

"[B]rain health should be as much on people's minds as heart health, breast cancer, and the war on smoking have been for decades."

Former U.S. Surgeons General, Drs. Richard Carmona, Joycelyn Elders, Antonia Novello and David Satcher, "U.S. Surgeons General: Dementia Is Our Top Public Health Crisis. Commentary." *Orlando Sentinel*, October 10, 2019.

Reducing cognitive impairment is a public health imperative because the prevalence of dementia may nearly triple by midcentury as the baby-boom generation ages. Hypertension prevention and management should be part of that population-level response. Hypertension is a risk factor not only for stroke and heart disease, but also for cognitive impairment, including vascular dementia.

One-third of U.S. adults has hypertension^{a,2} and another third has prehypertension.^{b,3} Thus, addressing high blood pressure — by preventing, delaying, or managing hypertension — has noteworthy potential for reducing the incidence of cognitive impairment. In particular, prevention of stroke and management of high blood pressure may reduce the risk of progression from mild cognitive impairment (MCI) to dementia.⁴

Further, addressing hypertension and other cardiovascular risk factors is essential to maintaining and promoting "brain health," the concept of making the most of the brain's capacity to remember, learn, play, concentrate, and maintain a clear, active mind.⁵ Brain health contributes to quality of life and optimal cognitive functioning throughout the lifespan. More and more evidence demonstrates that a healthy brain needs a healthy heart.

While research must continue to reveal the heart-brain relationship, one facet of this connection — high blood pressure — is actionable now. Public health has helped stem the tide of other chronic conditions (notably heart disease, diabetes, and HIV/AIDS) through comprehensive risk reduction strategies. The application of similar strategies to avert and control hypertension early and continuously across the lifespan has the potential to prevent stroke and related cognitive impairment and improve and maintain brain health at a population level.

^a Defined as systolic blood pressure of 140 mm Hg or above, or diastolic blood pressure of 90 mm Hg or above, or currently taking medication to lower blood pressure.

Defined as blood pressure readings that are higher than normal, but not yet in the high blood pressure range.

EXPLORING THE HEART-BRAIN CONNECTION:

THE RELATIONSHIP BETWEEN VASCULAR AND COGNITIVE HEALTH

The heart and brain are so closely linked that the conditions that damage or harm one can affect the other. When blood enters the brain, a complex network of blood vessels delivers oxygen and nutrients to brain cells. High blood pressure can damage, scar, and narrow these vessels over time. Eventually, parts of the brain may become damaged as well, lacking access to oxygen and nutrients. This damage may begin in midlife (ages 45-65) and eventually may be associated with memory and movement problems related to dementia. In fact, experts have long recognized the relationship between vascular brain

pathology — including damage to the cerebrovascular network — and syndromes of cognitive decline and dementia.⁶

Dementia — the term used to describe symptoms characterized by the loss of cognitive function — is a chronic condition, usually caused by disorders that progressively damage and eventually destroy brain cells. Dementia develops along a continuum (see Figure 1). Alzheimer's is the most common cause of dementia, while vascular dementia is the second most common cause.¹

FIGURE 1: LIFE COURSE PERSPECTIVE ON ALZHEIMER'S AND OTHER DEMENTIAS⁵



Dementia occurs along a continuum. Although most older adults have healthy cognitive functioning, some will experience pre-symptomatic changes in the brain that may eventually lead to cognitive impairment or dementia. In dementia, symptoms become noticeable and the disruption to cognition and everyday life can range from mild to severe.

Many changes in the brain associated with dementia are now known to occur years, sometimes decades, before clinical symptoms develop. Blood vessels in the brain are particularly susceptible to damage due to high blood pressure, and this damage increases the risk for stroke and may increase the risk of dementia. Preventing, delaying, and managing hypertension and chronic conditions that damage blood vessels or block blood flow to the brain may help protect the brain and reduce the risk of future cognitive impairment.

