

An approach to the prevention of Alzheimer's dementia – can we get there from here?

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Alzheimer's 1st reported case



“Auguste D.” 1903 - 4

First . . . jealous of her husband. Soon she “developed a **rapid loss of memory**. . . **disoriented** in her home, . . . carried things from one place to another and hid them, . . . thought somebody was trying to kill her . . . When reading . . . skips from line to line or **reads by spelling words individually** . . . In writing, she **repeats syllables, omits others**, . . . In speaking, she uses gap-fills and paraphrased expressions (“milk-pourer” instead of cup); She **no longer remembers the use of some objects**. . .”

The rising pandemic of dementia

- Dementia is a syndrome that can have many causes
- Alzheimer's disease (AD) is the most common neuro-degenerative disease of brain – causes 2/3 – 3/4 of all cases of dementia worldwide
- Today the world has >35 million cases of AD dementia. By 2050 this number will rise to 115 million cases . . . *unless we learn to prevent AD dementia*



The crushing costs of dementia

- In 2010, best estimates indicated worldwide costs > US \$604 billion each year.
- Costs in Canada exceeded \$5 billion / yr.
- By 2050, cumulative costs of Alzheimer care in U.S. estimated at \$10,000,000,000,000 – \$20,000,000,000,000 (\$10 to 20 trillion) -- more than the current US government debt!



Crushing costs of dementia (2)

- By 2050, annual costs for 115 million cases worldwide X \$20,000 / case = \$2.3 trillion
- By 2050, 24% of Chinese population will be ≥ age 65. Some 40 million with dementia.
- All this is foreordained unless we can learn to prevent AD dementia



Can we get there from here?

Yes!! If we understand that . . .

1. Alzheimer's disease is a chronic disease, similar to heart disease and cancer.
2. The disease has a biology that extends well into the decades before symptoms are seen.
3. As we learn more about the biology of the disease, we will learn how to prevent or control it.



The “take home” messages (2)

4. **Improved methods of detection and early intervention will undoubtedly motivate physicians and other health professionals to seek and treat early signs of disease.**
5. **We are “on the verge” of an explosion in knowledge about the biology of Alzheimer’s disease and the prevention of its symptoms.**

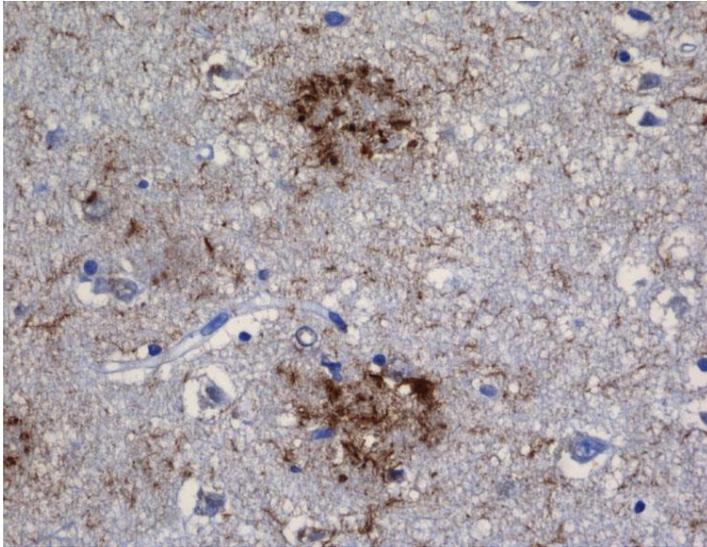


The “take home” messages (3)

