

Update on Alzheimer's Research

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Medical & Scientific Relations

Overview

- Role of the Alzheimer's Association
- Landscape of Alzheimer's and dementia
- Alzheimer's disease
- Risk related to Alzheimer's
- Emerging research for early detection
- Modernized criteria for diagnosis
- Current pipeline of clinical trials
- New generation of clinical trials - possible prevention

Our vision is a world without Alzheimer's disease



Our mission:

- Advance research
- Provide care and support
- Increase Concern & Awareness
- Public Policy & Advocacy Efforts

Research Roundtable

alzheimer's association®

The Global Leader in Alzheimer's Research



Connector • Convener Funder



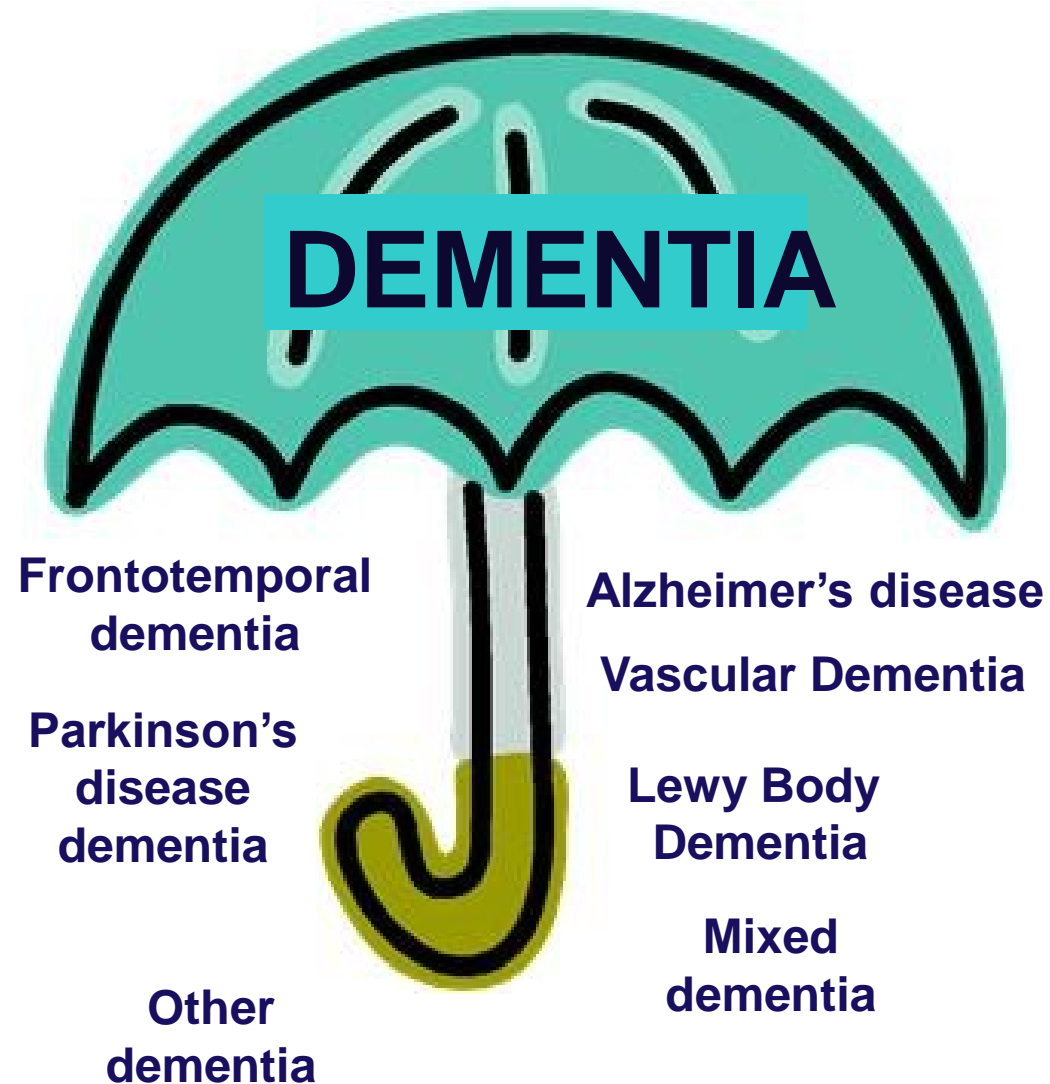
Global Leader in Alzheimer's Research

- Currently funding \$78 million of 350 active projects in 21 countries
- Over 1,000 scientists



Types of Dementia

- Dementia is the loss of memory due to changes in the brain
- Alzheimer's is the most common form
- Definite diagnosis used to require autopsy
- Many mixed cases
- Many memory disorders are reversible and not truly dementia



The Alzheimer's Epidemic Continues to Grow...

5.3

million Americans of **ALL** Ages
will have Alzheimer's in 2015

6

Of the top 10 killers,
Alzheimer's is the
only one that cannot
be prevented, cured
or even slowed.

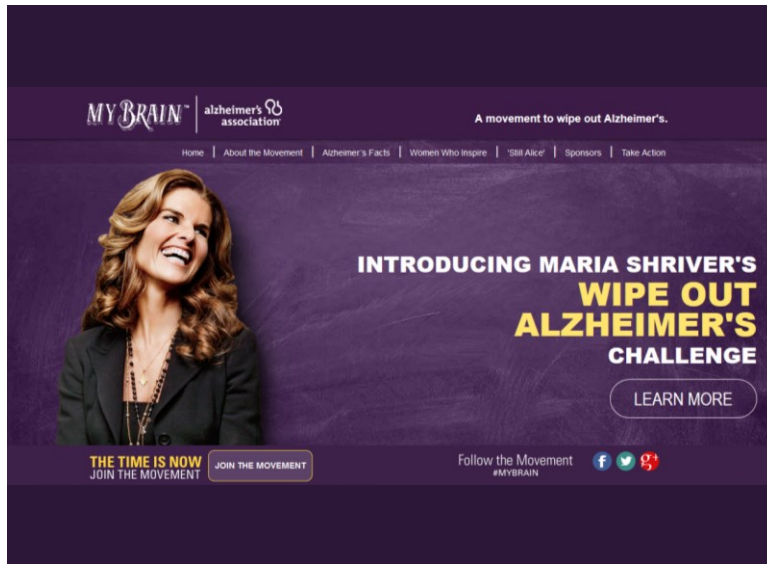
TH LEADING
CAUSE OF DEATH
IN THE U.S.



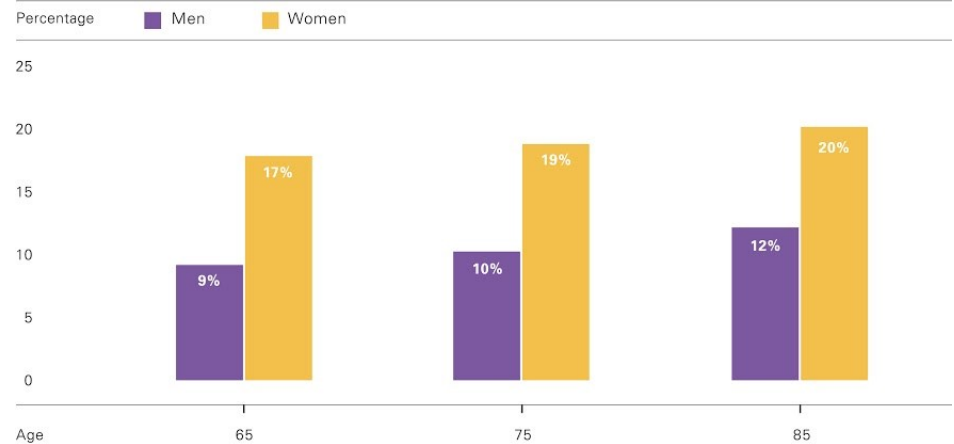
Total cost of care for those with Alzheimer's,
with more than two-thirds paid by Medicare and Medicaid

Source: Centers for Disease Control and Prevention (cdc.gov/nchs/fastats/leading-causes-of-death.html)

Women are at the Epicenter of the Alzheimer's Epidemic



Estimated Lifetime Risk for Alzheimer's, by Age and Sex, from the Framingham Study



Created from data from Seshadri et al.¹⁶⁶

Source: Alzheimer's Association 2015 Alzheimer's Disease Facts and Figures

Join the movement:
MYBRAIN.ALZ.ORG

Caregivers are More Susceptible to Disease & Health Complications

Due to the physical and emotional toll of caregiving, Alzheimer's and dementia caregivers had

