

Novel Diagnostic and Therapeutic Approaches for Alzheimer's Disease

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JOHNS HOPKINS
M E D I C I N E

8 issues in 2024

- *Definitions: dementia v. Alzheimer's*
- *Epidemiology: the next pandemic*
- *Diagnosis of dementia: highly accurate*
- *Diagnosis of course: markers*
- *Comprehensive care: effective*
- *Novel medications: controversial*
- *Prevention: possible*
- *The future: precision medicine*

Definitions: dementia v. Alzheimer's

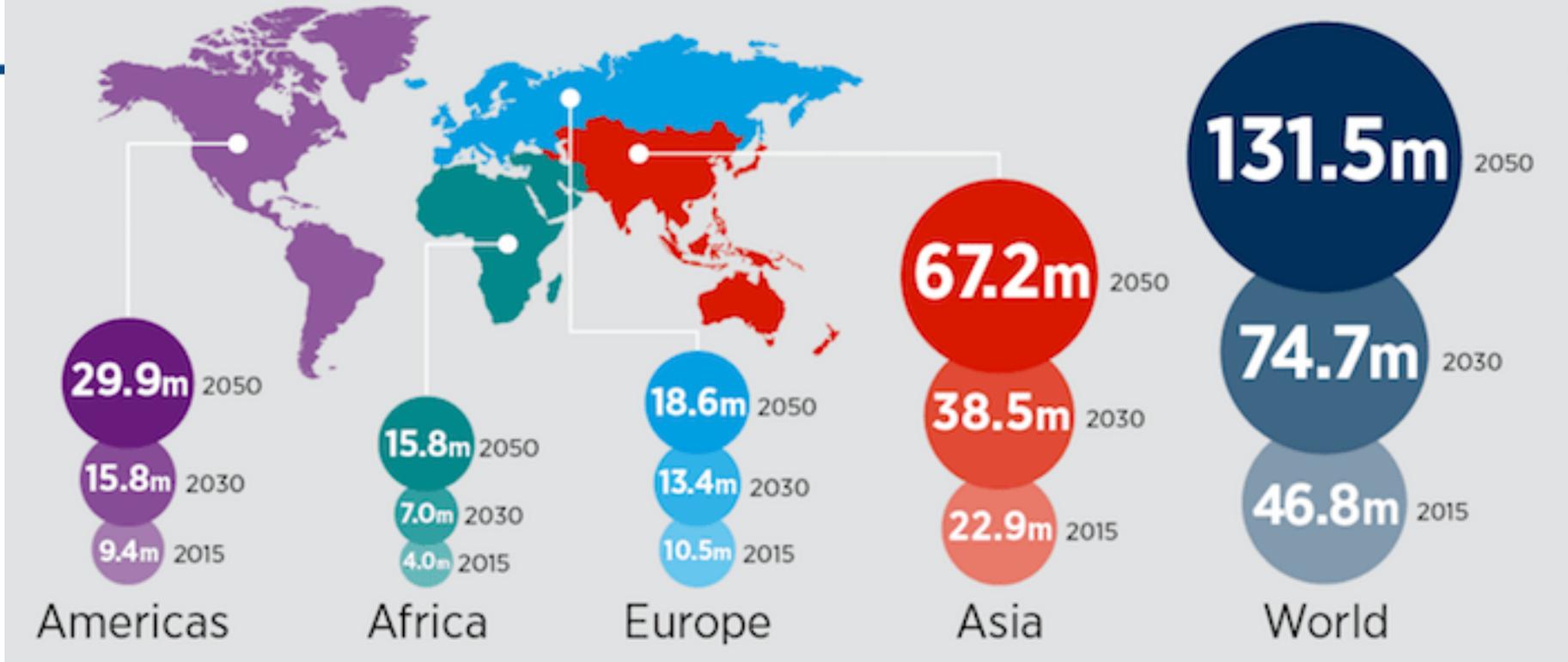
CLINICAL PICTURE

- Usual cognitive aging
- Prodromal states: MCI, MBI
- Dementia: functional impact

ORGAN

- Alzheimer's: brain disease

People living with dementia around the world



For every person ADD 1-3 affected caregivers

in 2024

| MEMORY | FACE | VELVET | CHURCH | DAISY | RED | POINTS |
|--|-----------|--------|--------|-------|-----|-----------|
| Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes. | 1st trial | | | | | No points |
| | 2nd trial | | | | | |

| ATTENTION | | |
|-----------------------------------|--|------------------------------------|
| Read list of digits (1 digit/sec) | Subject has to repeat them in the forward order | <input type="checkbox"/> 2 1 8 5 4 |
| | Subject has to repeat them in the backward order | <input type="checkbox"/> 7 4 2 |

Read list of letters. The subject must tap with their hand at each letter A. No points if ≥ 2 errors

FBACMNAAJKLBAFAKDEAAAJAMOFA

Serial 7 subtraction starting at 100 93 86 79 72

4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt 0 correct: 0 pt

| LANGUAGE |
|--|
| Repeat: I only know that John is the one to help today. <input type="checkbox"/> |
| The cat always hid under the couch when dogs were in the room. <input type="checkbox"/> |
| Fluency / Name maximum number of words in one minute that begin with the letter F <input type="checkbox"/> ____ (N ≥ 11 words) |

| ABSTRACTION |
|---|
| Similarity between e.g. banana – orange = fruit <input type="checkbox"/> train – bicycle <input type="checkbox"/> watch – r |

