



Alzheimer's Disease and Other Related Dementias: REDUCING THE RISK OF COGNITIVE DECLINE AND DEMENTIA

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Disclosure



The Public Health Center of Excellence on Dementia Risk

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Center of Excellence on Risk Reduction



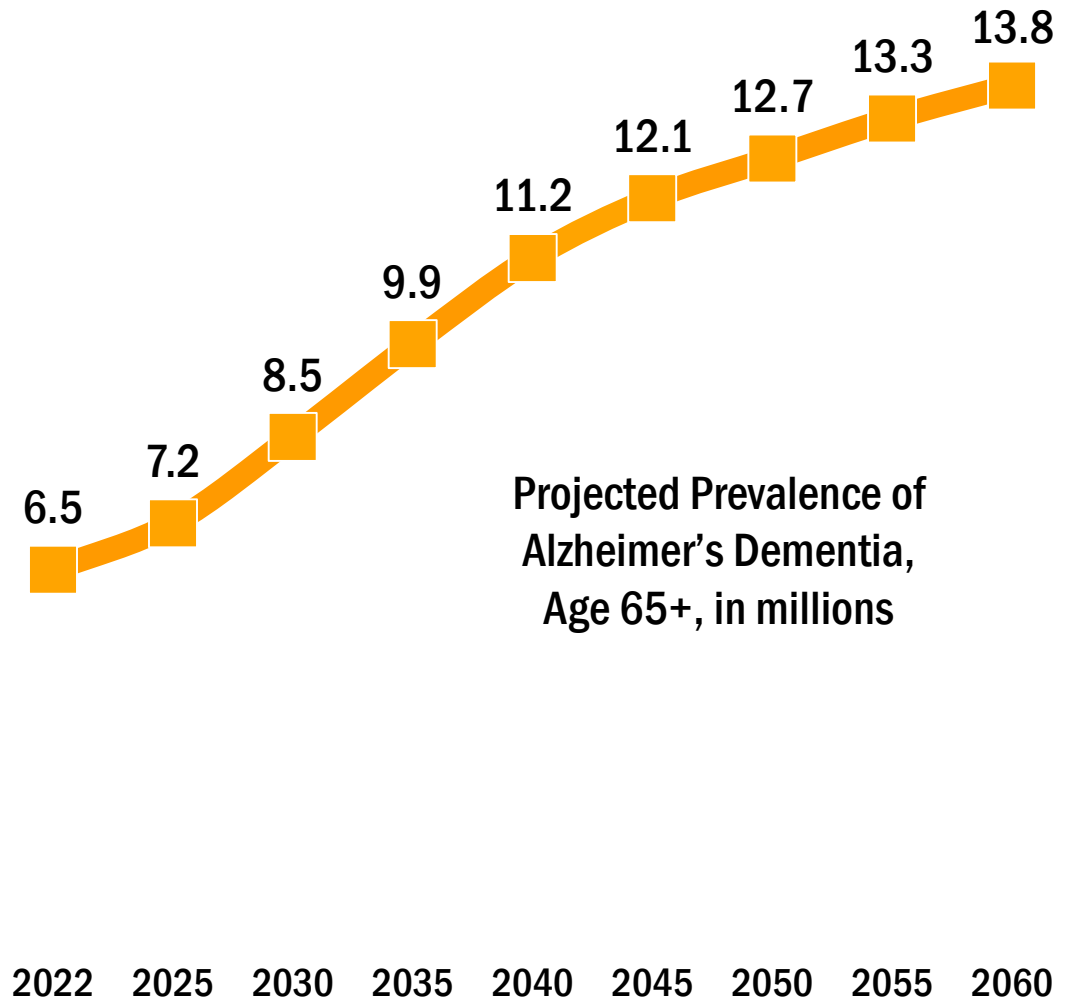
- Part of a broader effort created by Congress to expand public health efforts to address cognitive health and Alzheimer's
- One of three dementia Public Health Centers of Excellence named by the CDC
- Intended to provide state, local, and Tribal public health agencies the tools and resources necessary to act in the community



