NEW GENERATION AD AND OTHER TREATMENTS IN THE SETTING OF MCCS

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DISCLOSURES

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OUTLINE

- Anti-amyloid antibody treatments in MCC
  - Generalizability
  - Competing risk for anti-thrombotic treatment
- Treating cardiovascular MCC decreases ADRD risk
  - Hypertension
  - Atrial fibrillation

MULTIPLE CHRONIC CONDITIONS DOMINATE ADRD

- More than 95% of people with ADRD have one or more other chronic conditions.
- Cardiovascular diseases are common chronic conditions among people with ADRD.
- Having six or more chronic conditions is nearly 4-fold higher in those with ADRD.

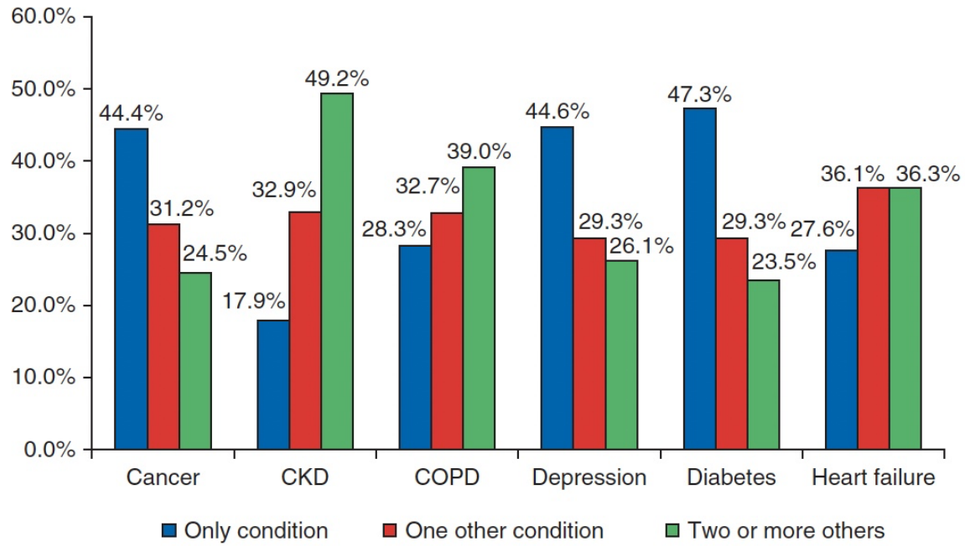


FIGURE 41-2. Proportion (%) of Medicare beneficiaries with multiple chronic conditions by select chronic condition (2005).

Boyd, C in Hazzard's Geriatrics and Gerontology, 2022

OUTCOMES STRATIFIED BY MCC ARE NOT REPORTED IN ANTI-AMYLOID ANTIBODY TRIALS

- CLARITY AD – Lecanemab

Table 1. Characteristics of the Participants at Baseline (Modified Intention-to-Treat Population).*

Characteristic	Lecanemab (N=859)	Placebo (N=875)
Age — yr	71.4±7.9	71.0±7.8
Sex — no. (%)		
Female	443 (51.6)	464 (53.0)
Male	416 (48.4)	411 (47.0)
Race — no. (%)†		
White	655 (76.3)	677 (77.4)
Black	20 (2.3)	24 (2.7)
Asian	147 (17.1)	148 (16.9)
Other or missing	37 (4.3)	26 (3.0)
Hispanic ethnic group — no. (%)†	107 (12.5)	108 (12.3)
Time since diagnosis — yr	1.41±1.51	1.34±1.54
Time since onset of symptoms — yr	4.13±2.35	4.15±2.53
Global CDR score — no. (%)‡		
0.5	694 (80.8)	706 (80.7)
1	165 (19.2)	169 (19.3)
Clinical subgroup — no. (%)		
Mild dementia due to Alzheimer's disease	331 (38.5)	331 (37.8)
Mild cognitive impairment due to Alzheimer's disease	528 (61.5)	544 (62.2)

- TRAILBLAZER-ALZ 2 – Donanemab

Table 1. Baseline Demographics and Clinical Characteristics in the Low/Medium and Combined Tau Populations

