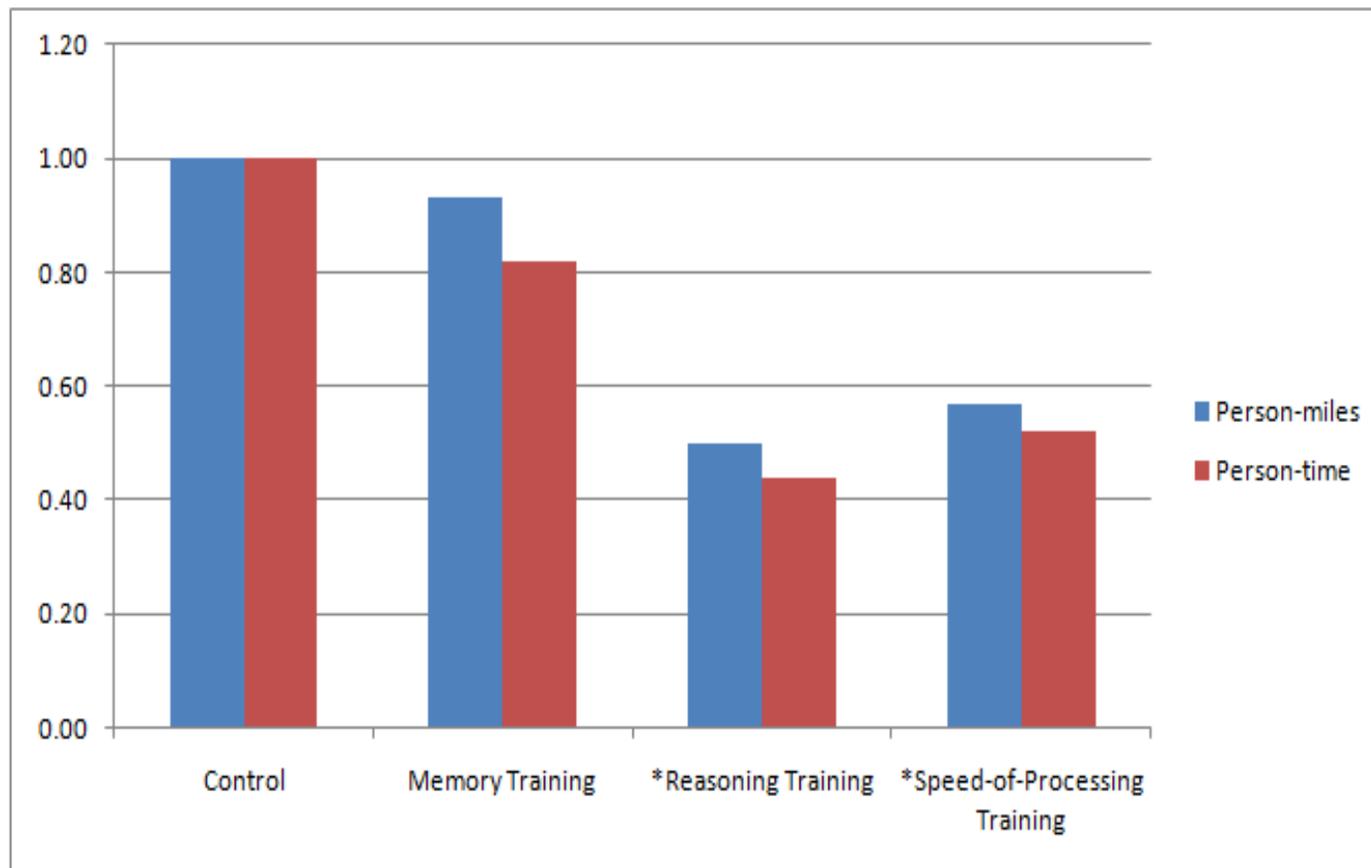
Karlene Ball (NIA grantee) was the co-developer of UFOV and has also shown that by *training* UFOV you can prospectively reduce crash rates (e.g., Ball, Edwards, and Ross, 2007)

MD, CA, and FL Motor Vehicle Departments are using and testing UFOV and State Farm and All State are offering discounts with this training.

UFOV Training Reduces Automobile Crashes

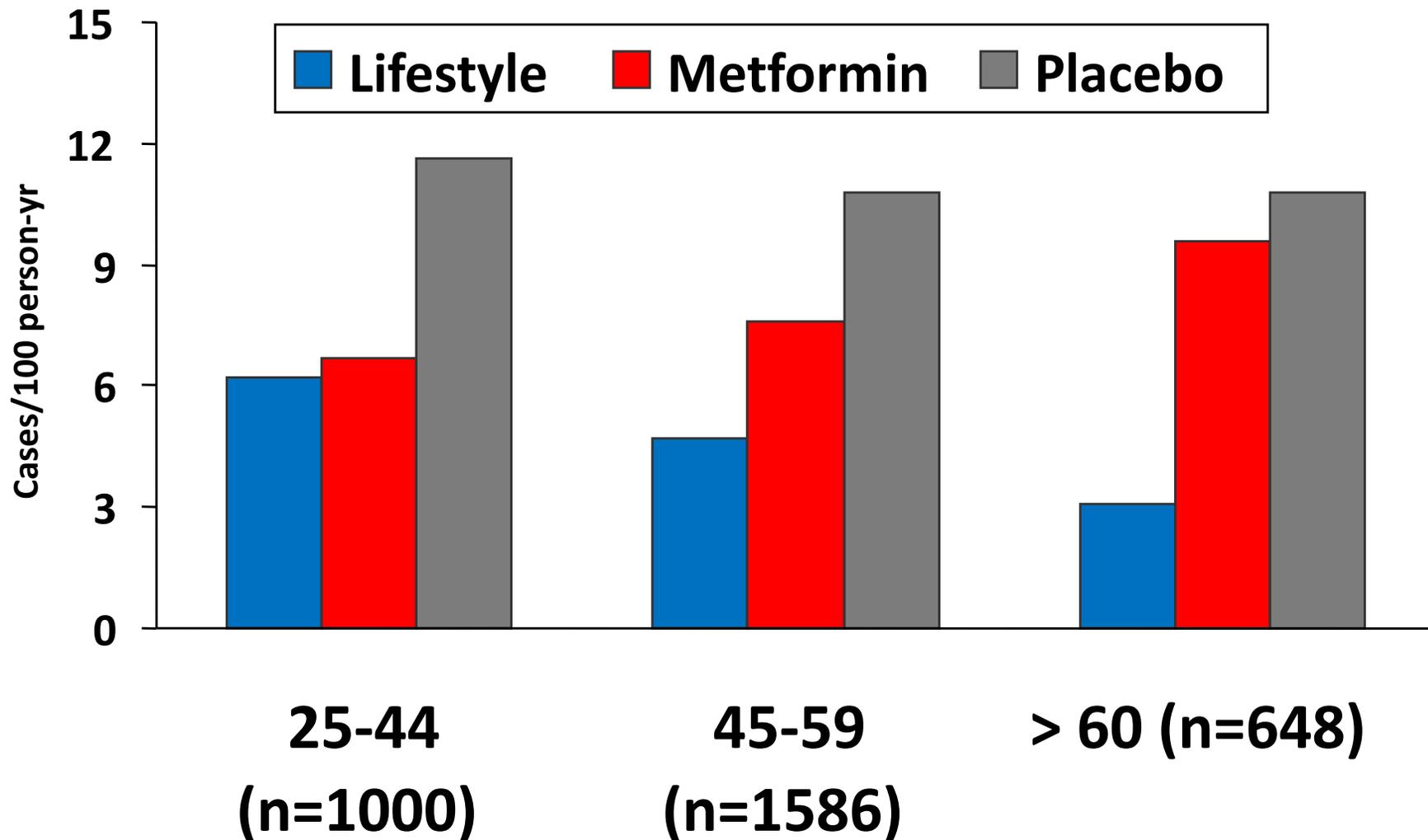
- Older adults randomized to training experienced half the number of at-fault crashes (results from ACTIVE)

Adjusted Odds Ratio for At-Fault Crashes (5-year Crash Data)



