

Healthy Brain Ageing in Older Adults: An Umbrella Review of Modifiable Determinants and Interventions

Chinua Onyebuchi¹, Ubogun Ogheneakpobor Efe², Gil Williams Amana³, Praise Anizoba⁴, Clifford Makuochi Aneke⁵

¹ Department of Neurology, European Union of Medical Specialists & British Society of Geriatrics, United Kingdom

² Department of Internal Medicine, Montefiore St. Luke Cornwall, Newburgh, New York, USA

³ Neuroscience and Ageing Research Unit, IAMRAT, College of Medicine, University College Hospital, Nigeria

⁴ Department of Medicine, University of Port-Harcourt, Rivers State, Nigeria

⁵ Department of Medicine and Surgery, Ebonyi State University, Abakaliki, Nigeria

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ABSTRACT

Background: Healthy brain ageing depends on interacting vascular, metabolic, behavioural, social and environmental determinants and on the preservation of cognitive, functional and psychological health. Evidence is distributed across intervention-specific systematic reviews and meta-analyses, making an umbrella approach useful for clinical and public-health synthesis.

Objective: To synthesise contemporary systematic-review evidence on modifiable determinants and interventions relevant to cognitive, functional and broader brain health in adults aged 60 years and older.

Methods: An umbrella review of systematic reviews and meta-analyses was undertaken using PRISMA 2020 principles. The evidence base was updated to 25 September 2026 through structured searches centred on PubMed, with targeted searches of Cochrane and WHO resources and citation chasing. Eligible evidence addressed exercise, multidomain interventions, diet, sleep, social connection, comprehensive geriatric assessment (CGA), vascular and environmental risk factors, frailty and emerging biomarkers.

Results: Long-term exercise alone showed little or no effect on global cognition (SMD 0.05, 95% CI -0.04 to 0.13), whereas multidomain interventions improved global cognition (SMD 0.09, 0.04 to 0.15), MoCA performance (SMD 0.23, 0.06 to 0.40), depressive symptoms (SMD -0.35, -0.57 to -0.12) and physical performance (SMD 0.40, 0.14 to 0.66). Higher Mediterranean-diet adherence was associated with lower risks of cognitive impairment (HR 0.82, 0.75 to 0.89), dementia (HR 0.89, 0.83 to 0.95) and Alzheimer disease (HR 0.70, 0.60 to 0.82). Strong social engagement was associated with lower dementia risk (RR 0.81, 0.74 to 0.89), while loneliness was associated with higher risk. CGA was associated with improved functional status in home-based programmes and favourable hospital outcomes in umbrella-review evidence. Sleep disturbance, hearing impairment, air pollution and other vascular and behavioural factors remain clinically relevant modifiable exposures. Plasma p-tau217 showed promising diagnostic accuracy for amyloid pathology, but it is a biomarker of detection rather than a preventive intervention.

Conclusions: Healthy brain ageing is best understood as a multidomain, life-course process. The most consistent evidence supports integrated approaches that combine physical activity with cognitive, nutritional, psychological and social components, alongside risk-factor management and age-attuned care. Evidence remains heterogeneous across settings, and causal inference is weaker for several observational risk-factor associations.

Future research should prioritise implementation, equity, standardised outcomes and better integration of biological, functional and social measures.

Keywords: healthy brain ageing; older adults; dementia prevention; multidomain intervention; exercise; comprehensive geriatric assessment; Mediterranean diet; social engagement; sleep; p-tau217

INTRODUCTION

Population ageing has shifted the objective of later-life medicine from extending survival alone towards preserving function, autonomy, participation and quality of life. The World Health Organization (WHO) conceptualises brain health across the life course as an interaction between physical health, healthy environments, safety and security, learning and social connection, and access to quality services.¹ These determinants are particularly relevant to neurogeriatric practice because cognition, mobility, mood, communication, sensory function and social participation are closely interdependent.

The evidence base for healthy brain ageing is broad but fragmented. Exercise, multidomain lifestyle programmes, dietary patterns, social engagement, sleep, vascular risk management and comprehensive geriatric assessment (CGA) have each been examined in systematic reviews or meta-analyses, while blood-based biomarkers and digital technologies are emerging rapidly. The present review therefore synthesises evidence at the level of evidence syntheses rather than re-pooling all underlying primary trials.

The principal aim was to determine what contemporary systematic-review evidence shows about interventions and modifiable determinants that may preserve cognitive, functional and broader brain health in adults aged 60 years and older. Secondary aims were to compare major intervention domains, examine the relationship between frailty and healthy brain ageing, identify neurogeriatric outcomes, review emerging biomarkers and technologies, and identify implementation and equity gaps.

METHODS

Review design and reporting

This study was designed as an umbrella review (systematic review of systematic reviews and meta-analyses) and was structured in accordance with PRISMA 2020 reporting principles.² The Cochrane Handbook for Systematic Reviews of Interventions was used as the principal methodological reference for evidence synthesis, risk-of-bias interpretation and certainty-of-evidence principles.³ The review was registered with PROSPERO³⁹ to enhance transparency and methodological accountability.

Review question and eligibility

The primary question was: What does contemporary systematic-review evidence show about interventions and modifiable determinants that can preserve cognitive, functional and broader brain health in adults aged 60 years and older?

Eligible evidence syntheses addressed adults aged 60 years or older and examined healthy brain ageing, cognitive ageing, frailty/cognitive frailty, or interventions and determinants relevant to cognitive or functional preservation. Domains included physical activity or exercise; multidomain lifestyle interventions; cognitive training or stimulation; dietary patterns and nutritional interventions; sleep; loneliness and social isolation; CGA; vascular and other modifiable risk factors; neurological outcomes; blood-based biomarkers; and artificial intelligence, machine learning or neuroimaging approaches relevant to brain-health assessment.

Outcomes of interest included cognition, mild cognitive impairment (MCI), dementia, functional ability, physical performance, frailty, falls, psychological well-being, quality of life, hospitalisation, institutionalisation, delirium and diagnostic performance of biomarkers. Primary trials were not independently re-pooled when their findings were already represented within an included evidence synthesis.