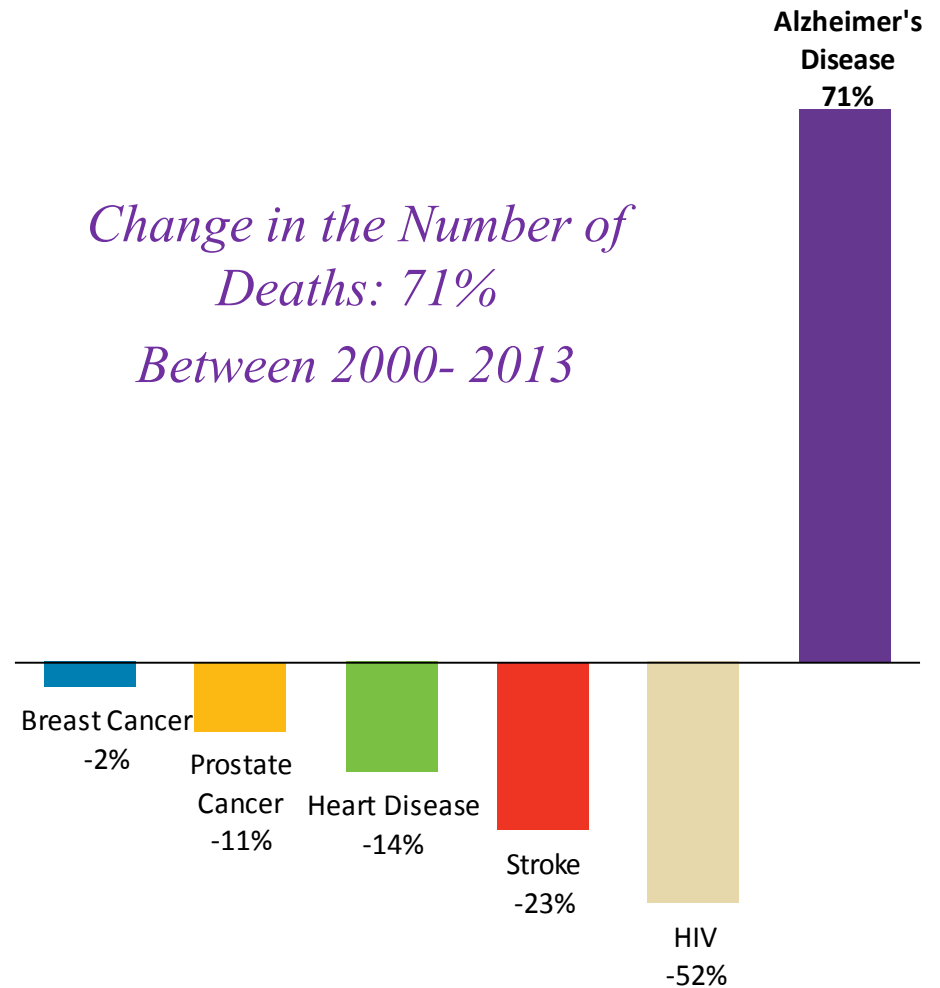
\$9.7

billion in additional health care costs
of their own in 2014

Hope In Research

- 6th leading cause of death across all ages
- 5th leading cause of death for those aged 65 and older
- Only cause of death among the top 10 in America without a way to prevent, cure or even slow its progression.

*Change in the Number of Deaths: 71%
Between 2000- 2013*



Facts & Figures 2015

National Plan to Address Alzheimer's disease

- Goal: “Prevent and Effectively Treat Alzheimer's by 2025”
- Key strategies:
 - Increase clinical studies enrollment
 - Expand scale and scope of research
 - Accelerate drug development



G8 Dementia Summit

London, England
December 11, 2013



Leaders for G8
countries commit to
work together to
**Prevent and
Effectively Treat
Alzheimer's Disease
by 2025!**



USA Russia
France
Germany
Italy
Canada
Japan
UK

theguardian

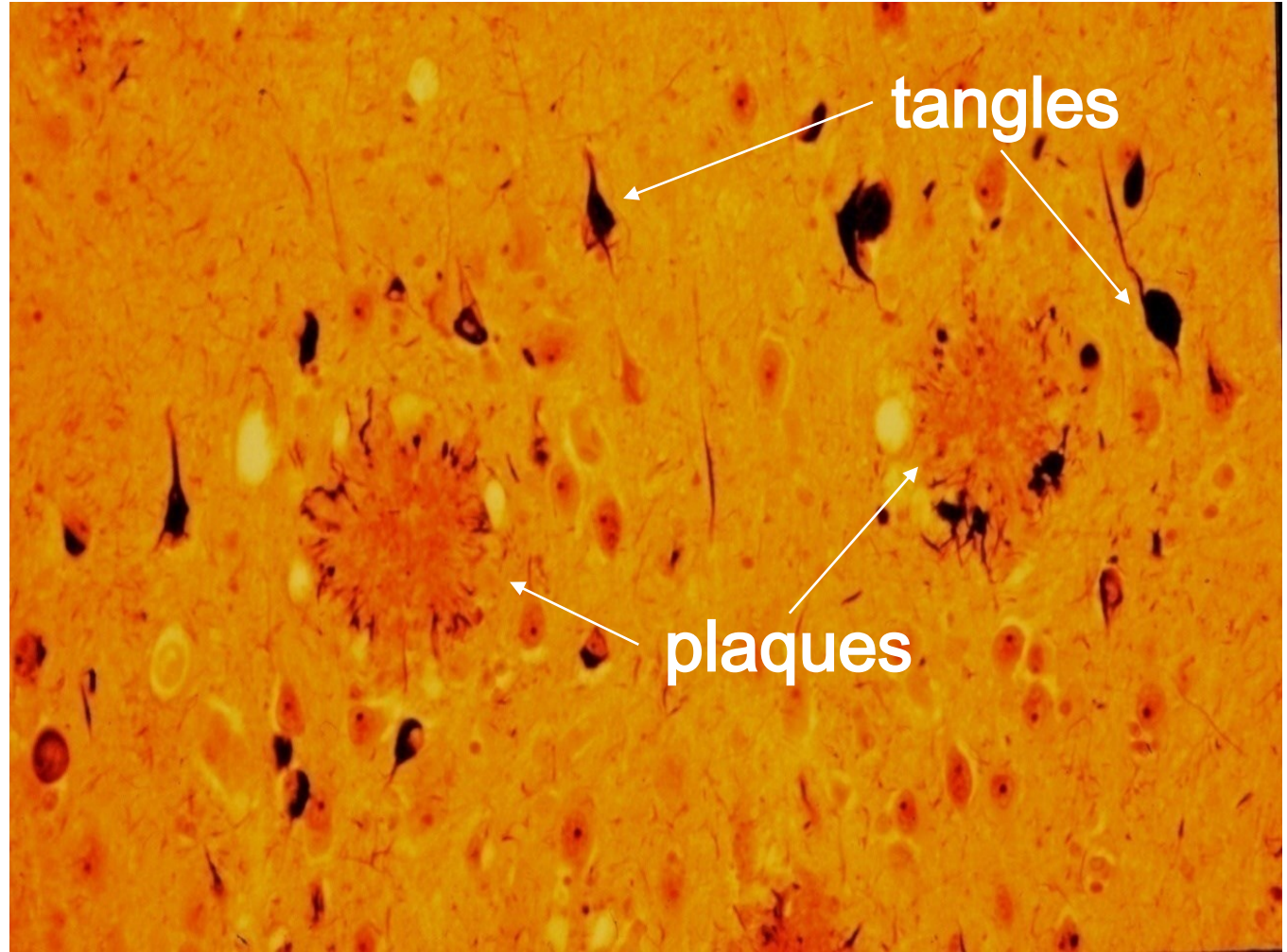
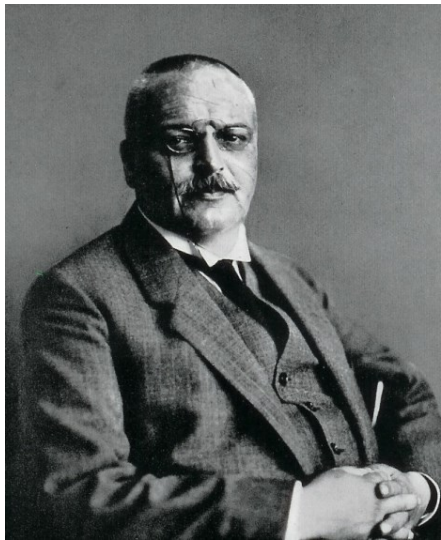
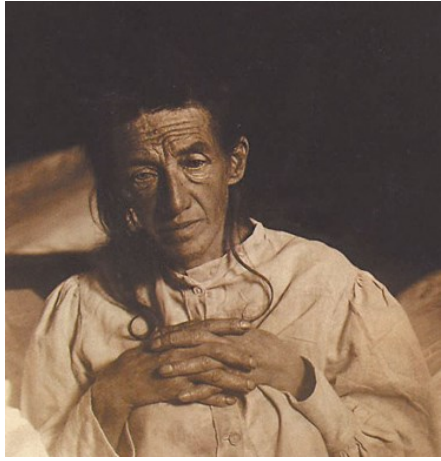
BBC

