

What's the Difference Between Alzheimer's Disease and Dementia?

Where this question came from and how we can finally answer it.

September 9, 2022

Jason Karlawish, MD

University of Pennsylvania

Perelman School of Medicine

www.jasonkarlawish.com

@jasonkarlawish

SPONSORED BY



CATHOLIC CHARITIES
HAWAII
CIRCLE OF CARE FOR DEMENTIA



Supported in part by grant No. 90ADPI0011-01-00 from the U.S. Administration for Community Living, Department of Health and Human Services, Washington, D.C. 20201. Grantees undertaking projects with government sponsorship are encouraged to express freely their findings and conclusions. Points of view or opinions do not, therefore, necessarily represent official ACL policy. The grant was awarded to Catholic Charities Hawaii for the Alzheimer's Disease Program Initiative.

Disclosures

- Jason Karlawish is a site investigator for clinical trials sponsored by Lilly, Biogen and Eisai

Topics I will talk about....

- Why the words we use in talking about Alzheimer's disease and other diseases that cause dementia matter to patients, clinicians, researchers, policy makers and advocates
- How Alzheimer's disease got its name
- The story of how the Alzheimer's Association got its name
- How MCI (Mild Cognitive Impairment) and biomarkers revolutionized research and care
- A vision for a nomenclature that serves patients, clinicians, researchers, policy makers and advocates

Topics I will talk about....

Why the words we use in talking about Alzheimer's disease and other diseases that cause dementia matter to patients, clinicians, researchers, policy makers and advocates.

- Patients: What's wrong with me? I am a person living with....
- Clinicians: The answer to the patient's chief complaint/concern. Communicating with others clinicians. Billing.
- Researchers: measurement, measurement, measurement
- Policy makers and Advocates: we have to rally lawmakers and the public to support patients, clinicians and researchers

The problem with our nomenclature...

- The terms “Alzheimer’s” and “Alzheimer’s disease” have at least three distinct usages.....
 - an umbrella term to capture a range of diseases that the U.S. has a national plan to address: “AD/ADRD”
 - a synonym for dementia (“*MCI progressed to Alzheimer’s*”)
 - a specific disease with identifiable pathologies (β -amyloid plaques & tau tangles) that cause of signs and symptoms
- Together, this creates mixed messages and misunderstandings

The problem with our nomenclature...

Abstract.

Background: Evaluating the risk of *Alzheimer's disease (AD)* in *cognitively normal (CN) and patients with mild cognitive impairment (MCI)* is extremely important. While *MCI-to-AD progression risk* has been studied extensively, few studies estimate CN-to-MCI conversion risk. The Cox proportional hazards (PH), a widely used survival analysis model, assumes a linear predictor-risk relationship. Generalizing the PH model to more complex predictor-risk relationships may increase risk estimation accuracy.

Objective: The aim of this study was to develop a PH model using an Xgboost regressor, based on demographic, genetic, neuropsychiatric, and neuroimaging *predictors to estimate risk of AD in patients with MCI*, and the risk of MCI in CN subjects.

From "Survival Analysis in Cognitively Normal Subjects and in Patients with Mild Cognitive Impairment Using a Proportional Hazards Model with Extreme Gradient Boosting Regression. J Alz Dis. 2022."

Google Books Ngram Viewer

Q dementia, Alzheimer, caregiver

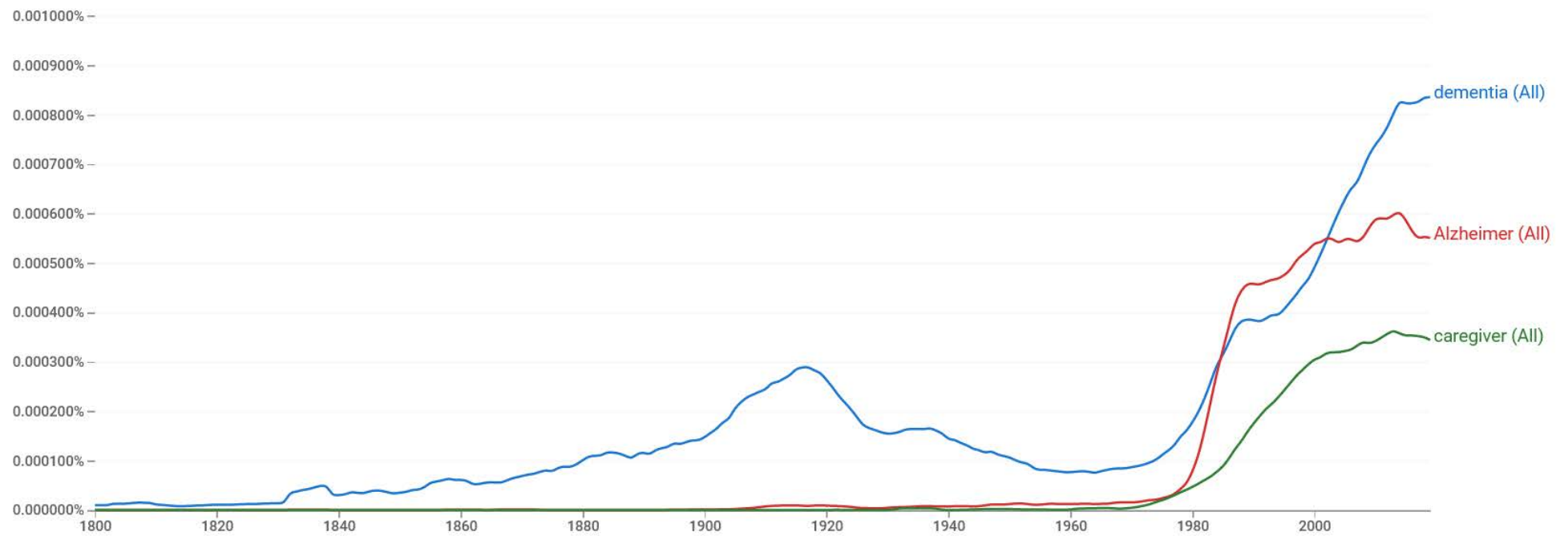


1800 - 2019

English (2019)

