The Brain Institute of Louisiana.

Healthy Brain Aging

Anne L. Foundas, M.D., FAAN

- **Cognitive Continuum**
- **Risk Reduction - Prevention**
- **Early Detection – Treatment**

NOLA Brain and Behavior

Dr. Foundas has nothing to disclose.

Cognitive Continuum

Preclinical
Pathologic brain changes, but cognitively normal

Mild Cognitive Impairment (MCI)
Some cognitive impairment, but independence in functional abilities intact

Dementia
Symptoms significant enough to impair functional independence

AA, Alzheimer's Association; NIA, National Institute on Aging.
a. Lloret A, et al. Int J Mol Sci. 2019;20:5536; b. Jack Jr CR, et al. Alzheimers Dement. 2018;14:535-562.

Criteria for Diagnosis
What does Alzheimer's Disease Looks Like?

Cognitive decline with objective cognitive deficits

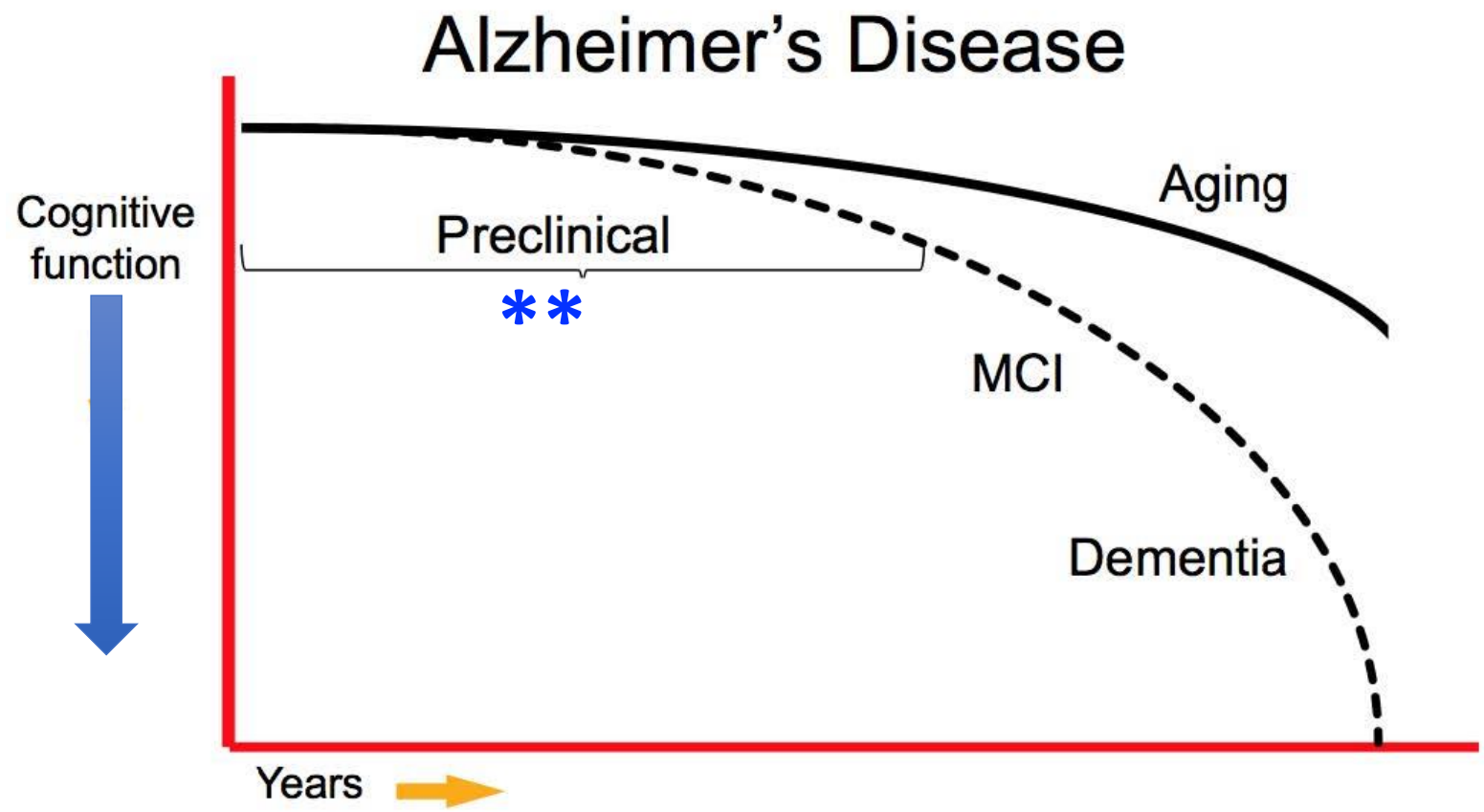
- Memory impairment and at least one of the following: *aphasia, apraxia, agnosia*, or a *disturbance in executive functioning*

Required criteria

- *Decline* from previous higher cognitive function
- *Functional deficits* - Severe enough to impair occupational or social function

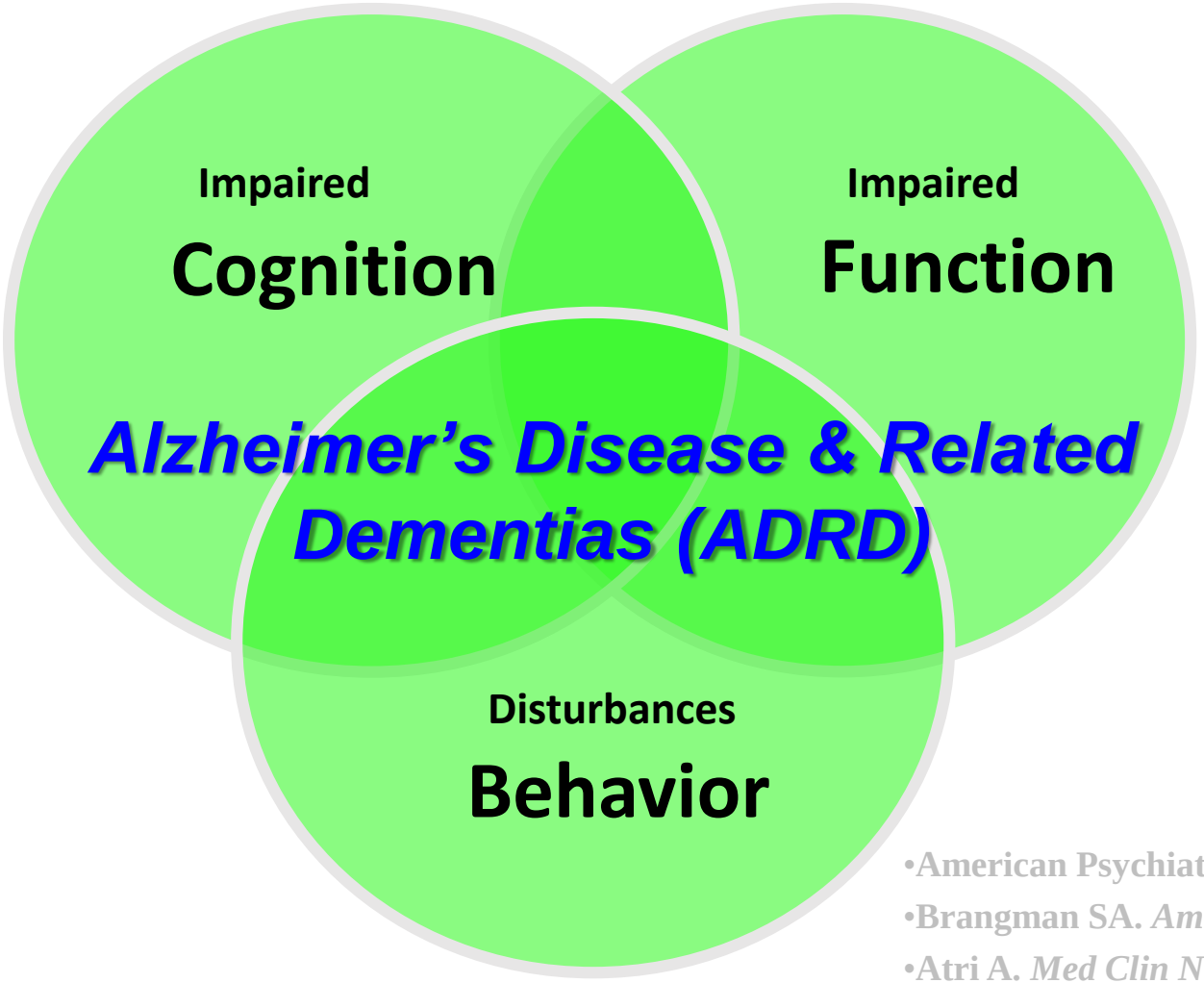
Gradual & slowly progressive cognitive decline

The Continuum of Alzheimer's Disease



Sperling RA *et. al. Alzheimer's Dementia*. 2011; 7: 280-292

Key Features of Dementia



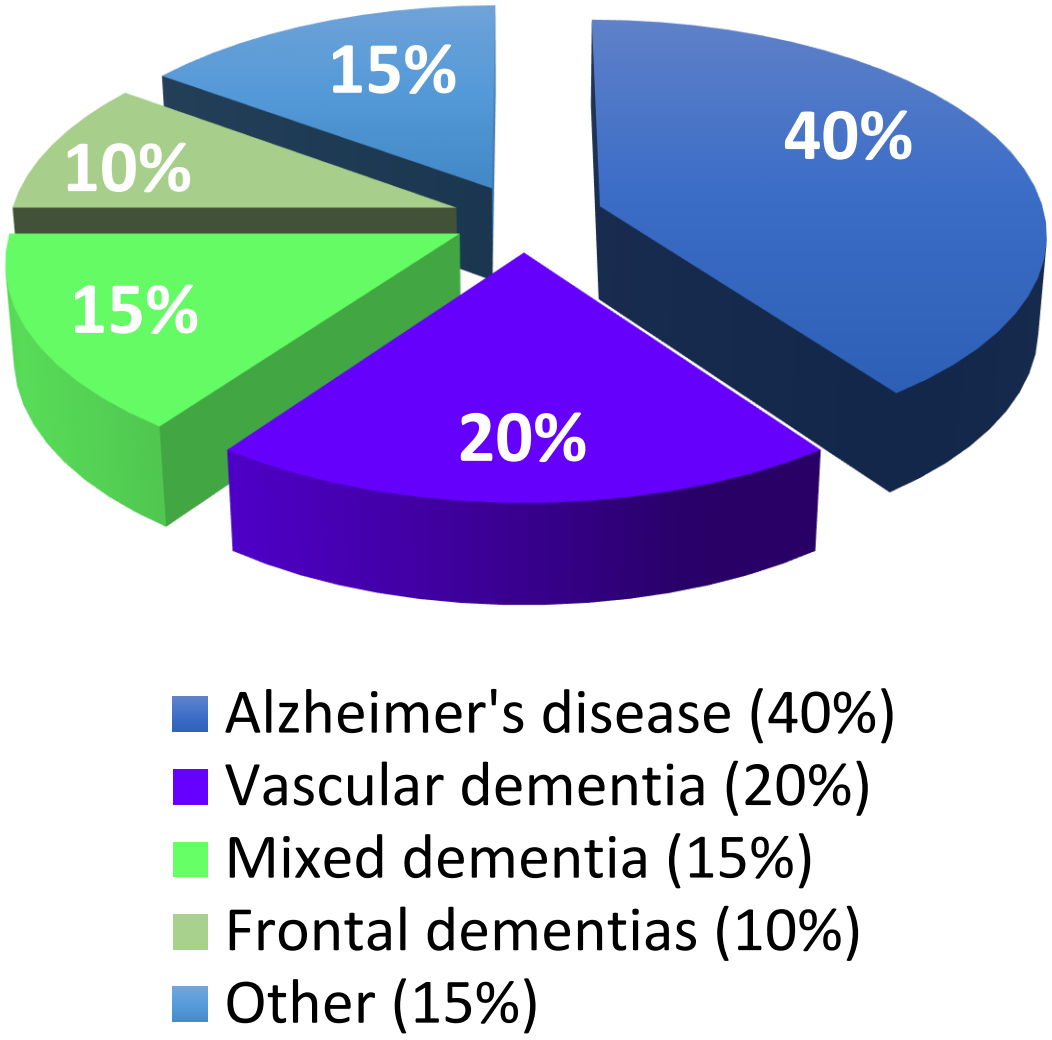
•American Psychiatric Association. *DSM-IV*. 1994.

•Brangman SA. *Am J Alzheimers Dis Other Demen.* 2003;18:79-84.

•Atri A. *Med Clin North Am*. 2019 Mar;103:263-293.

Cognitive decline is not one thing…..

Worldwide Prevalence
Dementia Subtypes

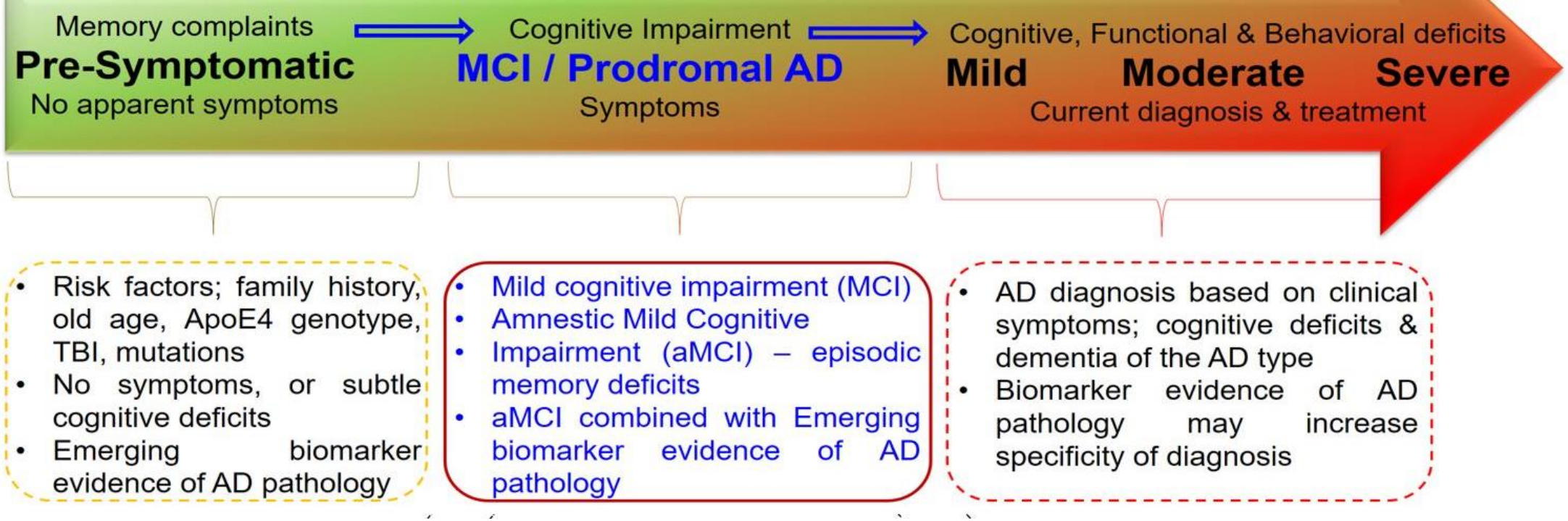


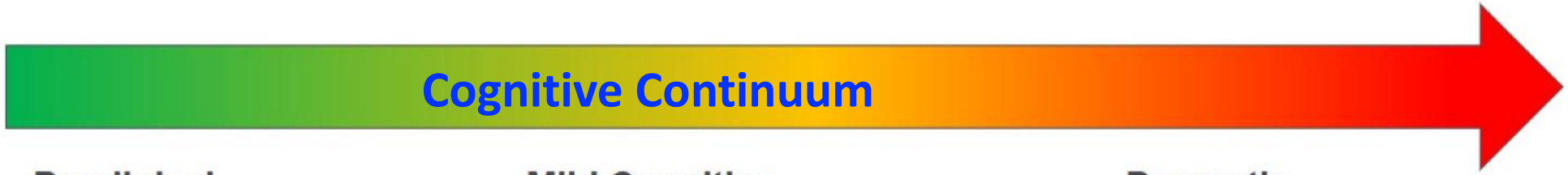
REFERENCE: Rougus-Pulia, Foundas, Mueller (2020) Chapter 14, Neurologic and Neurodegenerative Diseases of the Larynx

Dementia Subtypes

Rougus-Pulia, Foundas, Mueller (2020) Alzheimer's disease, Chapter 15, *Neurologic & Neurodegenerative Diseases of the Larynx*, pp177-190.