*significant associations

Lifestyle Influence on Diabetes Incidence



Neuropathologic Changes Characteristic of Alzheimer's Disease

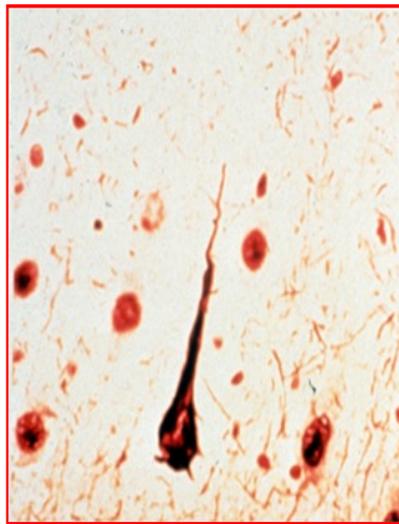
Normal



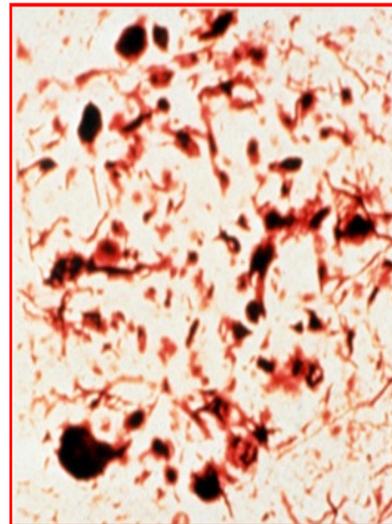
AD



**Neurofibrillary
Tangles**

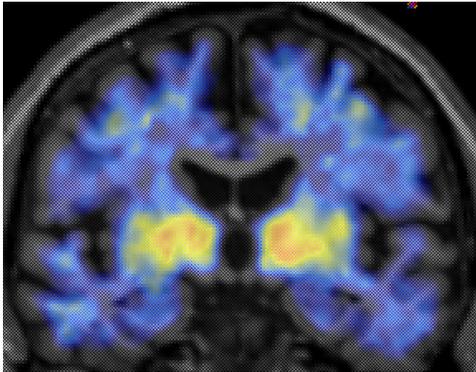


Senile Plaques

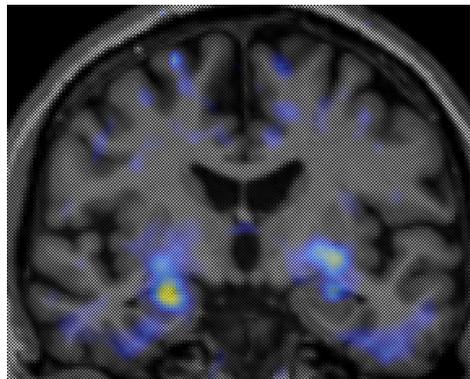


Amyloid and Tau PET Imaging

A β
(PiB)



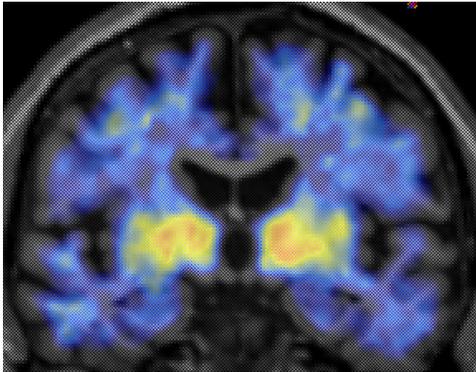
Tau
(T807)



CN

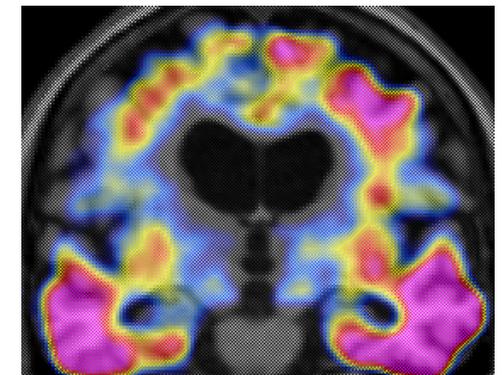
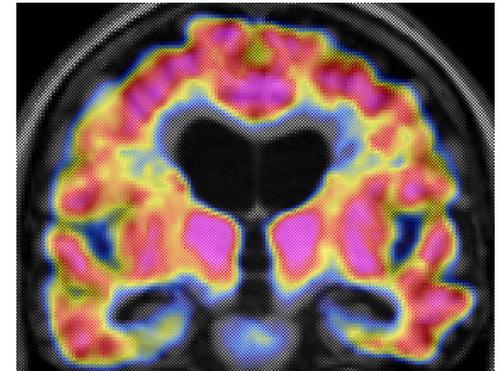
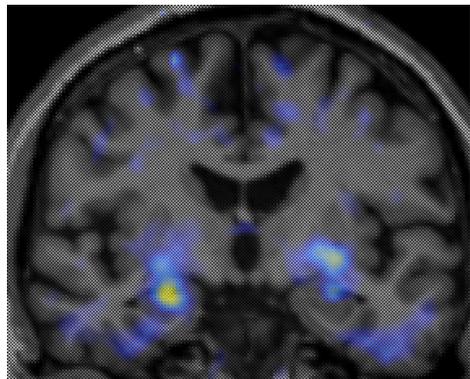
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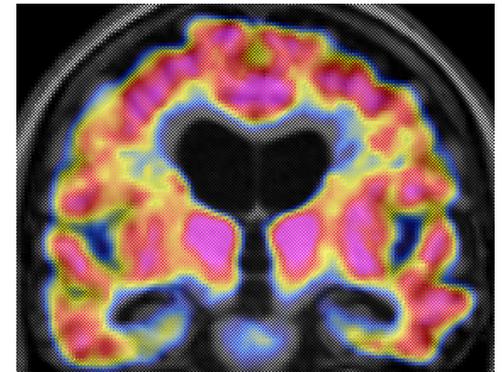
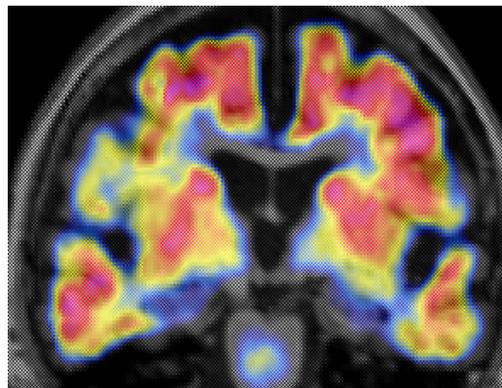
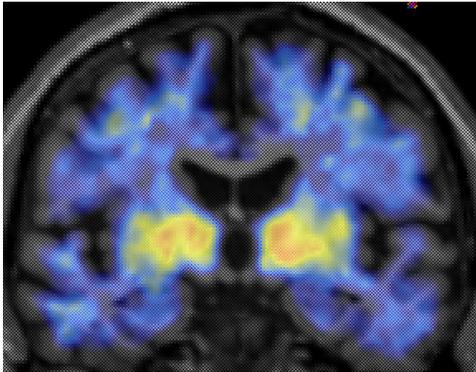
Tau
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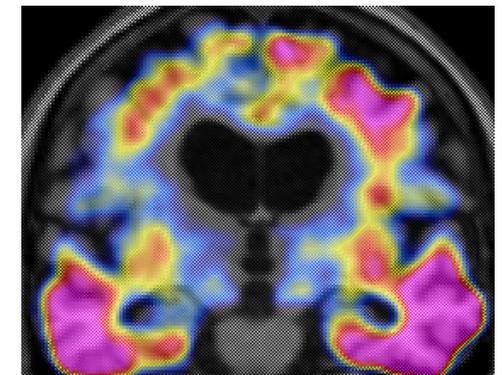
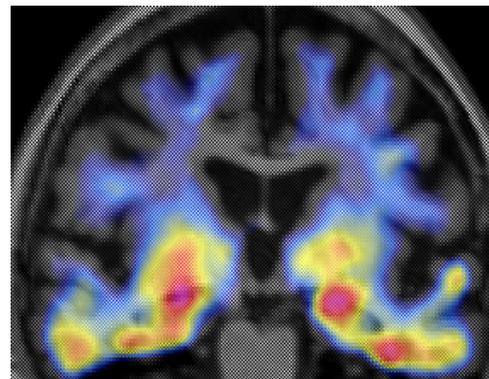
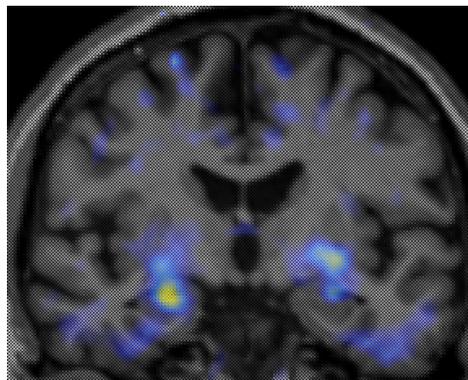
AD
Dementia

Amyloid and Tau PET Imaging

A β
(PiB)



Tau
(T807)