AP
Associated Press

REUTERS

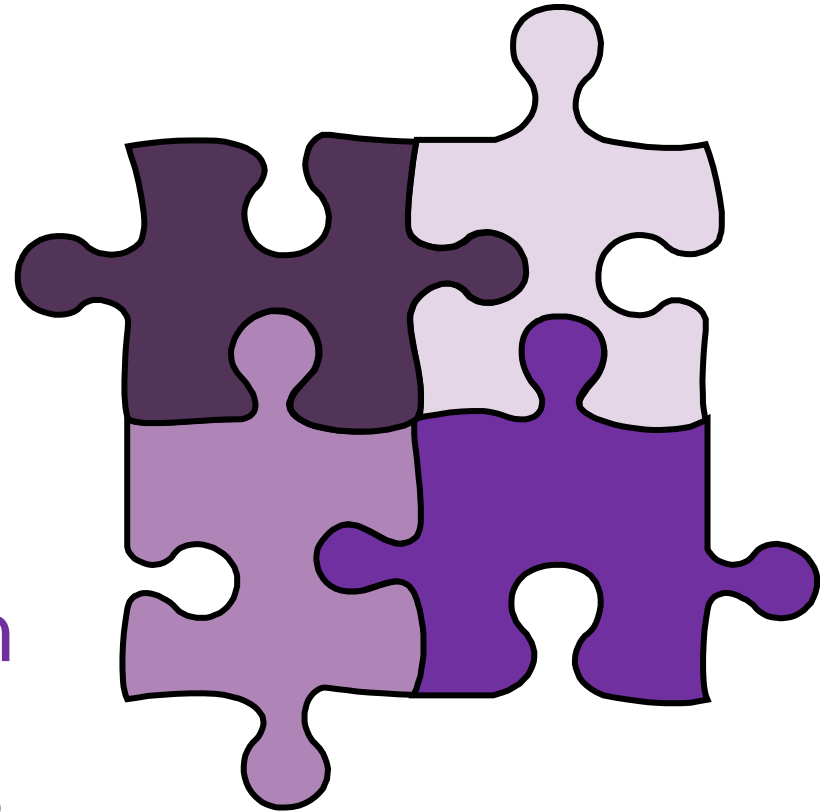
Forbes

Alzheimer's Disease



Alzheimer's Disease: Potential Risk Factors

- Age
- Family History and Genetic Susceptibility
- Heart/ Head Connection
- Other Lifestyle Factors?



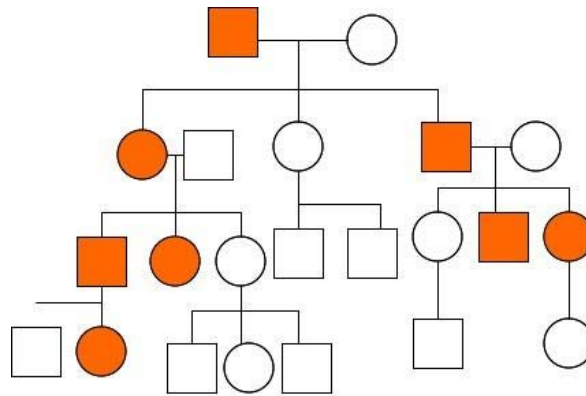
Age: Greatest Risk Factor for Alzheimer's disease



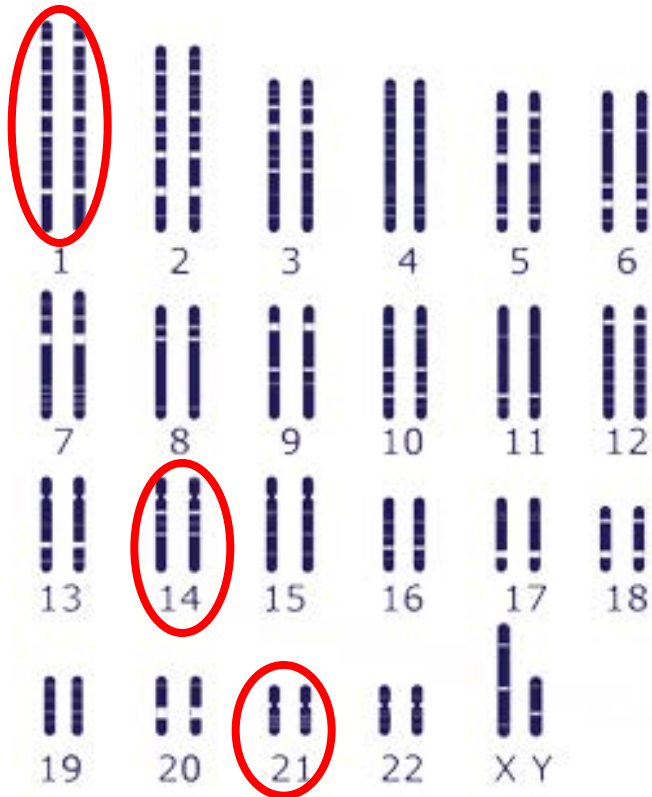
older Americans has
Alzheimer's disease.

Family History and Genetic Susceptibility

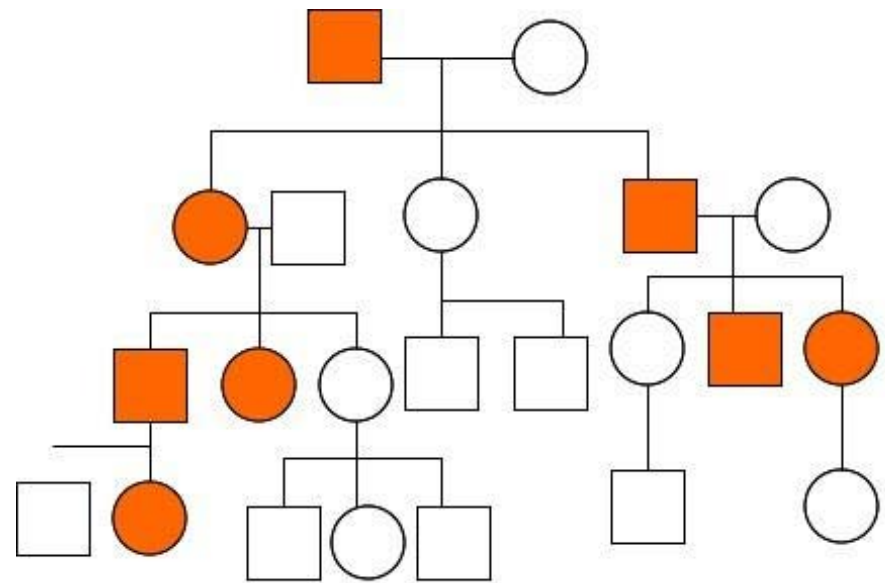
- First degree family member (parent or sibling) – increased risk
- Genetics: Deterministic and Risk



Understanding Genetics: Deterministic



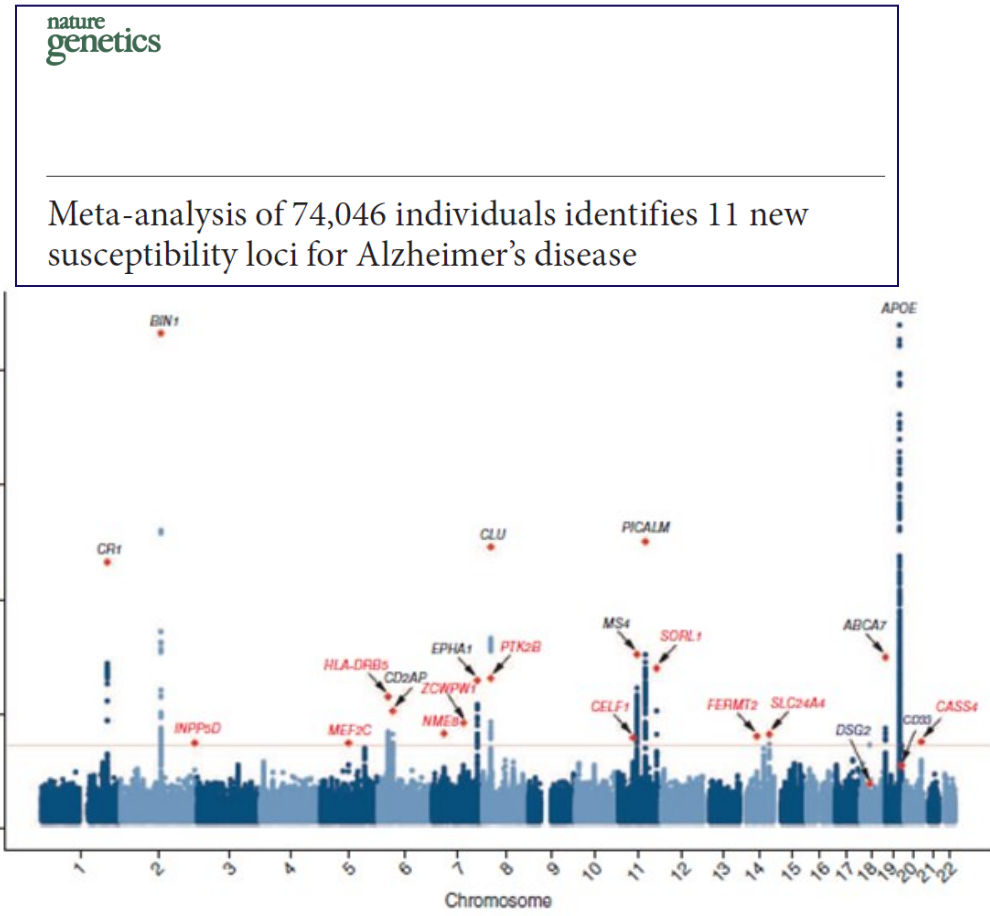
23 Chromosome Pairs



Relatively rare: 1-3% of all cases of Alzheimer's

Understanding Genetics: Risk

- International Genomics Alzheimer's Project (IGAP) compared genes from ~75,000 individuals'
- Confirmed 9, identified 11 new genetic areas of interest
- Approximately ~30 genes identified to date



