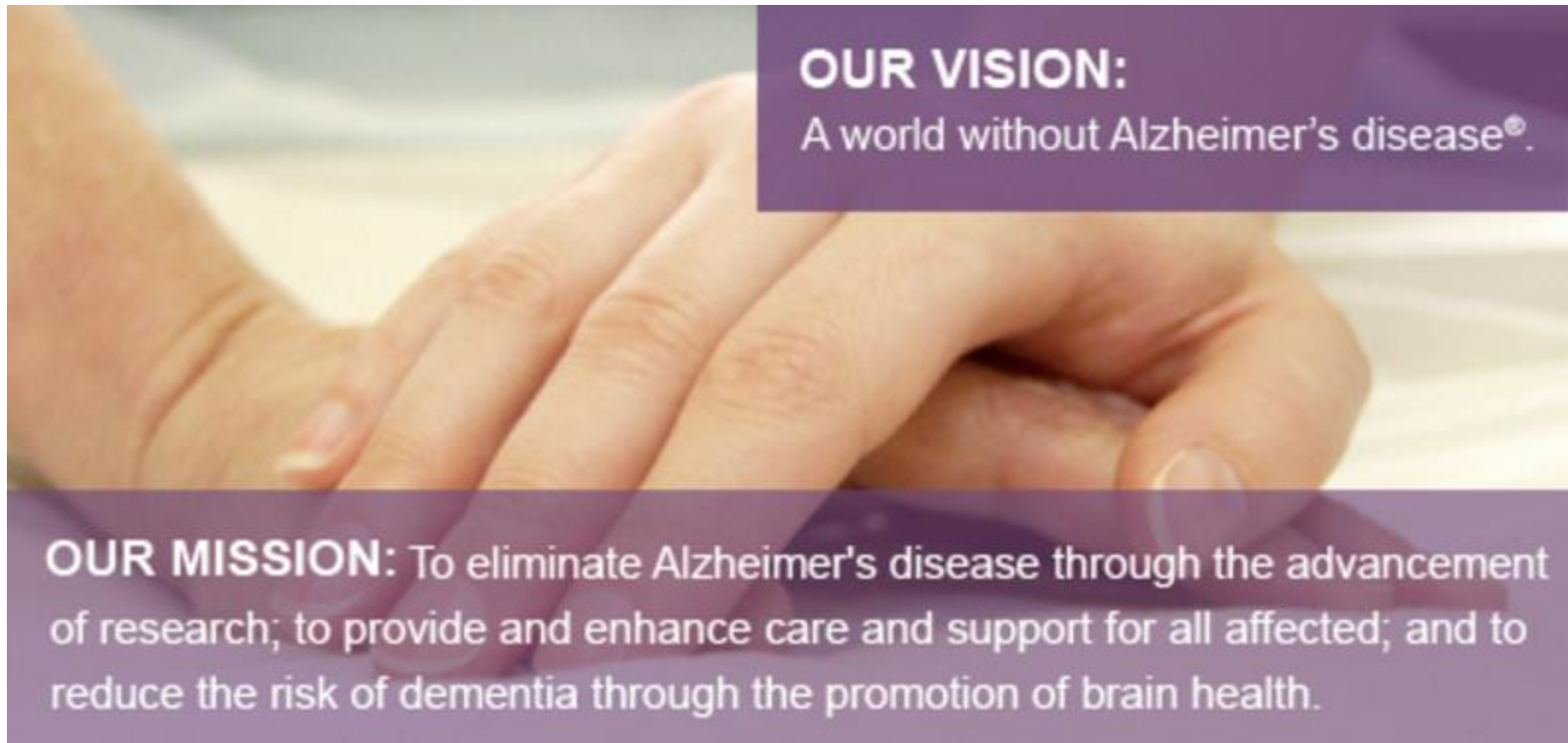


Public / Private Partnerships in Alzheimer's Biomarkers

James Hendrix, PhD
Alzheimer's Association
HRA Member's Meeting
September 18, 2017

Alzheimer's Association: Who We Are



alzheimer's association®

Research Roundtable

alzheimer's association®

Business Consortium

International Research GRANT PROGRAM

alzheimer's association®

Global Leader in Alzheimer's Research



Connector • Convener Funder



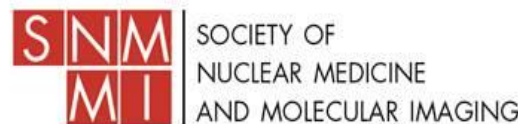
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THE BRAINS BEHIND SAVING YOURS™

Additional Partnerships



National Institutes of Health



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.

Jennifer J.