The Importance of Risk Reduction

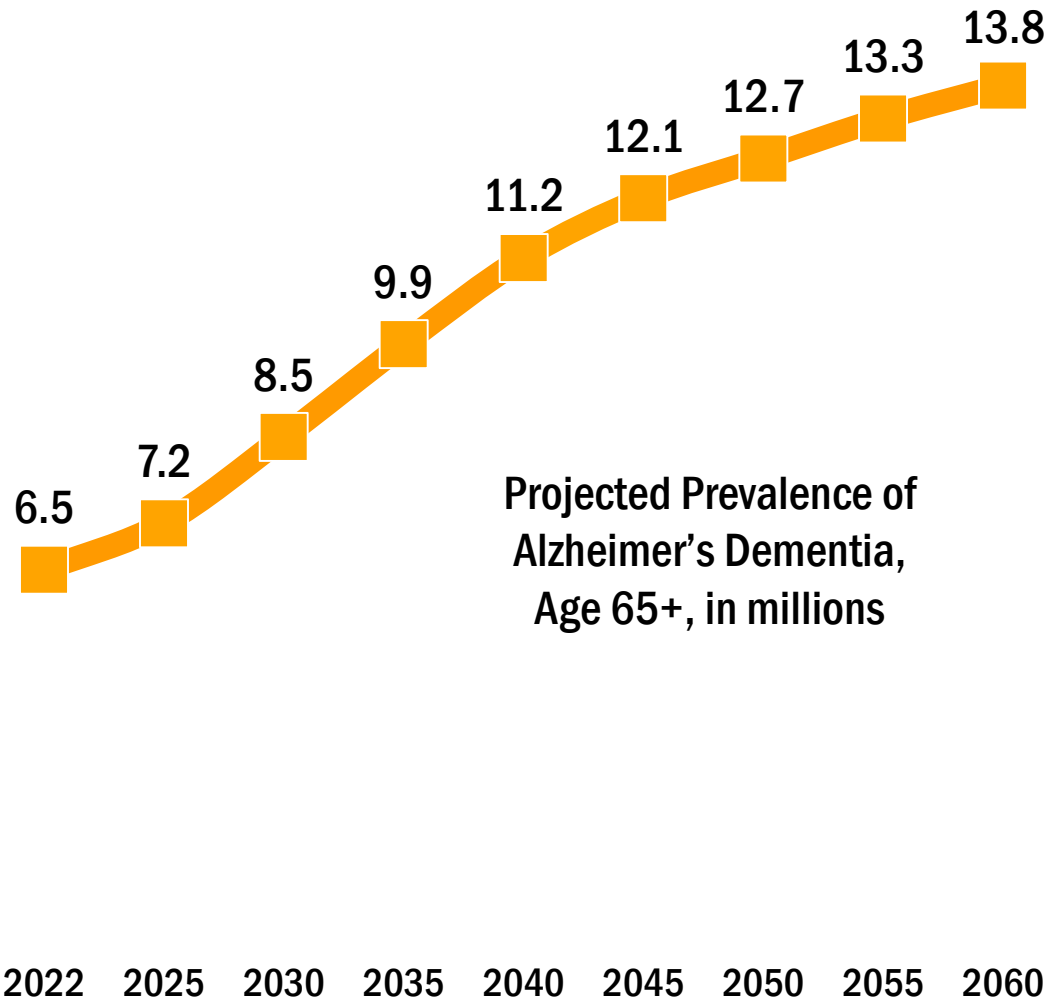
The Alzheimer's Tsunami

- More than 6 million Americans currently living with Alzheimer's
- Projected 75% increase in older adults by 2050, with 12 million more 85+
- In 2060, nearly 14 million living with Alzheimer's



Will the Tsunami Be Even Bigger?

- Projections based on studies of current (or recent) older Americans – a group that lived through a time of lower rates of obesity and diabetes



Projected Prevalence of Alzheimer's Dementia, Age 65+, in millions

- What happens to actual prevalence when a future cohort has higher rates?



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SAVING YOUR BRAIN



***PREVENTING ALZHEIMER'S
BEFORE IT'S TOO LATE***

By Matthew Baumgart

Don't Get Old!