Risk Related to Alzheimer's:

Possibly Able to Modify Behaviors

- Cardiovascular Risk Factors:
 - Diabetes
 - Mid-Life Obesity
 - Mid-Life Hypertension
 - Cholesterol



FINGER Study: Recipe of Lifestyle Interventions for Cognition

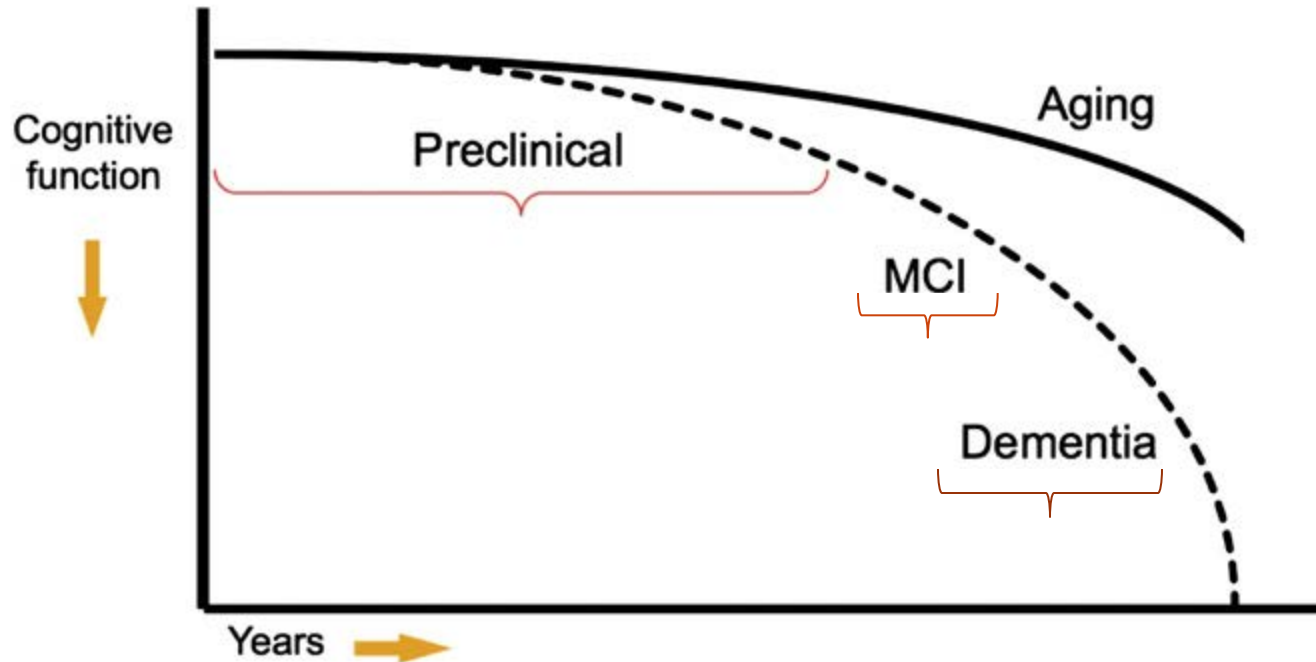
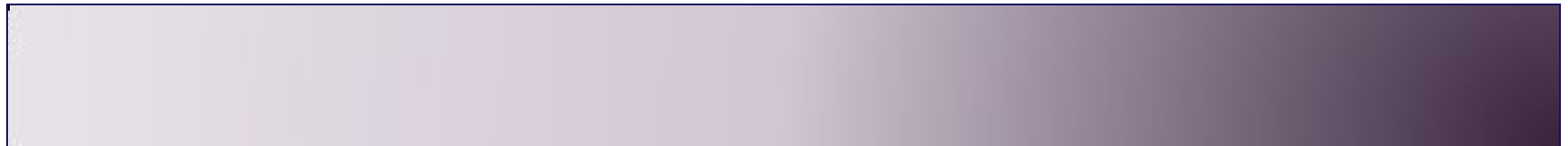
- Gold standard of testing any type of therapy or intervention – Randomized Control Trial (RCT)
- Large, rigorous study
- First solid evidence that recipe of lifestyle interventions reduces cognitive decline
- Needs to be replicated in more diverse populations



Continuum of Alzheimer's Disease

Normal

Alzheimer's disease



Adapted from Sperling et al. 2011

Modernizing the Diagnosis of Alzheimer's Based on a Continuum

2011

The diagnosis of dementia due to Alzheimer's disease:
Recommendations from the National Institute on Aging-Alzheimer's
Association workgroups on diagnostic guidelines for Alzheimer's disease

Guy M. McKhann^{a,b,*}, David S. Knopman^c, Howard Chertkow^{d,e}, Bradley T. Hyman^f,
Clifford R. Jack, Jr.^g, Jennifer L. Jordan^h,
Martin N. Rossorⁱ

The diagnosis of mild cognitive impairment due to Alzheimer's disease:
Recommendations from the National Institute on Aging-Alzheimer's
Association workgroups on diagnostic guidelines for
Alzheimer's disease

Marilyn S. Albert^{a,*}, Steven T. DeKosky^{b,c}, Dennis Dickerson^d, Bruno Dubois^e,
Richard H. Myers^f, Paul M. Pasquier^g, Ronald C. Peterson^h,
John C. Morris^{i,j}, William J. Jagust^k,
Richard D. B. Scahill^l, Creighton H. Phelps^p

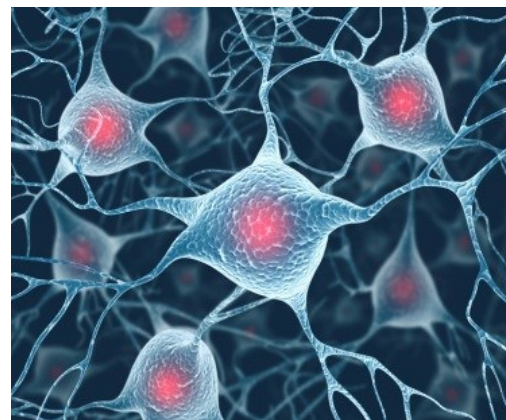
Toward defining the preclinical stages of Alzheimer's disease:
Recommendations from the National Institute on Aging-Alzheimer's
Association workgroups on diagnostic guidelines
for Alzheimer's disease

Reisa A. Sperling^{a,*}, Paul S. Aisen^b, Laurel A. Beckett^c, David A. Bennett^d, Suzanne Craft^e,
Anne M. Fagan^f, Takeshi Iwatsubo^g, Clifford R. Jack, Jr.^h, Jeffrey Kayeⁱ, Thomas J. Montine^j,
Denise C. Park^k, Eric M. Reiman^l, Christopher C. Rowe^m, Eric Siemersⁿ, Yaakov Stern^o,
Kristine Yaffe^p, Maria C. Carrillo^q, Bill Thies^q, Marcelle Morrison-Bogorad^r, Molly V. Wagster^r,
Creighton H. Phelps^r

Alzheimer's
&
Dementia

What is a Biomarker?

- Biological marker to measure change
- Reliable predictor and indicator of disease and disease progression
- Example
 - Glucose for Diabetes
 - Cholesterol for Heart disease



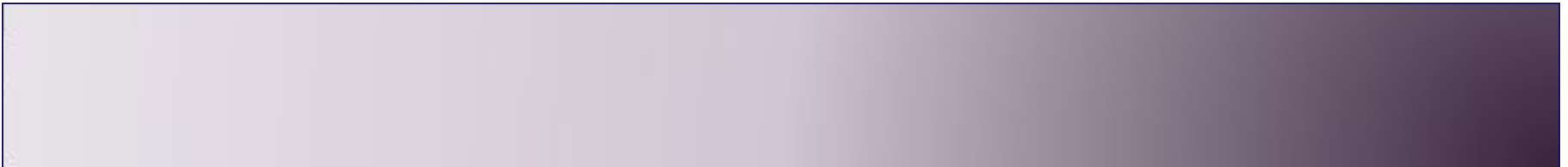
Modernizing the Diagnosis of Alzheimer's Based on a Continuum