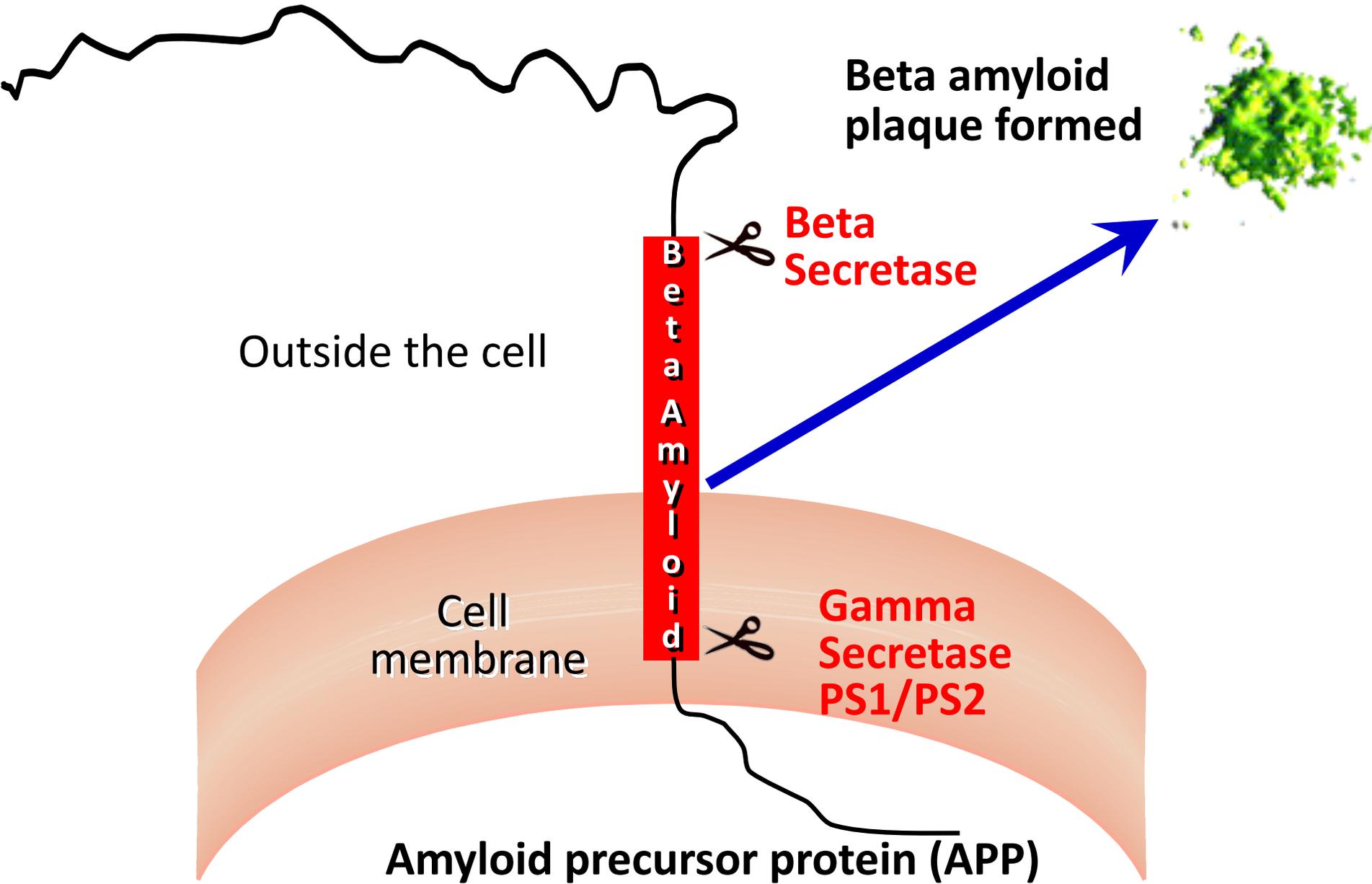


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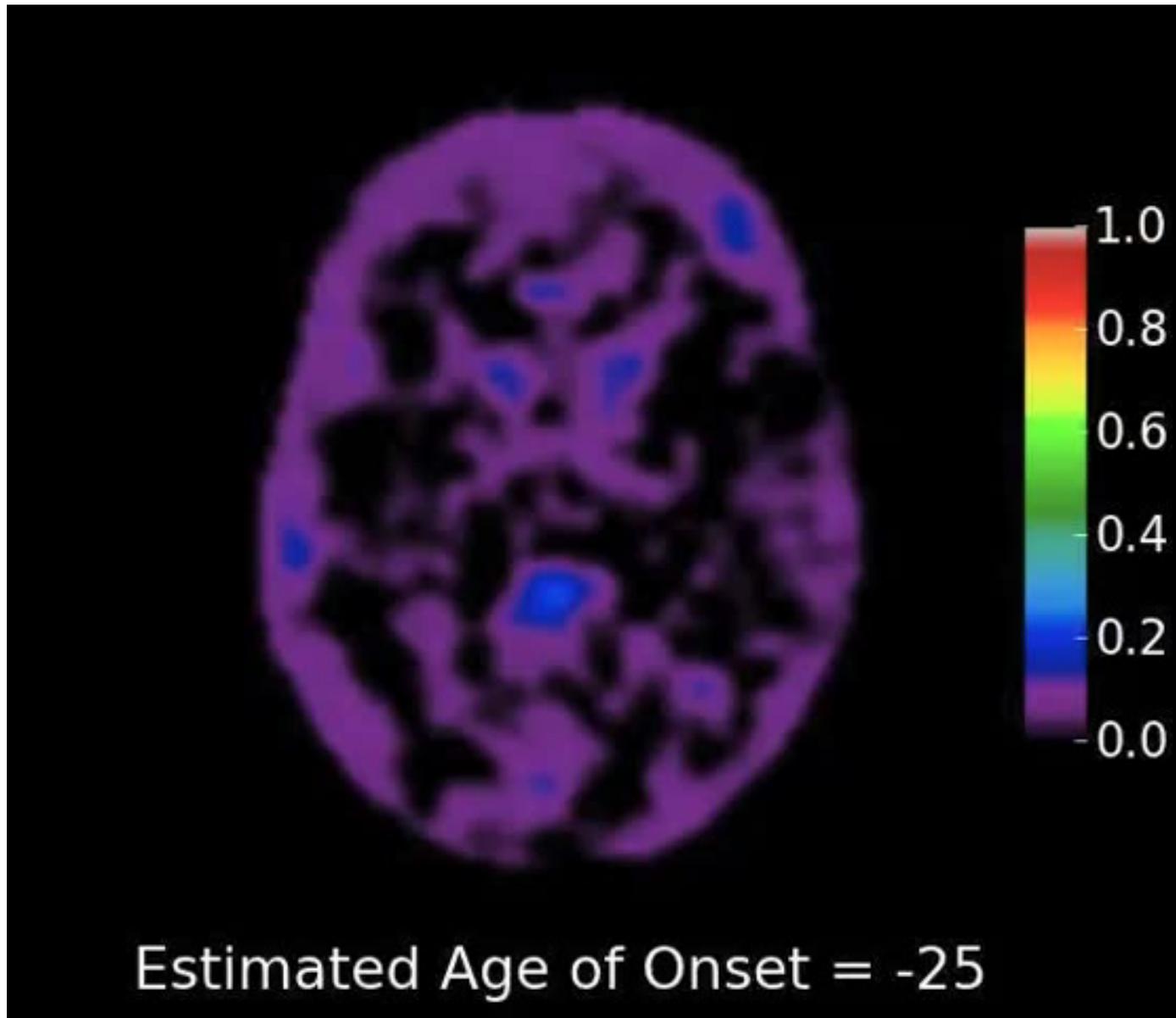
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AD
Dementia

