Primary Prevention of Dementia

Dr Mike Hall

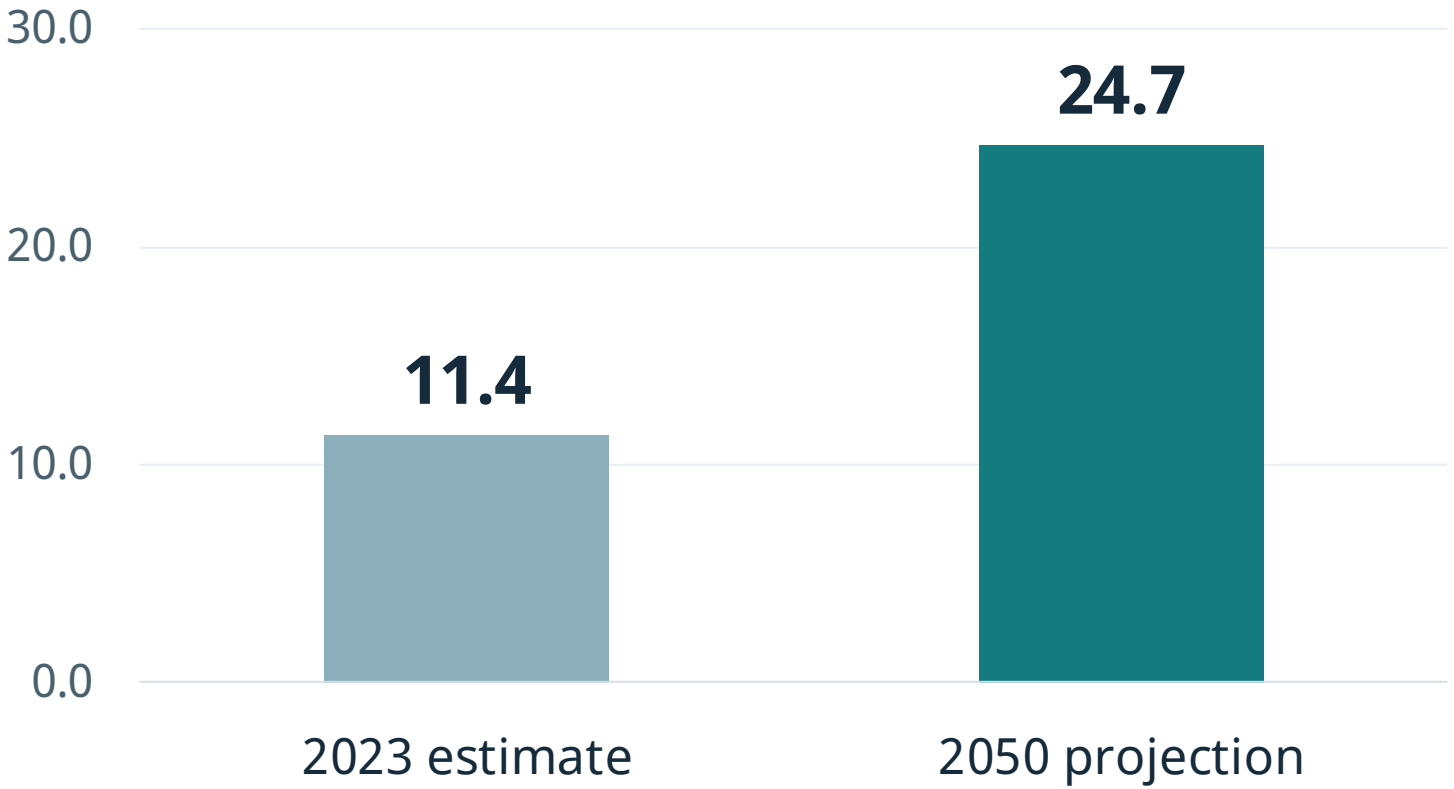
The prevention question

The patient	An adult without established cognitive impairment
The work	Vascular care, additional risks, and emerging therapies
The goal	Reduce risk while preserving function and participation

[1, 47] Livingston G et al. 2024 World Health Organization 2026

Global dementia incidence

Annual new cases worldwide, millions



38,418 adults
22 cohorts
18 countries and territories

Projection assumes constant age- and sex-specific incidence rates.

Population growth and aging increase the projected number of new cases.