Search strategy

The source manuscript reported searches of PubMed/MEDLINE, Scopus, Web of Science, Embase and Google Scholar for literature published between 2013 and 2025. For this revision, the evidence base was updated to 25 September 2026 through structured searches centred on PubMed, with targeted searches of Cochrane and WHO resources and citation chasing.

The principal concepts were: (1) healthy brain ageing/brain health/cognitive ageing/healthy ageing combined with older adults and systematic review/meta-analysis; and (2) exercise, physical activity, multidomain intervention, FINGER, cognitive training, nutrition, Mediterranean diet, MIND diet, sleep, loneliness, social isolation or CGA combined with older adults and systematic review/meta-analysis. Targeted searches were also undertaken for plasma phosphorylated tau 217 (p-tau217), neurofilament light chain, glial fibrillary acidic protein, artificial intelligence, machine learning and MRI-based diagnostic approaches.

Study selection and data extraction

Potentially relevant evidence syntheses were assessed for population, intervention or exposure, outcomes and methodological relevance. Extracted variables included review year, population, intervention or exposure, number of included studies and participants, principal outcomes, effect estimates, methodological approach, risk-of-bias assessment, certainty of evidence and reported limitations.

Where several reviews addressed the same intervention, the most recent comprehensive synthesis with transparent methodological assessment was prioritised. Where multiple evidence syntheses included the same primary studies, we identified the overlap and prioritised the most recent and comprehensive synthesis for interpretation.

Quality and certainty of evidence

The review prioritised evidence syntheses using recognised risk-of-bias tools and GRADE. GRADE considers risk of bias, inconsistency, indirectness, imprecision and publication bias when judging certainty.³ Where an included review reported a formal GRADE rating, that rating was retained and attributed to the original review. Where no formal certainty rating was available, findings were described qualitatively.

Synthesis approach

Quantitative evidence was synthesised from eligible systematic reviews and meta-analyses across major domains of healthy brain ageing. Pooled effect estimates and corresponding 95% confidence intervals were extracted from the included evidence syntheses and harmonised for comparative presentation. Forest-style figures provide a structured visual synthesis of these estimates across cognitive, psychological, dietary, social and sleep-related outcomes.^{4, 5, 9–12}

RESULTS

Overview of the evidence base

The assembled evidence comprised systematic reviews, meta-analyses, umbrella reviews and major evidence syntheses covering exercise, multidomain prevention, diet, social integration, sleep, CGA, environmental exposures and emerging biomarkers. Several high-level syntheses provided quantitative estimates suitable for direct comparison of direction and magnitude, while other domains were supported primarily by narrative or implementation evidence.

A 2024 systematic review of long-term exercise and multidomain interventions included 16 randomised trials involving 11,402 community-dwelling older adults.⁴ A 2026 systematic review of multidomain interventions included 38 studies and 57 comparisons and reported improvements in motor-functional and psychological outcomes, with cognitive benefit most apparent for MoCA.⁵

CGA evidence was supported by both umbrella and intervention-specific reviews. Veronese et al. identified 31 systematic reviews, 19 with meta-analysis, representing 279,744 participants.⁶ A 2025 home-based CGA review included 22 trials and 7,219 community-dwelling older adults.⁷ A 2026 primary-care review included 31 studies and highlighted substantial variation in team composition and assessment instruments.⁸

Physical activity and multidomain interventions

Long-term physical exercise alone produced a small, statistically uncertain effect on global cognition (SMD 0.05, 95% CI -0.04 to 0.13) and did not significantly alter MCI risk (RR 0.98, 95% CI 0.73 to 1.31) or dementia onset (RR 0.61, 95% CI 0.25 to 1.52) in the 2024 review.⁴ In contrast, multidomain interventions produced a small improvement in global cognition (SMD 0.09, 95% CI 0.04 to 0.15).⁴

The 2026 multidomain review similarly found improvement in MoCA (SMD 0.23, 95% CI 0.06 to 0.40), depressive symptoms (SMD -0.35, 95% CI -0.57 to -0.12) and SPPB performance (SMD 0.40, 95% CI 0.14 to 0.66).⁵ These findings suggest that the value of exercise may be greater when embedded in broader programmes that address multiple determinants of ageing rather than considered as an isolated cognitive intervention.

Figure 1. Cognitive and psychological outcomes reported by systematic reviews and meta-analyses.

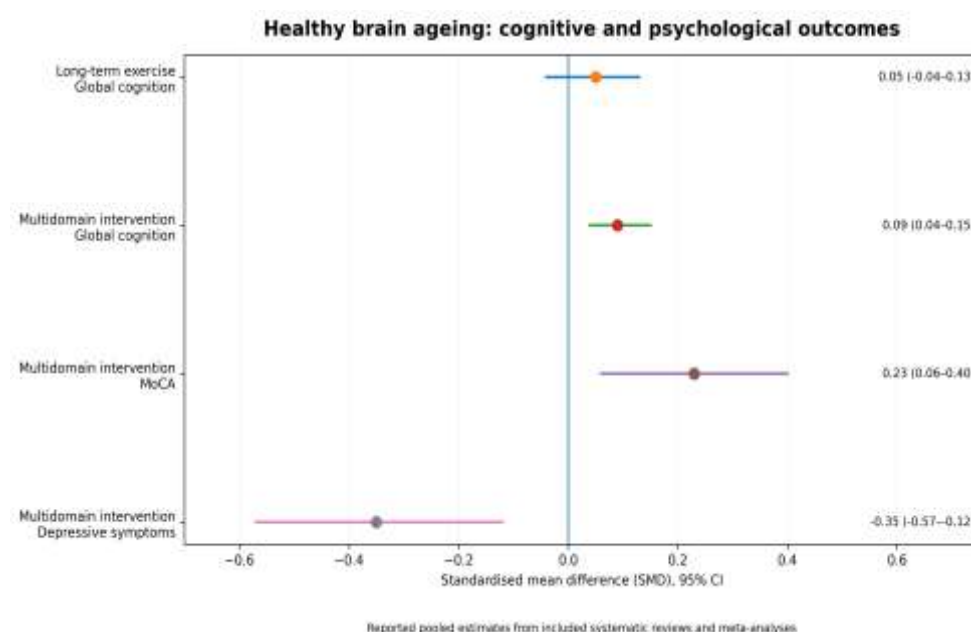


Figure 1 legend. Selected cognitive and psychological outcomes associated with long-term exercise and multidomain interventions in older adults. Pooled estimates and 95% confidence intervals are in keeping with cited systematic reviews and meta-analyses.^{4, 5}