Case-Insensitive

Smoothing



(click on line/label for focus, right click to expand/contract wildcards)

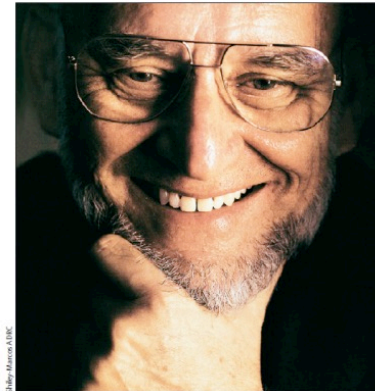
Editorial

The Prevalence and Malignancy of Alzheimer Disease

A Major Killer

Arch Neurol—Vol 33, April 1976

ROBERT KATZMAN, MD
Bronx, NY



Robert Katzman

Neurologist, researcher, and co-founder of the Alzheimer's Association. Born on Nov 29, 1925, in Denver, CO, USA, he died on Sept 16, 2008, in San Diego, CA, USA, aged 82 years.

“Senile as well as pre-senile forms of Alzheimer are a single disease, a disease whose etiology must be determined, whose course must be aborted, and ultimately a disease to be prevented.”



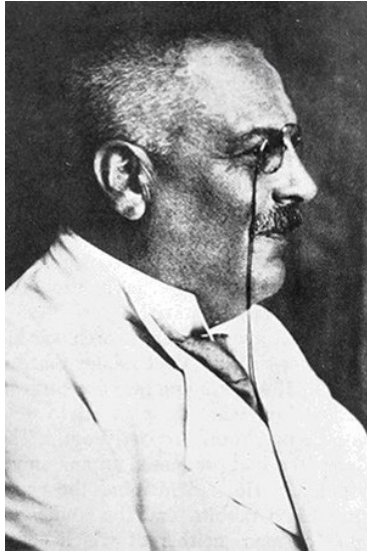
Alois Alzheimer (b. 1864 – d. 1915) and family

Hans, Maria, Cecilia, Alois, and Gertrud Alzheimer

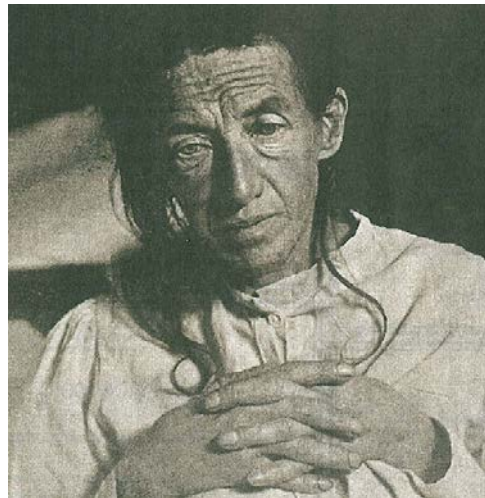


(Left to right) Alois Alzheimer, Emil Kraepelin, R. Gaupp, and Franz Nissl. About 1906

November 3rd 1906.
Tubingen, Germany
37th Assembly of the Southwest German Psychiatrists



"Soon she developed
a rapid loss of memory..."



"...only a tangle of fibrils indicates the place where a neuron was previously located."

Alois Alzheimer. "Über Eine Eigenartige Erkrankung der Hirnrinde."
Allgemeine Zeitschrift für Psychiatrie und Psychisch-Gerichtliche Medizin. 1907.
Translation: "About a peculiar disease of the cerebral cortex"



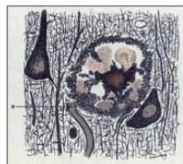
Stage I



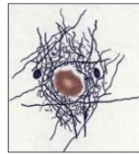
Stage IV



Stage VI



Stage VII



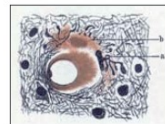
Stage II



Stage III



Stage V



Stage VI



Stage VIII



Oskar Fischer 1876 – 1942

Drawings of plaque stages I–VIII from the brains of patients with senile dementia. Compiled from the illustrations of Fischer's 1910 paper.

A. Alzheimer

Über eigenartige Krankheitsfälle des späteren Alters

(On certain peculiar diseases of old age)

With 10 Text figures and 2 Plates

(Received 11 January 1911)

I would like to begin by presenting one of the patients seen here recently as it illustrates some of the difficulties of making a clinical judgement about these cases.

⁴The 56-year-old labourer Johann F. was admitted to the psychiatric Clinic on 12 Nov. 1907. There was no history of excessive drinking. Two years before admission his wife died, since when he became quiet and dull. In the previous 6 months he had become forgetful, could not find his way, could not perform simple tasks or carried these out with difficulty. He stood around, did not appear to bother about food, but ate greedily whatever was put before him. He was not capable of buying anything for himself and did not wash. He was admitted by the service for the poor.