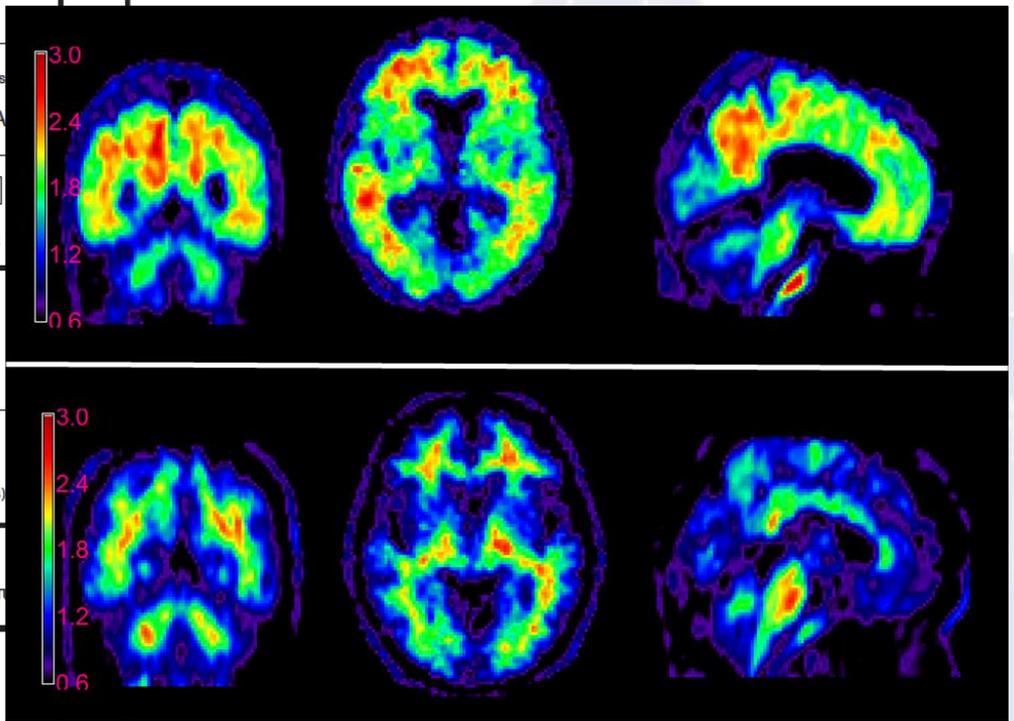
| DELAYED RECALL | Has to recall words WITH NO CLUE | FACE | VELVET | CHURCH | DAISY | RED | Points for UNCUE recall only |
|----------------|----------------------------------|------|--------|--------|-------|-----|------------------------------|
| Optional | Category cue | | | | | | |
| | Multiple choice cue | | | | | | |

| ORIENTATION | Date | Month | Year | Day | Place | City | _/6 |
|-------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----|
| | <input type="checkbox"/> | |

© Z.Nasreddine MD www.mocatet.org Normal ≥ 26 / 30 **TOTAL** ___/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