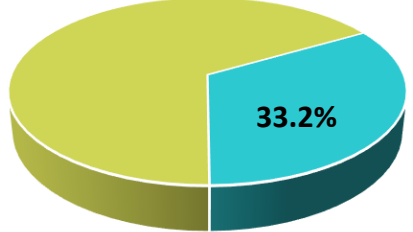
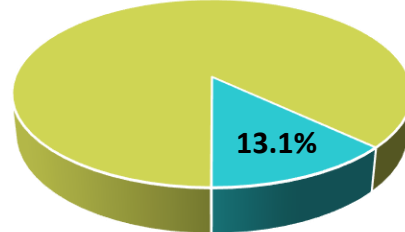
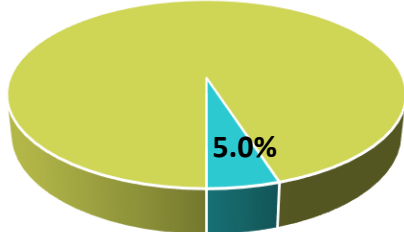




The Complex Reality

Unmodifiable Risk Factors

- Age



Prevalence, by Age Group:

Age 65-74

Age 75-84

Age 85+

- Family History



Accounts for <15% of known risk

- Genetics

- Apolipoprotein E ε4 allele
- Mutation/Trisomy 21



Estimated Percentage of Population with Forms of APOE Gene

e2/e2	0.5%	Elevated risk relative to e3/e3:
e2/e3	11%	
e2/e4	2%	3x
e3/e3	61%	--
e3/e4	23%	3x
e4/e4	2%	8-12x

Chance of Developing Alzheimer's with Mutation, by Gene

APP	100%
Presenilin 1	100%
Presenilin 2	95%

Percentage of Down Syndrome Cases with Alzheimer's, by Age

50s	~30%
60s	~50%

Modifiable Risk Factors



- In the vast majority of cases, Alzheimer's is a result of complex interactions among multiple factors
- While there are unmodifiable risk factors, there are also modifiable risk factors:
 - Certain medical conditions
 - Lifestyle behaviors
 - Social determinants of health
- According to the Lancet Commission, as many as 40% of dementia cases worldwide might be attributable to modifiable risk factors



Preliminary Points

Preliminary Points



- **Most evidence is population-based observational and epidemiological data, not randomized controlled trials**
- **There is a lot we are still learning – but there is sufficiently strong population-level evidence on some risk factors that we can no longer fail to act in the community**
- **Because this is not, by and large, evidence on a clinical level, you need to decide how best to use the evidence with your individual patients**
- **Be wary of shiny objects and easy answers**

A Little Help From My Friends



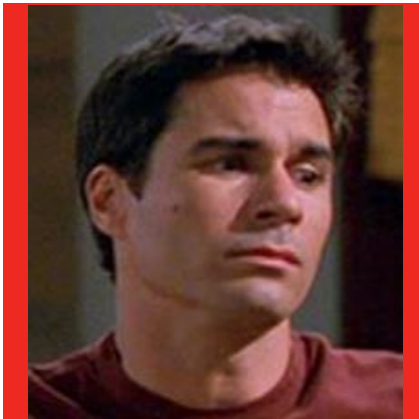
Will & Grace

WILL



The Beverly
Hillbillies

MAY



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WILL Affect Risk of Cognitive Decline and Dementia

Formal Education

- Years of formal education has some of the most consistent and strongest evidence as a protective factor against dementia
- Theory is that formal education builds “cognitive reserve”
- Fewer years of formal education is associated with lower socioeconomic status; lower education levels are also associated with less physical activity, more diabetes, more hypertension



Traumatic Brain Injury

- **Solid evidence that moderate and severe traumatic brain injury increases the risk of developing certain forms of dementia**
- **Repeated head injuries may increase risk even more**
- **Unclear what specific aspect of TBI leads to disrupted brain function**
- **May include damage to brain development, not just physical injury**





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WILL Affect Cognitive
Decline Risk and **MAY**
Affect Dementia Risk