[48] Vella AS et al. 2026

Reading prevention evidence

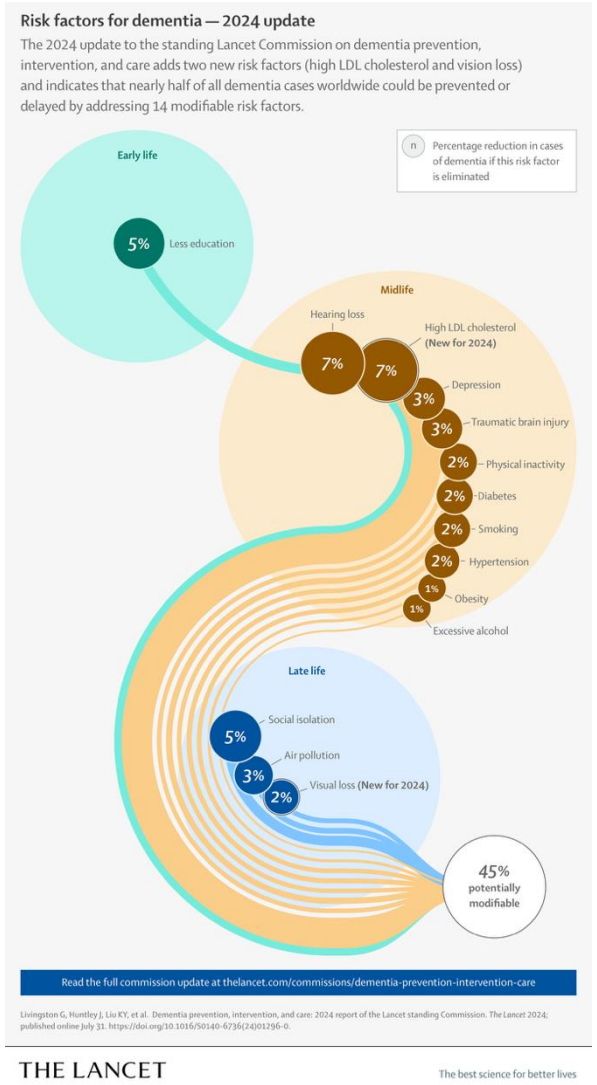
Outcome	What the result establishes
Incident dementia	A clinical prevention outcome
Cognitive test score	A change on the measured task or composite
Biomarker	A biological change requiring clinical interpretation

Illustrative arithmetic

10% to 8% = 20% relative reduction = 2 percentage points absolute

[1, 47] Livingston G et al. 2024 World Health Organization 2026

The 2024 Lancet Commission



45%

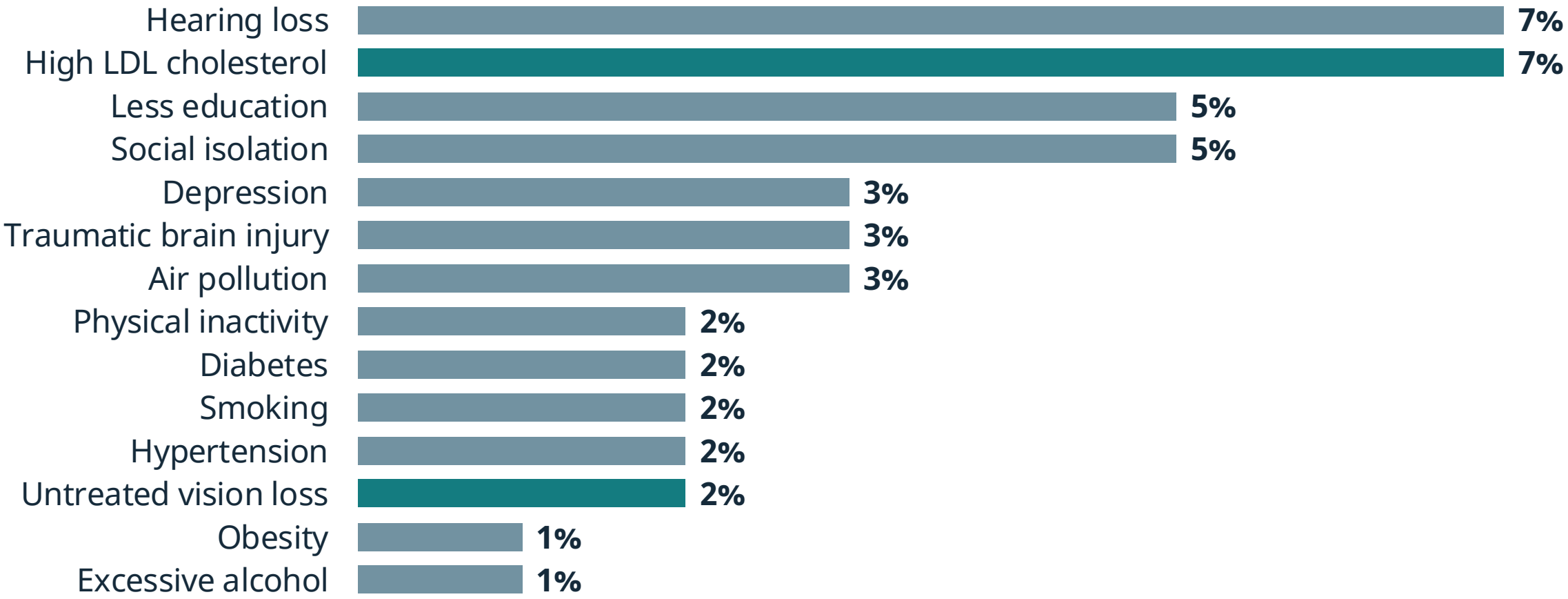
Estimated population share
potentially preventable or delayable