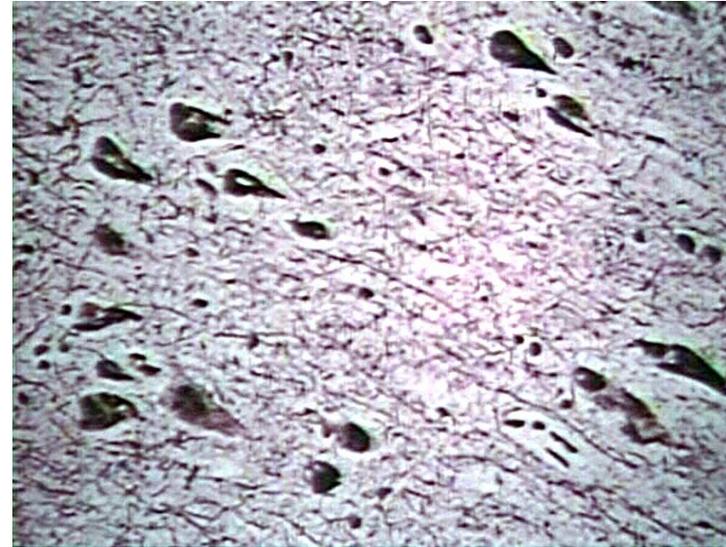
6. Prevention of Alzheimer’s dementia can be achieved without preventing the disease itself.
7. With research and resources similar to those dedicated to heart disease and cancer, we can achieve a similar measure of prevention – probably more!



Alzheimer's disease



Amyloid plaques



Neurofibrillary tangles

We know what it looks like . . .

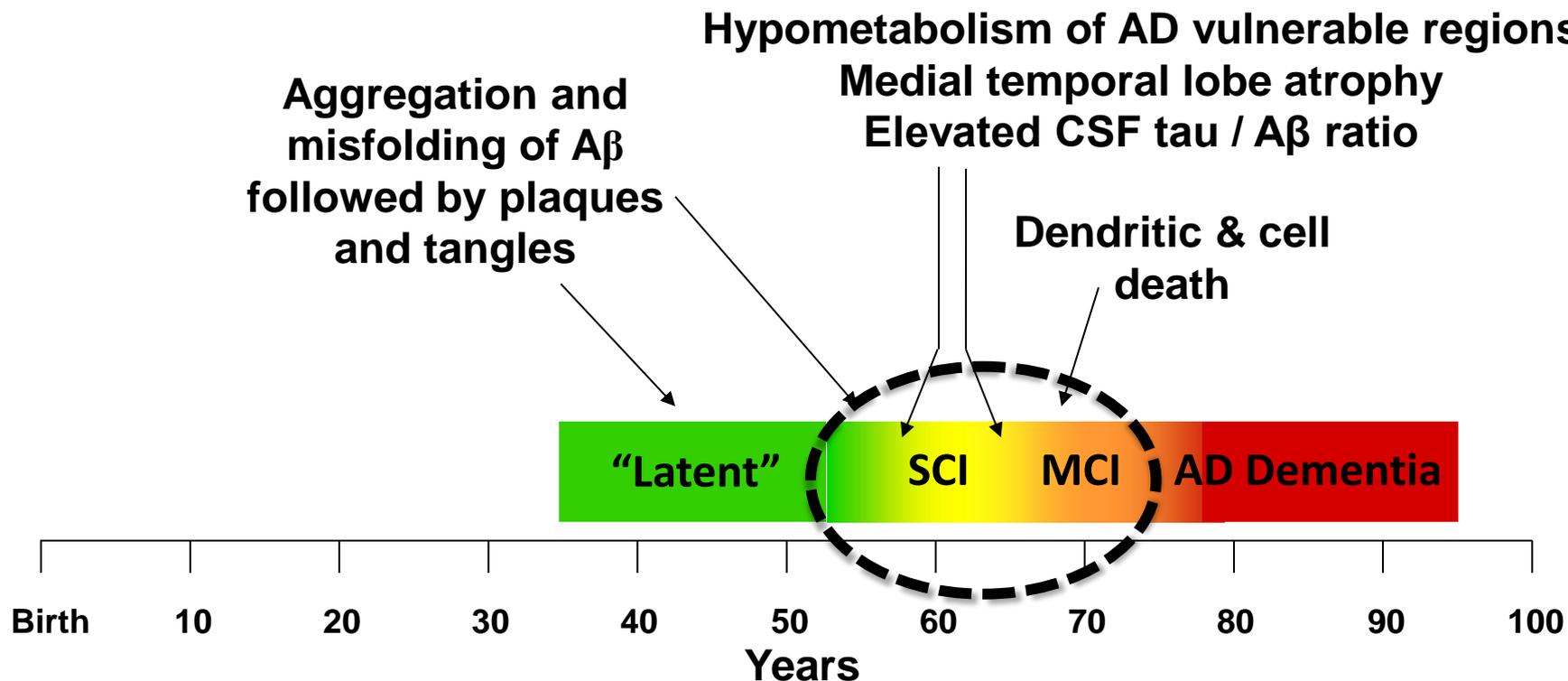


We don't know the cause. But we do know that . . .

