Risk reduction of cognitive decline and dementia

WHO guidelines, second edition

World Health Organization

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Design by Erica Lefstad.

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Foreword

More than 57 million people are living with dementia globally, a number that continues to rise, particularly in low-and middle-income countries. Behind these numbers are individuals, families, and communities navigating profound challenges that affect not only health, but dignity, independence, and well-being. This is not a distant issue; it touches all of us.

While the world continues to search for a cure for dementia, we already know that up to 45% of dementia risk can be attributed to modifiable risk factors, many of which are shared with noncommunicable diseases (NCDs). This is why dementia risk reduction is central to the *Global action plan on the public health response to dementia 2017–2025*, recently extended to 2031. Its goals are closely aligned with global action on NCDs, recognizing that shared risk factors require integrated, sustained responses across the life course.

These updated WHO guidelines are an important step forward. They provide practical, evidence-based actions to reduce dementia risk and promote brain health.

Universal health coverage provides the foundation for delivering this agenda. It ensures that people can access the services they need without financial hardship. Through strong, people-centred health systems, countries can better prevent, detect, and manage dementia and its risk factors over time, while responding to people's evolving needs as they age.

WHO is committed to supporting countries in this effort – through its leadership on healthy ageing, its work on NCDs, and its support to strengthen primary health care systems. But protecting brain health extends beyond the health sector. The conditions in which we are born, grow, live, play, work, and age all influence our risk of dementia.

These updated WHO guidelines are an important step forward. They provide practical, evidence-based actions to reduce dementia risk and promote brain health. Turning this guidance into impact will require commitment, investment, and collaboration across sectors.

By working together towards these actions, we can change the trajectory of dementia, protecting not only future generations, but also ourselves, and building healthier, more resilient societies for all.

Dévora Kestel

Director, a.i. Department of Noncommunicable Diseases and Mental Health

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WHO regional offices:

Chido Rwafa- Madzvamutse (Regional Office for Africa, Department of Mental Health and Substance Use); Renato Oliveira e Souza (Regional Office for the Americas, Department of Noncommunicable Diseases and Mental Health); Andrea Bruni (Regional Office for South-East Asia, Department of Noncommunicable Diseases, Mental Health and Disabilities); Ledia Lazeri (Regional Office for Europe, Department of Mental Health and Well-being); Khalid Saeed (Regional Office for the Eastern Mediterranean, Department of Mental Health, Neurological and Substance Use Disorders); and Atsuro Tsutsumi (Regional Office for the Western Pacific, Prevention and Management of Noncommunicable Diseases and Mental Health).

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Abbreviations

APOE	apolipoprotein E
ART	antiretroviral therapy
BMI	body mass index
CNS	central nervous system
CPAP	continuous positive airway pressure
DASH	Dietary Approach to Stop Hypertension
DOI	declaration of interest
ERT	evidence review team
EtD	evidence to decision
GDG	Guideline Development Group
GLP-1	glucagon-like peptide-1
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	hazard ratio
ICOPE	integrated care for older people
LDL	low-density lipoprotein
LMIC	low- and middle-income countries
MCI	mild cognitive impairment
MD	mean difference
MeDi	Mediterranean Diet
mhGAP	Mental Health Gap Action Programme
MHT	menopausal hormone therapy
MIND	Mediterranean-DASH Intervention for Neurodegenerative Delay
MMSE	Mini-Mental State Examination
NCD	noncommunicable disease
OR	odds ratio
OSA	obstructive sleep apnoea
PICO	population, intervention, comparator and outcome
PUFA	polyunsaturated fatty acids
RCT	randomized controlled trial
RR	relative risk
SAE	serious adverse event
SMD	standardized mean difference
T2D	type 2 diabetes
TBI	traumatic brain injury
United Kingdom	United Kingdom of Great Britain and Northern Ireland
USA	United States of America
WHO	World Health Organization

Executive summary

This is the second edition of the World Health Organization (WHO) guidelines on risk reduction of cognitive decline and dementia; the first edition was released in 2019. This updated edition reflects the latest evidence and advances in dementia risk reduction.

Background

In 2021, an estimated 57 million people globally were living with dementia, over 60% of whom resided in low- and middle-income countries. Because there is no widely accessible disease-modifying treatment or cure for dementia, prevention across the life course remains the most effective strategy to reduce future incidence. The guidelines reflect a life-course understanding of dementia risk, recognizing that exposure to risk factors accumulates over time and that certain risk factors may have a greater impact at specific life stages. This perspective also acknowledges that some associations of risk factors with dementia late in life may reflect early disease processes rather than causal effects, highlighting the importance of timing in risk reduction efforts. Several dementia risk factors overlap with those of other noncommunicable diseases, underscoring the need for integrated public health approaches.

Because there is no widely accessible disease-modifying treatment or cure for dementia, prevention across the life course remains the most effective strategy to reduce future incidence.

Since the first edition of the guidelines was published in 2019, evidence supporting individual-level, multidomain and population-level interventions has strengthened. These updated guidelines aim to identify interventions that effectively lower dementia risk; however, they do not replace clinical guidance for managing each specific risk factor.

Who are the updated guidelines for?

The guidelines apply to adults living without dementia, including adults with normal cognition, adults with mild cognitive impairment, and adults with normal cognition or mild cognitive impairment living with another health condition. They are intended primarily for health care providers working in first- and second-level facilities, including district-level outpatient and inpatient services. However, the guidelines may also be of use to policy-makers, for supporting population-level interventions and ensuring access to essential health services.

What's new?

In 2024, the WHO Secretariat conducted a scoping review to determine whether new evidence had emerged since the publication of the 2019 guidelines (**Annex 1**).

Based on this scoping review, the Guideline Development Group (GDG):

- validated existing recommendations for five risk factors – that is, the GDG reaffirmed the existing recommendations for interventions for which new evidence was considered unlikely to alter existing guidance; and
- requested comprehensive evidence syntheses for:
  - eight risk factors for which recommendations were made in the 2019 guidelines or for which evidence was insufficient at the time; for these risk factors, the GDG determined that the evidence warranted a full review, which might change the strength or content of the existing recommendation; and
  - eight new risk factors, not covered in the 2019 guidelines – that is, the GDG determined that expanded recognition of certain conditions (e.g. HIV, stroke and traumatic brain injury) as contributors to cognitive decline warranted a full review and the development of new recommendations.

Although population-level policies are important enablers of good brain health across the life course, high-quality evidence directly linking population-level policies to reduced incidence of dementia remains limited, with the exception of air pollution interventions.

The guidelines reflect a life-course understanding of dementia risk, recognizing that exposure to risk factors accumulates over time and that certain risk factors may have a greater impact at specific life stages.

Recommendations and existing guidance

The recommendations in the guidelines are organized into three groups:

- interventions promoting healthy behaviours and lifestyles for dementia risk reduction;
- treatments or management of health conditions or biological states that are associated with an increased risk of dementia; and
- interventions addressing environmental risk factors.

In the absence of direct data on dementia, evidence was inferred from cognitive functioning. When recommendations apply only to specific age groups or to individuals exposed to certain risk factors at a particular age, this is explicitly stated. If no age group is specified, the recommendations apply to all adults.

In addition to dementia-specific recommendations, for each risk factor, the updated guidelines include generic WHO guidance, with links to relevant WHO guidelines, technical tools and frameworks, as appropriate. Dementia-specific recommendations are issued in cases where there is evidence of benefit for reducing dementia risk or improving cognition that goes beyond the established benefits of treating individual risk factors.

Table A summarizes relevant generic WHO guidance (i.e. published WHO guidelines, technical documents and frameworks) and the dementia-specific recommendations.