Increasingly, many dementia cases are recognized as "mixed-cause" — such as a combination of Alzheimer's-vascular dementia or frontotemporal-vascular dementia. Autopsy studies report that about 40 percent of people who had the brain changes of Alzheimer's on autopsy also had the brain changes of vascular dementia, while only about 10 percent of brains from individuals with dementia show evidence of vascular dementia alone. ¹

The location, number, and size of brain injuries — whether caused by hypertension, stroke, or another source — determine whether vascular dementia will develop and how an individual's thinking and physical functioning may be impaired. Initial symptoms of vascular dementia are more likely to be impaired judgment and decision-making, rather than the memory loss associated with Alzheimer's. In addition to changes in cognitive functioning, vascular dementia can also impact movement, gait and balance.¹

While hypertension is a modifiable risk factor for dementia for much of the lifespan, late-life hypertension onset — when hypertension develops at age 80 or older — has been associated with a decreased risk of dementia. More research is needed to understand why the effects of some modifiable risk factors may change with age.

THE HEART-BRAIN CONNECTION:

DEMENTIA, HYPERTENSION AND STROKE IN THE UNITED STATES

Damage to the cerebrovascular system — the heart-brain connection — affects millions of Americans and is a leading cause of disability and death in the United States.

Alzheimer's, Dementia and Other Cognitive Impairment

In 2019, more than 5 million Americans were living with Alzheimer's dementia, including 10 percent of all Americans aged 65 and older. Prevalence projections estimate that by 2050, the number of Americans with Alzheimer's may reach 14 million.

Millions more are estimated to have mild cognitive impairment (MCI) — 11.6 million in 2018.9 And, in 2017, over 38 million Americans aged 30 and older were estimated to have elevated levels of beta-amyloid in their brains without any symptoms of cognitive impairment — a proposed preclinical stage of Alzheimer's.10

Most of these individuals with non-dementia cognitive impairment will not, in fact, develop dementia. However, these individuals are at greater risk of developing dementia than those without any cognitive impairment. For these individuals, risk reduction interventions may have the most pronounced effects, helping to delay or stall progression from MCI to dementia.

Hypertension

Prevalence estimates of hypertension among adults in the United States range from 75 million³ to 103 million.¹¹ These estimates represent one-third to one-half of all American adults. Additionally, another third of U.S. adults are estimated to have prehypertension³ — blood pressure readings that are higher than normal, but are not yet hypertensive. Prehypertension is a risk factor for later developing chronic high blood pressure.

Hypertension prevalence is even higher among older adults. Among adults aged 60 and older, two-thirds of U.S. adults are hypertensive¹¹ while three-fourths aged 80 and older have hypertension.¹² On average, only about half of adults with hypertension have their

condition controlled.¹³ And, large disparities exist among racial, ethnic, and national origin groups. For example, African Americans are more likely than their white peers to have hypertension (40.3 percent versus 27.8 percent, respectively, in 2015-2016)¹⁴ and American Indian/Alaska Native adults were 30% more likely to have hypertension than non-Hispanic white adults in 2004-2008.¹⁵ Management of hypertension also displays stark disparities: African Americans, Hispanic Americans, and Asian Americans are all less likely to have their high blood pressure controlled compared with white Americans.¹⁴

Stroke

Hypertension is a risk factor for all forms of stroke. Every year, 795,000 strokes occur in the United States. 11 Of these, nearly one in four occur in people who have had a previous stroke. 11 The vast majority (about 85 percent) of strokes are ischemic 16 — when blood flow through an artery in the brain becomes blocked, often due to a blood clot. Transient ischemic attacks (TIA) are also caused by blockage, but symptoms last less than 24 hours before disappearing. Both types of strokes are associated with vascular dementia. 17

In addition, about half of older individuals with Alzheimer's have pathologic evidence of silent strokes (also known as silent cerebral infarction). Silent strokes can damage the brain even when they do not induce other typical symptoms of stroke (such as confusion, slurred speech, or motor difficulty). Silent strokes increase the risk of having a symptomatic stroke in the future, and the cumulative damage from multiple silent strokes may increase the risk of vascular dementia.