- **Alzheimer's is a chronic disease . . .**
- **It begins in sometime in middle life**
- **Its earliest symptoms are barely noticeable and may be viewed as “normal for age.”**
- **As symptoms become more severe they may be recognized as Mild Cognitive Impairment**



Evolution in the Development of AD



Latent = No Cognitive Impairment

SCI = Subjective Cognitive Impairment

MCI = Mild Cognitive Impairment

AD = Alzheimer's dementia



'MCI' – Is that where we should intervene ?

- Significant compromise in cognitive ability leading to some difficulty in function, but . . .
- NO dementia (can maintain independent activity)
- Divided into types: amnestic (memory loss is predominant) vs. non-amnestic
- Amnestic type is thought to be the typical first blush (*prodrome*) of AD symptoms



'MCI' – What's the story?

- **Diagnosis is difficult to establish at first, but .**
..
- **Once it's clear MCI is there, ~ 80% of those who have it will develop dementia within 10 years.**
- **Helpful for optimum management (medical advice, planning for future events)**



However

Treatments for AD dementia have NOT been proven helpful for MCI, nor for delay of the later onset of dementia.

Has the train left the station?



More than half of people with MCI have a pathologic diagnosis of AD

Ann Neurol. 2009 August ; 66(2): 200–208. doi:10.1002/ana.21706.

The Neuropathology of Probable Alzheimer's Disease and Mild Cognitive Impairment

J.A. Schneider, M.D., M.S.^{1,2,3}, Z. Arvanitakis, M.D., M.S.^{1,2}, S.E. Leurgans, Ph.D.^{1,2}, and D.A. Bennett, M.D.^{1,2}

¹Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL

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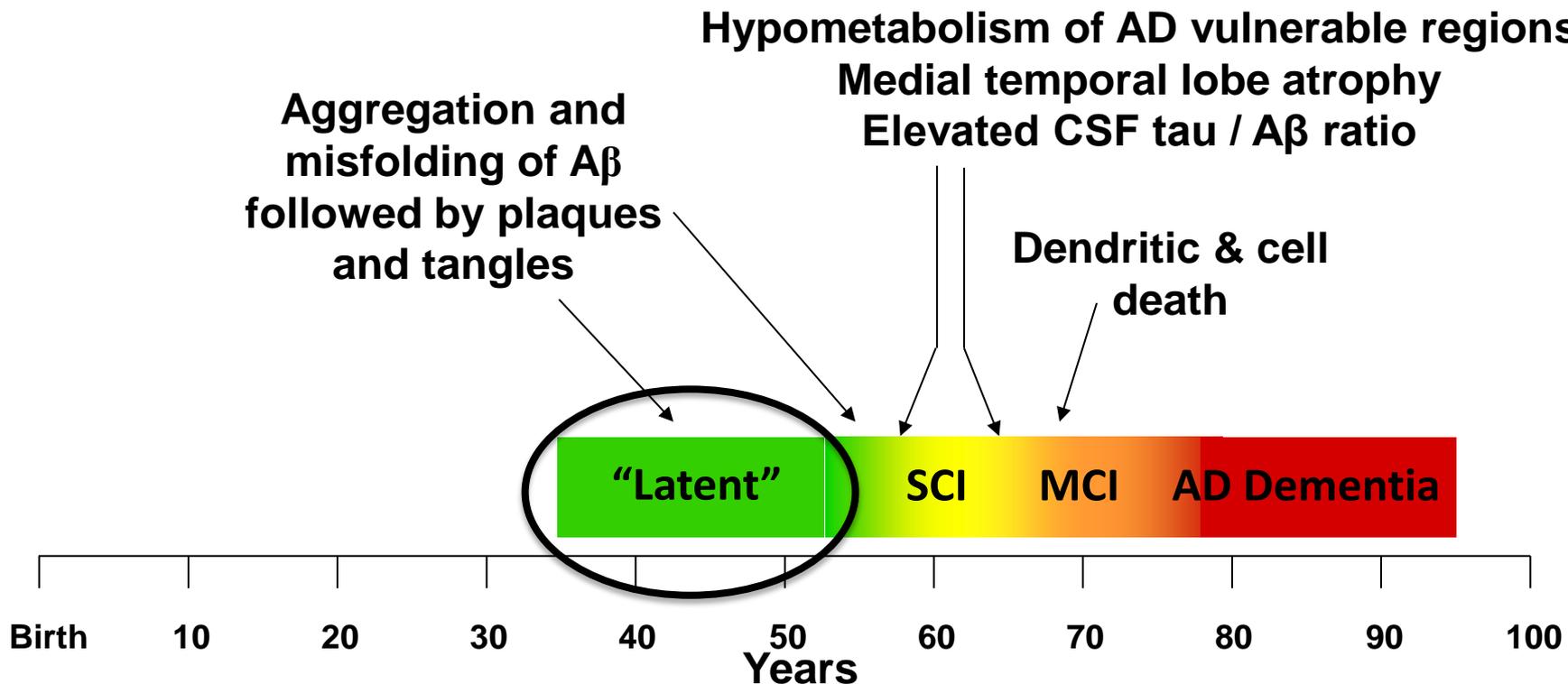