Table A.
Summary of generic WHO guidance and dementia-specific recommendations

Interventions promoting healthy behaviours

Cognitive activity

Generic WHO guidance

Lifelong learning through early nurturing interactions, equitable access to quality education, and cognitively stimulating work and environments should be promoted for everyone, to optimize brain health (including cognitive health) across the life course, in line with WHO guidance.

Clinical practice:

- *Integrated care for older people: guidelines on community-level interventions to manage declines in intrinsic capacity (1)*

Service delivery and care pathways:

- *Nurturing care for early childhood development: a framework for helping children survive and thrive to transform health and human potential (2)*
- *Framework to implement a life course approach in practice (3)*
- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (4)*

Public health and policy:

- *Optimizing brain health across the life course: WHO position paper (5)*

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, cognitive training[a] may be offered to older adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: low

NEW RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, engagement in cognitive stimulation[b] may be encouraged.

Strength of recommendation: conditional

Certainty of evidence: very low

[a] Cognitive training refers to a targeted and repetitive cognitive exercise or task that stimulates specific cognitive domains.

[b] Cognitive stimulation refers to structured activities or programmes in a group or social setting, within a set amount of time, as well as everyday activities that enhance general cognitive function such as reading, storytelling and playing games that individuals can undertake themselves.

Social activity

Generic WHO guidance

Social participation is strongly connected to good health and well-being throughout life, and should be supported over the life course, in line with WHO guidance.

Clinical practice:

- No dedicated WHO clinical guideline

Service delivery and care pathways:

- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (4)*

Public health and policy:

- *From loneliness to social connection: charting a path to healthier societies: report of the WHO Commission on Social Connection (6)*
- *Social isolation and loneliness among older people: advocacy brief (7)*

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, engagement in social activity interventions may be recommended to adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: very low

Physical activity

Generic WHO guidance

Regular physical activity across all ages and abilities – including aerobic movement, muscle strengthening activities and reduced sedentary behaviour – should be promoted for everyone, in line with WHO guidance.

Clinical practice:

- *WHO guidelines on physical activity and sedentary behaviour (8)*

Service delivery and care pathways:

- *Promoting physical activity through primary health care: a toolkit (9)*
- *Promoting physical activity for older people: a toolkit for action (10)*
- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*

Recommendations

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline specifically, physical activity should be recommended to adults with normal cognition.

Strength of recommendation: strong

Certainty of evidence: moderate

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline specifically, physical activity may be recommended to adults with mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: low

Reduce the harmful use of alcohol

Generic WHO guidance

Alcohol use is associated with many health risks, owing to its psychoactive, toxic and dependence-producing properties. Hence, alcohol should not be recommended in any amount for health benefits, in line with WHO guidance.

Clinical practice:

- *Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders – specifically, the module on alcohol use disorders (13)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *WHO Global strategy to reduce the harmful use of alcohol (14)*
- *Global alcohol action plan 2022–2030 (15)*
- *Global status report on alcohol and health and treatment of substance use disorders (16)*
- *The SAFER technical package: five areas of intervention at national and subnational levels (17)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*
- *Alcohol fact sheet (18)*

Recommendations

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, interventions aimed at reducing or ceasing hazardous and harmful drinking (including providing support to people with alcohol dependence) may be offered to adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: moderate

Tobacco cessation

Generic WHO guidance

Tobacco use should be avoided entirely. All people who use tobacco should be supported to quit through evidence-based behavioural and pharmacological cessation interventions, and all people should be protected from exposure to tobacco smoke, in line with WHO guidance.

Clinical practice:

- *WHO clinical treatment guideline for tobacco cessation in adults (19)*

Service delivery and care pathways:

- *Strengthening health systems for treating tobacco dependence in primary care to enhance skills and integrate evidence-based cessation practices into routine care (20)*
- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*

Recommendations

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline and dementia specifically, interventions for tobacco cessation should be offered to adults who use tobacco.

Strength of recommendation: strong

Certainty of evidence: low

Healthy, balanced diet and nutrition

Generic WHO guidance

A healthy, balanced diet should be recommended to all adults, in line with WHO guidance.

Clinical practice:

- *Carbohydrate intake for adults and children: WHO guideline (21,22)*
- *Guideline: sugars intake for adults and children (23)*
- *Use of non-sugar sweeteners: WHO guideline (24)*
- *Total fat intake for the prevention of unhealthy weight gain in adults and children: WHO guideline (25)*
- *Saturated fatty acid and trans-fatty acid intake for adults and children: WHO guideline (26)*
- *Guideline: sodium intake for adults and children (27,28)*
- *Guideline: potassium intake for adults and children (28)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *Healthy diet (12)*
- *Fiscal policies to promote healthy diets: WHO guideline (29)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, a healthy, balanced dietary pattern[a] may be recommended to adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: moderate

VALIDATED RECOMMENDATION AGAINST ✗

To reduce the risk of cognitive decline and/or dementia specifically, supplemention of vitamins B and E, omega-3 polyunsaturated fatty acids (PUFA) and multivitamins/minerals is not recommended.[b]

Strength of recommendation: strong

Certainty of evidence: moderate

[a] To be healthy, diets need to be *(22)*:

- **adequate:** providing enough essential nutrients to prevent deficiencies and promote health, without excess;
- **balanced:** in energy intake and energy sources (i.e. fats, carbohydrates and proteins);
- diverse: including a wide variety of nutritious foods within and across food groups to favour nutrient adequacy and consumption of other health-promoting substances; and
- **moderate:** in consumption of foods, nutrients or other compounds associated with detrimental health effects.

The exact makeup of a diet will vary depending on individual characteristics, preferences and beliefs, cultural context, locally available foods and dietary customs.

[b] This applies only to individuals without established vitamin deficiencies.

Management of health conditions and biological states

Management of obesity

Generic WHO guidance

Management of obesity should be offered to all adults[a] living with obesity, in line with WHO guidance.

Clinical practice:

- *Guideline on the use of glucagon-like peptide-1 (GLP-1) therapies for the treatment of obesity in adults (30)*

Service delivery and care pathways:

- *Health service delivery framework for prevention and management of obesity (31)*

Public health and policy:

- *WHO acceleration plan to stop obesity: a joint WHO/UNICEF operational model for designing and implementing the response (32,33)*
- *Recommendations for the prevention and management of obesity over the life course (34)*
- *Global action plan for the prevention and control of noncommunicable diseases (35)*

[a] WHO guidance applies to all non-pregnant adults with obesity.

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, interventions for reducing midlife overweight or obesity may be offered.

Strength of recommendation: conditional

Certainty of evidence: low to moderate

NEW RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, dietary restriction interventions may be offered to adults who are overweight or obese.

Strength of recommendation: conditional

Certainty of evidence: low to moderate

Management of diabetes

Generic WHO guidance

Management of diabetes should be offered to all adults with diabetes, in line with WHO guidance.

Clinical practice:

- *HEARTS D: diagnosis and management of type 2 diabetes (36)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *The WHO Global Diabetes Compact (37)*
- *Global action plan for the prevention and control of noncommunicable diseases 2013–2020 (35)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, management of diabetes may be offered to adults with diabetes.

Strength of recommendation: conditional

Certainty of evidence: very low

Management of hypertension

Generic WHO guidance

Management of hypertension should be offered to all adults with hypertension, in line with WHO guidance.

Clinical practice:

- *Guideline for the pharmacological treatment of hypertension in adults (38)*
- *HEARTS: technical package for cardiovascular disease management in primary health care (39)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *Global action plan for the prevention and control of noncommunicable diseases 2013–2020 (35)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, management of hypertension may be offered to adults with hypertension.

Strength of recommendation: conditional

Certainty of evidence: very low

Management of dyslipidaemia

Generic WHO guidance

Management of dyslipidaemia should be offered to all adults with dyslipidaemia, in line with WHO guidance.

