

# **Modifiable Risk Factors: How to Translate to Dementia Prevention?**

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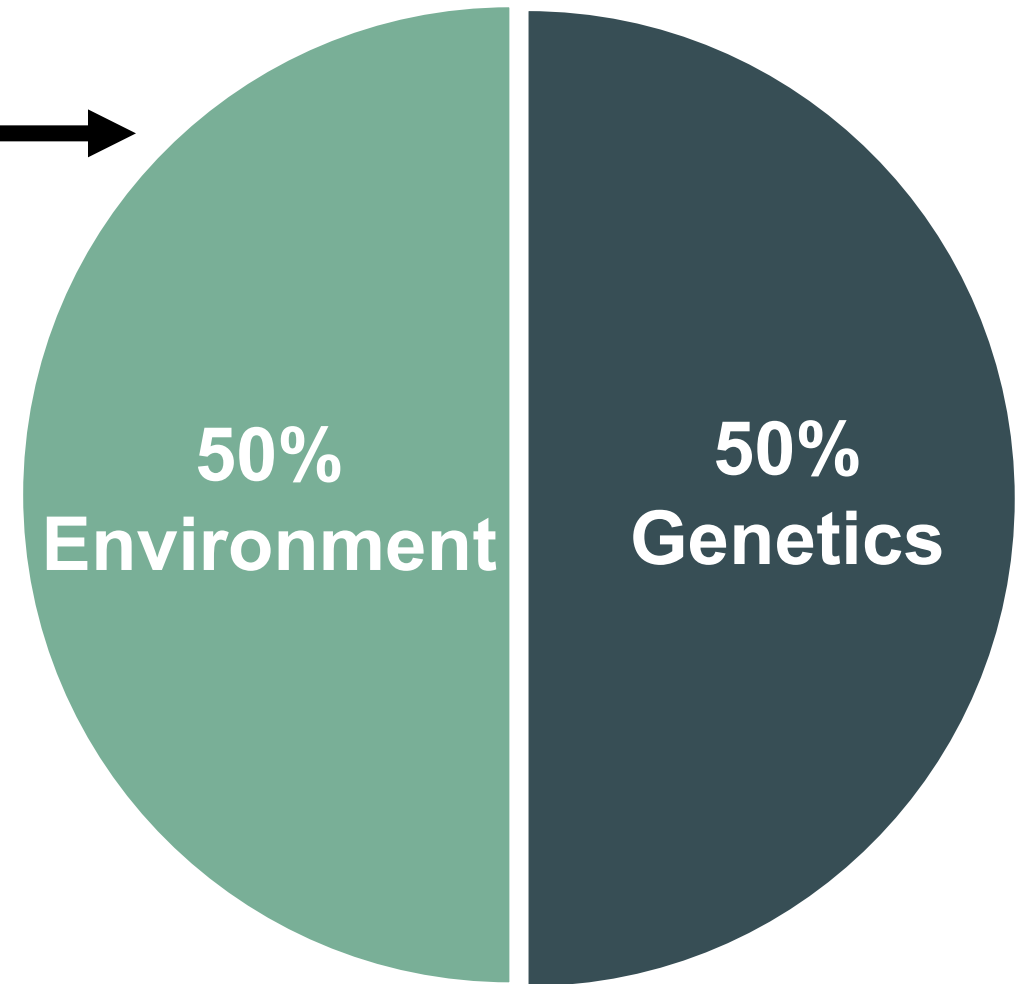
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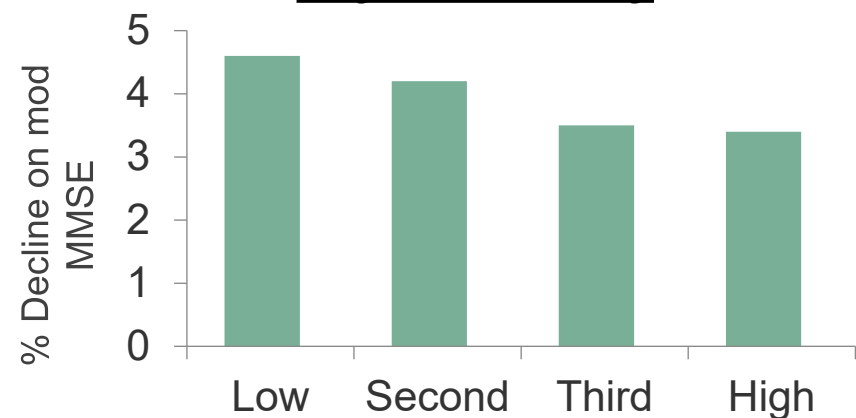
# Risk Factors for Dementia