Oskar Fischer

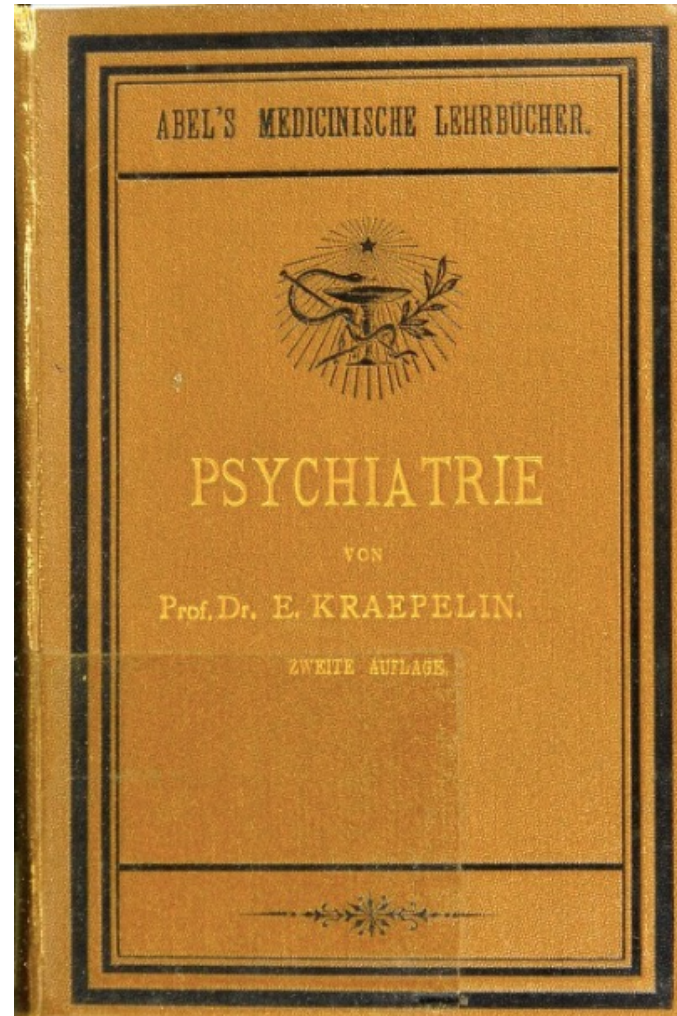
“These observations...demonstrate to us in an impressive way how difficult it is to define diseases solely with respect to their clinical features.”

“It cannot be doubted that the plaques in these specific cases do in all relevant aspects correspond to those which we find in dementia senilis.”

“The question therefore arises as to whether the cases of disease which I consider peculiar are sufficiently different clinically or histologically to be distinguished from senile dementia or whether they should be considered under that rubric.”



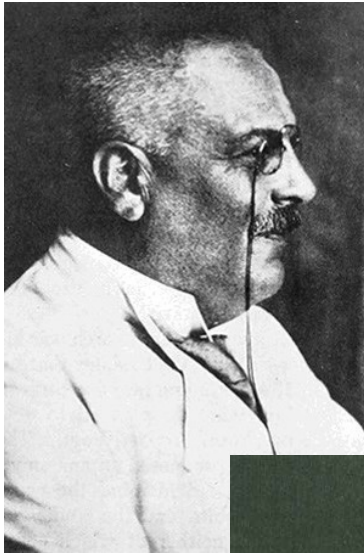
Emil Kraepelin 1856 – 1926



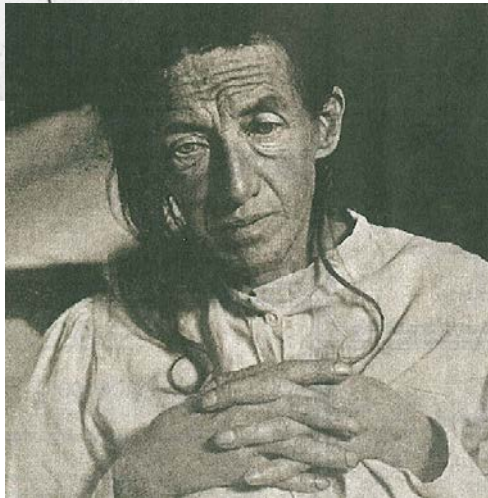
1887

Tubinger Chronik. "From City To Country."

On the Analysis of Psychotraumatic Symptoms....



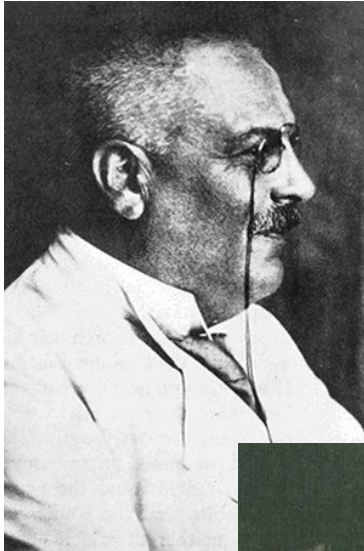
"Soon she developed
a rapid loss of memory..."



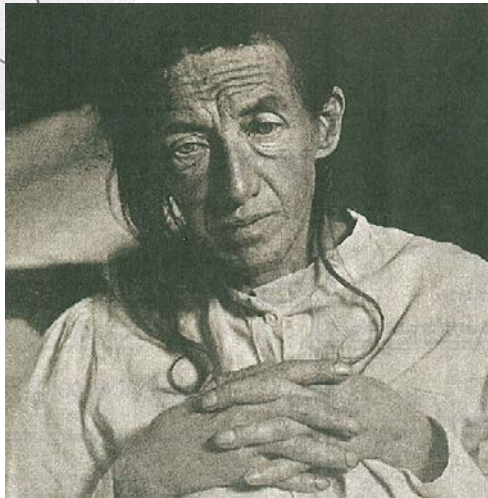
"...only a tangle of fibrils indicates the place
where a neuron was previously located."



Carl Jung
b. 1875 – d. 1961



"Soon she developed
a rapid loss of memory..."



"...only a tangle of fibrils indicates the place
where a neuron was previously located."

*"These are men whose minds the Dead
have ravished.
Memory fingers in their hair of murders,
Multitudinous murders they once
witnessed."*

Wilfred Owen, "Mental Cases."



EMIL KRAEPELIN

Psychiatrische Randbemerkungen zur Zeitgeschichte*

(Psychiatric observations on contemporary issues^(a))

The colossal events which have befallen the German people have struck at the root of their inner being. A variety of symptoms have appeared in the behaviour of the masses which, measured by traditional standards, appear foreign and inconceivable. Shifts falling entirely outside the bounds of linear development have occurred in public feeling and desire. Hence there has been no shortage of

“The frequency of psychopathic predisposition in Jews could have played a role, although it is their harping criticism, their rhetorical and theatrical abilities, and their doggedness and determination which are most important.” He bemoaned how “the war had carried out a terrible selection among our most able and self-sacrificing men; it was above all the unfit and selfish individuals who remained unscathed.” He regretted the “humanitarian efforts” that had helped “the suffering, sickly and the decrepit” and explained how “they load the shoulders of the able-bodied (on whom our hopes for the future rest) with ever greater burden under which the latter’s energies must ultimately expire.”