Martin N. Ro

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

Morley S. Albert^{a,*}, Steven T. DeKosky^{b,c}, Dennis Dickerson^d,

Bruno Dubois^e,
man^{i,j}, William J. Jagust^k,
s^o, 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



2001

Funded Dr. William Klunk for first studies on beta-amyloid imaging through RGP

2006

Added to the National Institute of Mental Health's (NIMH) list of priority review drugs leading to the imaging

IDEA TO INCEPTION:

Paving the way for the advancement of the field of

ACCELERATED BY FIVE YEARS!

JAMA Psychiatry publishes diagnostic NIA-Alzheimer's Association guidelines

2012

FDA approves beta-amyloid imaging agents for clinical use

2015

Launched IDEAS Study, working to ensure individuals can access beta-amyloid imaging

Alzheimer's Disease Neuroimaging Initiative (ADNI)

- To validate biomarkers for clinical AD trials
- To standardize biomarkers for clinical AD trials
- To optimize biomarkers for clinical AD trials
- AD trials include Phase 2 (POC) and Phase 3
- To provide all the data to those designing trials
- To help create a world wide network for AD trials
- Ultimately to facilitate development of a surrogate biomarker outcome measure: tau?

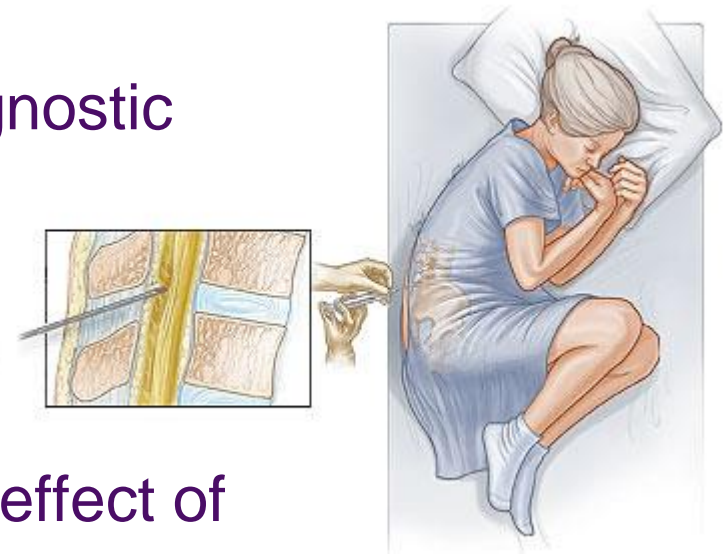


WW-ADNI – Worldwide Collaboration



Global Biomarkers Standardization Consortium (GBSC)

- CSF as a Potential Biomarker
- A Consortium of Academic Experts and Diagnostic Companies
- On-going research to improve diagnostic accuracy
- Potentially detects early biological changes
- Lumbar puncture (spinal tap)
- Identify & monitor the biochemical effect of a drug candidate in clinical trials
- Standardize $A\beta_{1-42}$, t-tau and p-tau₁₈₁ measurements



Background for starting the Alzheimer's Association CSF program

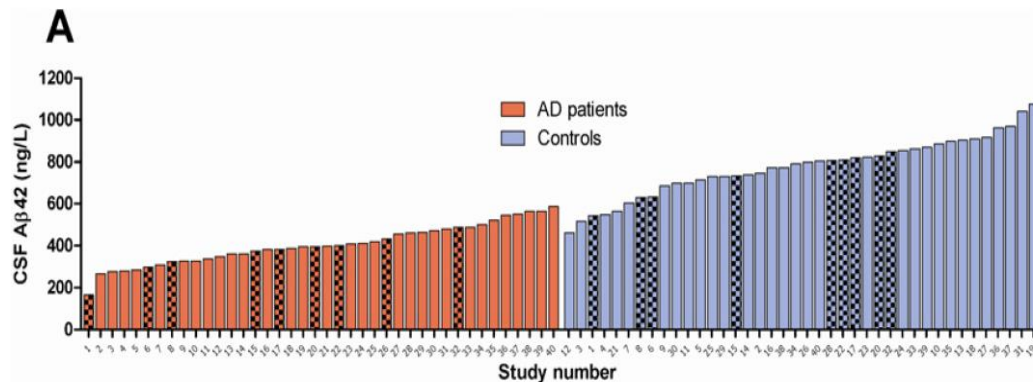


Alzheimer's
&
Dementia

Alzheimer's & Dementia 7 (2011) 386-395

The Alzheimer's Association external quality control program
for cerebrospinal fluid biomarkers