Clinical practice:

- *Hearts: technical package for cardiovascular disease management in primary health care: risk-based CVD management (39)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (11)*

Public health and policy:

- *Global action plan for the prevention and control of noncommunicable diseases (35)*

Recommendations

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, management of dyslipidaemia at midlife may be offered.

Strength of recommendation: conditional

Certainty of evidence: low

Management of hearing loss

Generic WHO guidance

Prevention, screening and management of hearing loss should be offered, in line with WHO guidance.

Clinical practice:

- *Package of interventions for rehabilitation: module 6: sensory conditions (40)*

Service delivery and care pathways:

- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (4)*

Public health and policy:

- *Hearing screening: considerations for implementation (41)*

Recommendations

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, hearing aids may be offered to adults with hearing loss.

Strength of recommendation: conditional

Certainty of evidence: low

Use of menopausal hormone therapy (MHT)

General clinical remark

MHT is primarily used for symptomatic relief of vasomotor symptoms and genitourinary syndrome of menopause, not for dementia prevention.

Recommendations

NEW RECOMMENDATION AGAINST

Menopausal hormone therapy is not recommended for specifically reducing the risk of cognitive decline and/or dementia in postmenopausal women aged 65 years and older.

Strength of recommendation: conditional

Certainty of evidence: very low

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For women aged below 65 years – including those experiencing premature ovarian insufficiency, early menopause or perimenopause – and for the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to advise for or against the use of menopausal hormone therapy.

Management of depression

Generic WHO guidance

Management of depression in the form of psychological interventions and/or antidepressants should be provided to all adults with depression, in line with WHO guidance.

Clinical practice:

- *Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders (13)*

Service delivery and care pathways:

- *mhGAP intervention guide – Version 2.0 (42)*
- *Depression module of the mhGAP training manuals (43)*
- *Depression module of the WHO Academy mhGAP training – mhGAP: Integrating mental health into primary care (44)*

Public health and policy:

- *Comprehensive mental health action plan 2013–2030 (45)*

Recommendations

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend the management of depression.

Management of stroke

Generic WHO guidance

Management of stroke should be provided to all adults, in line with WHO guidance.

Clinical practice:

- *Package of interventions for rehabilitation: module 3: neurological conditions (46)*

Service delivery and care pathways:

- *Framework for the care of acute coronary syndrome and stroke (47)*

Public health and policy:

- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (12)*
- *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (48)*

Recommendations

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend pharmacological interventions typically used to reduce the risk of recurrent stroke.

Management of traumatic brain injury (TBI)

Generic WHO guidance

Measures to prevent head injuries and traumatic brain injury should be consistently implemented and enforced across all populations. Prevention and management strategies should align with existing WHO guidance:

Clinical practice:

- *Package of interventions for rehabilitation: module 3: neurological conditions (46)*

Service delivery and care pathways:

- *Helmets: a road safety manual for decision-makers and practitioners (49)*
- The global concussion awareness campaign from WHO and the Fédération Internationale de Football Association (FIFA) *(50)*

Public health and policy:

- *Global plan for the decade of action for road safety 2021–2030 (51)*
- *Respect women: preventing violence against women (52)*

Recommendations

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend specific interventions after traumatic brain injury.

Management of vision impairment

Generic WHO guidance

Screening of suspected vision impairment should be offered to all adults, and management should be offered to those diagnosed with vision impairment, in line with WHO guidance.

Clinical practice:

- *Package of eye care interventions (53)*

Service delivery and care pathways:

- *Vision and eye screening implementation handbook (54)*
- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (4)*

Public health and policy:

- *World report on vision (55)*
- *Eye care in health systems: guide for action (56)*

Recommendations

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend vision impairment interventions.

Management of sleep

General clinical remark

Sleep is important for overall health and well-being. Maintaining good sleep – including getting enough hours of sleep, enjoying uninterrupted sleep, and achieving deep, restorative sleep – is advised throughout life.

Recommendations

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend interventions to treat sleep–wake disorders.

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend interventions to improve sleep[a] (quality or duration).

[a] Certain aspects of sleep contribute to sleep quality; for example, adequate sleep duration to ensure alertness the following day, continuity through uninterrupted sleep and deep sleep that provides restorative benefits.

Management of HIV

Generic WHO guidance

Antiretroviral therapy should be initiated for all people living with HIV, regardless of WHO clinical stage and CD4 cell count, to achieve and maintain viral suppression; the goal is to reach undetectable levels of HIV. Clinical management of HIV should be in line with WHO guidance.

Clinical practice:

- *WHO updated recommendations on HIV clinical management: recommendations for a public health approach (57)*
- *WHO guidelines on the management of advanced HIV disease (58)*

Service delivery and care pathways:

- *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach (59)*
- *Consolidated guidelines on differentiated HIV testing services (60)*

Public health and policy:

- *The role of HIV viral suppression in improving individual health and reducing transmission (61)*

Recommendations

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend one anti-retroviral therapy (ART) combination over another; therefore, ART regimens should be used according to disease control needs and patient preferences.

Interventions addressing environmental risk factors

Reduce exposure to air pollution

Generic WHO guidance

Air pollution is toxic and contributes substantially to the global burden of communicable and noncommunicable diseases, including dementia. Reducing exposure to air pollution, both indoors and outdoors, is critical to improving health and well-being for all people, across the entire life course, in line with guidance from WHO and other organizations:

Public health and policy:

- *WHO global air quality guidelines: particulate matter ($PM_{2.5}$ and PM_{10}), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide (62)*
- *Integrated science assessment (ISA) for particulate matter (final report, Dec 2019) (63)*

Recommendations

NEW RECOMMENDATION

Reducing exposure to household air pollution may reduce the risk or incidence of cognitive decline and/or dementia.

Strength of recommendation: conditional

Certainty of evidence: very low

NEW RECOMMENDATION

Reducing exposure to ambient air pollution (especially $PM_{2.5}$) may reduce the risk or incidence of cognitive decline and/or dementia.

Strength of recommendation: conditional

Certainty of evidence: very low

Interventions addressing multiple risk factors

Multidomain interventions

General clinical remark

Dementia risk factors should be addressed holistically, because multiple risks often coexist and accumulate over the life course.

Recommendations

NEW RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, tailored[a], multidomain[b] interventions may be offered.

Strength of recommendation: conditional

Certainty of evidence: moderate to high

[a] "Tailored" refers to customizing multidomain interventions to the specific needs and context of the individual or population. This includes selecting components that address relevant modifiable risk factors that are present in a person; adjusting intensity and delivery format; and considering cultural, socioeconomic and resource constraints. Tailoring ensures that interventions are adapted to optimize feasibility, adherence and effectiveness.

[b] "Multidomain" refers to targeting multiple dementia risk factors at once.

Implementation of dementia risk reduction interventions is shaped by health system, structural and sociocultural factors that are beyond individual control and thus require action beyond behaviour change alone.

Implementation considerations

Implementation of dementia risk reduction interventions is shaped by health system, structural and sociocultural factors that are beyond individual control and thus require action beyond behaviour change alone. Cross-cutting considerations include addressing structural and policy-level barriers; multisectoral collaboration and integrated, multidomain approaches; and embedding interventions within existing programmes for primary care, noncommunicable diseases, ageing and community. Strategies should balance digital and in-person delivery, strengthen workforce capacity, support public awareness and stigma reduction, and include monitoring and evaluation. Equity considerations cut across all risk factors and should be central to all implementation strategies.

