Hypertension and Dementia

BRAIN HEALTH ACADEMY
UsAgainstAlzheimer's

November 16, 2022

Acknowledgements

This course is presented and developed in partnership with the American Heart Association

Presenters

Mitchell Elkind, MD, MS is a tenured Professor of Neurology and Epidemiology at Columbia University and Chief Clinical Science Officer of the American Heart Association.

He received his medical degree from Harvard Medical School and trained in Neurology at Massachusetts General Hospital. He completed a fellowship in Vascular Neurology and Neuroepidemiology at Columbia University and holds a degree in Epidemiology from Columbia's Mailman School of Public Health. His research focuses on stroke prevention, risk prediction, atrial cardiopathy, and vascular causes of cognitive aging.

Course Description

Hypertension is one of the most important known modifiable risk factors for dementia. Managing blood pressure can reduce the risk of cognitive decline.

This course provides actionable guidance and tools to help health professionals effectively address this opportunity with patients and families.

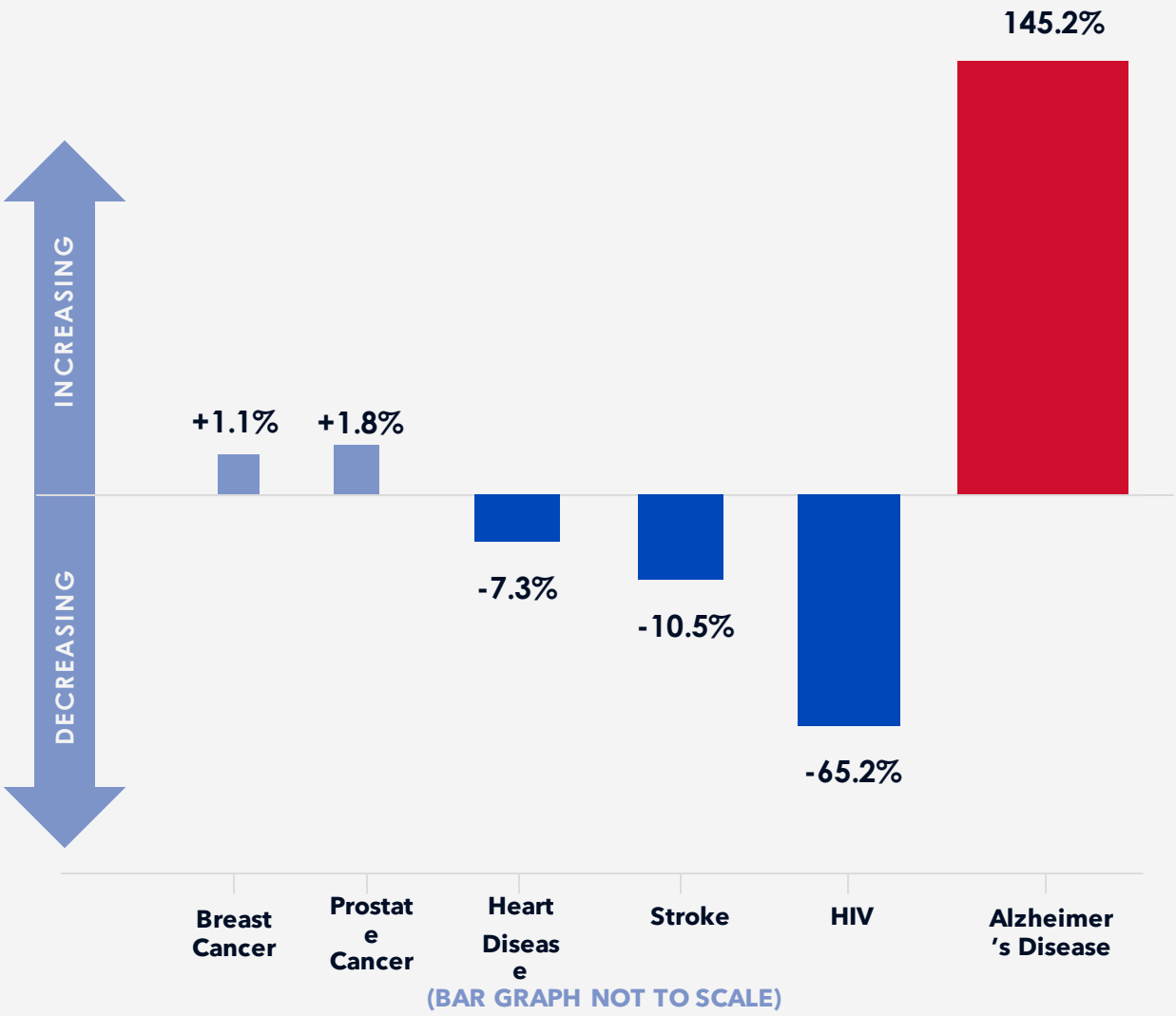
Learning Objectives

- Participants will be able to list 6 or more modifiable risk factors for dementia.
- Participants will be able to summarize the link between **hypertension** and dementia.
- Participants will be able to identify effective interventions and strategies to address **hypertension** with a special focus on adults aged 45+ years.
- Participants will be able to identify special considerations for high-risk populations.

Alzheimer's and Dementia Facts

Scope of the Epidemic (U.S.)[1]

- 6.5 million adults
- 1 in 9 adults age ≥65
- 1 in 3 adults age ≥85
- 2/3 are women
- Alzheimer's deaths increased 145% from 2000-2019, while other top causes of death have declined



Inequities in Brain Health[2, 3, 4]