Association of Subjective Cognitive Decline and Hypertension

National prevalence estimates of the number of Americans living with dementia, MCI, and elevated beta-amyloid levels who also have hypertension are not yet published. However, a population-based, nationwide proxy is available: subjective cognitive decline (SCD). SCD is the self-reported experience of worsening or more frequent confusion or memory loss.²⁰ It is one of the earliest noticeable warning signs of Alzheimer's disease and other dementias.²¹

In 2015, 58.8 percent of adults aged 45 and older who reported SCD also reported having high blood pressure (Table 1). c,22 Both SCD and hypertension increase the risk of later developing dementia, and

individuals reporting both conditions may be at an even higher risk.

Association of Dementia and Stroke

At the population-level, stroke doubles the chance of developing dementia.²³ There are many mechanisms that may influence this risk — including stroke type, dementia type, and underlying pathophysiology — and researchers do not yet fully understand the connection between stroke and dementia.²⁴ Nonetheless, since up to an estimated 90 percent of strokes are preventable,^{25,26} mitigating stroke risk across a population provides a promising opportunity to reduce the rates of both stroke and dementia. Hypertension management is one of the best-established stroke prevention strategies.²⁴

HYPERTENSION AND SCD PREVALENCE, SELECTED STATES 2015 BRFSS C.22

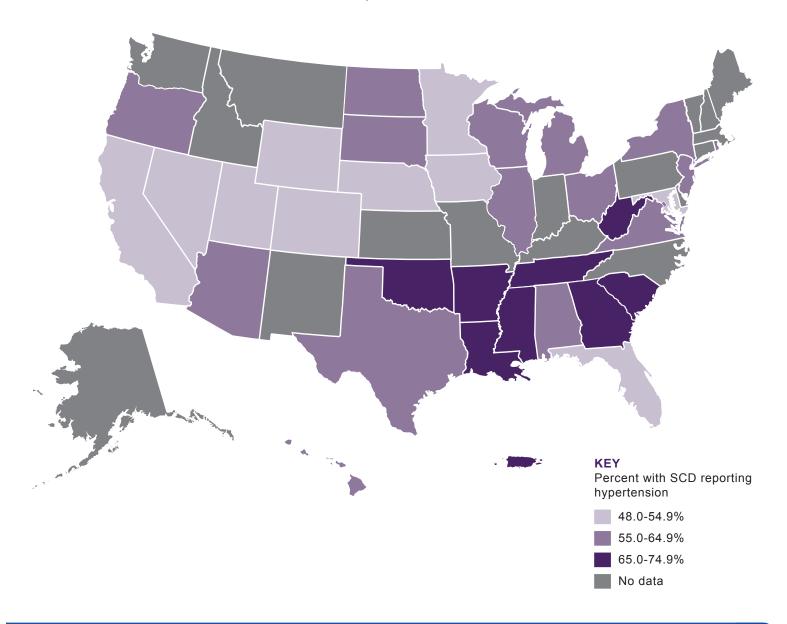


TABLE 1: Hypertension and Subjective Cognitive Decline (SCD) Prevalence, Selected States 2015 (Behaviorial Risk Factor Surveillance System)^{c,22}