Production of Amyloid Plaques

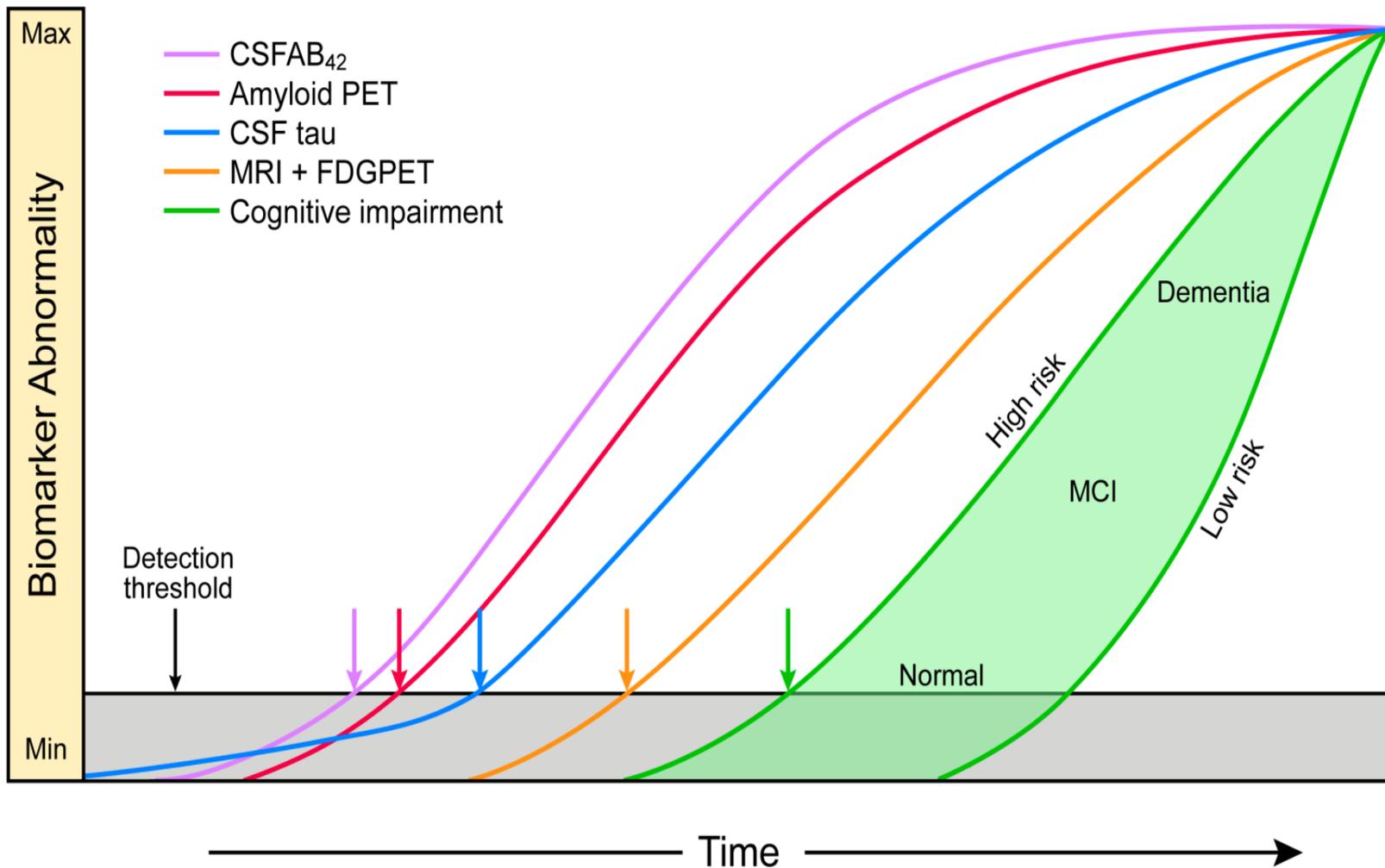


A β Deposition in Autosomal Dominant Alzheimer's Disease Years before Expected Clinical Symptoms

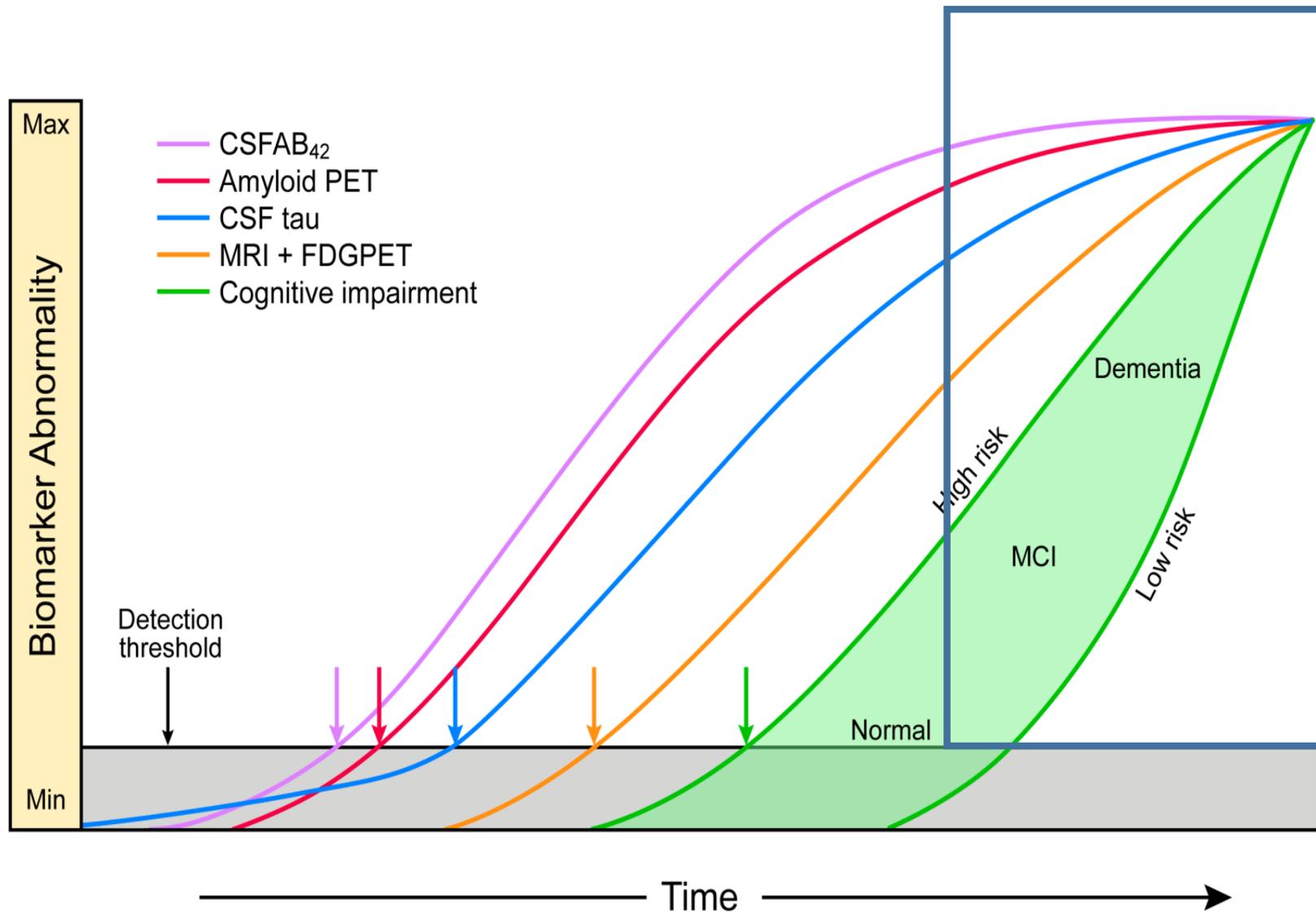


Courtesy of Tammie Benzinger; Bateman, R et al. (2012) *N Engl J Med* 367(9):795-804.

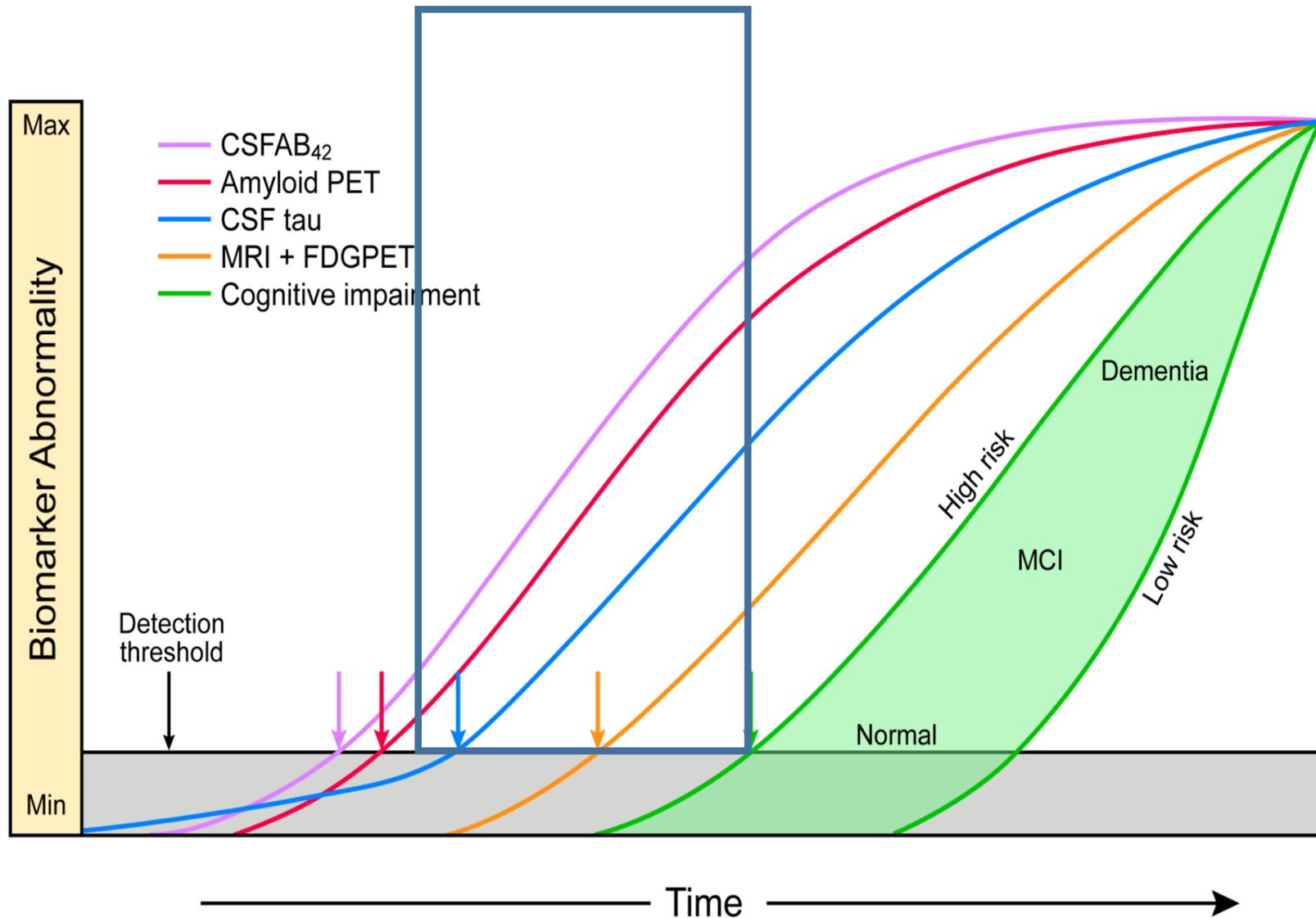
Alzheimer's disease: Biomarker progression