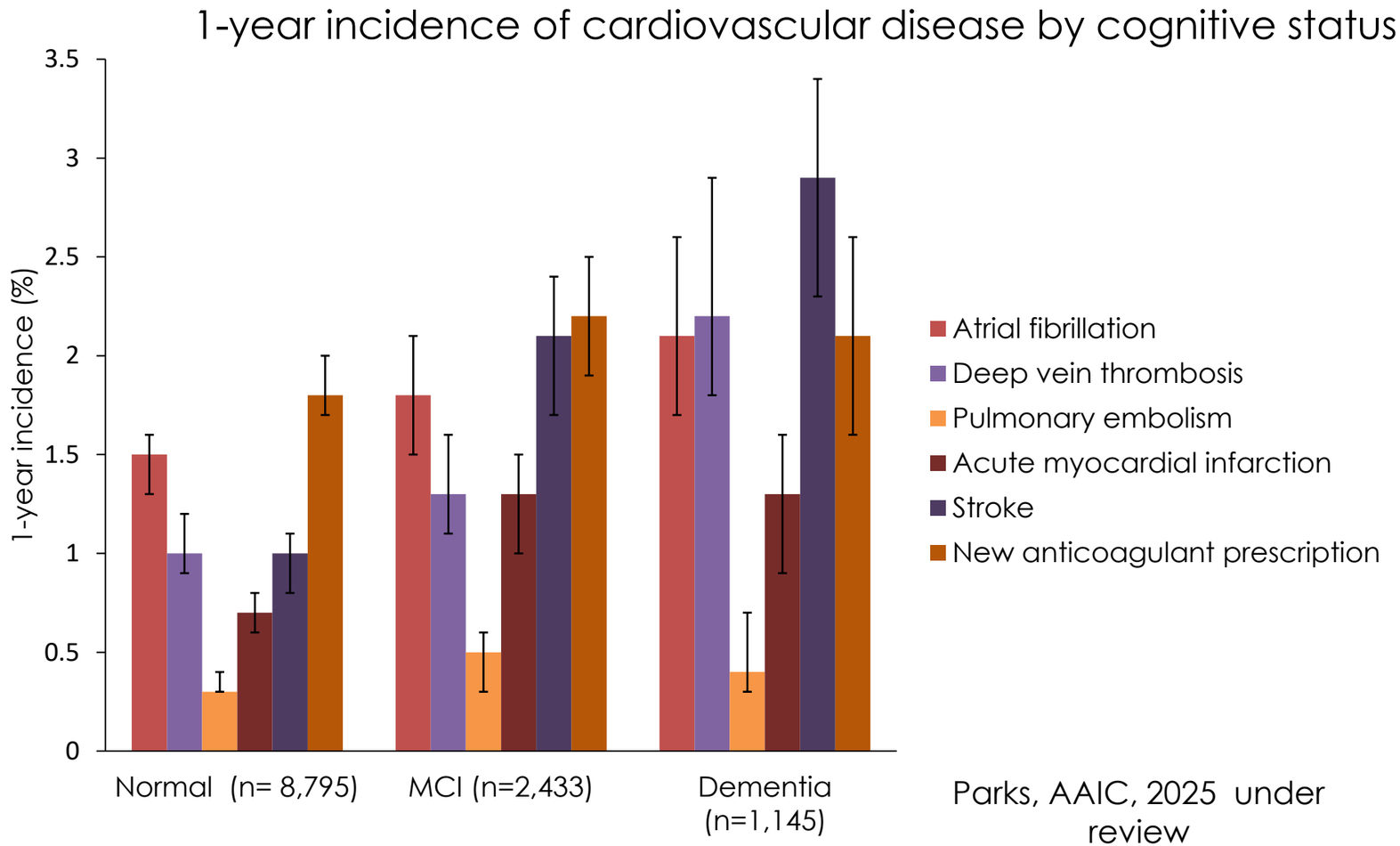
Characteristic	Low/medium tau		Combined tau	
	Donanemab (n = 588)	Placebo (n = 594)	Donanemab (n = 860)	Placebo (n = 876)
Sex, No. (%)				
Women	325 (55.3)	321 (54.0)	493 (57.3)	503 (57.4)
Men	263 (44.7)	273 (46.0)	367 (42.7)	373 (42.6)
Age, mean (SD), y	74.3 (5.7)	74.3 (5.8)	73.0 (6.2)	73.0 (6.2)
Race, No. (%)[a]				
American Indian or Alaska Native	1 (0.2)	0	2 (0.2)	0 (0.0)
Asian	48 (8.2)	38 (6.4)	57 (6.6)	47 (5.4)
Black or African American	17 (2.9)	17 (2.9)	19 (2.2)	21 (2.4)
White	522 (88.8)	539 (90.7)	781 (90.9)	807 (92.1)

CLARITY-AD SUPPLEMENTAL DATA

Overall representativeness of this trial	The participants in the present trial demonstrated more females than male and the expected age and ApoE4 distribution for Alzheimer's disease. Biological sex was reported by the participants; options were female, male. Gender was not assessed. The proportion of Black participants that underwent randomization overall was small (4.5% in US). The proportion of Hispanic participants was 22.5% in US, somewhat larger than the total population distribution of Hispanic people in the US. The incidence of common comorbidities (hypertension, hypercholesterolemia, diabetes, heart disease) were consistent with proportion in the US elderly population. No patient was enrolled in South America or Africa.