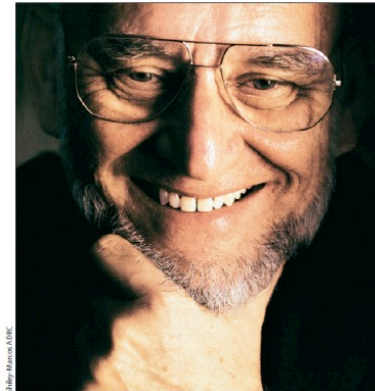
Editorial

The Prevalence and Malignancy of Alzheimer Disease

A Major Killer

Arch Neurol—Vol 33, April 1976

ROBERT KATZMAN, MD
Bronx, NY

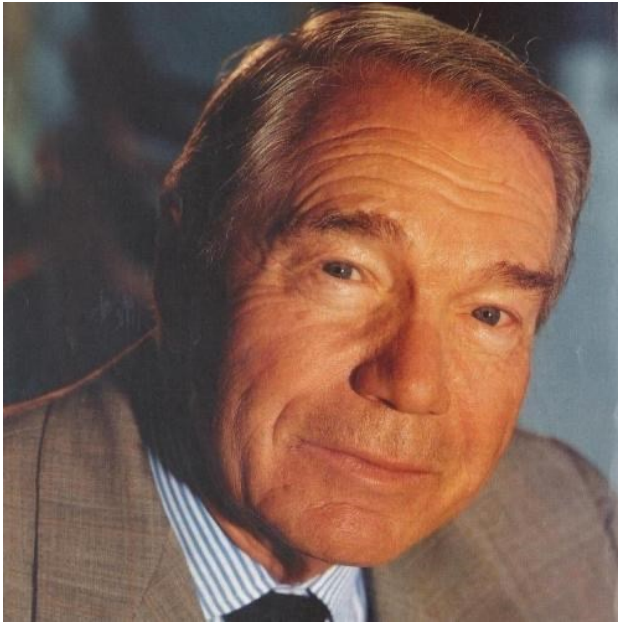


Robert Katzman

Neurologist, researcher, and co-founder of the Alzheimer's Association. Born on Nov 29, 1925, in Denver, CO, USA, he died on Sept 16, 2008, in San Diego, CA, USA, aged 82 years.

“Senile as well as pre-senile forms of Alzheimer are a single disease, a disease whose etiology must be determined, whose course must be aborted, and ultimately a disease to be prevented.”

A self-help group for the self-made man



Jerry Stone 1914 – 2015



Bethesda, Maryland
October 29, 1979.....

Jerry Stone

Robert Katzman & Lonnie Wollin, Alzheimer Disease Society

Hilda Pridgeon & Bobbie Glaze, Alzheimer's and Related Diseases Association

Ann Bashkiroff & Suzanne Harris, Family Survival Project

“During that day, with much good will dissipating into acrimonious debate, I could appreciate with full force the torment that our founding fathers must have gone through trying to satisfy 13 colonies who did not want to give up local autonomous rights for the national good.”

Jerry Stone

Bethesda, Maryland

October 29, 1979.....

“I’ll trade my little house in Sausalito anytime for your paper box company.”

Ann Bashkiroff, Family Survival Project

“Idiots.”

Lonnie Wollin

“If we go before Congress and we want something – whether it’s a change in the law or funds – and they see in our mission statement that we assist families that deal with trauma, then when we ask for money, Congress will say, ‘Oh, we had the trauma people in here last month and we gave them eight million dollars. *When we go to Congress, we’re there for Alzheimer’s.*”

Robert Katzman

Bethesda, Maryland
October 29, 1979.....

The Bethesda Compromise...

Alzheimer's Disease and Related Disorders Association

“Cumbersome tongue twisting name.”