Limitations, and gaps in evidence and research

Although the evidence base has increased since the first edition of the guidelines, important limitations remain. Across most risk factors, the evidence base is restricted to observational studies or only a few randomized controlled trials, short follow-up periods, and infrequent use of dementia or mild cognitive impairment as outcomes. Also, evidence is largely derived from high-income countries, with limited subgroup analyses and variable definitions of interventions and outcomes. Additionally, evidence on interactions between multiple risk factors remains limited, as does evidence on feasibility, scalability, cost–effectiveness and policy-level interventions. Addressing these gaps is essential to strengthen the evidence base, and to inform equitable, effective and context-appropriate dementia risk reduction strategies and future guideline updates.

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1. Introduction

1.1 Context

Dementia refers to a group of disorders characterized by a decline in cognitive function from a previous level, significantly affecting daily functioning. In 2021, 57 million people were living with dementia globally, with more than 60% residing in low- and middle-income countries (LMIC) *(1)*. As a leading cause of disability and dependency globally, dementia represents one of the most pressing global health and social care challenges of the 21st century.

Currently, there are no effective, widely accessible, disease-modifying treatments and no cure for dementia. Hence, dementia prevention and risk reduction are the most promising public health approaches to alter the future trajectory of dementia globally.

Dementia prevention and risk reduction

Dementia risk is influenced by a wide range of interconnected determinants, including health, behavioural and environmental factors throughout the life course. According to a 2024 Lancet Commission report on dementia prevention, intervention and care, up to 45% of dementia risk is attributed to 14 modifiable risk factors *(2)*. These factors include **unhealthy behaviours** such as poor diet and physical inactivity, **health conditions** such as diabetes mellitus (hereafter referred to as diabetes) and hypertension, and **environmental exposures** such as air pollution. For a list of all risk factors and intervention targets included in this guideline see **Table 1**.

Life-course patterns of risk exposure and the role of reverse causality

Dementia develops gradually over decades. Similarly, dementia risk accumulates over the life course, with different risk factors exerting their greatest influence at specific stages. For instance, the likelihood of developing dementia in later life (i.e. aged ≥65 years) increases as a result of exposure – particularly in midlife (i.e. aged 19–65 years) – to hypertension, hearing loss, obesity, smoking, depression, dyslipidaemia, diabetes, excessive alcohol consumption, physical inactivity and traumatic brain injury (TBI).[1] Similarly, the chances of developing dementia may be greater in those experiencing social isolation, air pollution and untreated vision impairment in later life *(2)*. A given risk factor may not have uniform effects across age groups. For instance, higher body weight appears to be harmful in midlife but may be protective in later life, because weight loss in older age may signal early cognitive decline. Similarly, depressive symptoms emerging in older age compared with midlife may reflect early or prodromal neuropathological changes rather than being an independent causal factor.

Fig. 1 illustrates the risk factors considered in these guidelines as intervention targets for dementia risk reduction, and the periods in life for which exposure has been established as particularly harmful (if known).

Mechanisms of action

Several biological pathways have been proposed to mediate the relationship between risk factors and the onset of dementia. Pathways for reducing the risk of dementia include decreasing underlying neuropathology or vascular damage, reducing inflammation, treating metabolic dysfunction and increasing neuronal resilience. **Fig. 2** illustrates the hypothetical mechanisms of action by which addressing each risk factor can potentially reduce dementia risk.

Table 1. Risk factors and intervention targets covered by the updated WHO guidelines

Promoting healthy behaviours	Management of conditions	Reduce exposure to environmental factors
Alcohol reduction Tobacco cessation Physical activity Healthy diet	Hypertension Diabetes Dyslipidaemia Obesity Stroke	Air pollution
Social activity Cognitive activity	Depression Hearing loss Vision impairment Sleep TBI Use of MHT[a] HIV	

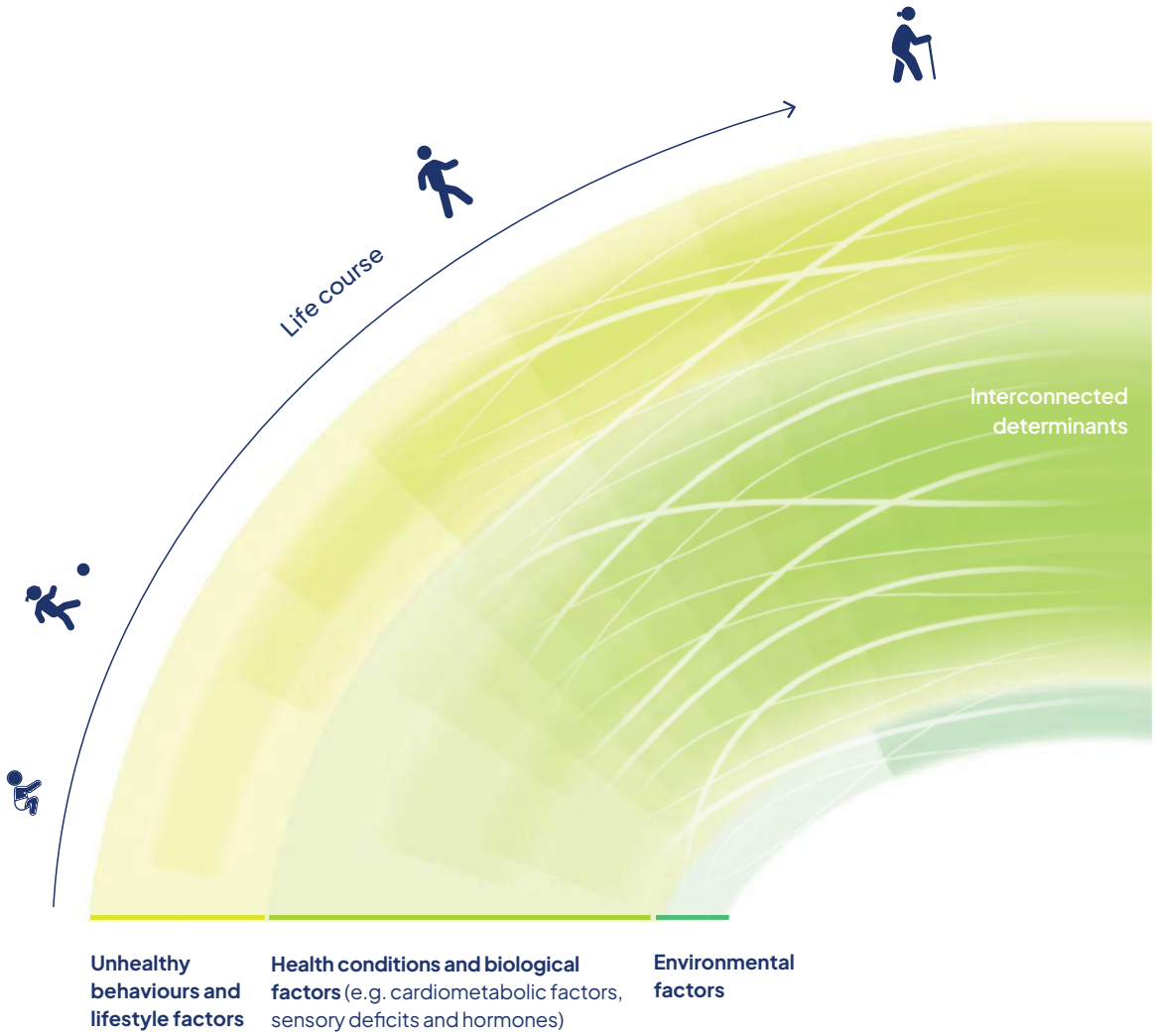
[a] Menopausal hormone therapy

Legend: The dotted lines indicate risk factors and intervention targets commonly shared with other cardiometabolic conditions.

[1] TBI is damage to the brain caused by an external force (e.g. a blow, jolt or penetration) resulting in temporary or permanent impairment of cognitive, physical or psychosocial function.