Degenerative Dementias	**Percent**	**Subtypes**	**Symptoms**	**Pathology**
Alzheimer's disease (AD)	40%	Early-onset (before age 65) Late-onset (after age 65)	Profound memory loss; Cognitive decline	Amyloid (AB 42) plaques; Neurofibrillary (tau) tangles
Frontal Dementias (FTD)	10%	Frontotemporal dementia (FTD) behavioral variant; Pick's disease; Semantic dementia; Primary Progressive Aphasia	Variable; Less memory loss than AD	Heterogeneous; Tau vs. Non-tau types
Mixed Dementia types	15%	AD plus VaD; Lewy body disease; Cortitocobasal degeneration	Variable	Heterogeneous
Vascular Dementia (VaD)	**20%**		Variable	Vascular disease
Multi-infarct dementia (large-vessel stroke); Small-vessel disease (chronic microvascular disease); Mixed type (Large and small vessel disease)			Variable	Vascular disease
Other Dementia types	**15%**	**Subtypes**	**Symptoms**	**Pathology**
Parkinson's Disease (PD) with dementia		Degenerative disease with about 30% of PD patients developing dementia; 60-80% have depression	Variable	Lewy body; Alpha synuclein
Traumatic Brain Injury (TBI)		Concussion; Intracranial hemorrhage; Hematomas – subdural; epidural	Greater Executive function deficits	Heterogeneous
Toxic, Metabolic, Endocrine, Deficiency		Alcoholic Dementia; B12 deficiency; Hypothyroidism		Deficiency states; Endocrine
Infectious/Inflammatory/ Autoimmune		Creutzfeldt-Jacob disease (CJD); Herpes simplex encephalitis; HIV dementia; Multiple sclerosis/demyelinating disorders		Heterogeneous
Chronic medical diseases		Chronic Renal disease; Hepatic disorders		Toxic/metabolic
Others disorders with cognitive decline		Multiple sclerosis; Brain tumors; Normal pressure hydrocephalus; Huntington's disease; Chronic major psychiatric disorders; Substance abuse syndromes		Heterogeneous





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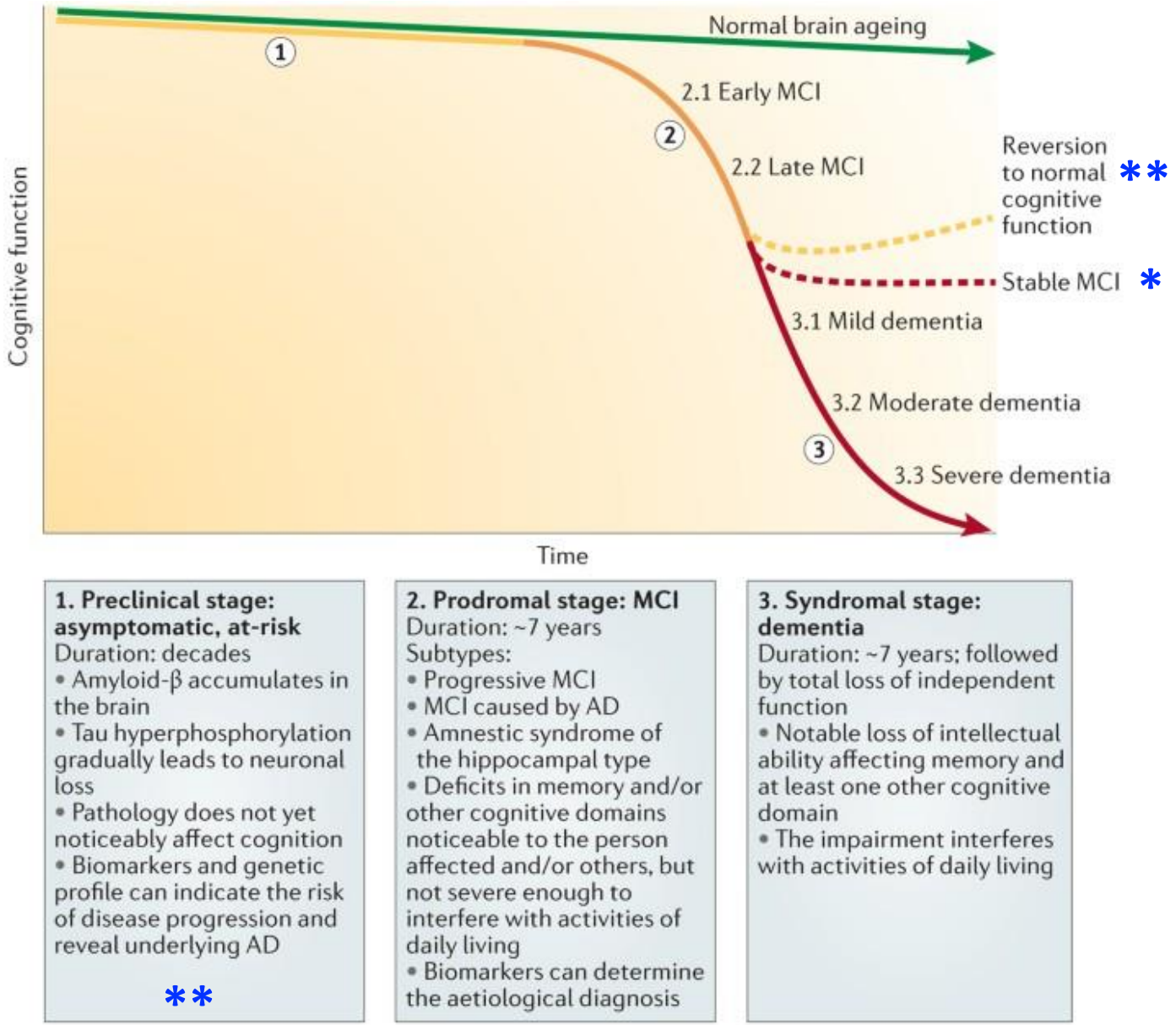
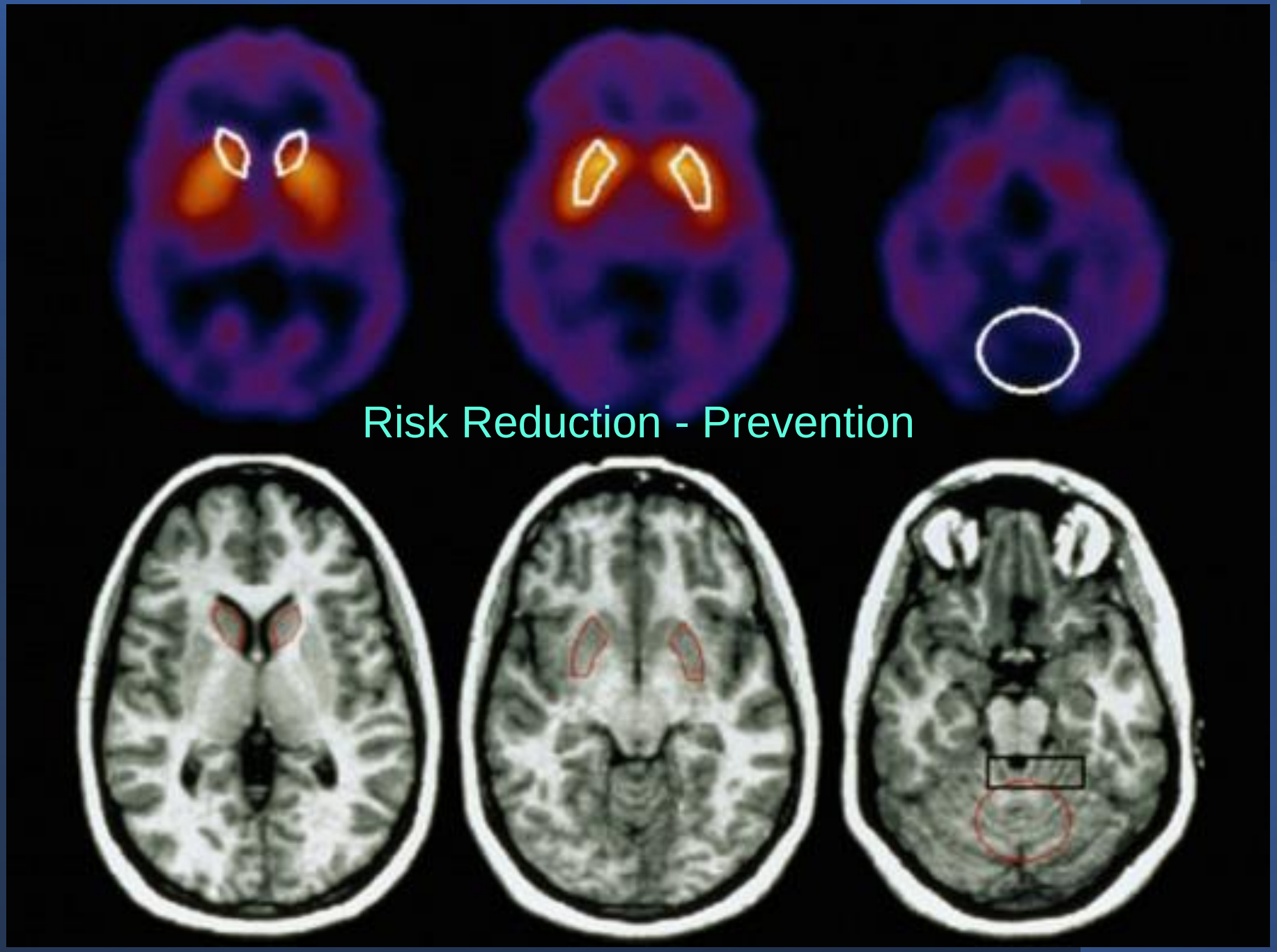
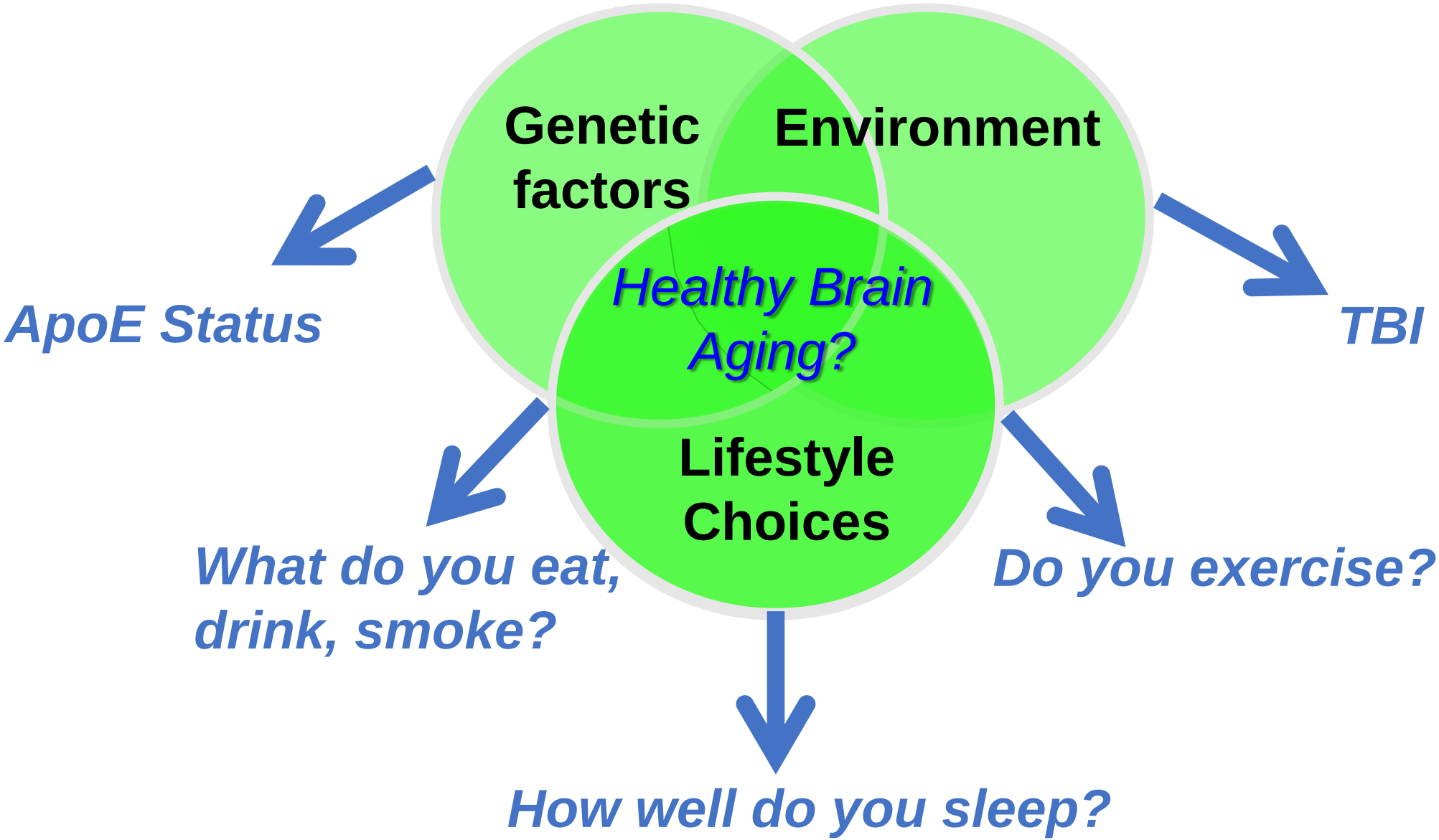
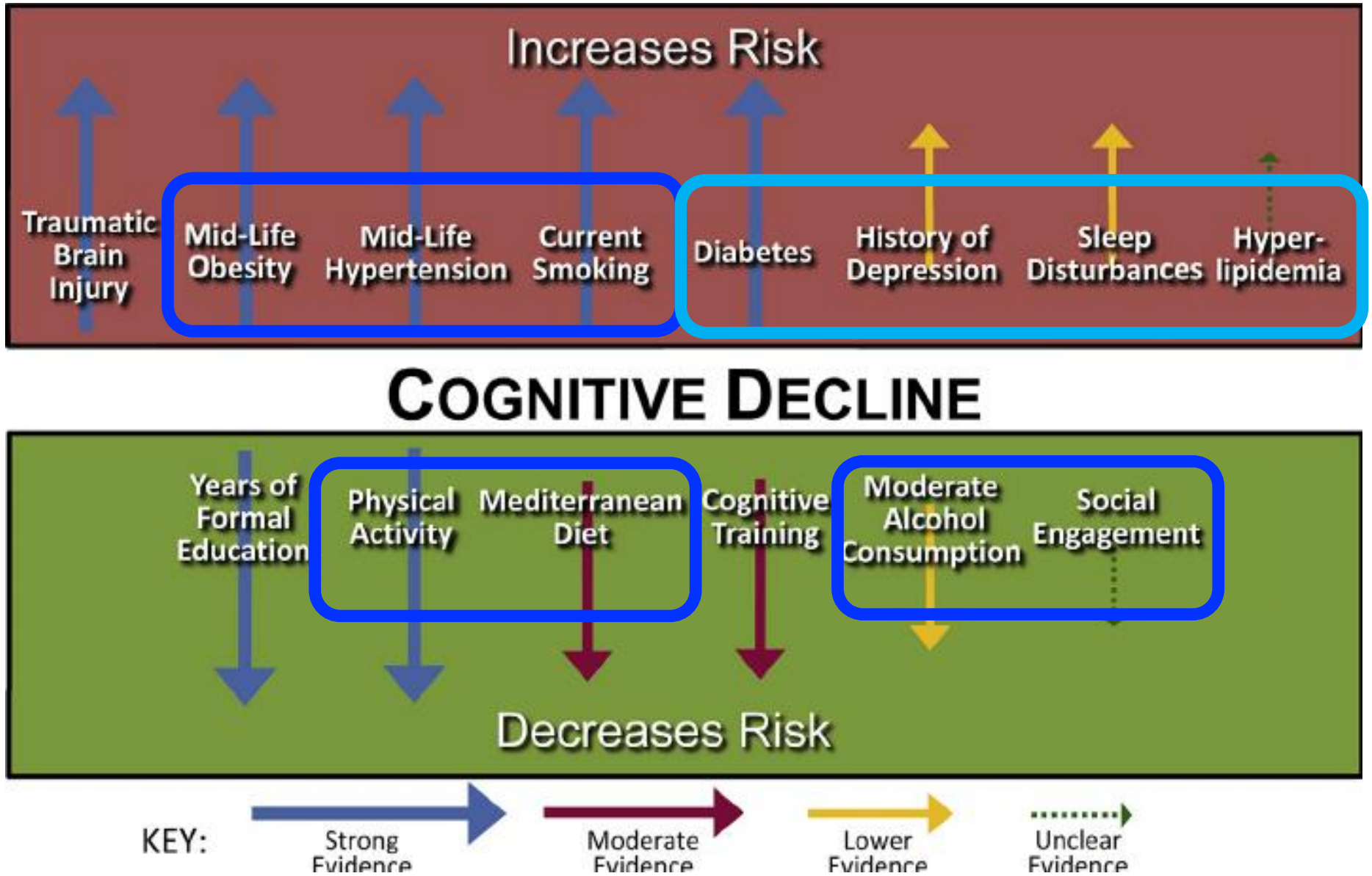


Reference: Hampel & Lista (2016) The rising tide of cognitive impairment. *Nature Reviews Neurology*. 12, 131-132


Risk Reduction - Prevention

Healthy Brain Aging: *What can you do?*





Baumgart et al (2015) Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimer's & Dementia*.

10 HEALTHY HABITS FOR YOUR BRAIN

TAKE CHARGE OF YOUR BRAIN HEALTH. THESE HEALTHY HABITS CAN LOWER THE RISK OF DEVELOPING COGNITIVE DECLINE AND POSSIBLY DEMENTIA. THIS IS TRUE EVEN FOR PEOPLE WITH A HISTORY OF DEMENTIA IN THEIR FAMILIES.

Follow as many of these tips as possible to achieve the most benefits for your brain and body. It's never too late or too early. Start now!

Challenge your mind

Be curious. Put your brain to work and do something that is new or hard for you. Learn a new skill. Try something artistic. Challenging your mind may have short- and long-term benefits for your brain.

Stay in school

Education reduces your risk of cognitive decline and dementia. Encourage youth to stay in school and pursue the highest level of training possible. Continue your own education by taking a class at a local library, college or online.

Protect your head

Help prevent an injury to your head. Wear a helmet for activities like biking, and wear a seatbelt. Protect yourself while playing sports. Do what you can to prevent falls, especially for older adults.

Control your blood pressure

Medications can help lower high blood pressure. And healthy habits like eating right and physical activity can help too. Work with a health care provider to control your blood pressure.

Eat right

Eating healthier foods can help reduce your risk of cognitive decline. This includes more vegetables and leaner meats/proteins, along with foods that are less processed and lower in fat. Choose healthier meals and snacks that you enjoy and are available to you.

Be smoke-free

Quitting smoking can lower the risk of cognitive decline back to levels similar to those who have not smoked. It's never too late to stop.

Manage diabetes

Type 2 diabetes can be prevented or controlled by healthier eating, increasing physical activity and medication, if necessary.

Maintain a healthy weight

Talk to your health care provider about the weight that is healthy for you. Other healthy habits on this list — eating right, physical activity and sleep — can help with maintaining a healthy weight.

Get moving

Engage in regular exercise. This includes activities that raise your heart rate and increase blood flow to the brain and body. Find ways to build more movement into your day — walking, dancing, gardening — whatever works for you!

Sleep well

Good quality sleep is important for brain health. Stay of screens before bed and make your sleep space as comfortable as possible. Do all you can to minimize disruptions. If you have any sleep-related problems, such as sleep apnea, talk to a health care provider.

Learn more at alz.org/healthyhabits.

ALZHEIMER'S ASSOCIATION®

RISK REDUCTION

What does the research show?