**Absolutely, we need to keep looking for better ways to care for and to treat people who already have symptoms,
*but***

Ultimately, we must find ways to attack the disease in its pre-symptomatic stages and prevent the emergence of symptoms.



Development of Alzheimer's disease



LATENT = No Cognitive Impairment
SCI = Subjective Cognitive Impairment

MCI = Mild Cognitive Impairment
AD = Alzheimer's dementia



Can we do that?

Can we

‘get there from here’?

If so, how?



Two broad approaches:

- 1. Find and replicate factors that predispose some people to delay or avoid onset of dementia ('lifestyle interventions')**
- 2. Pharmacological interventions keyed toward interruption of the disease process ('disease modification')**



Several lifestyle intervention strategies appear to reduce risk of AD

- Regular exercise
- Reduce weight (Body Mass Index)
- Control blood pressure (in mid-life)
- Reduce insulin resistance and Type II (obesity-associated) diabetes
- Improved diet (“Mediterranean vs McDonald’s”)



What's good for the heart is good for the brain!



But . . . rates of heart disease and stroke have come down enormously in the last few decades. Shouldn't that mean that rates of AD dementia would also be dropping?



They are!!

- Age-specific rates are actually declining – for first time ever observed
- But the rapid aging of populations will more than offset any improvement in age-specific rates
- Effects of aging most clearly evident in the developing world



We can be glad for now.

- **There really are things we can do to reduce our risk of AD dementia**
- **... but we won't win the battle against AD this way. Ultimately, we'll need to deal with the biology of the disease.**
- **How?**