Alzheimer's disease: Treating symptomatic disease



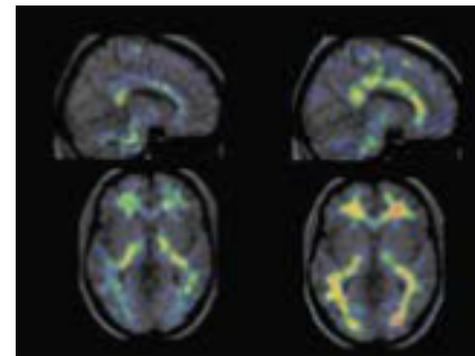
Alzheimer's disease: Intervening early



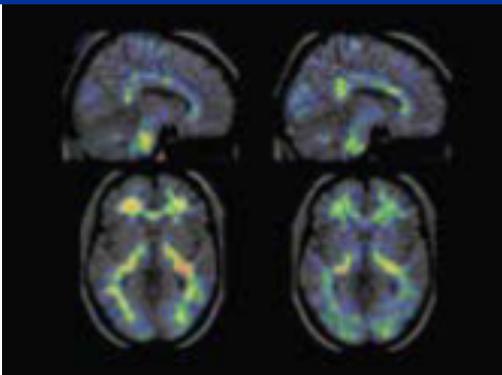
Early Interventions are in Trials Now

A family in Colombia that develops AD early is generously working with researchers

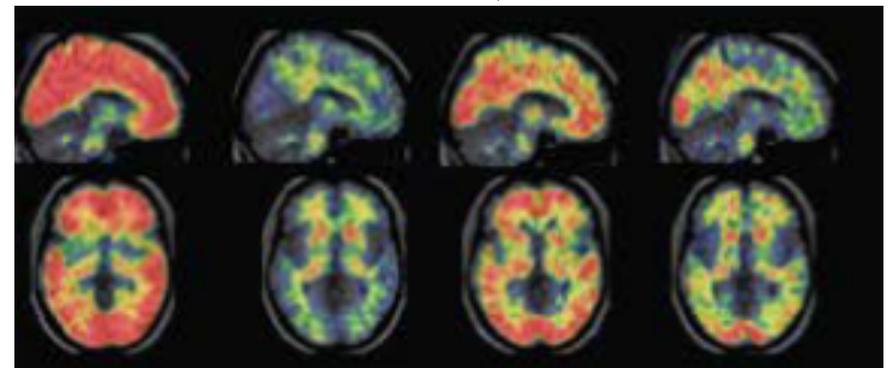
Non-Carriers, late 30's



Beta-amyloid, late 20's



Gene Carriers, late 30's

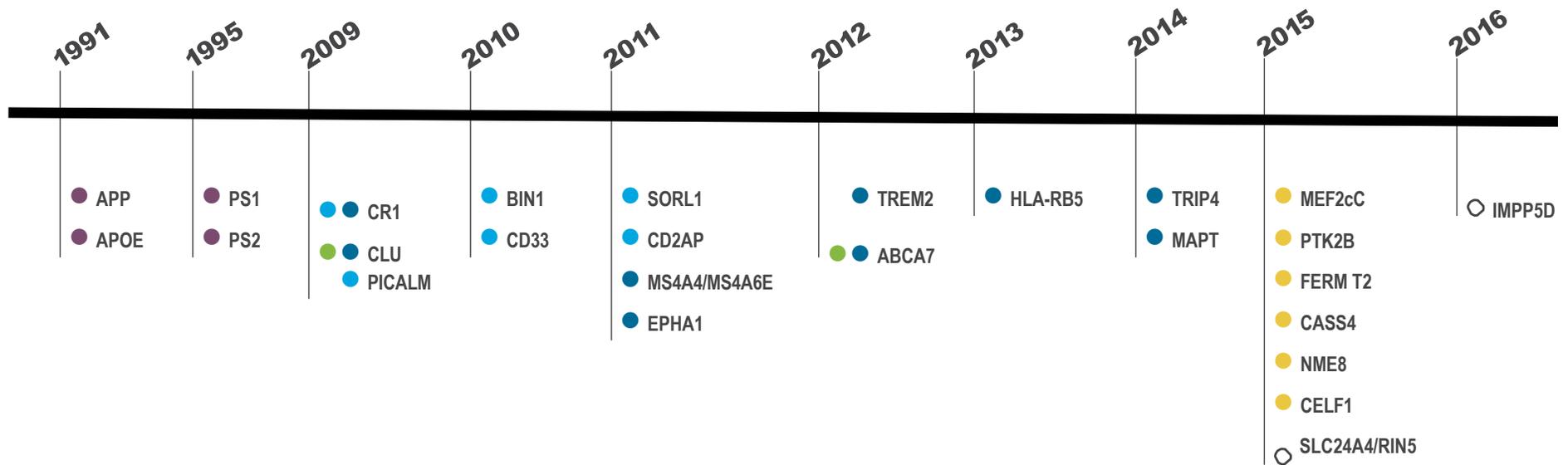


Dementia onset is in late 40's

Genetic Regions of Interest in Alzheimer's Disease

By year of discovery

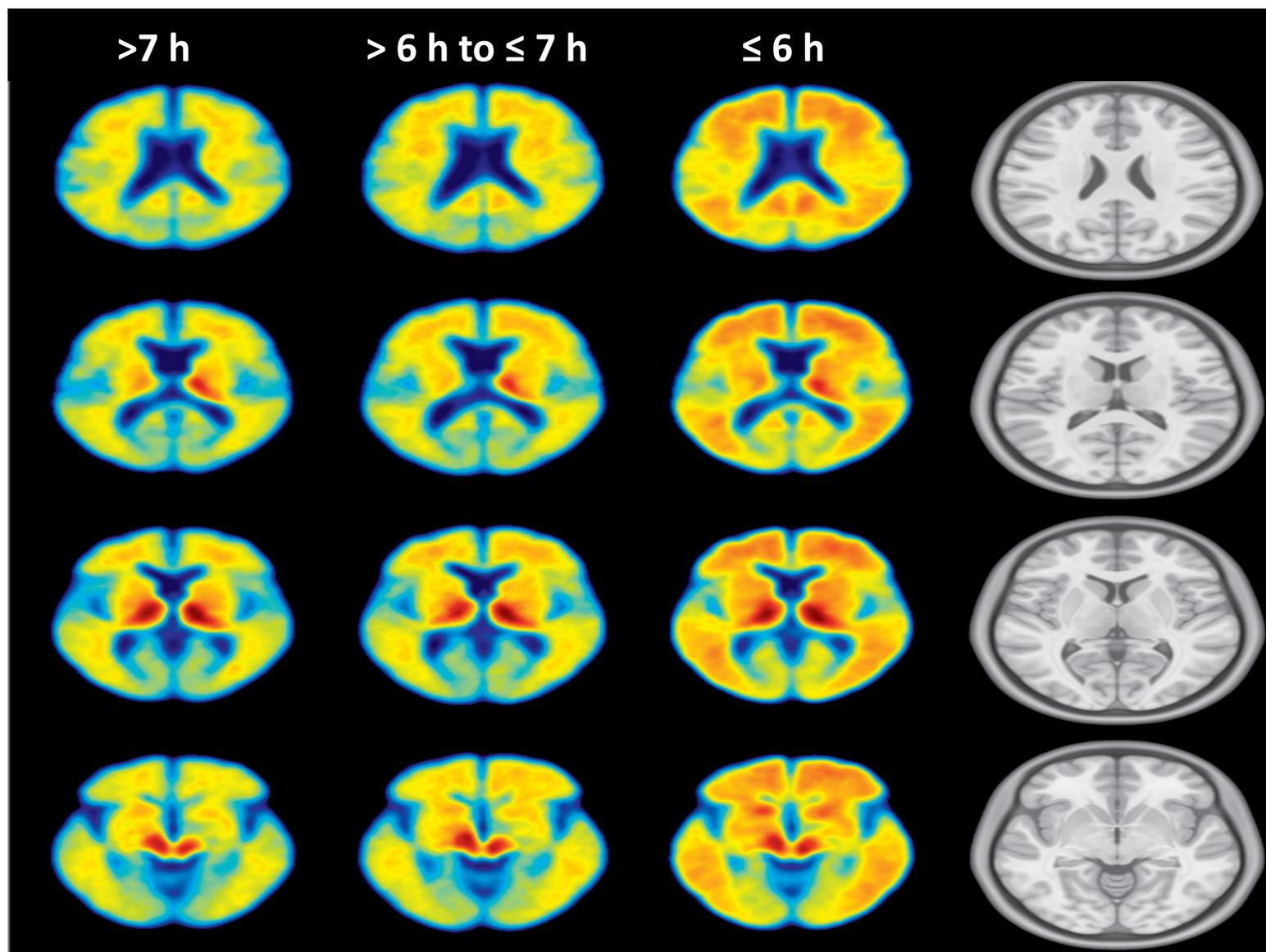
NOTE: Color indicates mechanism of action in the body. See key below.



