

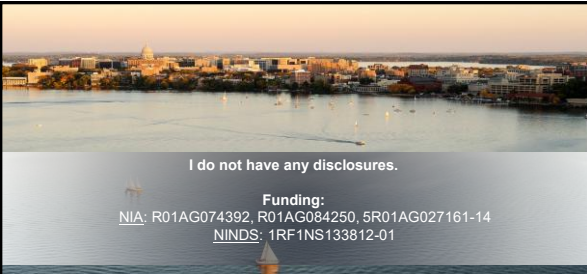
Healthy cognitive aging and lifestyle interventions

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Wisconsin Registry for Alzheimer's Prevention

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Overview

Define key terms

Discuss brain health support as prevention

Review evidence for brain health intervention

Describe practical applications



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Defining brain health



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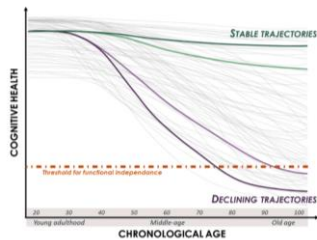
Brain health can have different meanings



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Some errors are part of healthy aging



Abrous, et al., 2026, Aging Research Reviews

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Risk and resilience impact brain health

Risk: factors related to our genetics, environment, and behavior that decrease odds of good brain health with aging

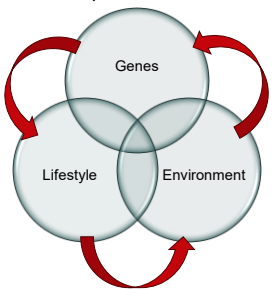
Resilience: factors related to our genetics, environment, and behavior that increase odds of good brain health with aging



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Risk and resilience impact brain health

- APOE ε4
- XX vs. XY



- Smoking
- Exercise

- Pollution
- Stress
- Social disadvantage
- Opportunity



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Brain health support as prevention



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Some risk and resilience factors can be changed

• XX vs. XY

• APOE ε4

Genes

Lifestyle

Environment

• Smoking

• Exercise

• Pollution

• Opportunity

• Social disadvantage

• Stress

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Many of us recommend these changes



Peres, 2015; Alcoro, Aurelio, Borba, Ordoño, & Zimmerman

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Lower risk and greater resilience improve outcomes

• Better cognition in healthy aging and dementia

• Social activity

• Cognitive activity

• Sleep

• Exercise

• Reducing alcohol

• Reducing stress

• Diet

• Greater well-being and healthy mood

Bratzke et al., 2018; Fields, Mueller et al., 2020; Jonaitis et al., 2013; Kivimäki, et al., 2020; Livingston, et al., 2024; Mueller et al., 2020; Okonkwo et al., 2014; Zuelsdorff et al., 2013, 2016, 2017

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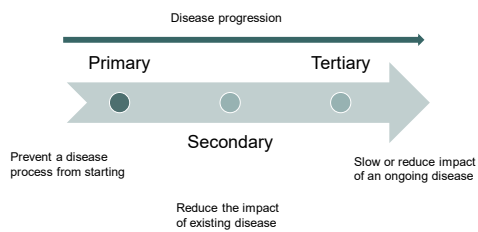
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Preventative practices aim to decrease risks and increase resilience to disease.

Prevention can be primary, secondary, or tertiary.

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Prevention has different goals



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Mild cognitive impairment and dementia are tertiary prevention targets

MCI	Dementia	Alzheimer's disease
• Modest cognitive decline in one or more domains • ADL independence	• Measurable decline in one or more cognitive domains • Impairment in ADL function	• Disease including amyloid and tau pathology and neurodegeneration • Causes dementia

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Tertiary prevention is impactful

- HABIT program for MCI:
 - Wellness education improves well-being and mood
 - Cognitive activity relates to cognition
 - Yoga related to better functional status
- Home-based interventions for MCI:
 - Improve at least one domain of cognition
- Intensive lifestyle intervention for MCI and early dementia (strict, provided diet; moderate exercise, stress management, support groups)
 - Improved cognition
 - Ab42/40 changes



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Levy, et al., 2022; Chirish, et al., 2024; Zou, et al., 2024

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Secondary dementia prevention addresses people with no cognitive symptoms



Pharmacological

Non-pharmacological

Examples:

- In cognitively normal people, provide medication or lifestyle change for those who have:
 - Alzheimer's disease pathology
 - Cerebrovascular risk factors
 - Family history of dementia

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Up to 45% of dementia cases may be avoidable



EARLY LIFE RISKS:

MIDLIFE RISKS:

LATER LIFE RISKS:

Low education

High LDL cholesterol
High blood pressure
Diabetes
Obesity
Physical inactivity

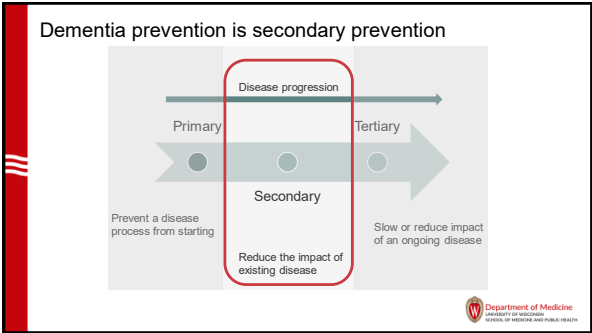
Depression
Smoking
>7 drinks/week
Head injury
Hearing loss

Vision loss
Social isolation
Air pollution

Levine, et al., in preparation; Livingston, et al., Lancet, 2024

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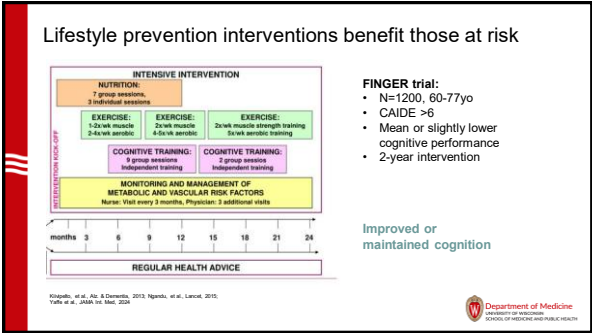
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Personalized interventions benefit those at risk



SMART Trial:

- N=172, 70-89yo
- > 2 dementia risks
- 2-year intervention
- Personalized intervention (medical, lifestyle) with health coaching

Improved cognition and total dementia risks

Kivimäki, et al. *Am J Geriatr*. 2013; Ngandu, et al. *Lancet*. 2015; Yaffe, et al. *JAMA Int Med*. 2014



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Structured interventions show more benefit than self-guided

POINTER Trial:

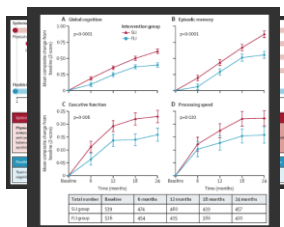


Baker LD, Espeland MA, Whitmer RA, et al. Structured vs self-guided multimodal lifestyle interventions for global cognitive function: the POINTER randomized clinical trial. *JAMA*. Published online July 28, 2015. doi:10.1001/jama.2015.12912



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Culturally adapted structured intervention benefits more than health advice



- N=1065 individuals
- 11 countries
- Mean age=67.6
- High dementia risk and suboptimal cognition
- 2 years

Improved cognition

Kivimäki, et al. *Am J Geriatr*. 2013; Ngandu, et al. *Lancet*. 2015; Yaffe, et al. *JAMA Int Med*. 2014

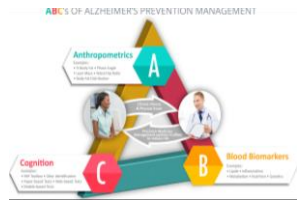


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Clinical prevention interventions impact early disease

- Isaacson personalized medical management:
 - N=174, 25-86yo
 - Cognitively normal/MCI
 - 18 months
 - Personalized lifestyle, pharmacological, educational

Improved cognition



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Isaacson, et al., *Alz & Demen*, 2019, 2019

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Psychology-informed approaches may add

Women's Alzheimer's Movement Prevention and
Research Center at Cleveland Clinic



Levin, et al., in Preparation

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Psychology informed approaches impact risk

- N=295 women
- Age ranges= 30-85
- N=104 with follow-up
- Cognitively normal
- Family history of AD
- 5 visits of personalized psychosocial and medical risk evaluation and recommendations

Lower drinking, lower
perceived cognitive
decline, better diet

Cognitive scores
greater at follow up
(practice effect)