Normal

Pre-clinical

MCI

Alz dementia

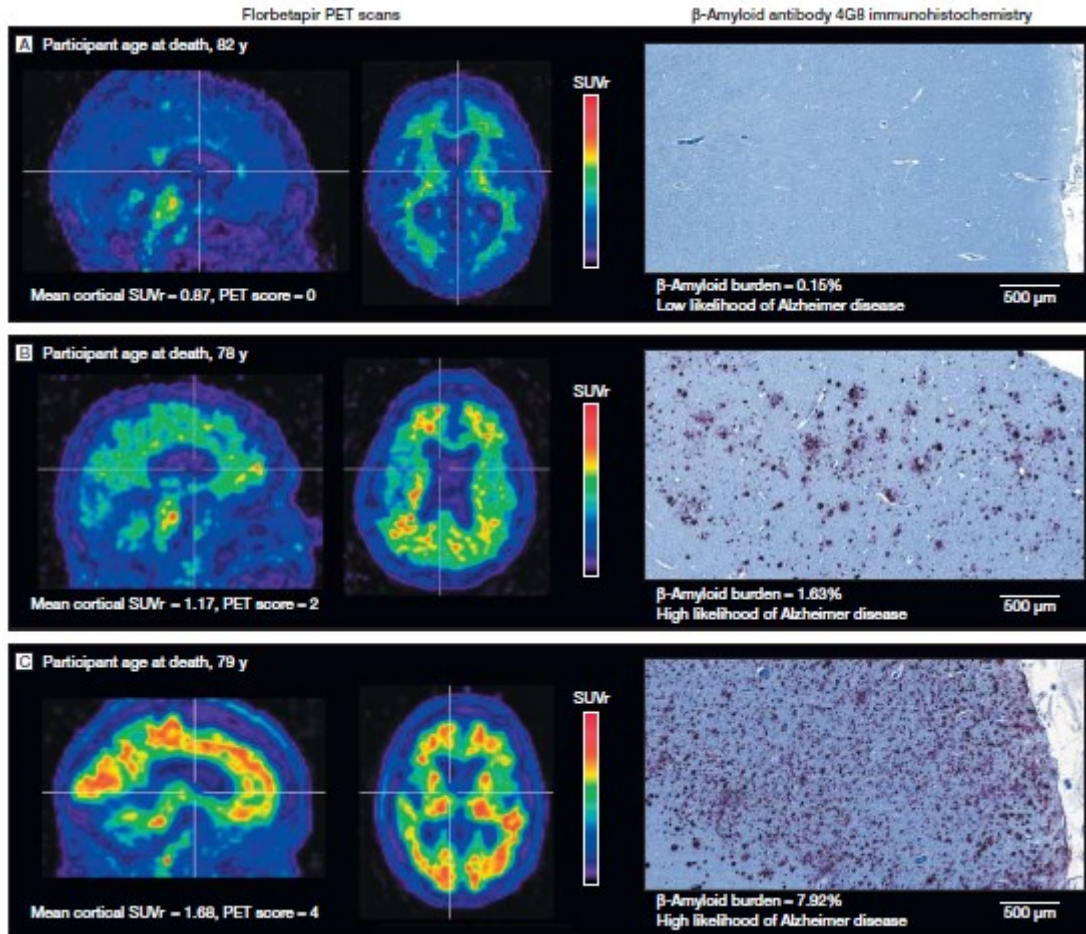


APOE
Protein or gene
“barcodes”
Family history
Tau/Abeta (CSF,
blood, eye)
MRI, CT
PET, fMRI

Subjective problem
in memory or another
domain, informant
corroborated and
measurable on tests;
normal overall
cognition and ADLs

Clear deficits in 2 or
more core cognitive
domains;
ADLs affected

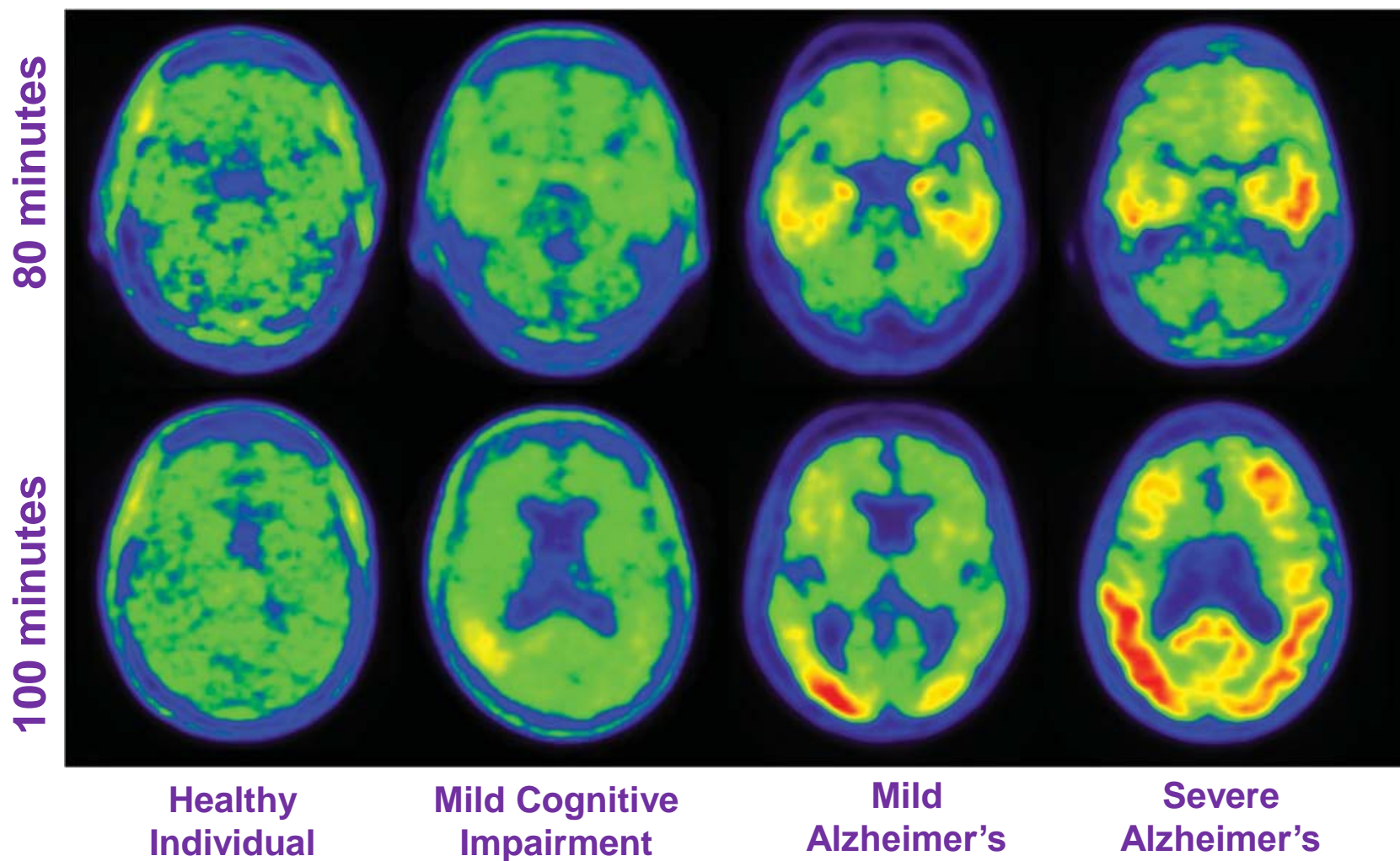
Amyloid PET Imaging



RED = maximum uptake

VIOLET = minimum uptake

Alzheimer's disease: Tau Imaging

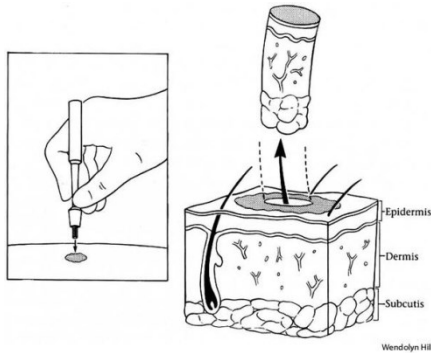


Emerging Research: Blood Test?

- Active area of research
- State of Science meeting – April 2013
- ISTAART PIA working on standardization and developing resources to accelerate discovery
- Today: no blood test available for use



Emerging Research: Skin Test?



- Skin biopsies of healthy individuals, people with Alzheimer's and people with Parkinson's disease
- Small study detected increased tau for Alzheimer's & Parkinson's; also α -Synuclein in Parkinson's
- Very early work
- Needs confirmation in larger populations and by independent research teams