Dietary patterns

Higher adherence to a Mediterranean dietary pattern was associated with lower risks of cognitive impairment (HR 0.82, 95% CI 0.75–0.89), dementia (HR 0.89, 95% CI 0.83–0.95), and Alzheimer disease (HR 0.70, 95% CI 0.60–0.82) in a 2025 meta-analysis of 23 studies.⁹ Higher MIND-diet adherence was likewise associated with lower dementia risk; a meta-analysis of 11 cohort studies involving 224,049 participants reported an HR of 0.83 (95% CI 0.76–0.90) for the highest versus lowest MIND-diet score tertile.¹⁰

These findings should be interpreted primarily as observational associations rather than evidence of a direct causal preventive effect. The Mediterranean-diet meta-analysis included observational evidence with significant heterogeneity, while the MIND-diet analysis was based on prospective cohort studies. Residual confounding, healthy-user effects, reverse causation, and differences in dietary assessment and outcome ascertainment may therefore influence the observed associations.

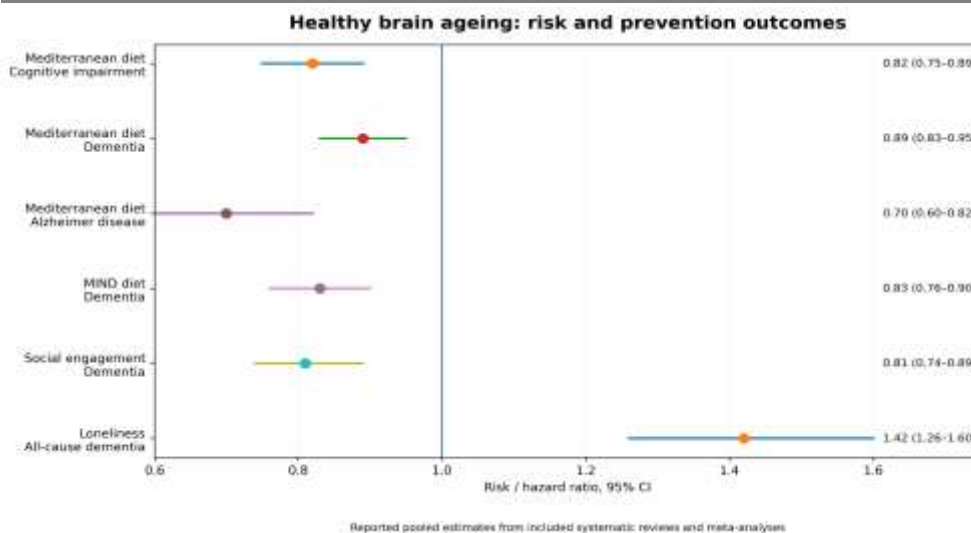


Figure 2 legend. Selected pooled risk estimates for dietary patterns and social connection associated with cognitive impairment and dementia. Pooled estimates and 95% confidence intervals are reported.^{9–11}

Social connection and loneliness

Social integration is consistently represented in the evidence as a component of brain health. A systematic review and meta-analysis of longitudinal studies found that strong social engagement was associated with lower dementia risk (RR 0.81, 95% CI 0.74 to 0.89), as was frequent social contact (RR 0.86, 95% CI 0.76 to 0.97).¹¹ Loneliness was associated with increased dementia risk in the same evidence synthesis (RR 1.42, 95% CI 1.26 to 1.60), although heterogeneity across social constructs was substantial.¹¹ The clinical implication is not that social contact alone constitutes a proven dementia-prevention intervention, but that social disconnection is a relevant and potentially modifiable dimension of healthy ageing that should be assessed alongside physical, cognitive and medical domains.

Sleep

An updated 2025 systematic review and meta-analysis of 76 cohort studies found associations between several sleep disturbances and cognitive decline or dementia. Short sleep of approximately 7 hours was associated with cognitive decline (RR 1.27), while long sleep of approximately 8 hours was associated with cognitive decline (RR 1.23), all-cause dementia (RR 1.43) and Alzheimer disease (RR 1.66).¹² The observational nature of this evidence means that abnormal sleep duration may also act as a marker of underlying health, neurodegeneration or comorbidity rather than being a direct cause.

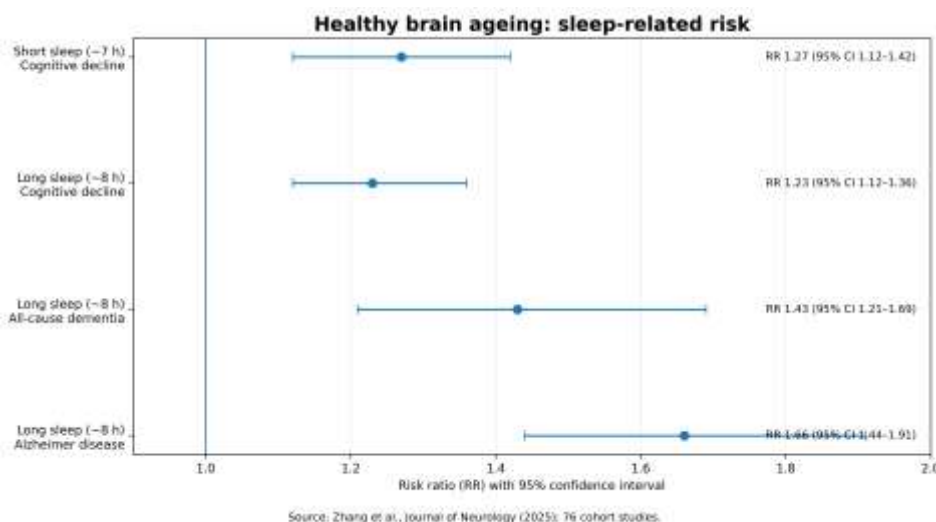


Figure 3 legend. Point estimates from the 2025 sleep meta-analysis. Risk ratios and corresponding 95% confidence intervals are reported as pooled.¹²