African American people are
2X AS LIKELY
to have Alzheimer's

AND

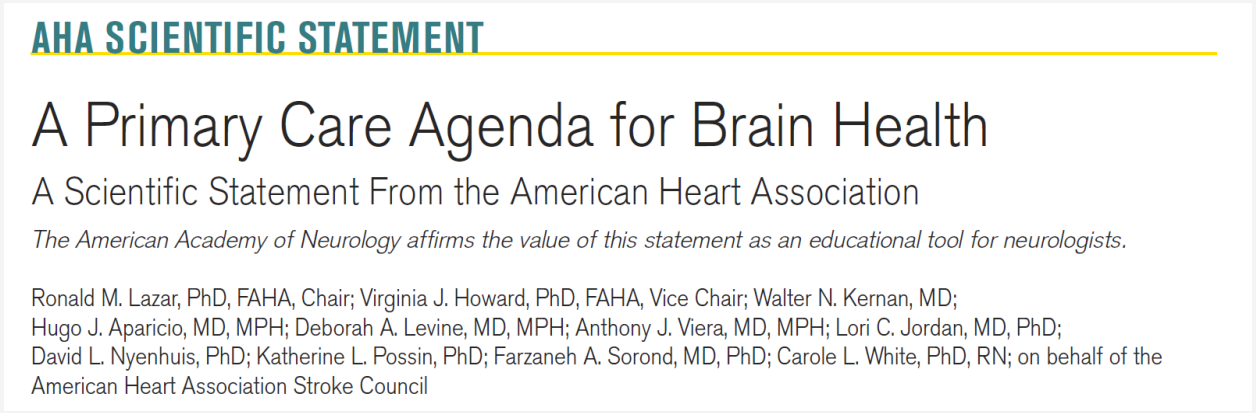
Latino people are
1.5X AS LIKELY
to have Alzheimer's

Less likely than White patients to receive a timely diagnosis;

More likely to report experiencing racial discrimination along their patient and caregiver journeys;

Less likely to be enrolled in cutting-edge Alzheimer's and brain health research.

What is Optimal Brain Health?



AHA SCIENTIFIC STATEMENT

A Primary Care Agenda for Brain Health

A Scientific Statement From the American Heart Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Ronald M. Lazar, PhD, FAHA, Chair; Virginia J. Howard, PhD, FAHA, Vice Chair; Walter N. Kernan, MD; Hugo J. Aparicio, MD, MPH; Deborah A. Levine, MD, MPH; Anthony J. Viera, MD, MPH; Lori C. Jordan, MD, PhD; David L. Nyenhuis, PhD; Katherine L. Possin, PhD; Farzaneh A. Sorond, MD, PhD; Carole L. White, PhD, RN; on behalf of the American Heart Association Stroke Council

Clinically: absence of cognitive impairment/dementia, stroke, and other brain diseases

Pathologically: absence of neurodegenerative, cerebrovascular, and comorbid brain pathology that interfere with everyday physical and cognitive functioning

Pragmatically: preservation of neuronal function to meet demands of everyday life, operationally defined in terms of the capacity to function adaptively in one's environment

Source: Lazar RM et al. *Stroke* 2022.


Modifiable Risk
Factors for Dementia

Alzheimer's: Non-Modifiable Risk Factors[6, 1, 7, 8]

Age

- Number one risk factor is advancing age.
- Risk doubles every 5 years after age 65.

Family History

- Genetics vs environmental factors.

Education

- Fewer years of formal education and lower levels of cognitive engagement may be risk factors.

Sex

- 2/3 of those with Alzheimer's are women.
- 16% of women age ≥ 71 (11% of men).
- After age 65, have more than 1 in 5 chance (1 in 11 for men).

Vascular/Modifiable Risks and Dementia

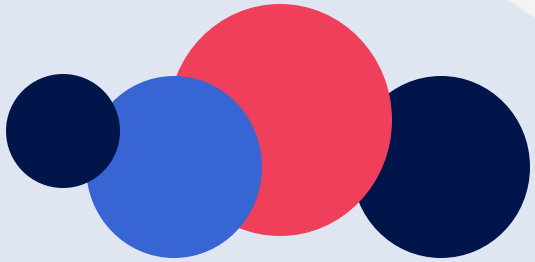
	Population prevalence	Relative risk (95% CI)	PAR (confidence range)	Number of cases attributable (thousands; confidence range)
USA				
Diabetes mellitus	8·7%	1·39 (1·17–1·66)	3·3% (1·5–5·4)	174 (77–288)
Midlife hypertension	14·3%	1·61 (1·16–2·24)	8·0% (2·2–15·1)	425 (119–798)
Midlife obesity	13·1%	1·60 (1·34–1·92)	7·3% (4·3–10·8)	386 (226–570)
Depression	19·2%	1·90 (1·55–2·33)	14·7% (9·6–20·3)	781 (506–1078)
Physical inactivity	32·5%	1·82 (1·19–2·78)	21·0% (5·8–36·6)	1115 (308–1942)
Smoking	20·6%	1·59 (1·15–2·20)	10·8% (3·0–19·8)	574 (159–1050)
Low education	13·3%	1·59 (1·35–1·86)	7·3% (4·4–10·3)	386 (236–544)
Combined (maximum)	..	..	54·1%	2 866 951*

PAR=population attributable risk. *Absolute number.

Others: Hearing loss, alcohol consumption, social isolation, pollution

Source: Barnes & Yaffe, *Lancet Neurol* 2011; 10: 819-28

Modifiable Risk Factors[9,10]