- **Diet**
- **Exercise**
- **Sleep**
- **Stress Reduction**
- **Social Engagement**
- **Learn New Things**

10 Healthy Habits is available in English and Spanish

Sleep

Sleep & Alzheimer's Disease

Role of the Glymphatic System

This process helps clearance of waste substances and other materials out of the central nervous system

Sleep modulates the glymphatic system

Aβ concentrations in the brain's extracellular milieu fall during sleep and rise during wakefulness

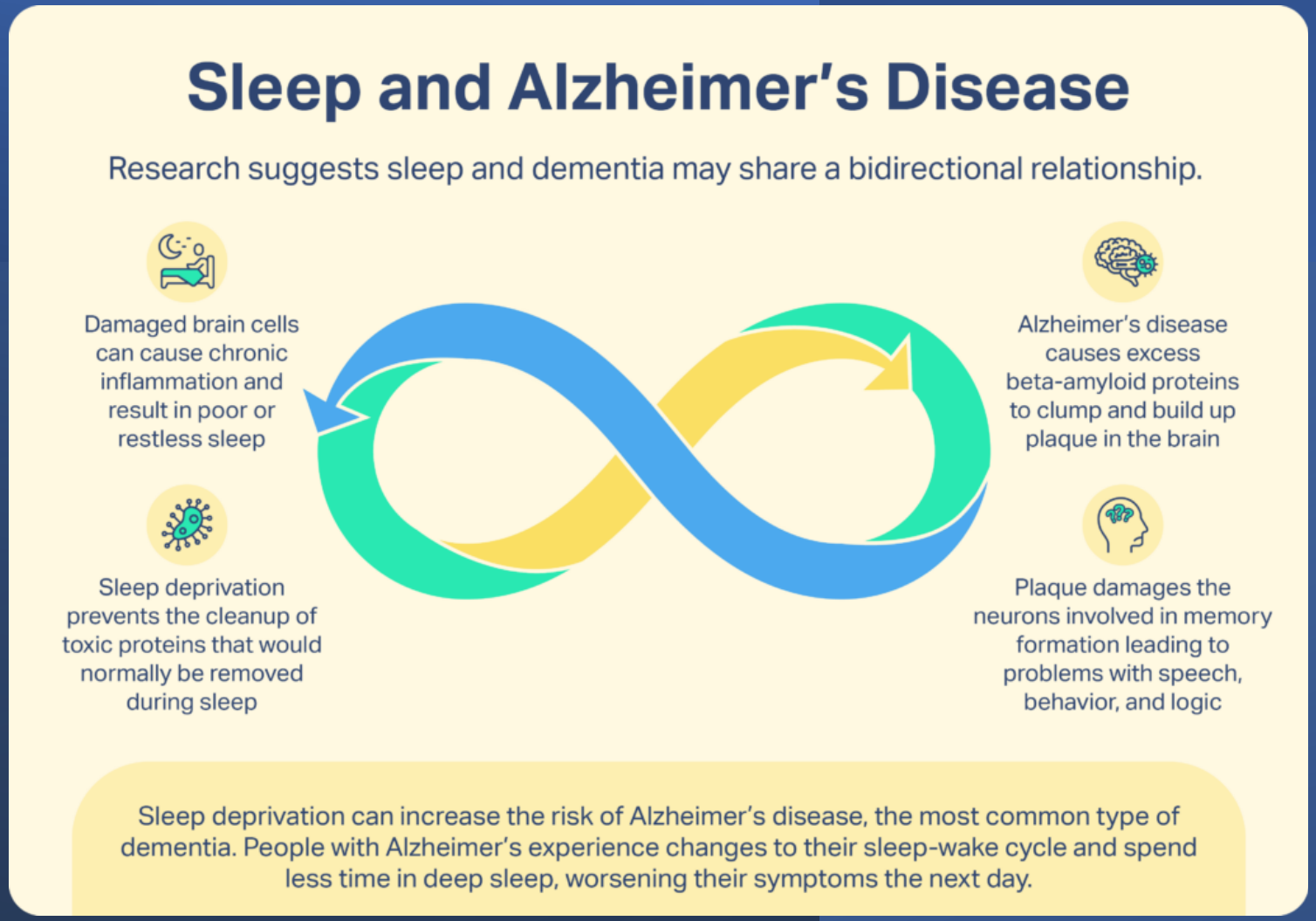
Glymphatic flow may help remove soluble extracellular Aβ peptide from the brain

Sleep disruptions can interfere with this process and thus increase the deposition of toxic soluble extracellular Aβ, the primary molecular species that accumulates in amyloid plaques

References:

Shenker JI, Singh G. Sleep and Dementia. Mo Med. 2017 Jul-Aug;114(4):311-315.

Wong R, Lovier MA. Sleep Disturbances and Dementia Risk in Older Adults: Findings From 10 Years of National U.S. Prospective Data. Am J Prev Med 2023;64(6):781−787.



Source: Fry A, Rehman A. Dementia & Sleep. Updated 11-16-2023

https://www.sleepfoundation.org/mental-health/dementia-and-sleep

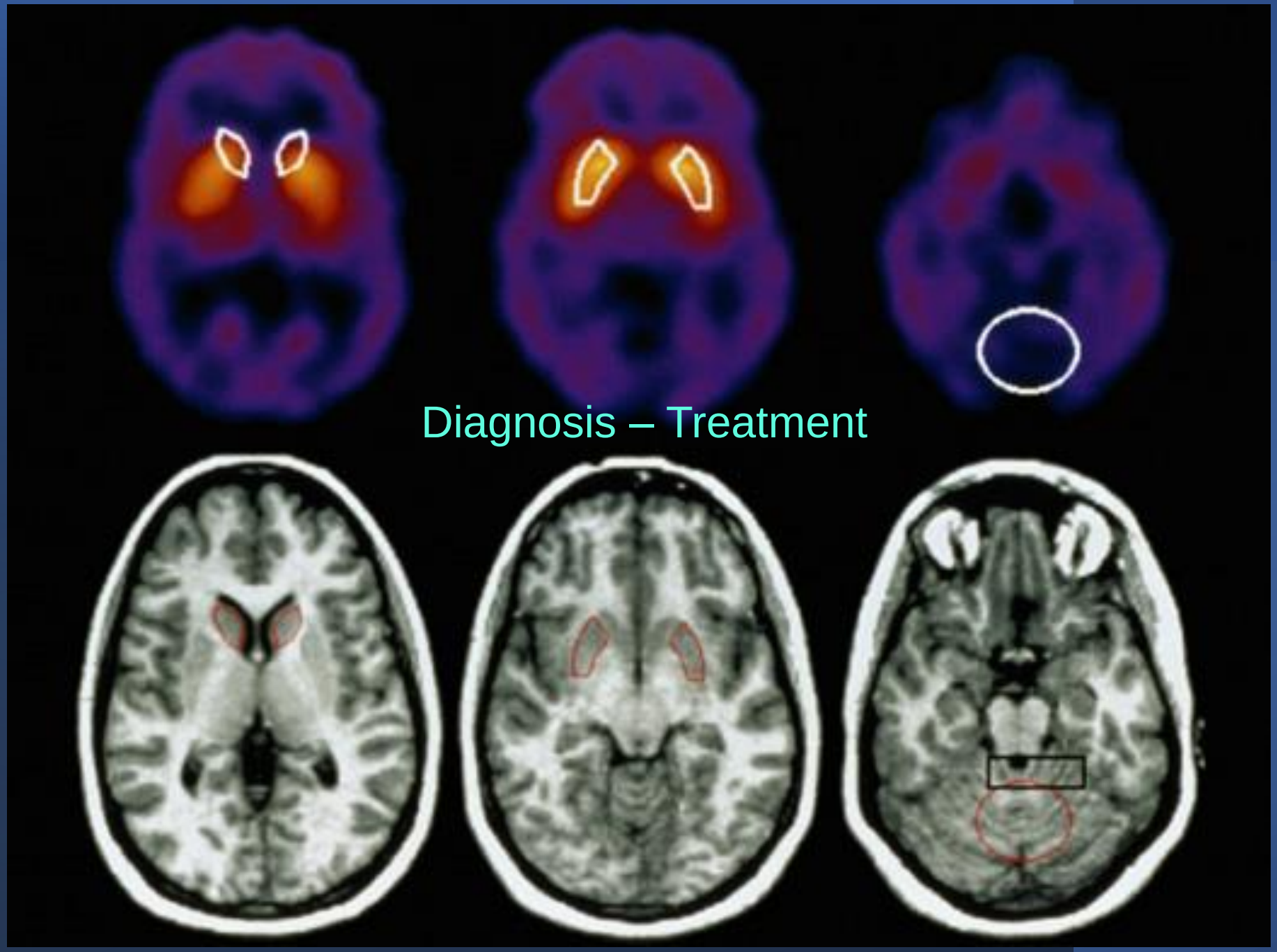
SUMMARY

Lifestyle
- Diet & Exercise
- Moderate

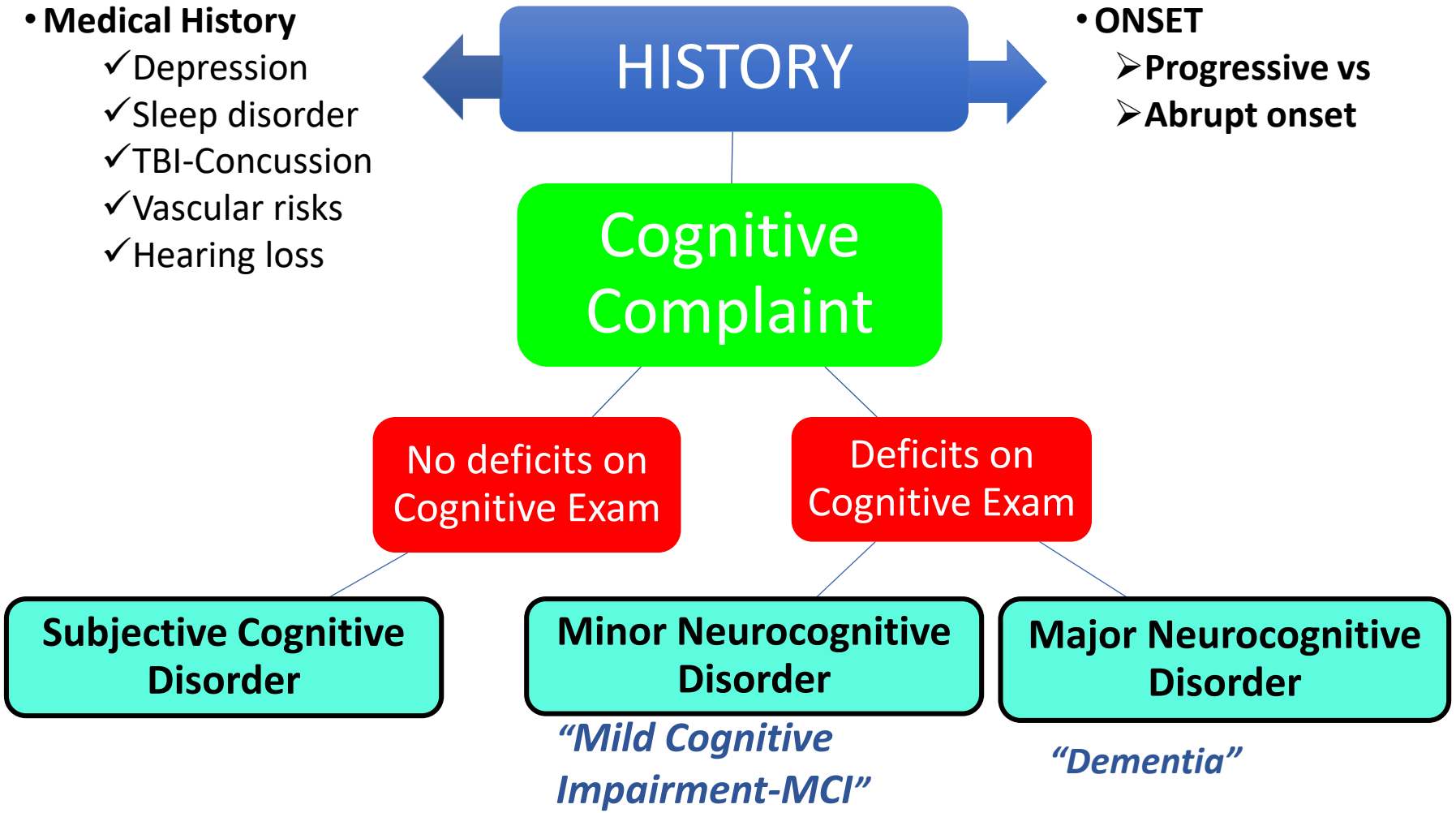
Health
- Manage Chronic Medical Conditions
- Treat Acute Risks

Early Treatment
- Baseline Screening
- Disease Modifying Drugs

https://alzheimers.org.nz/about-dementia/reducing-the-risk/


Diagnosis – Treatment

How to approach a patient with Cognitive Decline?



Diagnostic Studies

- **Laboratory Studies**
  - B12/folate, Vitamin D, Thyroid panel, Syphilis Serology [VDRL]
- **Structural Brain Imaging**
  - MRI Brain scan or CT brain [if contraindicated]
- **Electroencephalography [EEG]**
- **Other Diagnostic studies - Biomarkers**
  - PET imaging – Amyloid, Tau, Dopamine
  - CSF Studies

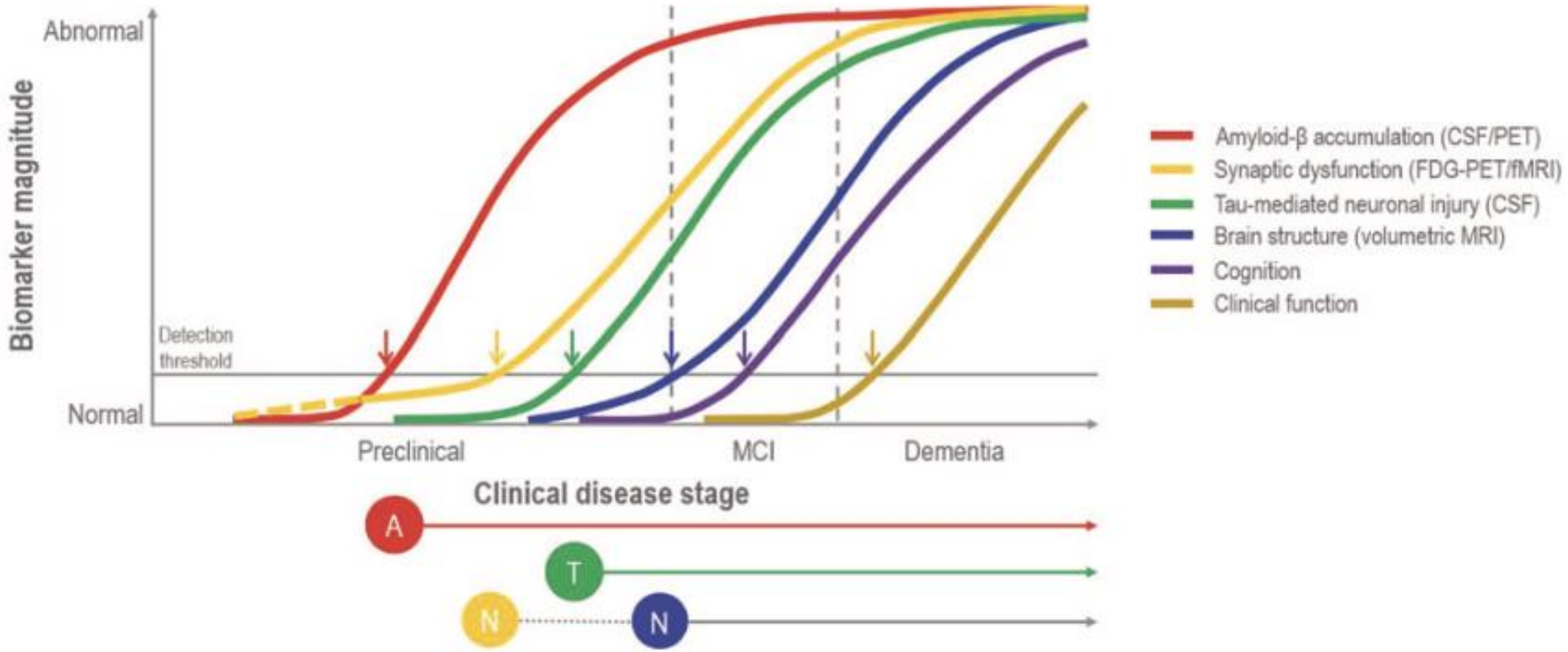
Evidence-Based Support for Earlier Detection of Alzheimer's Risk

- Emerging Classification Schemas based on the use of “biomarkers”
  - CSF profile of AD risk
  - Molecular Imaging with PET Scan Amyloid & Tau
- The idea is that individuals will be diagnosed before the onset of cognitive decline
  - Earlier detection will lead to earlier treatment with emerging immunotherapy drugs that target AD cellular pathology (Amyloid & Tau)
  - Earlier diagnosis & treatment should delay symptom onset

AT(N) System Classification of Alzheimer's Disease

- **The AT(N) system categorizes individuals using biomarkers that chart core AD pathophysiological features**
  - Amyloid-β (Aβ) pathway (A)
  - Tau-mediated pathophysiology (T)
  - Neurodegeneration (N)
- **This biomarker matrix is expanding to ATX(N) system**
  - **X represents** *novel candidate biomarkers* for additional pathophysiological mechanisms including: *neuroimmune dysregulation, synaptic dysfunction and blood–brain barrier alterations*