- What can we do about this? →
- Efficacy and broad benefits of newest therapies are evolving
- US Adults are concerned about dementia
  - 48% say that they will likely have dementia
  - 84% say would change behavior if knew dementia risk and risk factors



# Tremendous Progress Identifying Modifiable Risk Factors

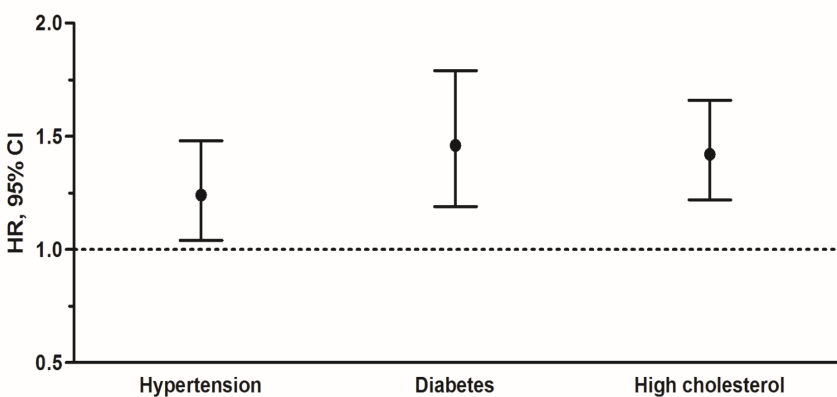
## Physical Activity



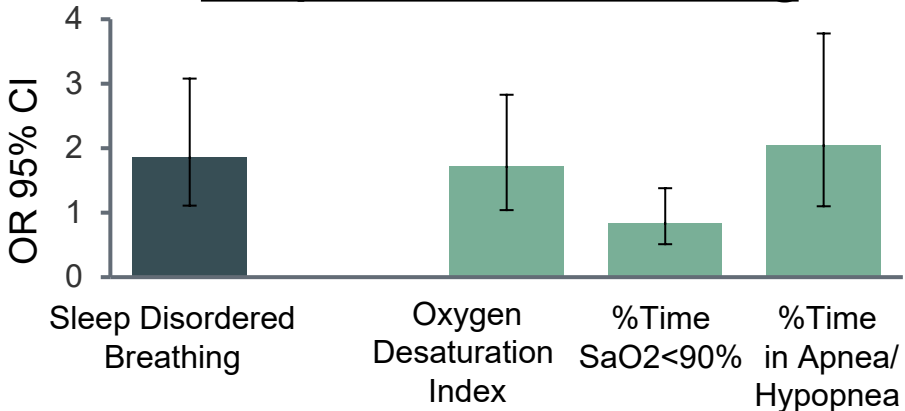
## Depression

| Number of Depressive Symptoms | Adjusted OR (95% CI) |               |
|-------------------------------|----------------------|---------------|
|                               | Cognitive Decline    | Dementia      |
| 0-2                           | 1.00                 | 1.00          |
| 3-5                           | 1.6 (1.2-2.1)        | 1.7 (0.9-3.5) |
| ≥6                            | 2.1 (1.4-3.1)        | 2.3 (0.9-5.9) |