State	Percent Reporting Subjective Cognitive Decline	Percent Reporting Hypertension	Percent With Subjective Cognitive Decline Reporting Hypertension
Alabama	12.9%	57.9%	63.5%
Arizona	13.4%	45.6%	57.6%
Arkansas	16.2%	56.7%	66.3%
California	11.7%	41.3%	48.9%
Colorado	10.8%	38.5%	48.0%
District of Columbia	12.1%	49.5%	63.5%
Florida	11.3%	47.0%	54.3%
Georgia	14.0%	55.2%	74.8%
Hawaii	8.9%	45.9%	60.7%
Illinois	9.6%	48.5%	57.9%
lowa	9.3%	45.5%	49.8%
Louisiana	14.6%	58.0%	68.4%
Maryland	10.6%	47.9%	53.0%
Michigan	12.1%	48.7%	62.8%
Minnesota	8.7%	40.4%	52.6%
Mississippi	12.9%	61.3%	71.9%
Nebraska	9.4%	46.6%	54.9%
Nevada	16.3%	43.5%	52.5%
New Jersey	9.1%	46.3%	56.7%
New York	11.1%	46.9%	59.0%
North Dakota	9.9%	48.3%	60.3%
Ohio	10.7%	49.4%	61.8%
Oklahoma	13.6%	55.0%	66.4%
Oregon	13.0%	44.5%	55.1%
Puerto Rico	6.6%	61.1%	69.4%
Rhode Island	11.5%	49.0%	55.7%
South Carolina	12.1%	55.2%	68.5%
South Dakota	6.0%	45.1%	62.2%
Tennessee	13.3%	56.6%	72.5%
Texas	13.1%	47.7%	59.6%
Utah	11.0%	39.6%	53.2%
Virginia	8.9%	48.6%	60.5%
West Virginia	10.0%	57.3%	66.3%
Wisconsin	10.9%	43.8%	58.5%
Wyoming	11.2%	44.6%	53.4%
Aggregate	11.5%	47.8%	58.8%

Source: Unpublished tabulations by the Alzheimer's Association based on data from the 2015 Behavioral Risk Factor Surveillance System from 33 states, the District of Columbia (D.C.), and Puerto Rico. Aggregate is of the 33 states, D.C., and Puerto Rico.

e Hypertension and subjective cognitive decline data are intermittently collected by the Behavioral Risk Factor Surveillance System (the former collected every other year and the latter at states' discretion); 2015 is the most recent year with the largest number of states collecting these data.

GROWING EVIDENCE:

HYPERTENSION AND THE RISK OF COGNITIVE DECLINE

Researchers do not yet fully understand what causes Alzheimer's and which specific actions may prevent dementia. However, the existing evidence base is sufficient to support addressing hypertension as a viable intervention strategy.^{27,28}

Intervention Potential

Results from the Systolic Blood Pressure Intervention Trial (SPRINT) Memory and Cognition in Decreased Hypertension (MIND) study show that the risk of developing mild cognitive impairment (MCI) among older adults can be significantly reduced through intensive blood pressure control. Older adults (aged 50 and older) who maintained a lower systolic blood pressure (targeted to be ≤120 mm Hg) had a 19 percent lower rate of developing MCI than older adults with a higher systolic blood pressure (targeted to be ≤140 mm Hg).²⁹

SPRINT is a randomized clinical trial examining older adults at increased risk for cardiovascular disease, but who have not been diagnosed with diabetes, dementia, or previous stroke. One-third of the participants were African American and 10 percent were Hispanic.³⁰ Using a combination of antihypertensive medications, researchers examined differences between the lower, intensive blood pressure goal and a higher, standard target goal.

In 2019, a meta-analysis examined the connection between incident dementia and the use of antihypertensive medications.³¹ Among individuals with high blood pressure, those using antihypertensive medications had a reduced risk of later developing dementia compared with those who did not use these medications. For individuals with normal blood pressure, no effect was found through antihypertensive medication use suggesting that the benefit is related to hypertension.

In 2017, the Lancet Commission on Dementia Prevention, Intervention and Care issued a comprehensive set of recommendations, based on its own evidence review. The global results estimated that the population attributable fraction — the proportion of cases in a population attributable to a

specific risk factor — of hypertension in midlife (ages 45-65) is as much as 5 percent of all-cause dementia. In response, the Commission recommends treating hypertension both in midlife (age 45-65 years) and in later life (age 65+) to reduce future dementia risk.

Other meta-reviews have examined hypertension as a modifiable risk factor for cognitive decline and dementia. Together, they largely support increased attention to hypertension as a modifiable risk factor for cognitive decline and potentially dementia across populations (see Appendix for additional detail).