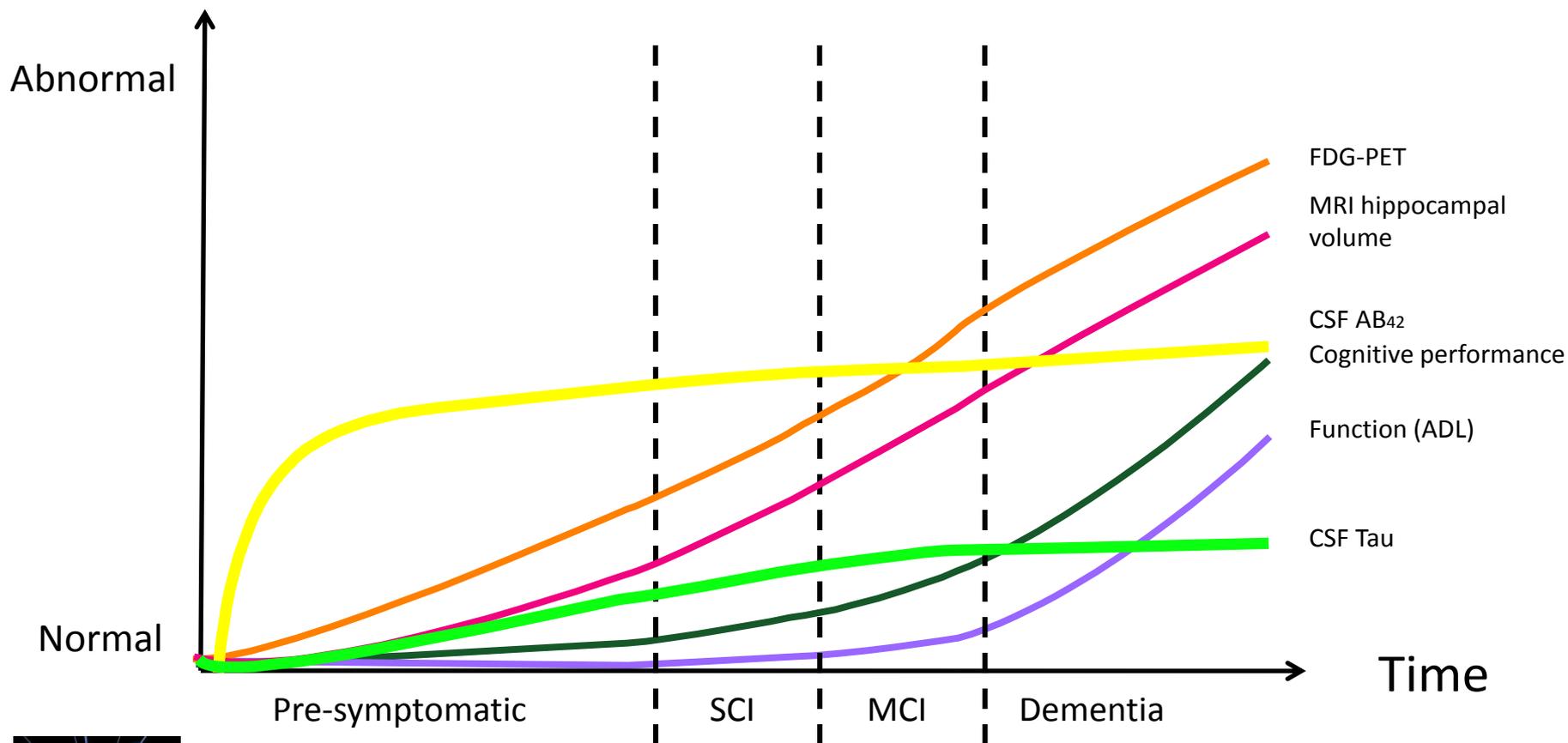


Biomarkers of AD may be useful for early diagnosis, before dementia is evident.

We may also be able to use biomarkers to measure the progress of AD in pre-symptomatic stage . . .