Fig. 1

Dementia risk factors accumulate across the life course



Unhealthy behaviours and lifestyle factors

- Cognitive inactivity
- Social isolation
- Physical inactivity
- Harmful alcohol use
- Smoking
- Unhealthy diet

Health conditions and biological factors (e.g. cardiometabolic factors, sensory deficits and hormones)

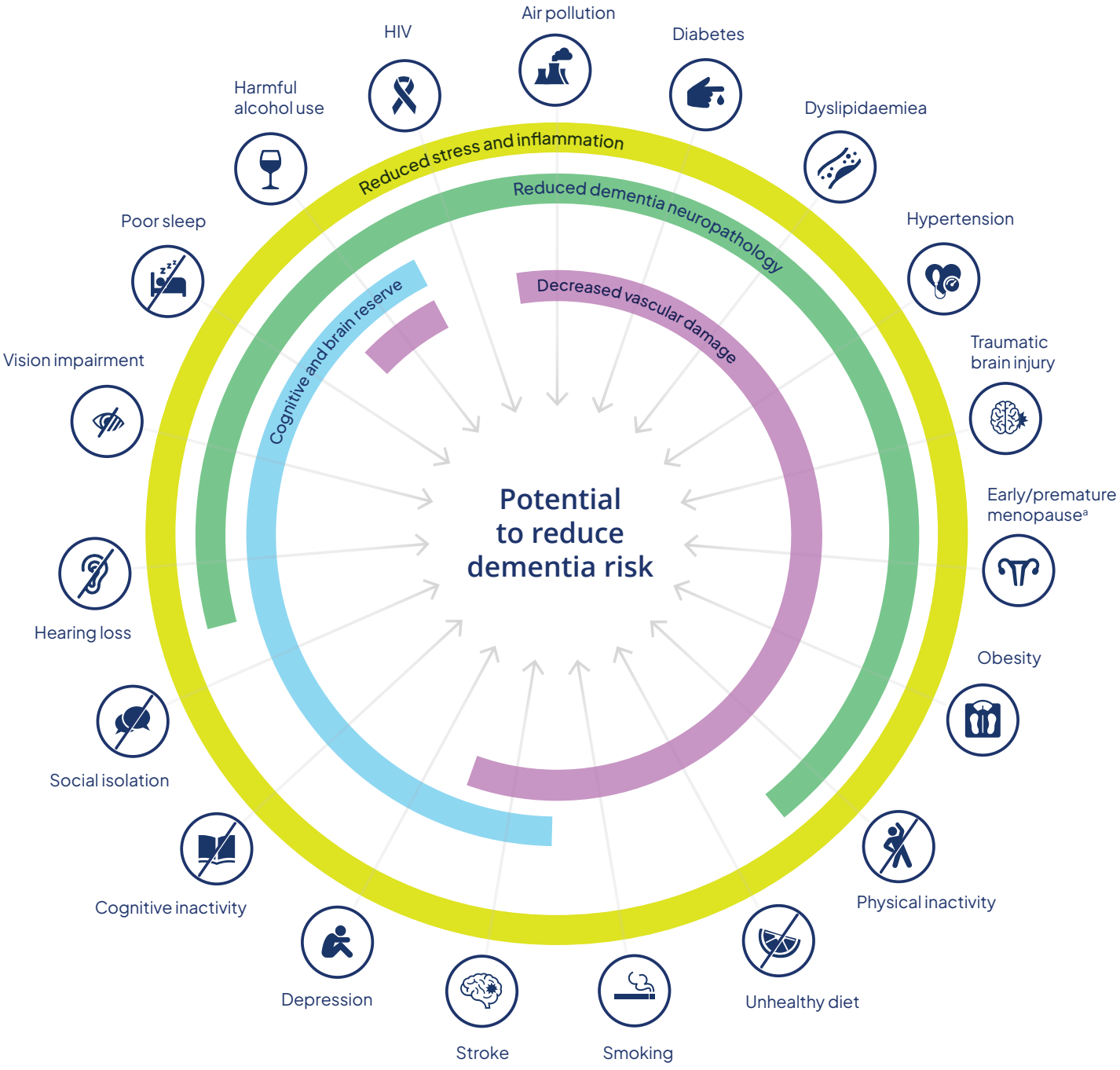
- Obesity
- Recurring stroke
- High cholesterol
- Hypertension
- Traumatic brain injury
- Vision impairment
- Diabetes
- Hearing loss
- Poor sleep
- Depression
- Menopause
- HIV

Environmental factors

- Air pollution

Fig. 2

How treating modifiable risk factors may prevent or delay dementia



[a] Premature or early menopause, occurring either naturally or iatrogenically before the age of 40 or between the ages of 40–44, respectively, has been implicated as a distinct risk factor for dementia and cognitive decline. However, most intervention evidence relates to treatment of persons experiencing natural menopause.

Individual- versus population-level risk reduction for dementia

Individual-level interventions target specific risk factors through primary or secondary prevention. However, achieving meaningful reductions in dementia risk and therefore incidence requires population-level action, such as policies that improve education, expand access to preventive health services, regulate air quality, and promote safe and active living environments. In the absence of such enabling conditions, individual-level recommendations are less effective and less equitably adopted. Thus, sustained change at policy and system levels is essential to maximize the reach and impact of dementia risk reduction strategies.

Social determinants such as poverty, deprivation, and inequities in education and socioeconomic opportunities can have strong and lasting effects on dementia risk. These determinants influence, for instance, early life and midlife opportunities for quality education, stable income, nutritious food and access to health care; thus, they influence dementia risk in later life.

Global mandates for dementia risk reduction

The *Global action plan on the public health response to dementia 2017–2025 (3)*, which has been extended to 2031 *(4)*, envisions *"a world in which dementia is prevented and people with dementia and their carers live well and receive the care and support they need to fulfil their potential with dignity, respect, autonomy and equality"*. One of the seven action areas of the plan focuses on dementia risk reduction; it tasks the World Health Organization (WHO) Secretariat with strengthening and disseminating evidence to support policy interventions targeting modifiable risk factors.

Many dementia risk factors are shared with other noncommunicable diseases (NCDs); hence, the global targets for dementia risk reduction are tied to those for NCD prevention and control, highlighting the importance of integrated public health strategies. This aligns with WHO's updated guidance on cost-effective interventions for NCD prevention and control, including the 2024 *Best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*, which provides a complementary framework for implementing dementia risk reduction strategies at scale.

In 2019, WHO released its first guidelines on reducing the risk of cognitive decline and dementia *(6)*, offering evidence-based recommendations on lifestyle and behavioural interventions to delay or prevent cognitive decline and dementia. Since the release of those guidelines, the field of dementia risk reduction has evolved significantly. More and stronger evidence is now available for the efficacy of individual-level interventions, multidomain interventions (addressing three or more risk factors) for dementia risk reduction and population-level policy interventions *(7–11)*. Similarly, when the guidelines were first developed, most of the available studies were conducted in high-income countries, potentially impacting generalizability; now, studies are available from a range of countries.

These new developments, along with WHO's commitment to regularly review and disseminate emerging evidence, warrant the release of this new edition of the guidelines.

> *"…a world in which dementia is prevented and people with dementia and their carers live well and receive the care and support they need to fulfil their potential with dignity, respect, autonomy and equality…"*
>
> Global action plan on the public health response to dementia 2017–2025

1.2 Purpose

The purpose of these guidelines is to identify which interventions aimed at treating established dementia risk factors are effective in reducing the risk of cognitive decline and dementia. These guidelines are not intended to replace existing clinical guidelines for the prevention and management of each individual risk factor (though relevant cross-references are provided), nor do they aim to determine which exposures qualify as dementia risk factors. **Fig. 3** provides a schematic overview of the scope and focus of these guidelines.