Modernizing the Diagnosis of Alzheimer's Based on a Continuum

Normal

Pre-clinical

MCI

Alz dementia



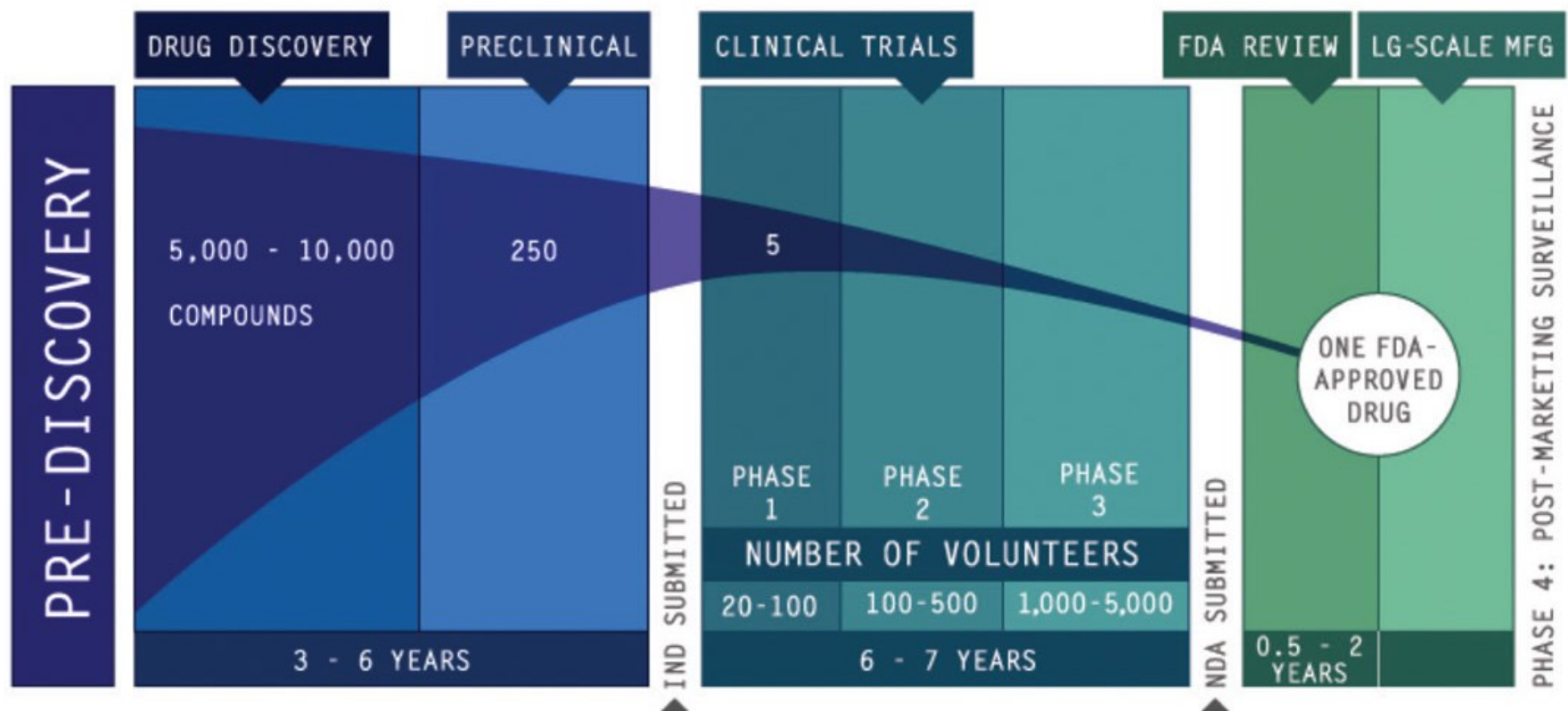
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Pathway to Your Medicine Cabinet

Drug Discovery and Development: A LONG, RISKY ROAD



Current Alzheimer's Therapies: Symptomatic

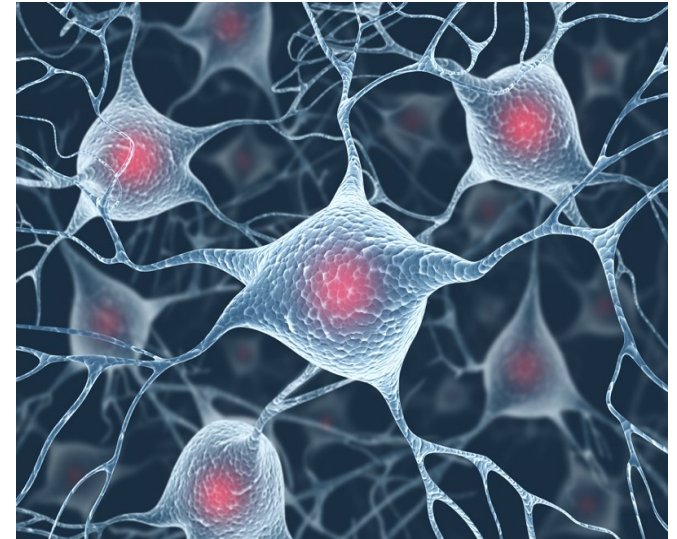
Cholinesterase Inhibitors

tacrine (Cognex)

donepezil (Aricept)

rivastigmine (Exelon)

galantamine (Razadyne)



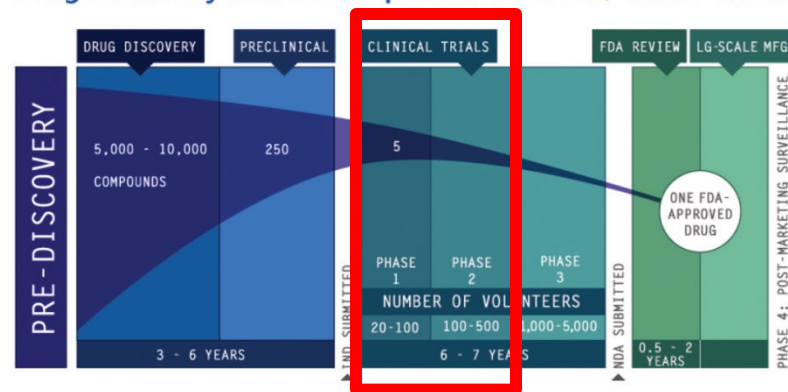
Glutamate Moderators

Memantine (Namenda)

Therapeutic Agents in Phase I and II Clinical Trials for Alzheimer's Disease

- AADvac1
- ABT-957
- Allopregnenalone
- Atomoxetine
- AZD0530
- AZD3293
- BAN2401
- Bexarotene
- **BIIB037**
- Blood plasma
- Bryostatin 1
- CPC-201
- Crenezumab (MABT5102A)
- DAIO-B
- DBS-f (Deep brain stimulation of the fornix)
- E2609
- Encenicline
- Exendin-4
- Insulin
- IVIg
- JNJ-54861911
- KHK6640
- Ladostigil
- L-arginine
- Levetiracetam
- Liraglutide
- LY3002813
- LY3202626
- MEDI1814
- Mesenchymal stem cells
- Metformin
- MK-7622
- NIC5-15
- Nicotinamide
- RO4602522
- RPh201
- R-Pramipexole
- SAR228810
- Sargramostim
- Simvastatin
- T-817MA
- Tetrahydrobiopterin
- TPI-287
- Transcranial direct current stimulation (tDCS)
- Transcranial magnetic stimulation (TMS)

Drug Discovery and Development: A LONG, RISKY ROAD



Phase 1b Results for Aducanumab

- BIIB037 or Aducanumab shows solid safety and tolerability profile (Phase 1b) in PRIME trial
- Also secondary outcomes: dose dependent slowing of cognition in individuals with mild disease/ confirmed beta-amyloid in brain
- Measures of cognition show statistical benefit at 54 weeks and reduced levels of beta-amyloid
- Need larger, longer trial (Phase 3)
- Monoclonal antibody targeting beta-amyloid clumps



BIOTECH AND PHARMACEUTICALS

HEALTH CARE | HOSPITALS | EBOLA | PHARMA | EQUIPMENT & SI

Biogen Alzheimer's drug exceeds expectations

Meg Tirrell | @megtirrell
3 Hours Ago



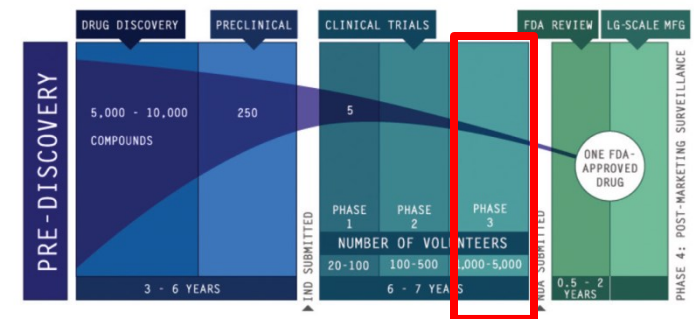
BloombergBusiness 

Biogen Soars as Alzheimer's Drug Slows Disease in Trial

Therapeutic Agents in Phase III Clinical Trials for Alzheimer's Disease

- Encenicline
Forum Pharmaceuticals
Nicotinic receptor agonist
- Gantenerumab
Hoffman-La Roche
Monoclonal antibody against beta amyloid
Part of DIAN-TU
- Gantenerumab + Solanezumab
Eli Lilly, Hoffman-La Roche
- Insulin
Alzheimer's Disease Cooperative Study
- IVIg and Albumin
Grifols
Intravenous immunoglobulin
- LU AE58054
H. Lundbeck
5HT6 receptor antagonist
- Masitinib
AB Science
Inhibitor of c-KIT cell signaling
- MK-8931
Merck
BACE inhibitor
- Nilvadipine
St. James Hospital
Calcium Channel Blocker
- Pioglitazone
Takeda
PPAR-gamma activator
- Sodium Oligo-mannurate
– Shanghai Greenvalley Pharmaceuticals
- Solanezumab
Eli Lilly
Humanized antibody against beta-amyloid
- TRx0237
TauRX
Tau aggregation inhibitor