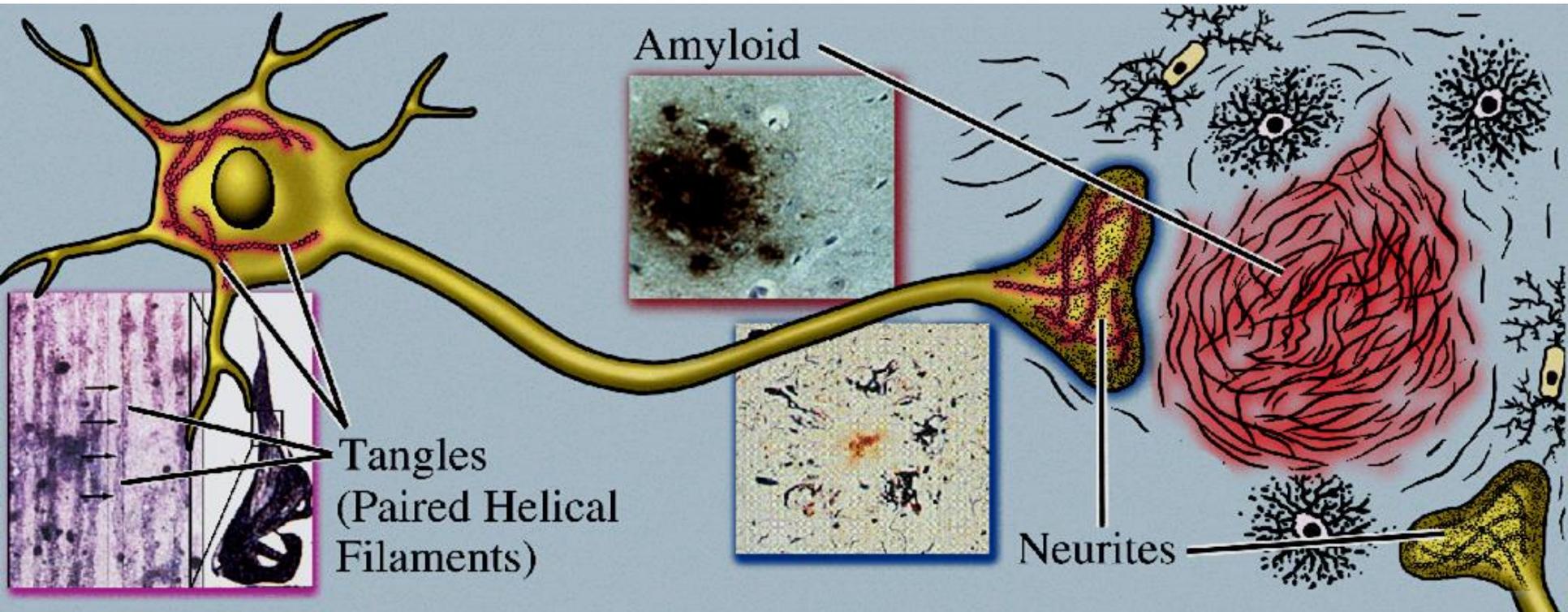


The brain in Alzheimer's dementia

NFT

**Neuronal
loss**

**Neuritic Plaques
Congophilic Angiopathy**



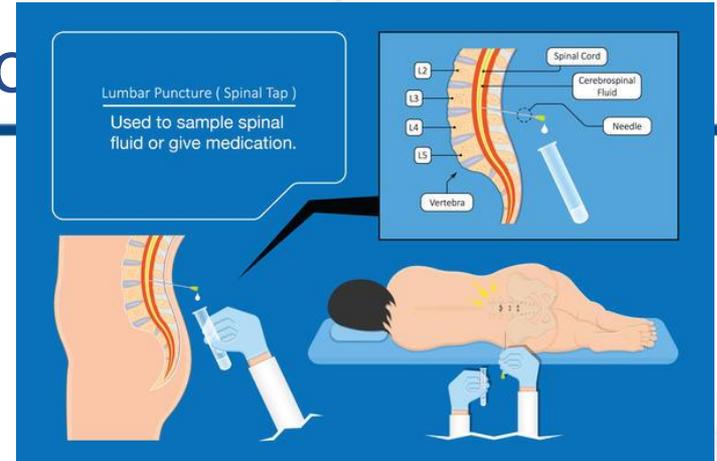
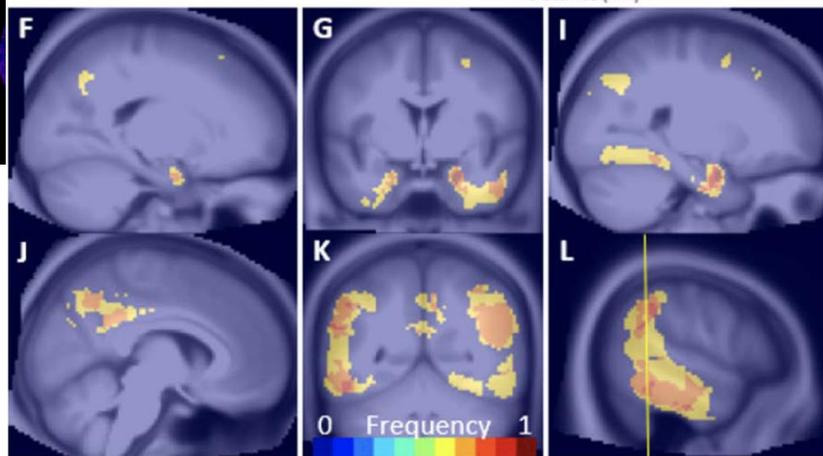
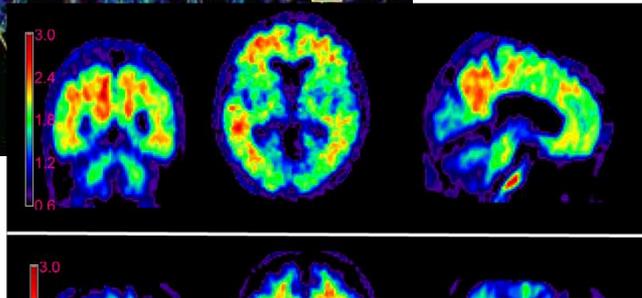
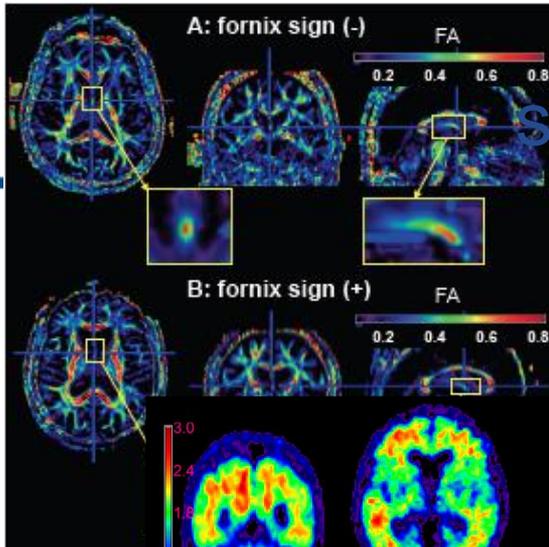
Phospho-tau - PHF