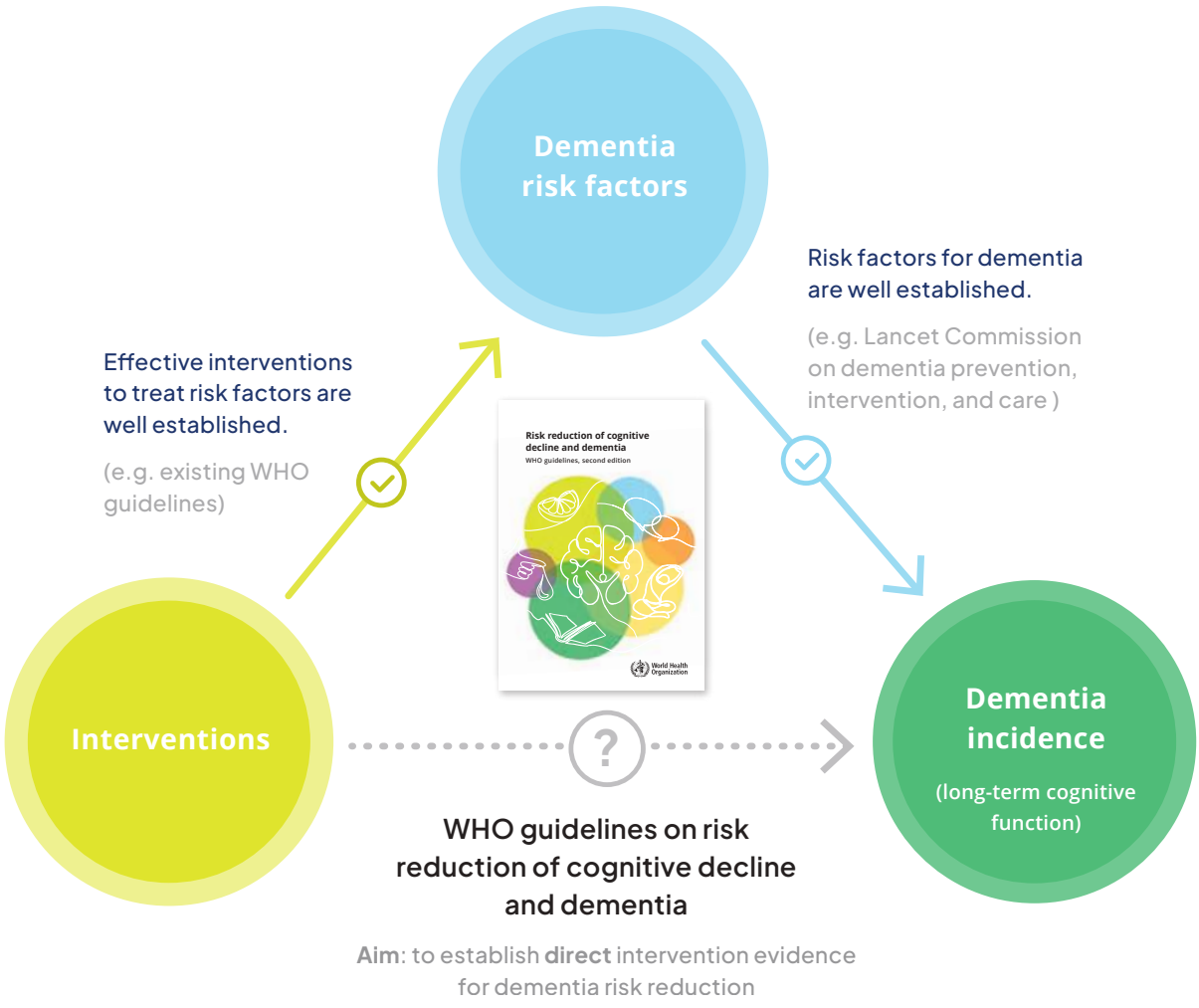
Specifically, these guidelines provide up-to-date, evidence-based recommendations for interventions:

- promoting healthy behaviours to reduce the risk of cognitive decline and/or dementia;
- managing specific health conditions and biological factors that are associated with dementia risk; and
- targeting environmental factors that are associated with cognitive decline and dementia.

Although treating individual risk factors is important, there is strong evidence for lifelong accumulation of multiple risk factors and coexisting health conditions (multimorbidity) *(12)*. Therefore, these guidelines also synthesized evidence for multidomain interventions.

Fig. 3

Evidence framework for dementia risk reduction



1.3 Scope

The scope of these guidelines is prevention or risk reduction of cognitive decline[1] and/or dementia[2] (main outcomes of interest). The guidelines are intended for adults without dementia, including:

- adults with normal cognition;[3]
- adults with mild cognitive impairment (MCI);[4] and
- adults with normal cognition or MCI living with another health condition.

These updated guidelines expand the scope beyond conditions caused by neurodegenerative processes, such as Alzheimer disease, and vascular dementia, to now also include dementia associated with medical conditions such as HIV, TBI and stroke. Although those forms of dementia may be preventable or manageable by treating the underlying cause, they can also contribute to long-term cognitive decline and dementia risk. Their inclusion in these updated guidelines reflects a growing recognition of their public health relevance, particularly in LMIC where conditions such as HIV and stroke are prevalent, and are often underdiagnosed or undertreated, supporting a more comprehensive approach to dementia risk reduction.

Risk factors considered in these updated guidelines include various factors known to increase the risk of dementia: **unhealthy behaviours** (e.g. tobacco use or smoking, harmful use of alcohol, physical inactivity and unhealthy diets), **health conditions** (e.g. diabetes, hypertension, HIV, depression and sleep–wake disorders), **biological states** (e.g. menopause) and **environmental factors** (e.g. air pollution) *(7–11)* (**Table 1**). Other potentially modifiable risk factors for cognitive decline and/or dementia (e.g. childhood malnutrition, infections other than HIV and systemic inflammation) are outside the scope of these guidelines.

Dementia prevention includes addressing these risk factors through individual- and population-level interventions (e.g. changing broader environmental, social and economic conditions) *(9,13)*. Although many modifiable risk factors are influenced by public policy (e.g. the design of urban environments and alcohol taxation), there is a lack of high-quality evidence assessing how public policy truly impacts dementia incidence *(2)*. Action on air pollution was the only public policy that was taken into consideration and was within the scope of this guideline update. Effective policy options may be available (e.g. policies addressing tobacco cessation and alcohol-use reduction), but substantive evidence gaps remain linking those options to reduced dementia incidence. It is vital to fill these evidence gaps before public policy can be fully reflected in dementia-prevention strategies.

[1] **Cognitive decline** is defined as a noticeable and measurable loss or abnormality in attention functions, memory functions or higher level cognitive functions, including attention, language reasoning and visuospatial abilitiy.

[2] **Dementia** is a syndrome that includes cognitive decline and other symptoms and can be diagnosed based on International Classification of Diseases 11th Revision (ICD-11) criteria. It involves a decline in two or more cognitive domains such as memory, skilled movements (limb apraxia), language (aphasia) or executive function (e.g. planning, attention and abstract reasoning). Memory impairment is present in most forms of dementia, but cognitive impairment is not restricted to memory. This decline should represent a change from previous behaviour, and impair participation in daily activities, and social and/or occupational functioning.

[3] That is, adults with no cognitive impairment or decline and who do not meet criteria for MCI or dementia.