RATES OF NEW INDICATION FOR ANTITHROMBOTIC DRUGS IN PEOPLE WITH COGNITIVE IMPAIRMENT

Nearly 8% of people with MCI/ADRD develop a CV condition requiring antithrombotic drugs per year.

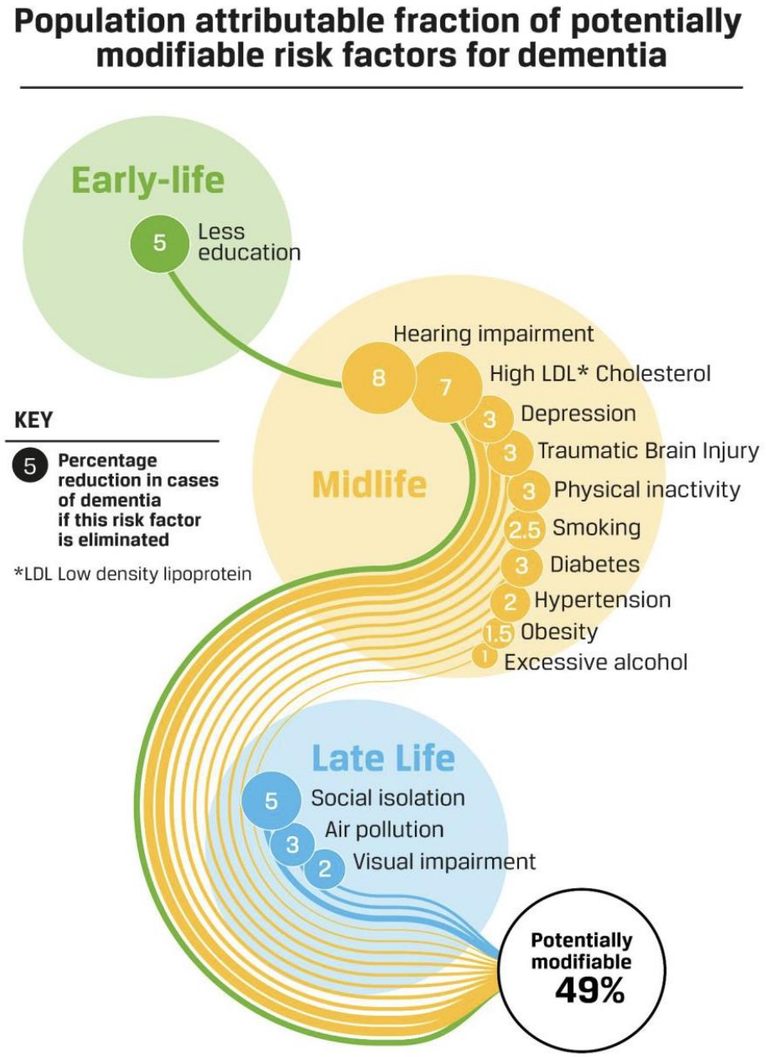


Parks, AAIC, 2025 under review

CONCLUSION – 1

Real world data from registries of patients receiving anti-amyloid antibody treatments are needed to determine the risks and benefits among patients with MCCs.

MODIFIABLE ADRD RISK FACTORS



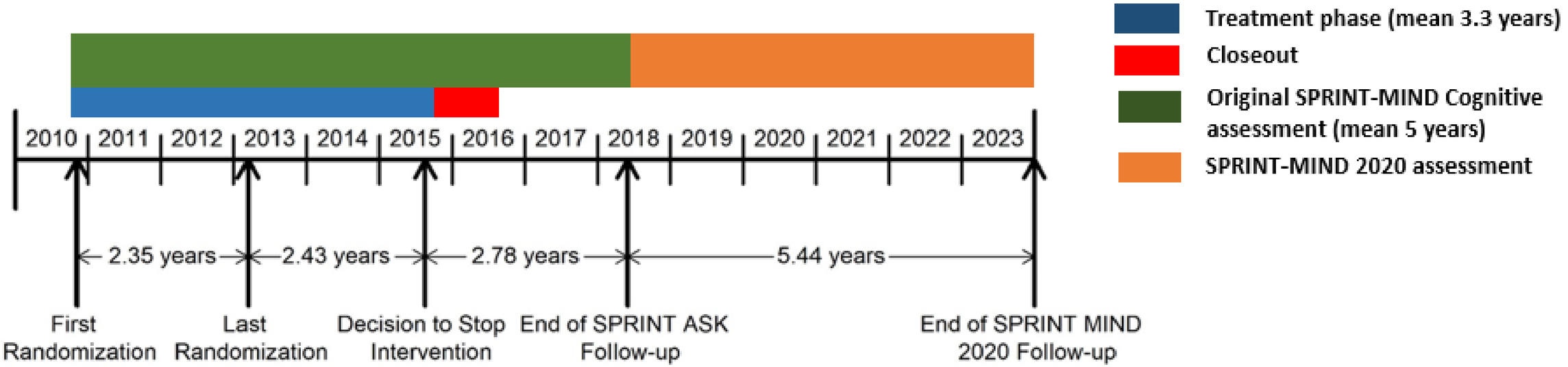
Livingston, 2024

Common conditions among persons with ADRD include:

- Hypertension (84%)
- Hyperlipidemia (67%)
- Depression (41%)
- Diabetes (37%)

Zhang, 2025

SYSTOLIC BLOOD PRESSURE INTERVENTION TRIAL (SPRINT) MIND 2020 - TIMELINE



SPRINT MIND 2020 OUTCOMES

RESEARCH ARTICLE

Long-Term Effect of Intensive vs Standard Blood Pressure Control on Mild Cognitive Impairment and Probable Dementia in SPRINT

David M. Reboussin,[1] Sarah A. Gaussoin,[1] Nicholas M. Pajewski,[1] Byron C. Jaeger,[1] Bonnie Sachs,[2] Stephen R. Rapp,[3] Mark A. Supiano,[4] Maryjo L. Cleveland,[5] Valerie Hunter,[5] Jamehl L. Demons,[5] Paula K. Ogrocki,[6] Alan Jay Lerner,[6] Gordon J. Chelune,[7] Virginia G. Wadley,[8] Margaret L. Scales,[9] Nancy F. Woolard,[5] Letitia H. Perdue,[1] Kathryn E. Callahan,[5] and Jeff D. Williamson[5]

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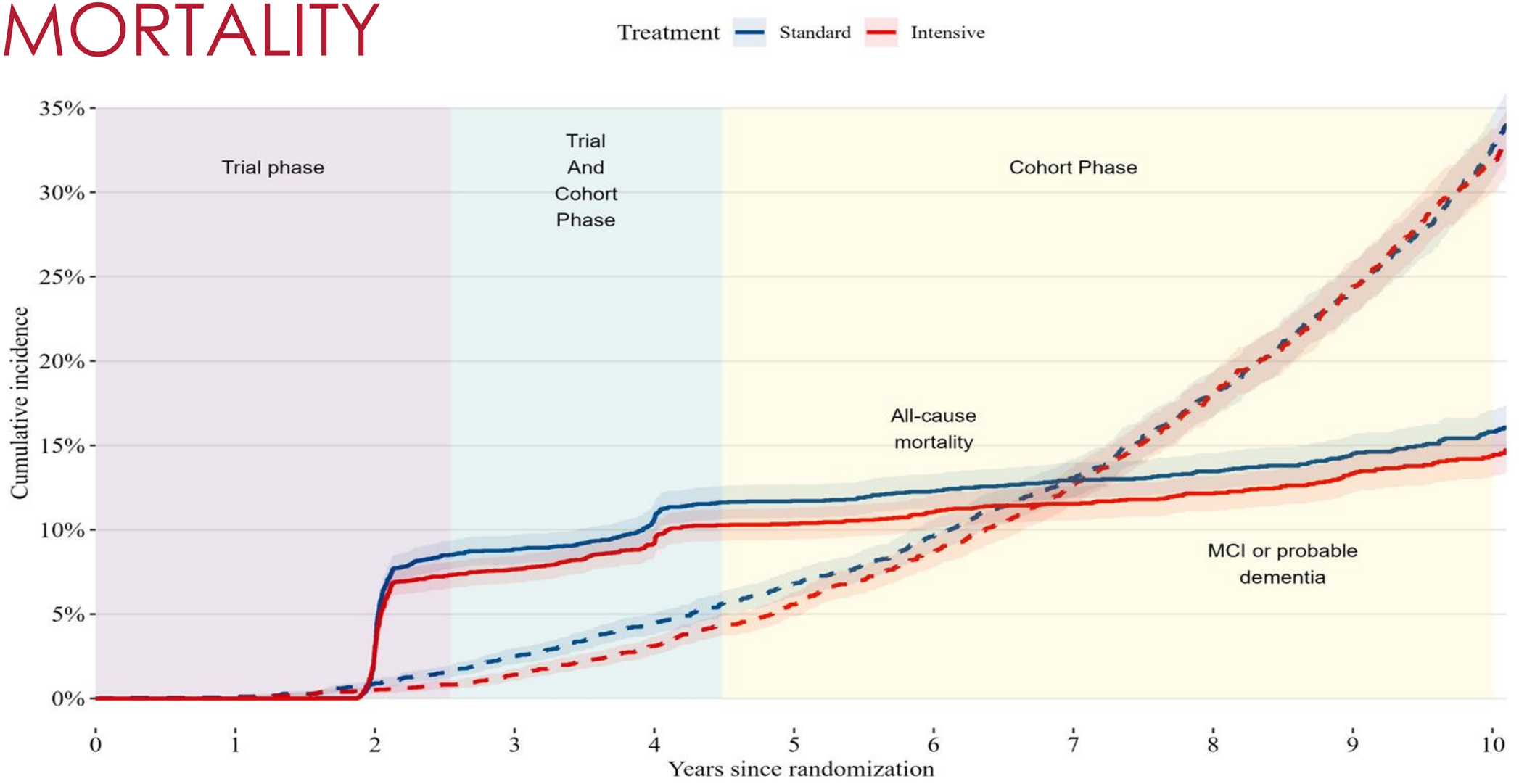
OVERALL LEGACY RESULTS: INCIDENCE OF PROBABLE DEMENTIA, MCI AND THE COMPOSITE