Niklas Mattsson^{a,*}, Ulf Andreasson^a, Staffan Persson^a, Hiroyuki Arai^b, Sat Dev Batish^c, Sergio Bernardini^d, Luisella Bocchio-Chiavetto^e, Marinus A. Blankenstein^f, Maria C. Carrillo^g, Sonia Chalbot^h, Els Coartⁱ, Davide Chiasserini^j, Neal Cutler^k, Gunilla Dahlfors^l, Stefan Duller^m, Anne M. Faganⁿ, Orestes Forlenza^o, Giovanni B. Frisoni^p, Douglas Galasko^q, Daniela Galimberti^r, Harald Hampel^s, Aase Handberg^t, Michael T. Heneka^u, Adrianna Z. Herskovits^v, Sanna-Kaisa Herukka^w, David M. Holtzman^x, Christian Humpel^w, Bradley T. Hyman^a, Khalid Iqbal^h, Mathias Jucker^s, Stephan A. Kaeser^s, Elmar Kaiser^r, Elisabeth Kapakiⁱ, Daniel Kidd^m, Peter Klivenyi^{bb}, Cindy S. Knudsen^s, Markus P. Kummerⁱ, James Lui^{cc}, Albert Llado^{dd}, Piotr Lewczuk^{cc}, Qiao-Xin Li^{ff}, Ralph Martins^{cc}, Colin Masters^{ff}, John McAuliffe^e, Marc Mercken^{gg}, Abhay Moghekar^{hh}, José Luis Molinuevo^{dd}, Thomas J. Montineⁱⁱ, William Nowatzke^h, Richard O'Brien^{hh}, Markus Otto^{jj}, George P. Paraskevas^e, Lucilla Parnettiⁱ, Ronald C. Petersen^{kk}, David Prvulovic^e, Herman P. M. de Reus^{ll,mm}, Robert A. Rissman^p, Elio Scarpiniⁱⁱ, Alessandro Stefaniniⁿⁿ, Hilka Soininen^e, Johannes Schröder^e, Leslie M. Shaw^{oo}, Anders Skinningsrud^{pp}, Brith Skrogstad^{pp}, Annette Spreer^{qq}, Leda Talib^o, Charlotte Teunissen^l, John Q. Trojanowski^{oo}, Hayretin Tumanian^{jj}, Robert M. Umek^{ff}, Bianca Van Broeck^{ee}, Hugo Vanderstichele^l, Laszlo Vecsei^{bb}, Marcel M. Verbeek^{ll,mm}, Manfred Windischⁿ, Jing Zhangⁱⁱ, Henrik Zetterbergⁿ, Kaj Blennow^a



→ Large variability for CSF Aβ42 across laboratories
 → Need of standardization efforts

CSF Pre-Analytic Protocol Working Group

Variability due to:

- Pre-analytical factors
- Analytical factors
- Assay manufacturing

- e.g. type of test tube, CSF transfer, freeze-thaw effects,
- e.g. analytical procedures, technician training, run acceptance
- e.g. reagent purity, plate coating variability, calibrator stability, lot-to-lot consistency (batch bridging procedure)