40%

of dementia cases could be prevented by addressing these lifestyle factors

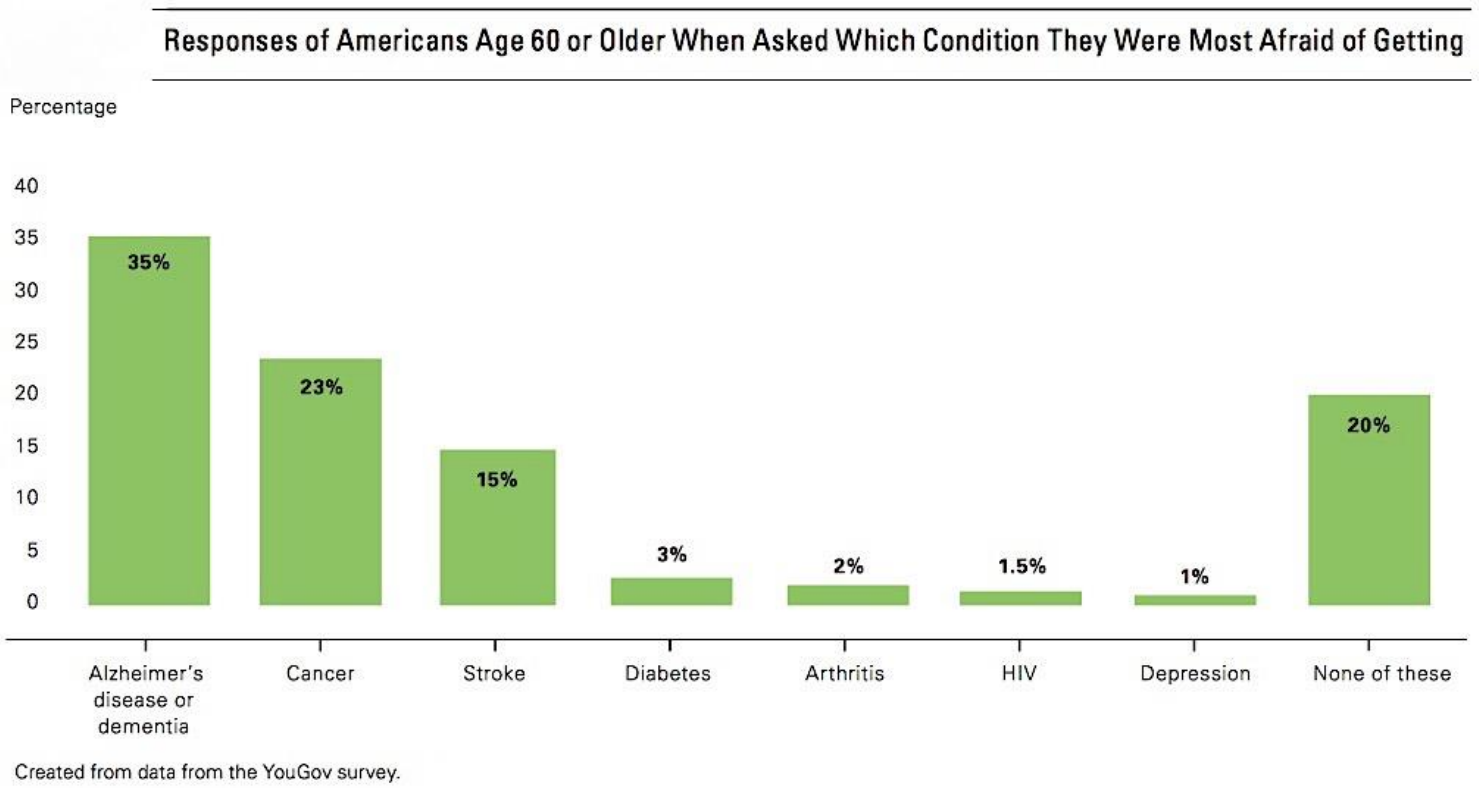
INCREASE

- Education
- Physical Activity
- Social Contact

DECREASE

- Hearing Loss
- Hypertension
- Obesity
- Smoking
- Depression
- Diabetes
- Excessive Alcohol Intake
- Head Injury
- Air Pollution

What Patients Think

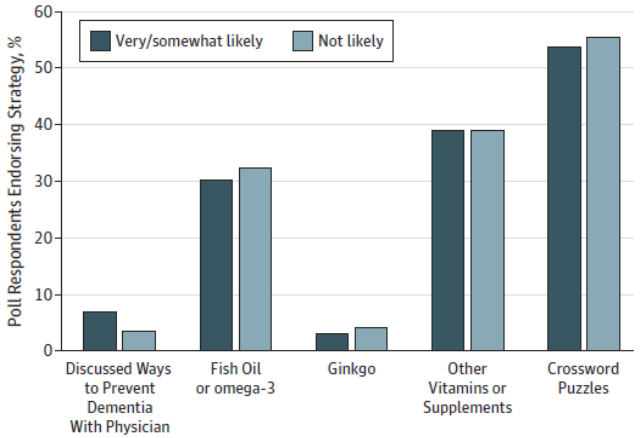


"O let me not be mad, not mad, sweet heaven!"
King Lear, *1.5*

Primary Care Practice:
Conversation about risk factors and dementia not taking place

- University of Michigan National Poll on Healthy Aging
- Survey of 1,019 respondents between 50 – 64 years old
  - Only 5.2% had discussed dementia prevention
  - Black patients perceived their risk as lower, rather than higher
  - Respondents did not perceive physical health as a risk factor for dementia
  - Few discussions about managing risk factors to reduce dementia risk
  - Respondents were engaging in strategies that were not evidence-based

Figure. Actions Taken to Prevent Memory Loss by Perceived Likelihood of Developing Dementia



The percentage of poll respondents who endorsed specific strategies in response to the following question: "Do you take or do any of the following to maintain or improve your memory?" Responses are grouped by perceived likelihood of developing dementia (somewhat/very likely vs not likely). A χ^2 test was used to compare particular strategies endorsed by perceived likelihood of developing dementia. All comparisons were nonsignificant with the exception of discussion with a physician, which was endorsed more frequently by those who believed they were at least somewhat likely to develop dementia (7.1% [95% CI, 5.1%-9.8%] vs 3.6% [95% CI, 2.2%-5.7%]; $P = .02$).

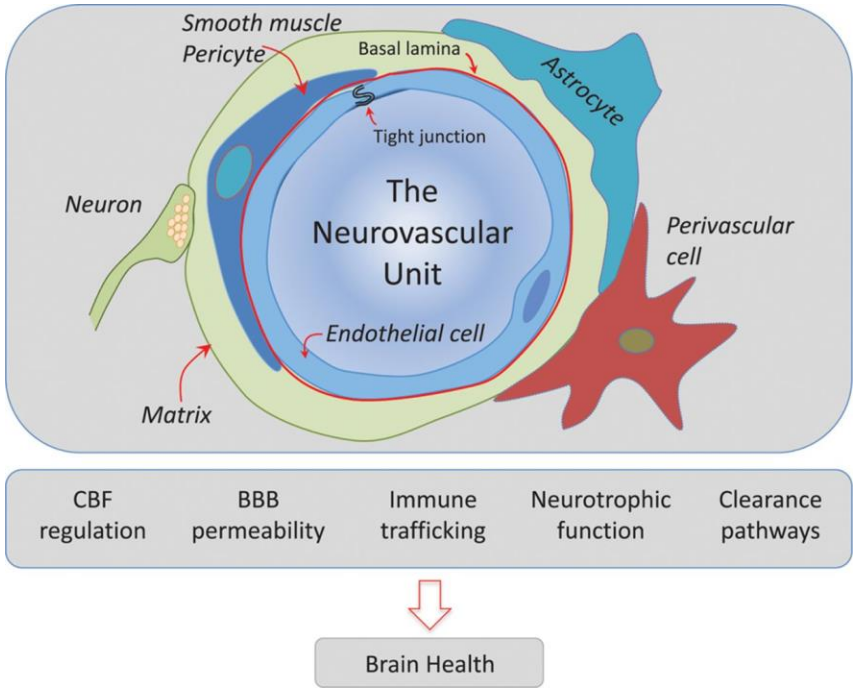
Source: Maust D et al. JAMA Neurol 2020;77:259-261.