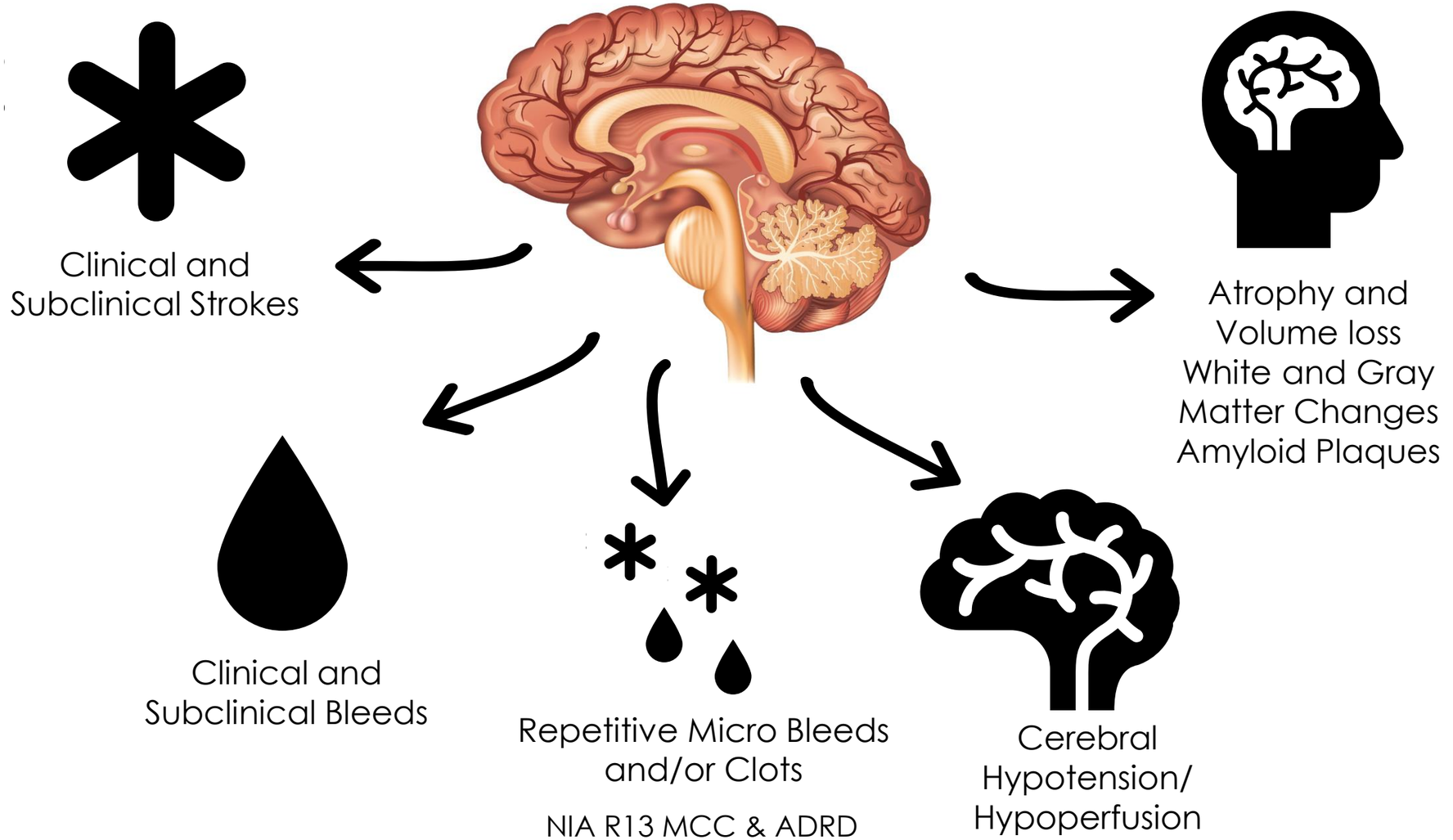
	Intensive Treatment		Standard Treatment			
Outcome	No. With Outcome / Person-Years	Cases per 1000 Person-Years	No. With Outcome / Person-Years	Cases per 1000 Person-Years	Hazard Ratio (95% Confidence Interval)	P Value
Probable dementia	248 / 29,122	8.5	293 / 28,855	10.2	0.86 (0.72, 1.02)	0.08
MCI	380 / 27,075	14.0	430 / 26,465	16.2	0.87 (0.76, 1.00)	0.04
MCI or Probable dementia	555 / 27,622	20.1	622 / 27,117	22.9	0.89 (0.79, 1.00)	0.04