KEY

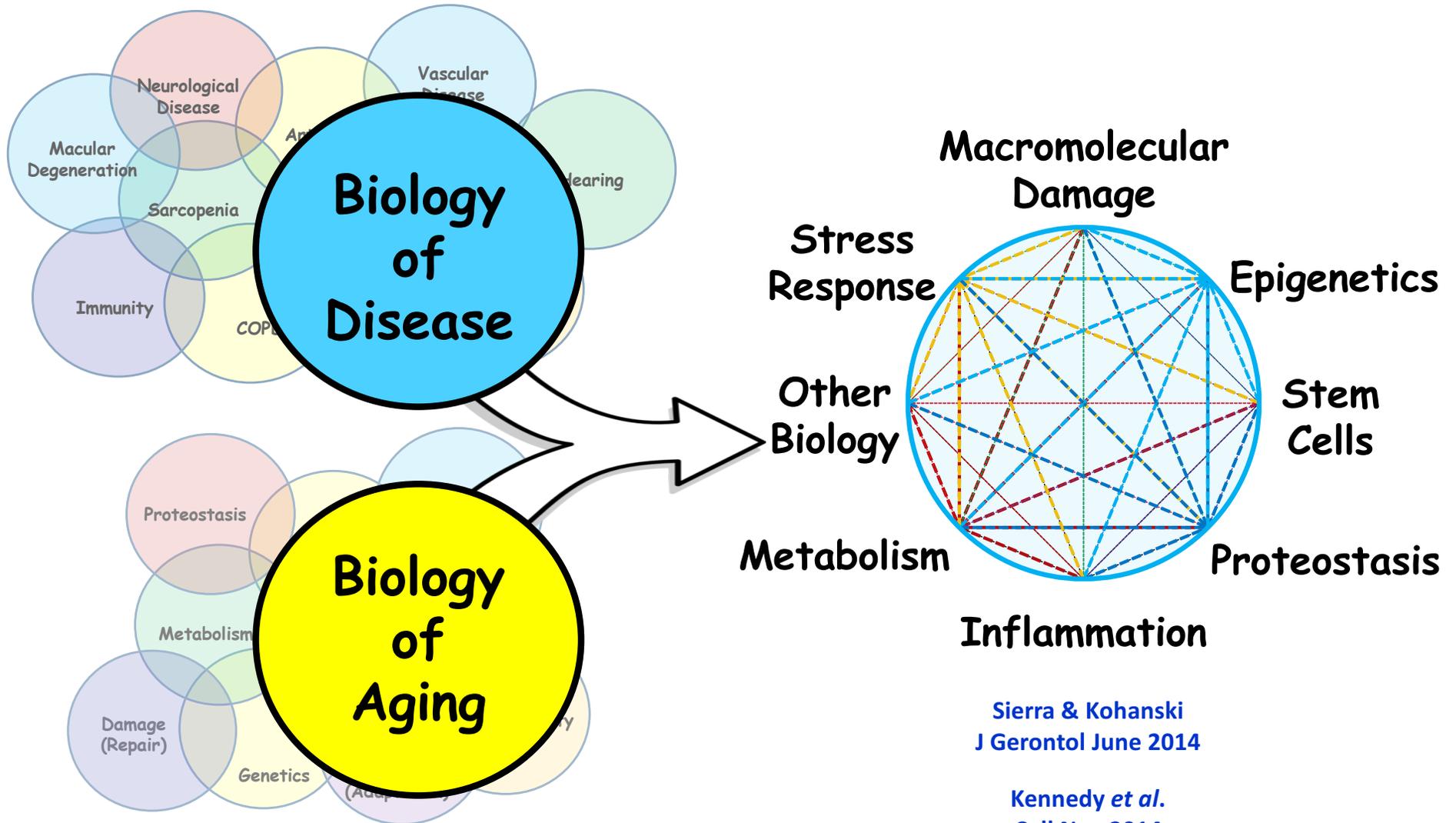
- Early-onset genes
- Innate immune/brain inflammatory response genes
- Endocytosis and cellular protein trafficking, including APP trafficking and Aβ processing
- Lipid transport/metabolism
- Synaptic transmission
- Cytoskeletal function, including tau
- No assigned mechanism of action

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

The Emergence of Geroscience

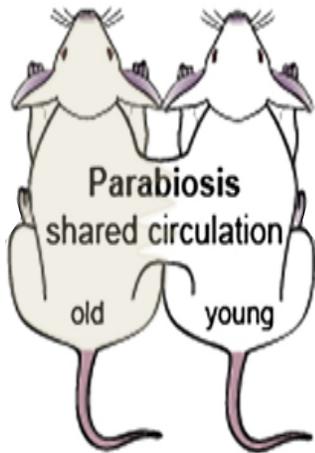


Sierra & Kohanski
J Gerontol June 2014

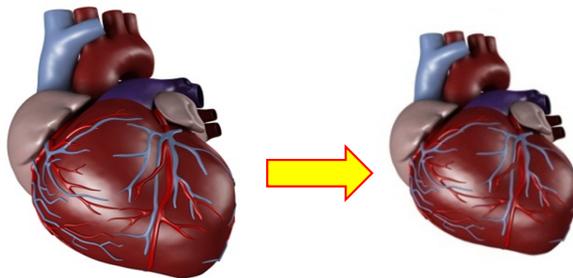
Kennedy *et al.*
Cell Nov 2014

Aging Intervention Affects Multiple Health Parameters

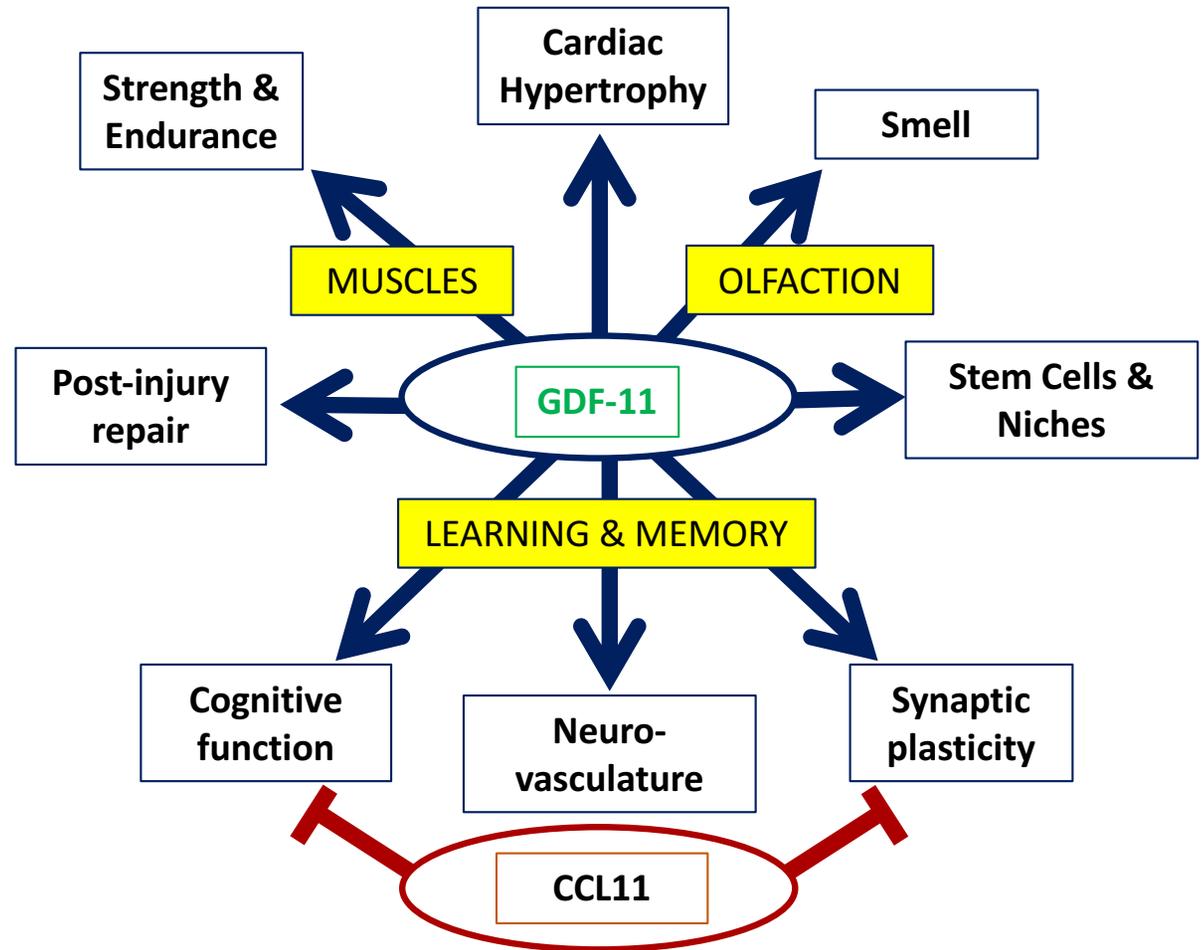
Heterochronic parabiosis



Conboy et al.
Nature 433: 760 (2005)