What Matters Most Insights Survey: Hypertension

UsA2 will complete this slide.

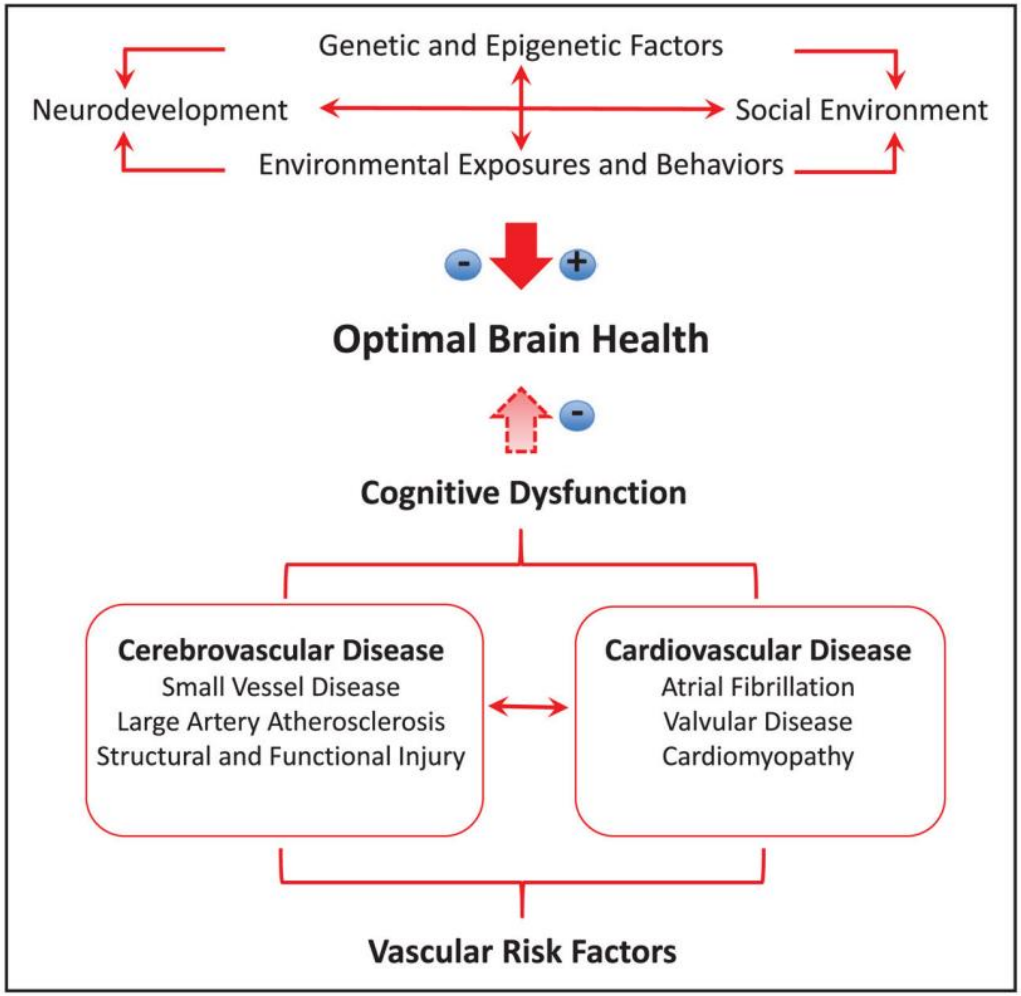
The Link Between Hypertension and Dementia

Brain physiology



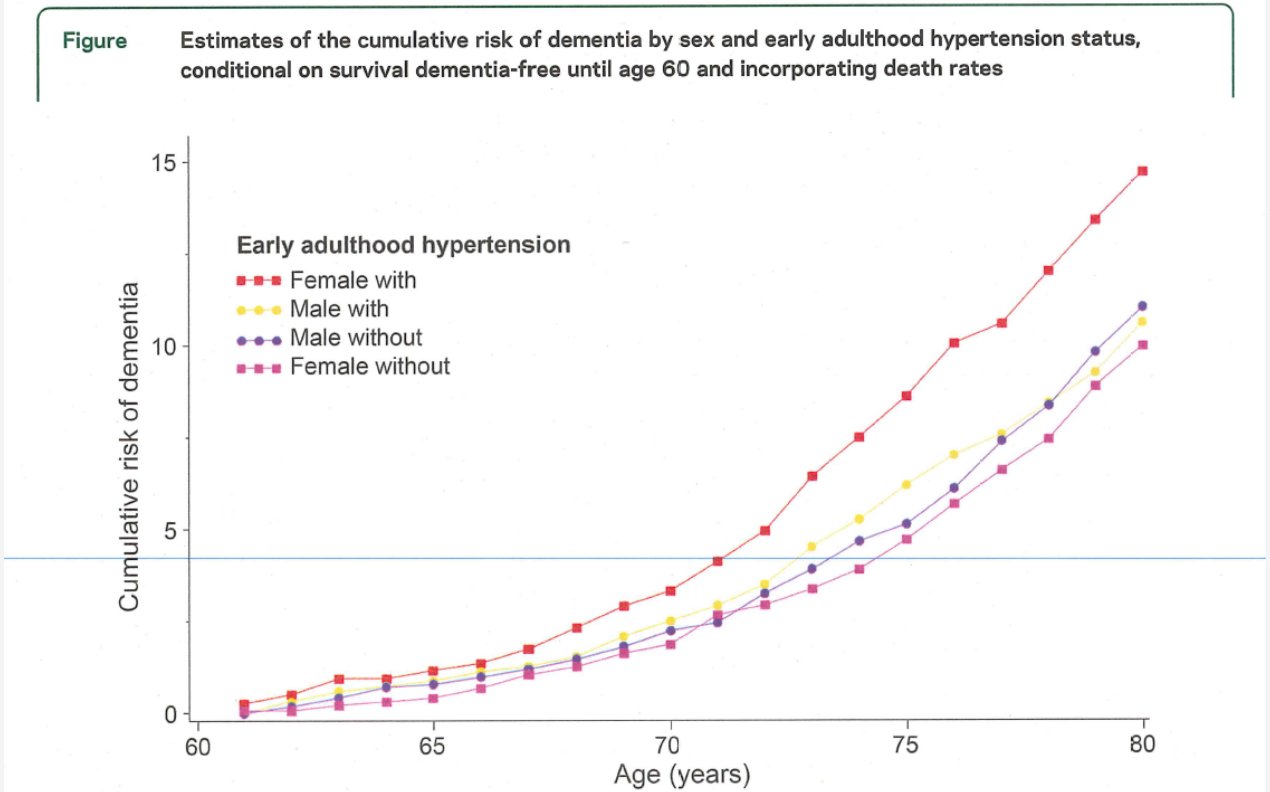
Defining Optimal Brain Health in Adults: A Presidential Advisory From the American Heart Association/American Stroke Association, Volume: 48, Issue: 10, Pages: e284-e303, DOI: (10.1161/STR.0000000000000148)