New in 2024
High LDL cholesterol
Untreated vision loss

[1] Livingston G et al. 2024

Fourteen potentially modifiable risks

Weighted population attributable fractions, rounded



Global model with causal assumptions and overlapping exposures. These are population estimates.

[1] Livingston G et al. 2024

SPRINT MIND

Randomized systolic targets below 120 versus below 140 mm Hg

Outcome, original report	Hazard ratio	95% CI
Probable dementia	0.83	0.67 to 1.04
Mild cognitive impairment	0.81	0.69 to 0.95

MCI favored intensive treatment. Dementia alone remained inconclusive.

[2, 3] SPRINT MIND Investigators 2019 Reboussin DM et al. 2025

Supported blood pressure treatment

China Rural Hypertension Control Project

0.85

Risk ratio for all-cause dementia
95% CI 0.76 to 0.95

33,995 participants
48 months of follow-up

Stepped treatment with community providers and physician supervision

Target below 130/80 mm Hg

The trial tested a supported treatment program in uncontrolled hypertension.

[4] He J et al. 2025

Blood pressure in practice

Measurement	Correct cuff, rest, useful home readings
Target	Below 130/80 mm Hg for many adults, individualized
Follow-up	Symptoms, standing pressure when relevant, renal function and electrolytes

[5] AHA and ACC Joint Committee 2025

Diabetes care and cognitive risk

Question	Evidence and clinical response
Intensive control in ACCORD MIND	A1c target below 6% did not improve the principal cognitive outcome
Healthy older adults	A1c often around 7 to 7.5%, individualized
More complex health	Less stringent goals, often around 8%, with hypoglycemia prevention

The patient must be able to use the regimen safely.

[6, 7] Launer LJ et al. 2011 American Diabetes Association 2026

Newer glucose-lowering drugs

Evidence	Population and result
SGLT2 versus DPP4 inhibitors	Observational diabetes cohort associated SGLT2 initiation with lower dementia incidence
EVOKE and EVOKE plus	Randomized early symptomatic Alzheimer disease trials found no slowing of clinical progression with oral semaglutide

Current prescribing follows established metabolic, cardiovascular, renal, or weight indications.

[8, 9] Shin A et al. 2024 Cummings JL et al. 2026

Lipids and statins

Evidence	Interpretation
High LDL in midlife	A modeled dementia risk factor in the Lancet Commission
Randomized statin trials	No consistent adverse cognitive effect
STAREE 2026	Major cardiovascular events favored atorvastatin. The death, dementia, or disability composite was not significantly improved

Lipid treatment follows cardiovascular risk, tolerance, patient preference, and time to benefit.

[1, 10, 11, 47] Livingston G et al. 2024 Ott BR et al. 2015 Zoungas S et al. 2026 World Health Organization 2026

Structured lifestyle trials

Trial	Result measured
FINGER 2015	Small advantage on cognitive testing over 2 years
US POINTER 2025	Structured versus self-guided programs. Difference 0.029 SD/year in global cognition
LatAm-FINGERS 2026	Systematic program favored a global cognitive composite over flexible advice
2026 trial, 513 participants	No significant global cognitive difference with exercise, vascular treatment, or their combination

Cognitive outcomes support feasible programs. Incident dementia effects remain a separate question.

[12, 13, 14, 15] Ngandu T et al. 2015 Baker LD et al. 2025 Crivelli L et al. 2026 Zhang R et al. 2026

An activity plan patients can use

150

Minutes of moderate aerobic activity per week as a longer-term goal

Strengthening on at least 2 days

A feasible start
Ten minutes with a neighbor after breakfast

General health targets require adjustment for ability, symptoms, and fall risk.