*3.3 years of intensive treatment, 6.9 years median follow-up time

CUMULATIVE INCIDENCE WITH ALL-CAUSE MORTALITY



SPECTRUM OF BRAIN INJURY IN PATIENTS WITH ATRIAL FIBRILLATION



Arrhythm Electrophysiol Rev. 2019; 8(1):8-12.

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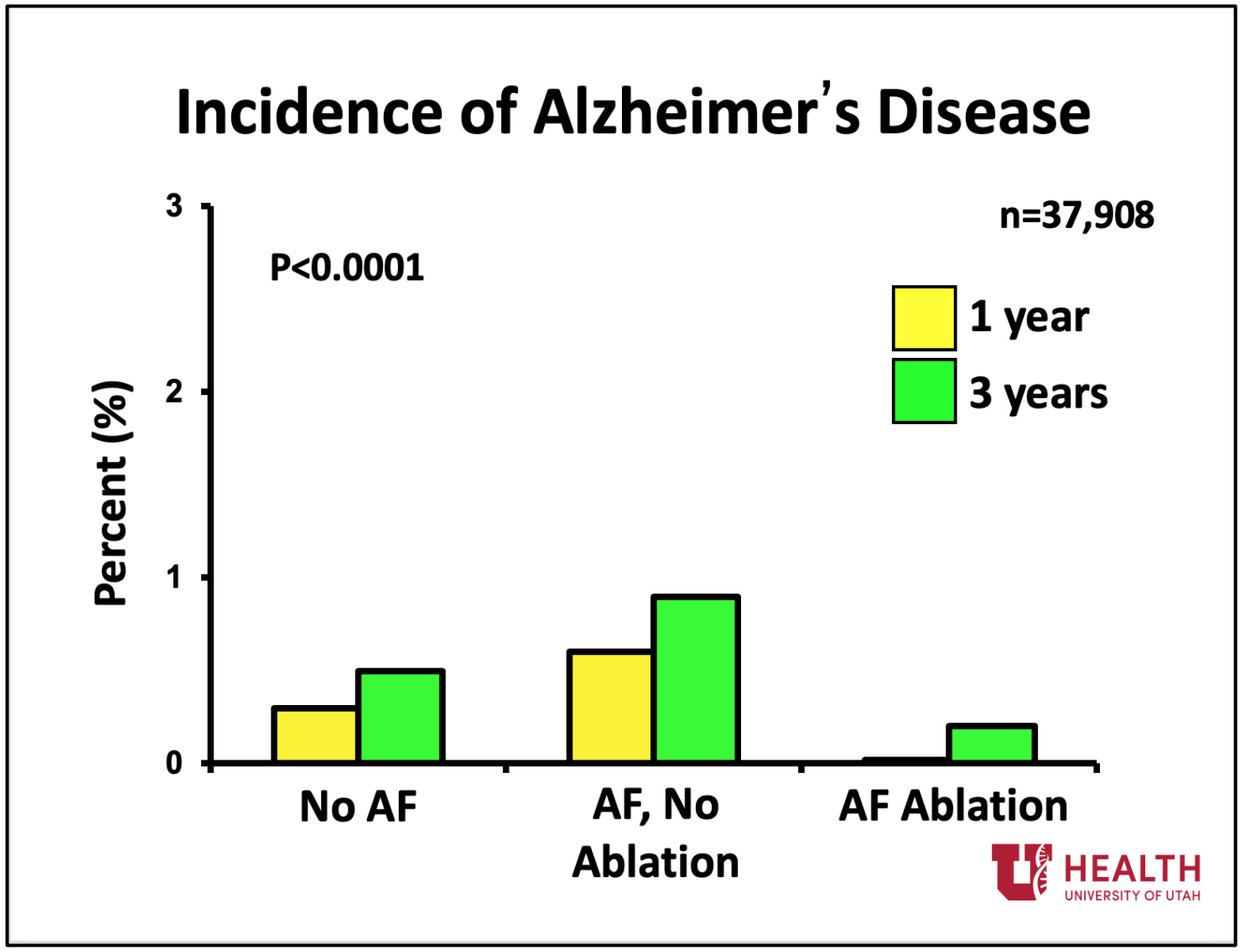
NIA R13 MCC & ADRD
March 2025