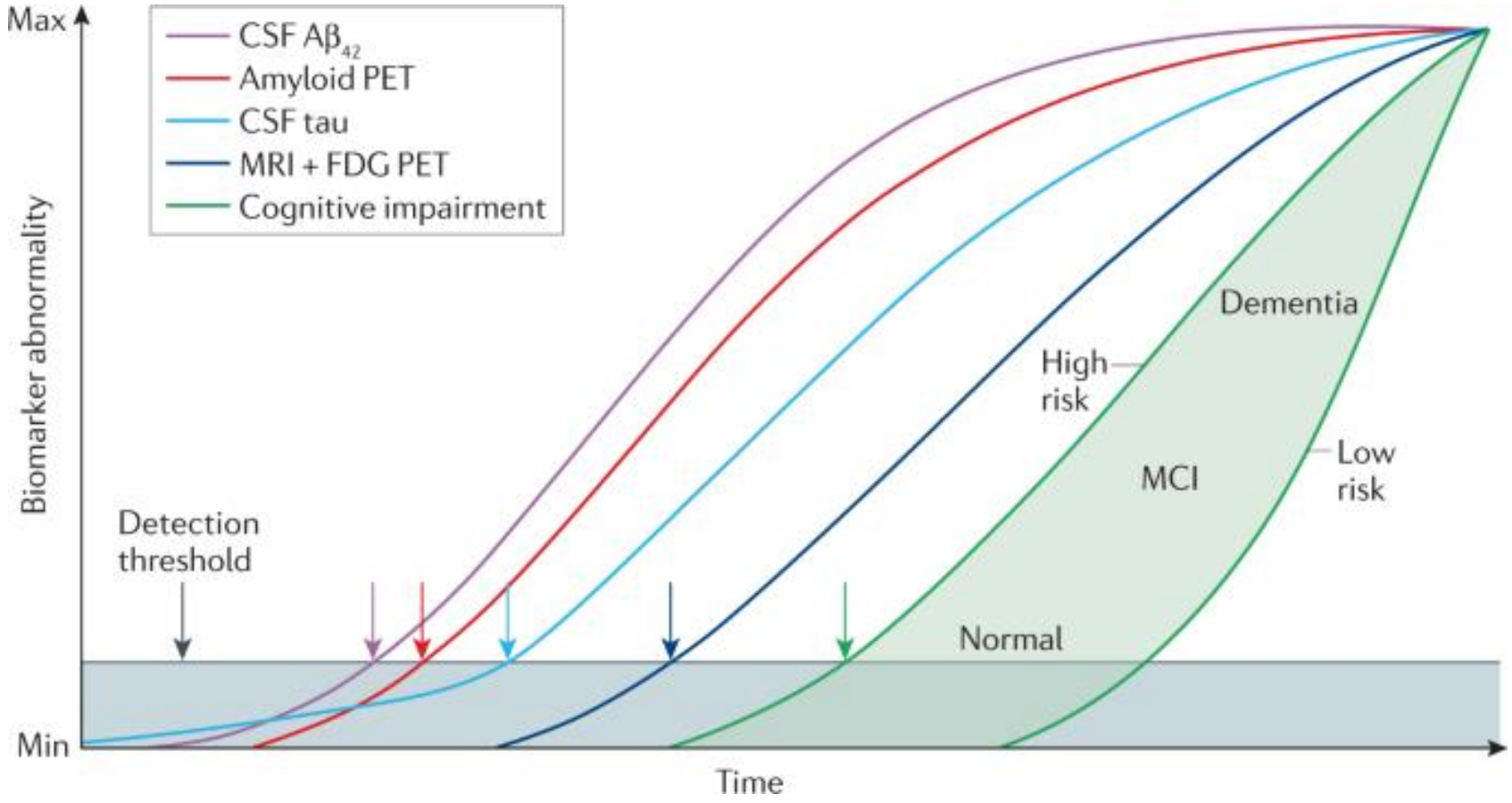
References: Hampel et. al. (2021) Developing the ATX(N) classification for use across the Alzheimer disease continuum. Nature Reviews Neurology. 17: 580-589.



Amyloid-β Pathway in Alzheimer's Disease

- **Reference: Hampel et. al. (2021) The Amyloid-β Pathway in Alzheimer's Disease. Molecular Psychiatry. 25: 5481-5503**.

AT(N) System Classification of Alzheimer's Disease



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PERSPECTIVE
https://doi.org/10.1038/s43587-022-00269-x

nature aging

Check for updates

NATURE AGING | VOL 2 | AUGUST 2022 | 692–703 |
www.nature.com/nataging

Designing the next-generation clinical care pathway for Alzheimer's disease

Harald Hampel[1]✉, Rhoda Au[2], Soeren Mattke[3], Wiesje M. van der Flier[4], Paul Aisen[5], Liana Apostolova[6], Christopher Chen[7], Min Cho[1], Susan De Santi[1], Peng Gao[1], Atsushi Iwata[8], Ricky Kurzman[1], Andrew J. Saykin[9], Stefan Teipel[10,11], Bruno Vellas[12], Andrea Vergallo[1], Huali Wang[13] and Jeffrey Cummings[14]

The reconceptualization of Alzheimer's disease (AD) as a clinical and biological construct has facilitated the development of biomarker-guided, pathway-based targeted therapies, many of which have reached late-stage development with the near-term potential to enter global clinical practice. These medical advances mark an unprecedented paradigm shift and requires an optimized global framework for clinical care pathways for AD. In this Perspective, we describe the blueprint for transitioning from the current, clinical symptom-focused and inherently late-stage diagnosis and management of AD to the next-generation pathway that incorporates biomarker-guided and digitally facilitated decision-making algorithms for risk stratification, early detection, timely diagnosis, and preventative or therapeutic interventions. We address critical and high-priority challenges, propose evidence-based strategic solutions, and emphasize that the perspectives of affected individuals and care partners need to be considered and integrated.

Biomarkers – Diagnosis before Cognitive Deficits

Table 1 | ATX(N) biomarkers and their contexts of use in Alzheimer's disease[5,8,9,136]

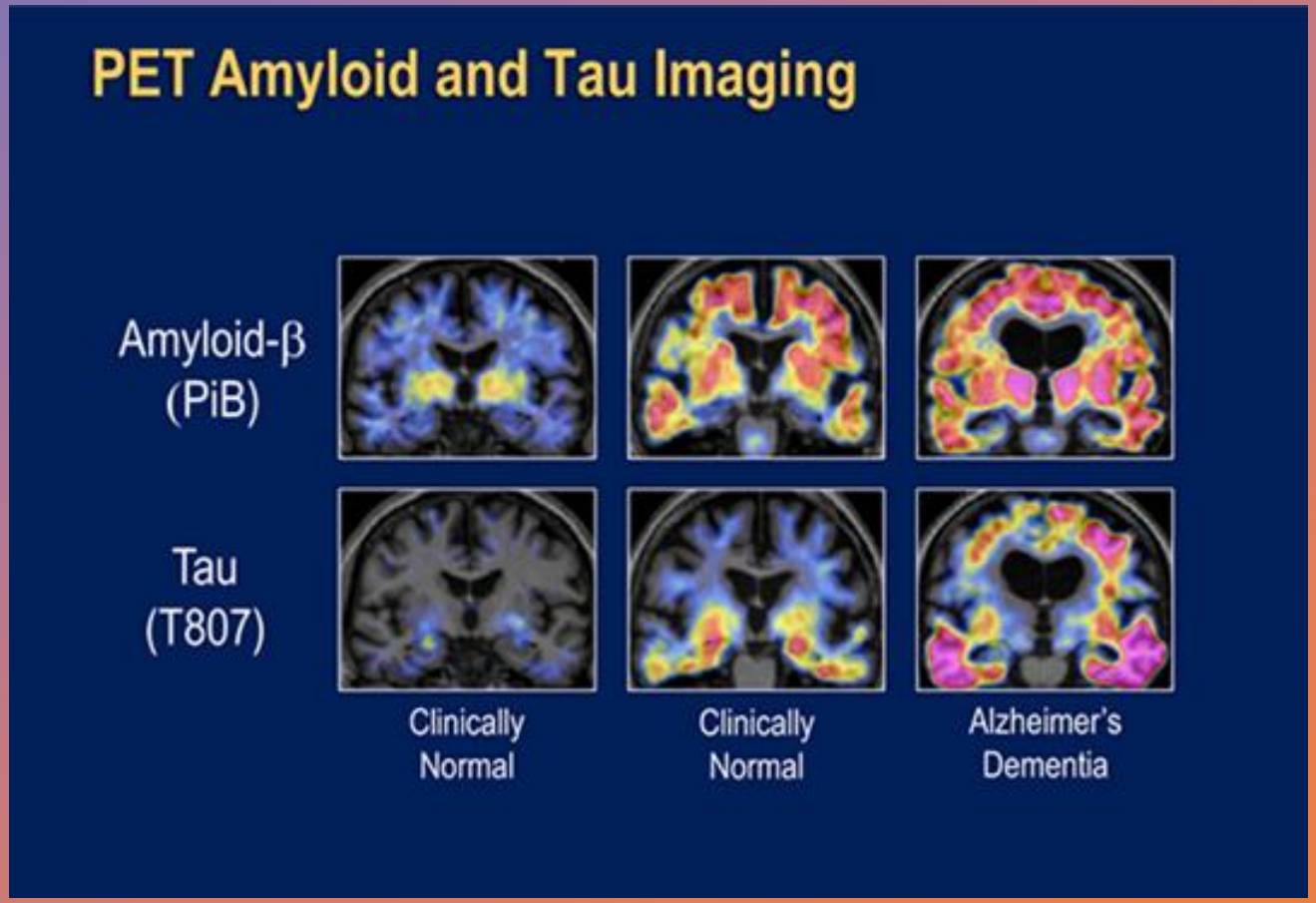
AT(N)	Imaging	CSF	Blood	FDA Class
A/amyloid	Amyloid PET	$A\beta_{42}$, $A\beta_{42}/A\beta_{40}$	$A\beta_{42}/A\beta_{40}$	Diagnostic monitoring
T/tau	Tau PET	p-tau_{181}, p-tau_{217}	p-tau_{181}, p-tau_{217}	Prognostic monitoring
N/neurodegeneration	MRI, FDG PET	NfL, tau	NfL, tau, GFAP	Pharmacodynamic monitoring
ATX(N) examples	SV2A PET, microglial PET, astrocytosis PET	Synaptic analytes, inflammatory measures	Synaptic analytes, inflammatory measures	Pharmacodynamic monitoring

The various biomarkers under the AT(N) system can be measured by neuroimaging or by detection in blood and CSF. ATX(N) demonstrates the dynamic and evolving nature of the AT(N) classification system where the X component represents additional biomarkers, for example, inflammatory biomarkers, that improve classification, based on the pathophysiology of disease.

Hampel et al. (2022) Designing the next-generation clinical care pathway for Alzheimer's disease. *Nature aging*. 2; 692-703.

PET Scan Methods *Molecular Imaging of Age-Related Changes*

Biomarkers of Disease



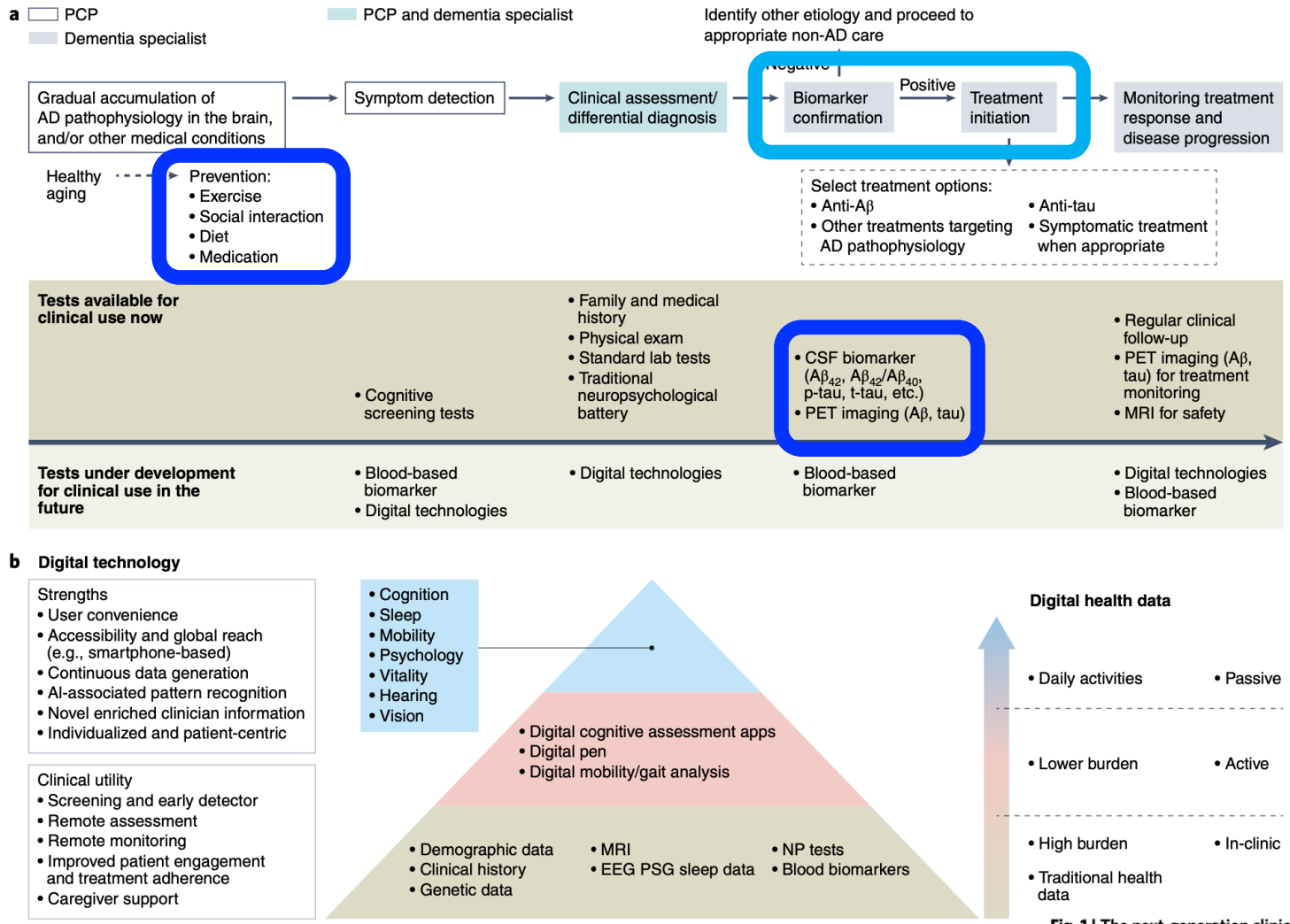
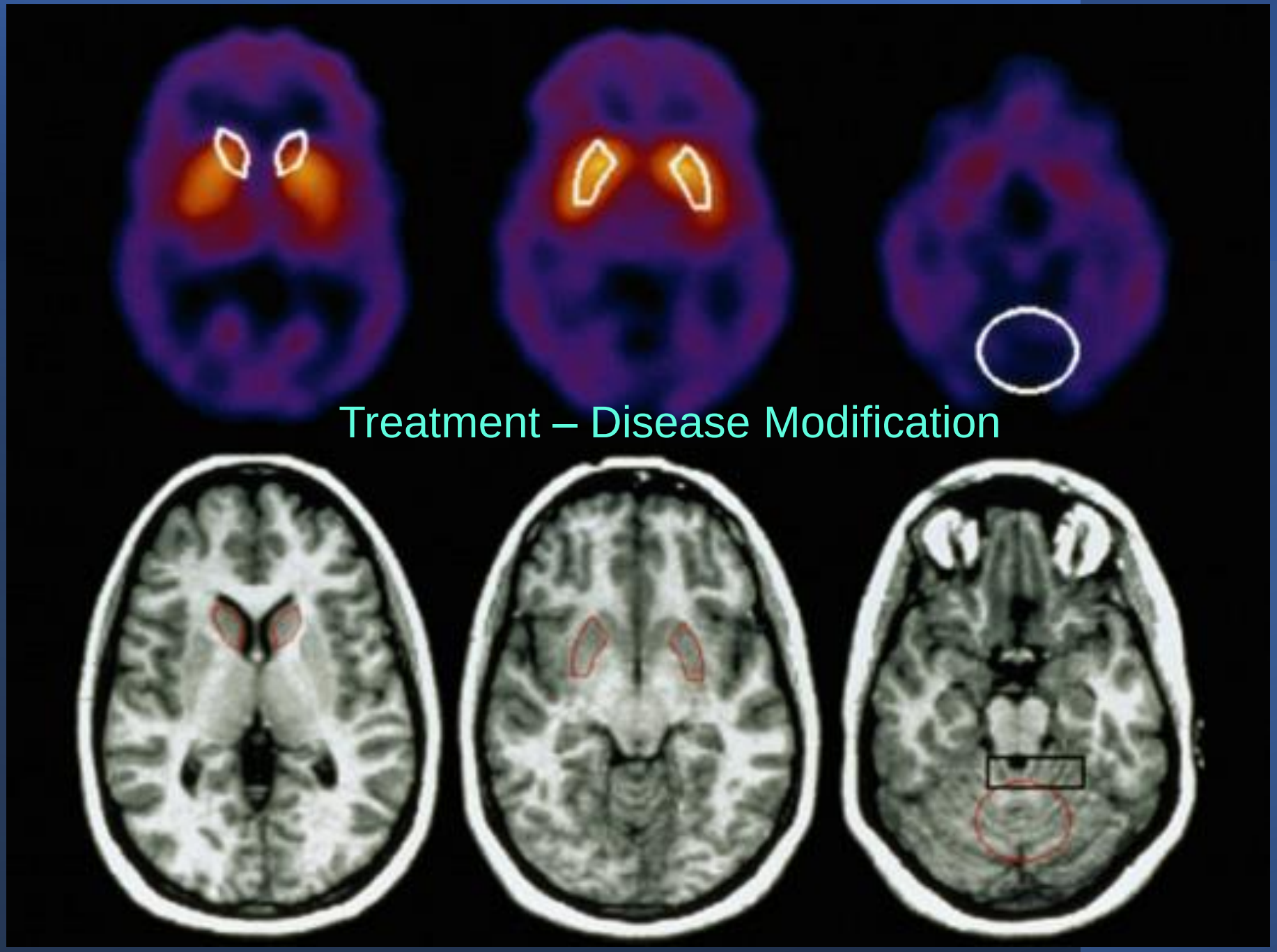
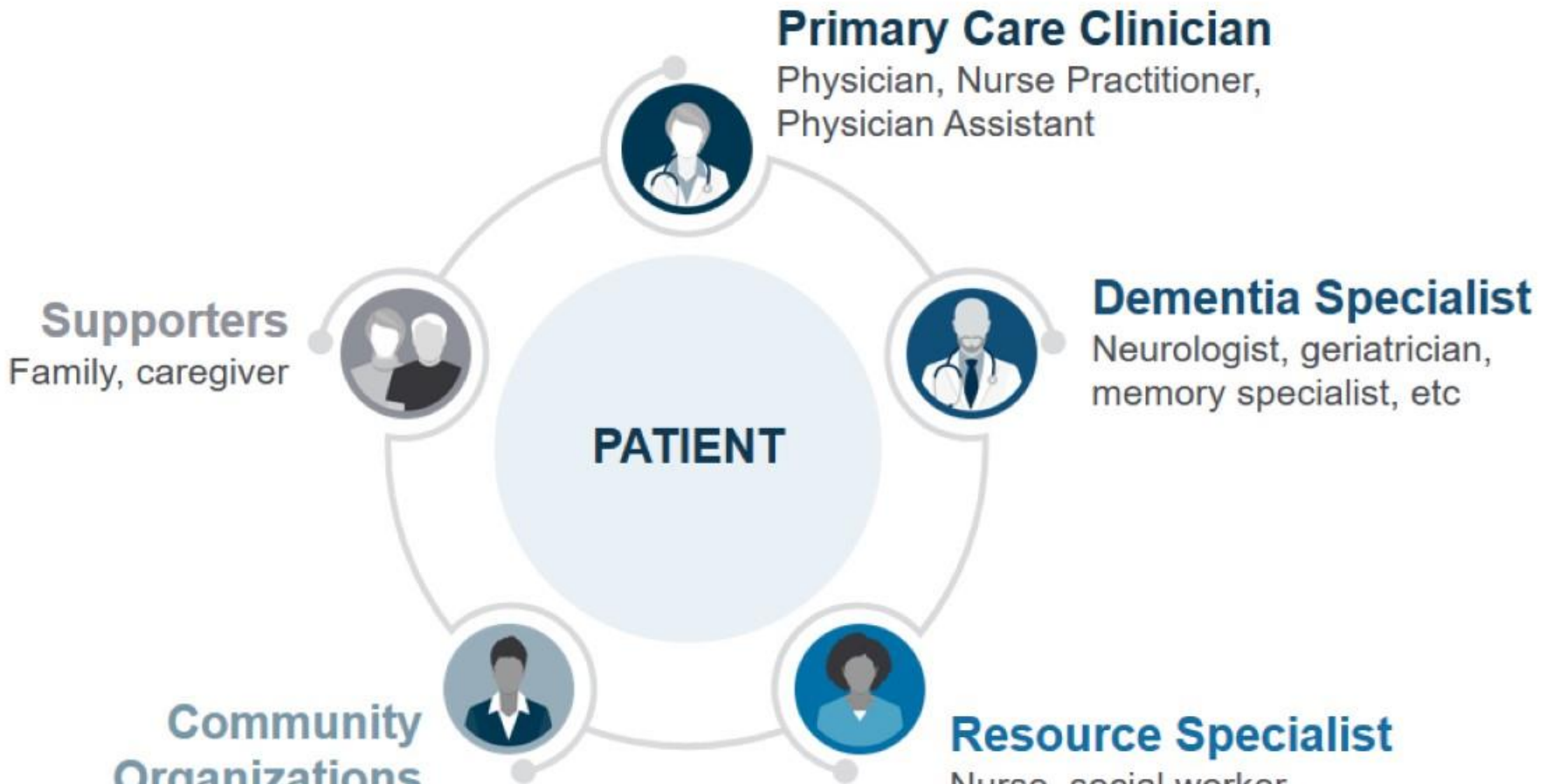