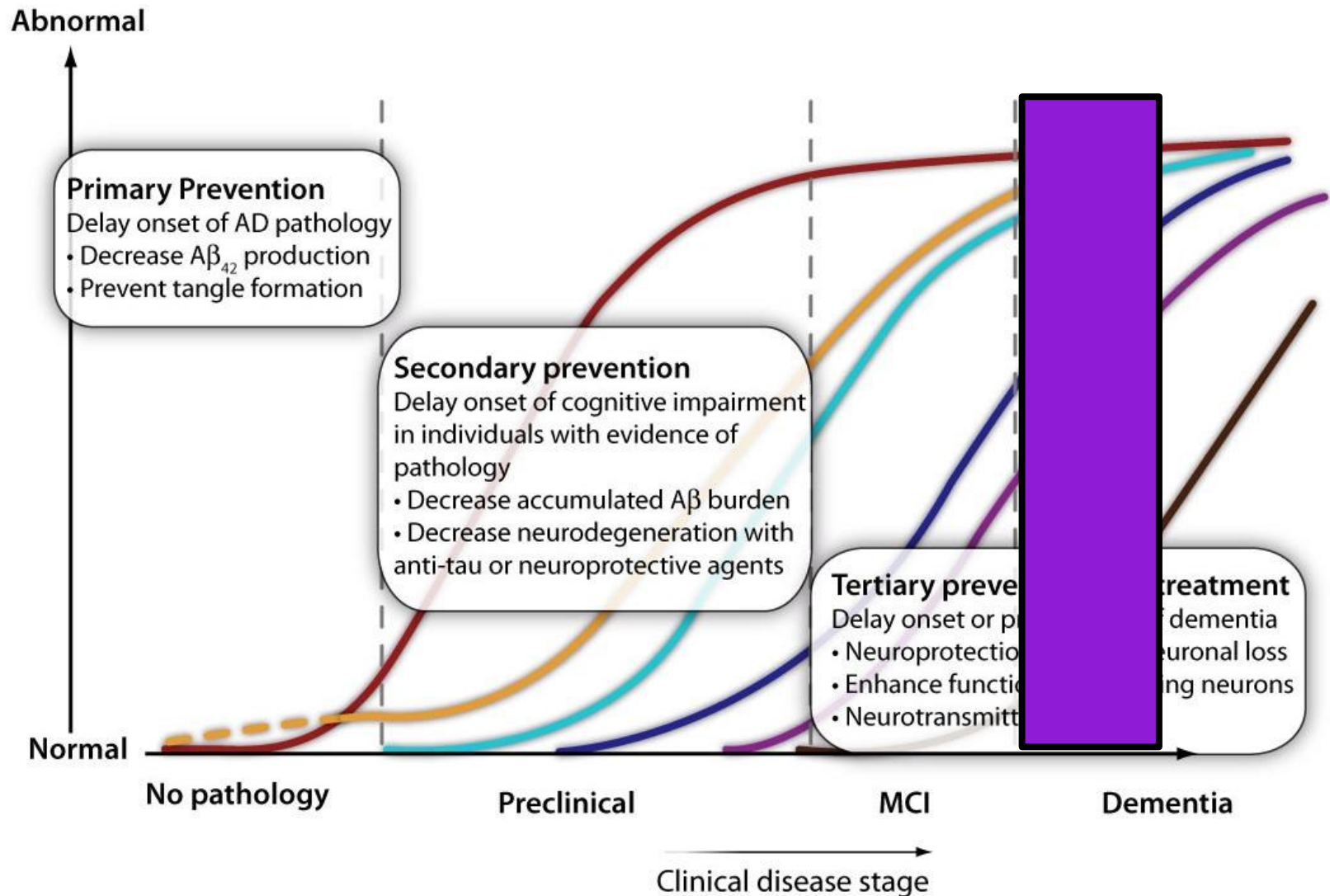
Drug Discovery and Development: A LONG, RISKY ROAD



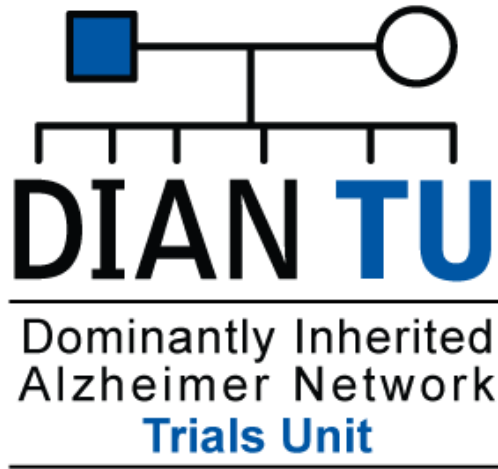
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Possible Prevention of Alzheimer's?



Five On-Going Prevention Efforts



ALZHEIMER'S
PREVENTION
INITIATIVE

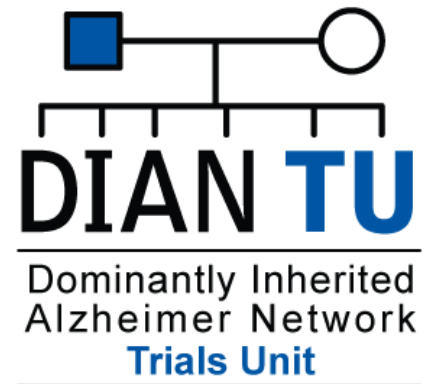


TOMMORROW

Dominantly Inherited Alzheimer's Network Trial (DIAN-TU)

- DIAN: Autosomal dominant Alzheimer's disease (ADAD)
- \$4.2 million award to launch
- Testing three simultaneous drugs:
 - Gantenerumab (Roche, Ab antibody)
 - Solanezumab (Lilly, Ab antibody)
 - TBD
- 22 months later: Received \$6 million from NIH
- And a year later ... Received \$23 million additional from NIH

alzheimer's 
association®

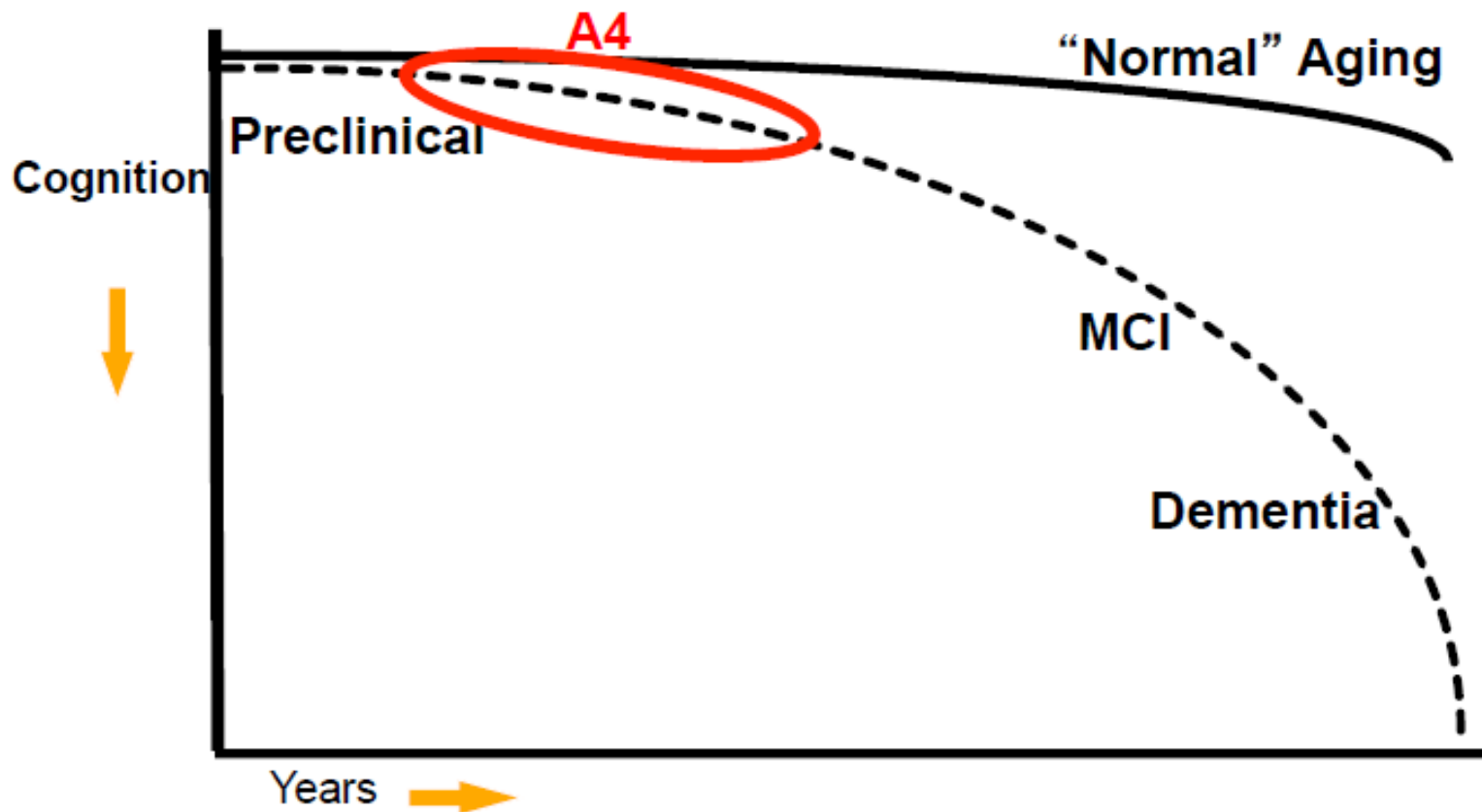


Anti-Amyloid in Asymptomatic Alzheimer's (A4) Study

- Clinically normal, Age 65+
- Positive Amyloid PET
- Testing Solanezumab (Lilly)
- Including both beta-amyloid and tau imaging (tau made possible by Alzheimer's Association)
- Lead Investigators:
Dr. Reisa Sperling &
Dr. Paul Aisen