- Most common risks:
- low fruit/vegetable intake (64.4%)
 - depression (39.0%)
 - obesity (38.4%)
 - low cognitive activity (31.2%)
 - high cholesterol (25.1%)

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Levin, et al., in Preparation

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Other prevention trials have shown no impact



PreDIVA (Netherlands)

6-year nurse-led vascular risk intervention
Community-dwelling adults aged 70-78 years
No significant reduction in all-cause dementia



MAPT (France)

Omega-3 ± multidomain intervention (exercise, nutrition, cognitive training)
Community-dwelling, 70+ with SCD
No significant reduction in cognitive decline over 3 years.

Slide modified from Julia Owens, PhD

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Growing support for intensive, structured lifestyle intervention on cognitive change in people at risk

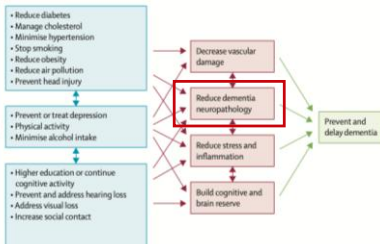


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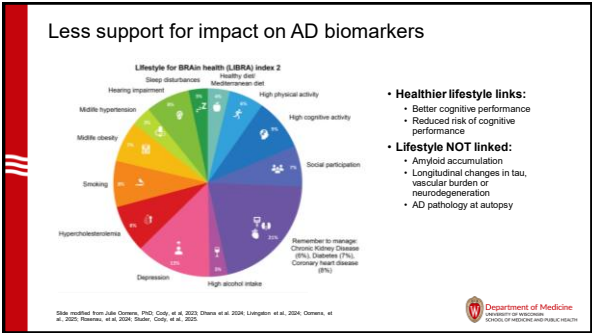
Many interactive mechanisms for lifestyle intervention are proposed



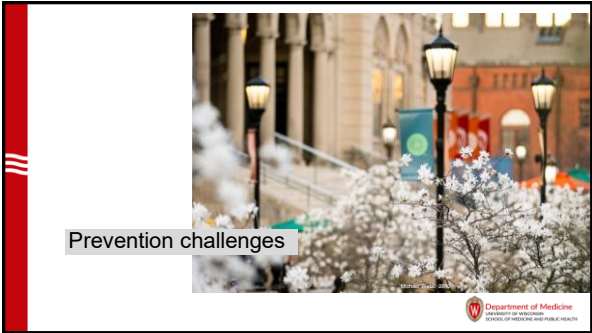
Slide modified from Julia Owens, PhD, Chaturvedi et al. 2024, Livingston et al. 2024

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Intervention must reach those at highest risk

- Cleveland Clinic survey showed 57% of women are concerned
- 24% knew women are at greater risk
- Transgender individuals have higher dementia risk scores and subjective cognitive decline
 - Transgender women with subjective cognitive decline less likely to receive help
 - Transfeminine adults 1.4-1.75x risk

Brady, et al., 2023, Alz & Dementia; Cleveland Clinic, 2024; Cicero, et al., 2023, Alz & Dementia; Lambreau, et al., 2020, Alz & Dementia; van Heeswijk, et al., 2023, International Journal of Transgender Health

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Intervention must reach those at highest risk

- Black/African American individuals have 2x risk
 - Represented 1% of AD trial participants
- Hispanic/Latino individuals have 1.5x risk
 - Large cross-sectional study, 1/4 Hispanic/Latino
 - 30% of respondents knew about ethnicity risk



Careweli, et al., 2019, Neurosci. Biobehavioral Review; Chen, et al., 2024, GSA; Hsieh, et al., 2024, The Journals of Gerontology: Series B; Takad, et al., 2024, The Journal of Aging Research & Lifestyle; Sun, et al., 2025, JPAD; Tran, et al. 2025, AlabiDennis; Wang, et al., 2024, eClinicalMedicine;

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Lifestyle risks are modifiable *in theory*

- Some changes take global or national intervention
 - Pollution
 - Education about risk
- Other changes need work from the health care system
 - Health Literacy
 - Access



Kivimäki, et al., 2025, Nature Medicine; Rohr, et al., 2025, Lancet Healthy Longevity; Wilson & Antsey, 2024, The Gerontologist; Images Pixels RDNE Stock Project and August de Richelieu