Fig. 1 | The next-generation clinical care pathway for Alzheimer's disease. a, An overarching illustration. The next-generation clinical care pathway begins with healthy aging and participation in preventive lifestyle measures to slow or prevent accumulation of AD pathophysiology, with the goal of extending healthspan across populations. Symptom detection, triggered by concerned individuals or family members, or detected during a routine wellness visit, may involve cognitive testing and, in the future, blood-based biomarkers and digitally based assessments. This will be accompanied by clinical assessments involving standard laboratory tests and physical examination. Any recorded cognitive impairment will be confirmed with standardized biomarker tests. Individuals with confirmed disease will proceed to treatment initiation with relevant AD therapy followed by long-term monitoring, of which digital technologies and blood-based biomarkers will play a key role in the future. **b**, Digital health technologies in future AD clinical care and the path toward a precision monitoring and detection platform. A precision monitoring and detection platform will require a transformation from the traditional data collection methods to the inclusion of digital technologies. This will include active engagement technologies that require individual interaction and engagement to passive engagement technologies that collect data in the background while the individuals keep to their daily routine. AI, artificial intelligence; EEG, electroencephalogram; NP, neuropsychiatric; PSG, polysomnography.


Treatment – Disease Modification

The Care Team

- Interprofessional, multidisciplinary team
- The exact makeup of the care team will differ by patient and by what is available in the PCP's locale



a. Galvin JE, et al. Front Neurol. 2021;11:592302; b. Expert opinion.

Addressing Other Causes of Cognitive Decline

Physical Examination

- Contributory comorbidities[a]
- Medication review[a]
- General health[a]
- Hypoglycemia[b]
- Hypotension[b]

Neurologic Examination[b]

- Signs of FTD, LBD, NPH, PD, or stroke
- Focal weakness
- Gait changes
- Neuropathy
- Psychotic features
- Speech, hearing, or vision issues

Laboratory Tests

- CBC count[a,c]
- Comprehensive metabolic panel[a,c]
- Thyroid function[a,c]
- Serum B12, folate[a]
- HIV[a,c]
- Rapid plasma reagin[a,c]

Structural Imaging

- MRI preferred (or CT)[c]
- Abnormalities like NPH, stroke, or tumor[b]
- Atrophy patterns[a]

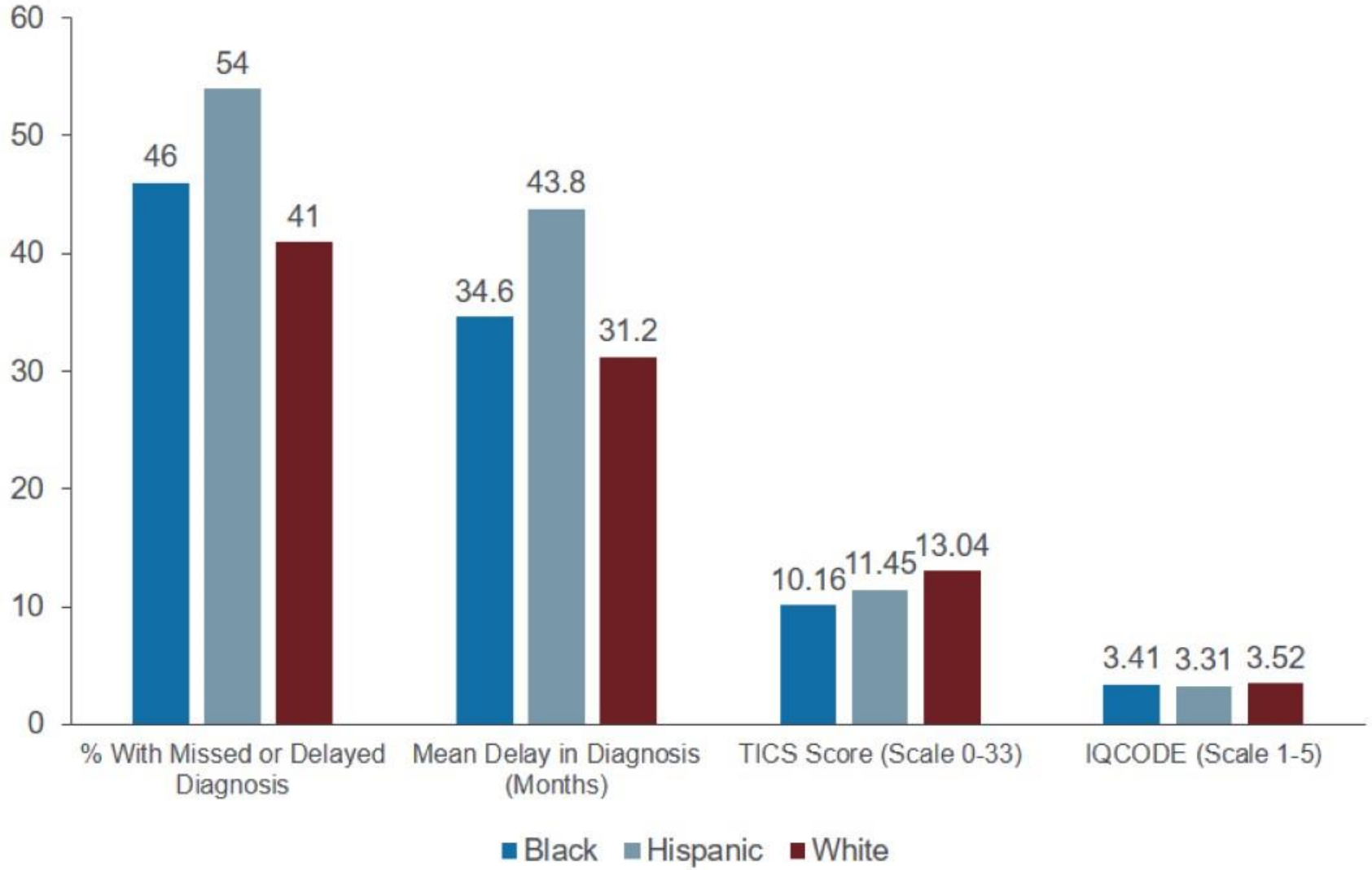
CBC, complete blood cell; CT, computed tomography; FTD, frontotemporal dementia; LBD, Lewy body dementia; MRI, magnetic resonance imaging; NPH, normal pressure hydrocephalus; PD, Parkinson disease.

a. Porsteinsson AP, et al. J Prev Alz Dis. 2021;3:371-386; b. Langa KM, et al. JAMA. 2014;312:2551-2561; c. Liss JL, et al. J Intern Med. 2021;290:310-334.

Missed or Delayed Diagnoses

Study based on Health and Retirement Study data

- More Black and Hispanic participants had a missed or delayed dementia diagnosis, compared with White participants
- Black and Hispanic patients showed poorer cognitive function and functional limitations at the time of diagnosis
- Overall, 24% of participants never received a dementia diagnosis
- Among Hispanic participants, that proportion was 32%



IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; TICS, Telephone Interview for Cognitive Status.
Lin PJ, et al. Med Care. 2021;59:679-686.

Expert Insights: A Major Shift in Thinking

"Alzheimer's disease" refers to pathologic change

NOT a specific syndrome

Alzheimer's disease is identified postmortem by pathologic changes or *in vivo by biomarkers*

Symptoms are part of the disease continuum

NOT part of its definition

Expert opinion from R. Petersen, MD

Biomarker Profiles

ATN Profile	Biomarker Category
A-T-N-	Normal AD biomarkers
A+T-N-	AD pathologic change
A+T-N+	AD and concomitant suspected non-AD pathologic change
A+T+N-	AD
A+T+N+	AD
A-T+N-	Non-AD pathologic change
A-T-N+	Non-AD pathologic change
A-T+N+	Non-AD pathologic change

AD Continuum

a. Lloret A, et al. Int J Mol Sci. 2019;20:5536; b. Jack Jr CR, et al. Alzheimers Dement. 2018;14:535-562.

FDA-Approved Drugs for Dementia

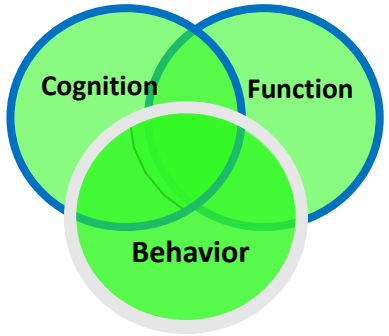
- Anti-AD pharmacotherapies approved by the US Food and Drug Administration
  - **Acetylcholinesterase inhibitors:** donepezil (Aricept), galantamine, and rivastigmine
  - **N-methyl-D-aspartate antagonist:** memantine (Namenda)
- These drugs provide *modest* but meaningful benefits
  - Mitigate symptoms, slow clinical progression, and delay functional disability.
- These drugs do *NOT* treat the underlying pathology

FDA-Approved Anti-Amyloid Drugs

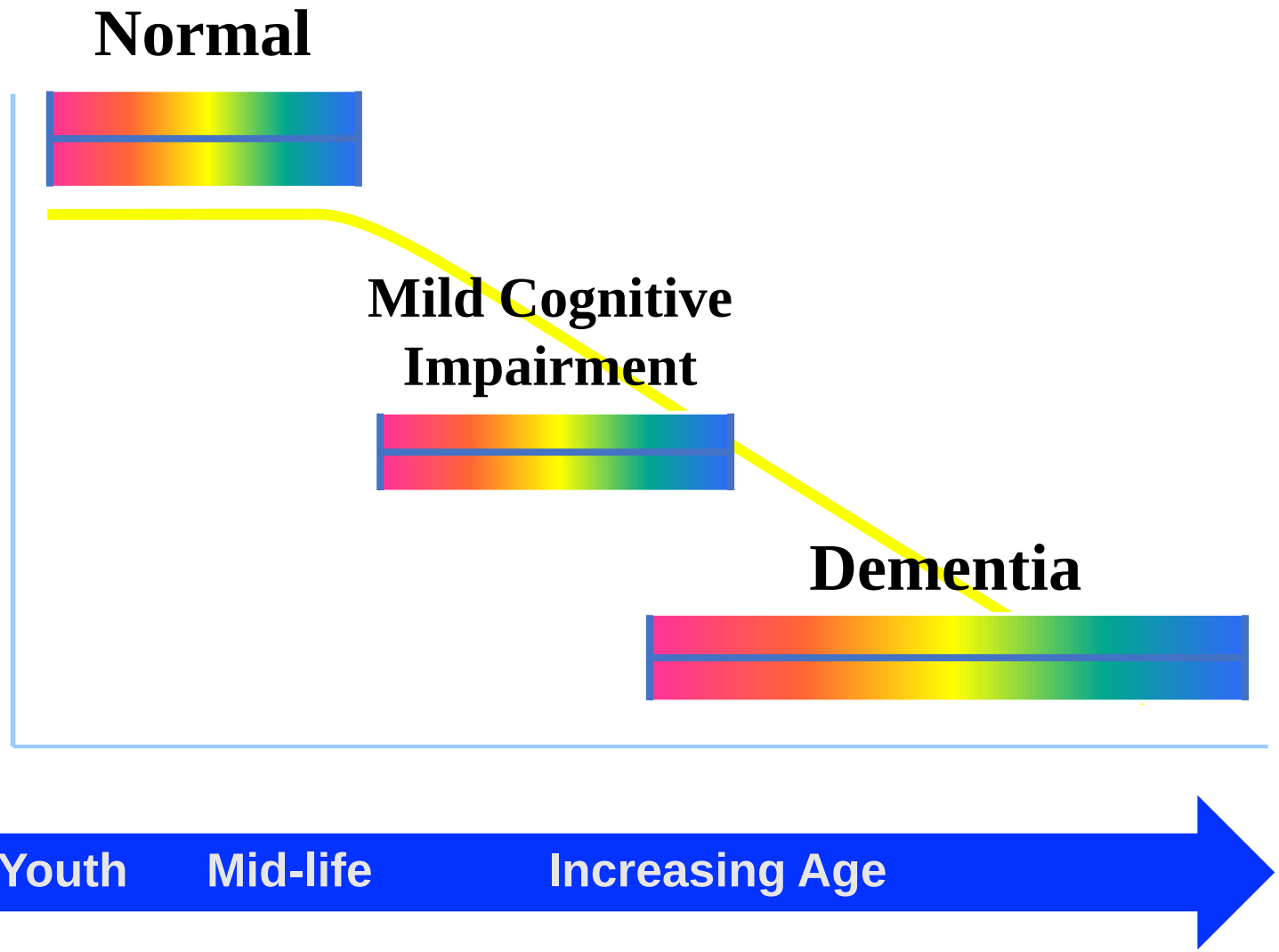
- **Amyloid plaques are a defining feature of Alzheimer's disease, disrupt cell-signaling, & lead to cell death.**
  - ✓ One hypothesis is that if you can get rid of these toxic plaques, you can keep the brain cells from dying and curb cognitive decline.
- **Two anti-amyloid drugs have had FDA-approval**
  - **Aducanumab (Aduhelm, Biogen/Eisai)** – no longer
  - **Lecanemab (Leqembi, Eisai)**
    - ✓ Both drugs are monoclonal antibodies designed to signal the immune system to clear amyloid plaques
    - ✓ Both drugs are administered via infusion therapy
    - ✓ Both drugs had fast-track approval
      - ➢ Current limitations: need for longitudinal study in larger diverse populations
      - ➢ Cost is prohibitive for many prospective patients

Brain Health – Healthy Brain Aging
Can you modify age-related brain changes?