[4] **MCI** refers to a condition characterized by mild deficits in one or more cognitive domains (e.g. attention, executive function, language, memory, perceptual-motor abilities or social cognition) that exceed what is expected for a person's age and reflect a decline from their previous level of functioning. These impairments are not severe enough to significantly interfere with daily activities related to personal, social, educational or occupational functioning, and do not meet the criteria for a diagnosis of dementia. However, individuals with MCI are at increased risk of developing dementia. Their inclusion in these guidelines enables the use of targeted interventions to help slow the progression of cognitive decline and delay the transition from MCI to dementia.

[5] For the purposes of this document, references to Alzheimer disease are intended in line with ICD-11 category 6D80, Dementia due to Alzheimer disease; that is, a clinical dementia syndrome presumed to be attributable to underlying Alzheimer disease on the basis of clinical assessment and supportive evidence.

1.4 Target audience

These updated guidelines are primarily targeted at health care providers working at a first- or second-level facility or at district level, including basic outpatient and inpatient services. The health care providers could be doctors, nurses or other cadres of health workers. Quality improvement teams at all levels of the system will benefit from the work.

In addition, the guidelines and their derivative products have implications for policy-makers, health care planners and programme managers at both the national and international level, and for the general population. The involvement of policy-makers remains important for supporting population-level interventions and ensuring access to essential health services.

Achieving meaningful reductions in dementia risk requires population-level action, including policies that improve education, access to health services and healthier environments.

2. Methods

This document – *Risk reduction of cognitive decline and dementia: WHO guidelines, second edition* – was prepared in accordance with the WHO standards and methods for guideline development. Details of this approach can be found in the WHO handbook for guideline development *(14)*.

2.1 Guideline contributors

The different groups involved in the development of the guidelines are described below. Further details are provided in **Annex 2**.

2.1.1 WHO Steering Group

The WHO Steering Group was established to guide and oversee the guideline development process. It included WHO staff members from various departments at WHO headquarters: Department of Noncommunicable Diseases and Mental Health; Department for HIV, Tuberculosis, Hepatitis and Sexually Transmitted Infections; Department of Sexual, Reproductive, Maternal, Child, Adolescent and Ageing Health; Department of Health Determinants, Promotion and Prevention; Department of Environment, Climate Change, One Health and Migration; and Department of Nutrition and Food Safety. It also included regional advisers for mental health from all regional offices.

The role of the WHO Steering Group was to identify priority questions and outcomes, in consultation with the Guideline Development Group (GDG), and the guideline methodologist. The WHO Steering Group also decided on composition of the proposed GDG and provided overall support to guideline development.

2.1.2 Guideline Development Group

The GDG was established as a diverse panel comprising individuals with extensive expertise in clinical practice, research, health policy and guideline development, alongside representatives with lived experience. Members were selected to ensure both geographical and gender balance, and representation across countries with different income levels.

Two co-chairs were nominated by the WHO Steering Group and confirmed by GDG members before the first meeting. Their selection was based on prior experience with WHO's guideline development processes and subject matter expertise.

The GDG's responsibilities included defining the scope of the guidelines, supporting the WHO Steering Group in updating and formulating key questions in PICO (population, intervention, comparator and outcome) format, and assessing the evidence to develop recommendations. The group also reviewed the draft guideline document.

2.1.3 Evidence review teams

Five evidence review teams (ERTs) were selected based on their thematic and technical expertise. The ERTs conducted quantitative systematic reviews and assessed the certainty of evidence using standard systematic review and grading processes, as detailed in the *WHO handbook for guideline development* (14).

2.1.4 Guideline methodologist

A guideline methodologist was appointed by the WHO Steering Group to ensure expert input throughout the guideline development process. Their responsibilities included prioritizing questions and outcomes, synthesizing evidence, assessing the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, translating evidence into recommendations and overseeing the overall methodology. The methodologist supported the planning, scoping and formulation of guideline questions, and assisted the GDG in developing evidence-informed recommendations in a transparent and systematic manner.

2.1.5 External peer reviewers

External experts were invited to review the draft guidelines. These external peer reviewers included individuals with expertise in dementia risk reduction, clinical practice, research and health policy, and people with lived experience. Reviewers were selected to ensure geographical diversity, representation across country income levels and gender balance. Their role was to identify any errors or gaps in the evidence and to provide feedback on clarity, context-specific issues and implications for implementation. They were not expected to alter the recommendations formulated by the GDG. Comments from external peer reviewers were incorporated where appropriate, and the final draft was subsequently shared with the GDG.

2.2 Declarations of interest

In accordance with the *WHO handbook for guideline development (14)*, GDG members, ERT members and external peer reviewers were asked to declare in writing any competing interests – academic, financial or otherwise – at the time of their invitation to participate in the guideline development process. Each expert completed and signed the standard WHO declaration of interest (DOI) form, which was submitted electronically to the coordinating team before their involvement.

GDG members, ERT members, external peer reviewers and the guideline methodologist were also required to sign a confidentiality agreement using the standard WHO confidentiality undertaking form, covering the guideline development process and its outcomes. Upon receipt of the DOI forms, the WHO Secretariat reviewed the forms and conducted supplementary checks (e.g. internet and bibliographic database searches) to identify any potential conflicts of interest and determine whether a management plan was necessary.

Biographies of proposed GDG members were published on the WHO website for public consultation *(15)* and shared via social media. Final group composition was confirmed following this process.

At the start of the GDG meeting, a summary of the DOI declarations was presented, and members were invited to update their disclosures by notifying the WHO Secretariat of any relevant changes. Overall, the declared interests were found to be relatively minor and unlikely to affect the expert's judgement. All decisions were documented (see **Annex 2**).

Recommendations were formulated through a structured process that considered benefits and harms, certainty of evidence, and broader contextual factors.

2.3 Identifying, appraising and synthesizing available evidence

2.3.1 Appraising existing review questions and recommendations

To support the guideline update process, the WHO Secretariat conducted an initial scoping review to identify:

- new evidence related to existing PICOs;
- emerging evidence on dementia risk factors not included in the 2019 guidelines; and
- individual- and population-level interventions targeting these risks (see **Annex 1**).

The purpose of this scoping review was to inform the development of potential new questions structured using the PICO framework for inclusion in the updated guidelines, and to determine which existing recommendations need to be updated.

The findings from the scoping review were shared with the WHO Steering Group and GDG members for their input and discussion. Based on the presented evidence and their clinical and research expertise, GDG members were asked to select one of the following actions for each existing recommendation:

- **Remove:** The recommendation is outdated or no longer relevant. A review of the evidence is not required and the recommendation should be deleted.
- **Validate:** The recommendation remains well-established and widely accepted. No further evidence review or decision-making is needed. Minor edits to wording may be made to improve clarity or ensure consistency across recommendations, without altering the recommendation's strength or intent.
- **Update:** New evidence warrants a full review by the GDG, including a complete GRADE evidence to decision (EtD) process. This may result in changes to the strength or content of the recommendation *(14)*.

For proposed new risk factor interventions, GDG members were asked to choose one of the following options:

- **Include:** The topic (i.e. risk factor or condition) is sufficiently established as posing an independent risk for developing dementia. A full evidence synthesis of interventions addressing the risk factor is required, followed by a complete EtD process.
- **Exclude:** The topic is not to be included in the updated guidelines and no evidence synthesis will be required.

The GDG held a series of virtual meetings to define the scope of the guideline research questions. Through these discussions, the GDG formulated 16 research questions for the guideline update: eight updated questions based on the 2019 recommendations pertaining to cognitive training, depression, diabetes, diet and nutrition, hearing loss, hypertension, obesity and social activity; and eight new questions pertaining to air pollution, HIV, menopausal hormone therapy (MHT), multidomain interventions, sleep, stroke, TBI and vision impairment (see **Annex 1** for details). The GDG also validated six recommendations pertaining to five risk factors: alcohol, dyslipidaemia,[1] physical activity, tobacco cessation and use of dietary supplements.