Midlife Hypertension

- **Solid evidence that hypertension in midlife will increase risk of cognitive decline and possibly dementia**
- **Gold standard evidence, obtained in randomized controlled trials of diverse populations, that treating elevated blood pressure is a pathway to reducing cognitive impairment**
- **U.S. guideline is systolic blood pressure <130 mmHG – can be achieved in 90% of people with generic medications (SPRINT trial targeted <120 mmHG)**



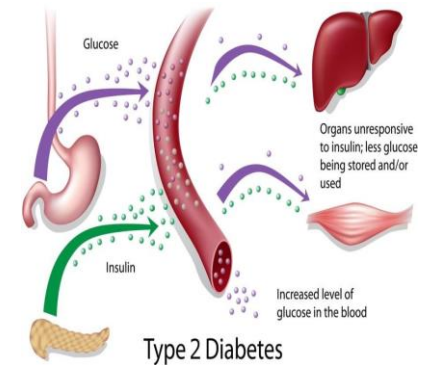
Midlife Obesity

- **Compelling evidence that midlife obesity increases risk for cognitive decline and possibly dementia**
- **Less compelling evidence that:**
 - Obesity is generally preventable long term
 - Treating obesity subsequently reduces risk
- **Relationship between obesity and cognitive decline/dementia is less clear with late-life obesity**



Diabetes

- **Compelling evidence that:**
 - Type 2 diabetes increases risk for cognitive decline and possibly dementia
 - Diabetes is preventable through lifestyle intervention



- **Risk may occur not only through vascular pathways but also through biological mechanisms related to diabetes itself**
- **Less compelling evidence that treating diabetes subsequently reduces risk**

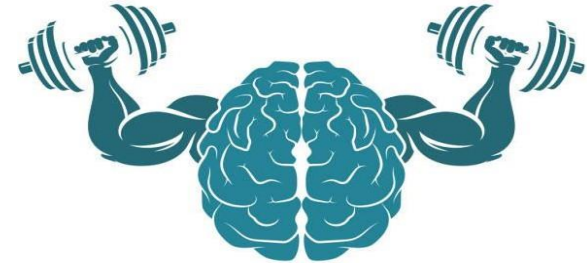
Current Smoking

- Strong evidence that smoking increases risk of cognitive decline and possibly dementia
- Some studies have suggested that heavy smoking in middle-age may double the risk for dementia later in life
- Smoking shortens survival among those with dementia
- Quitting smoking appears to reduce the associated risk to levels comparable to those who have never smoked



Physical Inactivity

- Growing evidence to support favorable effects of aerobic exercise on preserving cognition – and possibly dementia
- Studies consistently show exercise must be regular and more vigorous, but the exact “prescription” (i.e., duration, frequency, and intensity) is unclear
- Success of intervention strategy will depend on sustainability of delivery within the community



Poor Sleep

- Strong evidence for a risk relationship between poor sleep and cognitive decline and possibly dementia
- Exact nature of sleep problems (duration, disruptions, overall quality) and increased risk is the subject of ongoing study
- Lacking large trial data for sleep intervention strategies to reduce risk; existing interventions include some low-cost options
- Targeting sleep is beneficial for multiple organ systems





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MAY Affect Risk of Cognitive Decline

Diet and Nutrition

- **Healthy dietary factors are associated with better cognitive function and may reduce risk of cognitive decline**
- **Evidence supports a healthy dietary pattern over time**

(e.g. Mediterranean Diet, DASH Diet, MIND Diet) – but most recent evidence suggests key is balanced nutrition
- **Interpretation is tricky: dietary pattern is tied to other lifestyle factors and social determinants of health**
- **No effect seen for dietary supplements**



Cognitive Stimulation

- **Systematic reviews and RCTs show improvements in recall among those who undertake cognitive stimulation or training – and in the “trained” skill**
- **Most trials have been fairly small and many had inconclusive data**
- **The “recipe” for successful engagement/intervention is unknown**
- **Long-term effect on dementia risk is unclear**





