How Much Forgetfulness Is Too Much?

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2020 Brock Institute Glennan Center Lecture

EVMS

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Disclosures

- Roche, Inc.
- Merck, Inc.
- Genentech, Inc.
- Biogen, Inc.
- Eisai, Inc.

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- U01 AG006786
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- U01 AG011378
- R01 AG011378
- R01 AG041581
- GHR Foundation
- Mayo Foundation for Education and Research

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Outline

- The Problem
- What is MCI?
- MCI therapies
- Clinical acceptance of MCI
- Subjective Cognitive Decline

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Major question

What is normal aging?

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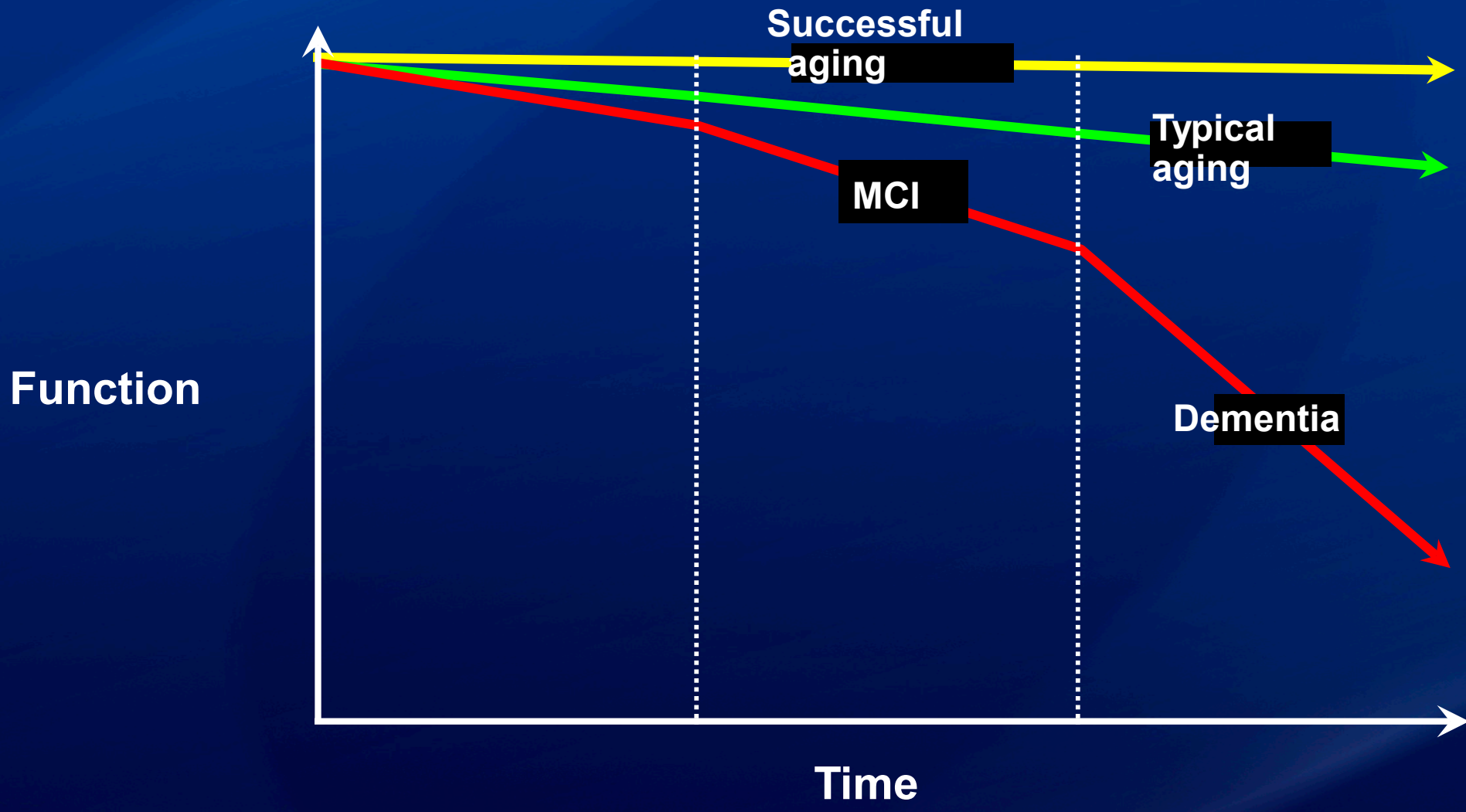
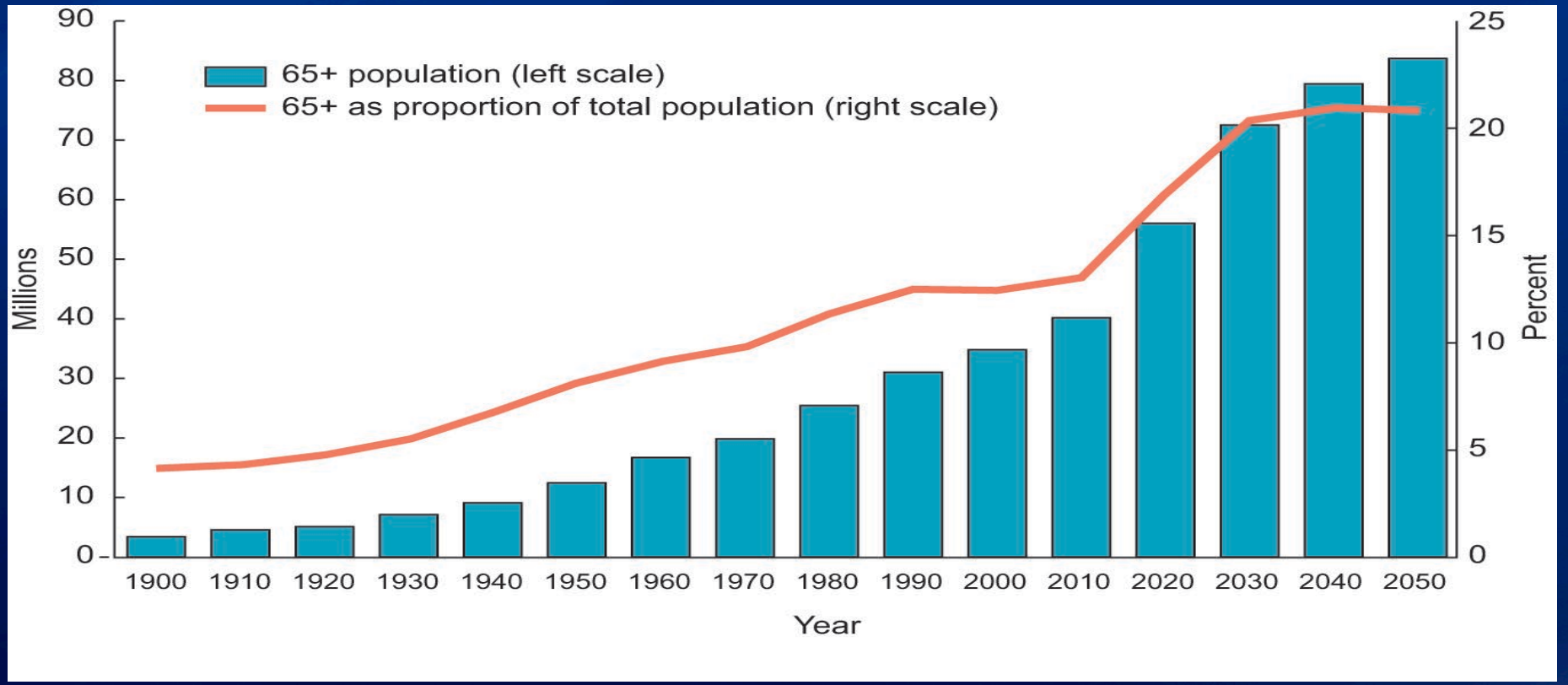


What is Cognitive Aging?

- **Cognition** refers to the mental functions involved in attention, thinking, understanding, learning, remembering, solving problems, and making decisions.
- **Cognitive aging** is a process of gradual, ongoing, yet highly variable changes in cognitive functions that occur as people get older.
- Cognitive aging is a **lifelong process**. It is not a disease or a quantifiable level of function.
- In the context of aging, **cognitive health** is exemplified by an individual who maintains his or her optimal cognitive function with age.

Demographics



SOURCE: West, L. A., S. Cole, D. Goodkind, and W. He. 2014. *65+ in the United States: 2010. U.S. Census Bureau Special Studies*.

Key Features of Cognitive Aging

- **Inherent in humans** and animals as they age
- Occurs **across the spectrum of individuals** as they age regardless of initial cognitive function
- Highly dynamic process with **variability within and between individuals**
- Includes cognitive domains that may not change, may decline, or may actually improve with aging, and there is the potential for older adults to **strengthen some cognitive abilities**
- **Only now beginning to be understood biologically** yet clearly involves structural and functional brain changes
- **Not a clinically-defined neurological or psychiatric disease such as Alzheimer's disease** and does not inevitably lead to neuronal death and neurodegenerative dementia.

Cognitive Continuum

Normal

MCI

Dementia

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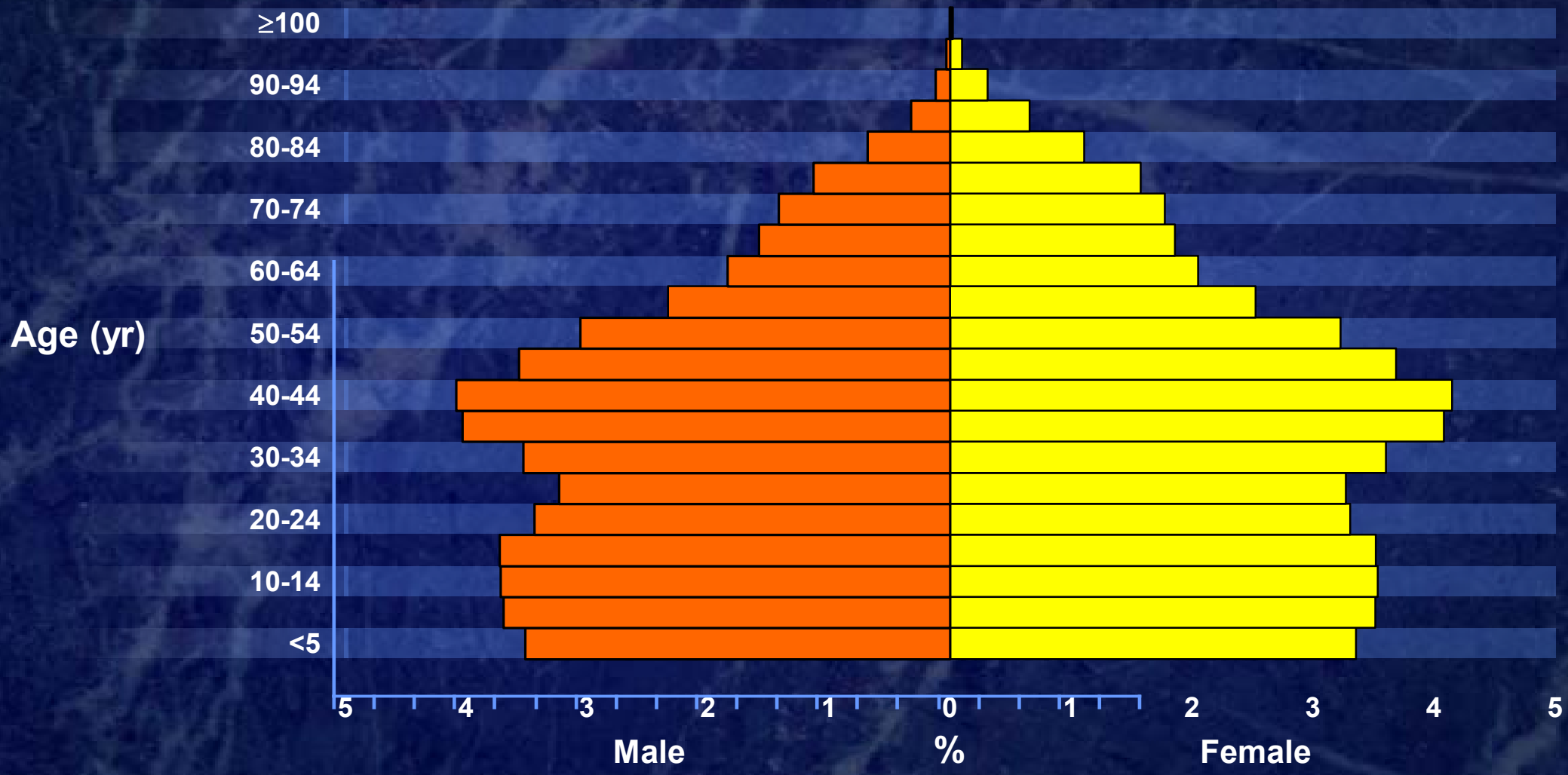
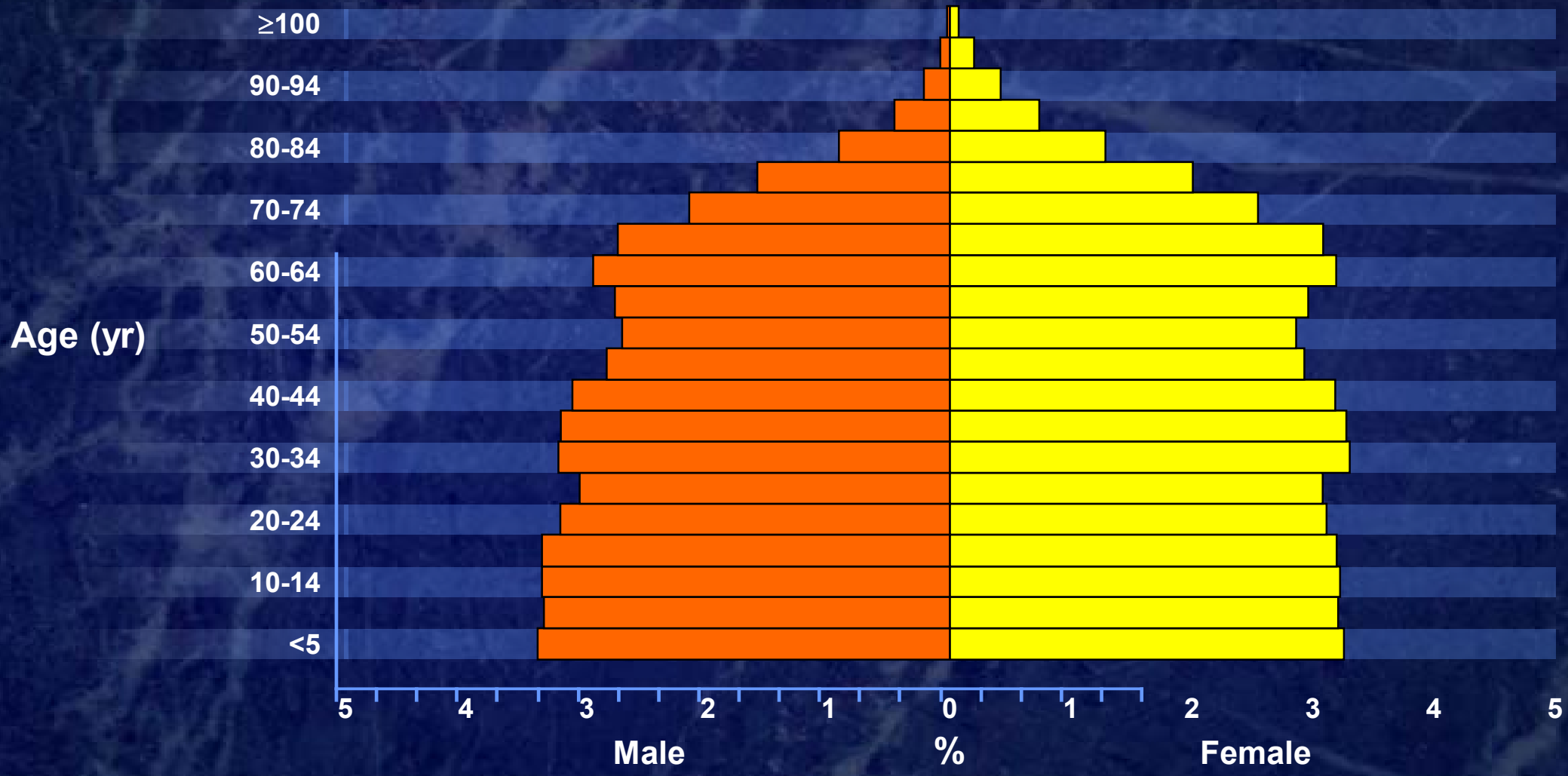
Population of the United States as of July 1, 2000



National Projections Program, Population Division,
U.S. Census Bureau, Washington, DC 20233

CP1319882-1

Projected Population of the United States as of July 1, 2025



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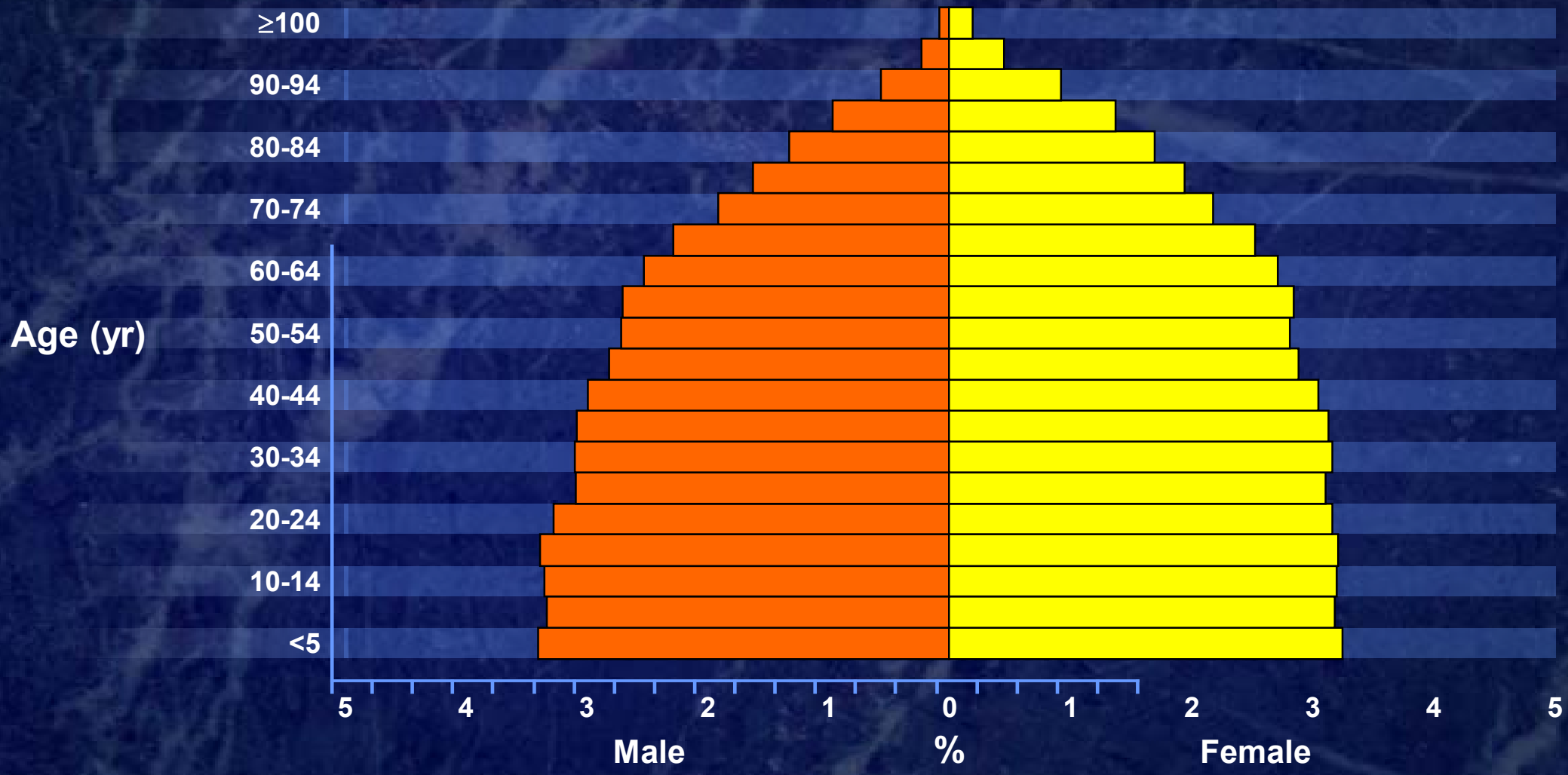
Projected Population of the United States as of July 1, 2050