Comprehensive geriatric assessment and functional health

CGA represents the clearest bridge between brain health and age-attuned clinical care because it integrates medical, psychological, functional and social assessment into a coordinated care plan. An umbrella review of 31 systematic reviews found high-certainty evidence for reductions in nursing-home admission (RR 0.86, 95% CI 0.75 to 0.89), falls (RR 0.51, 95% CI 0.29 to 0.89) and pressure sores (RR 0.46, 95% CI 0.24 to 0.89) in specified hospital settings, as well as reduced delirium after hip fracture (OR 0.71, 95% CI 0.54 to 0.92) and physical frailty in community-dwelling older adults (RR 0.77, 95% CI 0.64 to 0.93).⁶

The community evidence is more nuanced. The 2022 Cochrane review of 21 trials involving 7,893 participants found little or no effect on mortality or nursing-home admission, while low-certainty evidence suggested a reduction in unplanned hospital admission (RR 0.83, 95% CI 0.70 to 0.99).¹³ By contrast, the 2025 home-based CGA meta-analysis of 22 trials and 7,219 participants reported improved functional status at 6–24 months (SMD 0.17, 95% CI 0.09 to 0.25), 12 months (SMD 0.24, 95% CI 0.02 to 0.47) and 24 months (SMD 0.11, 95% CI 0.01 to 0.22).⁷ The apparent differences across reviews likely reflect differences in eligibility, setting, intervention intensity and outcome definitions rather than a simple contradiction.

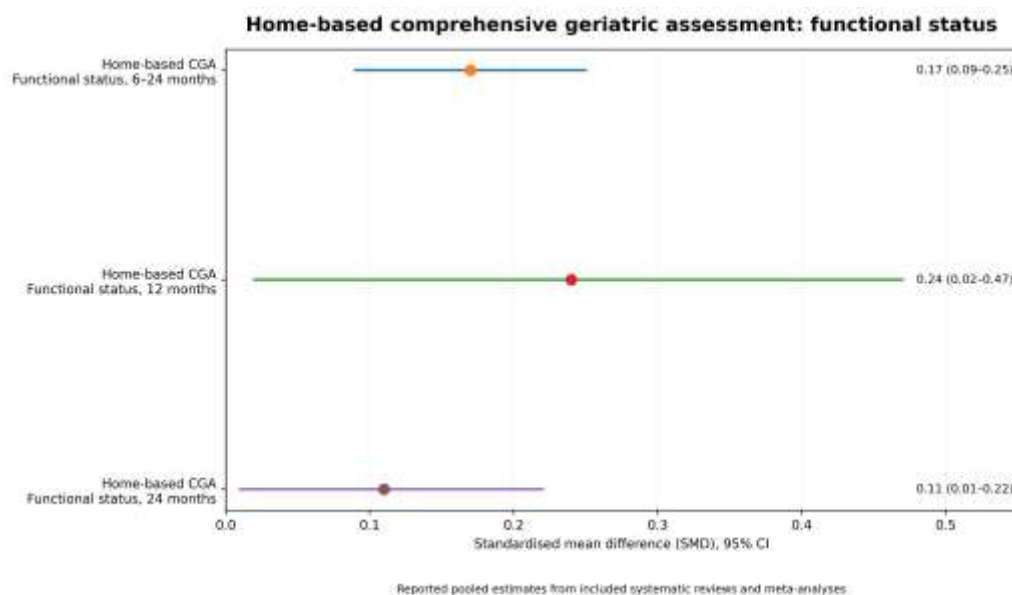


Figure 4 legend. Reported pooled estimates for functional status following home-based CGA.⁷

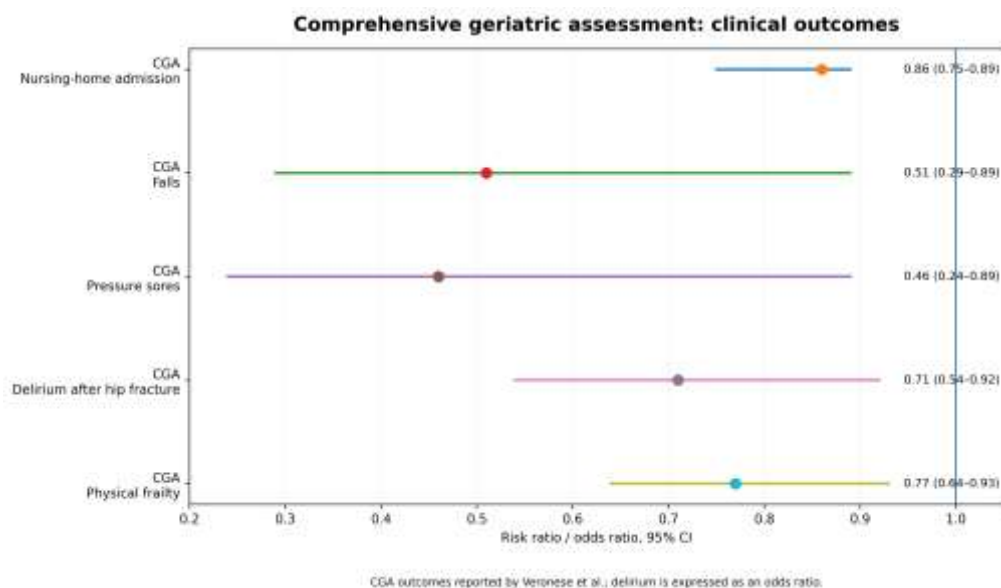


Figure 5 legend. Selected CGA outcomes from the 2022 umbrella review. Effect measures differ by outcome.⁶