A Few Others Often Mentioned

Lower Level or Unclear Evidence

- **Hearing Loss**: meta-analyses support a link
- **Air Pollution**: growing body of evidence; length of exposure, amount of exposure, age of exposure, etc. are still research questions
- **Depression**: does depression increase risk or is it an early marker of brain changes?
- **Hyperlipidemia**: unclear evidence of risk; inconsistent evidence on statins to reduce risk
- **Alcohol Abuse**: unclear evidence
- **Moderate Alcohol Use**: some evidence suggests it is associated with better brain health
- **Social Engagement**: seen as element of healthy aging in general



Multi-Factor Tactic

FINGER Study



- **Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER)**
- **Enrolled people with higher cardiovascular risk profiles**
- **Intervention involved physical activity, nutritional guidance, cognitive stimulation, social activities, and management of cardiovascular risk factors**
- **Cognitive performance and executive function improved significantly among those receiving the lifestyle intervention**

U.S. POINTER



- **U.S. Study to Protect Brain Health Through Lifestyle Intervention to Reduce Risk – to evaluate effect of multi-domain lifestyle intervention on cognitive function**
- **Six-site randomized controlled trial of 2,000 adults aged 60-79 through 2024**
- **Intervention of physical activity, diet, cognitive stimulation, and management of cardiovascular health**





To Summarize

The Scientific Conclusions

WILL



**AFFECT RISK OF COGNITIVE
DECLINE AND DEMENTIA**

➤ **Education**

➤ **TBI**

WILL



**AFFECT RISK OF
COGNITIVE DECLINE**

➤ **Midlife
Hypertension**

➤ **Physical
Inactivity**

MAY



AFFECT RISK OF DEMENTIA

➤ **Midlife Obesity**

➤ **Diabetes**

➤ **Smoking**

➤ **Poor Sleep**

MAY



**AFFECT RISK OF
COGNITIVE DECLINE**

➤ **Balanced
Nutrition**

➤ **Cognitive
Stimulation**

Key Takeaways

- What's good for your heart is good for your brain**

Current population-level evidence suggests risk for cognitive decline and possibly dementia can be reduced, especially by focusing on cardiovascular risk factors

Risk Factors for Cognitive Decline/Dementia

	Cognitive Decline	Dementia	Life's Essential 8 (AHA Heart Health)
Formal Education	WILL	WILL	
TBI	WILL	WILL	
Midlife Hypertension	WILL	MAY	✓
Midlife Obesity	WILL	MAY	✓
Diabetes	WILL	MAY	✓
Current Smoking	WILL	MAY	✓
Physical Inactivity	WILL	MAY	✓
Poor Sleep	WILL	MAY	✓
Diet/Nutrition	MAY	<i>Lower Level Evidence</i>	✓
Cognitive Stimulation	MAY	<i>Lower Level Evidence</i>	