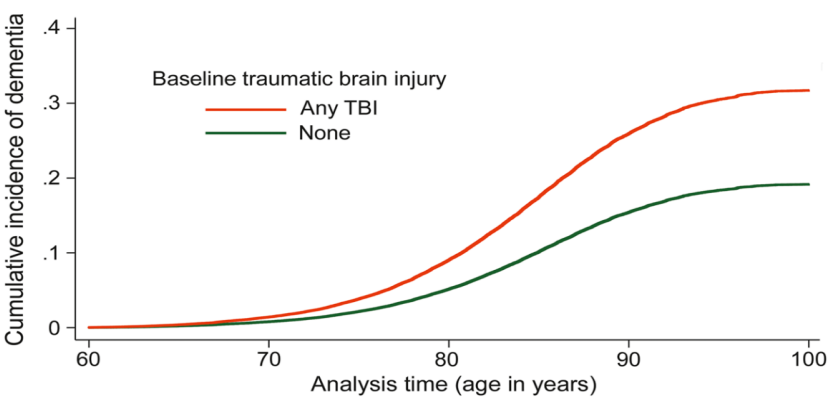
## Cardiovascular Risk Factors



## Sleep Disordered Breathing



## Traumatic Brain Injury



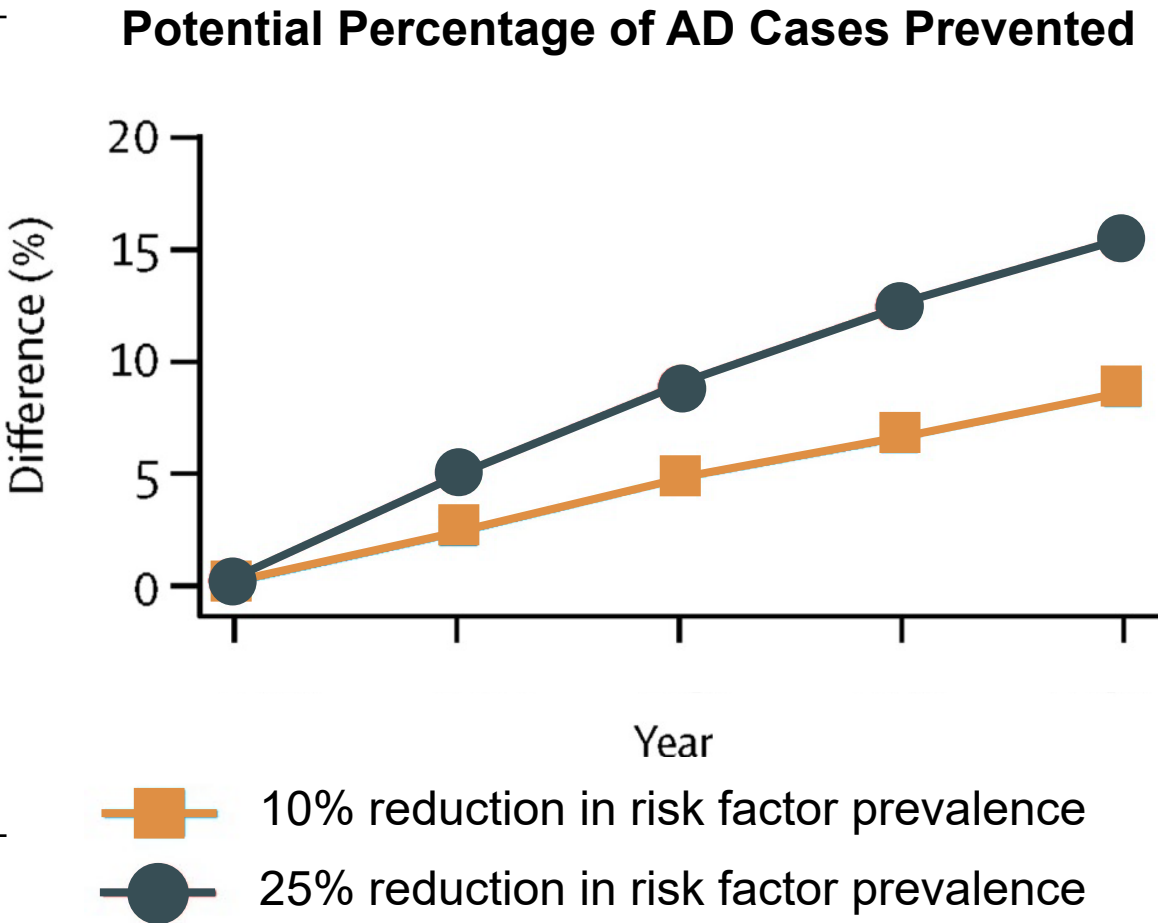
Yaffe et al, *Arch Intern Med*, 2001; Yaffe et al, *JAMA*, 2011; Yaffe et al, *Arch Gen Psychiatry*, 1999; Whitmer et al, *Neurology*, 2004; Barnes et al, *Neurology*, 2014.