Hypertension and Dementia Link



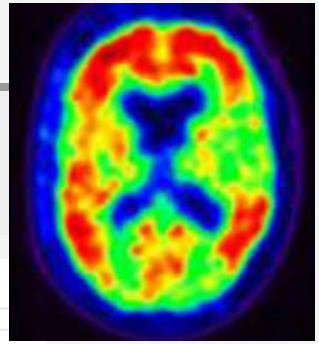
Source: Gorelick et al. 2017; *Stroke*

Mid-life Risk Factors Predict Late-Life Dementia



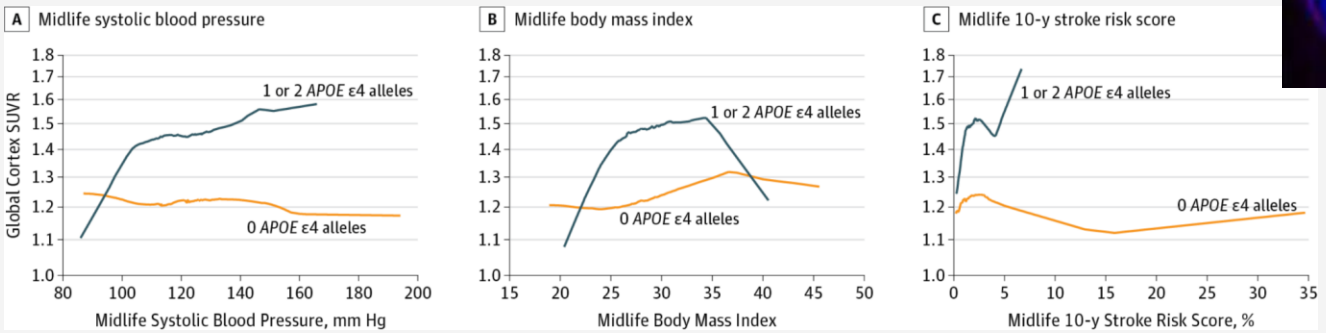
Source: Gilsanz P et al. Neurology 2017.

The JAMA Network



Association Between Midlife Vascular Risk Factors and Estimated Brain Amyloid Deposition

Gottesman RF, et al. JAMA. 2017;317(14):1443-1450. doi:10.1001/jama.2017.3090



Associations Between Midlife Vascular Risk Factors and Global Cortex Florbetapir SUVRs >1.2.

In individuals without dementia from 3 US communities, a cumulative number of midlife vascular risk factors was associated with elevated brain amyloid. Relationships did not differ by race or carrier status of *APOE* ε4 allele.

These data support the concept that midlife, but not late-life, exposure to these vascular risk factors is important for amyloid deposition.

From: **The Prevention of Dementia With Antihypertensive Treatment: New Evidence From the Systolic Hypertension in Europe (Syst-Eur) Study**

Arch Intern Med. 2002;162(18):2046-2052. doi:10.1001/archinte.162.18.2046

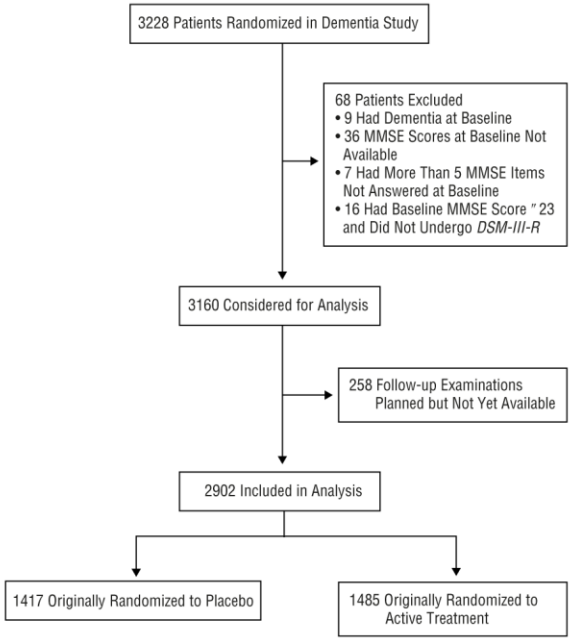


Figure Legend:

Study profile. MMSE indicates Mini-Mental State Examination; DSM-III-R, Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition.

From: **The Prevention of Dementia With Antihypertensive Treatment: New Evidence From the Systolic Hypertension in Europe (Syst-Eur) Study**

Arch Intern Med. 2002;162(18):2046-2052. doi:10.1001/archinte.162.18.2046

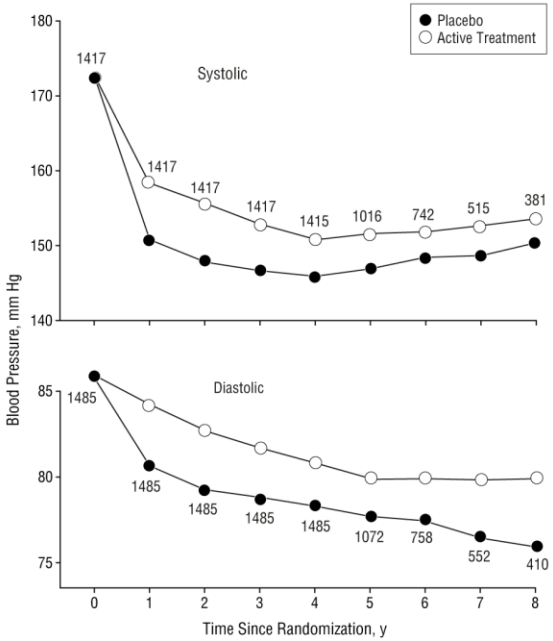


Figure Legend:

Average sitting systolic and diastolic blood pressure at randomization and during follow-up. For each mean value, the number of patients is given.