Key Takeaways



- **What's good for your heart is good for your brain**

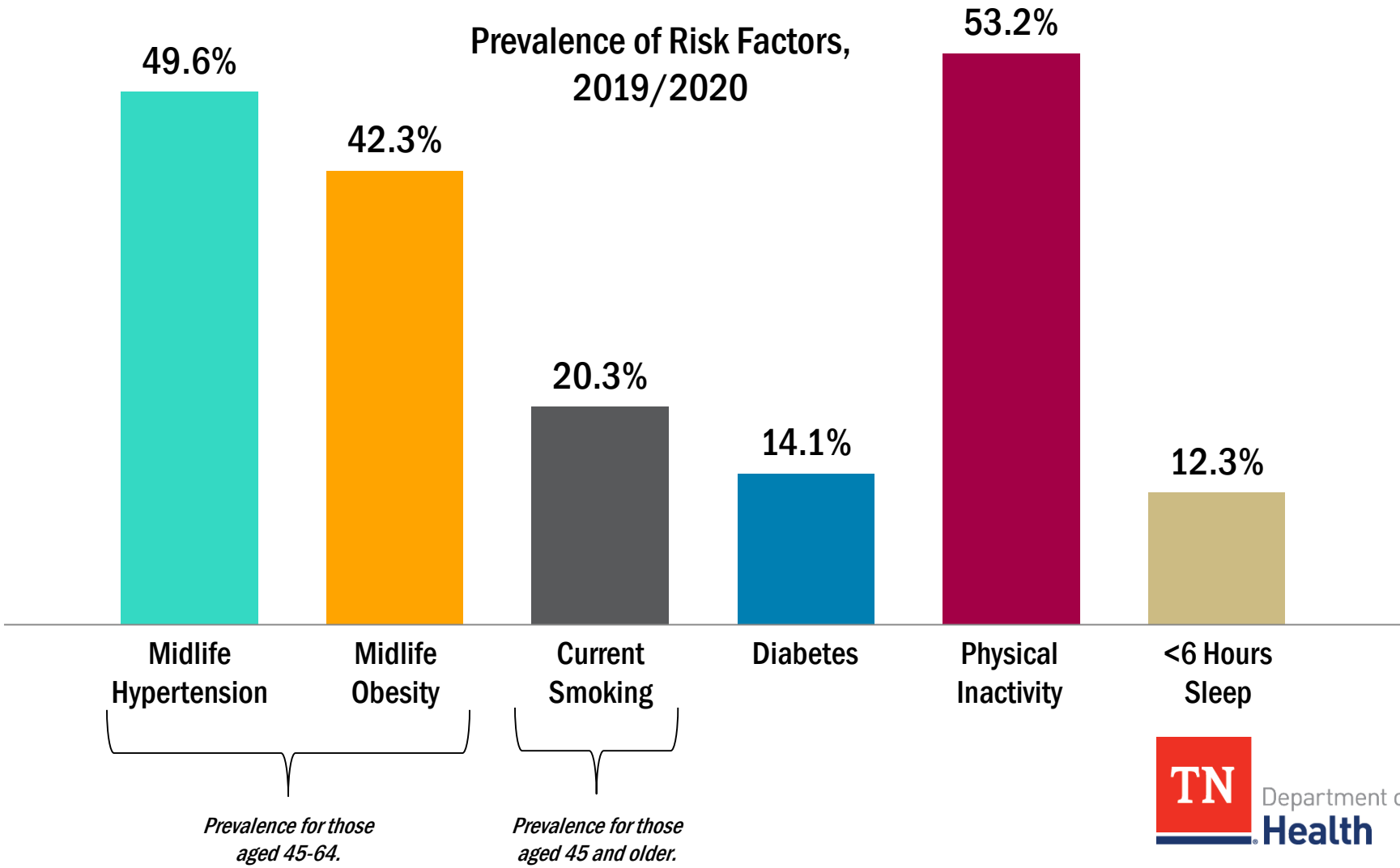
Current population-level evidence suggests risk for cognitive decline and possibly dementia can be reduced, especially by focusing on cardiovascular risk factors