**Microglia
Astrocytes**

**Ab Peptides
Oligomers
Fibrils**

Biomarkers

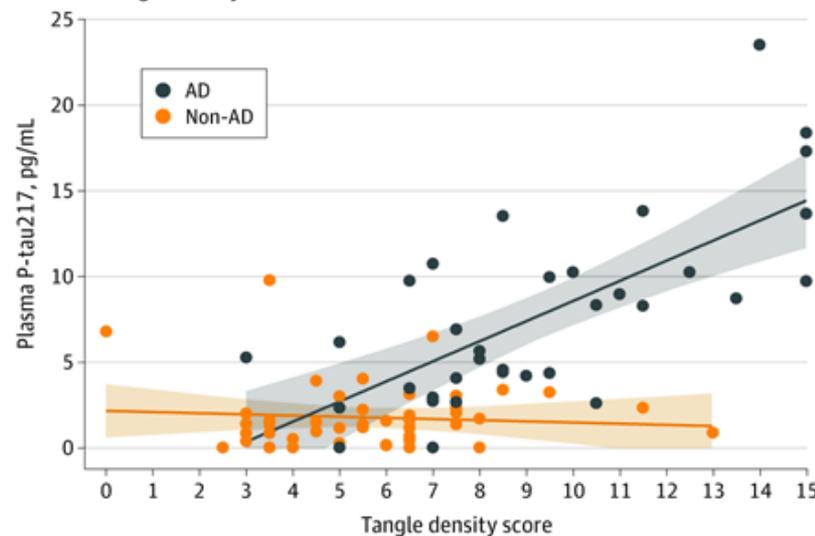
significant developments



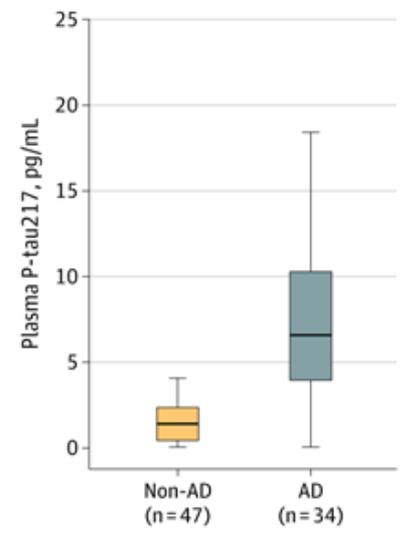
Blood biomarkers in development

- Mass-spec
- A β 40
- A β 42
- A β 40/42
- P-tau-217

A Correlations between plasma P-tau217 concentration and total tangle density score