From: **The Prevention of Dementia With Antihypertensive Treatment: New Evidence From the Systolic Hypertension in Europe (Syst-Eur) Study**

Arch Intern Med. 2002;162(18):2046-2052. doi:10.1001/archinte.162.18.2046

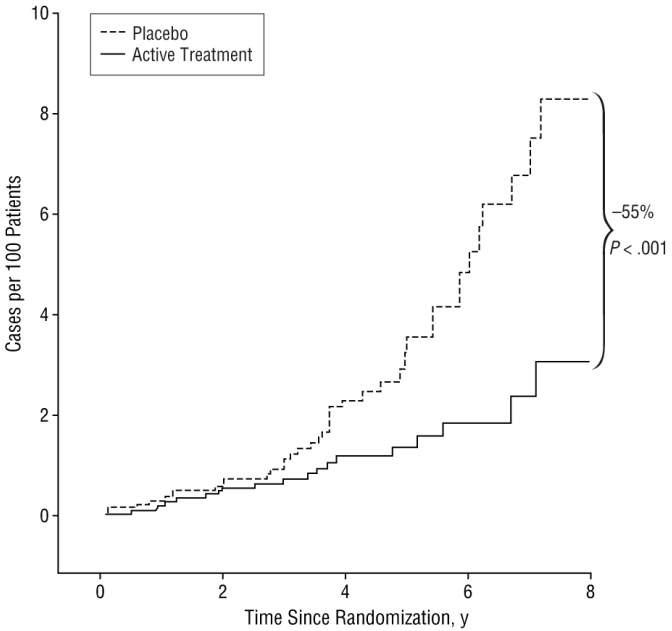


Figure Legend:

Culmulative rate of dementia by treatment group.

Reductions in BP associated with less cognitive decline

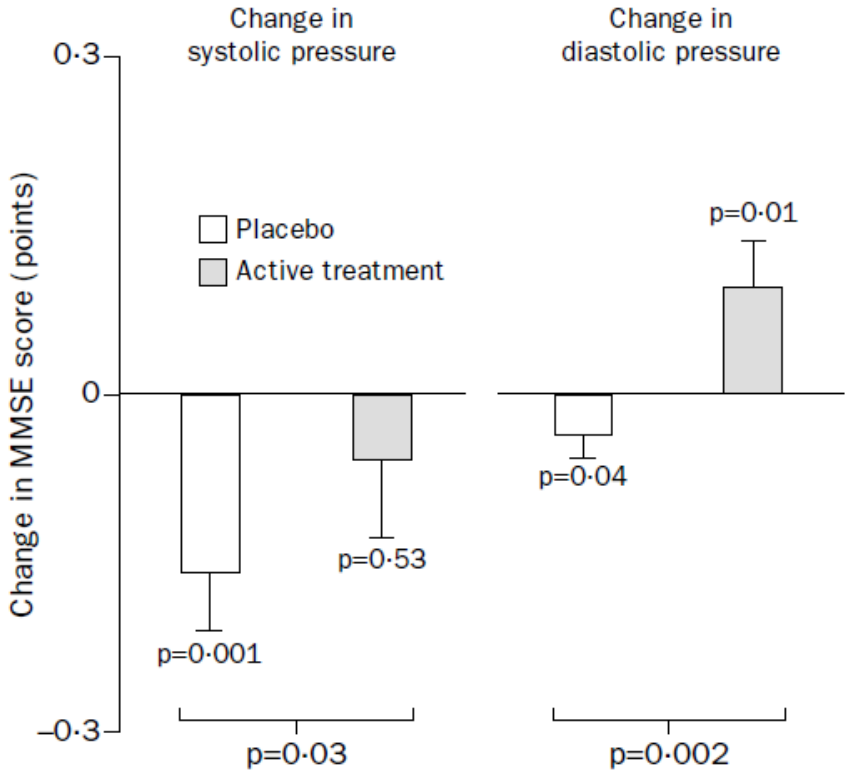


Figure 3: **Changes in MMSE score associated with mean decrease in systolic and diastolic blood pressure in placebo and active treatment groups**

Association sizes adjusted for sex, age, educational level, previous cardiovascular complications, antihypertensive treatment before enrolment, smoking, and alcohol consumption at randomisation.

Forette F et al. Syst-Eur trial. Lancet 1998;352(9137):1347-51.

JAMA Network™

From: **Effect of Intensive vs Standard Blood Pressure Control on Probable Dementia: A Randomized Clinical Trial**

JAMA. 2019;321(6):553-561.

Intensive blood pressure control (<120 mm Hg systolic) reduced incidence of MCI and of Probable Dementia or Mild Cognitive Impairment

Table 2. Incidence of Probable Dementia and Mild Cognitive Impairment by Treatment Group

	Treatment Group					
	Intensive		Standard			
Outcomes	No. With Outcome/Person-Years	Cases per 1000 Person-Years	No. With Outcome/Person-Years	Cases per 1000 Person-Years	Hazard Ratio (95% CI)[a]	*P* Value
Probable dementia	149/20 569	7.2	176/20 378	8.6	0.83 (0.67-1.04)	.10
Mild cognitive impairment[b]	287/19 690	14.6	353/19 281	18.3	0.81 (0.69-0.95)	.007
Composite of mild cognitive impairment or probable dementia	402/19 873	20.2	469/19 488	24.1	0.85 (0.74-0.97)	.01

[a] Intensive treatment group vs standard treatment group based on Cox proportional hazards regression.

[b] Participants adjudicated as having probable dementia at the first follow-up visit (year 2) do not contribute to the analyses of mild cognitive impairment.