# Connecting Risk Factors to Public Health Implications

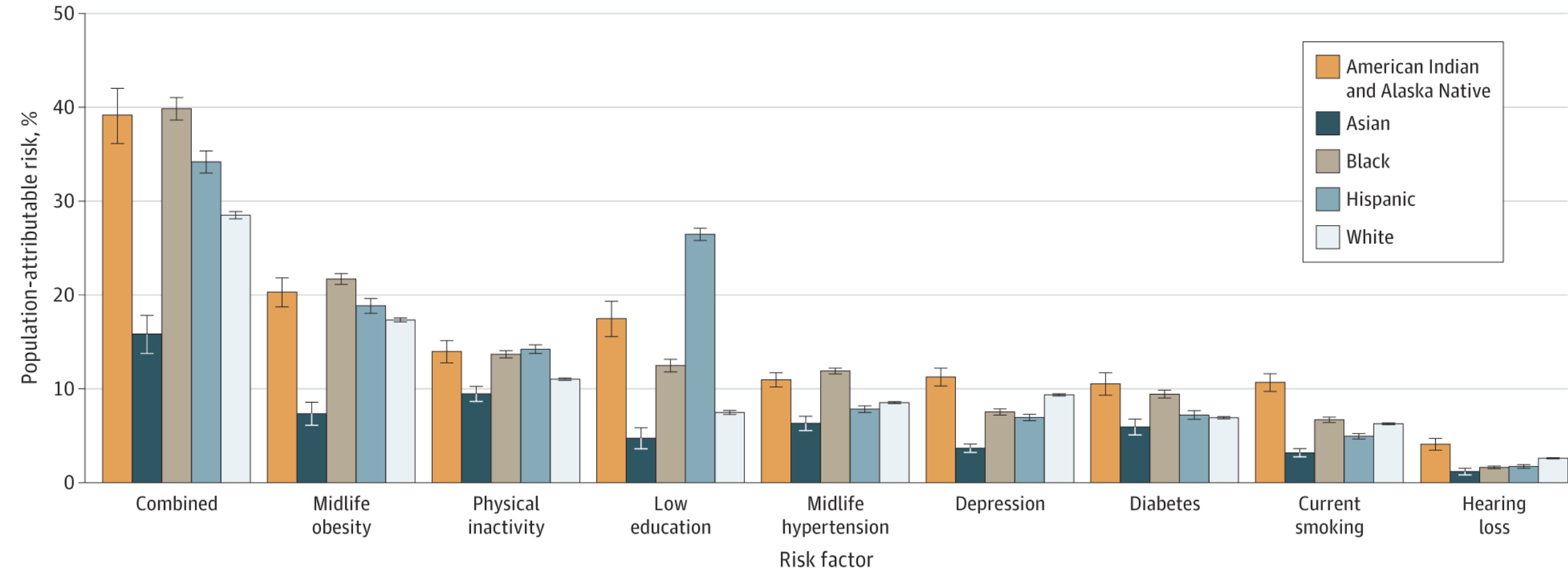
- Compelling evidence for several (not all) modifiable risk factors
- What is the potential impact on disease burden?
- But how does this translate to population-based prevention strategies?
- How to get at risk adults to change behavior?
- How to couple with pharmacological therapy?

# Up to 30% of Dementia Attributable to Modifiable Risk Factors

| Risk Factor           | Population Prevalence | Relative Risk (95% CI) | PAR % (Range) |
|-----------------------|-----------------------|------------------------|---------------|
| Low education         | 40%                   | 1.6 (1.4, 1.9)         | 19% (12-26%)  |
| Smoking               | 27%                   | 1.6 (1.2, 2.2)         | 14% (4-25%)   |
| Physical inactivity   | 18%                   | 1.8 (1.2, 2.8)         | 13% (3-24%)   |
| Depression            | 13%                   | 1.7 (1.4, 1.9)         | 8% (5-11%)    |
| Mid-life hypertension | 9%                    | 1.6 (1.2, 2.2)         | 5% (1-10%)    |
| Diabetes              | 6%                    | 1.5 (1.2, 1.8)         | 3% (1-5%)     |
| Mid-life obesity      | 3%                    | 1.6 (1.3, 1.9)         | 2% (1-3%)     |
| Combined (max.)       |                       |                        | 49%           |
| Combined (adj.)       |                       |                        | 28%           |



# Differences in the Potential of Modifiable Risk Factors By Race/Ethnicity, United States



# Modifiable Risk Factors and Individual Risk Reduction

Conventional intervention protocols may be difficult to implement, costly, and have low adherence... need to be pragmatic