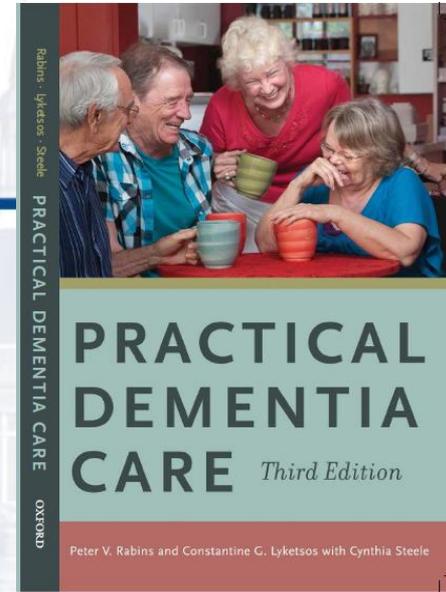


B Antemortem plasma P-tau217 concentration



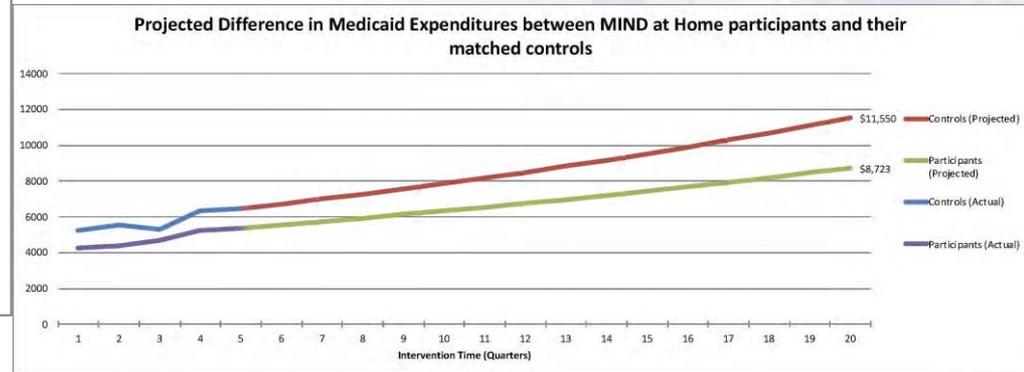
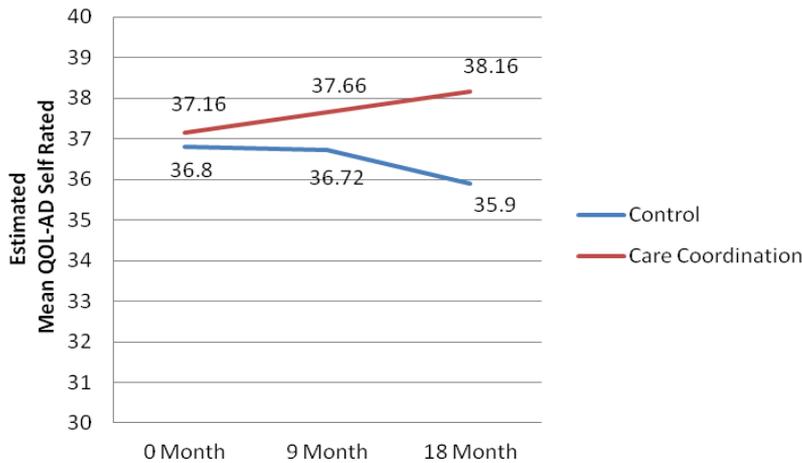
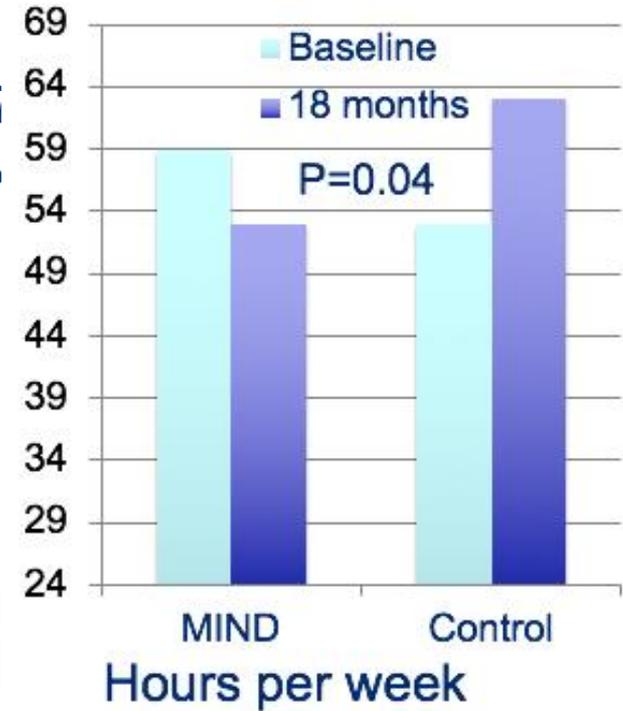
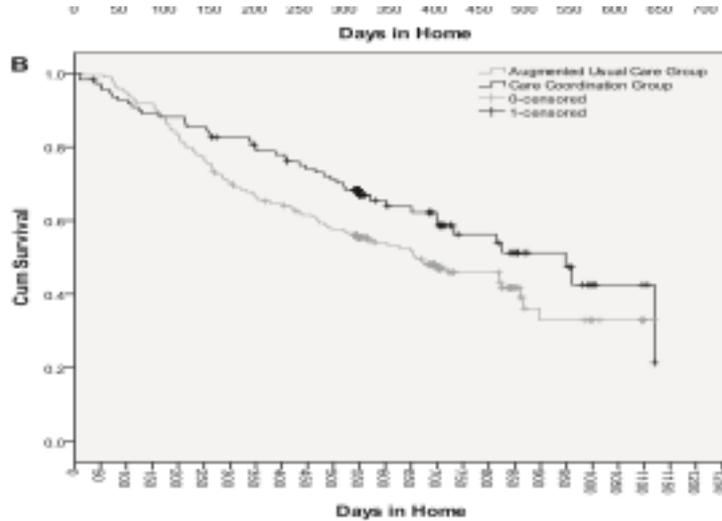
Dementia Care activities

- Treat cognitive symptoms
- Treat neuropsychiatric symptoms
- Reduce medication load
- Manage co-morbidities: HTN, DM, CVD
- Prevent delirium: early detection, anesthesia
- Support patients: activities, safety
- Caregivers: communication, skills, respite



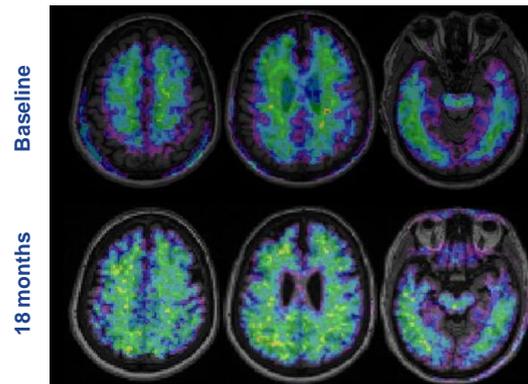
Care at Home

Current

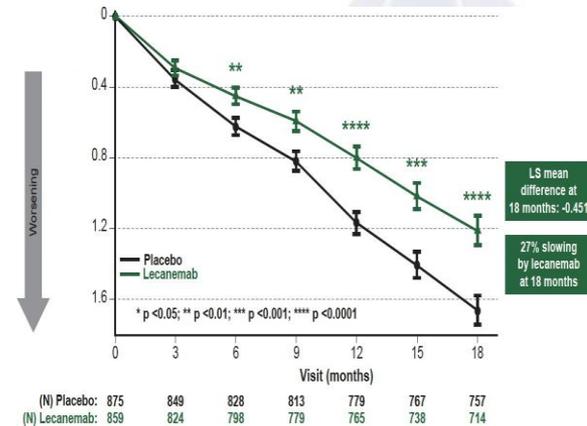
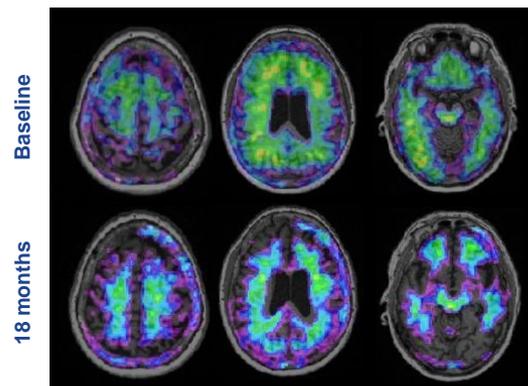