[16] US Department of Health and Human Services

Dietary patterns

A feasible pattern	Vegetables, legumes, whole grains, nuts, and fish where appropriate
The MIND randomized trial	No significant cognitive or MRI difference over 3 years
Clinical use	An affordable eating pattern that the patient can sustain

[17] Barnes LL et al. 2023

Cognitive and social participation

Meaning	A class, music, a book group, volunteering, or a new skill
Access	Hearing, vision, pain, transport, and affordability
Follow-up	An activity the person actually continues

[1, 12, 13, 47] Livingston G et al. 2024 Ngandu T et al. 2015 Baker LD et al. 2025 World Health Organization 2026

Hearing intervention

Study	Primary result and boundary
ACHIEVE, 977 participants	Overall 3-year cognitive primary outcome was neutral
Prespecified ARIC subgroup	About 48% less cognitive decline in the higher-risk subgroup
CHOICE 2026, existing MCI	No significant reduction in progression to dementia-level impairment over 2 years

Communication benefits justify care while the dementia effect remains uncertain.

[18, 19, 47] Lin FR et al. 2023 Chen Y et al. 2026 World Health Organization 2026

Vision and everyday function

The evidence	Cataract extraction is associated with lower subsequent dementia risk in cohort data
The indication	Treat vision loss for established ophthalmic and functional reasons
The practical question	Can this person see well enough to participate in the proposed plan?

[1, 20] Livingston G et al. 2024 Lee CS et al. 2022

Medication review

Ask by name	Nighttime products, allergy tablets, bladder drugs, and medicines to settle down
Review cumulative burden	Strong anticholinergics and sedating medicines
Change deliberately	Confirm the indication, account for withdrawal, and arrange follow-up

[21] American Geriatrics Society 2023

Sleep complaints

Problem	Clinical response and evidence
Chronic insomnia	CBT-I is an established initial treatment
Possible sleep apnea	Assess when the history suggests it and treat established indications
CPAP and dementia	APPLES measured cognition over 6 months. It did not establish long-term dementia prevention

A sleep history can reveal a treatable problem before a specialized biomarker does.

[22, 23] Kushida CA et al. 2012 Qaseem A et al. 2016

Other risks that belong in the visit

Tobacco	Offer cessation treatment
Alcohol	Address hazardous use. Abstainers need no alcohol prescription
Depression	Assess and treat the current burden
Head injury	Review falls, protection, and relevant exposures
Environment and isolation	Ask about air quality, social contact, and barriers to participation

[1, 47] Livingston G et al. 2024 World Health Organization 2026

Zoster vaccination and dementia

3.5

Percentage-point reduction
in new dementia diagnoses
over 7 years

~20%

Relative reduction
near the eligibility threshold

Welsh birth-date natural experiment using the live zoster vaccine.

[24] Eyting M et al. 2025

Vaccination evidence is still developing

Cohort results	Associations change with the comparator and healthcare-selection effects
Methodological debate	A 2026 reanalysis challenges implied effects in natural experiments
Clinical action	Keep recommended vaccines current for their established indications

[25, 26, 27, 28] Rayens E et al. 2026 Kivimaki M et al. 2026 DAN ZOSTER 2025 Centers for Disease Control and Prevention 2026

Bisphosphonates and dementia

Nitrogen-containing agents in osteoporosis or fragility fracture

121,492

Hong Kong adults aged 60 and older

Comparison	Matched pairs	ADRD HR, 95% CI
Versus untreated	10,833	0.84 (0.78 to 0.90)
Versus other osteoporosis drugs	3,080	0.76 (0.66 to 0.89)

Observational association. Prescribing follows established fracture-risk indications.

[49] Sing CW et al. 2025

Menopausal hormone therapy

	UK Biobank 2026	WHIMS 2003
Design and population	Observational 183,450 postmenopausal women	Randomized 4,532 women aged 65+
Dementia outcome	All-cause dementia HR 0.90 (0.84 to 0.96)	Probable dementia HR 2.05 (1.21 to 3.48)
Exposure	Historical HRT use Regimen detail limited	Oral conjugated equine estrogen plus medroxyprogesterone

Design, timing, and regimen matter. HRT solely for dementia prevention remains unestablished.