**How do we get people to change their behaviors?**



Personalized, multidomain risk factor profiles and tailored intervention plans

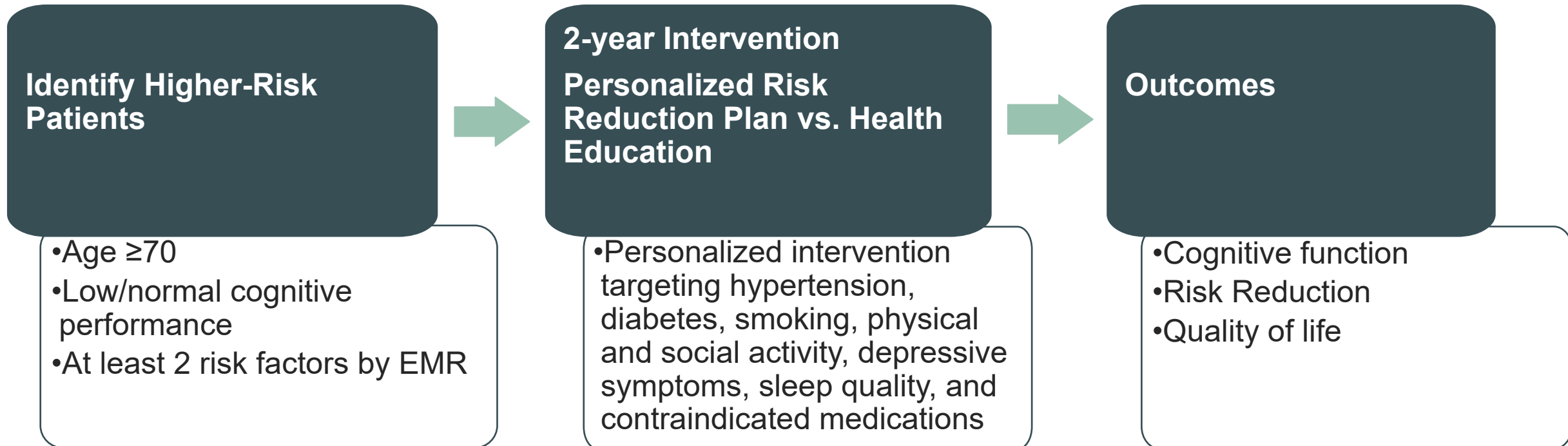


Changes in risk factors? Benefit in cognition?