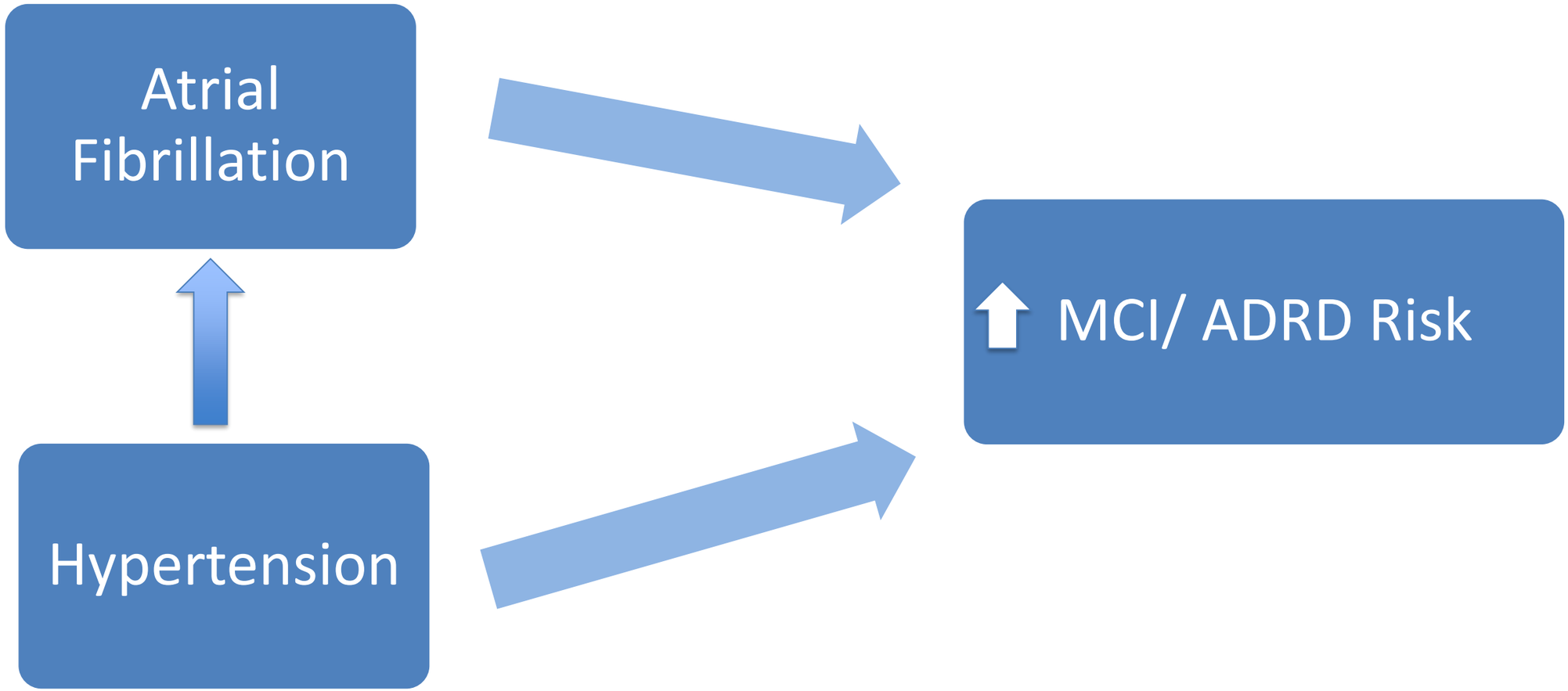
CATHETER ABLATION FOR ATRIAL FIBRILLATION