[45, 50] Shumaker SA et al. 2003 Squires S et al. 2026

Other medication research

Approach	Evidence boundary
PDE5 inhibitors, including sildenafil	Inconsistent observational associations. No validated dementia-prevention regimen
Lecanemab and donanemab	Pivotal trials concern early symptomatic Alzheimer disease
AHEAD 3-45	An earlier, biomarker-selected research population

Disease stage and treatment selection change the question being answered.

[38, 39, 40, 41, 42, 43] Fang J et al. 2021 Adesuyan M et al. 2024 Desai RJ et al. 2022 AHEAD 3 45 van Dyck CH et al. 2023 Sims JR et al. 2023

Natural therapies

“Show me the product, tell me what you hope it will do, and let’s look at the evidence together.”

The formulation, dose, patient population, and clinical outcome still matter.

[47] World Health Organization 2026

Multivitamins and cognition

0.07 SD

Pooled global cognition difference

Modest benefits on some cognitive measures

The incidence analysis did not establish fewer MCI or dementia cases over 3 years.

A cognitive-test effect and an incident dementia effect require separate claims.

[29, 30, 47] Vyas CM et al. 2024 Sachs BC et al. 2023 World Health Organization 2026

Common supplements

Product	Relevant randomized evidence
Ginkgo biloba	GEM, over 3,000 adults, about 6 years. No significant reduction in dementia or Alzheimer incidence
Marine omega-3	The tested VITAL regimen did not improve cognitive change over 2 to 3 years
Vitamin D	VITAL ancillary studies found no benefit for the overall cognitive trajectory

Deficiency treatment and other established indications remain separate clinical decisions.

[31, 32, 33] DeKosky ST et al. 2008 Kang JH et al. 2022 Kang JH et al. 2021

Products with limited human evidence

Product	What has actually been studied
Lion’s mane	Small MCI trial, 30 participants. No demonstrated dementia-prevention outcome
Turmeric extracts	Small trials of selected formulations and cognitive endpoints
Low-dose lithium	Experimental biology and an MCI pilot. LATTICE met none of its 6 primary significance thresholds

No established routine dementia-prevention regimen for these products.

[34, 35, 36, 37] Mori K et al. 2009 Saji R et al. 2026 Lithium deficiency and the onset of Alzheimer disease 2025 Gildengers AG et al. 2026

One patient, several useful actions

Age 64, independent
Family history of dementia
Home systolic BP in the high 140s
Diabetes, knee pain
Nightly OTC sleep product
Difficulty in group conversations

What would you address first?

What would you ask before changing treatment?

Hypothetical teaching case. Priorities depend on assessment and the patient’s goals.

The next prevention visit

Vascular care	Accurate pressure, safe diabetes treatment, appropriate lipid management
Participation	Hearing, vision, movement, and meaningful social contact
Avoidable burden	Medication effects, poor sleep, and hazardous exposures
A usable plan	One achievable change, barriers addressed, and a follow-up date

References 1, 5, 7, 21, 28, 47. Full citations in speaker notes and reference slides.

Memory, on a different stage

“But we in it
shall be remember’d”

William Shakespeare
Henry V, Act IV, Scene iii



HENRY V

St. Crispin’s Day
Act IV, Scene iii

“We few, we happy few,
we band of brothers”

William Shakespeare

The lives our patients want to keep

Risk reduction is part of helping patients keep living their own lives.

Thank you

Questions

Primary Prevention of Dementia

PDE5 inhibitors: the numerical results

Backup discussion

Study or analysis	Estimate	Interpretation
2021 sildenafil claims study	HR 0.31	Observational Alzheimer association
2024 UK PDE5 cohort	HR 0.82	Men with erectile dysfunction, versus nonuse
2024 cohort, 3-year lag	HR 0.93 95% CI 0.80 to 1.08	No longer statistically significant
DREAM active comparator	No reduced risk	Different population and comparator

Inconsistent observational evidence does not identify a validated preventive dose.

[38, 39, 40] Fang J et al. 2021 Adesuyan M et al. 2024 Desai RJ et al. 2022

Aspirin

Backup discussion

ASPREE

No demonstrated reduction in dementia, MCI, or cognitive decline

Current decision

A separate cardiovascular indication requires its own benefit and bleeding-risk assessment

[44] Ryan J et al. 2020

Biomarkers and family history

Backup discussion

Blood biomarkers	Specialty diagnostic guidance addresses objective cognitive impairment after clinical assessment
Healthy adults	Diagnostic recommendations do not automatically establish population screening
Family history	Risk reduction remains worthwhile. Unusually early disease may warrant a more specific assessment

[1, 46] Livingston G et al. 2024 Alzheimers Association 2025

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