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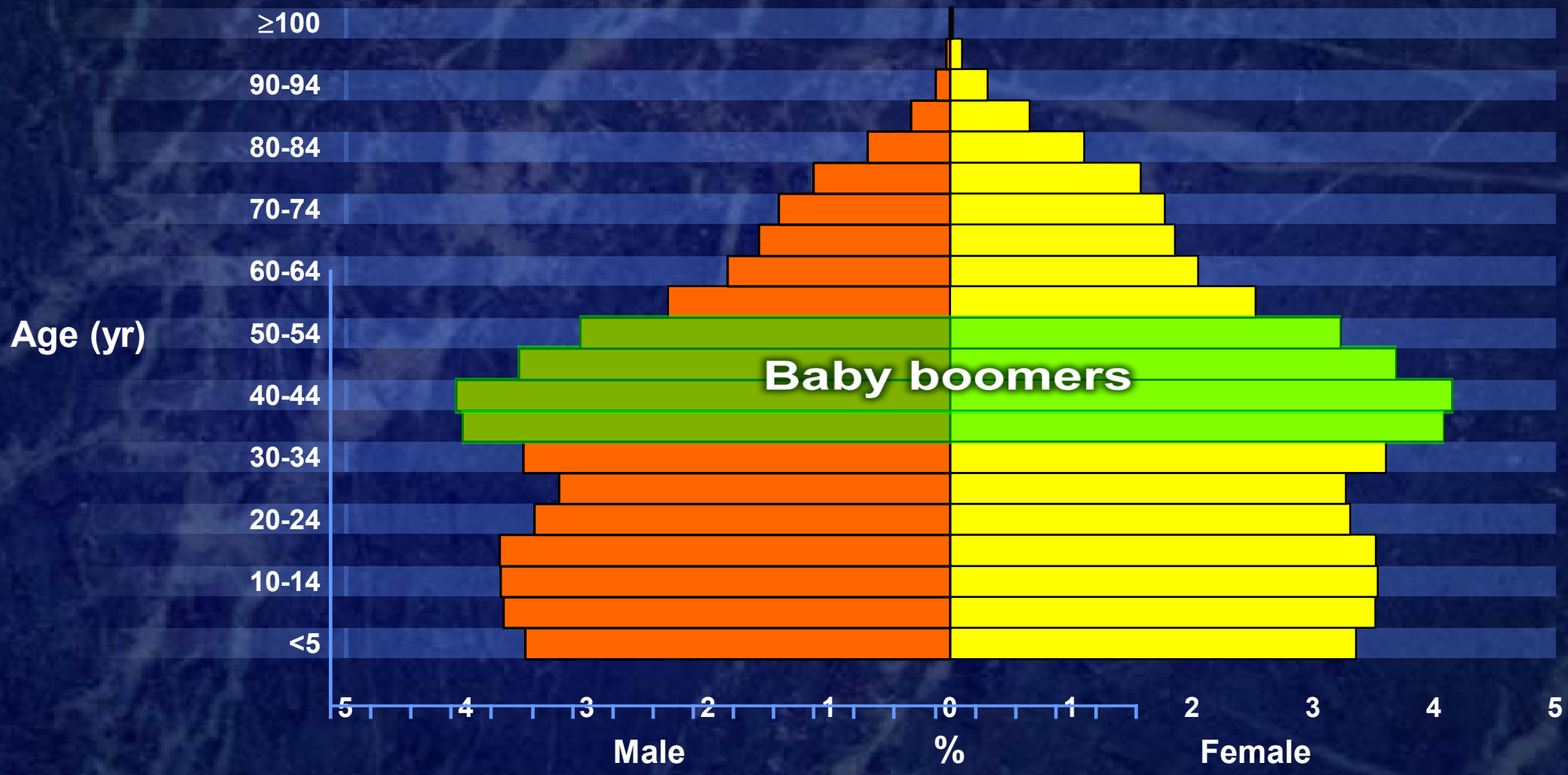
U.S. Census Bureau, Washington, DC 20233

CP1319882-3

Population of the United States as of July 1, 2000



National Projections Program, Population Division,
U.S. Census Bureau, Washington, DC 20233

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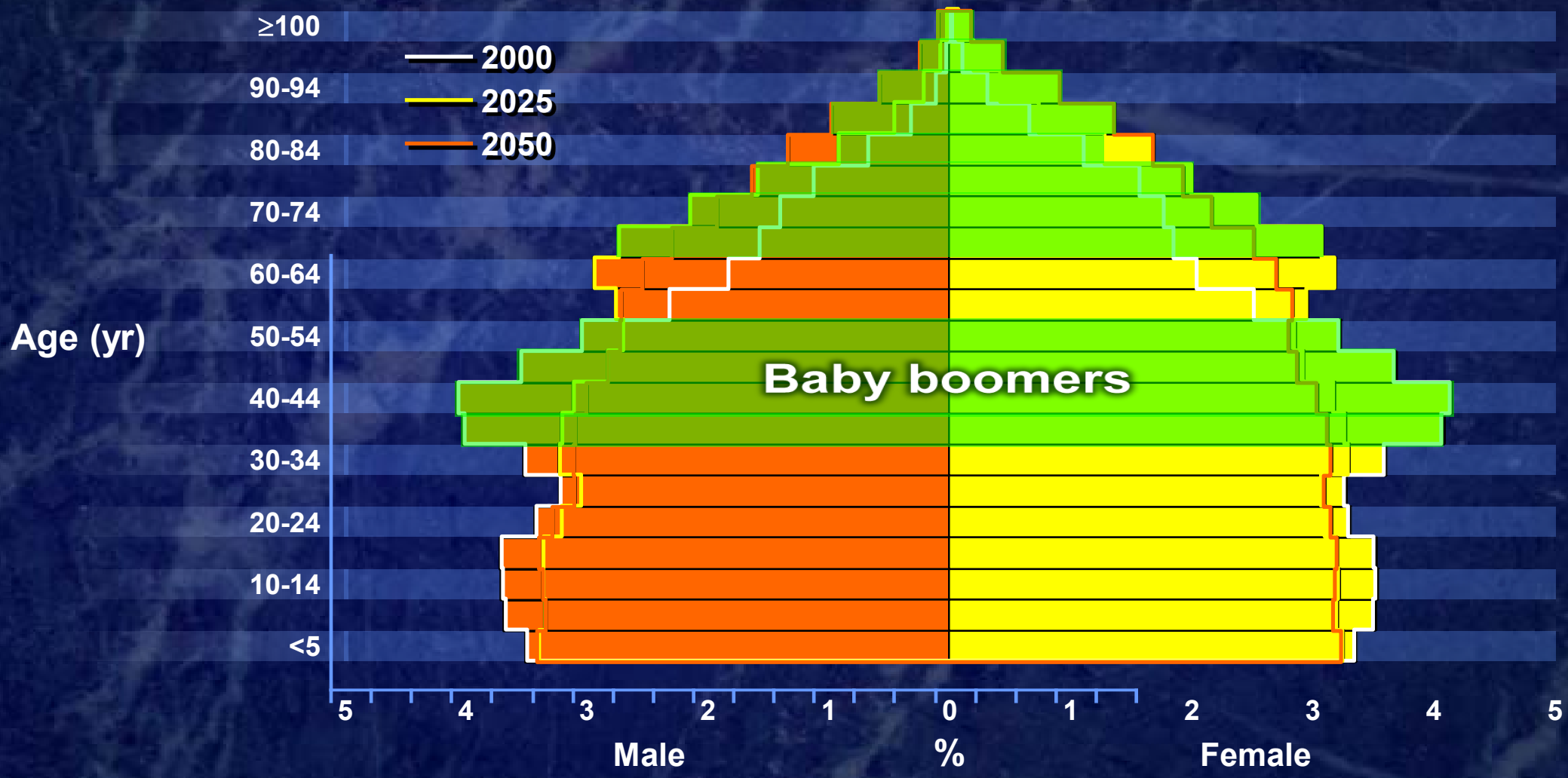
Projected Population of the United States as of July 1, 2050



National Projections Program, Population Division,
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- Subjective Cognitive Decline

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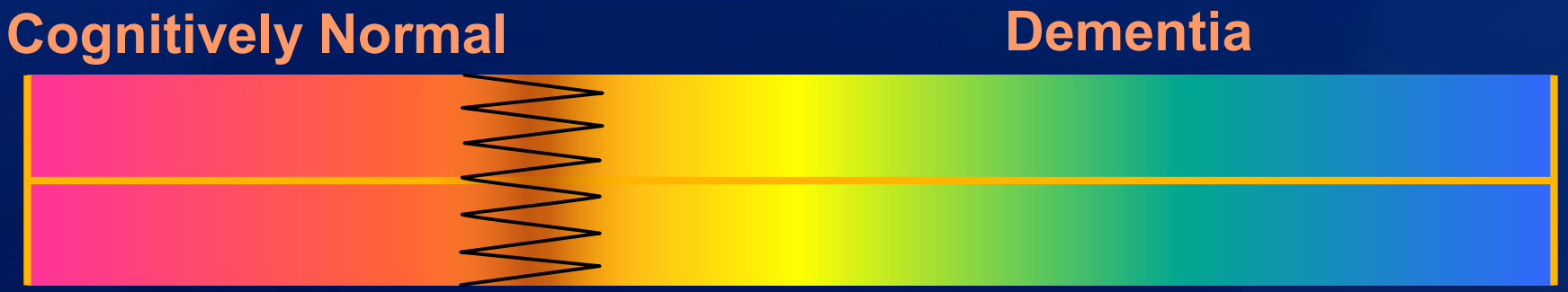
Old Conception of Alzheimer's Disease



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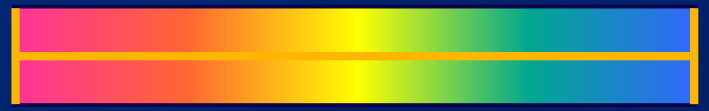
Cognitive Continuum

Normal



MCI

Dementia

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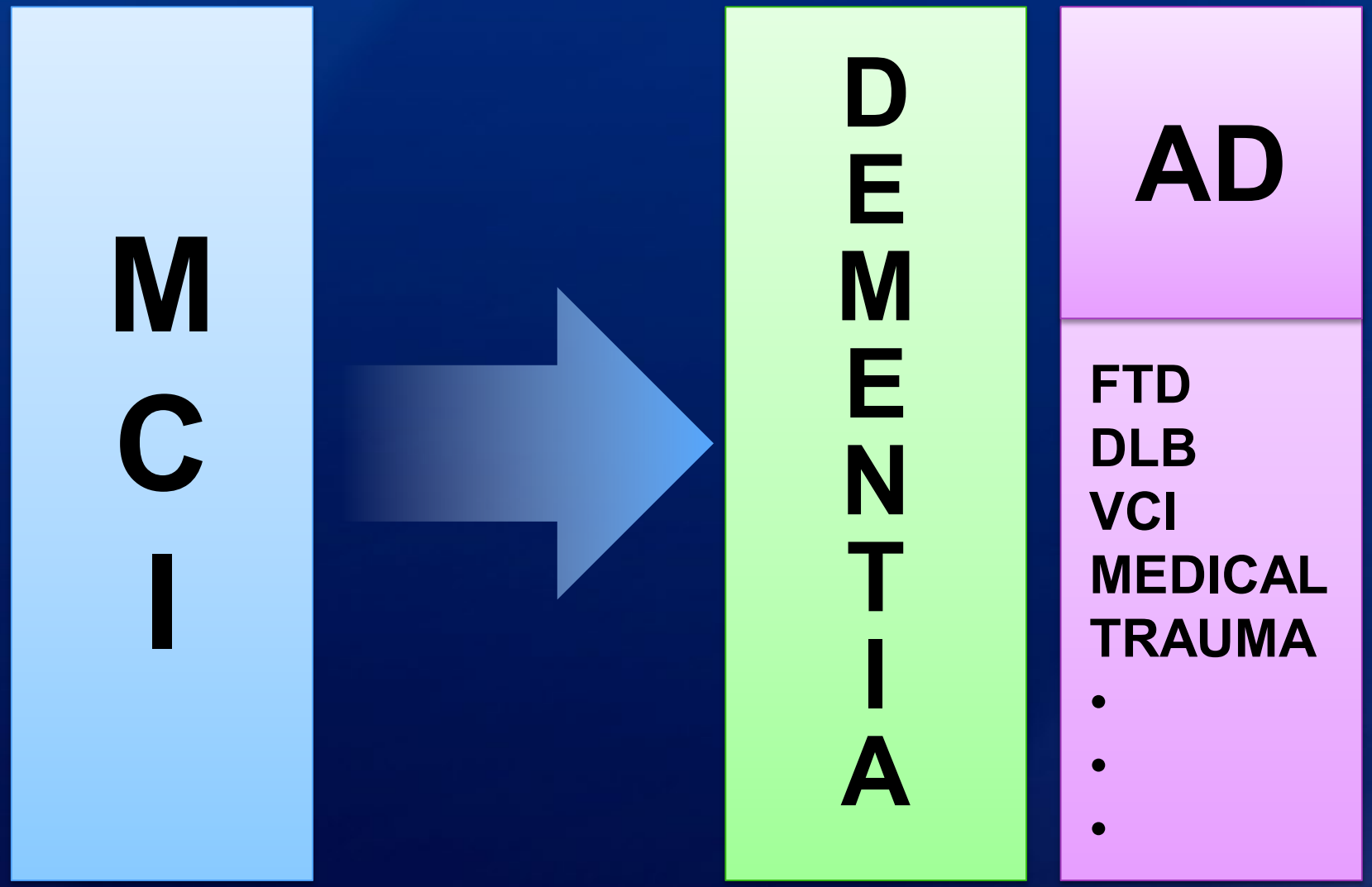

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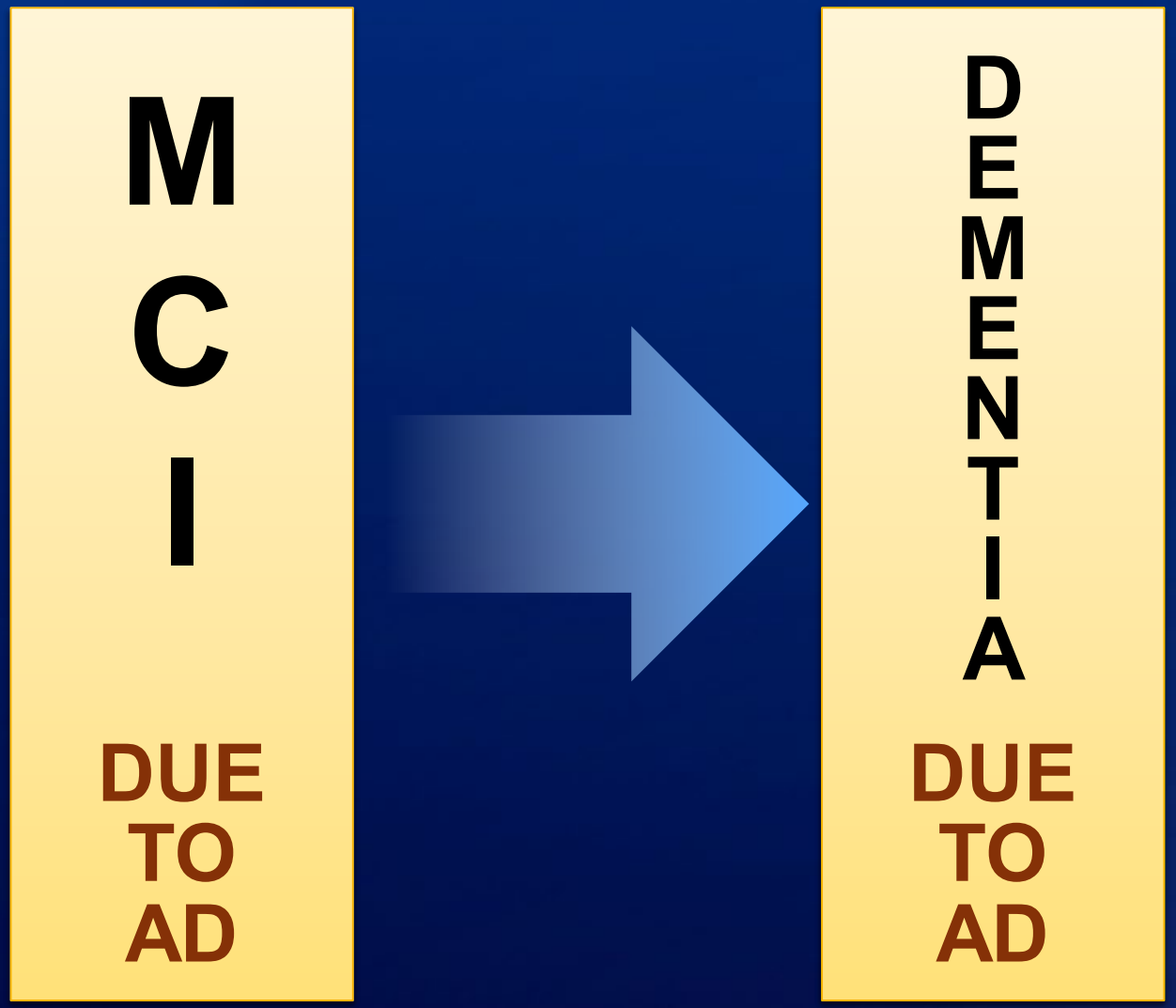