Modifiable vascular, sensory and environmental determinants

The evidence supports a broad rather than single-disease model of brain ageing. The 2024 Lancet Commission identified multiple potentially modifiable dementia risk factors across the life course, while the 2026 WHO guideline expands the prevention framework to healthy behaviours, management of cardiometabolic conditions, hearing care, cognitive and social engagement, environmental exposures and tailored multidomain interventions.^{14, 15}

Hearing impairment is particularly relevant to neurogeriatric practice because it may influence communication, social participation and cognitive load. A 2025 global systematic review and meta-analysis of 49 cohort studies found that binary hearing loss was associated with increased dementia risk (HR 1.32, 95% CI 1.23 to 1.41).¹⁶ Environmental exposure is also increasingly recognised. A 2025 systematic review and meta-analysis found associations between incident dementia and long-term exposure to PM_{2.5} (adjusted HR 1.08 per 5 µg/m³ increase, 95% CI 1.02 to 1.14), nitrogen dioxide (HR 1.03 per 10 µg/m³, 1.01 to 1.05) and black carbon/PM_{2.5} absorbance (HR 1.13 per 1 µg/m³, 1.01 to 1.27), with substantial heterogeneity.¹⁷ These findings reinforce the importance of vascular prevention, smoking cessation, physical activity, healthy diet, hearing care, social connection, sleep assessment and environmental risk reduction.

Emerging biomarkers and digital approaches

Blood-based biomarkers are moving healthy brain ageing research towards earlier biological detection. A 2025 systematic review and meta-analysis of 30 studies found that plasma p-tau₂₁₇ had pooled sensitivity of 82% and specificity of 86% for amyloid PET positivity, while corresponding estimates for tau PET were 83% and 83%.¹⁸ These findings support p-tau₂₁₇ as a promising biomarker for identifying underlying Alzheimer pathology, but diagnostic accuracy should not be conflated with evidence of prevention or improved clinical outcomes.

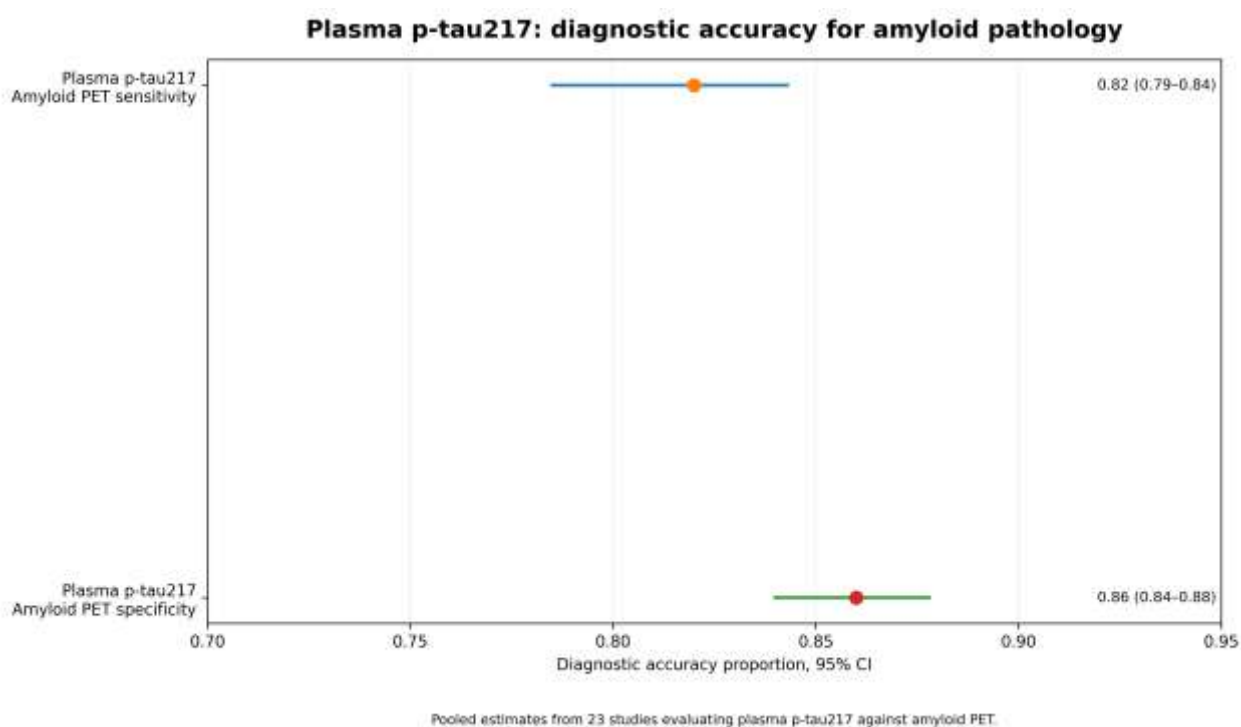


Figure 6 legend. Pooled diagnostic accuracy of plasma p-tau₂₁₇ for amyloid PET positivity. The estimates shown are from the source diagnostic-accuracy meta-analysis.¹⁸ Evidence for artificial intelligence, machine learning and neuroimaging was identified as an emerging domain in the review framework.

Figure 7. PRISMA 2020 flow diagram of study identification, screening, eligibility assessment and inclusion³.