New medications: the “MABs” lecanemab, donanemab

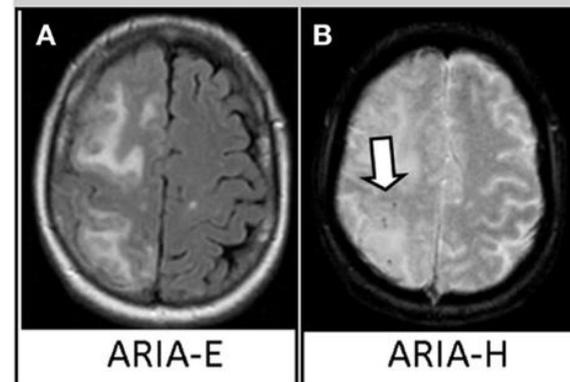
Placebo



Lecanemab



Immunotherapy-induced ARIA



TIPS FOR HEALTHY COGNITIVE LONGEVITY

Constantine G. Lyketsos, M.D., M.H.S.



BASIC RULES

Track activity, sleep, steps, weight (e.g., FitBit).

Understand and practice variety.

Remember brain health = heart health.

WHAT TO AVOID

- ✓ Avoid unnecessary medication use. Don't take pills you don't absolutely need.
- ✓ Be wary of what is being sold in alternative health care. Make sure you are getting what you pay for and understand potential risks.
- ✓ Don't fully retire unless you must. If you do retire, keep as active as possible.

GOOD THINGS TO DO

- ✓ **Stay healthy:** manage weight, blood pressure, blood sugar, and other health conditions. Stay engaged with a good **primary care doctor**.
- ✓ **Sleep well**—at least **seven hours** a night. Make sure you get enough rest.
- ✓ **Limit the effects of stress** on your body (e.g., meditation).
- ✓ **Keep physically active:** Emphasize variety, combine different forms of physical activity over time. Formal exercise is only one form of physical activity. Change your regimen at least once a year (e.g., NYC ballet workout).
- ✓ **Keep mentally active.** Learn new things: a language (e.g., Mandarin) or a musical instrument (e.g., piano). Take a course in a field outside your past experience and your comfort zone (e.g., bonsai garden). Try an online brain-training program.
- ✓ **Keep socially active.** Stay engaged with family, religious activities, social organizations, etc.
- ✓ **Combine physical, mental and social activities.** Examples are group sports, ballroom dancing, and group travel with a lot of walking.
- ✓ Follow a **Mediterranean diet**. Eat lots of fruits, vegetables, fish, and olive oil.
- ✓ **Consume antioxidants.** Examples are blueberries, red wine, or dark chocolate.

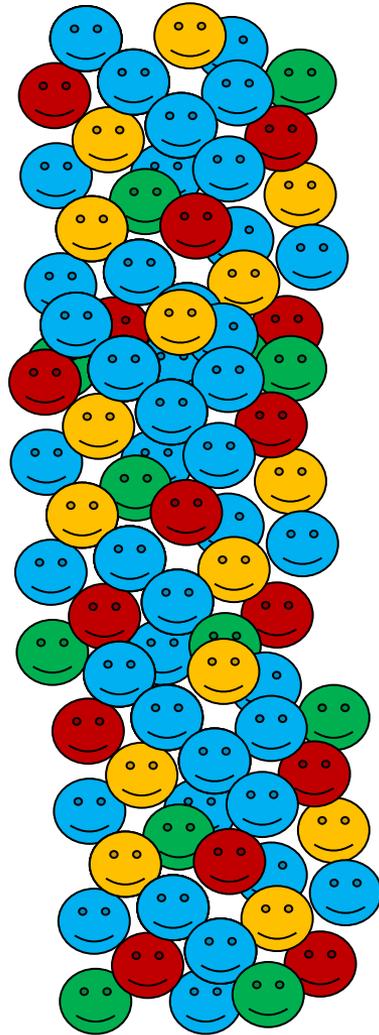
THE BOTTOM LINE

1. There is no single answer—you need to do lots of things at the same time.
2. It does not come in the form of the pill.
3. There are limits to what you can do—ultimately genetics play the major role.