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Mild Cognitive Impairment

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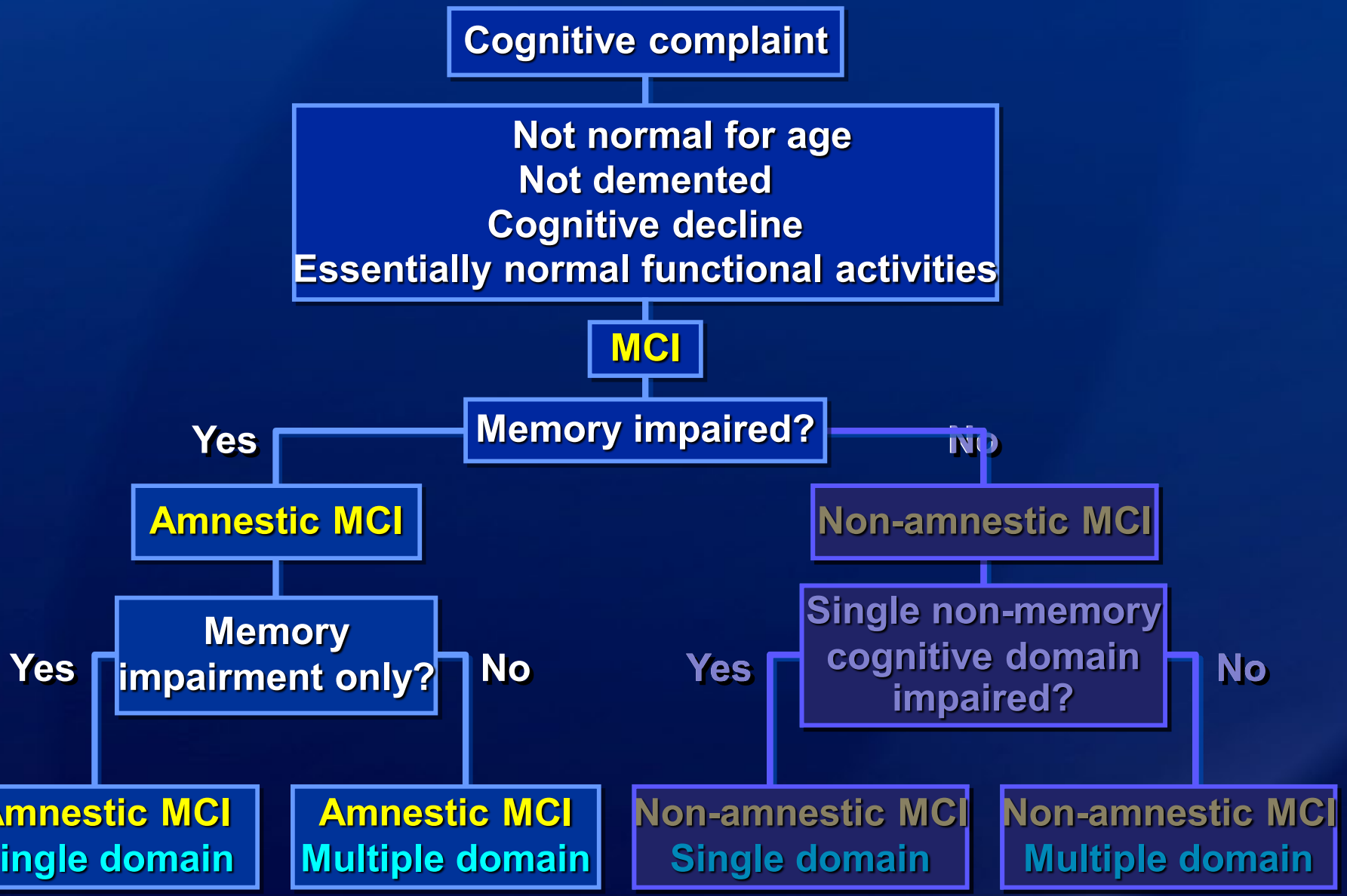
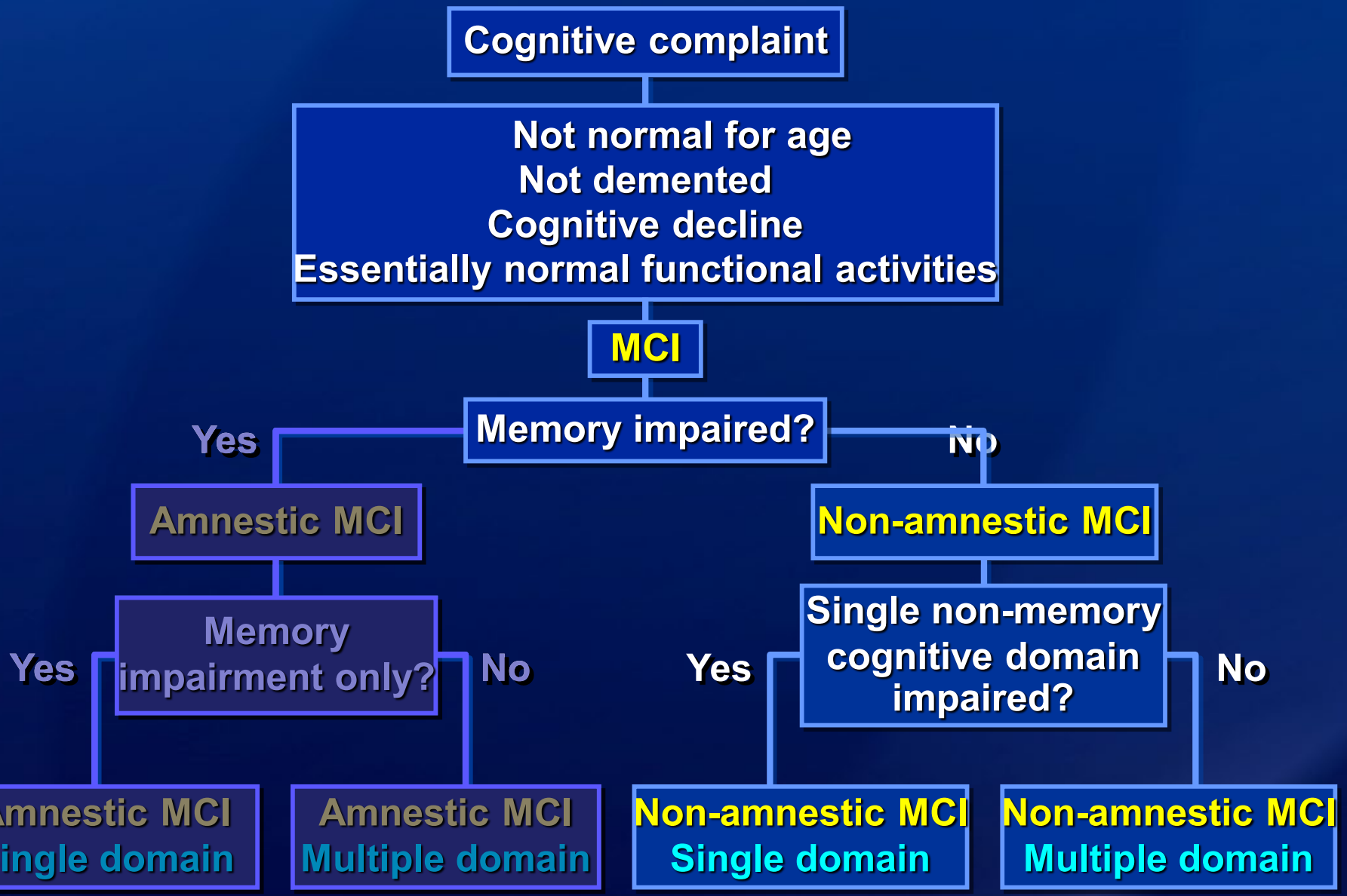
Mild Cognitive Impairment



Petersen: J Int Med, 2004

CP1265413-2

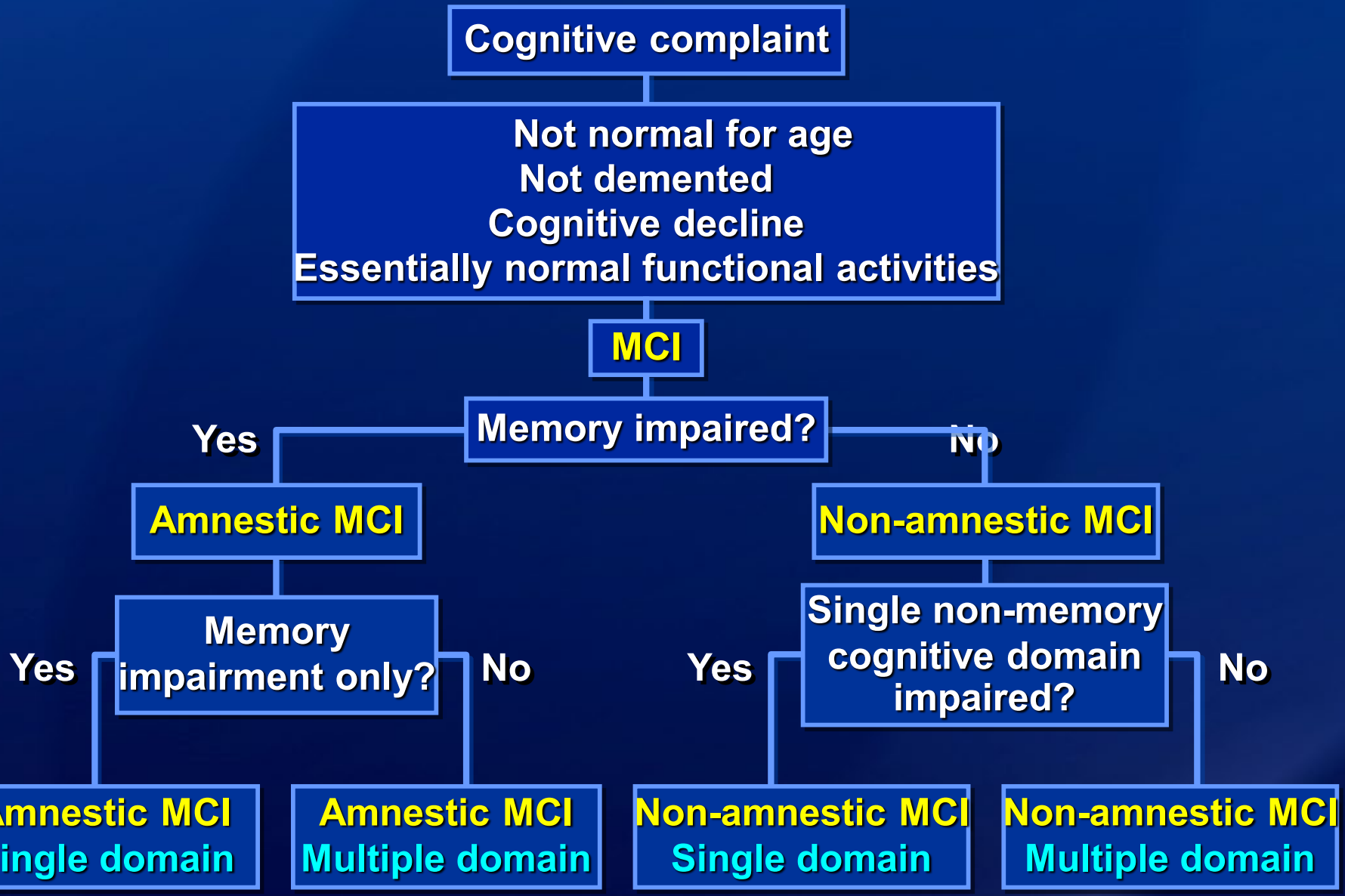
Mild Cognitive Impairment



Petersen: J Int Med, 2004

CP1265413-3

Mild Cognitive Impairment



Petersen: J Int Med, 2004

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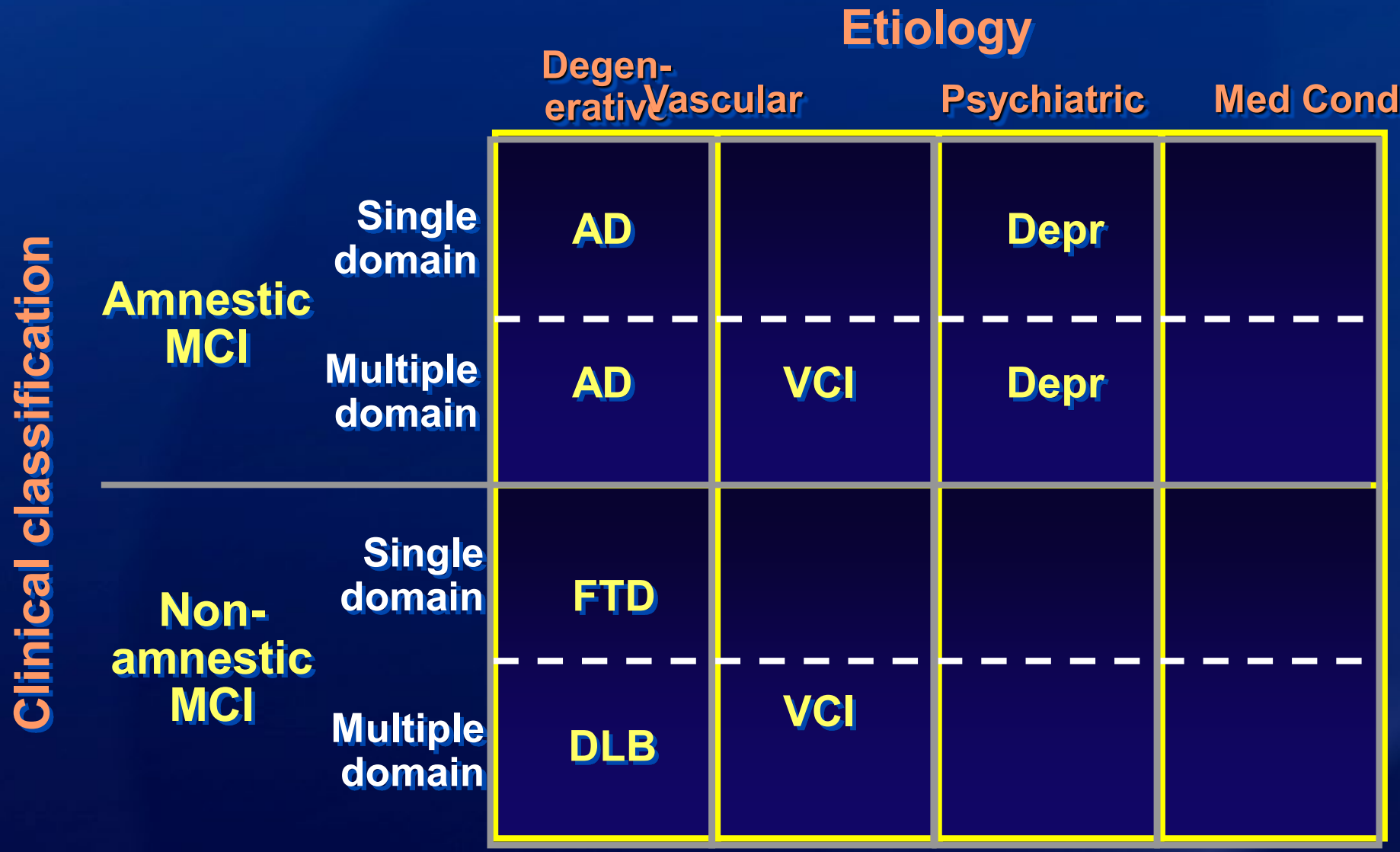
MCI Outcomes (examples)



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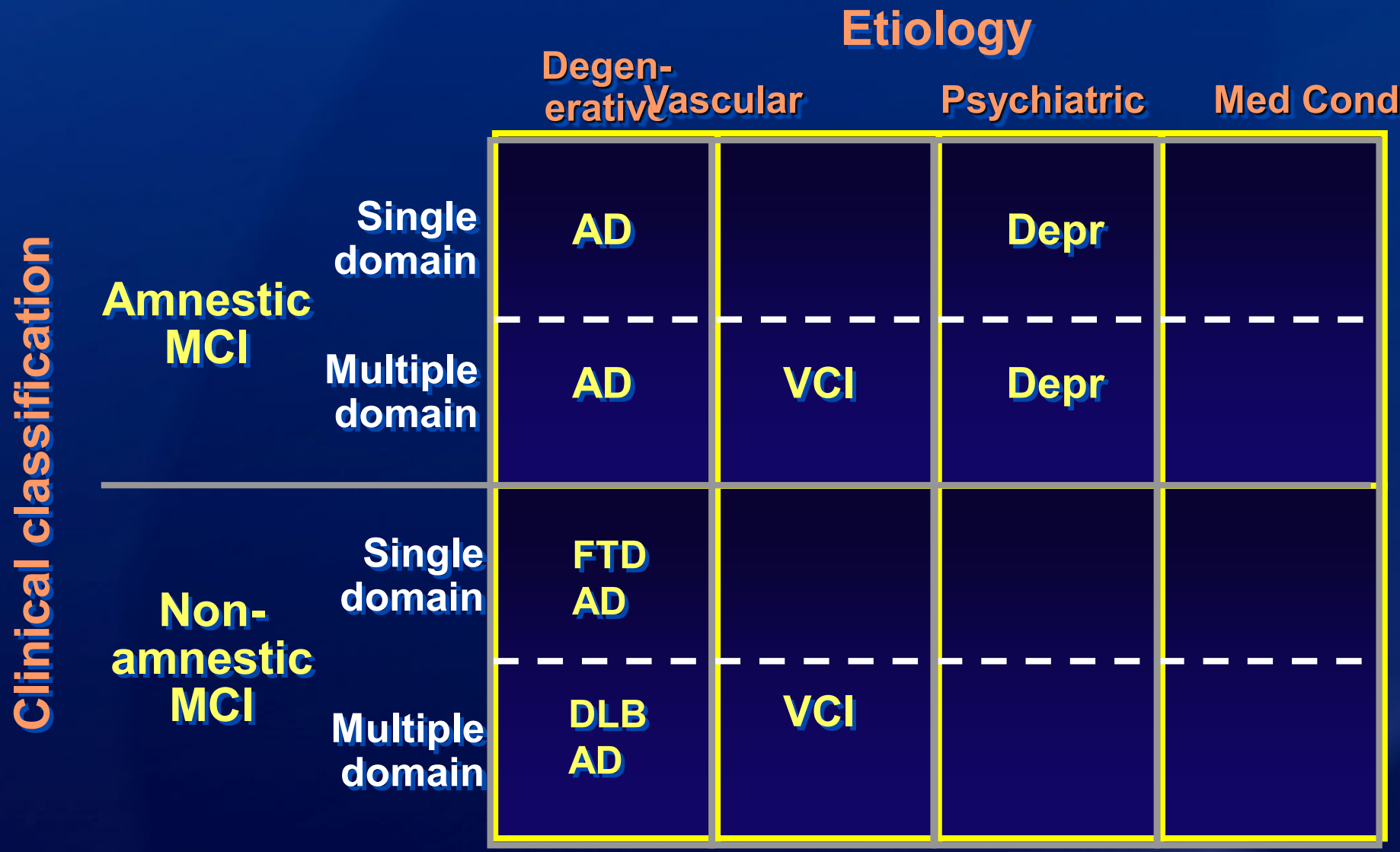
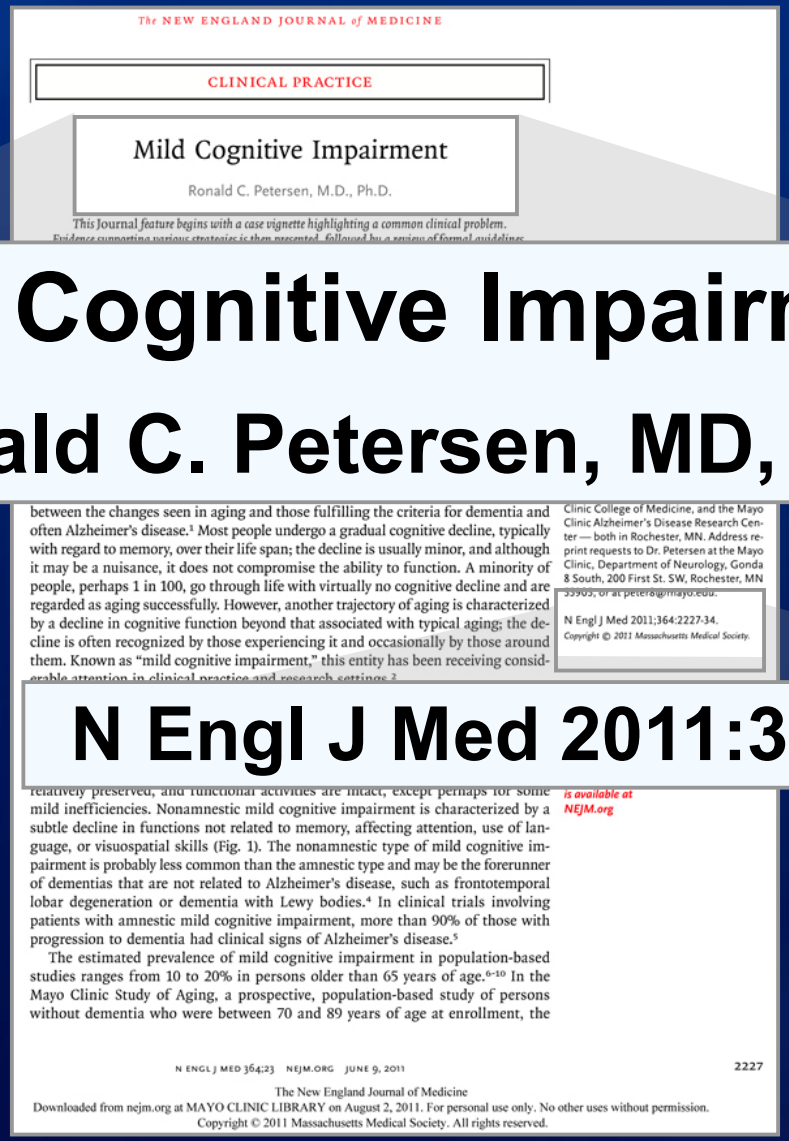
MCI Outcomes



CP1265413-6



The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Mild Cognitive Impairment

Ronald C. Petersen, M.D., Ph.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines

between the changes seen in aging and those fulfilling the criteria for dementia and often Alzheimer's disease.[1] Most people undergo a gradual cognitive decline, typically with regard to memory, over their life span; the decline is usually minor, and although it may be a nuisance, it does not compromise the ability to function. A minority of people, perhaps 1 in 100, go through life with virtually no cognitive decline and are regarded as aging successfully. However, another trajectory of aging is characterized by a decline in cognitive function beyond that associated with typical aging; the decline is often recognized by those experiencing it and occasionally by those around them. Known as "mild cognitive impairment," this entity has been receiving considerable attention in clinical practice and research settings.[2]

Clinic College of Medicine, and the Mayo Clinic Alzheimer's Disease Research Center — both in Rochester, MN. Address reprint requests to Dr. Petersen at the Mayo Clinic, Department of Neurology, Gonda 8 South, 200 First St. SW, Rochester, MN 55905, or at peterse@mayo.edu.