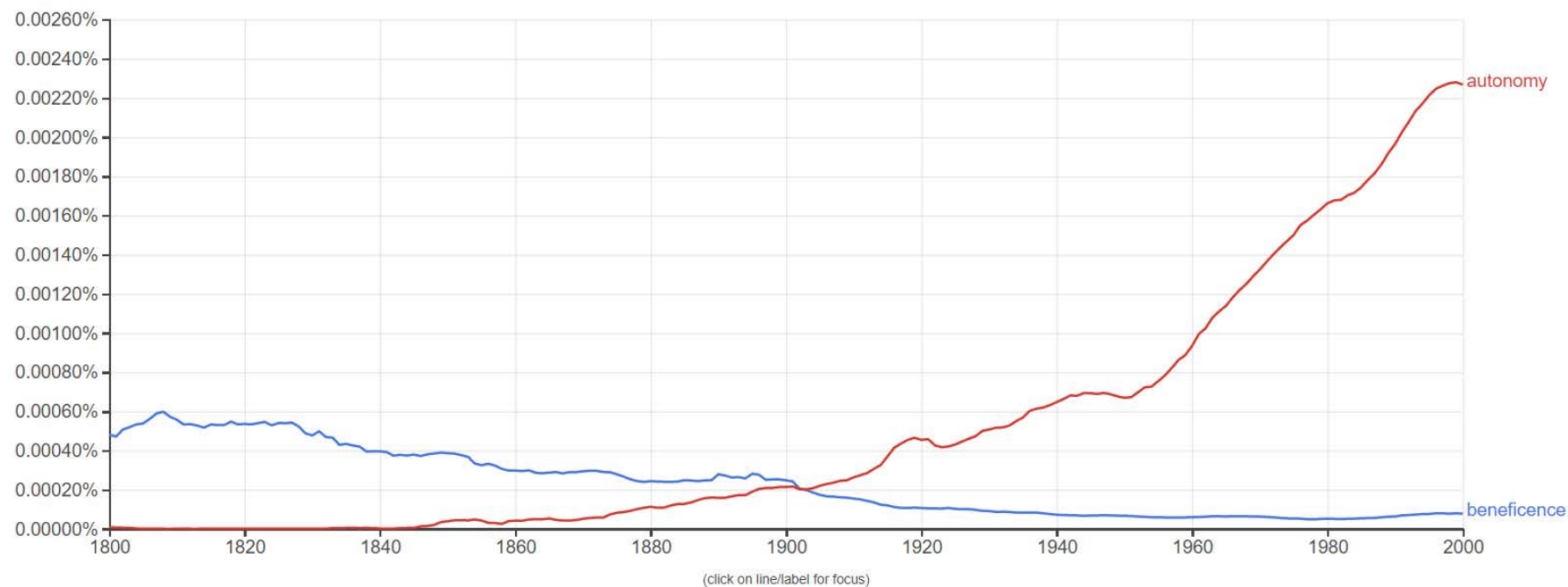
Lonnie Wollin

1988, Katzman argues the name distracts from convincing congress to fund research for a cure. The board of directors rebrands the organization the “Alzheimer's Association” and the tag line “*Someone to Stand By You.*”

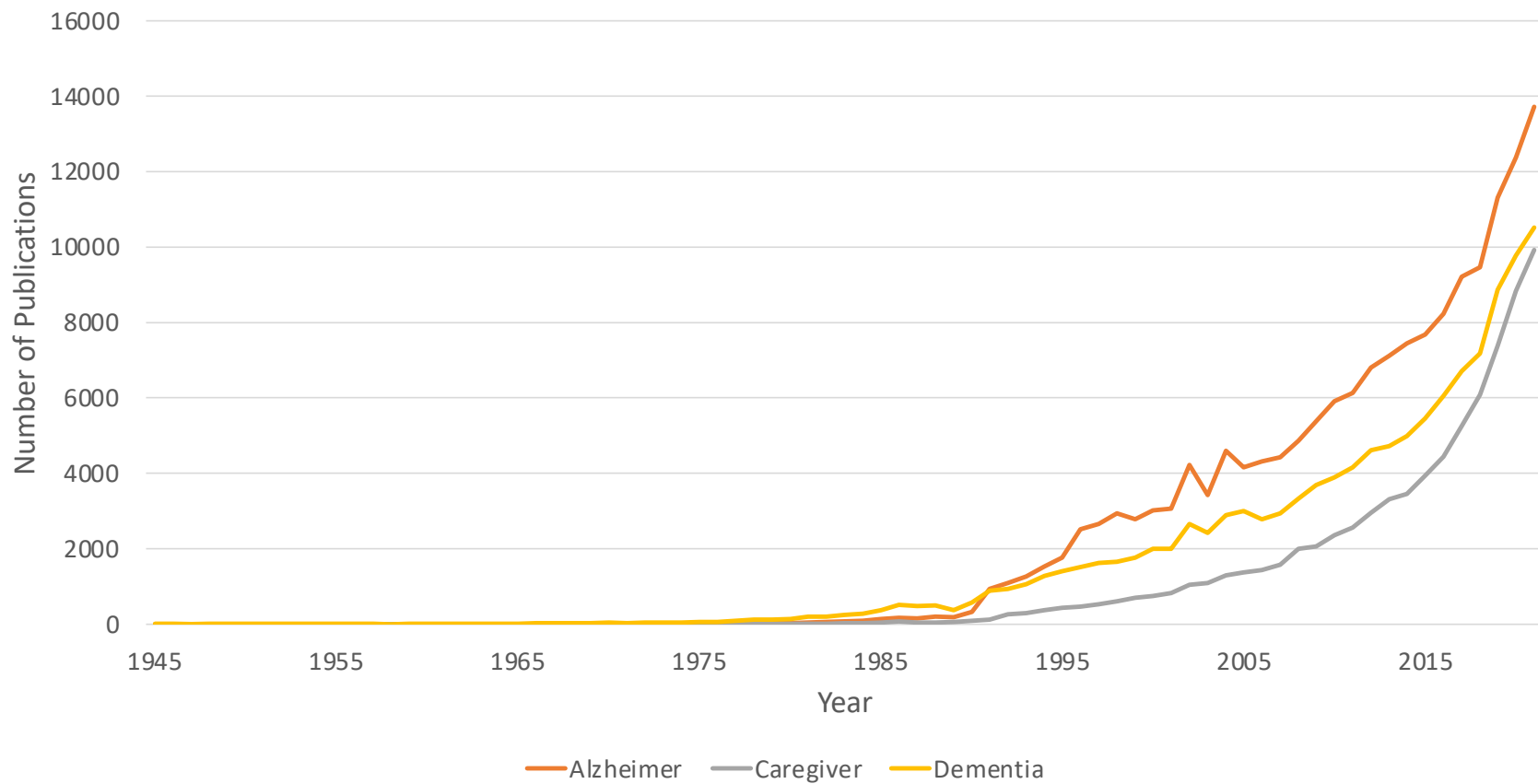
Google Books Ngram Viewer

Graph these comma-separated phrases: ☐ case-insensitive

between and from the corpus with smoothing of [Search lots of books](#)



Number of Web of Science publications containing terms "caregiver," "Alzheimer," and "dementia" in title or abstract by year