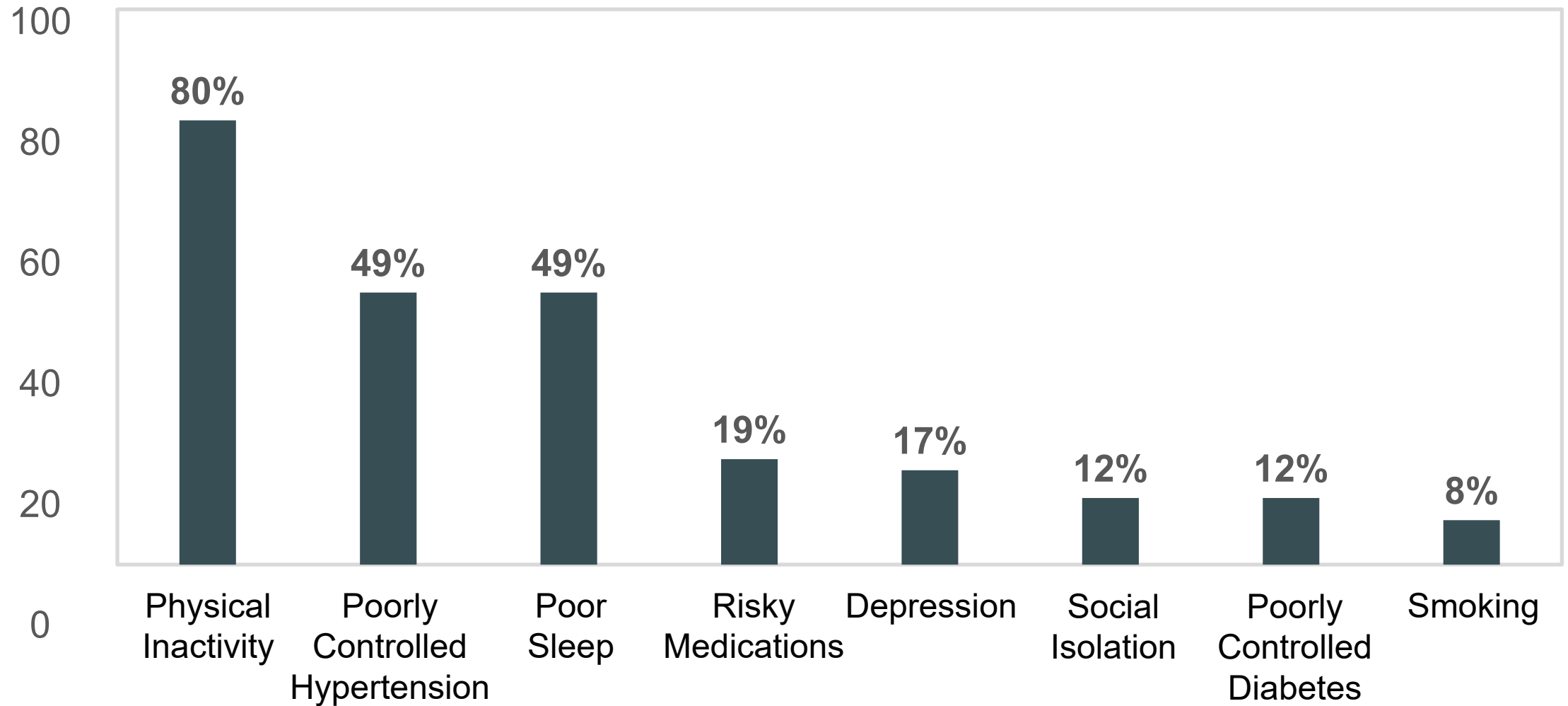


# Systematic Multi-domain Alzheimer's Risk Reduction Trial (SMARRT)

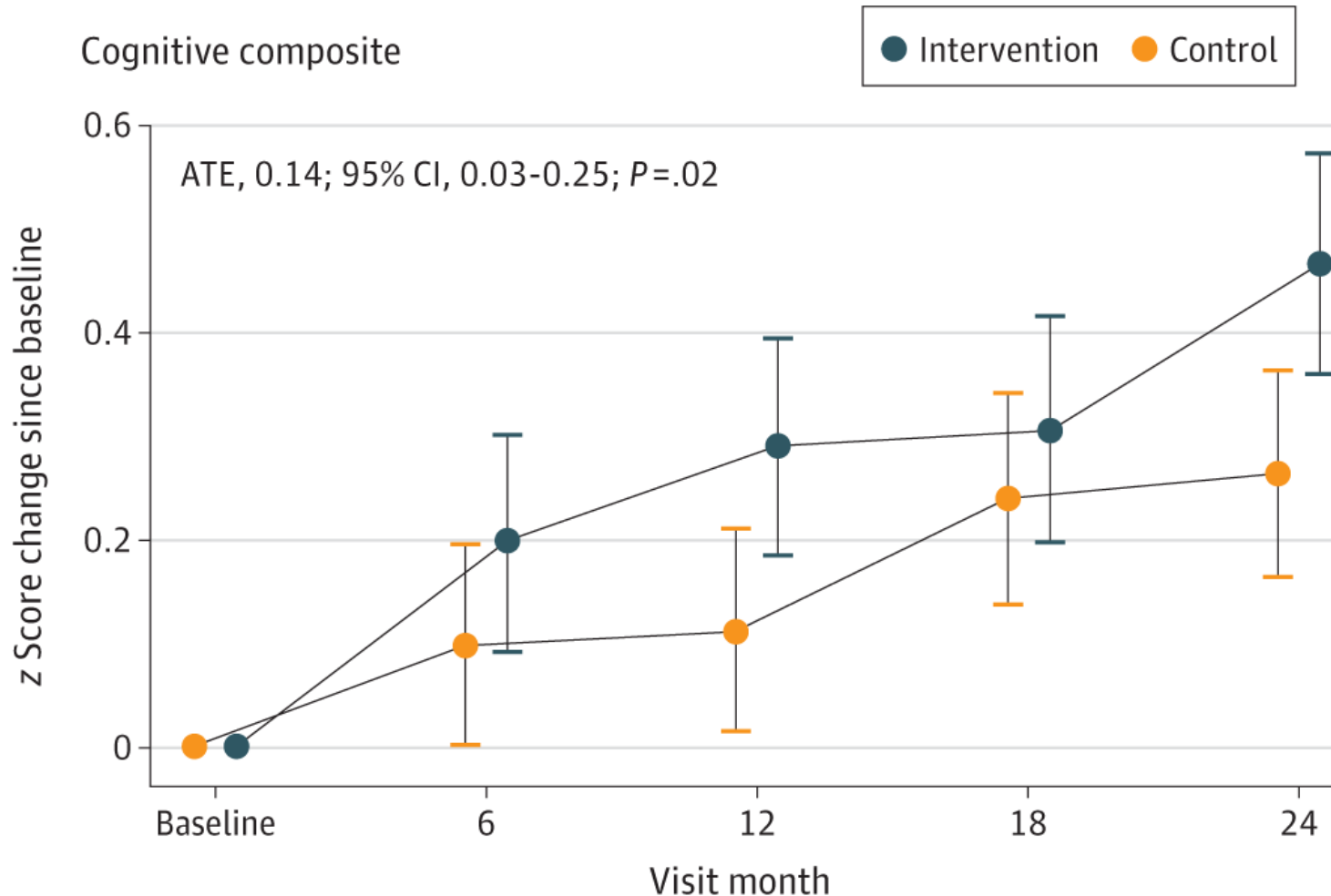
- Previous multi-domain interventions relatively intensive and all standardized, may be difficult to implement in real-world settings
- Personalized risk reduction intervention delivered through a U.S. integrated healthcare delivery system, and leverage advancements in digital health