N Engl J Med 2011;364:2227-34.

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relatively preserved, and functional activities are intact, except perhaps for some mild inefficiencies. Nonamnestic mild cognitive impairment is characterized by a subtle decline in functions not related to memory, affecting attention, use of language, or visuospatial skills (Fig. 1). The nonamnestic type of mild cognitive impairment is probably less common than the amnestic type and may be the forerunner of dementias that are not related to Alzheimer's disease, such as frontotemporal lobar degeneration or dementia with Lewy bodies.[4] In clinical trials involving patients with amnestic mild cognitive impairment, more than 90% of those with progression to dementia had clinical signs of Alzheimer's disease.[5]

The estimated prevalence of mild cognitive impairment in population-based studies ranges from 10 to 20% in persons older than 65 years of age.[6-10] In the Mayo Clinic Study of Aging, a prospective, population-based study of persons without dementia who were between 70 and 89 years of age at enrollment, the

is available at NEJM.org

N ENGL J MED 364;23 NEJM.ORG JUNE 9, 2011

2227

Mild Cognitive Impairment

Ronald C. Petersen, MD, PhD

N Engl J Med 2011:364-2227-34

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Case

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53 y/o woman

- 1 ½ yr history loss of self-confidence
- Not want to move
- Says “can’t think”
- Forgets rapidly in conversation
- Daughters have noticed x 1 yr
- Decreased reading comprehension
- Family human compass
- Sleep ok
- Concerned but not depressed

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53 y/o woman

- Family history negative for dementia
- PMH: Good health, postpartum hemorrhage
- Med: supplements, Zoloft, ASA

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53 y/o woman

- STMS: 37/38
- VIQ: 107, PIQ: 97
- Attention/Executive
  - Trails A and B: 50th %ile
  - Stroop: 50th %ile
- Language
  - Fluency: 90th %ile
  - BNT: 59/60

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53 y/o woman

- **Visuospatial**
  - Rey O copy: 50th %ile
  - JLO: 50th %ile

- **Memory**
  - Logical Memory: 17/10
  - Visual Reproductions: 64/21
  - AVLT: 7,6,11,10,8; DR 3

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Diagnosis

Amnestic Mild Cognitive Impairment

Memory impaired for age
Other cognitive domains preserved
Largely normal daily functions

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Practical Stuff

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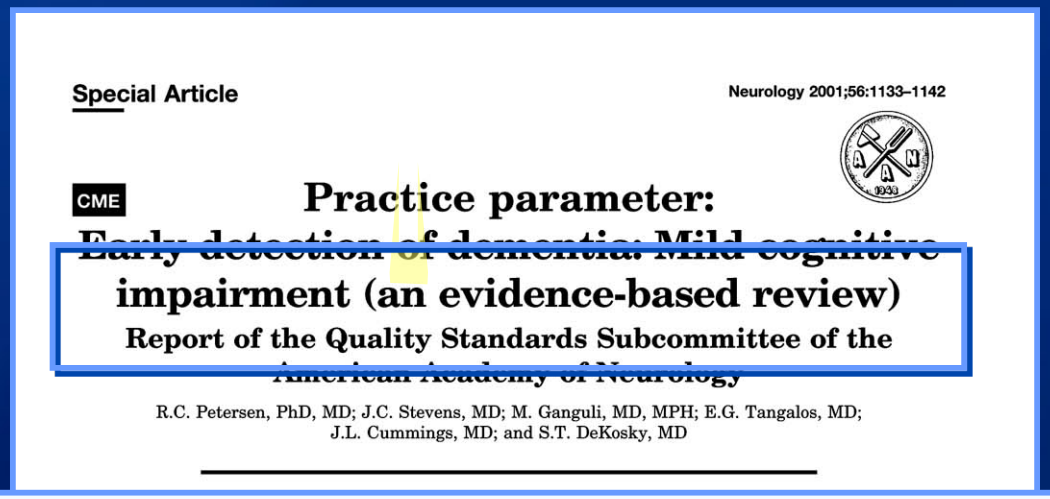
Special Article

Neurology 2001;56:1133–1142

CME

Practice parameter:
Early detection of dementia: Mild cognitive impairment (an evidence-based review)
Report of the Quality Standards Subcommittee of the American Academy of Neurology

R.C. Petersen, PhD, MD; J.C. Stevens, MD; M. Ganguli, MD, MPH; E.G. Tangalos, MD; J.L. Cummings, MD; and S.T. DeKosky, MD

Practice Parameter: Early Detection of Dementia: Mild Cognitive Impairment (an Evidence-Based Review)

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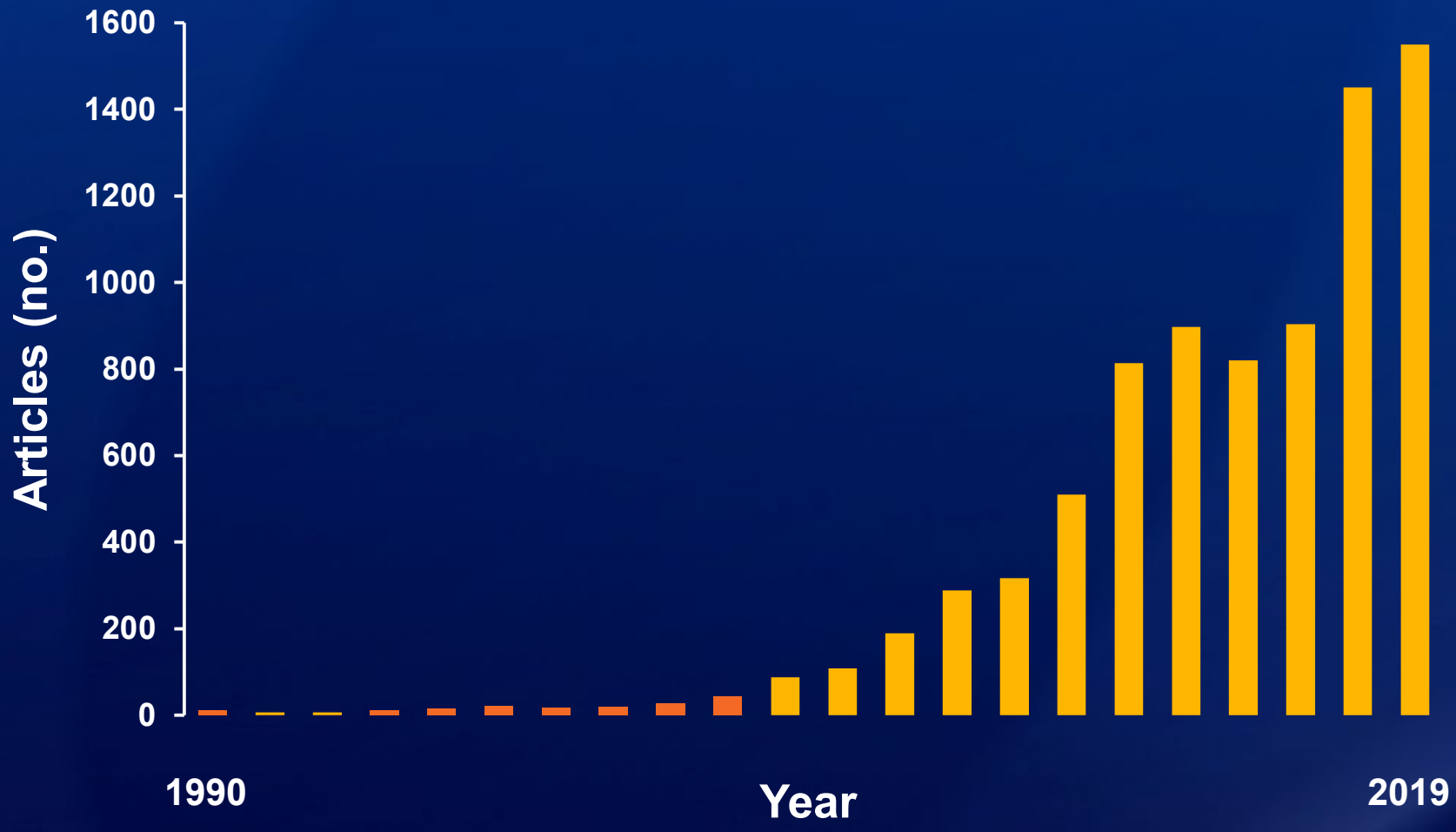
Publications on MCI



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SPECIAL ARTICLE LEVEL OF RECOMMENDATION

Practice guideline update summary: Mild cognitive impairment

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology

Ronald C. Petersen, MD, PhD, Oscar Lopez, MD, Melissa J. Armstrong, MD, MSc, Thomas S.D. Getchius, Mary Ganguli, MD, MPH, David Gloss, MD, MPH&TM, Gary S. Gronseth, MD, Daniel Marson, JD, PhD, Tamara Pringsheim, MD, Gregory S. Day, MD, MSc, Mark Sager, MD, James Stevens, MD, and Alexander Rae-Grant, MD

Correspondence
American Academy of Neurology
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Neurology® 2018;90:126-135. doi:10.1212/WNL.0000000000004826

Ronald C. Petersen, MD, PhD, Oscar Lopez, MD, Melissa J. Armstrong, MD, MSc, Thomas S.D. Getchius, Mary Ganguli, MD, MPH, David Gloss, MD, MPH&TM, Gary S. Gronseth, MD, Daniel Marson, JD, PhD, Tamara Pringsheim, MD, Gregory S. Day, MD, MSc, Mark Sager, MD, James Stevens, MD, and Alexander Rae-Grant, MD

Results

MCI prevalence was 6.7% for ages 60–64, 8.4% for 65–69, 10.1% for 70–74, 14.8% for 75–79, and 25.2% for 80–84. Cumulative dementia incidence was 14.9% in individuals with MCI older than age 65 years followed for 2 years. No high-quality evidence exists to support pharmacologic treatments for MCI. In patients with MCI, exercise training (6 months) is likely to improve cognitive measures and cognitive training may improve cognitive measures.

Major recommendations

Clinicians should assess for MCI with validated tools in appropriate scenarios (Level B). Clinicians should evaluate patients with MCI for modifiable risk factors, assess for functional impairment, and assess for and treat behavioral/neuropsychiatric symptoms (Level B). Clinicians should monitor cognitive status of patients with MCI over time (Level B). Cognitively impairing medications should be discontinued where possible and behavioral symptoms treated (Level B). Clinicians may choose not to offer cholinesterase inhibitors (Level B); if offering, they must first discuss lack of evidence (Level A). Clinicians should recommend regular exercise (Level B). Clinicians may recommend cognitive training (Level C). Clinicians should discuss diagnosis, prognosis, long-term planning, and the lack of effective medicine options (Level B), and may discuss biomarker research with patients with MCI and families (Level C).

AMERICAN ACADEMY OF NEUROLOGY

From the Department of Neurology (R.C.P.), Mayo Clinic, Rochester, MN; Department of Neurology (O.L.), University of Pittsburgh Medical Center, PA; Department of Neurology (M.J.A.), University of Florida College of Medicine, Gainesville; Heart Rhythm Society (T.S.D.G.), Washington, DC; Department of Psychiatry (M.G.), University of Pittsburgh, PA; Department of Neurology (D.G.), Charleston Area Medical Center, WV; Department of Neurology (G.S.G.), University of Kansas Medical Center, Kansas City; Department of Neurology (D.M.), University of Alabama, Birmingham; Department of Clinical Neurosciences, Psychiatry, Pediatrics and Community Health Sciences (T.P.), Cumming School of Medicine, University of Calgary, Canada; Knight Alzheimer Disease Research Center (G.S.D.), Washington University School of Medicine, St. Louis, MO; Wisconsin Alzheimer's Institute (M.S.), School of Medicine and Public Health, University of Wisconsin, Madison; Department of Neurology (J.S.), Fort Wayne Neurological Center, IN; and Department of Neurology (A.R.-G.), Cleveland Clinic, OH.

Approved by the Guideline Development, Dissemination, and Implementation Subcommittee on July 16, 2016; by the Practice Committee on August 22, 2016; and by the AAN Institute Board of Directors on October 5, 2017.

This guideline was endorsed by the Alzheimer's Association on May 1, 2017.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Petersen et al., Neurology, 90:126-135, 2018

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AAN Practice Parameter on MCI

- Evidence-based medicine review of the literature
  - 11,500+ studies evaluated
  - 326 full review
- 3 primary questions
  - What is the prevalence of MCI?
  - What is the outcome of MCI?
  - Are there any treatments for MCI?
    - Pharmacologic
    - Non-pharmacologic

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AAN Practice Parameter on MCI Conclusions

1. Prevalence
    - 20 Class I studies
    - Prevalence age-related but overall
        - 15-20% in age 65 and up
2. Outcome
    - 9 Class I studies
    - Rates of progression to dementia
        - age related: 5-20%/year (10-15%)

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AAN Practice Parameter on MCI Conclusions

3. Treatments
   - Pharmacological
   - 10 Class II studies, 1 Class I
   - No FDA approved drugs

   - Non-pharmacological
   - 4 Class II studies
     - exercise
     - intellectual activities

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Outline

- The Problem
- What is MCI?
- **MCI therapies**
- Clinical acceptance of MCI
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Pharmacological Therapies for MCI

- Currently there are no FDA approved therapies for MCI (due to AD)
- Lifestyle
  - Physical exercise
  - Cognitive training
  - Blood pressure control (SPRINT MIND trial)

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Pharmacologic treatment of MCI

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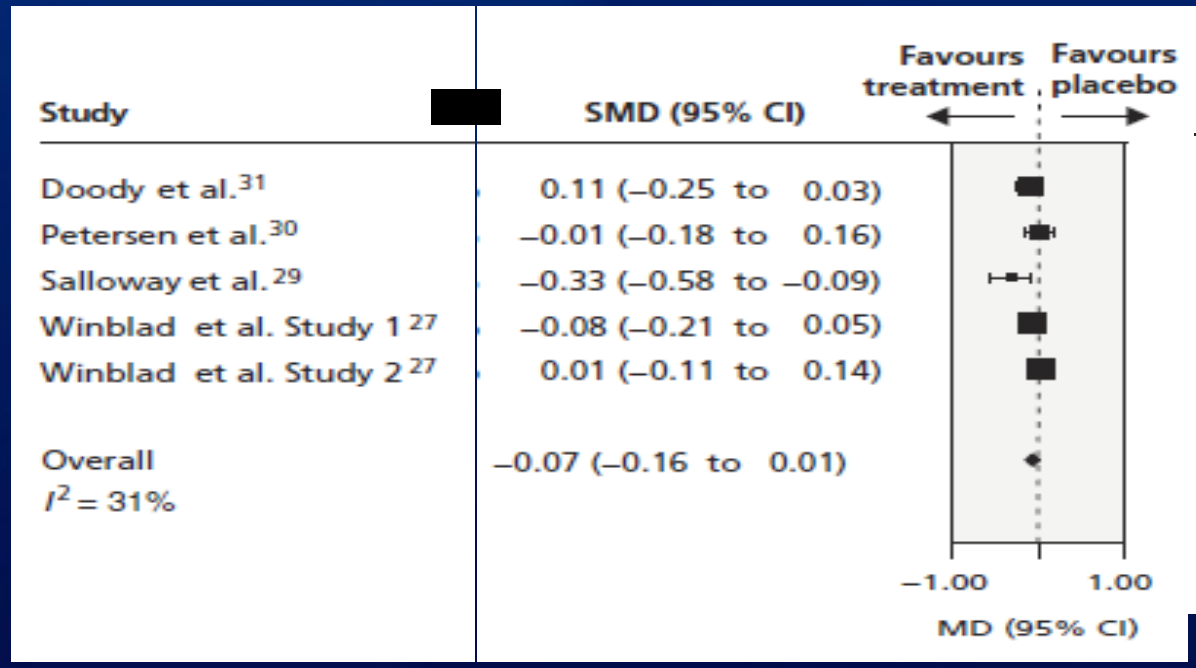
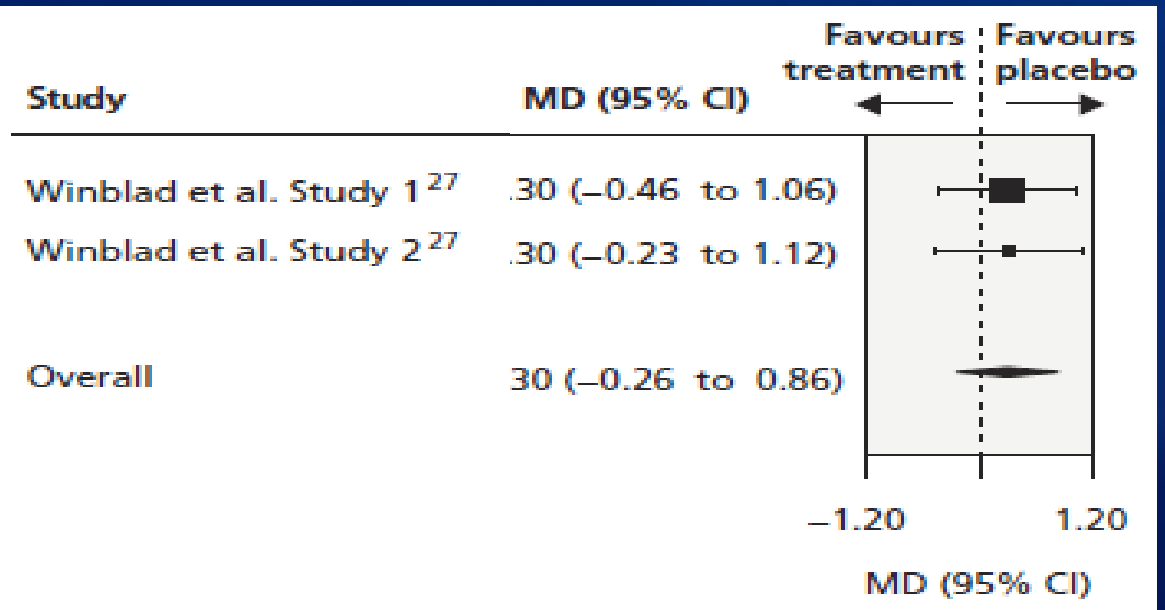
Do cholinesterase inhibitors work in MCI?

Cognitive outcomes for donepezil



Activities of daily living for galantamine



Tricco, et. al. CMAJ. 2013

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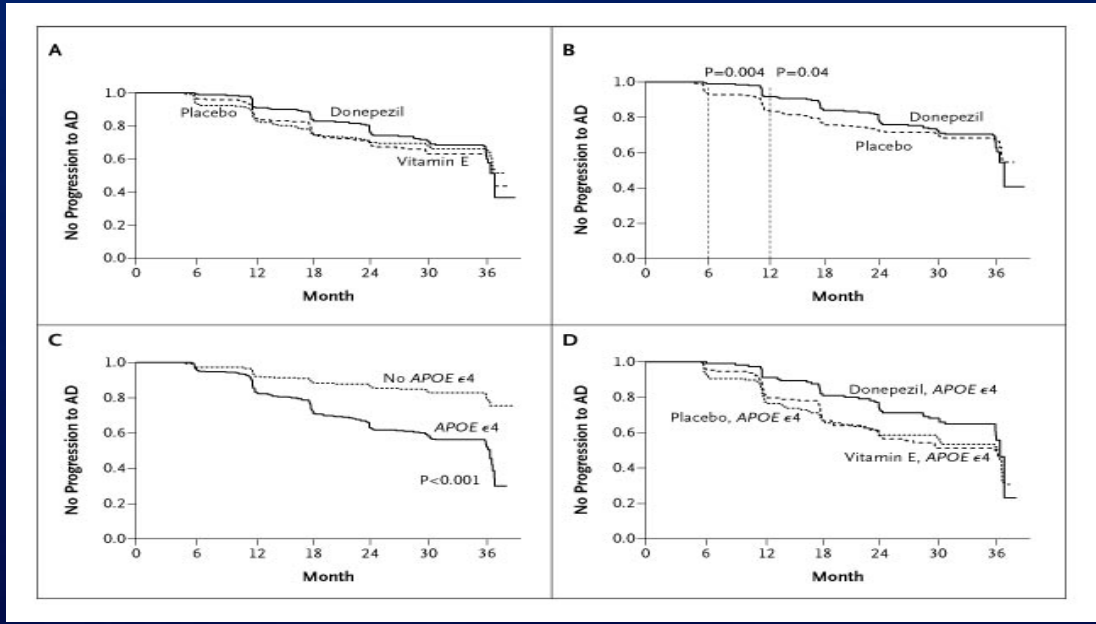
Do cholinesterase inhibitors prevent progression to dementia?