From: **Mild Cognitive Impairment: Clinical Characterization and Outcome**

Arch Neurol. 1999;56(3):303-308. doi:10.1001/archneur.56.3.303

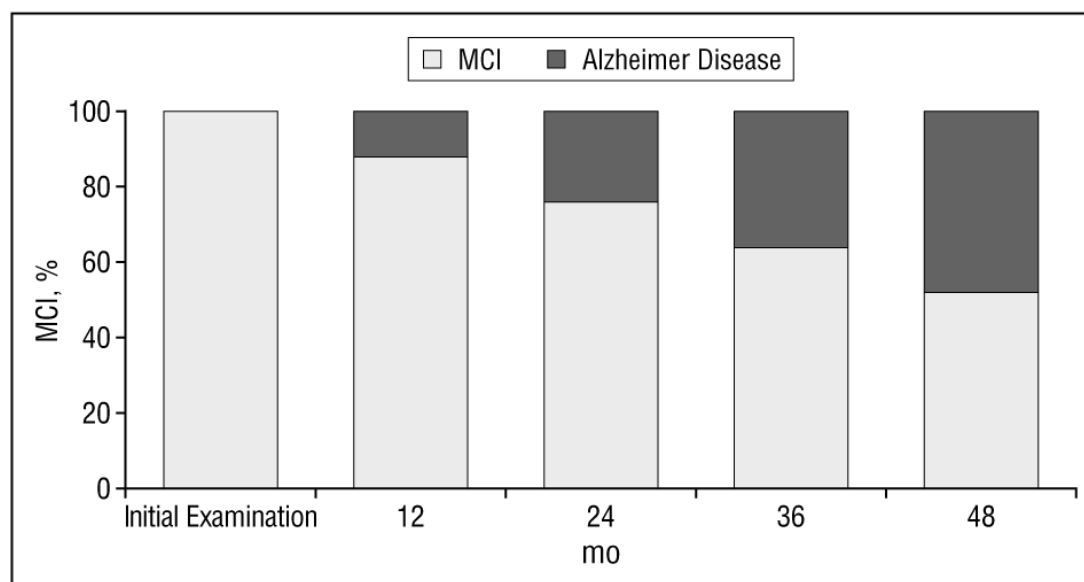


Figure Legend:

Annual rates of conversion from mild cognitive impairment (MCI) to dementia over 48 months.

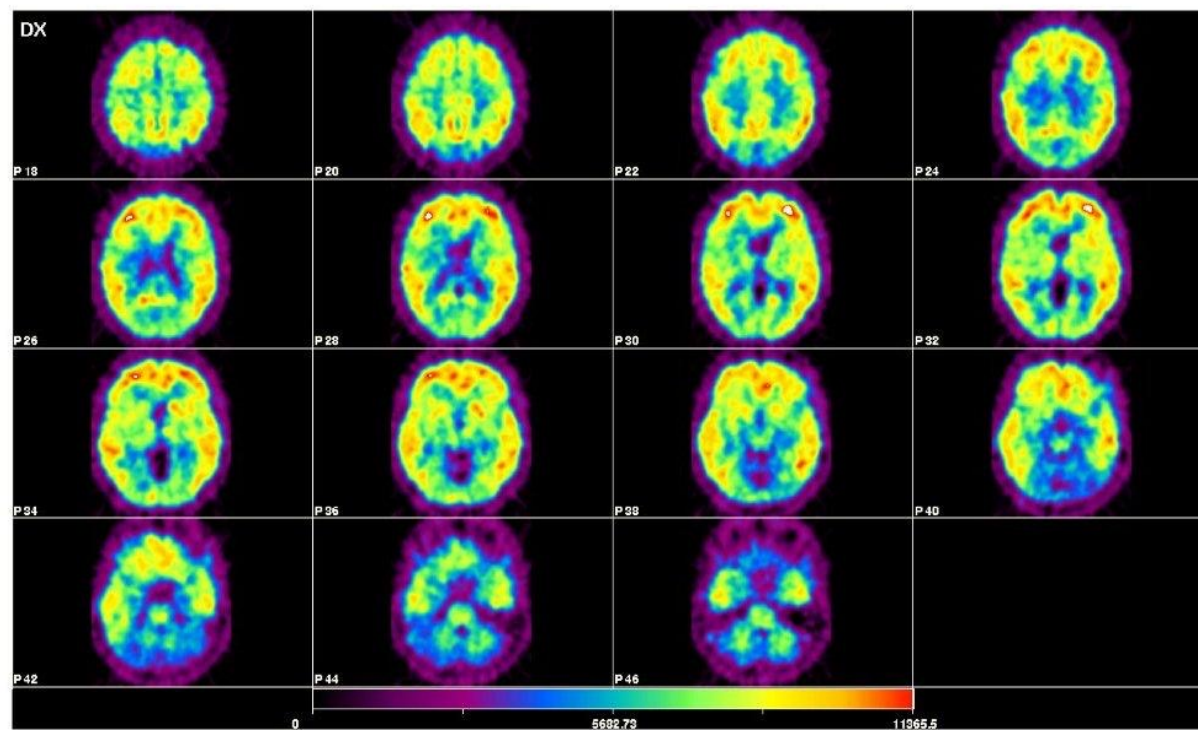


Chet Mattis & Bill Klunk holding Coho Salmon they caught on the Salmon River in Pulaski, NY