Source: SPRINT Mind investigators for the SPRINT Research Group et al. 2019; *JAMA*

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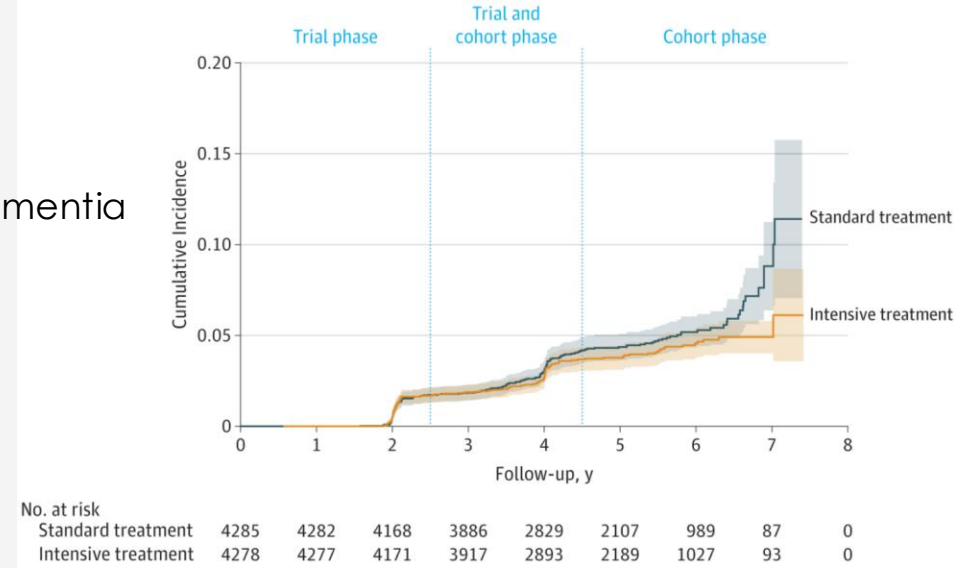
Probable dementia



HR 0.83,
95% CI 0.67-1.04;
P=0.10

Probable Dementia by Treatment GroupShaded regions indicate 95% confidence intervals. Median follow-up time was 5.14 years (interquartile range, 3.91-6.00) for the intensive treatment group and 5.07 years (interquartile range, 3.87-5.98) for the standard treatment group. For group comparison of incidence, hazard ratio, 0.83; 95% CI, 0.67-1.04; P=.10.

Source: SPRINT Mind investigators for the SPRINT Research Group et al. 2019; JAMA

From: **Association of Blood Pressure Lowering With Incident Dementia or Cognitive Impairment: A Systematic Review and Meta-analysis**

JAMA. 2020;323(19):1934-1944. doi:10.1001/jama.2020.4249

Study	Participants with dementia or cognitive impairment/total No.		Absolute risk reduction (95% CI), %	Odds ratio (95% CI)	Weight, %
	Blood pressure lowering group	Control group			
Dementia (criterion-referenced)					
SHEP,[22] 1994	37/2365	44/2371	0.29 (-0.45 to 1.03)	0.84 (0.54 to 1.31)	1.69
PROGRESS,[23] 2003	193/3051	217/3054	0.78 (-0.48 to 2.04)	0.88 (0.72 to 1.08)	8.14
Syst-Eur,[5] 2002	21/1485	43/1417	1.62 (0.54 to 2.70)	0.46 (0.27 to 0.78)	1.18
SCOPE,[24] 2003	62/2477	57/2460	-0.19 (-1.04 to 0.67)	1.08 (0.75 to 1.56)	2.48
HYVET-COG,[6] 2008	126/1687	137/1649	0.84 (-0.99 to 2.67)	0.89 (0.69 to 1.15)	5.17
ADVANCE,[25] 2009	39/5569	37/5571	-0.04 (-0.34 to 0.27)	1.05 (0.67 to 1.66)	1.61
SPRINT MIND,[12] 2019	149/4278	176/4285	0.62 (-0.18 to 1.43)	0.84 (0.67 to 1.05)	6.64
Random-effects model for subgroup ($Q_6 = 7.92$; $P = .24$; $I^2 = 0.0\%$)				0.87 (0.78 to 0.97)	
Dementia (clinical-based)					
PRoFESS,[26] 2008	408/8624	409/8646	0.00 (-0.63 to 0.63)	1.00 (0.87 to 1.15)	16.62
HOPE-3,[13] 2019	10/811	6/815	-0.50 (-1.46 to 0.46)	1.68 (0.61 to 4.65)	0.32
Random-effects model for subgroup ($Q_1 = 0.99$; $P = .32$; $I^2 = 0.0\%$)				1.01 (0.88 to 1.16)	
Dementia and mild cognitive impairment (composite)					
TRANSCEND,[7] 2011[a]	239/2694	245/2689	0.24 (-1.29 to 1.77)	0.97 (0.81 to 1.17)	9.41
ON TARGET (Dual),[7] 2011[a]	618/7807	326/3932.5	0.37 (-0.68 to 1.42)	0.95 (0.83 to 1.09)	16.75
ON TARGET (ARB),[7] 2011[a]	584/7797	326/3932.5	0.80 (-0.24 to 1.84)	0.90 (0.78 to 1.03)	16.44
SPS3,[27] 2014[a]	506/1323	535/1345	1.53 (-2.17 to 5.23)	0.94 (0.80 to 1.10)	13.55
Random-effects model for subgroup ($Q_3 = 0.57$; $P = .90$; $I^2 = 0.0\%$)				0.93 (0.87 to 1.01)	
Test for overall effect: $z = -2.50$; $P = .01$			0.39 (0.09 to 0.68)	0.93 (0.88 to 0.98)	
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 12.14$; $P = .43$; $I^2 = 0.0\%$					

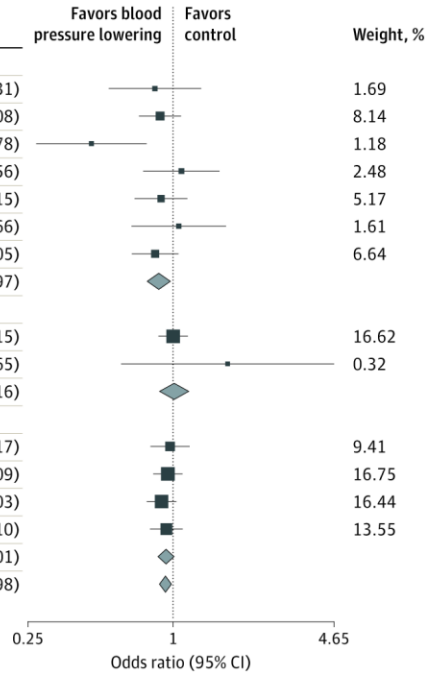


Figure Legend:

Association of Blood Pressure Lowering With Dementia or Cognitive Impairment The squares and bars represent the mean values and 95% CIs of the effect sizes and the area of the squares reflects the weight of the studies. Diamonds represent the combined effects and the vertical dotted line represents the line of no association.