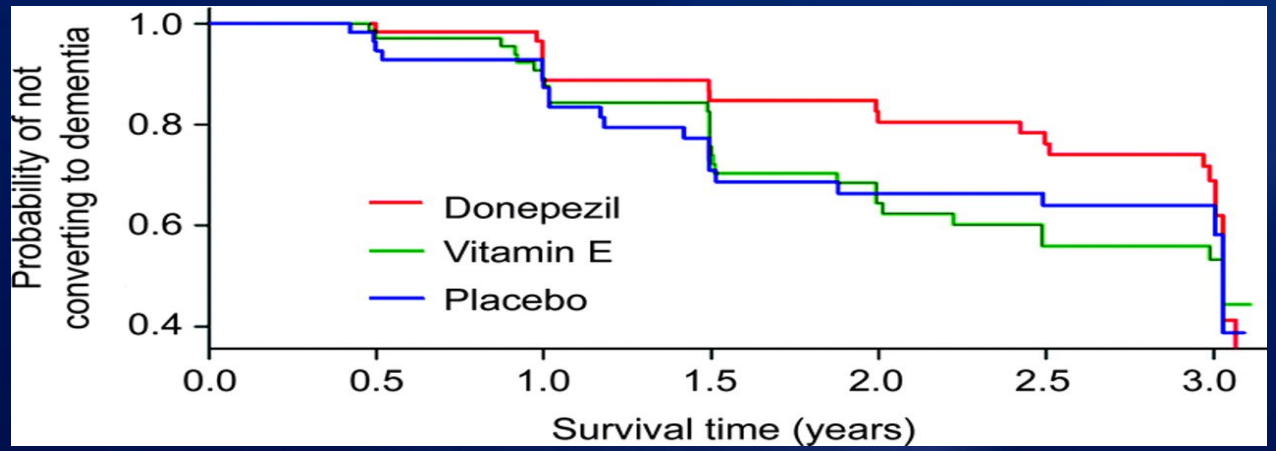
Category	Gal-INT-18 [33]: Galantamine	Gal-INT-11 [32]: Galantamine	InDDEX [31]: Rivastigmine	Salloway [36]: Donepezil	Petersen [37]: Donepezil	Koontz [34]: Galantamine
Duration of the study	2 y	2 y	3–4 y	24 wk	3 y	16 wk
Subjects completing the study (ChEI; placebo)	—	—	51%; 63%	68%; 83%	64%; 74%	50%; 36%
Conversion rate (ChEI; placebo)	17%; 21%	13%; 18%	17%; 21%	—	25%; 28%	—
Jadad quality score (0–5)	2	2	3	3	3	3

Raschetti, et. al. PLoS. 2007



Petersen, et. al. NEJM. 2005

Amnestic MCI with depressive symptoms



Lu, et. al. Neurology. 2009

Recommendations

1. Clinicians should counsel the patients and families that there are no pharmacologic or dietary agents currently shown to have symptomatic cognitive benefit in MCI and that no medications are US Food and Drug Administration approved for this purpose
2. Clinicians may choose not to offer cholinesterase inhibitors
3. If clinicians choose to offer cholinesterase inhibitors, they must first discuss with patients the fact that this is an off-label prescription not currently backed by empirical evidence

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Non-pharmacologic treatment of MCI

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Lancet Commission Report

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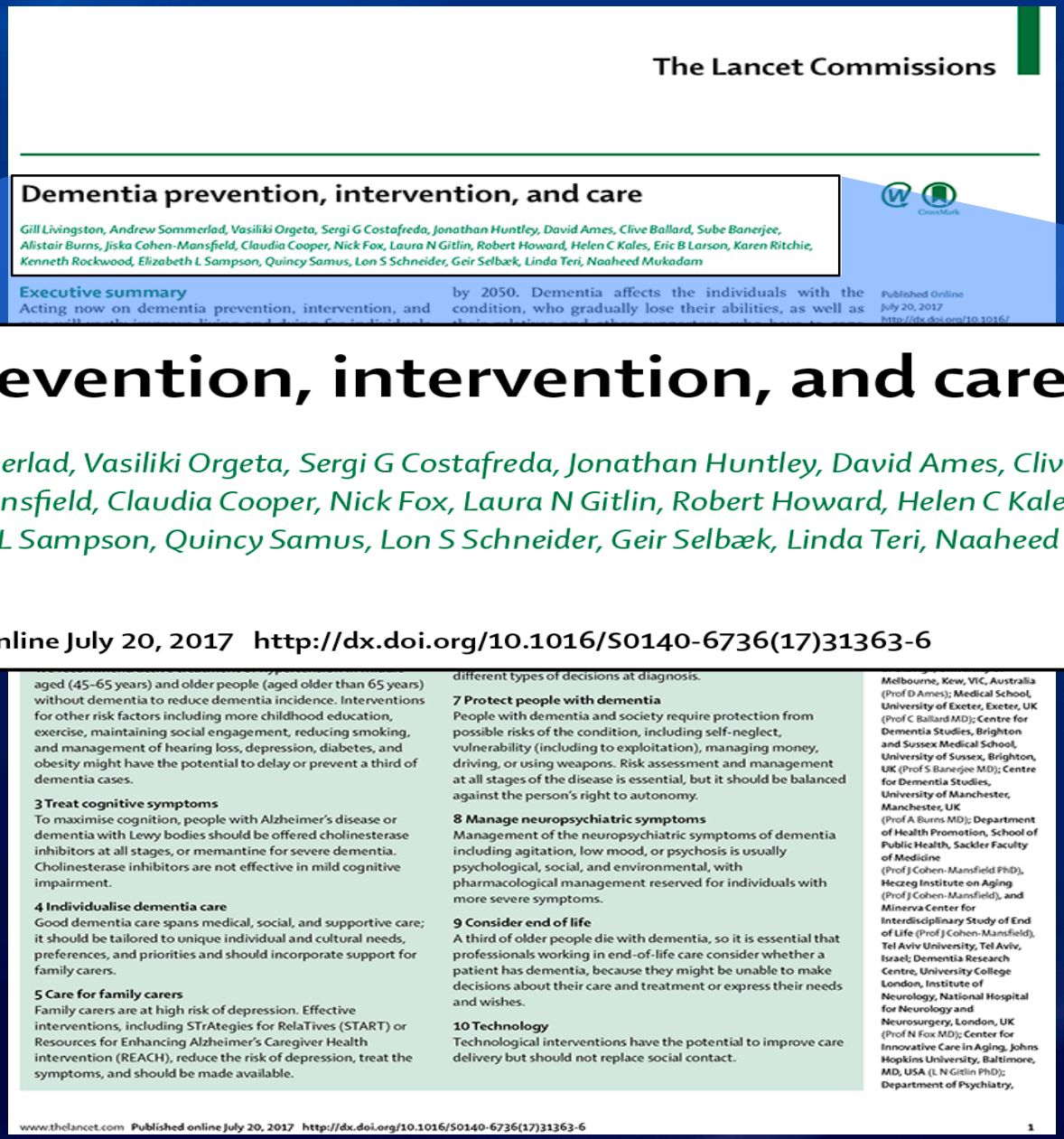

The Lancet Commissions

Dementia prevention, intervention, and care

Gill Livingston, Andrew Sommerlad, Vasiliki Orgeta, Sergi G Costafreda, Jonathan Huntley, David Ames, Clive Ballard, Sube Banerjee, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Eric B Larson, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

Executive summary

Acting now on dementia prevention, intervention, and

by 2050. Dementia affects the individuals with the condition, who gradually lose their abilities, as well as

Published Online July 20, 2017 http://dx.doi.org/10.1016/

aged (45–65 years) and older people (aged older than 65 years) without dementia to reduce dementia incidence. Interventions for other risk factors including more childhood education, exercise, maintaining social engagement, reducing smoking, and management of hearing loss, depression, diabetes, and obesity might have the potential to delay or prevent a third of dementia cases.

3 Treat cognitive symptoms

To maximise cognition, people with Alzheimer's disease or dementia with Lewy bodies should be offered cholinesterase inhibitors at all stages, or memantine for severe dementia. Cholinesterase inhibitors are not effective in mild cognitive impairment.

4 Individualise dementia care

Good dementia care spans medical, social, and supportive care; it should be tailored to unique individual and cultural needs, preferences, and priorities and should incorporate support for family carers.

5 Care for family carers

Family carers are at high risk of depression. Effective interventions, including STrAtegies for RelaTives (START) or Resources for Enhancing Alzheimer's Caregiver Health intervention (REACH), reduce the risk of depression, treat the symptoms, and should be made available.

different types of decisions at diagnosis.

7 Protect people with dementia

People with dementia and society require protection from possible risks of the condition, including self-neglect, vulnerability (including to exploitation), managing money, driving, or using weapons. Risk assessment and management at all stages of the disease is essential, but it should be balanced against the person's right to autonomy.

8 Manage neuropsychiatric symptoms

Management of the neuropsychiatric symptoms of dementia including agitation, low mood, or psychosis is usually psychological, social, and environmental, with pharmacological management reserved for individuals with more severe symptoms.

9 Consider end of life

A third of older people die with dementia, so it is essential that professionals working in end-of-life care consider whether a patient has dementia, because they might be unable to make decisions about their care and treatment or express their needs and wishes.

10 Technology

Technological interventions have the potential to improve care delivery but should not replace social contact.

Melbourne, Kew, VIC, Australia (Prof D Ames); Medical School, University of Exeter, Exeter, UK (Prof C Ballard MD); Centre for Dementia Studies, Brighton and Sussex Medical School, University of Sussex, Brighton, UK (Prof S Banerjee MD); Centre for Dementia Studies, University of Manchester, Manchester, UK (Prof A Burns MD); Department of Health Promotion, School of Public Health, Sackler Faculty of Medicine (Prof J Cohen-Mansfield PhD), Herczeg Institute on Aging (Prof J Cohen-Mansfield), and Minerva Center for Interdisciplinary Study of End of Life (Prof J Cohen-Mansfield), Tel Aviv University, Tel Aviv, Israel; Dementia Research Centre, University College London, Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK (Prof N Fox MD); Center for Innovative Care in Aging, Johns Hopkins University, Baltimore, MD, USA (L N Gitlin PhD); Department of Psychiatry,

www.thelancet.com Published online July 20, 2017 http://dx.doi.org/10.1016/S0140-6736(17)31363-6 1

Dementia prevention, intervention, and care

Gill Livingston, Andrew Sommerlad, Vasiliki Orgeta, Sergi G Costafreda, Jonathan Huntley, David Ames, Clive Ballard, Sube Banerjee, Alistair Burns, Jiska Cohen-Mansfield, Claudia Cooper, Nick Fox, Laura N Gitlin, Robert Howard, Helen C Kales, Eric B Larson, Karen Ritchie, Kenneth Rockwood, Elizabeth L Sampson, Quincy Samus, Lon S Schneider, Geir Selbæk, Linda Teri, Naaheed Mukadam

www.thelancet.com **Published online July 20, 2017 http://dx.doi.org/10.1016/S0140-6736(17)31363-6**

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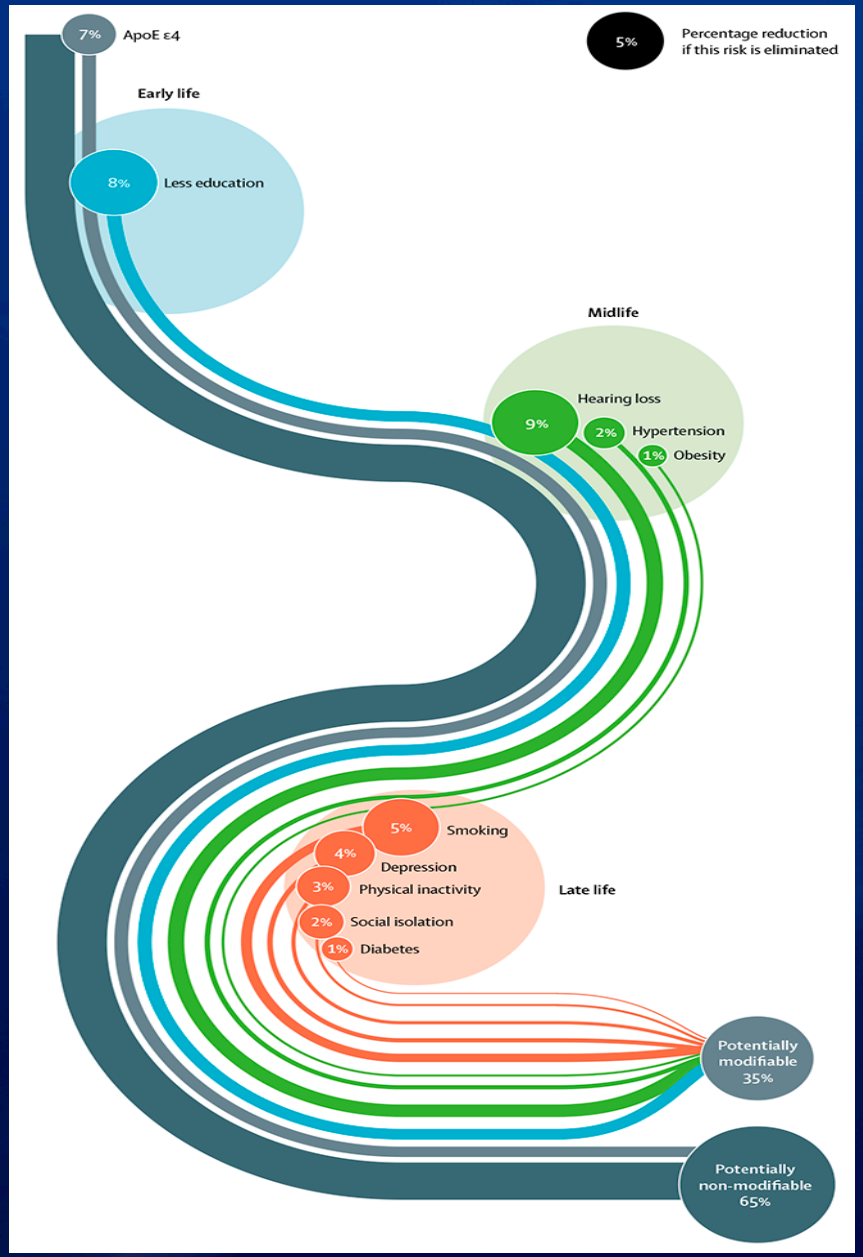
Life-Course Model of Contribution of Modifiable Risk Factors to Dementia



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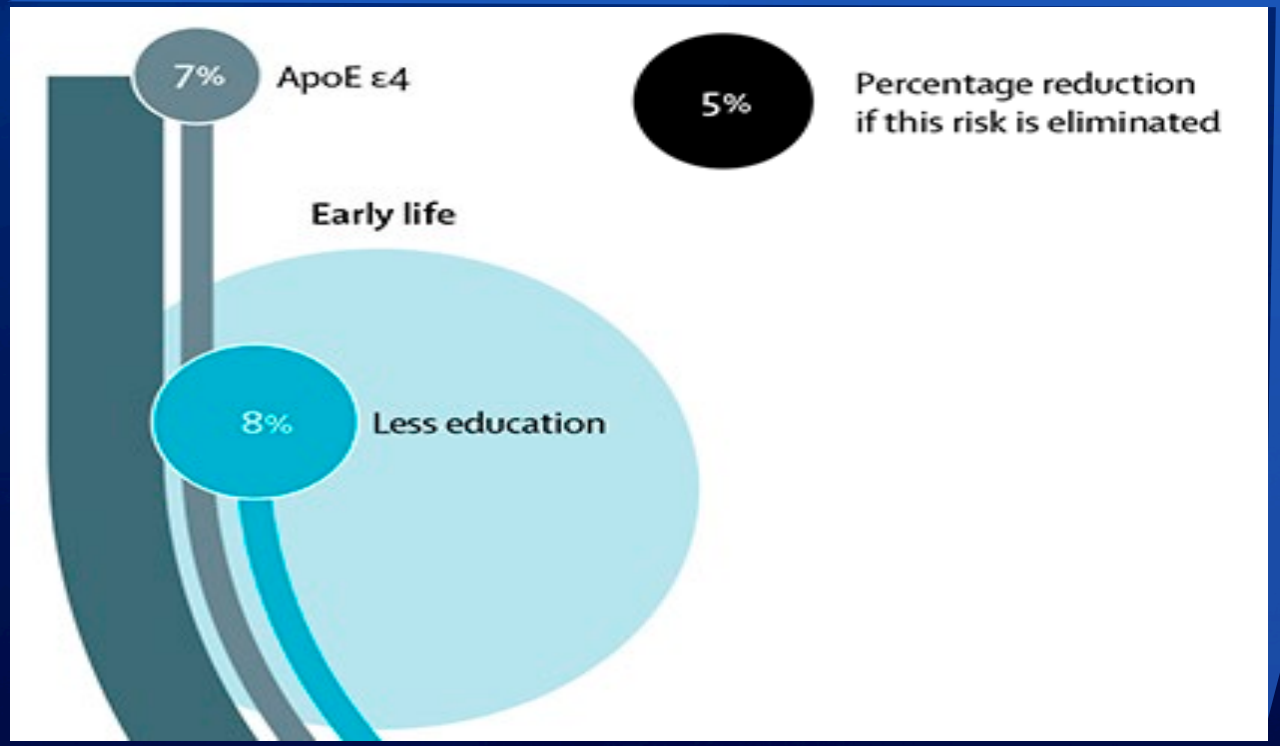