*Prevention
is possible*

*Follow these
tips*

The future: precision medicine



Genetic

Polygenic risk: overall
Polygenic risk: system

Stem Cells

Neuronal function
Effect of treatments

Imaging

Structure
Function

Physiology

Inflammation
Brain perfusion
Exosomes

Clinical

Cognition
Behavior

Subgroup 1



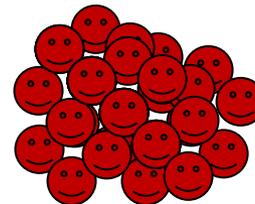
Subgroup 2



Subgroup 3



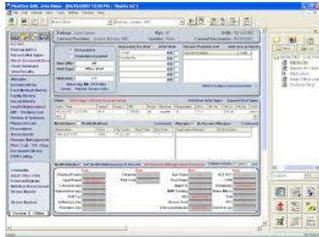
Subgroup 4



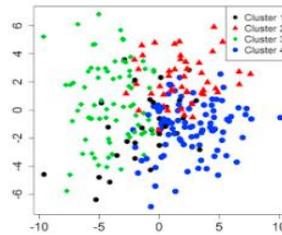
The real world meets AI

Precision Medicine Analytic Platform

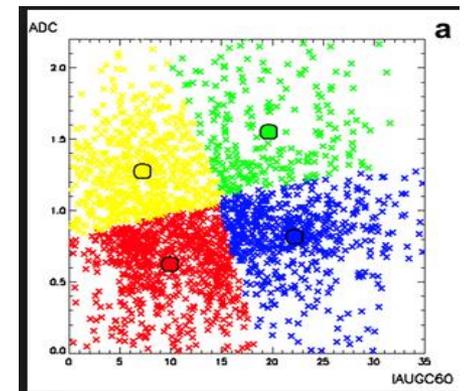
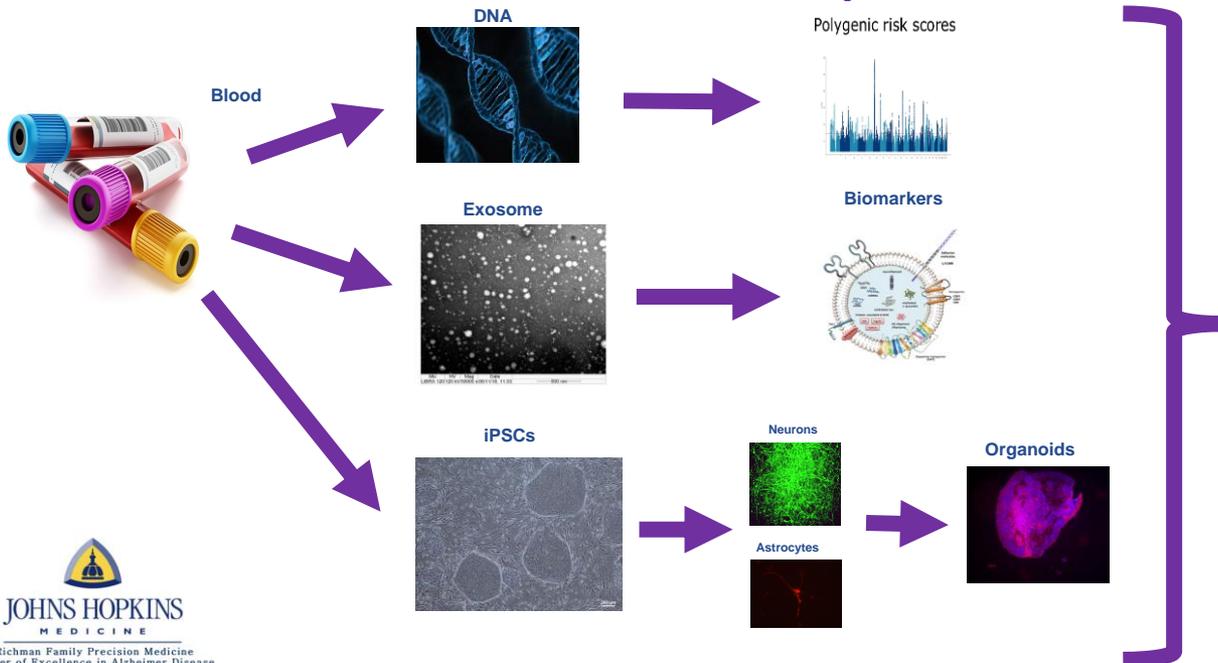
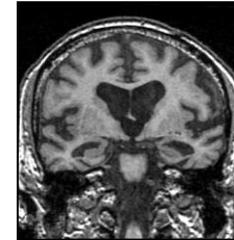
Medical records >700.000