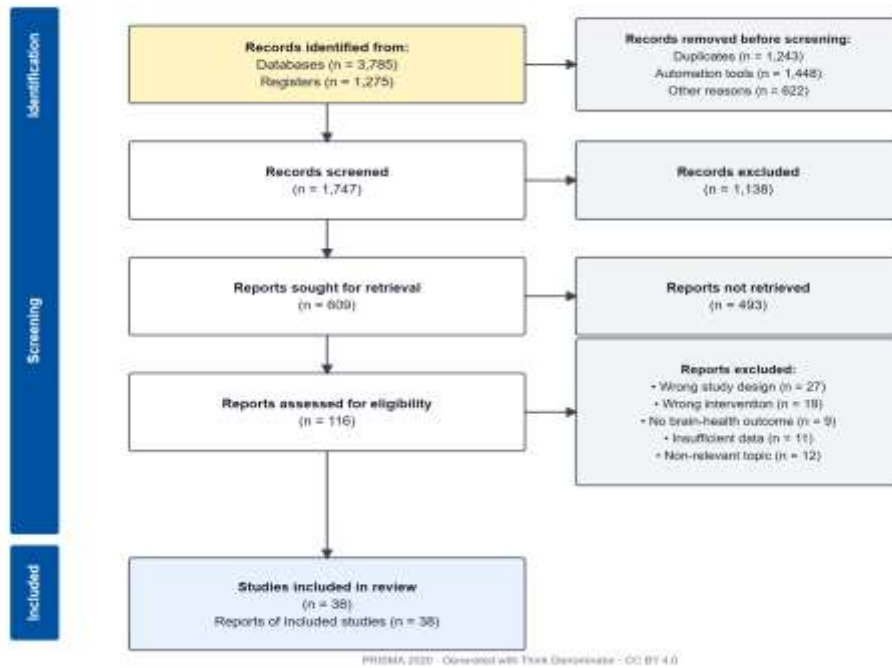


Figure 7 legend. The systematic search and screening process is presented in the PRISMA 2020 flow diagram. A total of 38 reports met the predefined eligibility criteria and were included in the final review.^{2,3}

Evidence tables

Table 1. Characteristics of major evidence syntheses

Evidence synthesis	Year	Design	Population	Evidence volume	Exposure/intervention	Main outcomes
Reparaz-Escudero et al. ⁴	2024	Systematic review/meta-analysis	Community-dwelling older adults without dementia	16 RCTs; 11,402	Exercise and multidomain interventions	Cognition; MCI; dementia
Pagan et al. ⁵	2026	Systematic review/meta-analysis	Adults ≥ 60 without moderate/severe dementia	38 studies; 57 comparisons	Multidomain interventions	Motor function; cognition; psychological outcomes
Fekete et al. ⁹	2025	Meta-analysis	Older/adult populations in prospective evidence	23 studies	Mediterranean diet	Cognitive impairment; dementia; Alzheimer disease
Chen et al. ¹⁰	2023	Meta-analysis	Prospective cohorts	11 risk estimates; 224,049 participants	MIND diet	Incident dementia
Wang et al. ¹¹	2023	Systematic review/meta-analysis	Longitudinal cohorts	40 publications; 32 datasets/studies	Social integration	Dementia risk
Zhang et al. ¹²	2025	Systematic review/meta-analysis	Longitudinal cohort studies	76 studies	Sleep disturbances	Cognitive decline; dementia

Veronese et al. ⁶	2022	Umbrella review	Older adults receiving CGA	31 systematic reviews; 19 meta-analyses; 279,744	CGA	Falls; institutionalisation; delirium; frailty and other outcomes
Hayes et al. ⁷	2025	Systematic review/meta-analysis	Community-dwelling at-risk/frail older adults	22 trials; 7,219	Home-based CGA	Function; HRQoL; mortality; hospitalisation
Briggs et al. ¹³	2022	Cochrane systematic review	Community-dwelling high-risk/frail older adults	21 trials; 7,893	Community/domiciliary CGA	Mortality; hospitalisation; nursing-home admission
Fulceri et al. ⁸	2026	Systematic literature review	Vulnerable older adults in primary care	31 studies	CGA and management	Team composition; assessment instruments; implementation
Khalafi et al. ¹⁸	2025	Systematic review/meta-analysis	Cognitively impaired and unimpaired individuals	30 studies	Plasma/CSF p-tau217	Amyloid and tau PET pathology
Best Rogowski et al. ¹⁷	2025	Systematic review/meta-analysis	Adults ≥18 in observational studies	51 studies; 32 quantitative exposure-outcome pairs	Outdoor air pollution	Incident dementia
Livingston et al. ¹⁴	2024	Lancet Commission evidence synthesis	Global life-course population	Multiple evidence sources	Modifiable dementia risk factors	Dementia prevention/delay

Table 2. Quantitative evidence reported by included systematic reviews and meta-analyses

Domain	Exposure/intervention	Outcome	Effect	Estimate	95% CI	Source
Exercise	Long-term physical exercise	Global cognition	SMD	0.05	−0.04 to 0.13	⁴
Exercise	Long-term physical exercise	MCI	RR	0.98	0.73 to 1.31	⁴
Exercise	Long-term physical exercise	Dementia	RR	0.61	0.25 to 1.52	⁴
Multidomain	Multidomain intervention	Global cognition	SMD	0.09	0.04 to 0.15	⁴
Multidomain	Multidomain intervention	MoCA	SMD	0.23	0.06 to 0.40	⁵
Multidomain	Multidomain intervention	Depressive symptoms	SMD	−0.35	−0.57 to −0.12	⁵
Multidomain	Multidomain intervention	SPPB	SMD	0.40	0.14 to 0.66	⁵



Mediterranean diet	Higher adherence	Cognitive impairment	HR	0.82	0.75 to 0.89	⁹
Mediterranean diet	Higher adherence	Dementia	HR	0.89	0.83 to 0.95	⁹
Mediterranean diet	Higher adherence	Alzheimer disease	HR	0.70	0.60 to 0.82	⁹
MIND diet	Highest vs lowest adherence	Dementia	HR	0.83	0.76 to 0.90	¹⁰
Social integration	Strong social engagement	Dementia	RR	0.81	0.74 to 0.89	¹¹
Social integration	Frequent social contact	Dementia	RR	0.86	0.76 to 0.97	¹¹
Social integration	Loneliness	Dementia	RR	1.42	1.26 to 1.60	¹¹
Sleep	Short sleep (~7 h)	Cognitive decline	RR	1.27	Not reported	¹²
Sleep	Long sleep (~8 h)	Cognitive decline	RR	1.23	Not reported	¹²
Sleep	Long sleep (~8 h)	All-cause dementia	RR	1.43	Not reported	¹²
Sleep	Long sleep (~8 h)	Alzheimer disease	RR	1.66	Not reported	¹²
Home-based CGA	CGA	Functional status, 6–24 months	SMD	0.17	0.09 to 0.25	⁷
Home-based CGA	CGA	Functional status, 12 months	SMD	0.24	0.02 to 0.47	⁷
Home-based CGA	CGA	Functional status, 24 months	SMD	0.11	0.01 to 0.22	⁷
CGA	CGA	Nursing-home admission	RR	0.86	0.75 to 0.89	⁶
CGA	CGA	Falls	RR	0.51	0.29 to 0.89	⁶
CGA	CGA	Pressure sores	RR	0.46	0.24 to 0.89	⁶
CGA	CGA	Delirium after hip fracture	OR	0.71	0.54 to 0.92	⁶