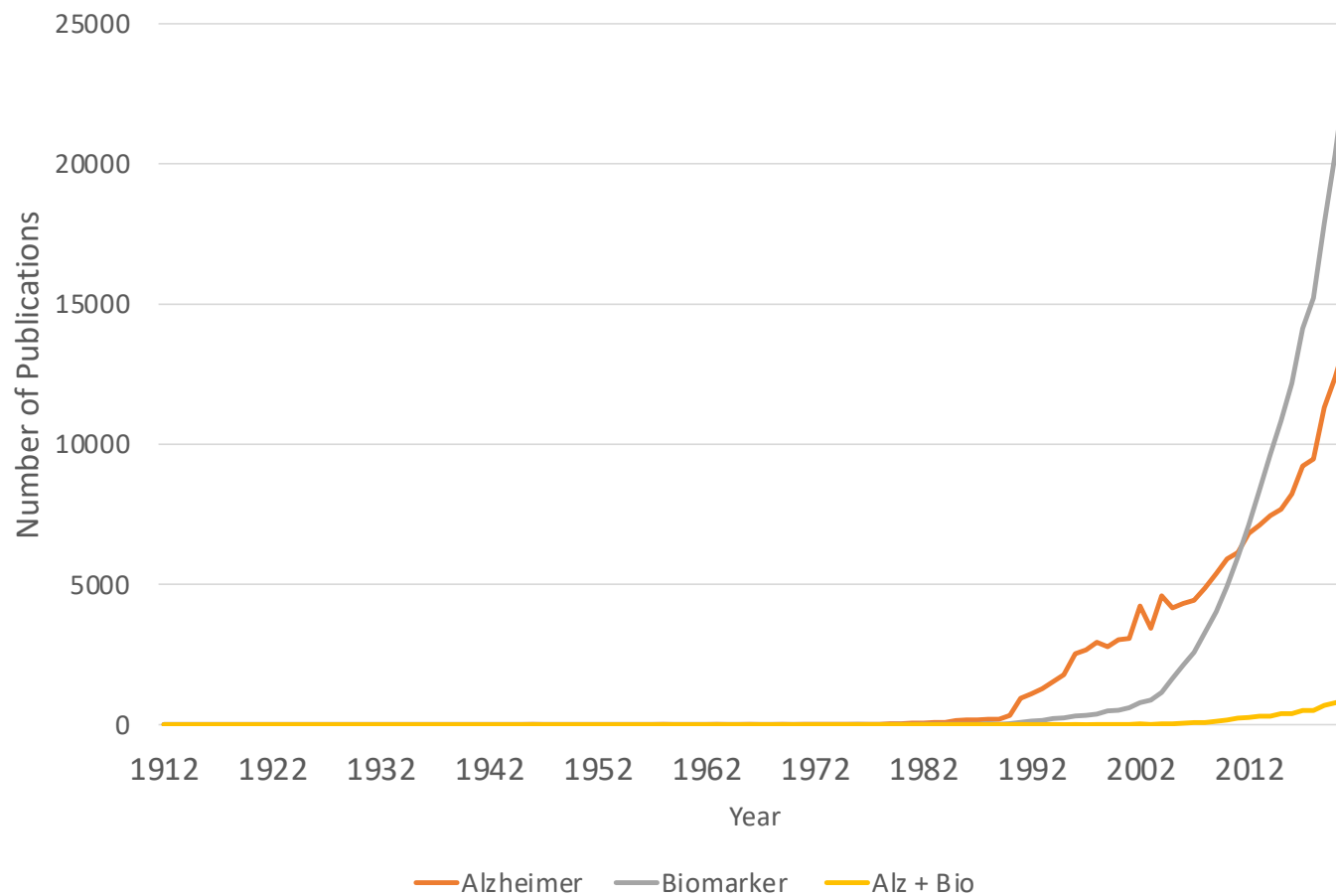
Patient Name: 1-summabild.Activity
Patient Id: 1
Study Date: Feb 14 2002
Radiopharmaceutical: C-11

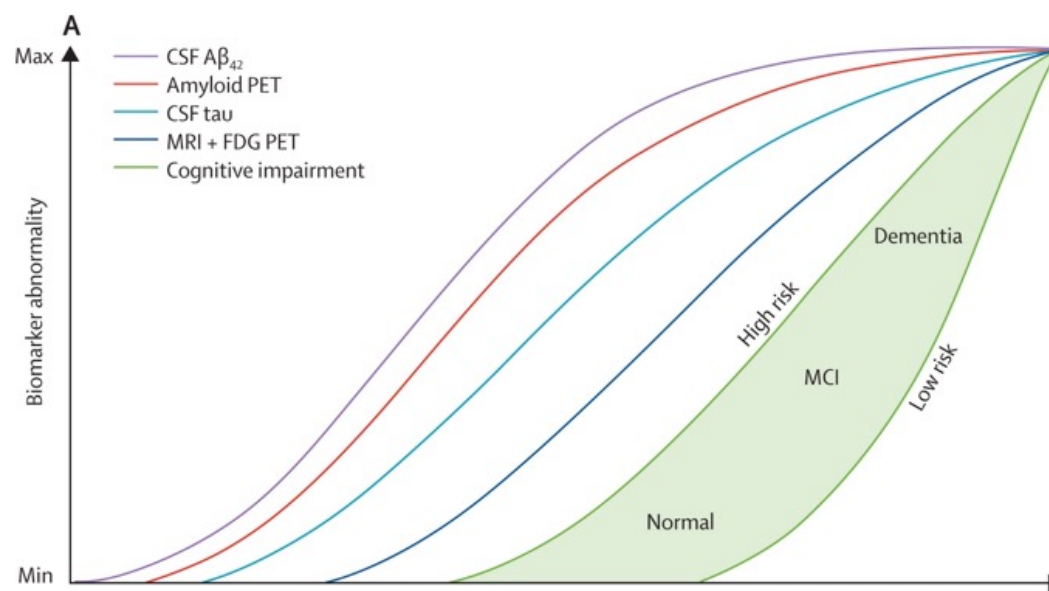
PET CENTRUM
UPPSALA UNIVERSITET

Transaxial View



Number of Web of Science publications containing terms "Alzheimer,"
"biomarker," and both "Alzheimer" and "biomarker" in title or abstract
by year



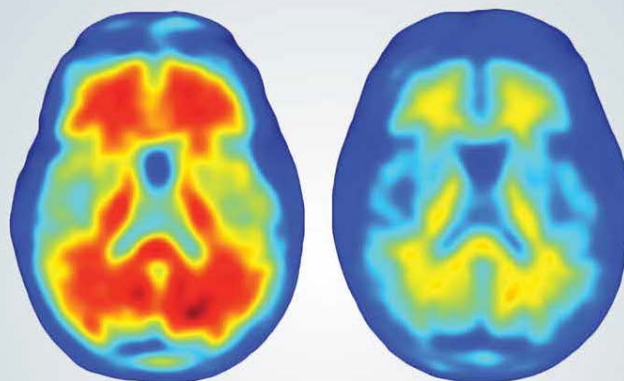


Jack CR, Knopman DS, Jagust WJ, et al. Tracking pathophysiological processes in Alzheimer's disease: an updated hypothetical model of dynamic biomarkers. *The Lancet Neurology*. 2013;12(2):207-216. doi:[10.1016/S1474-4422\(12\)70291-0](https://doi.org/10.1016/S1474-4422(12)70291-0)

nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

OUTLOOK
Science-led
economics



TARGETING AMYLOID

Antibody aducanumab reduces Alzheimer's
disease-associated amyloid in human brain **PAGES 36 & 50**