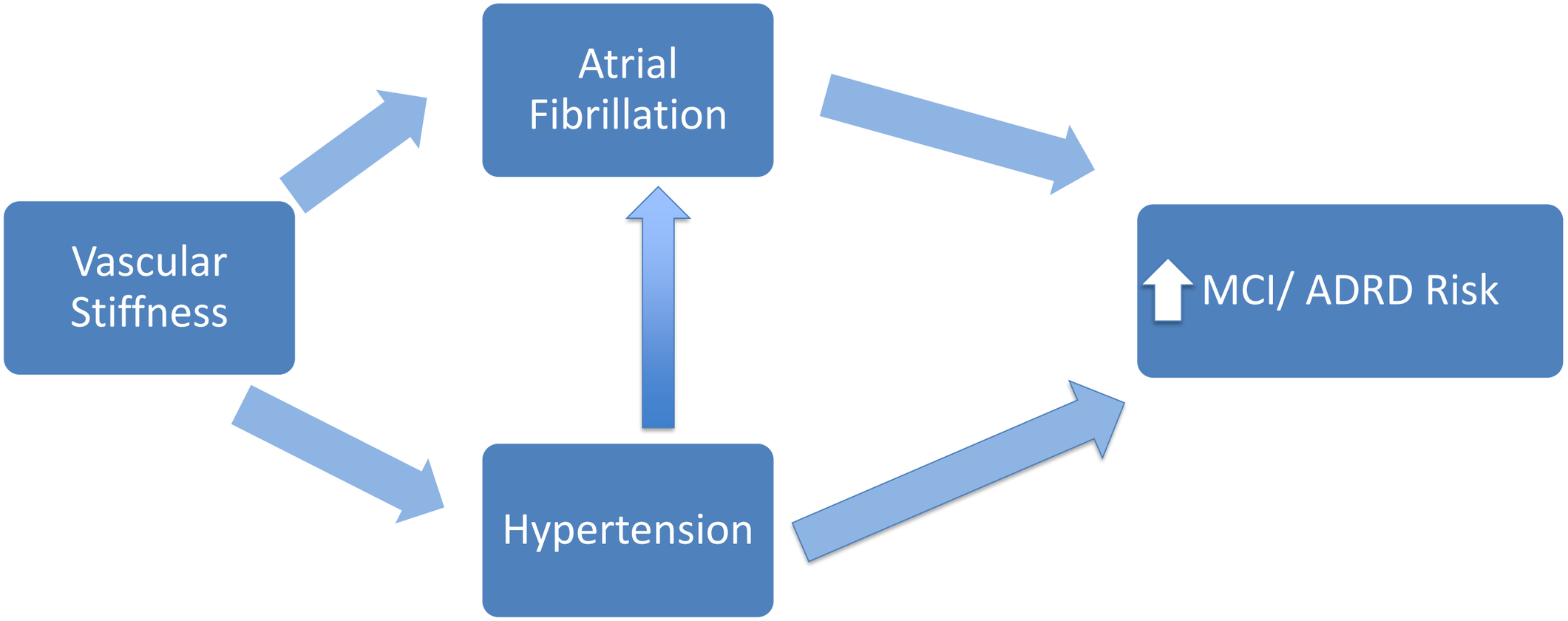
- Alzheimer's Disease incidence is high in A Fib patients
- AD incidence in A Fib patients post ablation was comparable to the no A Fib group
- Other forms of dementia were also significantly less.

Bunch, 2011

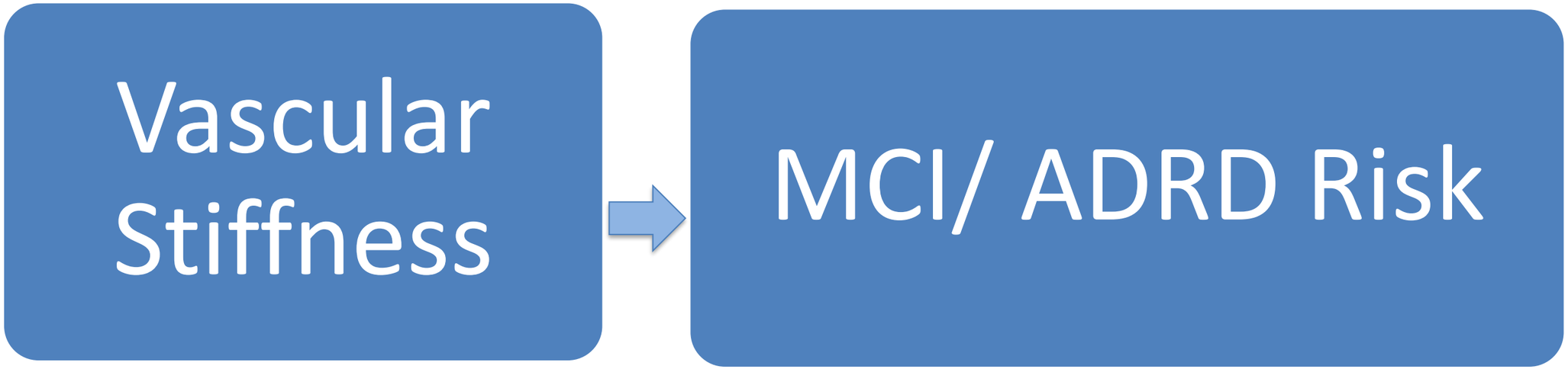
MCC AND ADRD RISK



VASCULAR STIFFNESS, MCC AND ADRD RISK



VASCULAR STIFFNESS AND ADRD RISK



Hughes, AAIC, 2025 under review

CONCLUSION – 2

- Improved recognition and management of lifestyle factors and MCC, especially CV conditions, is an effective treatment strategy to reduce ADRD risk.
- Vascular stiffness may play a mechanistic role in the associations between CV MCCs and ADRD.