'Biomarkers' of AD precede symptoms



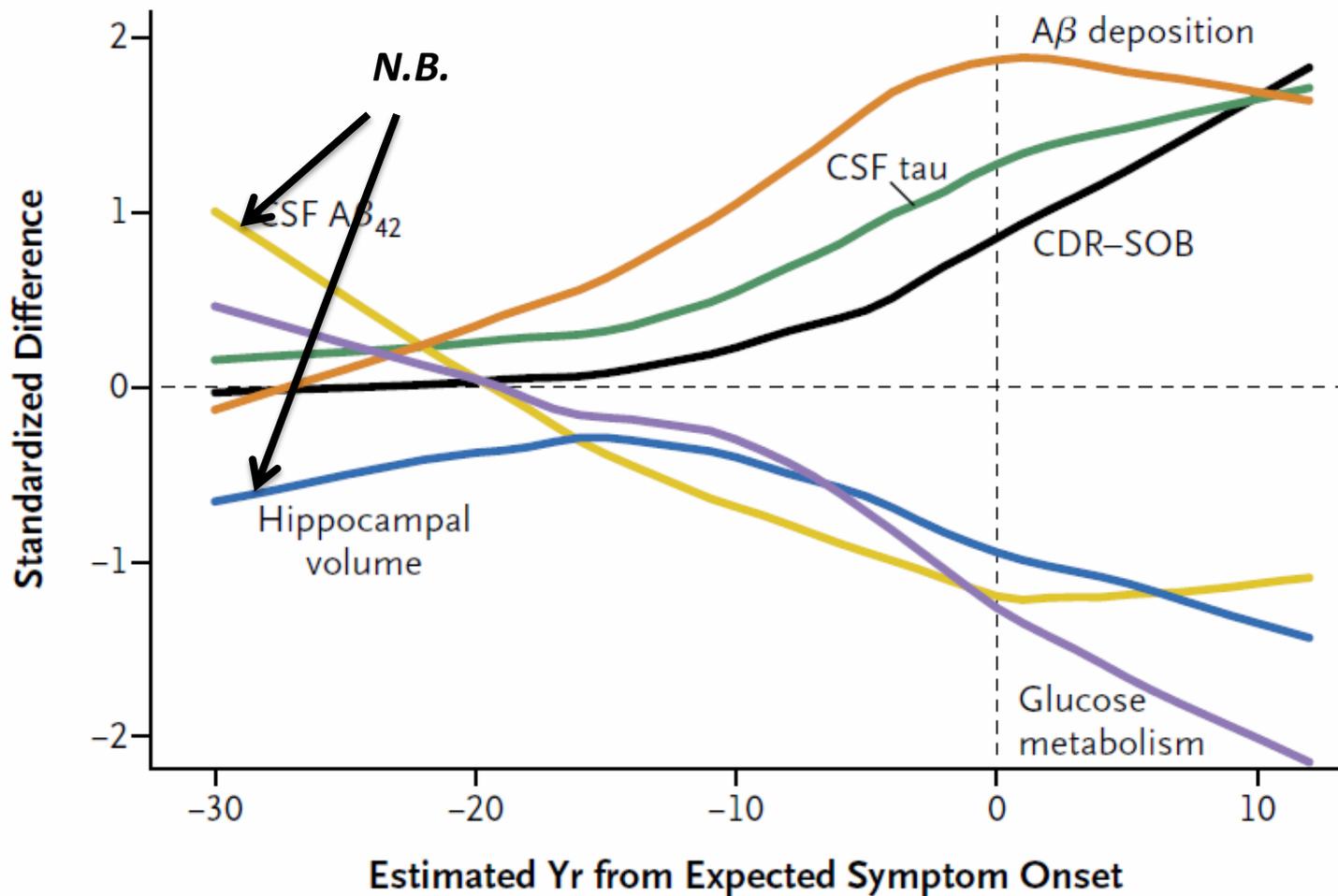
Aisen PS, Peterson RC, Donohue MC, et al. *Alzheimer's Dement.* 2010;6:239-246.



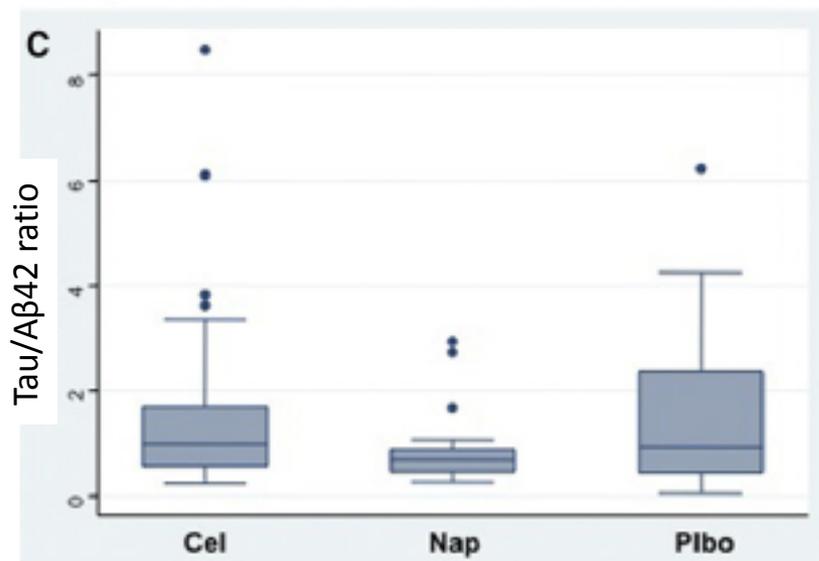
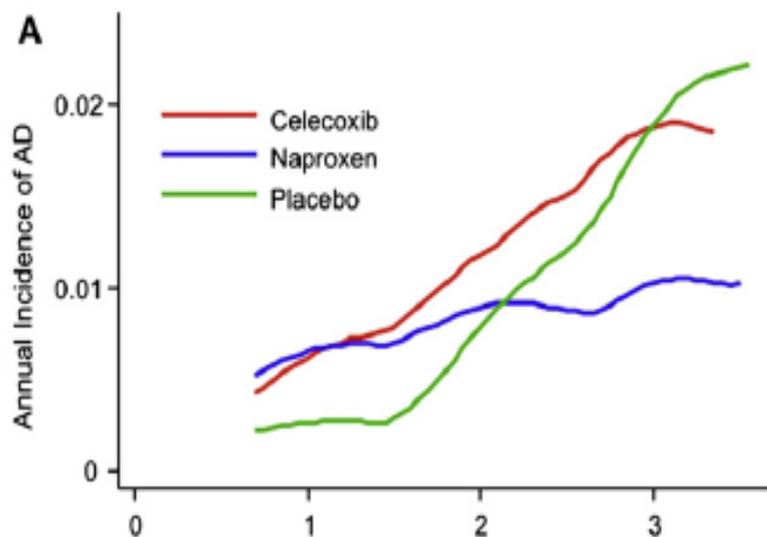
Can we use biomarkers to measure the effects of prevention strategies?