COMPUTING

DNA MEMORIES

Genomic technology
tackles big data

PAGE 22

RESEARCH MISCONDUCT

CHEATING HAPPENS

Don't ignore the fraud factor
in irreproducibility

PAGE 29

ATOMIC THEORY

SPHERES OF INFLUENCE

How John Dalton's wooden
models defined the atom

PAGE 32

NATURE.COM/NATURE

1 September 2016 \$20

Vol. 537, No. 7618



9 770028 083095

3.50

The National Alzheimer's Plan

“In this plan, ***the term "Alzheimer's disease," or AD, refers to Alzheimer's disease and related dementias, consistent with the approach Congress used in NAPA.*** Related dementias include frontotemporal, Lewy body, mixed, and vascular dementia. It is often difficult to distinguish between Alzheimer's disease and other dementias in terms of clinical presentation and diagnosis. Some of the basic neurodegenerative processes have common pathways. People with dementia and their families face similar challenges in finding appropriate and necessary medical and supportive care. ***Unless otherwise noted, in this plan AD refers to these conditions collectively.***”



OFFICE OF THE ASSISTANT SECRETARY
FOR PLANNING AND EVALUATION

Topics ▾

Collaborations, Committees, and Advisory Groups ▾

About ▾

Search



NAPA

[Alzheimer's Disease and Related Dementias \(AD/ADRD\)](#)

[Advisory Council on Alzheimer's Research, Care and Services](#)

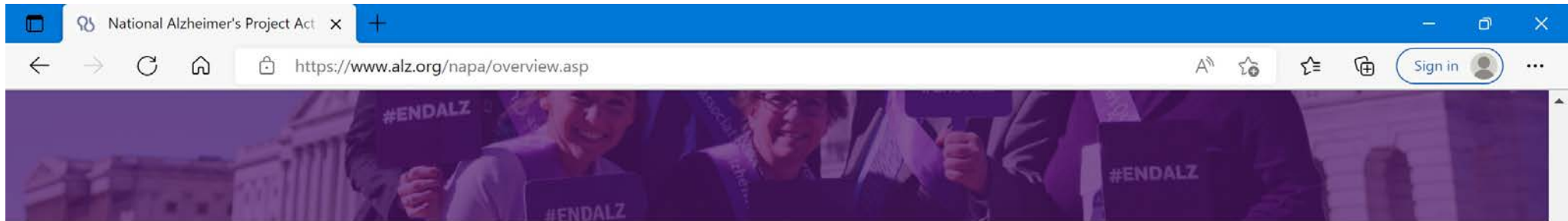
[National Plan and Other NAPA Documents](#)

[Additional AD/ADRD Information](#)

[ASPE](#) > [Collaborations, Committees, and Advisory Groups](#) > [NAPA National Alzheimer's Project Act](#)

NAPA – National Alzheimer's Project Act

The National Alzheimer's Project Act (NAPA) creates an important opportunity to build upon and leverage HHS programs and other federal efforts to help change the trajectory of Alzheimer's disease and related dementias (AD/ADRD). The law calls for a National Plan for AD/ADRD with input from a public-private Advisory Council on Alzheimer's Research, Care and Services. The Advisory Council makes recommendations to HHS for priority actions to expand, coordinate, and condense programs in order to improve the health outcomes of people with AD/ADRD and reduce the financial burden of these conditions on those with the diseases, their families, and society.



The Alzheimer's Association is leading the fight to make Alzheimer's a national priority

In 2010, the Alzheimer's Association and the Alzheimer's Impact Movement, a separately incorporated advocacy affiliate, worked with Congress to develop the National Alzheimer's Project Act (NAPA). Signed into law on Jan. 4, 2011, NAPA led to the creation of a national strategic plan to address the rapidly escalating Alzheimer's crisis and fundamentally changed the way the nation addresses Alzheimer's and all other dementia.

Working toward the national goal of preventing and effectively treating Alzheimer's by 2025, the Alzheimer's Association, AIM and our nationwide network of advocates are the driving force leading to unprecedented levels of federal research funding and improved access to care and support services.

Ask Congress to pass the NAPA Reauthorization

True or False....

1. If a person does not have dementia, she cannot have Alzheimer's disease. FALSE
2. MCI is a risk factor for Alzheimer's disease. FALSE
3. The US National Alzheimer's plan focuses on Alzheimer's disease. FALSE
4. In the US National Alzheimer's plan, AD/ADRD abbreviates "Alzheimer's disease and Alzheimer's disease related disorders." FALSE

My *new* practice @the Penn Memory Center

“The results of my assessment show *impairments in cognition*. [list out domains of cognition; e.g., memory and executive function].

A. These are *not causing problems* in day-to-day function.

B. These are causing *inefficiencies* in day-to-day function (i.e. MCI). [list & explain]

C. These are causing *disabilities* in day-to-day function (i.e. dementia). [list & explain]

There *are/are not psychiatric symptoms*. [list & explain]

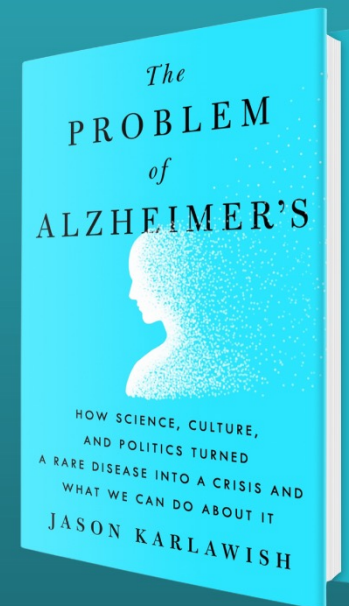
The results of history, exam, cognitive and biomarker testing show that the cause of these cognitive problems and [inefficiencies / disabilities] is [fill in the disease name].”

Note: my colleagues and I routinely speak of “persons living with....” (we do not say “demented”).

Thank you....

.....to Catholic Charities Hawai'i

WHY DID ALZHEIMER'S DISEASE
BECOME A CRISIS...
AND WHAT CAN WE DO ABOUT IT?



www.jasonkarlawish.com

@jasonkarlawish