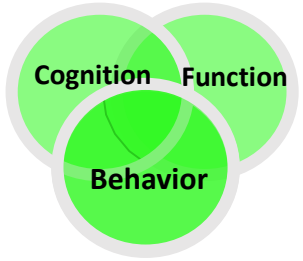
Petersen, RC. 2001

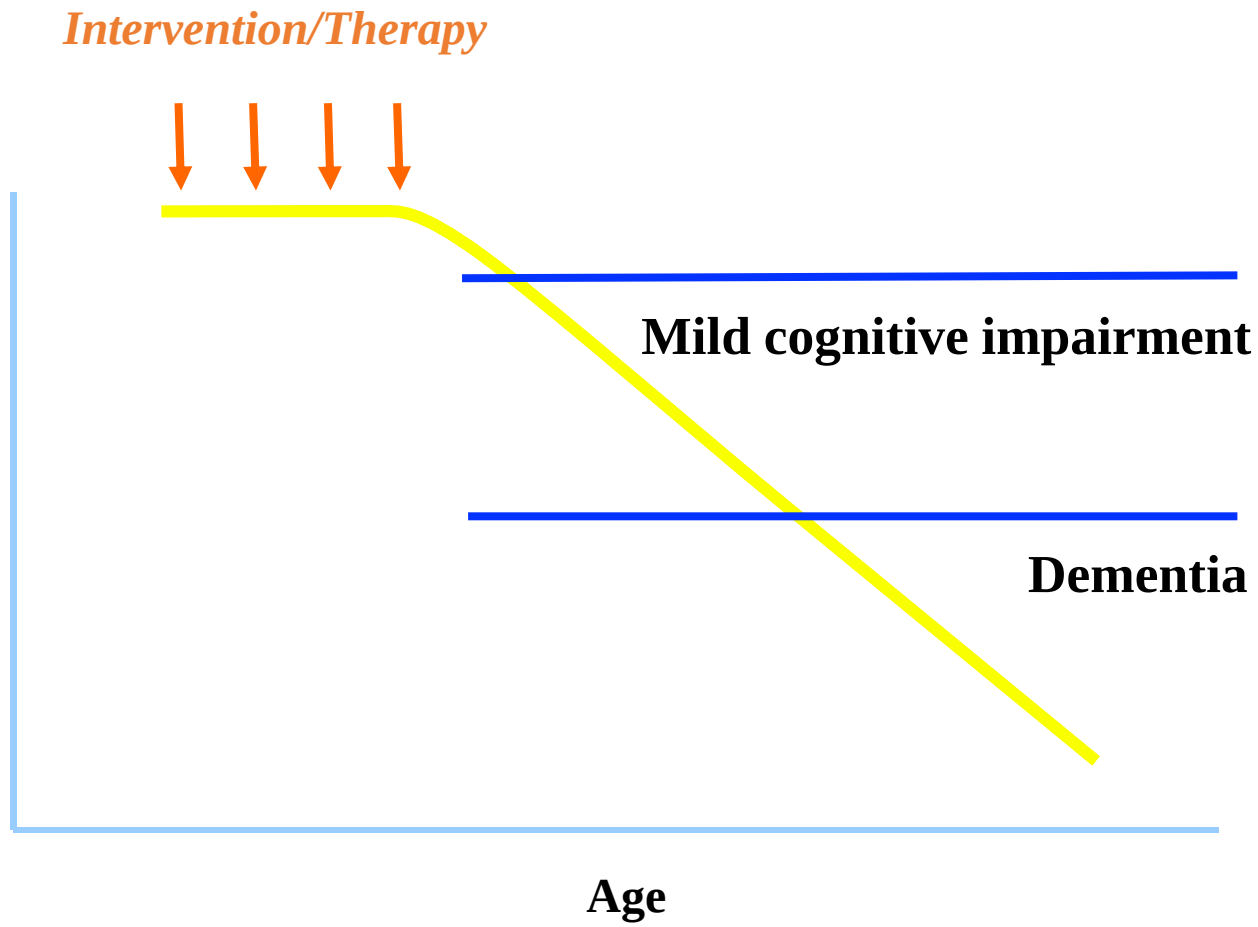


- Cognition
- Function
- Behavior

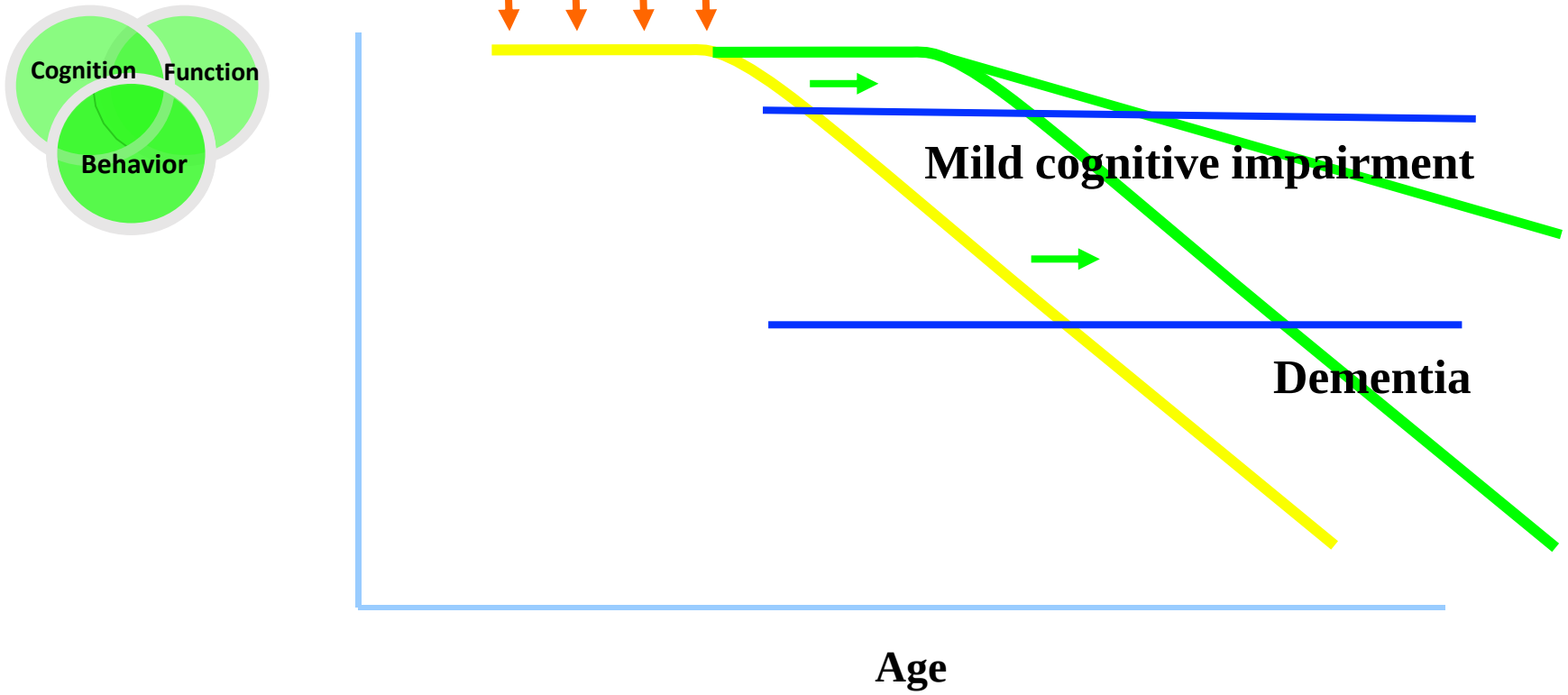


Brain Health – Healthy Brain Aging
Can intervention/Therapy alter brain aging?





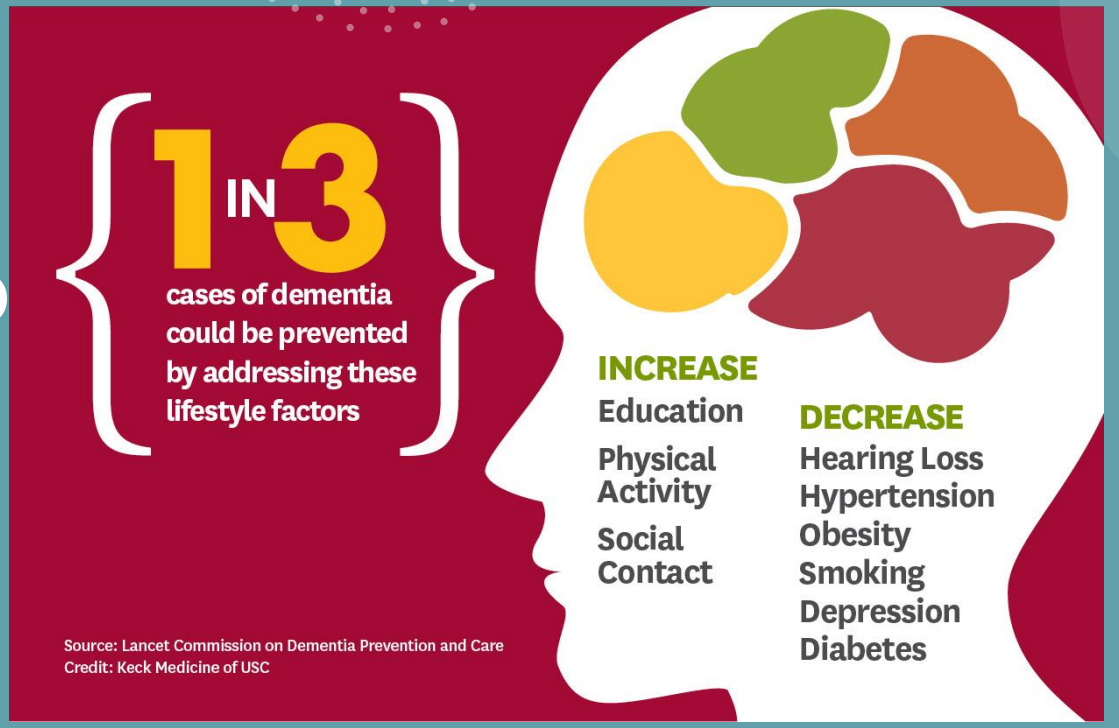
Brain Health – Healthy Brain Aging
Can intervention/Therapy alter brain aging?

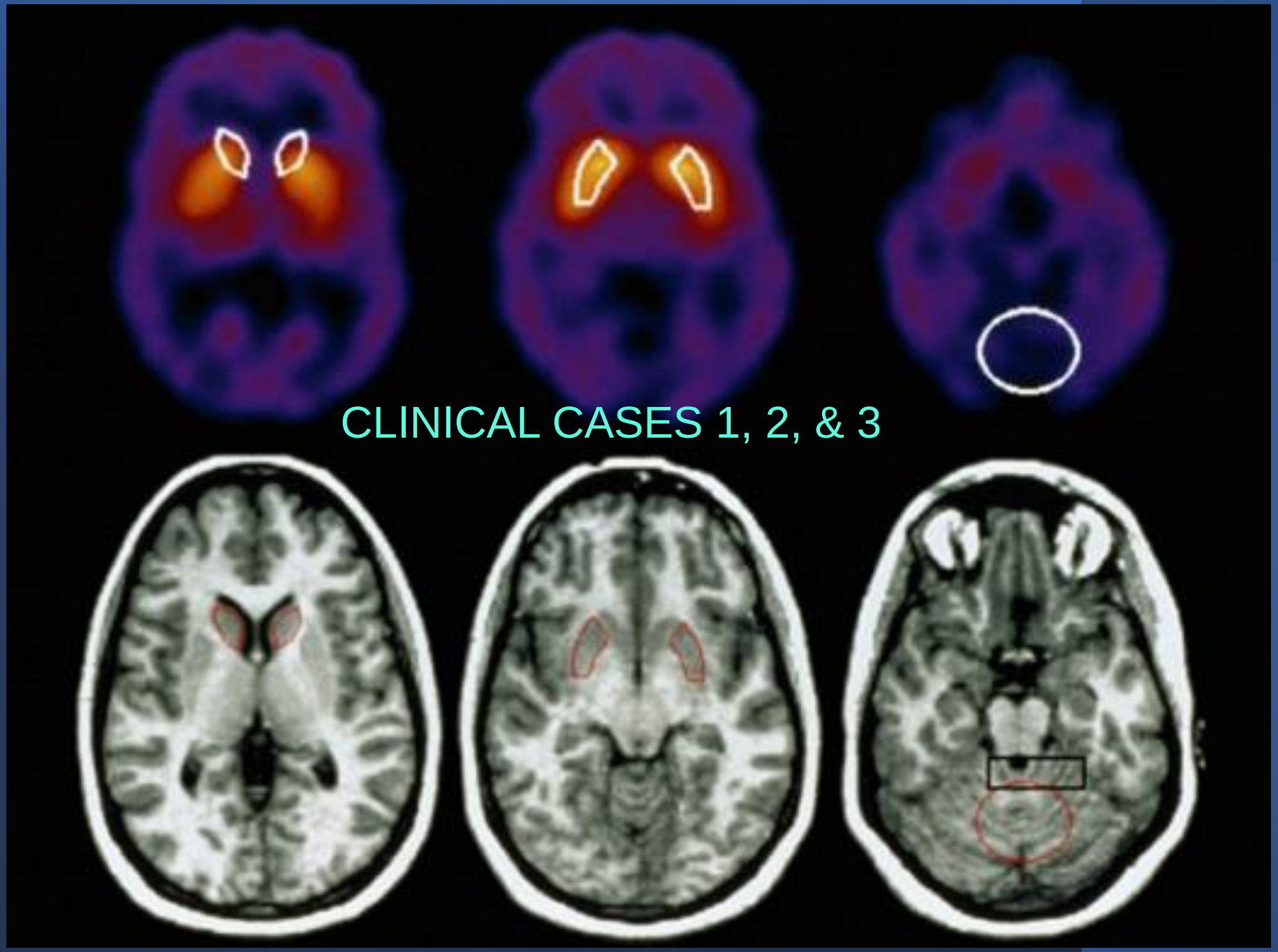


Innovative Memory Care
To promote brain health & Wellness

- Seek medical care early
  - Early diagnosis & treatment can improve outcome
  - Some causes of cognitive complaints are treatable!
  - Innovative therapies are emerging
    - Drug development to treat the underlying pathology
      - ✓ FDA-approved Anti-Amyloid infusions
      - ✓ Other drugs under development
    - Neural Stimulation to enhance brain function
      - ✓ Other innovative treatments
    - Supplements & Herbal therapy

How to promote healthy brain aging?




CLINICAL CASES 1, 2, & 3

Clinical Cases – Case 1

Chief Complaint: memory complaint

History of Present Illness: Mrs. Harris is a 71-year-old business owner who has been having trouble multi-tasking in the past 1-2 years. Her daughters are concerned about memory loss. She has had recent stressors. She is functionally independent.

Past Medical & Social History – unremarkable

Examination – Recall 2 of 3 words at 5 minutes, mild difficulty with serial 7s, no other cognitive deficits

Cranial nerves, Sensorimotor, Cerebellar, Gait & Station, DTRs intact, No Babinski response or pathological reflexes

Clinical Cases – Case 2

Chief Complaint: cognitive decline

History of Present Illness: Mrs. Lewis is a 59-year-old executive who has been having trouble learning new people's names. She often forgets about meetings that she arranges herself. Her ability to speak well is declining. She is functionally independent.

Past Medical & Social History – unremarkable

Examination – Delayed Recall 0 of 3 words, some word-finding pauses in conversation, no other cognitive deficits. Elemental neurological exam nonfocal.

Clinical Cases – Case 3

Chief Complaint: cognitive decline

History of Present Illness: Dr. Barnes is a 79-year-old Professor with a progressive cognitive decline. He has memory loss and word-finding difficulty. He stopped driving 1-year ago because he was getting lost. He moved into assisted living 2-years ago.

Past Medical & Social History – unremarkable

Examination – Recall 0 of 3 words at 5 minutes, impaired confrontation naming of low-frequency words, difficulty copying a complex figure. Elemental neurological examination nonfocal.

Clinical Cases – Diagnosis & Definitions

Case 1: **Subjective Cognitive Disorder (SCD)**

- *Cognitive complaint*
  - No objective cognitive deficits on exam
  - Functionally independent

Case 2: **Minor Neurocognitive Disorder**

- *Complains of Cognitive decline*
  - Cognitive deficits on exam
  - Functionally independent

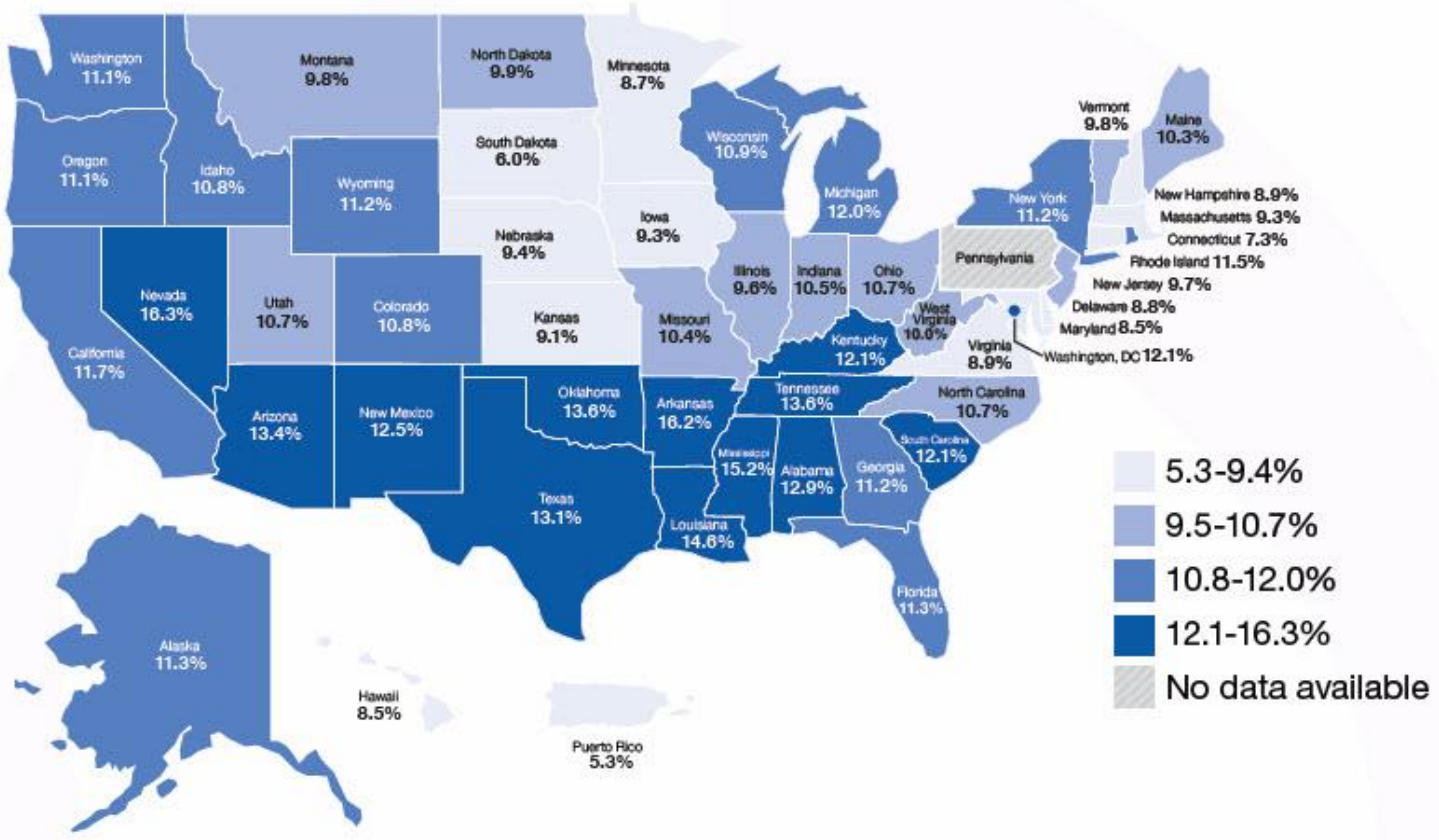
Case 3: **Major Neurocognitive Disorder**

- *Cognitive Deficits, Functionally impaired* ***– Dementia***

Cognitive Decline in Louisiana

Prevalence of Subjective Cognitive Decline in the U.S.