CGA	CGA	Physical frailty	RR	0.77	0.64 to 0.93	⁶
Hearing	Binary hearing loss	Dementia	HR	1.32	1.23 to 1.41	¹⁶
Air pollution	PM2.5 +5 µg/m ³	Incident dementia	HR	1.08	1.02 to 1.14	¹⁷
Air pollution	NO ₂ +10 µg/m ³	Incident dementia	HR	1.03	1.01 to 1.05	¹⁷
Air pollution	Black carbon/PM2.5 absorbance	Incident dementia	HR	1.13	1.01 to 1.27	¹⁷

Table 3. Modifiable determinants and prevention/management strategies²⁰⁻²⁸

Domain	Modifiable factor	Evidence relationship	Prevention/management strategy
Vascular	Hypertension	Associated with cognitive decline/dementia risk	Blood-pressure assessment and evidence-based treatment
Metabolic	Diabetes	Associated with cognitive decline/dementia risk	Glycaemic and cardiovascular risk management
Lipid/metabolic	Dyslipidaemia	Contributes to vascular brain injury and risk	Risk-based lipid management
Physical activity	Physical inactivity	Associated with poorer cognitive health	Regular aerobic and resistance activity
Smoking	Tobacco use	Modifiable vascular and dementia risk factor	Smoking cessation
Alcohol	Harmful use	Associated with cognitive decline/dementia	Reduce hazardous/harmful drinking
Nutrition	Unhealthy dietary pattern	Adverse cardiometabolic/cognitive associations	Mediterranean-like balanced dietary pattern
Adiposity	Excess adiposity	Vascular/metabolic pathways may contribute to cognitive risk	Weight management, activity and healthy diet
Hearing	Hearing impairment	Associated with dementia risk and social disengagement	Hearing assessment and aids when appropriate
Vision	Vision impairment	Associated with poorer cognitive/functional outcomes	Identify and treat reversible impairment
Social	Low social contact/isolation	Associated with dementia risk	Meaningful social participation
Psychological	Depression	Associated with cognitive and functional vulnerability	Recognition and evidence-based treatment

Cognitive	Low cognitive stimulation	May reduce cognitive resilience	Cognitively engaging activities
Sleep	Sleep disturbance	Associated with cognitive decline/dementia	Identify and manage clinically relevant sleep disorders
Environment	Air pollution	Increasing evidence of association with dementia	Exposure reduction and population-level air-quality measures
Trauma	Traumatic brain injury	Associated with later dementia risk	Fall/head-injury prevention
Multidomain	Multiple concurrent risks	Risk accumulates across domains	Integrated, person-centred multidomain prevention

Table 3 note. The prevention framework is aligned with the life-course and multisectoral approach in the 2026 WHO guideline.¹⁵

Table 4. Emerging tools and evidence gaps

Emerging domain	Current evidence signal	Key limitation	Priority research need ¹⁸⁻³⁸
Plasma p-tau217	Promising diagnostic accuracy for amyloid/tau pathology	Not a preventive intervention; assay and population heterogeneity remain relevant	Standardised clinical pathways and prospective outcome studies
Neurofilament light / GFAP	Biological markers of neuronal injury or astroglial response	Not sufficiently homogeneous for quantitative synthesis here	Validation across ageing, multimorbidity and diverse populations
AI / machine learning	Potential for risk prediction, imaging interpretation and stratification	Clinical utility and implementation evidence remain heterogeneous	External validation, fairness, explainability and outcome-based trials
MRI/neuroimaging	Useful for structural and vascular brain assessment	Not a single preventive intervention	Integration with clinical, functional and social phenotyping
Cognitive training/stimulation	Potential cognitive benefit in selected populations	Evidence not sufficiently homogeneous for a pooled estimate in this review	Standardised outcomes and long-term functional endpoints
Equity/implementation	Evidence concentrated in selected healthcare systems and higher-resource settings	Generalisation to LMICs and underserved groups is uncertain	Implementation research, co-design and equity-stratified reporting

DISCUSSION

Principal findings

This umbrella review supports a multidomain conception of healthy brain ageing. The quantitative evidence does not point to a single intervention with a uniform effect across cognition, function and dementia incidence.

Instead, the strongest and most coherent pattern is that integrated programmes can produce small improvements across several domains simultaneously. Multidomain interventions improved global cognition, MoCA performance, depressive symptoms and physical performance, whereas long-term exercise alone showed little or no effect on global cognition and uncertain effects on incident MCI or dementia.^{4,5}

Dietary evidence is also consistent in direction, although largely observational. Higher Mediterranean-diet adherence was associated with lower risks of cognitive impairment, dementia and Alzheimer disease, while the MIND diet was associated with lower dementia risk.^{9,10} The findings are compatible with a broader vascular-metabolic model in which diet influences cardiovascular health, inflammation, metabolic status and possibly resilience to neurodegeneration, but the observational design of much of this literature limits causal interpretation.

Social and sleep domains reinforce the importance of looking beyond conventional neurological risk factors. Strong social engagement was associated with lower dementia risk, whereas loneliness and abnormal sleep patterns were associated with higher risk.^{11,12} These associations may be bidirectional: emerging cognitive impairment and comorbidity can themselves lead to social withdrawal and altered sleep. Accordingly, these domains should be viewed as clinical targets for assessment and support rather than as isolated causal exposures.