'Biomarkers' of AD as measures of pre-symptomatic disease progress?



Naproxen may diminish incidence of AD and reduce AD biomarkers in non-demented elderly



*J C. Breitner et al. for ADAPT Research Group
 Alzheimers and Dementia, 2011;7:402-11*

PResymptomatic Evaluation of Experimental Novel or Treatments for Alzheimer's Disease (PREVENT-AD)



*Étude sur
la prévention
de la maladie
d'Alzheimer*

La maladie d'Alzheimer et les démences apparentées sont des maladies dégénératives du cerveau. Elles détruisent lentement la mémoire et la faculté de penser, conduisent à la perte d'autonomie et finissent par entraîner le décès. À ce jour, il n'existe aucun remède.

Avec la population vieillissante, environ un *baby boomer* sur cinq souffrira de la maladie d'Alzheimer au cours de sa vie. De plus, chez les personnes qui ont des antécédents familiaux de la maladie, le risque de développer l'Alzheimer s'accroît de deux à trois fois.

À l'heure actuelle, le seul remède, c'est la prévention.

Douglas
INSTITUT UNIVERSITAIRE EN SANTÉ MENTALE / MENTAL HEALTH UNIVERSITY INSTITUTE

Do you want to prevent Alzheimer's disease?

Study conducted by the Centre for Studies on Prevention of Alzheimer's Disease (StoP-Alzheimer) at the Douglas Mental Health University Institute.



*Study on
the prevention
of Alzheimer's
disease*

Alzheimer's and related dementias are caused by degenerative diseases of the brain. They slowly destroy memory and the ability to think, which leads to decreased independence and finally the loss of life. There is no cure.

With the aging of the population, about one in five baby boomers will suffer from Alzheimer's disease in his or her life. What's more, people with a family history of the disease have a two to three times higher risk.

The best hope for a cure is prevention.

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Voulez-vous prévenir la maladie d'Alzheimer ?

Étude menée par le Centre de recherche sur la prévention de la maladie d'Alzheimer (StoP-Alzheimer) à l'Institut universitaire en santé mentale Douglas.



PREVENT-AD *eligibility criteria*

- 60 years old or more
 - 55-59 years old if 15 years within relative onset of AD
- Parent or 2 siblings with probable AD
 - mother and/or father; sister and/or brother
- Cognitively intact at entry
 - determined by MoCA and CDR
- Good general health
- Willing and able to participate in >5 yrs of annual assessments



www.prevenir-alzheimer.ca

www.prevent-alzheimer.ca

1-855-888-4485



Ars longa, vita brevis

No time like the present . . .

Rome wasn't built in a day!

**Journey of 1000 miles begins
with first steps**

but

**No sensible enterprise would commit
than 0.5% of its expenditures to R & D**



The “take home” messages

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Merci beaucoup!