The CSF biomarker assays on fully automated clinical analyzers

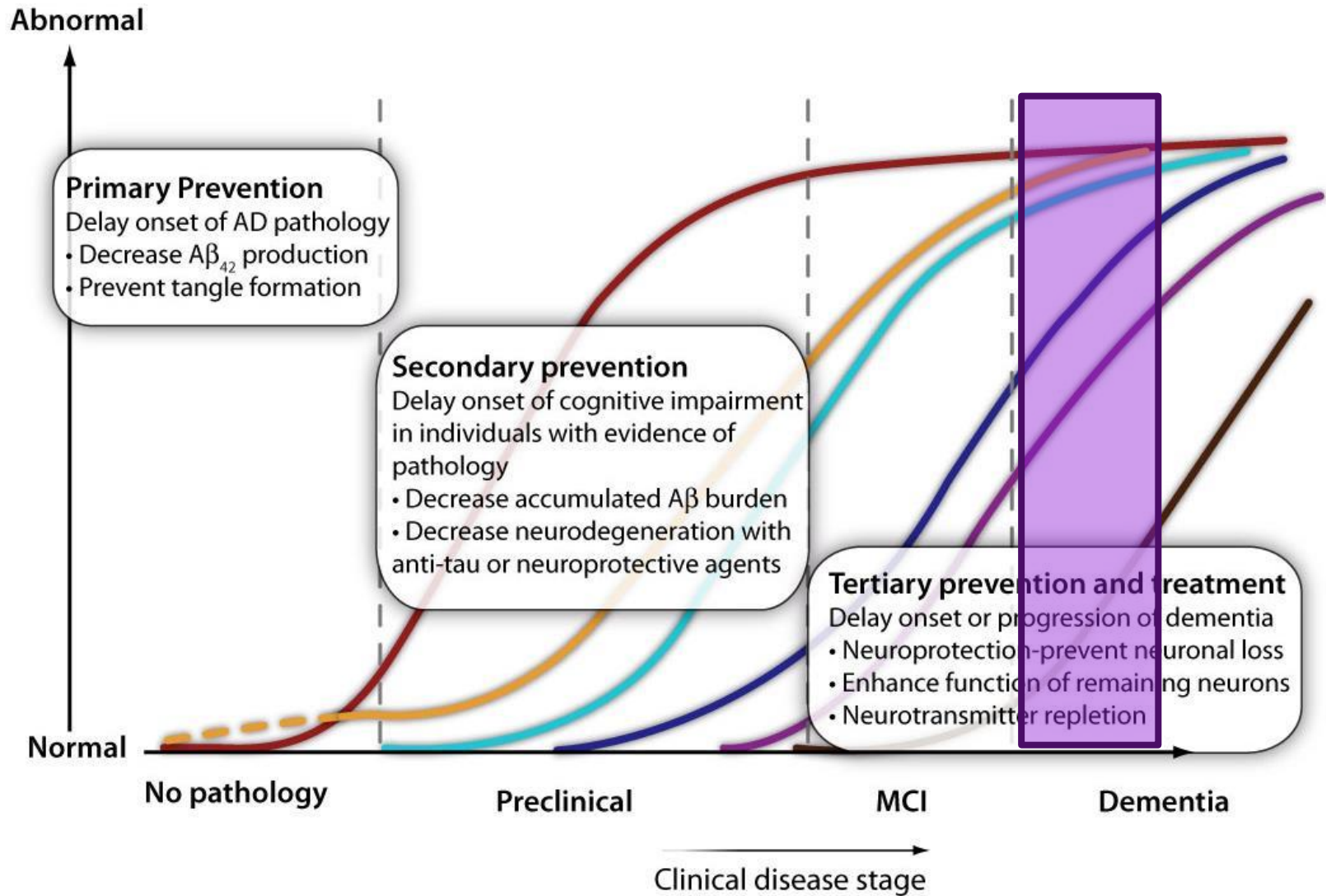
- Fully automated - minimize variations due to differences in laboratory procedures
 - reduced between-run, between-batch and between-lab variation
- Single sample analysis → fast results (< 30 min) to the clinician



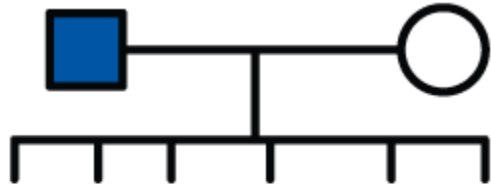
Fujirebio - Lumipulse

Appropriate Use Criteria for CSF in AD in Progress
– Led by the Alzheimer's Association

Prevention of Alzheimer's?



Collaboration for Alzheimer's Prevention (CAP)



DIAN TU
Dominantly Inherited
Alzheimer Network
Trials Unit



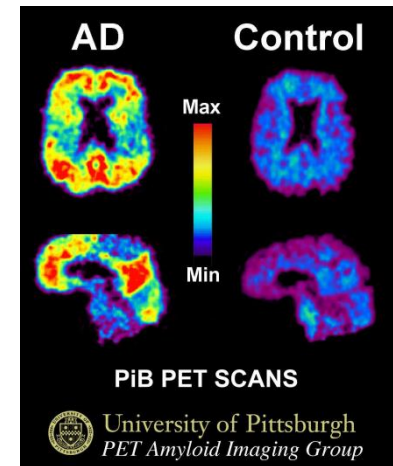
ALZHEIMER'S
PREVENTION
INITIATIVE

TOMMORROW



In the News: Published Report of **Aducanumab Phase 1B**

- First seen at AAIC 2015
- Using beta-amyloid PET for enrollment
- Promising Phase 1 monoclonal antibody
Aducanumab
 - Lowering levels of beta-amyloid, as measured by PET
 - Saw improvement in cognition, as measured by CDRsb & MMSE
- Currently recruiting for Phase 3
- Results expected in 2020



In Summary ...

- Alzheimer's Association is the global leader in research, providing care and support to all of those affected, and leading the public policy efforts
- Significant advances in biomarker research have been facilitated by the Alzheimer's Association led Public-Private Partnerships.
- Alzheimer's disease biomarkers tell us that the disease is a continuum; need to identify earliest biological change and intervene at that time point
- There is hope in research!

THE END OF
ALZHEIMER'S
STARTS
WITH YOU

alzheimer's  association®

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