Continuum of Alzheimer's disease

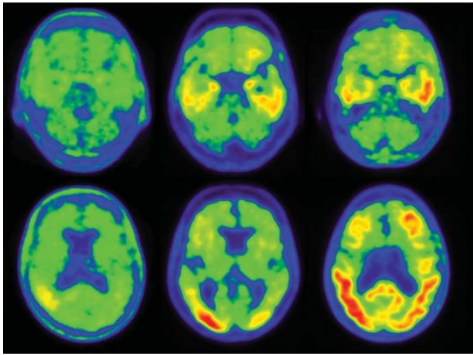


Adapted from Dr. Reisa Sperling

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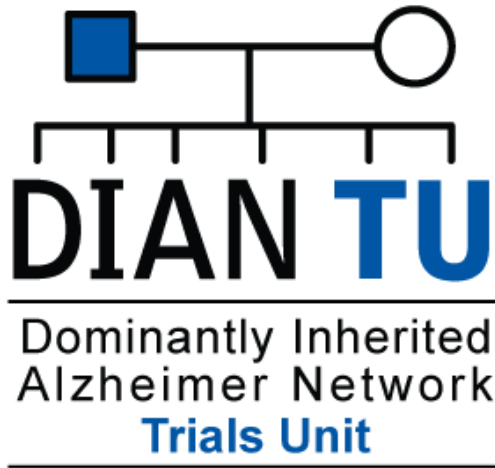
LEARN

- Longitudinal Evaluation of Amyloid Risk and Neurodegeneration (LEARN)
- Natural history study of 400 people with low/intermediate levels of amyloid
- Leveraging the A4 trial
- Focus on diverse populations
- ***Largest award ever given by Alzheimer's Association***
- ***First funded tau imaging study***



JT Chien et al. *Journal of Alz Dis* 2013

Collaboration for Alzheimer's Prevention



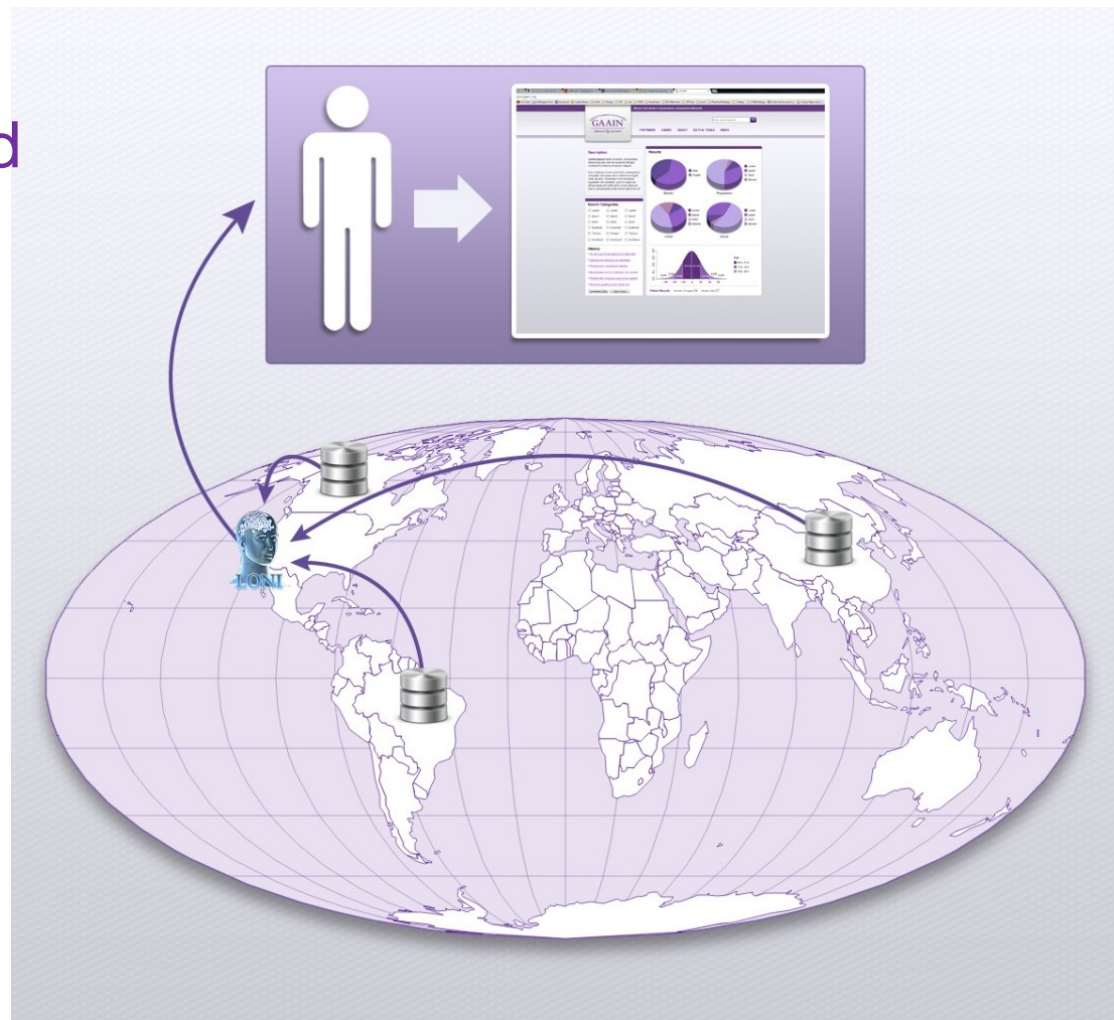
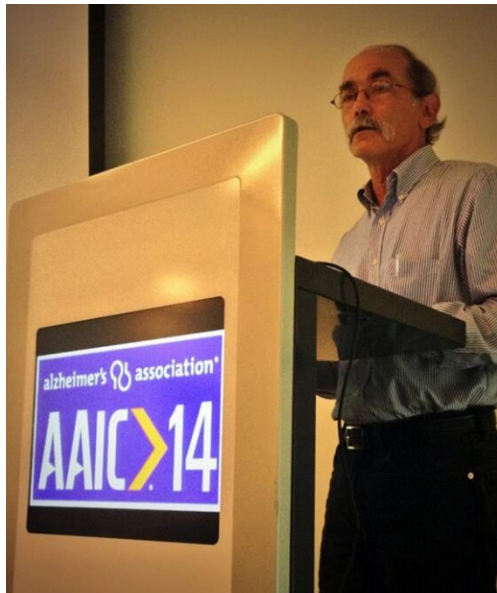
ALZHEIMER'S
PREVENTION
INITIATIVE

TOMMORROW




GAAIN is the first Global Data Network for Alzheimer's

Collaborative effort to provide researchers around the globe with access to a vast repository of Alzheimer's research data.



Alzheimer's Association Research Website

alz.org® | research center
advancing alzheimer's research worldwide



HOME | SCIENCE & PROGRESS | CLINICAL TRIALS | FUNDING & COLLABORATION | YOU CAN HELP | STAY CURRENT | VIDEO AND RESOURCES

alz.org >> Research Home Text Size [A](#) [A](#) [A](#)

A future without Alzheimer's

The race is on. Alzheimer's and related dementias research is a dynamic field, and momentum builds each year. This site is for [professional researchers](#) and anyone interested in following the [progress in research](#). The Alzheimer's Association has been involved in every major advancement in Alzheimer's and related dementias research since the 1980's and is a [leader in the global fight](#) for a world without Alzheimer's.



Discovering tomorrow's treatments

The Alzheimer's treatment horizon has never looked brighter. More potential treatments are in development than ever before as a result of 30 years of accelerating insight and identification of promising targets for intervention. The Alzheimer's Association is committed to sustaining this pace of discovery. [Learn more](#)

- 1
- 2
- 3
- 4
- 5

what we know today



➤ About Alzheimer's disease

tomorrow's answers



➤ Drug treatment pipeline

clinical trials



➤ Find a trial

www.alz.org/research

What Can You Do Now?

- Talk about your experience Alzheimer's disease
- Participate in Longest Day or Walk to End Alzheimer's
- Talk to your legislators
- Support research - join a clinical study
- Maintain overall health – physical, mental and social



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In Summary ...

- Alzheimer's Association is global leader
- Alzheimer's is 21st century health epidemic
- Significant advances in our understanding of risk, early biological changes – but still many unanswered questions
- Growing pipeline of clinical investigations
- New generation of clinical trials in possible prevention
- Alzheimer's Association is resource to all those facing this disease
- There is **hope** through research!

THE END OF
ALZHEIMER'S
STARTS
WITH YOU

alzheimer's  association®

[alz.org](https://www.alz.org)