CGA as a clinical model for brain health

CGA provides a practical clinical framework for translating the multidomain evidence into care. It explicitly integrates cognition, mood, mobility, nutrition, continence, medication, sensory function, social circumstances and environmental factors. The evidence is strongest for selected outcomes and settings rather than for a universal effect across all community populations.^{6,13} The newer home-based evidence suggests that functional gains can be sustained across 6–24 months, while the primary-care literature demonstrates considerable variation in team composition and assessment instruments.^{7,8}

For neurogeriatric practice, the implication is that brain health should be embedded within routine geriatric assessment rather than separated into a narrowly cognitive pathway. Screening for vascular risk, hearing impairment, depression, sleep problems, frailty, medication burden, mobility limitation and social isolation can identify modifiable contributors to loss of cognitive and functional reserve.

Prevention and public-health implications

The 2026 WHO guideline places dementia risk reduction within a life-course and multisectoral framework and estimates that up to 45% of dementia risk may be attributable to potentially modifiable factors.¹⁵ The present synthesis is concordant with this approach. Physical activity, healthy diet, cardiometabolic risk management, hearing care, social connection, sleep assessment and environmental risk reduction are not competing strategies; they address different pathways within the same ageing system.

The public-health implications are especially relevant where specialist neurogeriatric services are limited. Multidomain prevention can potentially be embedded in primary care and community programmes, while CGA provides an established mechanism for identifying high-risk older adults and coordinating interventions. Implementation should be adapted to local resources rather than assuming that models developed in high-income health systems can be transferred unchanged.

Biomarkers and the future of personalised prevention

The rapid development of plasma biomarkers may change the distinction between risk reduction and biological detection. Plasma p-tau217 shows promising diagnostic performance for amyloid pathology, but diagnostic accuracy is not equivalent to demonstrated clinical benefit from biomarker-guided prevention.¹⁸ Future research should therefore test whether biomarker-informed pathways improve patient outcomes, reduce inappropriate investigation and treatment, and add value beyond conventional clinical and functional assessment.

Strengths and limitations

A principal strength of this review is the integration of evidence across multiple determinants of healthy brain ageing, including clinical care models, lifestyle interventions, social factors, sleep, environmental exposures and emerging biomarkers. The review also avoids treating heterogeneous published estimates as if they were generated from a single *de novo* meta-analysis.

Several limitations should be considered. First, the review is dependent on the quality, scope and methodological robustness of the underlying systematic reviews and meta-analyses. Second, substantial clinical and methodological heterogeneity exists across populations, settings, outcome definitions and follow-up periods, limiting direct comparability between evidence syntheses. Third, many risk-factor estimates arise from observational cohorts and therefore remain vulnerable to residual confounding and reverse causation. Fourth, overlap between primary studies across systematic reviews may introduce potential duplication of evidence, despite efforts to prioritise the most comprehensive and methodologically robust contemporary syntheses. Finally, evidence for artificial intelligence, some cognitive interventions and several emerging biomarkers remains heterogeneous, limiting quantitative integration and interpretation.

CONCLUSION

Healthy brain ageing is a multidomain, life-course process in which cognitive health is closely interconnected with physical function, vascular and metabolic health, mood, sensory function, sleep, social connection and the broader care environment. The evidence synthesised in this review suggests that brain health should not be approached through isolated cognitive interventions alone, but through coordinated strategies addressing multiple interacting determinants of healthy ageing. Contemporary evidence is most supportive of integrated and multidomain approaches, particularly those combining physical activity with cognitive, nutritional, psychological and social components alongside systematic management of modifiable vascular and metabolic risk factors. These approaches are especially relevant to older adults experiencing frailty, multimorbidity or functional vulnerability, in whom cognitive, physical and psychosocial outcomes frequently overlap.

Comprehensive geriatric assessment (CGA) provides a practical clinical framework for translating this multidomain evidence into individualised and coordinated care. By integrating assessment of cognition, function, mobility, comorbidity, medication, nutrition, psychological wellbeing and social circumstances, CGA may help identify modifiable contributors to declining brain health while supporting broader functional outcomes. The findings also highlight the importance of prevention across the life course. Healthy dietary patterns, physical activity, meaningful social engagement, appropriate sleep, sensory health, vascular risk management and avoidance of harmful exposures represent interconnected opportunities for maintaining cognitive and functional resilience. Conversely, loneliness, physical inactivity, cardiometabolic risk, sensory impairment, sleep disturbance and other modifiable factors may contribute cumulatively to adverse ageing trajectories. Emerging technologies and biomarkers, particularly plasma phosphorylated tau 217 (p-tau217), offer opportunities to improve biological characterisation and detection of neurodegenerative disease. However, diagnostic utility should not be equated with demonstrated preventive benefit, and the clinical value of these technologies for population-level healthy brain ageing remains to be established.

Future research should therefore move beyond short-term cognitive endpoints and prioritise long-term functional independence, quality of life, patient-centred outcomes, healthcare utilisation and prevention of disability. Greater attention is also required to implementation within primary-care and community settings, equity across diverse populations, accessibility of interventions, and standardised outcome measurement. Well-designed longitudinal and pragmatic studies should clarify which combinations of interventions provide sustained benefit and how these strategies can be integrated into routine neurogeriatric and geriatric care. Overall, healthy brain ageing is best understood as an integrated clinical and public-health objective, requiring coordinated action across individual behaviours, medical risk-factor management, social determinants, healthcare systems and supportive environments.

Declarations

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Conflicts of interest: Nil

Ethics approval: Ethical principles were maintained through accurate referencing and acknowledgement of sources, responsible interpretation of evidence, respect for privacy, avoidance of ageist language and assumptions, and transparent reporting. The review promotes dignity, equity, inclusivity, and respectful representation of older adults throughout the research and reporting process.

Data availability: All evidence was derived from published systematic reviews, meta-analyses and other indexed sources. The search/update strategy is described in the Methods.

Author contributions: All authors contributed substantially to the conception, literature review, data synthesis, manuscript preparation, critical revision, and approval of the final manuscript.

Registration: The study has been registered with PROSPERO³⁹ to enhance transparency, methodological accountability, and reproducibility, while reducing selective reporting and strengthening confidence in the review process.

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