Figure 1: Adults 45 years of age and older with Subjective Cognitive Decline



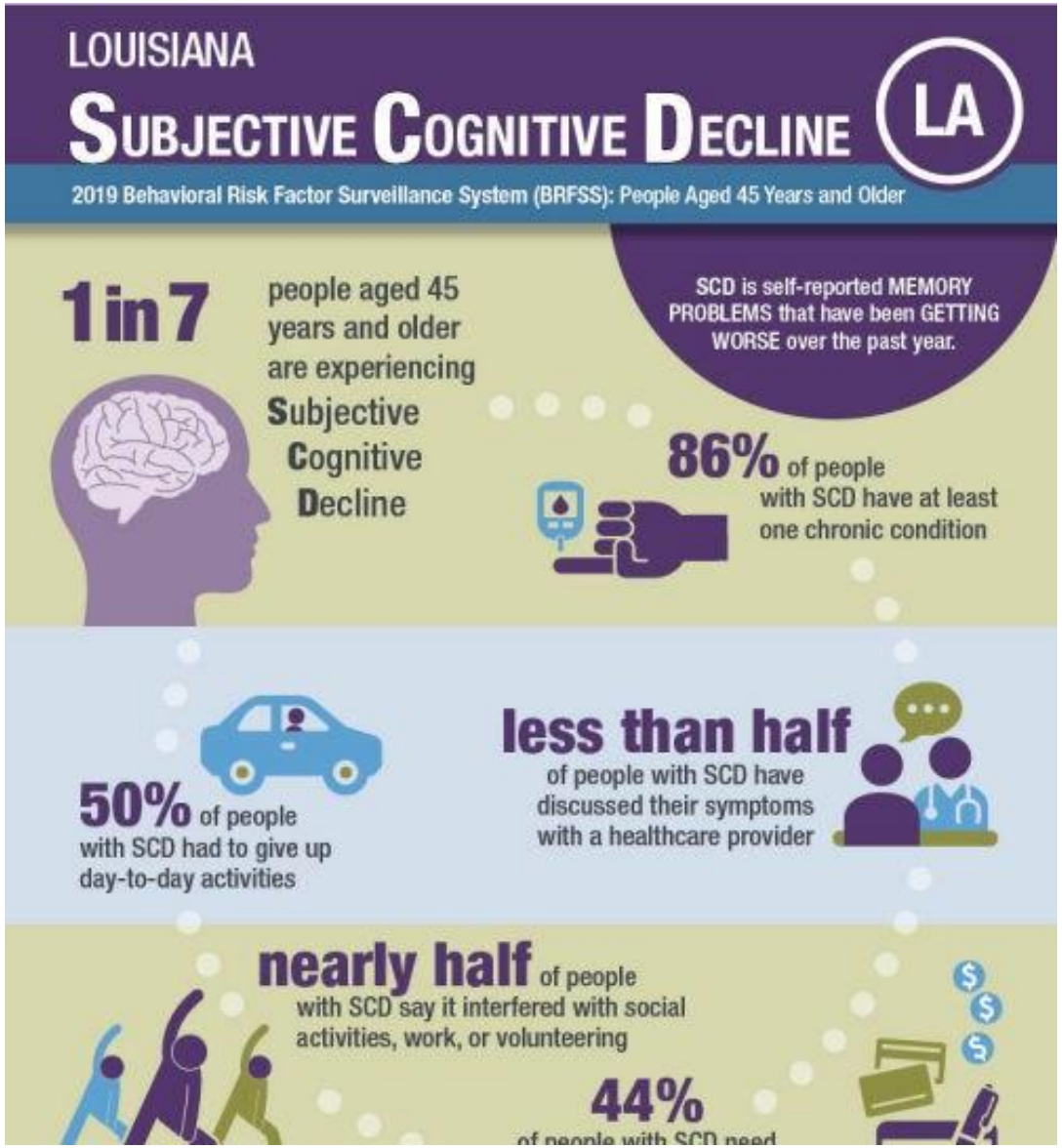
LOUISIANA POPULATION DATA		
45-54	528,974	11.42%
65-74	493,078	10.65%
75-84	232,006	5.01%
85+	85,306	1.84%
Total >45 yrs	1,339,364	

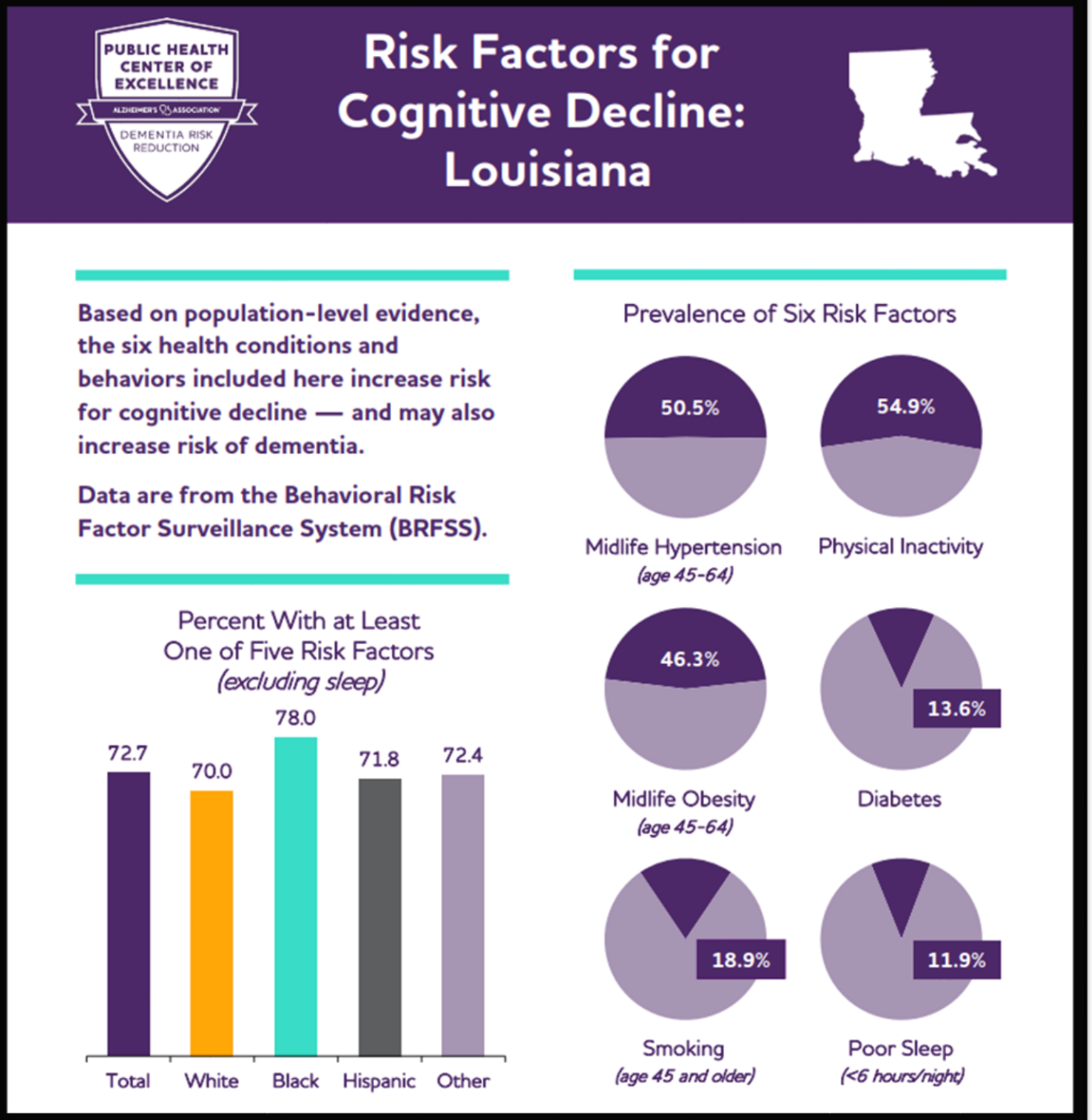
Total State Population 2021 = 4,624,000

29% of the State Population is over 45 years of age

According to the CDC, 14.6% of Louisiana residents over 45 years of age have Subjective Cognitive Decline (SCD) and are at risk for dementia.

Based on current population data, about 195, 547 Louisiana citizens are at risk.

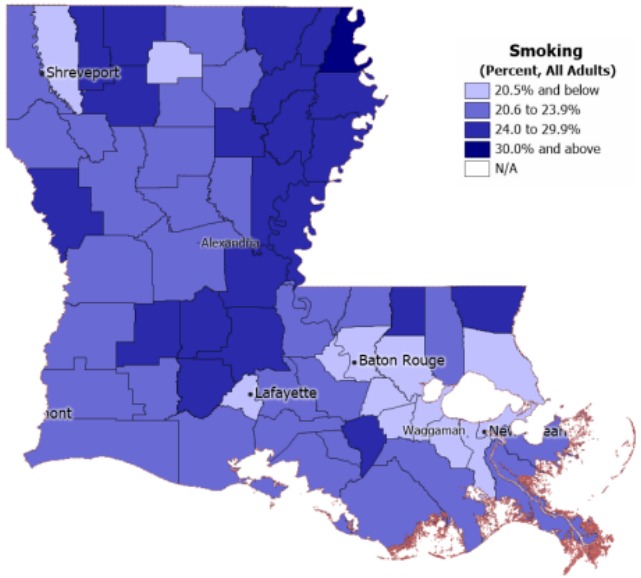

LOUISIANA
SUBJECTIVE COGNITIVE DECLINE
LA
2019 Behavioral Risk Factor Surveillance System (BRFSS): People Aged 45 Years and Older
1 in 7
people aged 45 years and older are experiencing Subjective Cognitive Decline
SCD is self-reported MEMORY PROBLEMS that have been GETTING WORSE over the past year.
86% of people with SCD have at least one chronic condition
50% of people with SCD had to give up day-to-day activities
less than half of people with SCD have discussed their symptoms with a healthcare provider
nearly half of people with SCD say it interfered with social activities, work, or volunteering
44%



- Opportunities to address the impact of dementia on Louisiana begin before a diagnosis.
- 36% of Louisiana adults have 2 or more of these risk factors

Risk Factors for Cognitive Decline
Louisiana

Smoking



Statewide Rate 19.5%

NOTE: Statewide rate may differ from other published figures due to differences in data year, age group, and survey question.

Source: Public Health Center of Excellence on Dementia Risk Reduction at the Alzheimer's Association, based on data from PLACES, Centers for Disease Control and Prevention, October 2023.
Mapping Software: © 2023 CALIPER

This Fact Sheet is supported by the Centers for Disease Control and Prevention (CDC) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award totaling $2,973,948. The contents are those of the Alzheimer's Association and do not necessarily represent official views of nor an endorsement by, CDC, HHS, or the U.S. government.

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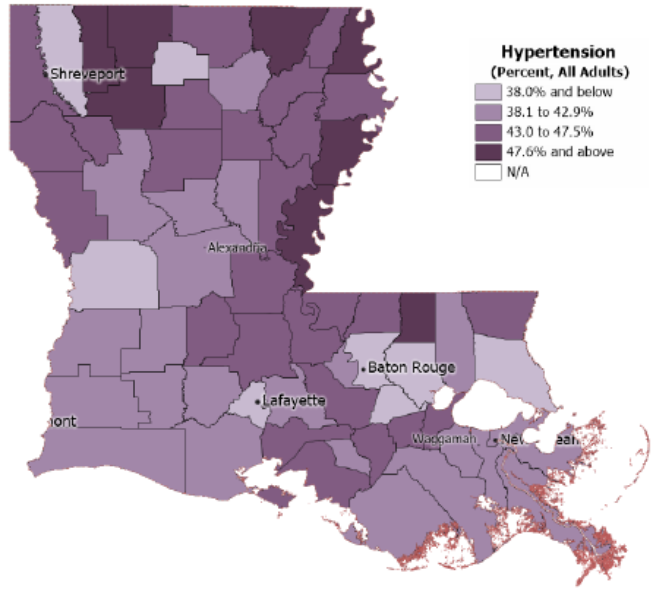
Risk Factors for Cognitive Decline
Louisiana

Hypertension



Statewide Rate 40.2%

NOTE: Statewide rate may differ from other published figures due to differences in data year, age group, and survey question.

Source: Public Health Center of Excellence on Dementia Risk Reduction at the Alzheimer's Association, based on data from PLACES, Centers for Disease Control and Prevention, October 2023.
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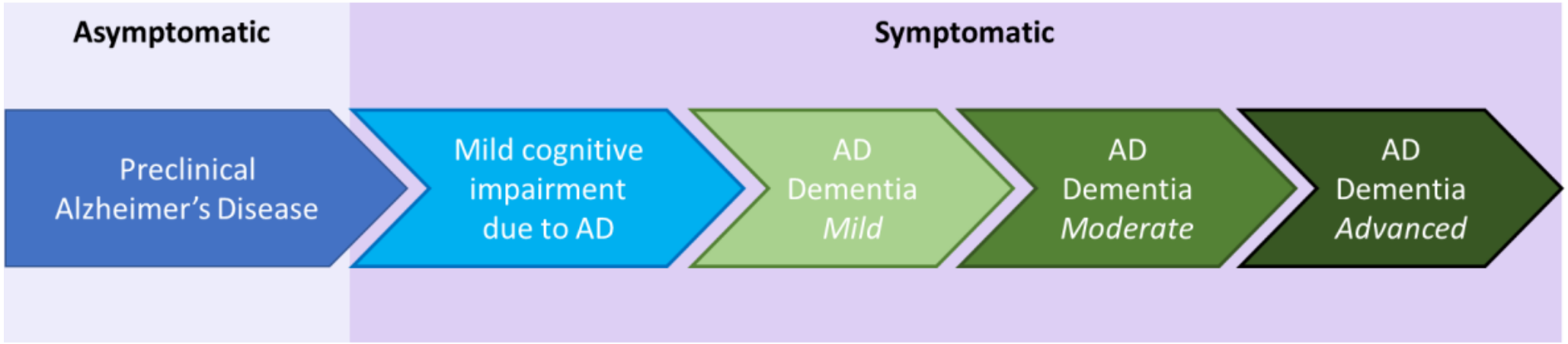
Mild Cognitive Impairment (MCI) - *Definition*

Cognitive decline	• Deficits on objective cognitive testing • Deficits can be in a Single or Multiple Cognitive domains
Functionally independent	• No significant functional changes
Not all patients with a diagnosis of MCI progress to dementia	



Alzheimer's disease (AD) continuum, based on the 2011 NIA-AA diagnostic guidelines

Neurodegenerative Diseases
Alzheimer's Disease – Case 3

Alzheimer's Disease	***Cortical Degeneration***

Clinical Deficits	
• Learning & Memory	Hippocampal formation Acetycholine – *Nucleus basalis of Meynert*
• Cognitive deficits	Bilateral Parietal Cortex
⑩***Right Parietal***	***Visuospatial & Visual Perception deficits***
⑩***Left Parietal***	***Anomia & Apraxia***

Localization	Anatomical, Neurochemical

Pathophysiology	Diagnosis & Treatment
• ***Neurofibrillary tangles***	***Tau protein***
• ***Neuritic plaques***	***Beta-amyloid deposition***

Louisiana Specific Data

Alzheimer's disease is a growing public health crisis in Louisiana. The impact of Alzheimer's is projected to rise, and the most recent data show:

- 92,000 people aged 65 and older are living with Alzheimer's in Louisiana.
- 13.6% of people aged 45 and older have subjective cognitive decline.
- 200,000 family caregivers bear the burden of the disease in Louisiana.
- 363 million hours of unpaid care provided by Alzheimer's caregivers.
- $4.8 billion is the value of the unpaid care.
- $765 million is the cost of Alzheimer's to the state Medicaid program.

These numbers show that a public health approach is necessary to lessen the burden and enhance the quality of life for those living with cognitive impairment and their families.

Learn more about Louisiana: Alzheimer's Statistics (PDF), Cognitive Decline (PDF), Dementia Caregiving (PDF), Risk Factors (PDF), County-Level Alzheimer's Prevalence (PDF)

LOUISIANA CAREGIVING

LA

2021 Behavioral Risk Factor Surveillance System (BRFSS) Data

1 in 4 adults are caregivers

CAREGIVERS provide regular care or assistance to a **FRIEND** or **FAMILY** member with a health problem or disability

CAREGIVING CAN BE

LENGTHY

Over half have provided care for at least two years

INTENSE

Over a third have provided care for at least 20 hours per week

WHO ARE CAREGIVERS?

60% are women

20% are 65 years old or older

34% are caring for a parent or parent-in-law

23% of caregivers are providing care to someone with dementia

HOW DO CAREGIVERS HELP?