Aligning with this evidence, research from 2019 indicates that sustained hypertension in midlife to late-life as well as a pattern of midlife hypertension and late-life hypotension^d were associated with increased risk for subsequent dementia when compared with normal blood pressure throughout midlife and late-life.³²

Lastly, many risk factors for developing hypertension are also risk factors for cognitive decline. These include smoking, diabetes, and obesity. Primary, secondary, and tertiary prevention efforts for these modifiable risk factors may reduce the risk of both hypertension and cognitive decline.

Research Outlook

Current research studies may further add to the existing, actionable evidence base that managing midlife hypertension can reduce the risk of future cognitive decline.

A two-year continuation of the SPRINT MIND study — called SPRINT MIND 2.0 — is further investigating the impact of intensive blood pressure treatment on reducing the risk of dementia. The additional two years will continue clinical follow-up with the SPRINT MIND participants to gather additional evidence on the interaction between hypertension intervention and future cognition.

Additionally, a two-year clinical trial called the U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk (U.S. POINTER) aims to evaluate whether lifestyle interventions that

^d Defined as systolic blood pressure of 90 mm Hg or below, or diastolic blood pressure of 60 mm Hg or below.

simultaneously target several risk factors can protect cognitive function in older adults who are at an increased risk for cognitive decline. Interventions include physical exercise, nutritional counseling and modification, cognitive and social stimulation, and improved self-management of health status, including blood pressure management. The study began participant recruitment in 2018.

THE PUBLIC HEALTH RESPONSE:

POPULATION-LEVEL ACTION TO REDUCE RISK OF COGNITIVE DECLINE

Hypertension prevention and management across the lifespan is an emerging opportunity for public health practitioners to pursue reductions in population-level risk of cognitive decline throughout their communities. The first priority should be populations most at risk of hypertension and dementia.

State and local public health agencies have existing, often deep, capacity and expertise in promoting cardiovascular health, helping the public understand and manage heart health, educating healthcare providers, and increasing the adoption of clinical best practices. The Healthy Brain Initiative's <u>State and Local Public Health Partnerships to Address Dementia, The 2018-2023 Road Map (HBI Road Map)</u> calls for integrating cognitive health into ongoing public health efforts. Integration then provides a foundation for public health practitioners to alter policies, systems, and environments to reduce risk for cognitive decline and impairment.

A companion guide from the Healthy Brain Initiative

— <u>The Road Map for Indian Country</u> — is designed for public health systems serving American Indian and Alaska Native (AI/AN) communities.³³ As a population with a high burden of hypertension, AI/AN communities may benefit greatly from public health efforts focused on their unique strengths, needs, and considerations.

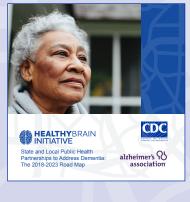
The HBI Road Map provides expert-guided actions for state and local public health agencies to address dementia. Mapped to Essential Services of Public Health, the following HBI Road Map actions (see Table 2) can serve as a starting point for public health engagement on hypertension and risk reduction for cognitive decline. The final column of Table 2 corresponds to tools and other resources (detailed in Table 3) that public health professionals can use to implement the actions.

FROM THE HEALTHY BRAIN INITIATIVE

Designed for state and local public health practitioners, the *State and Local Public Health Partnerships to Address Dementia: The 2018-2023 Road Map* encourages 25 actions that help promote brain health, address cognitive impairment, and support the needs of caregivers.

Designed for American Indian/Alaska Native (AI/AN) communities, the *Road Map for Indian Country* is a guide for AI/AN leaders to learn about Alzheimer's and begin planning their response to dementia.