- **The burden on communities can be reduced**

Risk Factor Prevalence in Tennessee



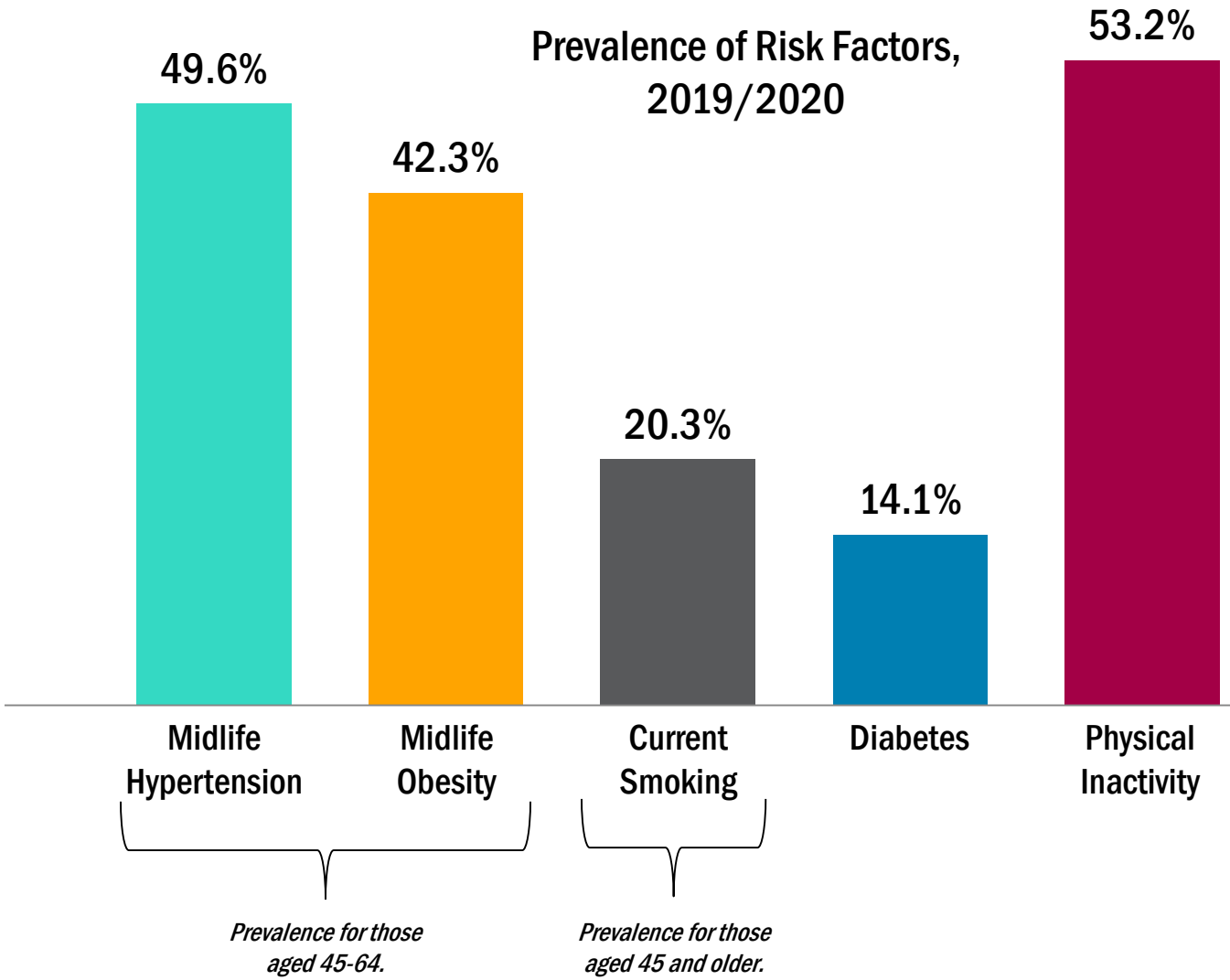
Prevalence of Risk Factors,
2019/2020



Risk Factor Prevalence in Tennessee



Prevalence of Risk Factors, 2019/2020



- 71% of adults have at least one of these risk factors; 37% have two or more
- 78% of Blacks have at least one; 43% have two or more

Key Takeaways

- What's good for your heart is good for your brain**

Current population-level evidence suggests risk for cognitive decline and possibly dementia can be reduced, especially by focusing on cardiovascular risk factors

- The burden on communities can be reduced**

An aggressive effort focused on dementia risk factors could reduce prevalence by more than 1 million Americans in 2050

Potential Effect of Risk Reduction Efforts

Unpublished analysis, 2017	5 risk factors	15% per decade improvement	~1.4 million fewer cases in 2050 than baseline
Unpublished analysis, 2018	5 risk factors	15% prevalence reduction over decade; 15% incidence reduction for additional decade	~1.1 fewer cases in 2050 than baseline
Norton, et al, 2014	7 risk factors	10% per decade improvement	~775,000 fewer cases in 2050 than baseline*
NAPA Advisory Council, 2021	8 risk factors	15% per decade improvement	~1.2 fewer cases in 2050 than baseline

*2050 baseline prevalence projection was 36% lower. Using the higher prevalence projection would have shown ~1.2 million fewer cases.



THANK YOU

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alz.org/publichealth