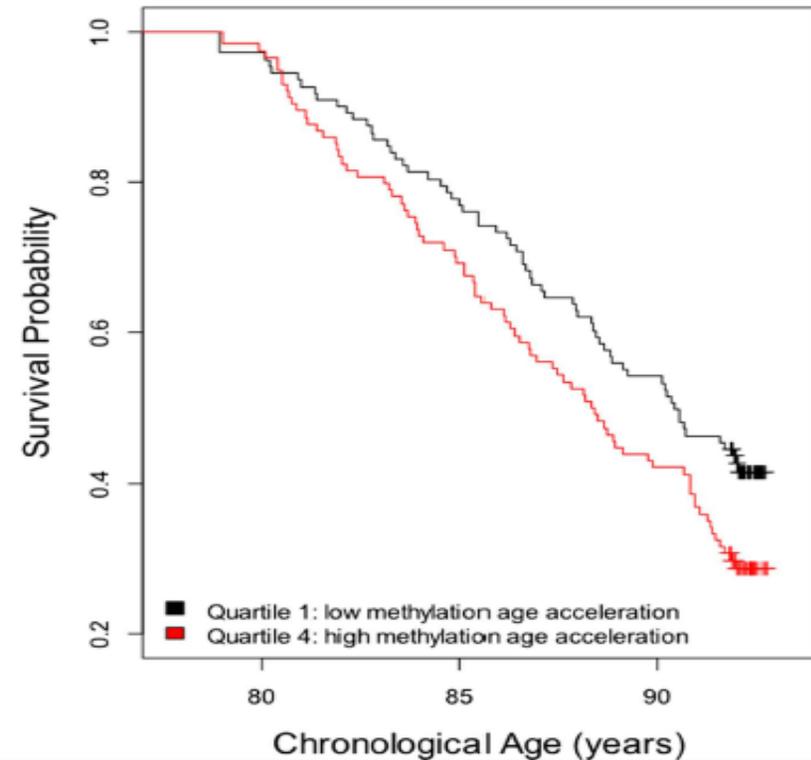
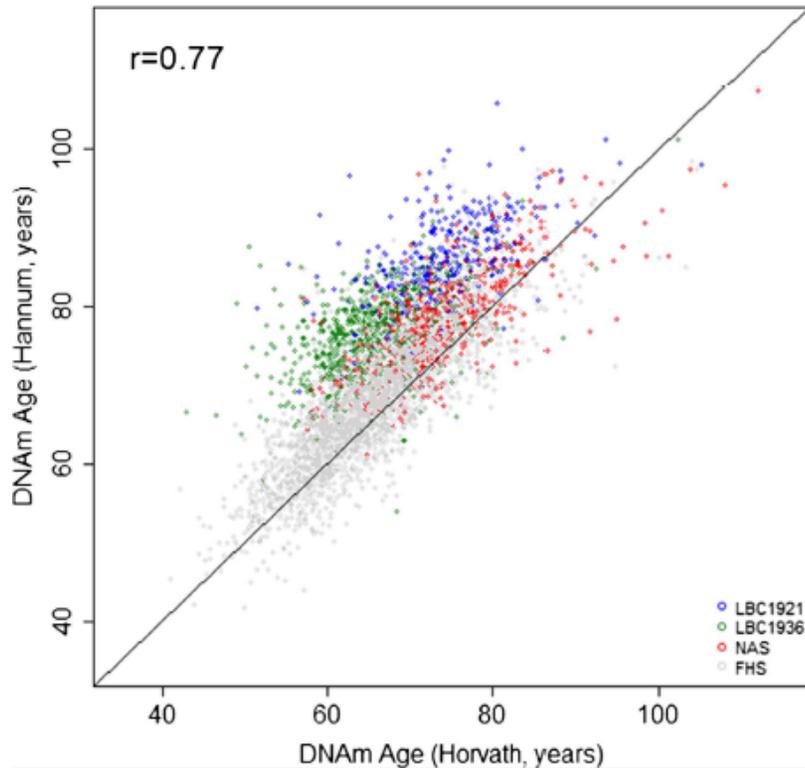


Loffredo et al. *Cell* 153: 828 (2013)



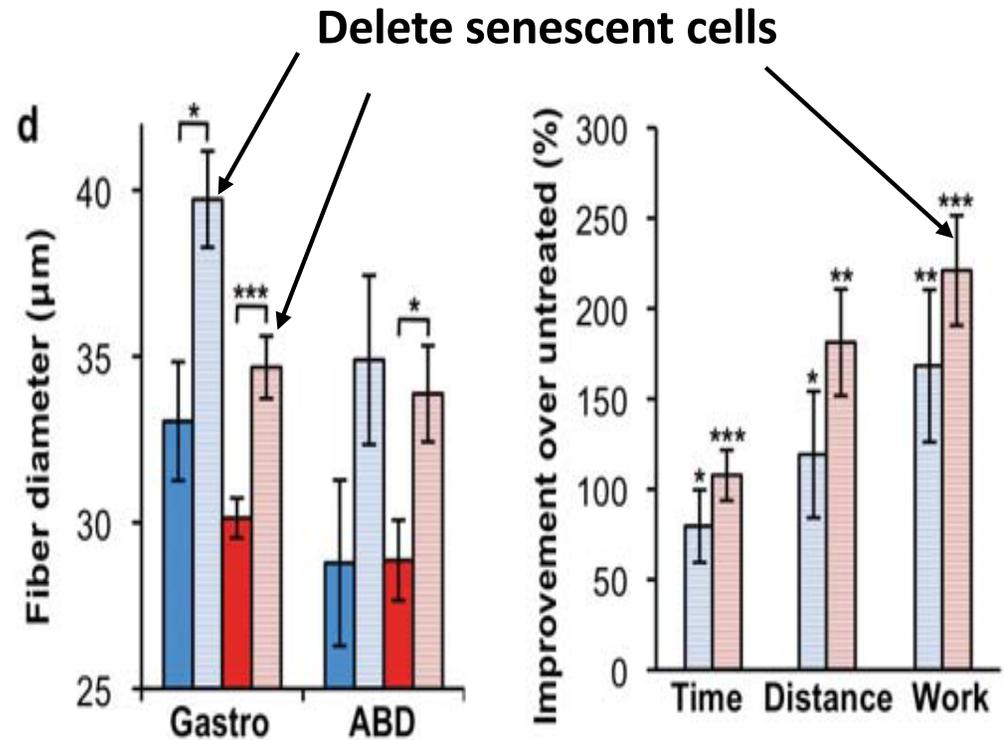
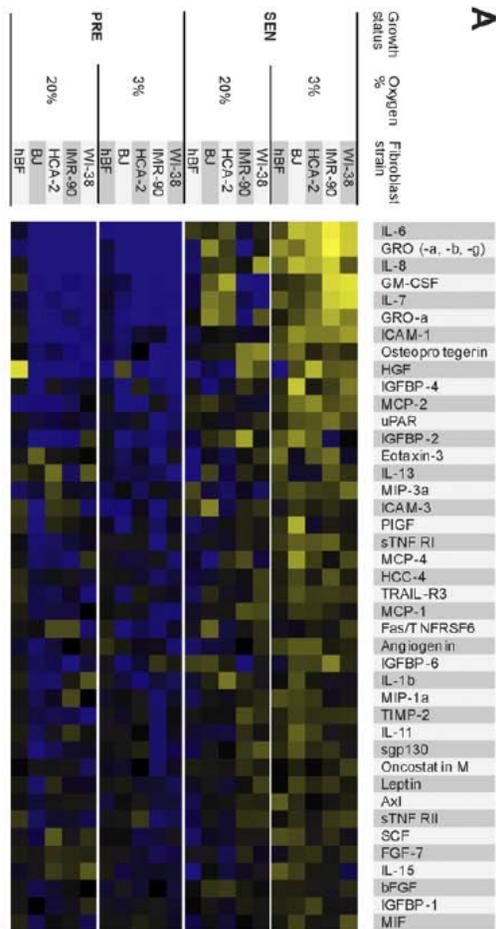
Villeda et al. *Nature* 477: 90 (2011); Villeda et al. *Nat Med* 20: 659 (2014);
Sinha et al. *Science* 344: 649 (2014); Katsimpardi et al. *Science* 344: 630 (2014)