Learn more at alz.org/publichealth



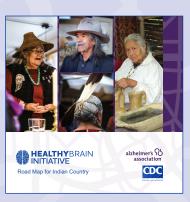


TABLE 2: HBI Road Map Actions Related to the Heart-Brain Connection and Resources to Support Implementation

HBI Road Map Action		Resource Letter
EDUCATE & EMPOWER		
E-2	Integrate the best available evidence about brain health and cognitive decline risk factors into existing health communications that promote health and chronic condition management for people across the life span.	A, B, D
E-7	Improve access to and use of evidence-informed interventions, services, and supports for people with dementia and their caregivers to enhance their health, well-being, and independence.	A, G

DEVELOP POLICIES & MOBILIZE PARTNERSHIPS		
P-1	Promote the use of effective interventions and best practices to protect brain health, address cognitive impairment, and help meet the needs of caregivers for people with dementia.	A, D, E, F
P-2	Assure academic programs, professional associations, and accreditation and certification entities incorporate the best available science about brain health, cognitive impairment, and dementia caregiving into training for the current and future public health workforces.	E, F

ASSURE A COMPETENT WORKFORCE		
W-1	Educate public health and healthcare professionals on sources of reliable information about brain health and ways to use the information to inform those they serve.	A, B, C, D, E, F, G
W-3	Educate public health professionals about the best available evidence on dementia (including detection) and dementia caregiving, the role of public health, and sources of information, tools, and assistance to support public health action.	A, E, F, G
W-6	Educate healthcare professionals about the importance of treating co-morbidities, addressing injury risks, and attending to behavioral health needs among people at all stages of dementia.	A, E, F, G

MONITOR & EVALUATE		
M-3	Use data gleaned through available surveillance strategies and other sources to inform the public health program and policy response to cognitive health, impairment, and caregiving.	G

RESOURCES AND TOOLS

The following free resources are available to help public health professionals address hypertension management as a reasonable and practicable means of reducing risk for cognitive decline. The resource letters correspond to HBI Road Map actions from Table 2.

TABLE 3: Resources to Support Public Health Action on Hypertension to Reduce Risk of Cognitive Decline	
Resource Letter	Resource Author and Description

Resource Letter	Resource Author and Description
A	Mind Your Risks National Institute of Neurological Disorders and Stroke (NINDS) Available at: mindyourrisks.nih.gov
	This public health campaign aims to educate health professionals and people with high blood pressure about the importance of controlling blood pressure, particularly in midlife, to reduce the risk of having a stroke and possibly developing dementia later in life. The campaign includes print and social media materials as well as the latest scientific research on high blood pressure and dementia.
	Take Brain Health to Heart South Carolina Department of Health and Environmental Control Available here
В	This public awareness campaign about brain health focuses on the heart-brain connection including how to control hypertension. The campaign also includes information for the public about the intersection between stroke and brain health. Read the <u>case study</u> for additional information about the development of this campaign.
С	Risk Reduction Messaging for Health Education Alzheimer's Association Available here
	Readymade messages about risk reduction of cognitive decline that can be easily incorporated into existing public health campaigns about hypertension as well as other chronic conditions.
D	Healthy Heart, Healthy Brain Association of State and Territorial Health Officials (ASTHO), International Association for Indigenous Aging (IA²) Available at: astho.org/Healthy-Aging/Healthy-Heart-Healthy-Brain/
	A series of communication materials tailored for American Indian and Alaska Native (AI/AN) communities. These materials emphasize the connection between heart health and brain health — including hypertension — and feature (1) radio PSAs, posters and fliers intended for community-wide distribution; (2) videos that can be shown in clinical settings; and (3) a guide for healthcare providers with culturally-appropriate messaging.

Resource Letter	Resource Author and Description
E	Brain Health – Benefits of Blood Pressure Management as a Potential Mechanism to Reduce the Risk of Cognitive Decline and Dementia American College of Preventive Medicine (ACPM) Available here
	This 1.5-hour continuing education module discusses the benefits of blood pressure management to reduce cognitive decline and dementia. The module is designed for physicians, but applicable for nurses, physician assistants, and other allied health professionals. It is offered as part of ACPM's <u>Lifestyle Medicine Core Competencies Program</u> , and those who complete the module will be eligible for 1.5 hours of continuing medical education (CME) or maintenance of certification (MOC) credits.
	ACPM's <u>Brain Health</u> landing page contains additional resources including educational resources, provider tools, and caregiver materials.
F	Clinical Practice Guidelines for the Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults American College of Cardiology, American Heart Association Available here
	These 2017 clinical care guidelines provide target recommendations for adult blood pressure management and care. The guidelines include a recommendation of lowering high blood pressure among adults with hypertension as a reasonable way to prevent cognitive decline. These guidelines were informed in part by results from the Systolic Blood Pressure Intervention Trial (SPRINT) study.
G	Accelerate Risk Reduction and Promote Brain Health Alzheimer's Association Available at: alz.org/professionals/public-health/core-areas/brain-health-risk-reduction
	This online portal includes information, resources, and examples of public health strategies to reduce the risk of cognitive decline. Find additional research and state-specific actions, too.