# Risk Profile of SMARRT Participants



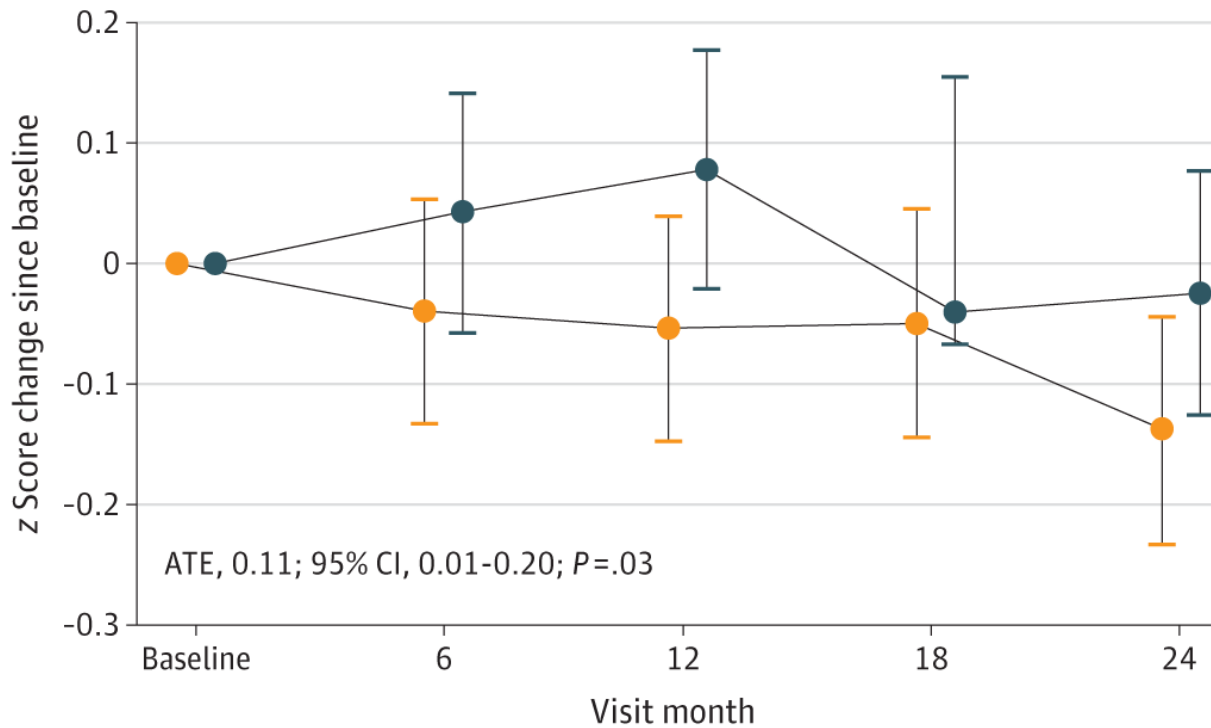
# SMARRT Primary Outcome



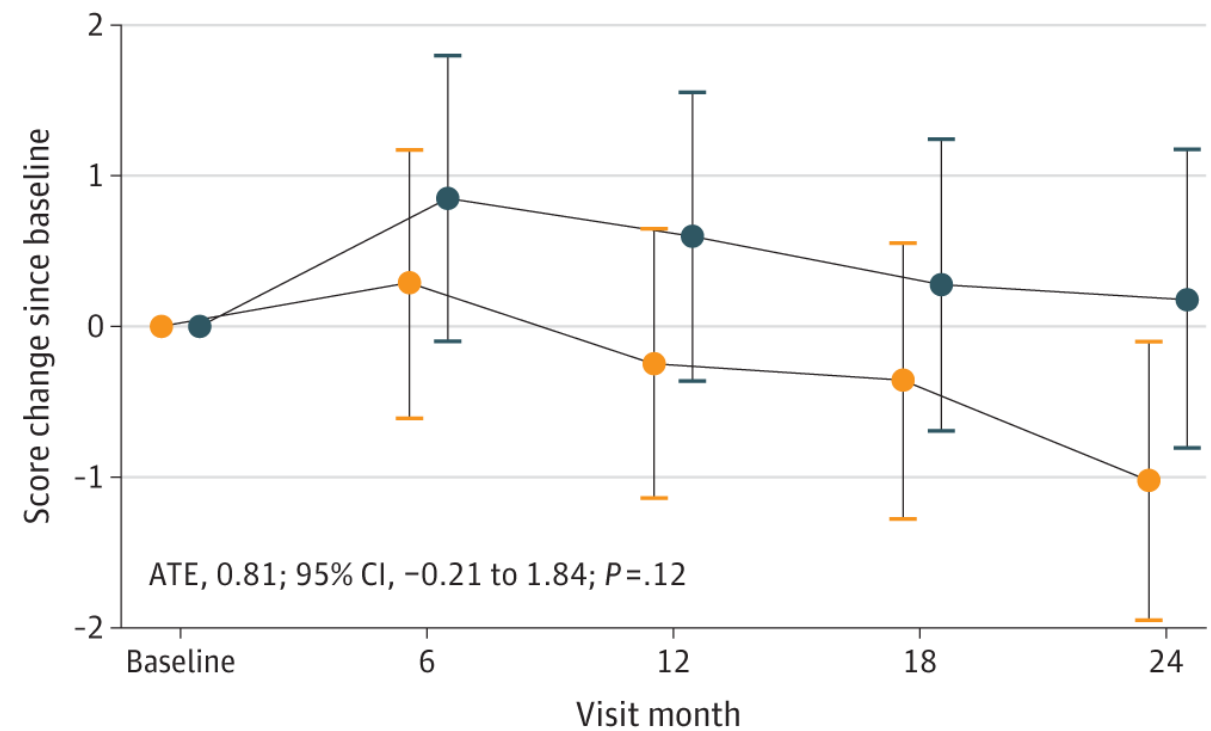
- 2-year cognitive change on the mNTB...highly statistically significant
- Intention-to-treat analysis adjusted for sex, race/ethnicity, education, comorbidity score, and phone assessment (to control for Covid)
- Improvement in intervention arm, 74% greater compared to HE change

# SMARTT Secondary Outcomes

Risk factor composite



Quality of life



● Intervention ● Control

# Next Steps for Dementia Prevention with Modifiable RF

- Recommend some strategies now as beneficial to overall health, low risk and cost...CVRF, sleep hygiene, TBI prevention, physical activity, depression RX
- CDC is rolling out to state health depts: education & behavioral change
- Expand the framework for dementia prevention encompassing the **life course** and **more diverse** populations... personalized to be more effective
- Need pharma trials to 1) measure these variables (usually not), 2) look at interactions/moderators 3) do combination therapies
- Ultimately, primary prevention will probably be like cardiovascular disease: managed by a combination of lifestyle/risk factors and medications

# Thank YOU!

## Funders

- Current NIH:
  - R35 AG071916
  - **R01 AG057508**
  - R01 AG063887
  - R01 AG066137
  - R01 AG069120
  - U19 AG078109
  - UCSF ADRC
- Department of Defense
- Department of Veterans Affairs