[a]Composite of dementia and cognitive impairment.

From: **Association of Blood Pressure Lowering With Incident Dementia or Cognitive Impairment: A Systematic Review and Meta-analysis**

JAMA. 2020;323(19):1934-1944. doi:10.1001/jama.2020.4249

Subgroup	No. of events/total No.		Absolute risk reduction (95% CI), %	Odds ratio (95% CI)
	Blood pressure lowering group	Control group		
Blood pressure lowering and dementia or cognitive impairment				
Overall	2992/49 968	2558/42 167	0.39 (0.09 to 0.68)	0.93 (0.88 to 0.98)
Cumulative systolic blood pressure change				
Above median	1032/14 189	1152/14 121	0.81 (0.20 to 1.40)	0.88 (0.80 to 0.96)
Below median	1960/35 779	1406/28 046	0.19 (-0.20 to 0.54)	0.96 (0.90 to 1.03)
Baseline systolic blood pressure				
Above median	478/16 634	535/16 522	0.37 (0.01 to 0.74)	0.88 (0.78 to 1.00)
Below median	2514/33 334	2023/25 645	0.39 (-0.03 to 0.82)	0.94 (0.88 to 1.00)
Blood pressure lowering and cognitive decline				
Overall	5513/37 504	4468/29 972	0. 71 (0.19 to 1.20)	0.93 (0.88 to 0.99)
Cumulative systolic blood pressure change				
Above median	2427/17 358	2617/17 321	1.10 (0.50 to 1.80)	0.89 (0.82 to 0.96)
Below median	3086/20 146	1851/12 651	0.21 (-0.60 to 1.00)	0.98 (0.92 to 1.05)
Baseline systolic blood pressure				
Above median	1669/14 746	1777/14 681	0.82 (0.10 to 1.50)	0.92 (0.85 to 0.99)
Below median	3844/22 758	2691/15 291	0.62 (-0.10 to 1.40)	0.94 (0.85 to 1.04)

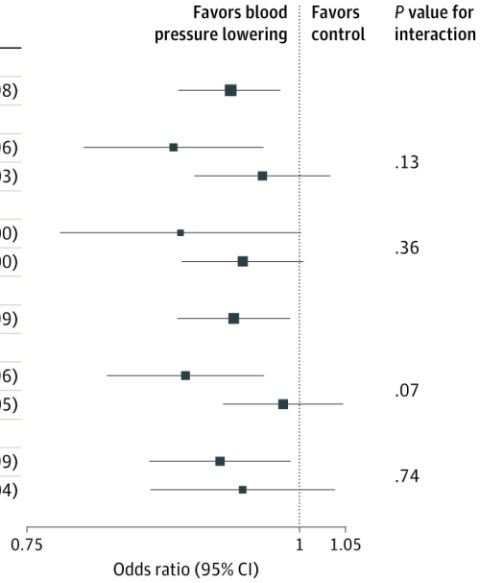


Figure Legend:

Association of Blood Pressure Lowering With Dementia or Cognitive Impairment/Decline by Cumulative Systolic Blood Pressure Change and Baseline Systolic Blood PressureThe squares and bars represent the mean values and 95% CIs of the effect sizes and the area of the squares reflects the weight of the studies. The vertical dotted line represents the line of no association.

From: **Association of Blood Pressure Lowering With Incident Dementia or Cognitive Impairment: A Systematic Review and Meta-analysis**

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Study	Participants with dementia or cognitive impairment/total No.		Absolute risk reduction (95% CI), %	Odds ratio (95% CI)
	Blood pressure lowering group	Control group		
PROGRESS,[23] 2003	276/3051	334/3054	1.89 (0.39 to 3.39)	0.81 (0.68 to 0.96)
SCOPE,[24] 2003	113/2477	125/2460	0.52 (-0.68 to 1.71)	0.89 (0.69 to 1.16)
HYVET-COG,[6] 2008	485/1687	486/1649	0.72 (-2.36 to 3.81)	0.97 (0.83 to 1.12)
PRoFESS,[26] 2008	795/7531	832/7518	0.51 (-0.48 to 1.50)	0.95 (0.86 to 1.05)
TRANSCEND,[7] 2011[a]	454/2642	412/2589	-1.27 (-3.28 to 0.74)	1.10 (0.95 to 1.27)
ON TARGET (Dual),[7] 2011	1240/7461	657/3801	0.67 (-0.80 to 2.13)	0.95 (0.86 to 1.06)
ON TARGET (ARB),[7] 2011	1279/7566	657/3801	0.38 (-1.09 to 1.85)	0.97 (0.88 to 1.08)
SPRINT MIND,[12] 2019	287/4278	353/4285	1.53 (0.42 to 2.64)	0.80 (0.68 to 0.94)
HOPE-3,[13] 2019	584/811	612/815	3.08 (-1.20 to 7.37)	0.85 (0.68 to 1.06)
Test for overall effect: $z = -2.28$; $P = .02$ Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 12.60$; $P = .13$; $I^2 = 36.1\%$			0.71 (0.19 to 1.2)	0.93 (0.88 to 0.99)

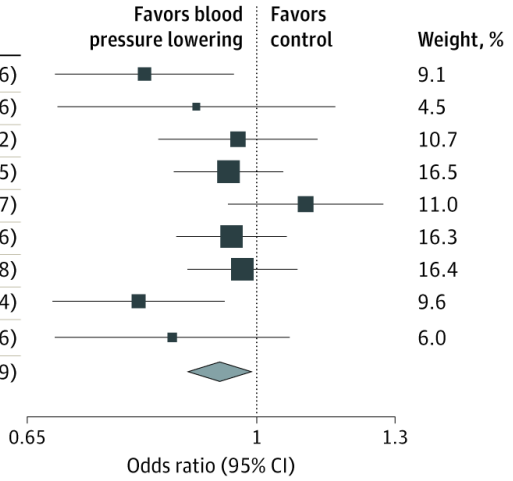

Figure Legend:

Association of Blood Pressure Lowering and Cognitive DeclineThe squares and bars represent the mean values and 95% CIs of the effect sizes and the area of the squares reflects the weight of the studies. The diamond represents the combined effect and the vertical dotted line represents the line of no association.