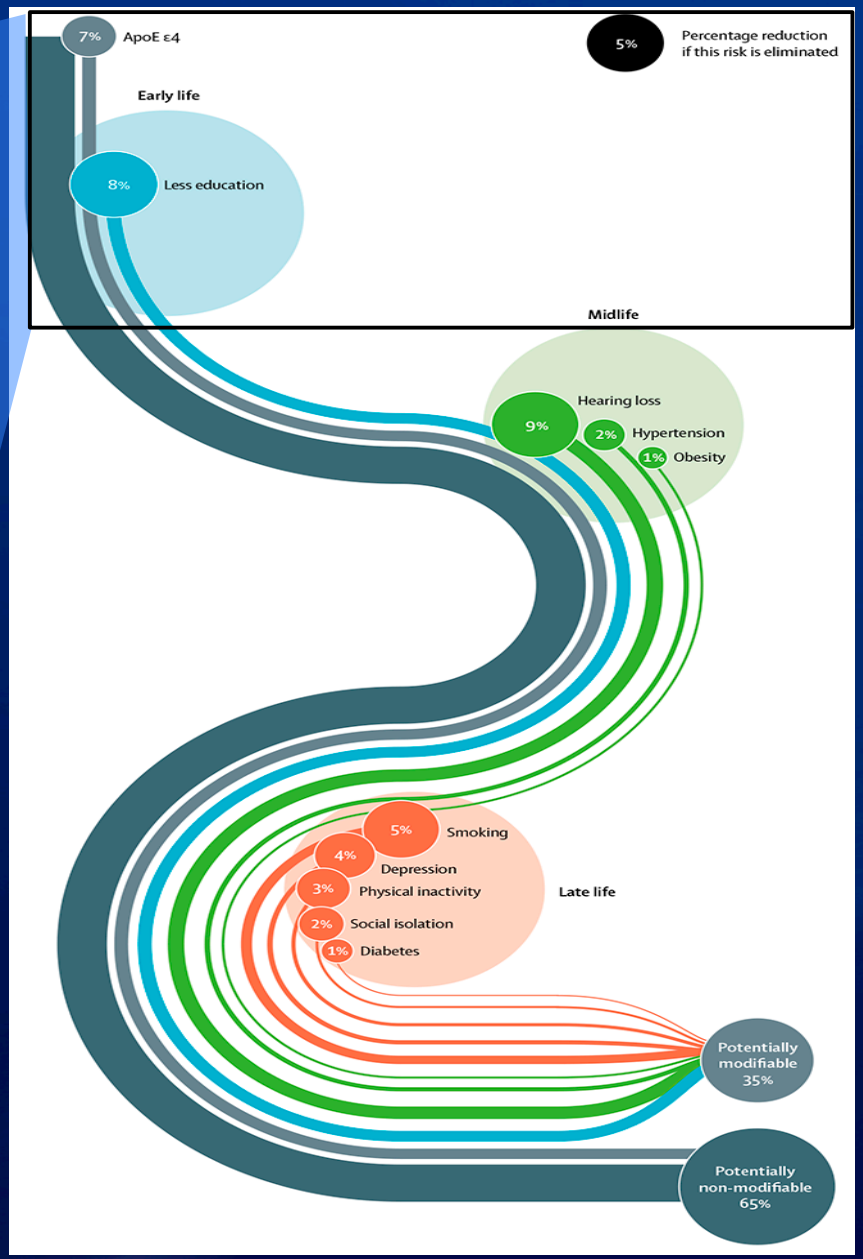

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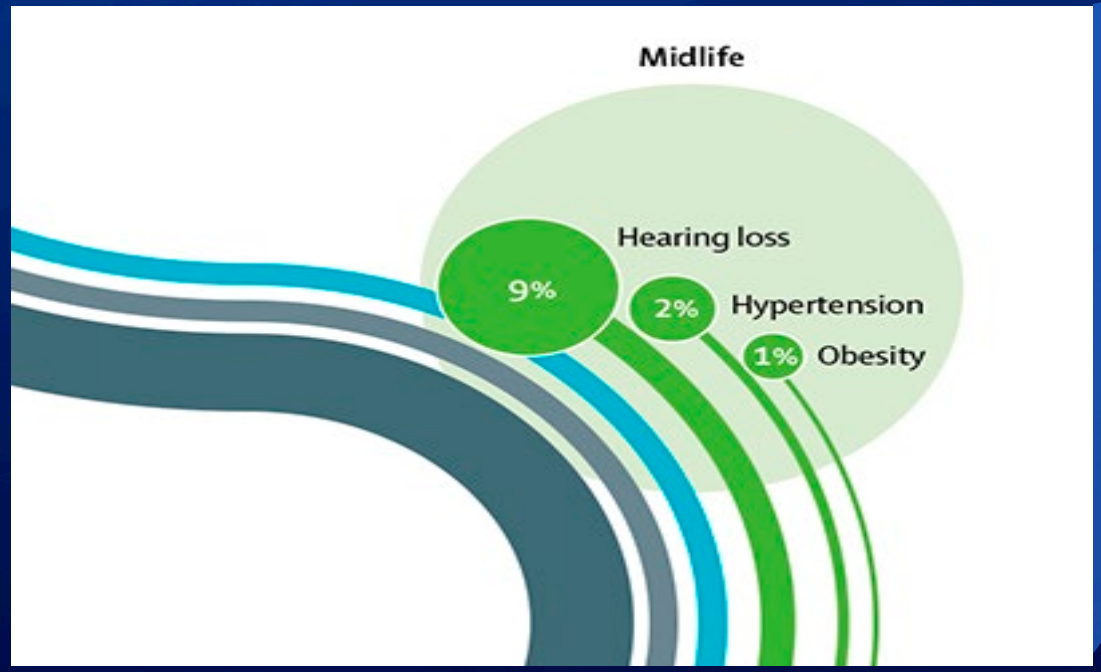

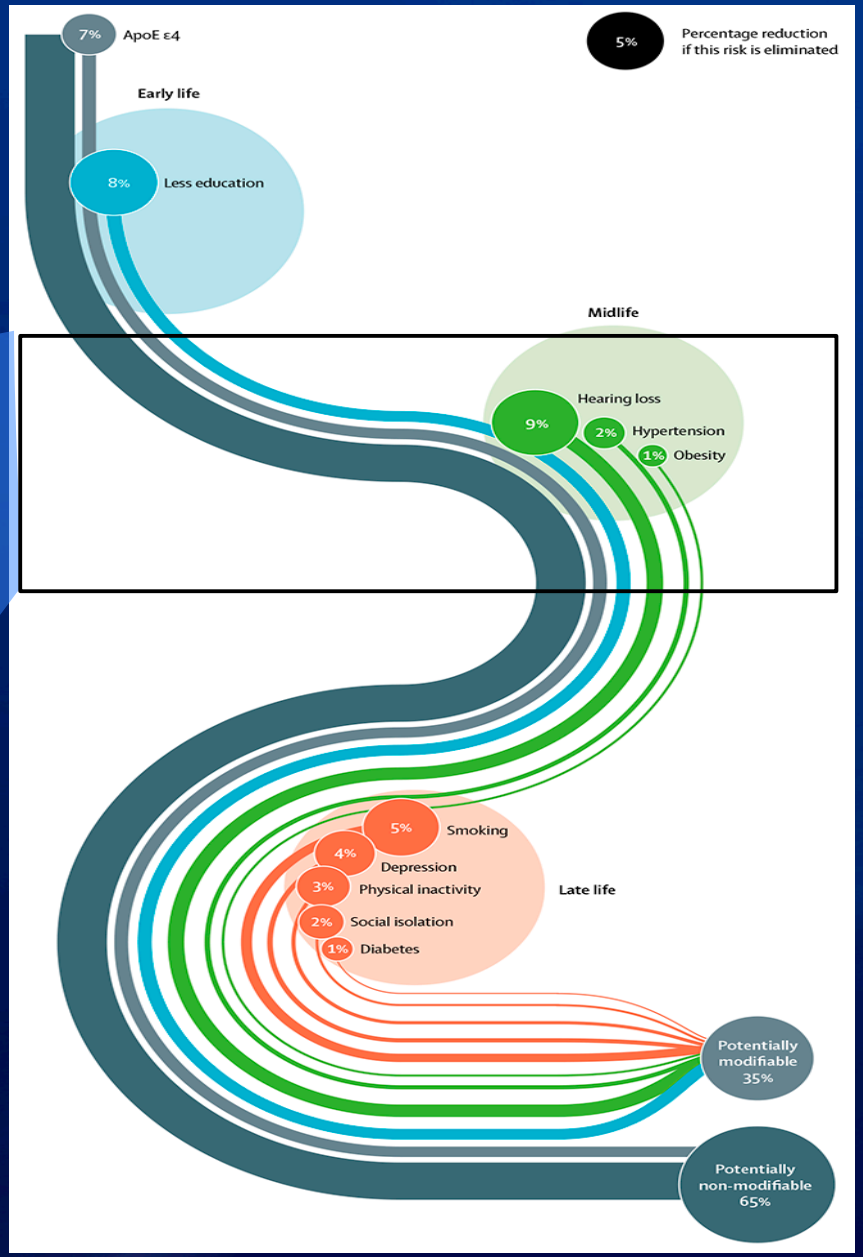

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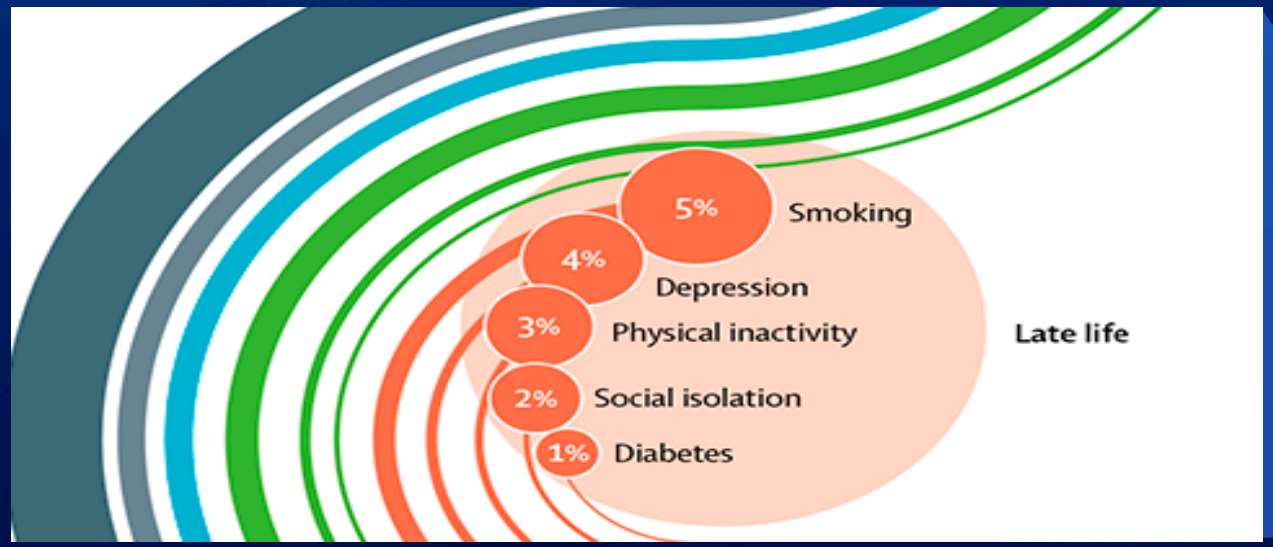

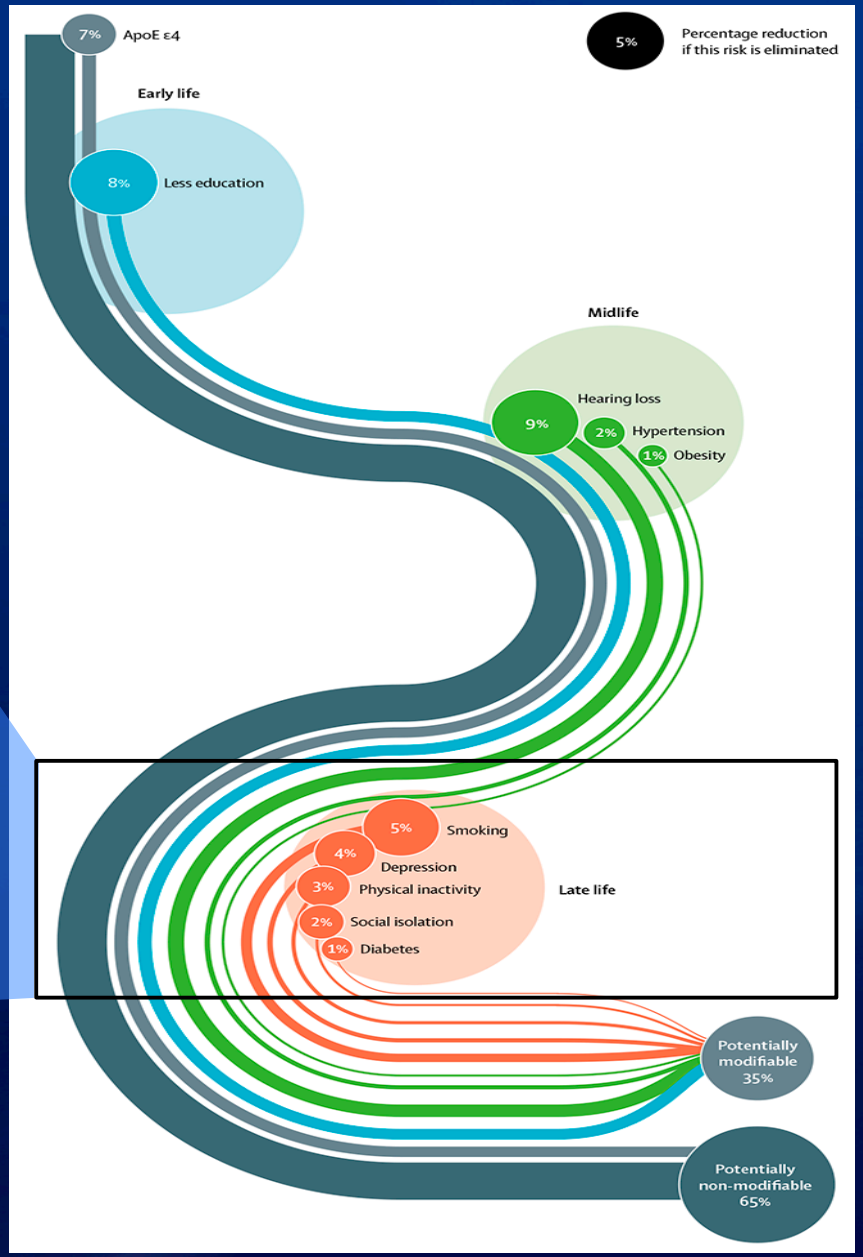

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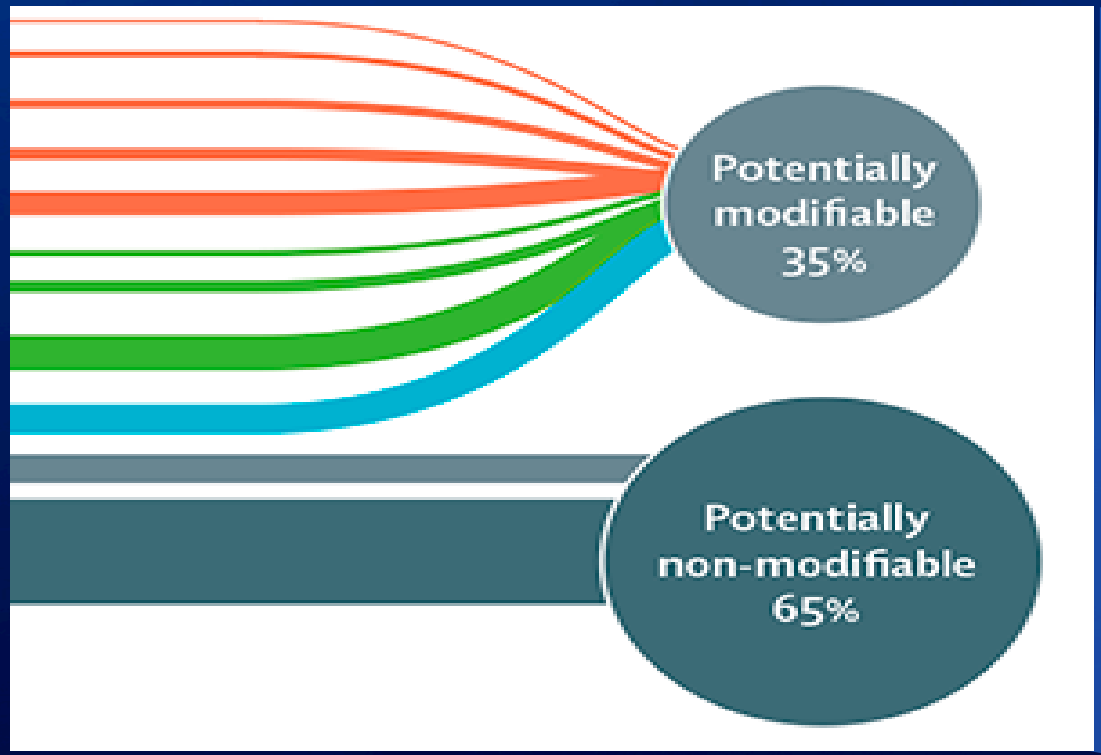

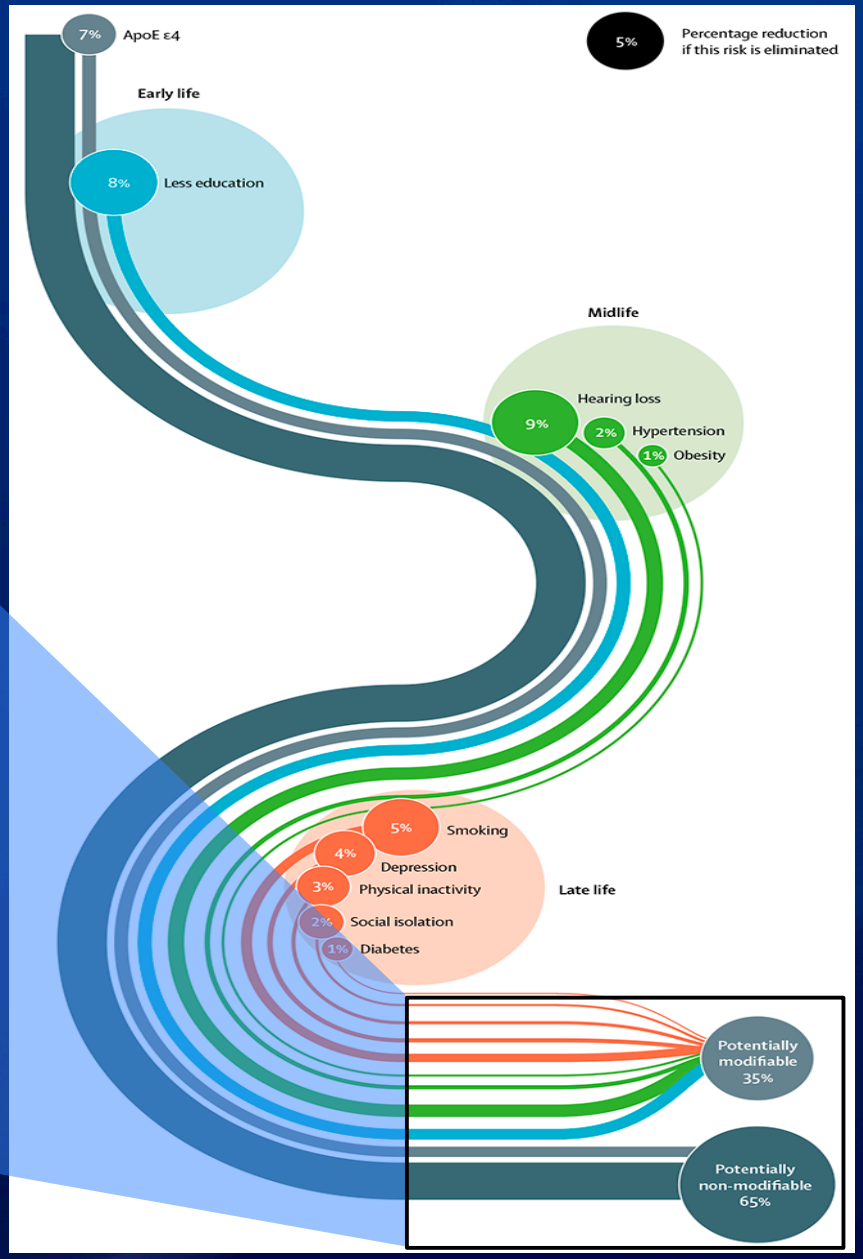

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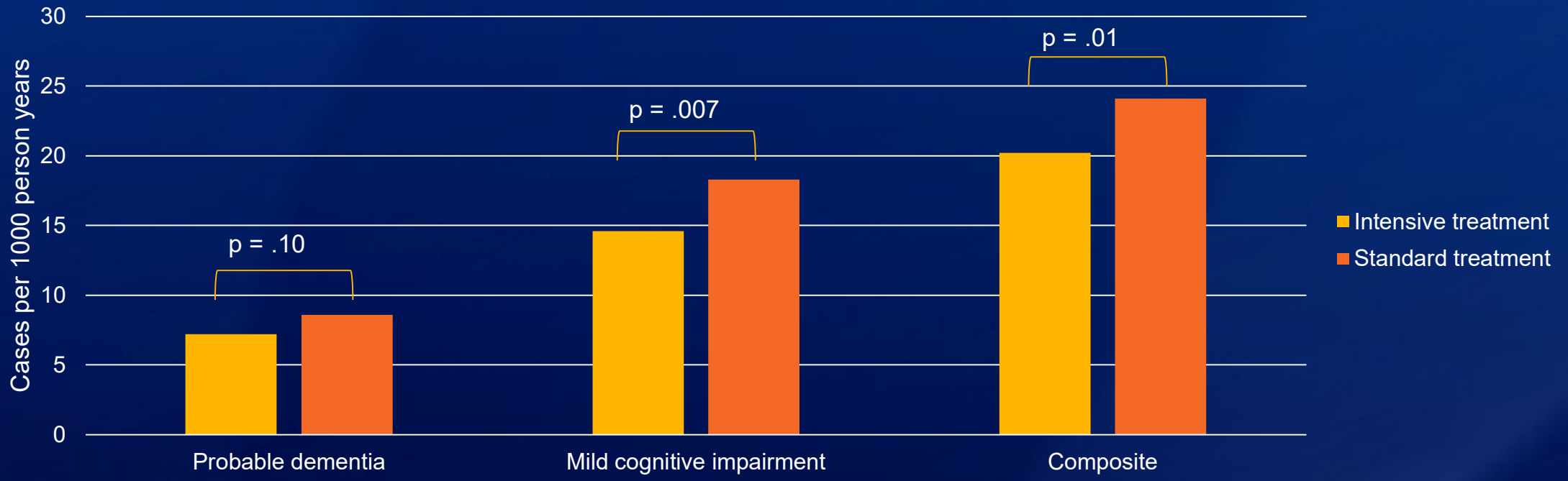
SPRINT MIND