Over 80% manage household tasks

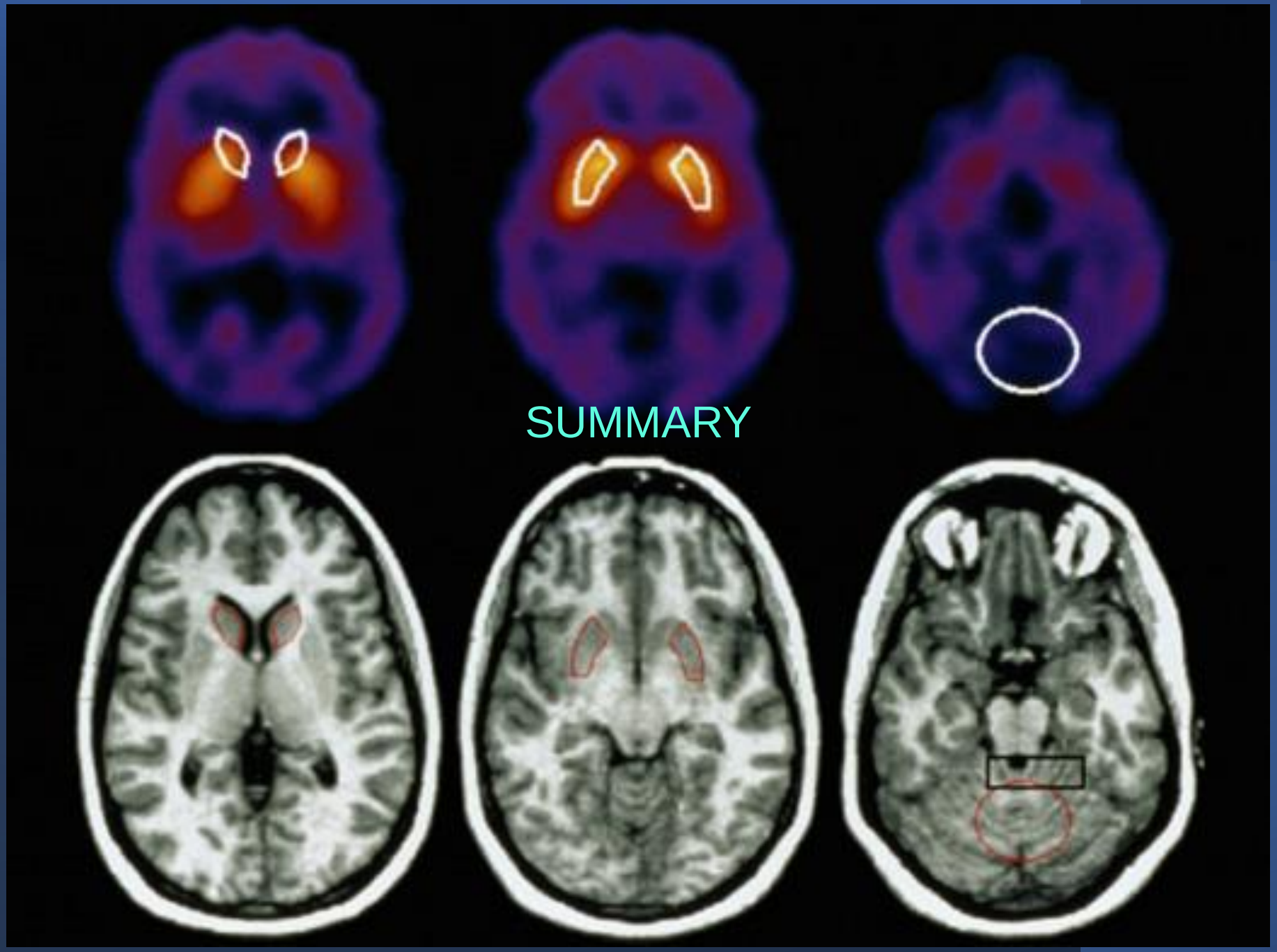
Over half assist with personal care

FUTURE CAREGIVERS

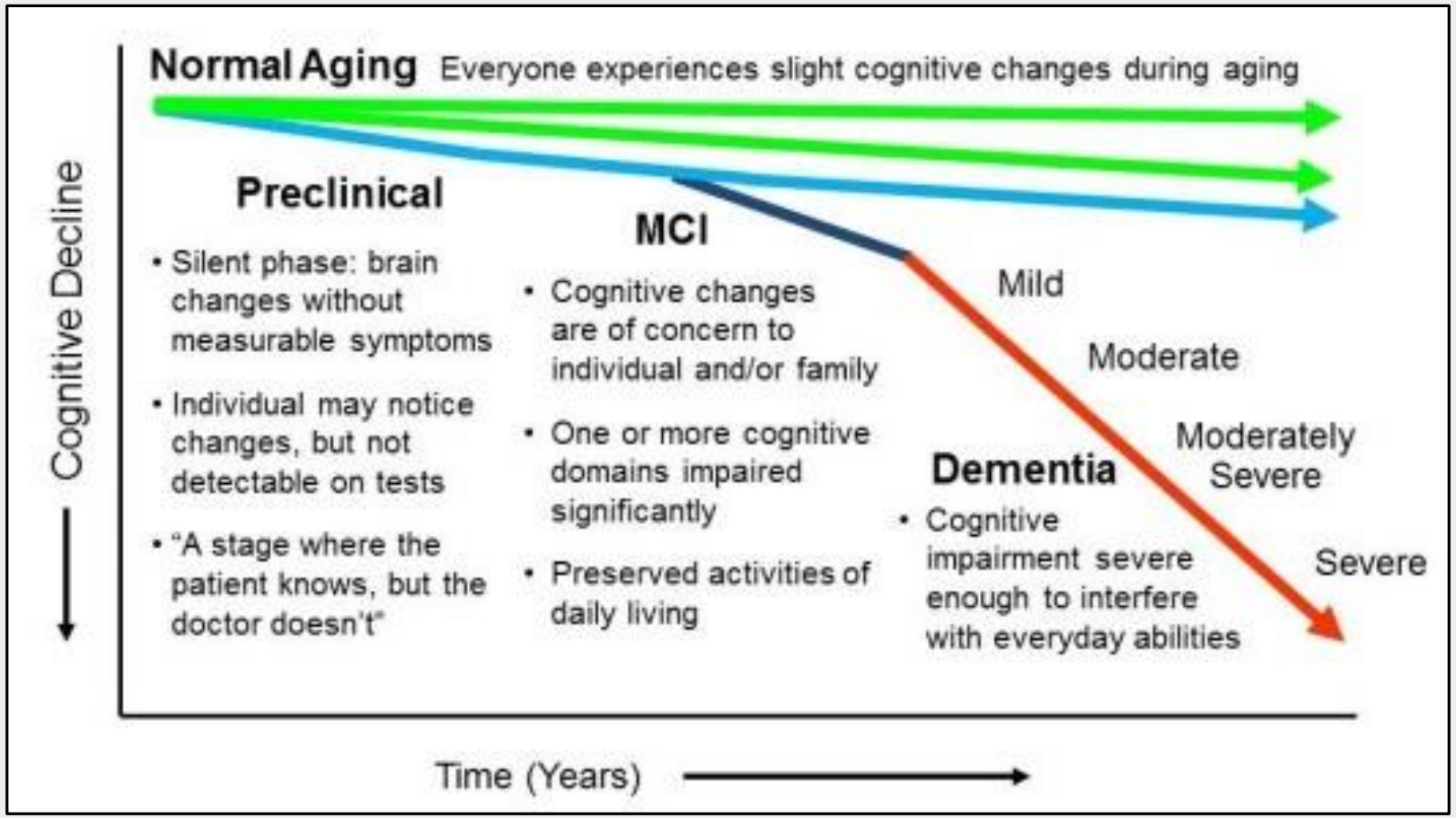
Nearly 1 in 5 NON-CAREGIVERS expect to **BECOME CAREGIVERS** within 2 years

alzheimer's association | CDC

For more information: www.alz.org/publichealth www.cdc.gov/aging


SUMMARY

Cognitive Continuum



- Cognitive Continuum
- Risk Reduction - Prevention
- Early Detection – Treatment

Reference: Temple University

Clinical Pearls

Early AD

- MCI: some cognitive impairment, functional independence intact
- Mild AD dementia: cognitive impairment significant enough to impair functional independence

Importance of early and timely diagnosis

- Development of an effective care plan
- Eligibility for available clinical trials or disease-modifying therapies
- More time for education and planning

Role of the primary care clinician

- Often the first to see signs and symptoms
- Investigates cognitive complaints
- Addresses remediable causes

When to assess

- Subjective cognitive complaints should be taken seriously
- Annual Wellness Visit includes cognitive assessment

Importance of Early/Timely Diagnosis of Early AD (MCI or Mild AD Dementia)

Lifestyle modifications to slow or delay progression[a]

- Exercise and diet
- Sleep
- Reduced tobacco use
- Reduced alcohol use
- Cognitive stimulation
- Vascular factors

More time for medical and estate planning[a]

Time to educate and counsel patients and their family members[a]

Treatment with available disease-modifying therapies[b]

a. Liss J, et al. J Intern Med. 2021;290:310-334; b. Porsteinsson AP, et al. J Prev Alz Dis. 2021;8:371-386.

Alzheimer's disease genetics

- Classified into two subtypes depending on the age of onset

1. Early onset Alzheimer's Disease [EOAD]: **also called familial AD**
   - Starts before the age of 65 years, typically in late 40s and early 50s
   - Accounts for 1-5% AD patients
   - Most obvious family aggregation of AD patients
   - Mendelian autosomal dominant pattern of inheritance [<1% AD patients
2. Late onset Alzheimer's Disease [LOAD]: **also called sporadic AD**
   - Starts after the age of 65 years
   - Accounts for >95% of cases

Alzheimer's Disease – Genetic Factors

The two main types of AD are *early-onset* and *later-onset*:

Early-onset AD

Familial Alzheimer's disease

Researchers have identified mutations in three genes

Presenilin 1	**Presenilin 2**	**APP (amyloid precursor protein)**

Later-onset AD

Sporadic Alzheimer's disease

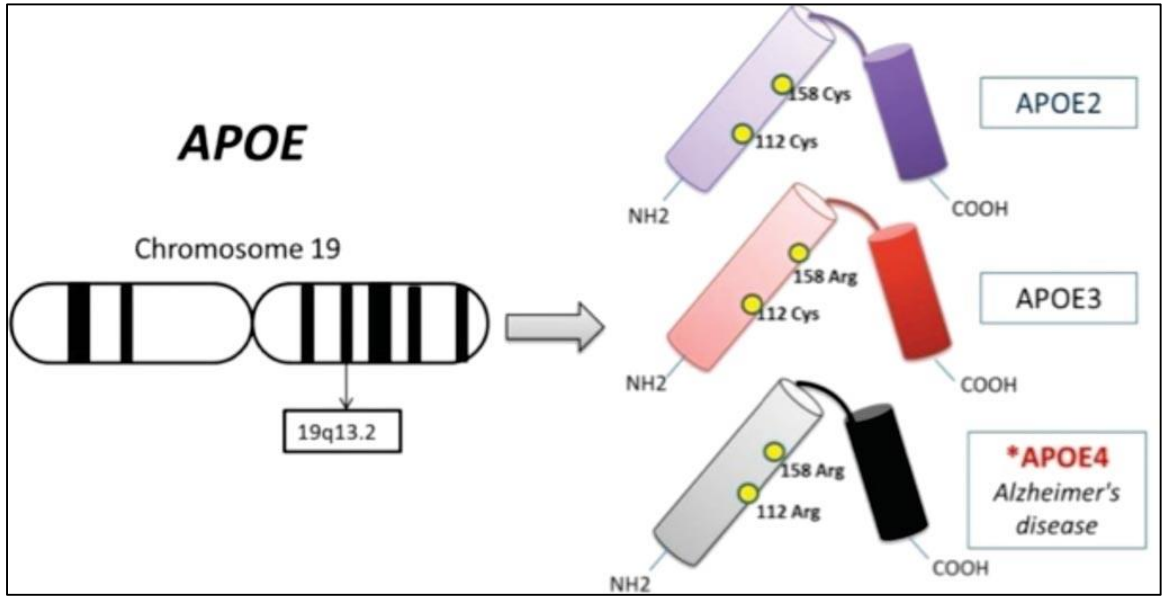
Linked to specific *Apolipoprotein E Alleles*

- ApoE - involved in beta-amyloid plaque formation
  - ✓ApoE2 protective
  - ✓ApoE4 increased risk

ε4 allele of apolipoprotein E (APOE)

- ✓ *e4/4 (homozygotes): 9.6% of the population*
- ✓ *3 times the risk of developing AD*

ApoE Genotype



Population estimates

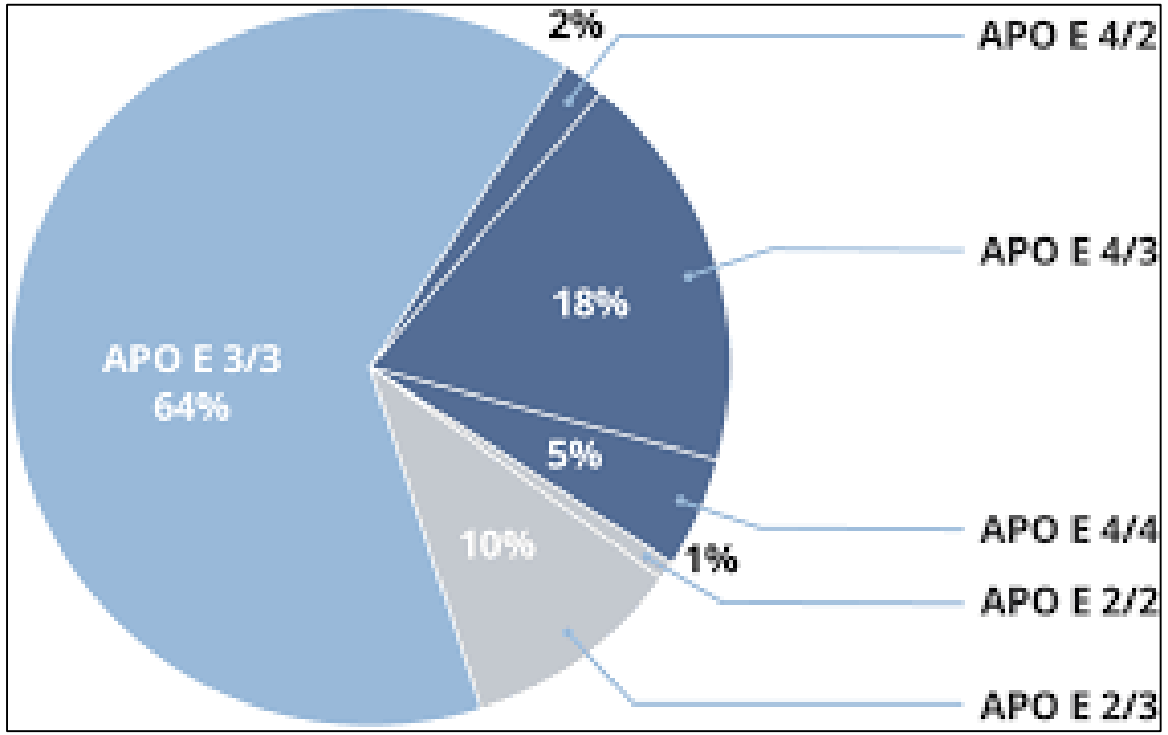
- ApoE3 = 64%

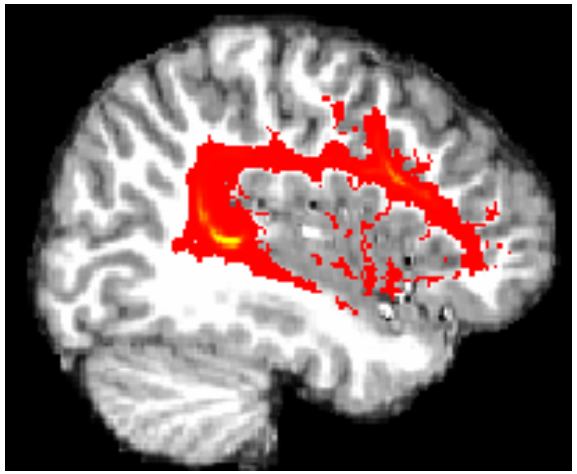
Increases Risk of AD

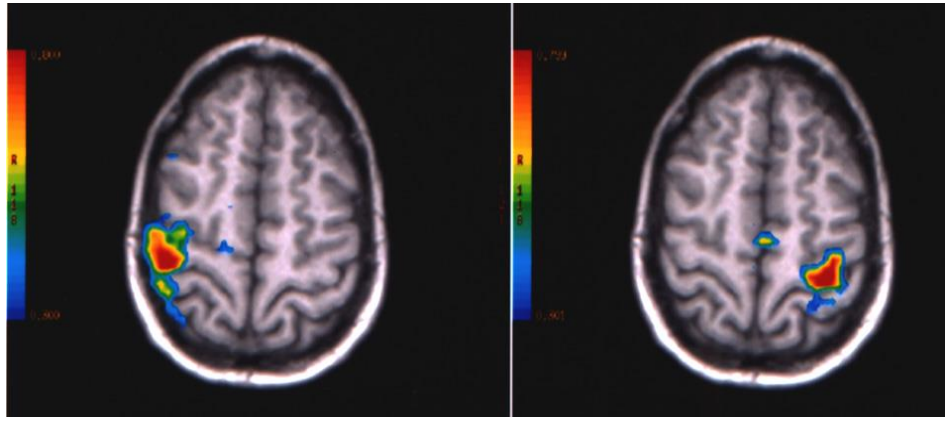
- ApoE4 = 25%

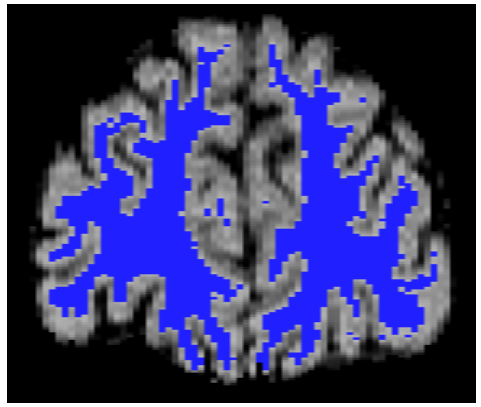
May be Protective of AD risk

- ApoE2 = 11%

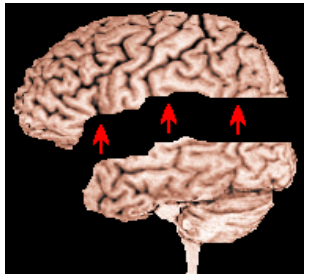


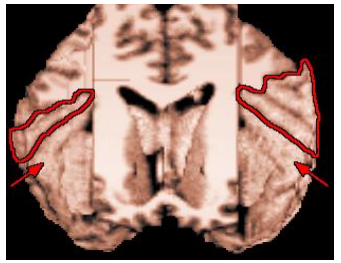


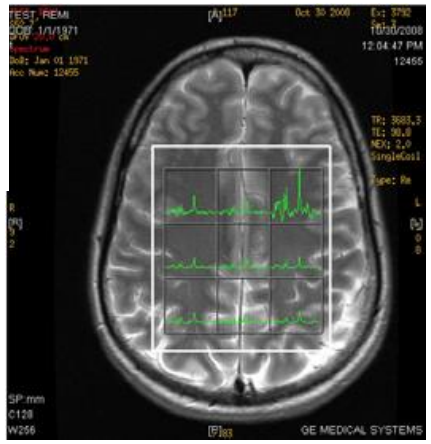




NOLA Brain and Behavior







The Brain Institute of Louisiana.

www.braininstituteoflouisiana.com