Deep phenotyping



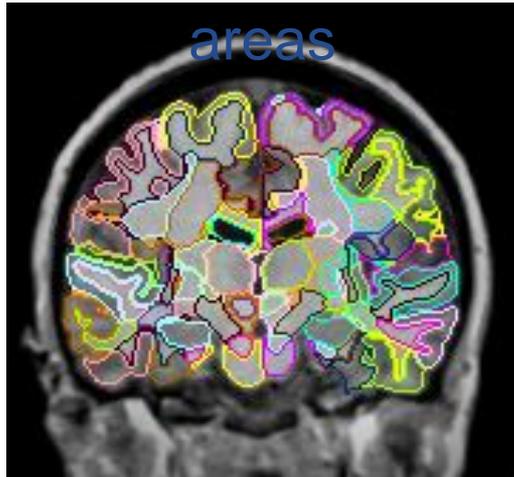
Clinical MRI



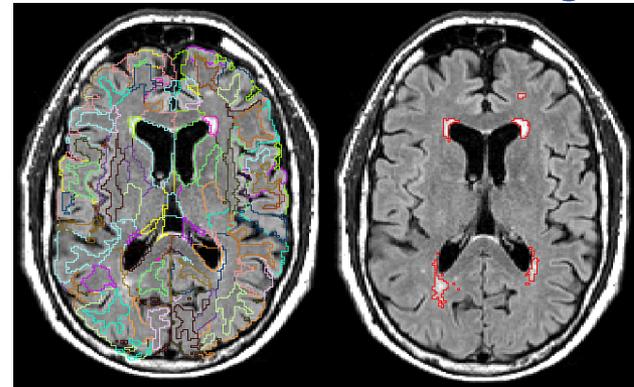
Final phenotyping

Automated analysis of brain MRI

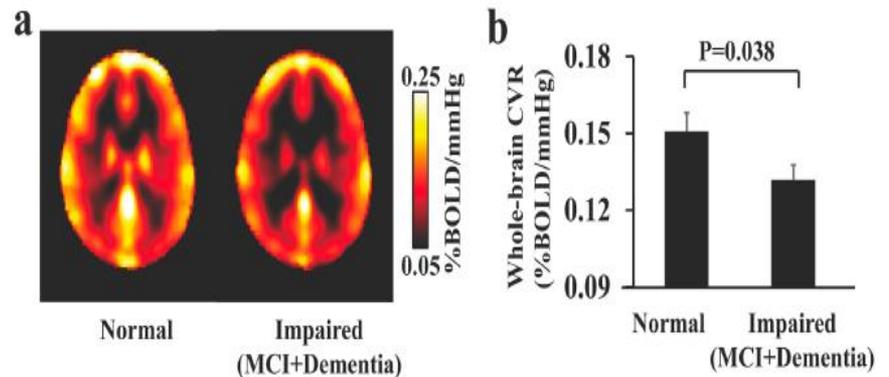
Volume of 190 brain areas



Size and distribution of white matter change

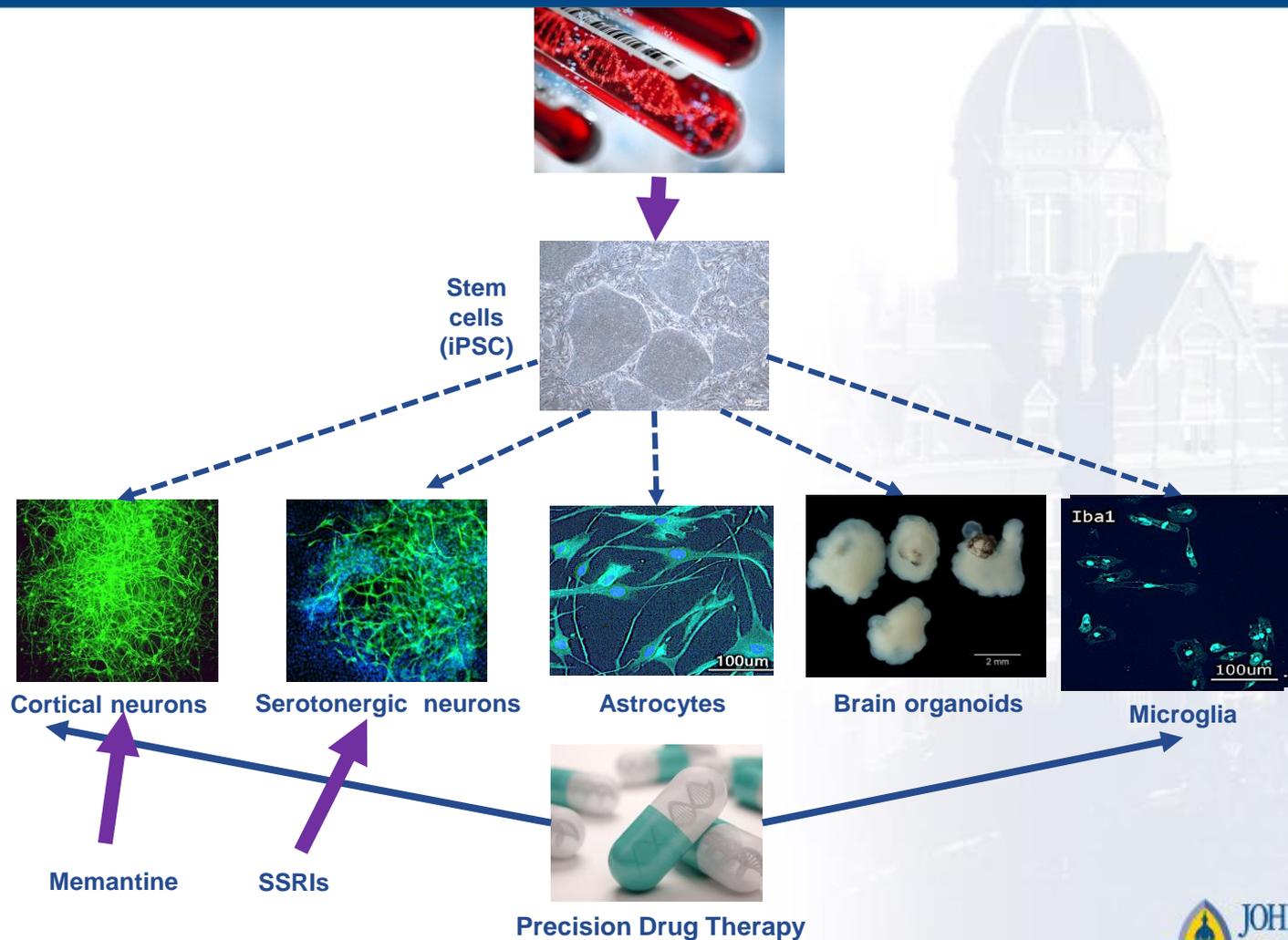


Brain Stress Test
Blood flow before and
after CO₂ inhalation



Individualized discovery platform for biomarkers and meds based on induced pluripotent stem cells

Machairaki Lab





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Thank you!
Ευχαριστω!



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