The SPRINT MIND investigators. JAMA. 2019

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Recommendations

1. Clinicians should recommend regular exercise (twice per week) as part of an overall approach to management
2. Clinicians may recommend cognitive interventions

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Outline

- The Problem
- What is MCI?
- MCI therapies
- **Clinical acceptance of MCI**
- Subjective Cognitive Decline

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Mild Cognitive Impairment Survey

American Academy of Neurology

Roberts et al., Neurology, 2010

Scott Roberts, PhD
University of Michigan

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MCI Survey

- Behavioral Neurology Section
- Geriatric Neurology Section
- Random sample of 900 AAN members of 2,338 eligible members
- Instrument approved by Exec Committees
- Response rate of 47.8% (420/879) 95% CI ±4.8%

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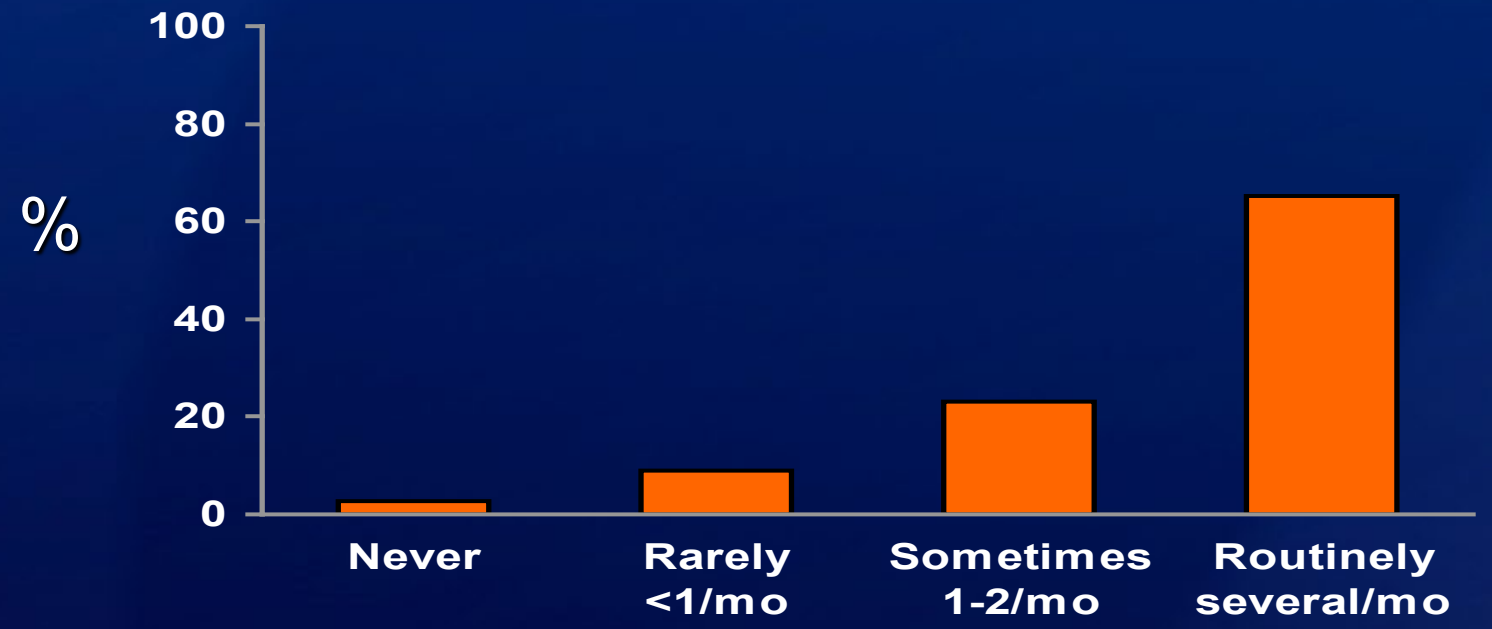
Current Practices

How Often Do You See Patients with Cognitive Symptoms of Mild Severity?



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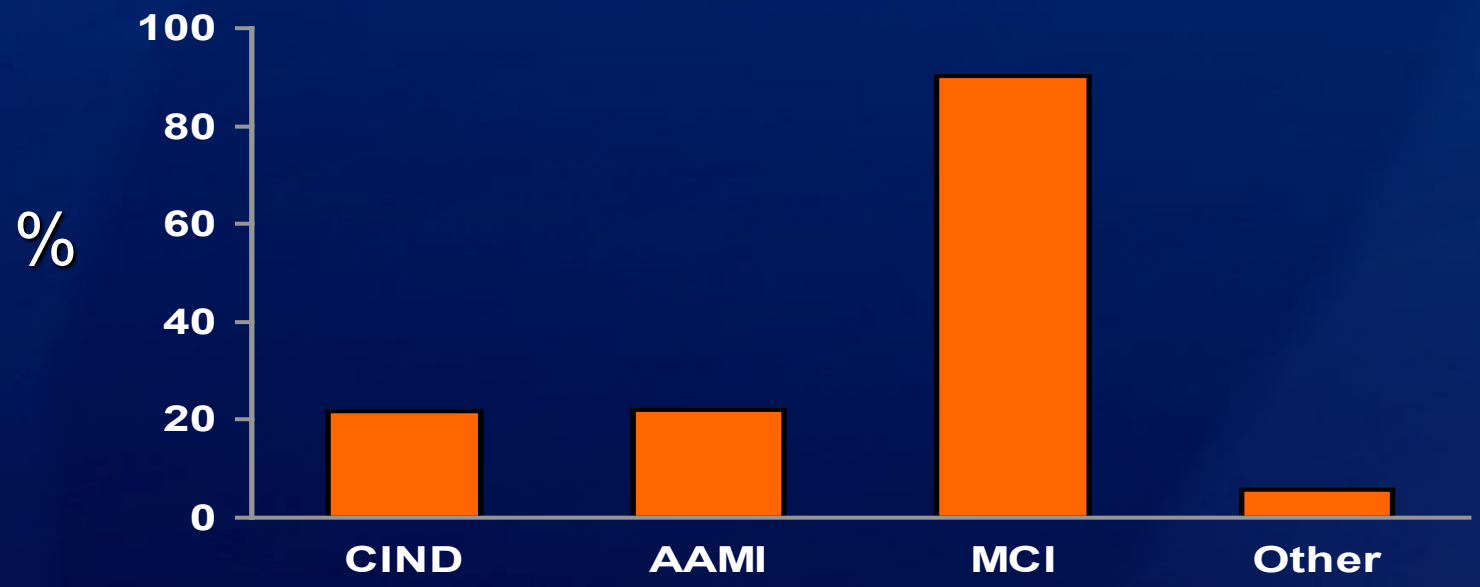
Terminology

Which Terms Do You Recognize as a Clinical Diagnosis?



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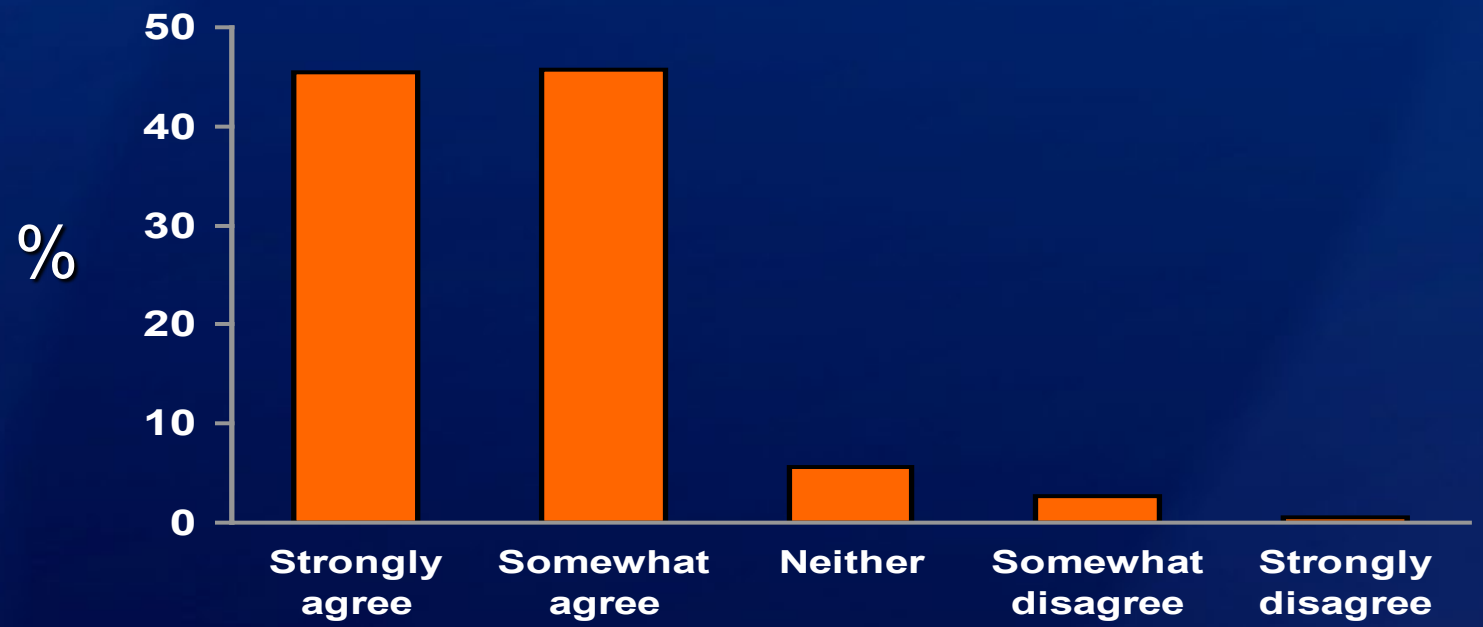
Attitude Towards MCI

Is This Label Useful



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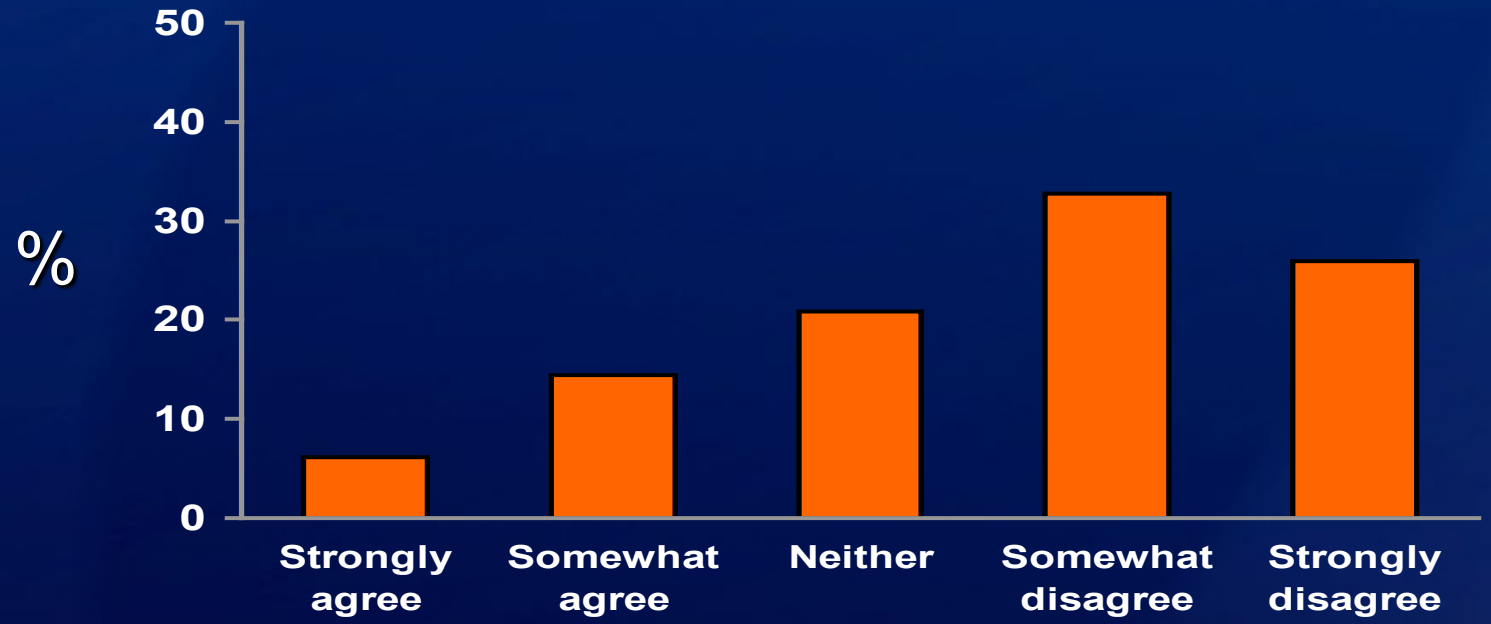
Attitude Towards MCI

Better Described as Early AD



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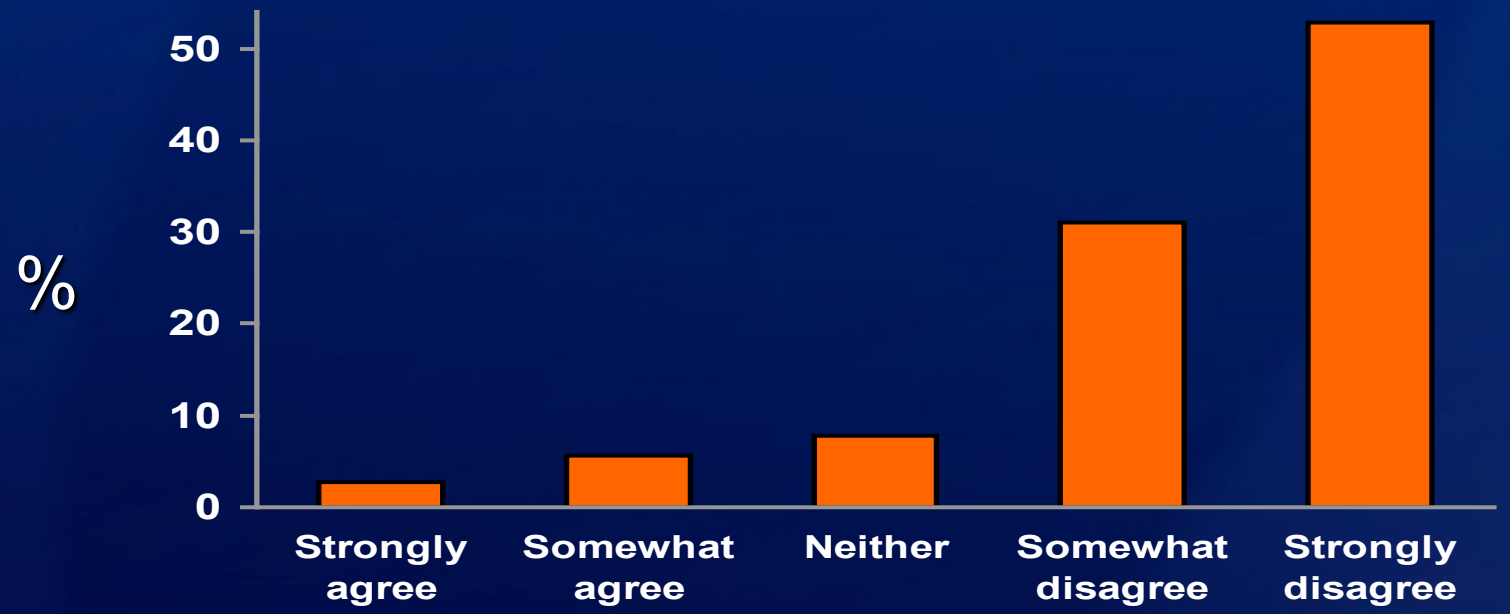
Attitude Towards MCI

No Treatment – No Sense to Diagnose



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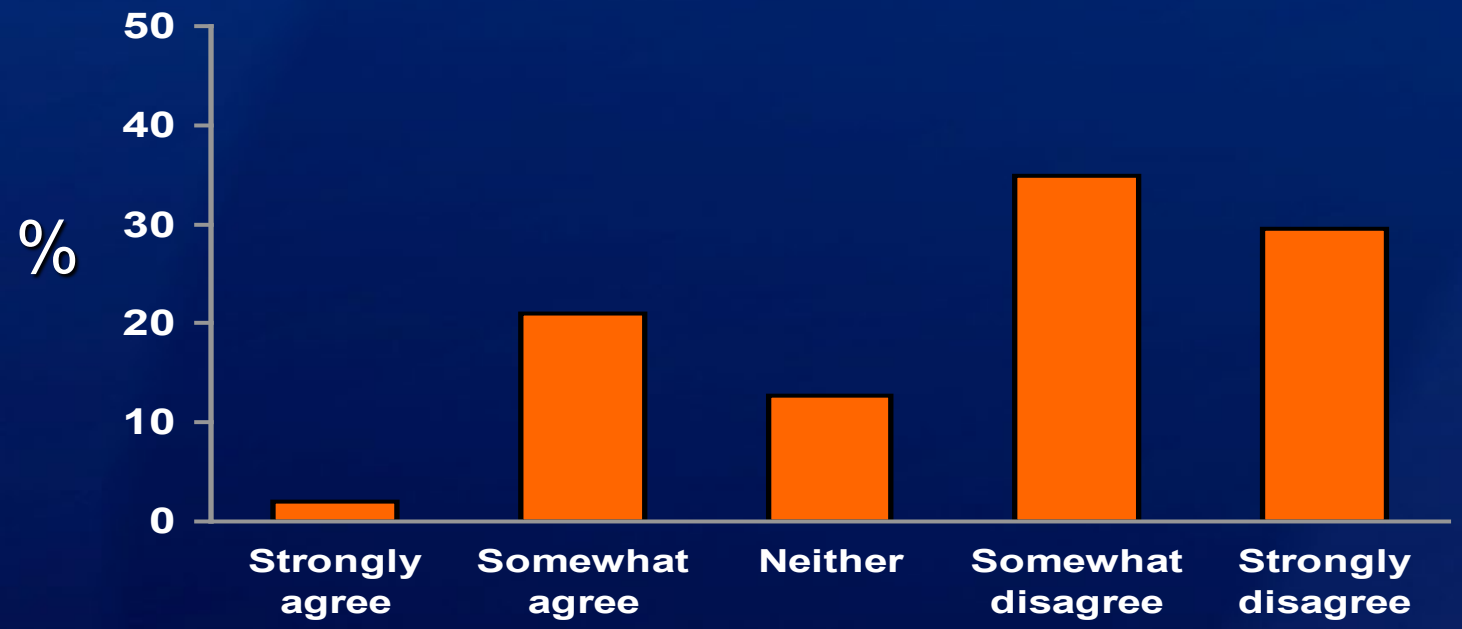
Attitude Towards MCI

Too Difficult to Diagnose Accurately or Reliably



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Physician Acceptance

- Neurologists see these patients regularly
- They use the term “MCI” (84%)
- They find it useful and prefer it over Pre-AD

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What About Outside the US?