DNA Methylation Predicts All-cause Mortality

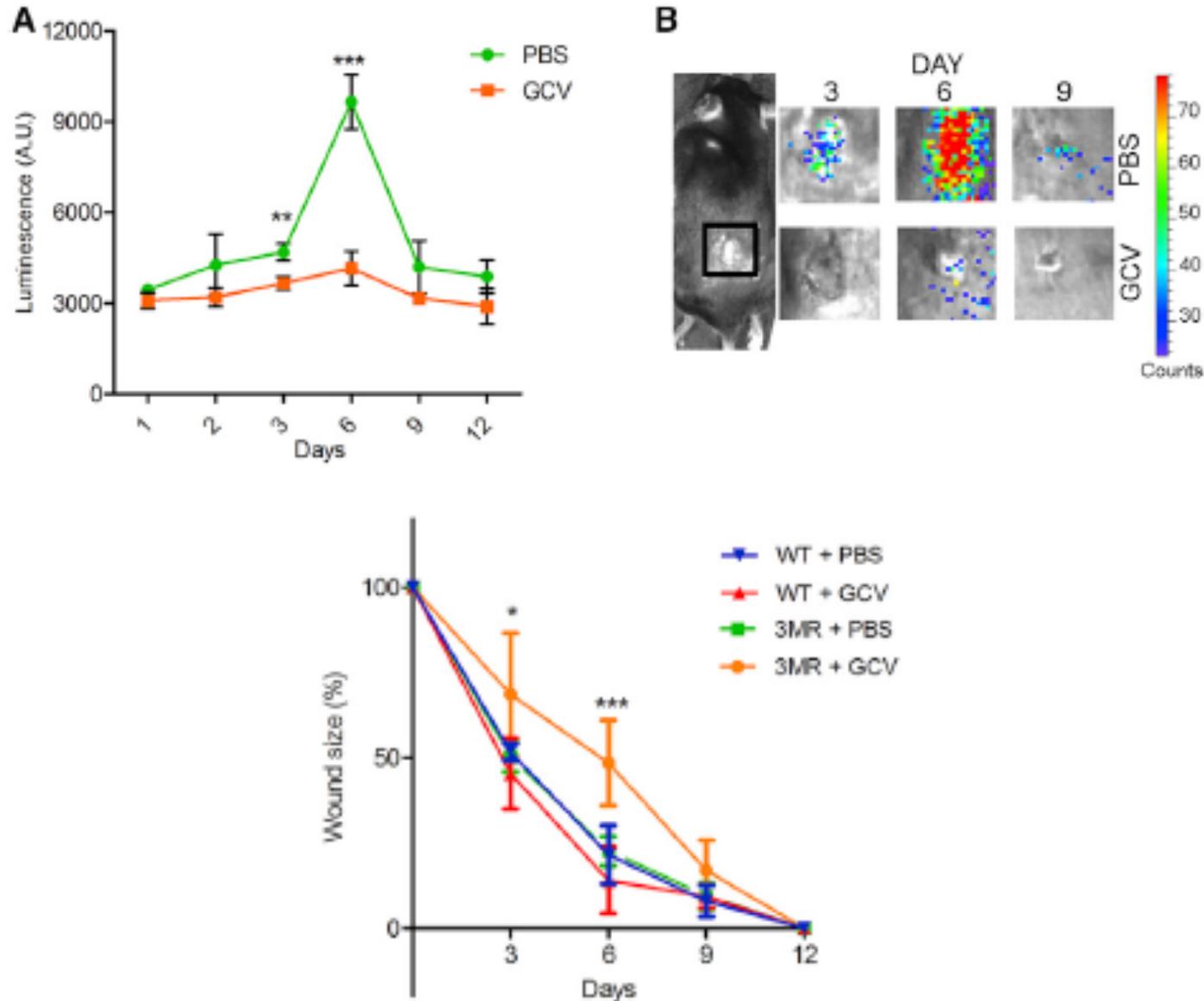


- High correlation between two papers addressing DNA Methylation (Hannum and Horvath)
- Methylation status correlates with all cause mortality

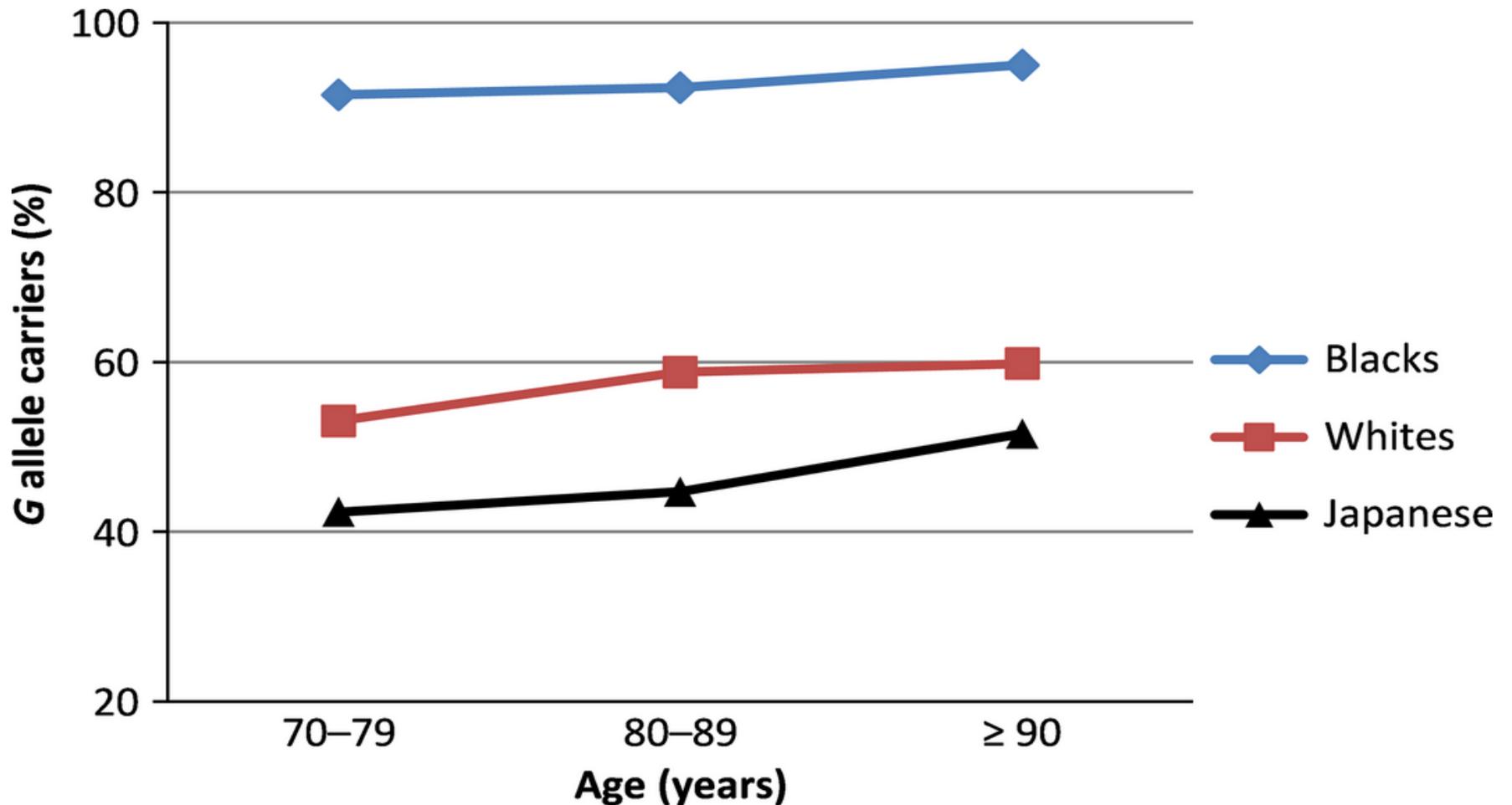
Senescent Cells are Physiologically Active



Senescent Cells have Beneficial Functions



FOXO3 genotype and age at death



Carrier status for the protective G allele increased with age for individuals in their 70s to ≥ 90 years old, consistent with protection against mortality for carriers in the three populations

Summary

- The world is growing older; but life expectancy is decreasing for several groups
- Age is a risk factor for many serious health conditions
- Research has contributed to advances in understanding many of these specific conditions and how to treat or prevent them
- Geroscience is an emerging field that helps us understand why aging is a risk factor – in the hope that we can extend *healthspan* as well as lifespan