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Intervention should reflect reality

Temporal inequity



Lifestyle stigma

- Focus on weight without reasoning or support
- Focus on "gold standard" exercise only
- Focus only on foods that may be financially inaccessible or ignoring cultural culinary context

Stigma of treatment

- CPAP
- Hearing aids
- Psychotherapy

Rohr, et al., 2025, Lancet Healthy Longevity; Wilson & Antsey, 2024, The Gerontologist

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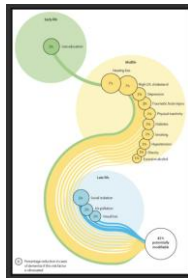
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Practical applications

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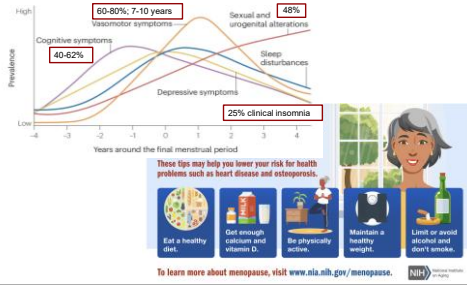
Screening can be powerful

- Midlife:
 - Hearing loss (7%)
 - High LDL (7%)
 - Depression (3%)
 - Physical inactivity (2%)
 - Diabetes (2%)
 - Smoking (2%)
 - Hypertension (2%)
 - Obesity (1%)
 - Alcohol over 7 drinks/week (1%)
- Later life:
 - Social isolation (5%)
 - Vision loss (2%)



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Ask about menopause



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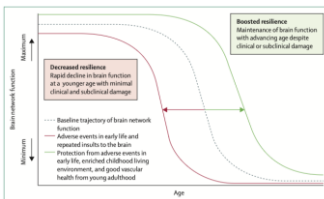
Talk about brain health

- Ask about:
 - Memory concerns
 - Family history of dementia
 - Cognitive challenge
 - Plans to stay mentally active



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Frame risks as *brain* risks



- Much is not new information
- Impact on the brain may be new to folks

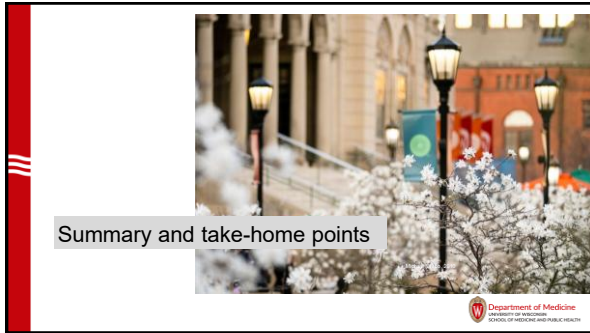
Sabayan, et al., 2023

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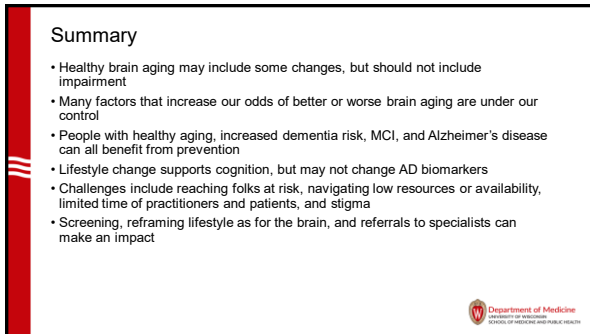
Refer for follow-up

- Sleep medicine
- Cognitive Behavioral Therapy for Insomnia (CBT-I)
- Smoking cessation
- Psychotherapy/counseling
- Stress resources
- Nutrition services

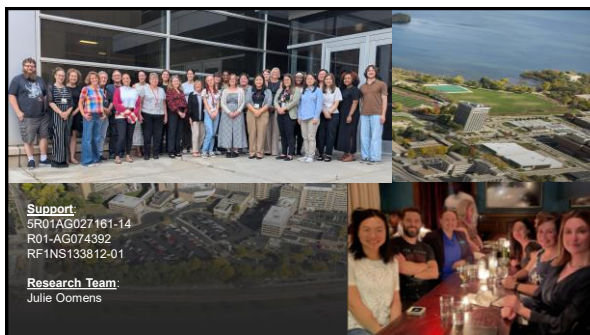
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