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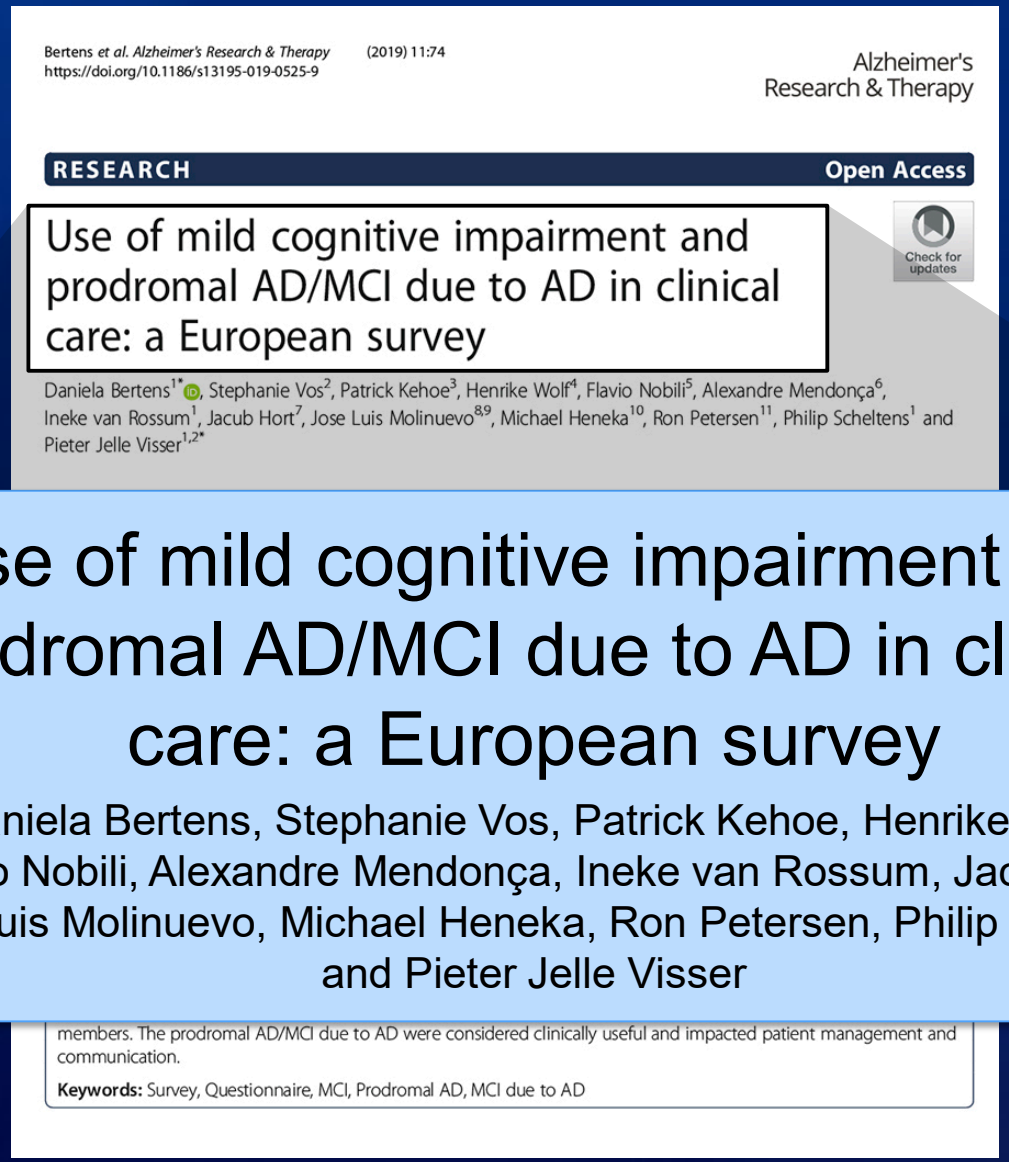

Bertens et al. Alzheimer's Research & Therapy (2019) 11:74
https://doi.org/10.1186/s13195-019-0525-9

Alzheimer's Research & Therapy

RESEARCH Open Access

Use of mild cognitive impairment and prodromal AD/MCI due to AD in clinical care: a European survey

Daniela Bertens[1*], Stephanie Vos[2], Patrick Kehoe[3], Henrike Wolf[4], Flavio Nobili[5], Alexandre Mendonça[6], Ineke van Rossum[1], Jacub Hort[7], Jose Luis Molinuevo[8,9], Michael Heneka[10], Ron Petersen[11], Philip Scheltens[1] and Pieter Jelle Visser[1,2*]

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members. The prodromal AD/MCI due to AD were considered clinically useful and impacted patient management and communication.

Keywords: Survey, Questionnaire, MCI, Prodromal AD, MCI due to AD

Bertens et al: Alzheimer's Res & Ther 11(74):1, 2019

Overall frequency of the use of the MCI term in Clinical Practice in Europe

91%

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Outline

- The Problem
- What is MCI?
- MCI therapies
- Clinical acceptance of MCI
- Subjective Cognitive Decline

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Subjective Cognitive Decline in the Community

Everyday Cognition (ECog)

- 12 questions about cognitive function
- Rate as “occasional” or “consistent”
- Does it bother you?
- Score of >/= 3

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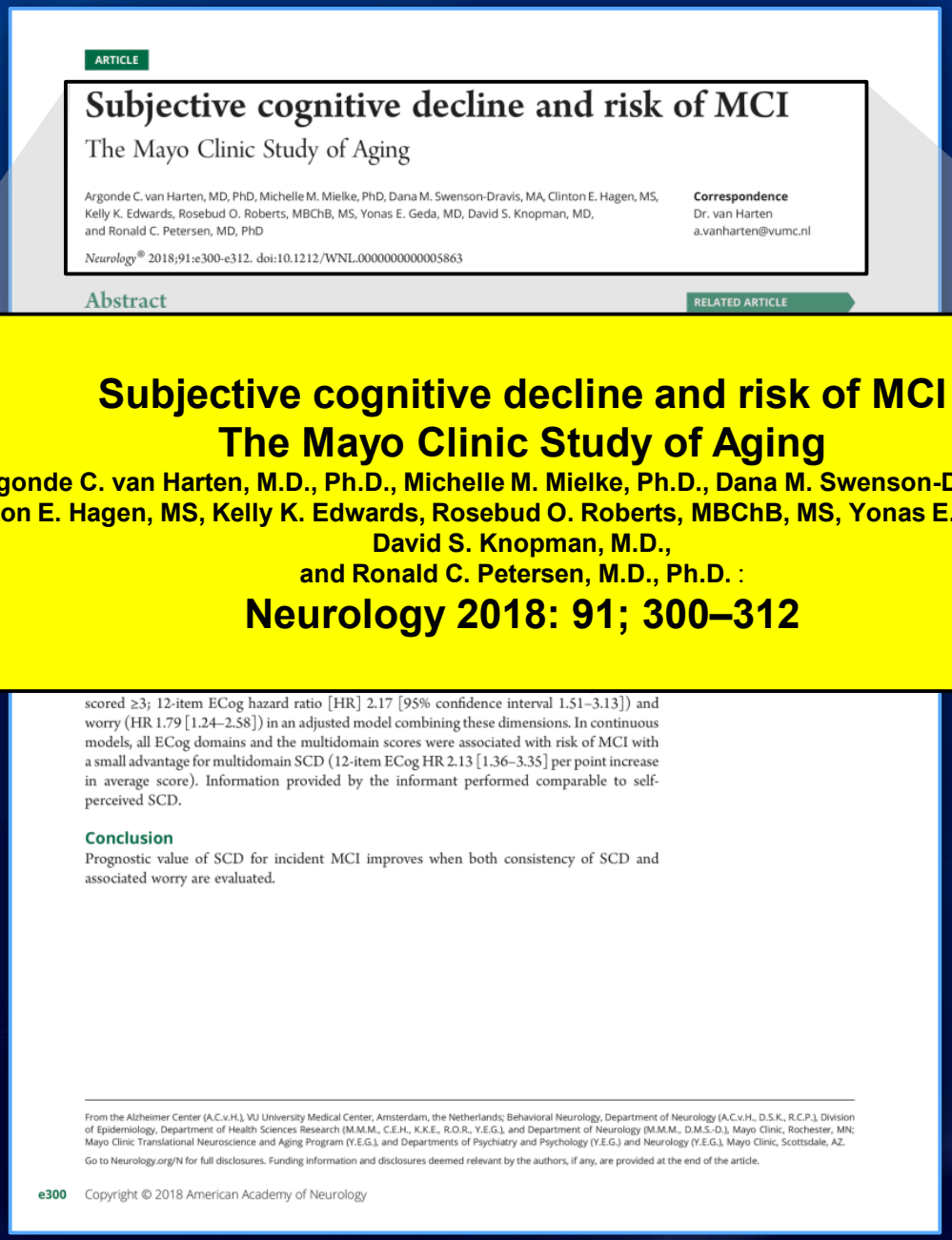

ARTICLE

Subjective cognitive decline and risk of MCI

The Mayo Clinic Study of Aging

Argonde C. van Harten, MD, PhD, Michelle M. Mielke, PhD, Dana M. Swenson-Dravis, MA, Clinton E. Hagen, MS, Kelly K. Edwards, Rosebud O. Roberts, MBChB, MS, Yonas E. Geda, MD, David S. Knopman, MD, and Ronald C. Petersen, MD, PhD

Correspondence
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Neurology® 2018;91:e300-e312. doi:10.1212/WNL.0000000000005863

Abstract

RELATED ARTICLE

Subjective cognitive decline and risk of MCI
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Neurology 2018: 91; 300–312

scored ≥3; 12-item ECog hazard ratio [HR] 2.17 [95% confidence interval 1.51–3.13]) and worry (HR 1.79 [1.24–2.58]) in an adjusted model combining these dimensions. In continuous models, all ECog domains and the multidomain scores were associated with risk of MCI with a small advantage for multidomain SCD (12-item ECog HR 2.13 [1.36–3.35] per point increase in average score). Information provided by the informant performed comparable to self-perceived SCD.

Conclusion

Prognostic value of SCD for incident MCI improves when both consistency of SCD and associated worry are evaluated.

From the Alzheimer Center (A.C.v.H.), VU University Medical Center, Amsterdam, the Netherlands; Behavioral Neurology, Department of Neurology (A.C.v.H., D.S.K., R.C.P.), Division of Epidemiology, Department of Health Sciences Research (M.M.M., C.E.H., K.K.E., R.O.R., Y.E.G.), and Department of Neurology (M.M.M., D.M.S.-D.), Mayo Clinic, Rochester, MN; Mayo Clinic Translational Neuroscience and Aging Program (Y.E.G.), and Departments of Psychiatry and Psychology (Y.E.G.) and Neurology (Y.E.G.), Mayo Clinic, Scottsdale, AZ.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

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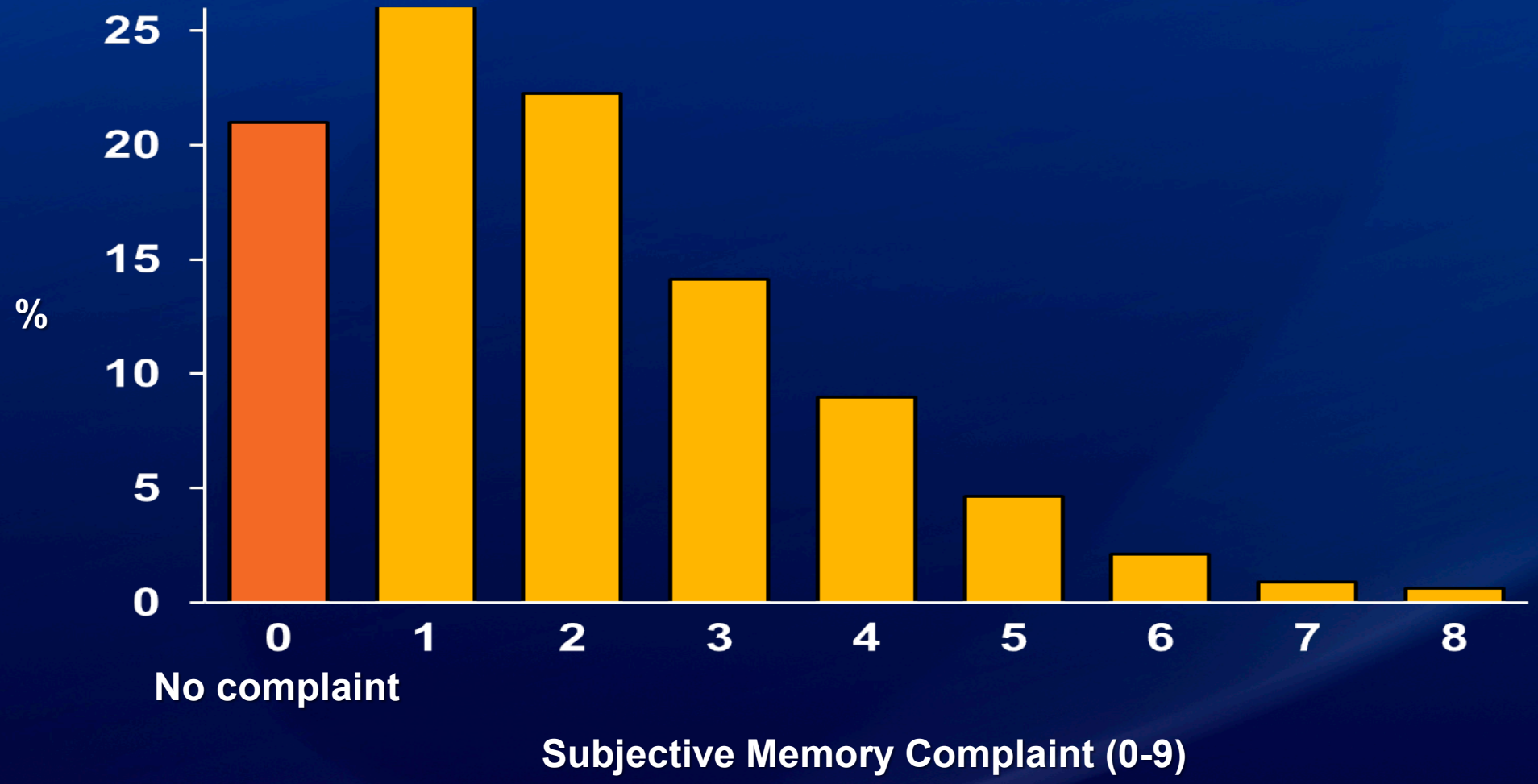
Frequency of Subjective Memory Complaints



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Multivariate Cox Proportional Hazard Model

Variable	HR (95% CI)	P
Degree of subjective memory complaints (0-9)	1.12 (1.06, 1.19)	<0.0001
Male	0.77 (0.63, 0.95)	0.013
Education	1.04 (1.00-1.07)	0.03
Depression/dysphoria	1.28 (0.85, 1.72)	0.011
Anxiety	1.27 (0.85, 1.92)	0.25
APOE carrier	1.44 (1.17, 1.77)	0.0005
zAttention	0.72 (0.60, 0.87)	0.0004
zMemory	0.57 (0.47, 0.68)	<0.0001
zGlobal	0.32 (0.49, 0.82)	0.0005
Charlson index	1.03 (1.00, 1.06)	0.073

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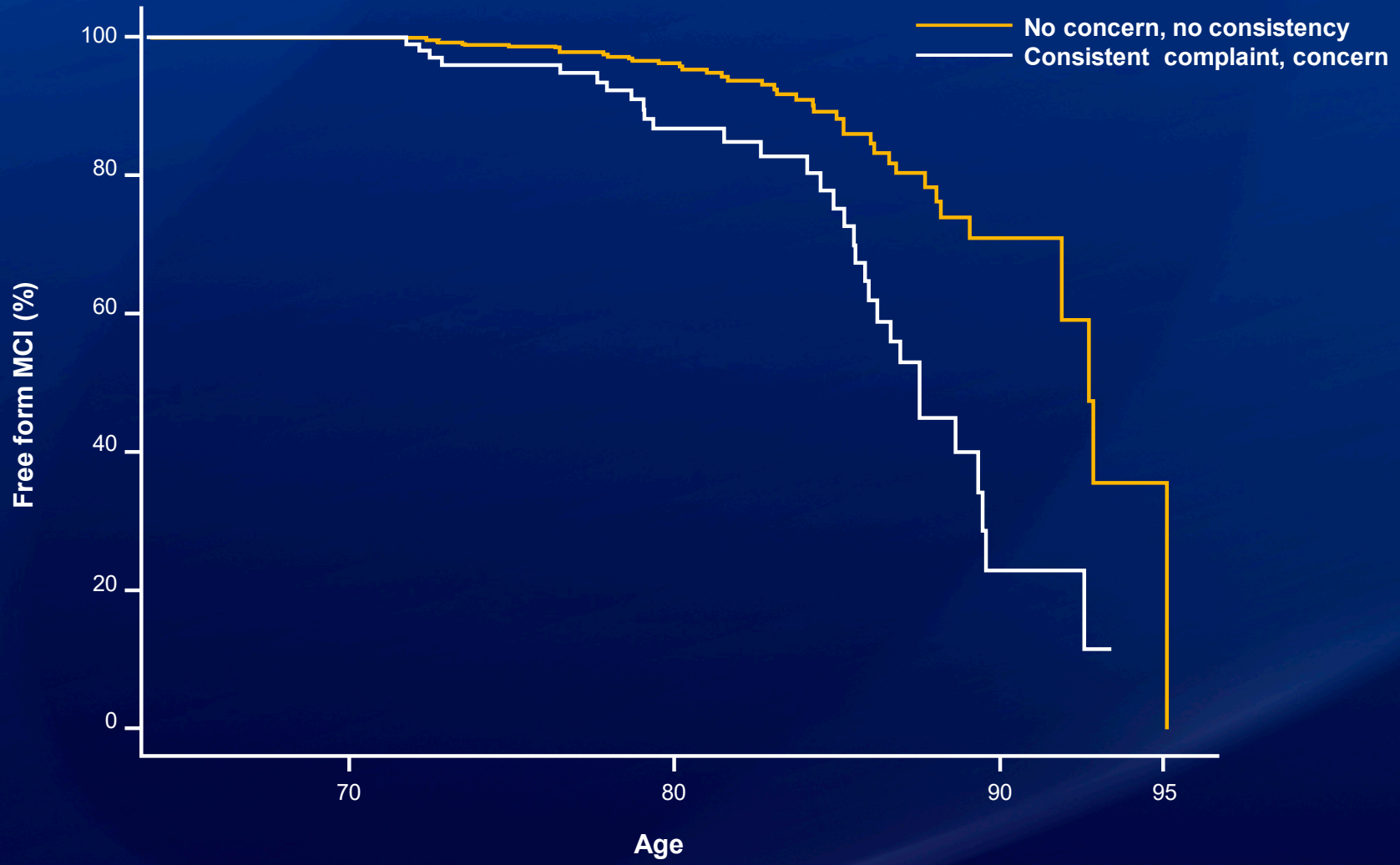
Kaplan-Meier curve combining consistency of complaints on the 12-item ECog and concern



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Subjective Concerns

- Frequent in the general community (79%)
- Subjective concerns in cognitively normal subjects predict progression to MCI
- Subjective concerns “reflect” biomarker status to some degree

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Summary

- MCI is a useful clinical and research entity
- Influencing dementia research
- Data more consistent
- Moving toward early identification

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Mayo Clinic Mayo Aging Research

Rochester

Brad Boeve
Dave Knopman
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Val Lowe
Mary Machulda
Michelle Mielke
Jon Graff-Radford
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Prashanthi Vemuri
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Terry Therneau
Walter Kremers
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Nikki Stricker
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Jacksonville

Neill Graff-Radford
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Nilufer Erketin-Taner
Len Petrucelli
Guojun Bu
Owen Ross

Scottsdale

Rick Caselli
Bryan Woodruff
Yonas Geda

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Thank You

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