APPENDIX — META-REVIEWS

Several large meta-reviews have reported on the connection between hypertension and risk of cognitive decline. While some reviews are older, they provided insights that later studies — including SPRINT MIND - further investigated. These meta-reviews, listed below, found varying evidence about the effectiveness of hypertension management as a risk reduction intervention for cognitive decline in part because of methodological differences. Scientists involved in the reviews noted the difficulty of determining the impact of hypertension treatment on cognitive decline since many studies included for meta-review were not specifically designed to detect cognitive effects. Additionally, many studies lacked specific trial parameters to control for potential confounding as many risk factors for developing hypertension are also risk factors for cognitive decline (including smoking, diabetes, and obesity). This is why studies with strong trial design and parameters — like SPRINT MIND and SPRINT MIND 2.0 — are so valuable.

The reviews listed below serve as an entry point for understanding risk reduction research. These evidence reviews align with population data that new cases of dementia — particularly in developed Western societies — have declined over the past several decades. Increasing levels of education, reduced incidence of cardiovascular and cerebrovascular diseases, and improved control of cardiovascular risk factors — especially smoking, stroke, and diabetes — are attributed to this lower dementia incidence rate.

- Preventing Cognitive Decline and Dementia:
 A Way Forward from the National Academies of Science, Engineering, and Medicine (2017)³⁶ this report suggests that while the evidence is inconsistent, observational data support the management of hypertension as a plausible intervention for reducing dementia.
- Interventions to Prevent Age-Related Cognitive Decline, Mild Cognitive Impairment, and Clinical

- Alzheimer's-Type Dementia from the Agency for Healthcare Research and Quality (2017)³⁷ this evidence review examined 16 random controlled trials of blood pressure management interventions among hypertensive populations. The review found generally low evidence that hypertension management was beneficial as a means to reduce the risk of cognitive decline and dementia. However, the review noted that all RCTs examined were not primarily designed to detect the effect of blood pressure management on dementia incidence.
- Summary of the evidence on modifiable risk factors for cognitive decline and dementia:
 A population-based perspective from the Alzheimer's Association (2015)²⁷ this meta-analysis found that management of mid-life hypertension can reduce the risk of cognitive decline, but did not find as strong of a connection between hypertension and future dementia risk.
- Cognitive Aging: Progress in Understanding and Opportunities for Action from the National Academies of Science, Engineering, and Medicine (2015)³⁸ (published as the Institute of Medicine) — this report notes that while there is no certain cognitive benefit of hypertension treatment, blood pressure management can help reduce the risk of heart attack and stroke (both of which are linked to cognitive decline).
- World Alzheimer Report: Dementia and Risk Reduction, An Analysis of Protective and Modifiable Factors from Alzheimer's Disease International (2014)³⁹ — this evidence review highlighted a strong association between mid-life hypertension and incident vascular dementia. The review notes that for other kinds of dementia, especially Alzheimer's dementia, the evidence is weak.

ACKNOWLEDGMENTS

Contributors to the development of this brief: Nancy Maddox, MPH, Maren Enterprises, Inc.; John Shean, MPH, Alzheimer's Association; Molly French, MS, Alzheimer's Association; and Raza Lamb, Alzheimer's Association. This issue brief is supported by Cooperative Agreement #5 NU58DP006115, funded by the Centers for Disease Control and Prevention. The findings and conclusions in this brief are those of the Alzheimer's Association and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the Department of Health and Human Services.

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