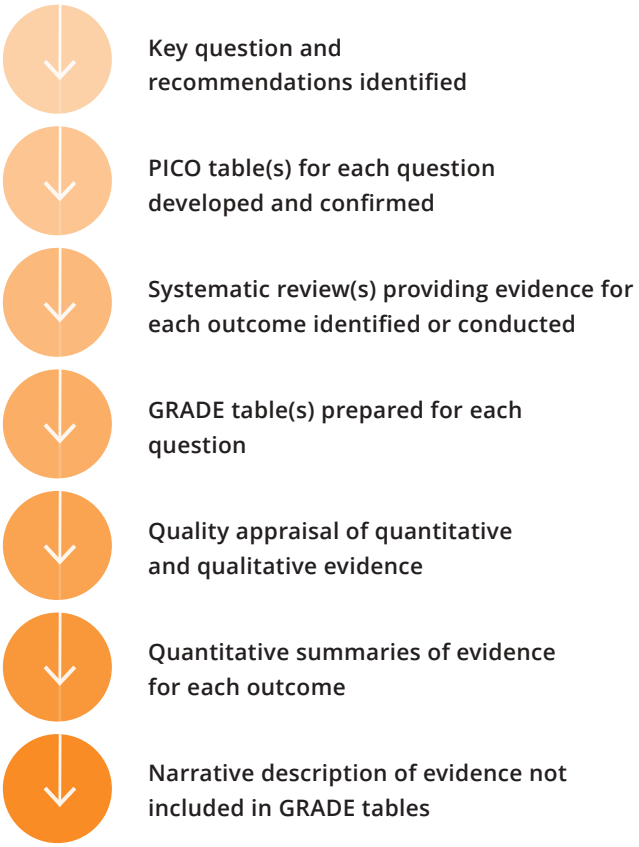
With support from the GDG, each question was structured using the PICO framework, with critical and important outcomes specified. The outcomes defined in the 2019 guidelines were retained for both the updated and new questions.

Following the meetings, the WHO Secretariat prepared a summary report outlining suggested actions for each existing recommendation and proposed new questions, informed by input from both the GDG and the WHO Steering Group.

2.3.2 Evidence retrieval

Evidence retrieval and synthesis followed the methods outlined in the *WHO handbook for guideline development (14)*, as presented in **Fig. 4**.

Fig. 4 Steps in evidence synthesis and GRADE process



GRADE: Grading of Recommendations Assessment, Development and Evaluation; PICO: population, intervention, comparator and outcome.

[1] Dyslipidaemia is a metabolic disorder that is characterized by abnormal levels of lipids in the blood. It constitutes a major risk factor for cardiovascular disease, including heart attack and stroke, which are leading causes of death globally (*16*).

2.3.3 Systematic review methods

The ERTs developed standardized protocols for each guideline question, outlining methods for assessing risk of bias and defining a data analysis plan before evidence retrieval and appraisal.

Systematic literature search strategies were designed by a WHO librarian, to ensure consistency across all reviews. These protocols were reviewed by the guideline methodologist, the WHO Technical Team and members of the WHO Steering Group.

Evidence was retrieved in accordance with standard operating procedures, formats and timelines established by the WHO Steering Group and the guideline methodologist. The systematic review methods applied to each guideline question are detailed in the evidence profiles available in the **web annexes**.

2.3.4 Types of evidence

This guideline update is based on quantitative evidence. ERTs received a briefing note as well as report templates from the WHO Technical Team, to ensure a consistent approach to quantitative evidence appraisal across the ERTs. The GRADE approach to rating the certainty of quantitative evidence was used for all critical outcomes identified in the guideline questions, and a GRADE evidence profile was prepared for each outcome.

The certainty of evidence for each outcome was rated as "high", "moderate", "low" or "very low", as defined in **Table 2**.

A body of evidence from randomized controlled trials (RCTs) was rated as being of high certainty at the outset, whereas evidence from nonrandomized trials and observational studies was considered to be of low certainty. For both types of studies, the initial ratings could be downgraded based on five factors: limitations in study design and execution (risk of bias), indirectness, imprecision, inconsistency and publication bias. The risk of bias was assessed at the level of the individual study and across studies, while the other four factors were assessed for each outcome across all included studies.

The traditional GRADE framework for rating the quality and certainty of evidence disadvantages areas of research that rely on observational evidence (i.e. areas where trial or intervention studies would be unethical or not feasible), because such evidence is automatically rated as low certainty. Thus, for certain risk factors, particularly environmental exposures, lower certainty ratings reflect the ethical and practical constraints of conducting randomized human studies rather than a lack of biological plausibility.

Evidence on the effectiveness of interventions was mostly extracted from systematic reviews or meta-analyses. For any reviews that were more than 2 years old, the guideline methodologist advised on suitability. New systematic reviews or meta-analyses were conducted where none had been identified.

Evidence on feasibility, sociocultural acceptability, cost–effectiveness of interventions, equity and human rights was also derived through scoping reviews and GDG member expertise.

Table 2. The GRADE quality of evidence grading

Quality level	Description
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.

GRADE: Grading of Recommendations Assessment, Development and Evaluation.

2.3.5 Evidence synthesis

For each guideline question, the ERTs produced an evidence profile that summarized the relevant findings from the systematic review (**web annexes**). Where possible, outcomes were presented as meta-analyses; if this was not possible, a narrative description of findings was provided. The WHO Technical Team reviewed the evidence profile and developed the relevant sections of the EtD frameworks, in collaboration with the WHO Steering Group and guideline methodologist (**web annexes**).

EtD frameworks

The GRADE EtD frameworks include explicit and systematic considerations of evidence on interventions across specified domains *(17)*. Certain domains were primarily informed by the quantitative evidence reviews; these domains were desirable effects, undesirable effects, certainty of evidence of effects, and balance between desirable and undesirable effects. By contrast, a scoping of evidence and expertise from the GDG and WHO Steering Group were used for the domains of values and preferences of intended users, resource requirements, certainty of evidence of resource requirements, cost–effectiveness, impact on health equity, equality and non-discrimination, feasibility, alignment with human rights principles and sociocultural acceptability. The evidence profiles and EtD frameworks were subsequently presented to the GDG (**web annexes**).

2.4 Decision-making during the GDG meetings

2.4.1 GDG meetings

Before the GDG meetings, the evidence profiles, the EtD frameworks and other relevant materials for each guideline question were shared with the GDG members. During the meeting, the ERTs presented a summary of findings for each research question. Under the leadership of the GDG co-chairs, the GDG members reached a consensus (i.e. full agreement among all GDG participants) on the judgement for each domain of the EtD framework, while providing additional input and technical considerations.

Based on the available evidence and their knowledge and experience, the GDG formulated the recommendations, and agreed on the strength of the recommendations and overall certainty of evidence. Where possible, the draft of each recommendation was made by consensus. If GDG members were unable to reach a consensus, the decision was put to a vote. A recommendation or decision stood if more than two thirds of the participants voted in support of it. Voting was done by a show of hands (physical or electronic, or both, depending on the meeting format), and dissent was documented when relevant.

The WHO Steering Group, ERTs, guideline methodologist and meeting observers did not participate in the voting process.

2.4.2 Types of recommendations and statements

The following types of directing statements are provided in the update guidelines:

- **Recommendations:** These are statements specific to the context of dementia risk reduction that were formulated by the GDG using the GRADE approach. Recommendations are supported by systematic reviews of the evidence, with a formal assessment of the certainty of evidence. Where evidence was insufficient to issue dementia-specific recommendations, this was noted.

- **Generic WHO guidance:** These are statements that reflect a consensus within the GDG that the net benefits of adhering to the statement are large and unequivocal, and that the implications of the statement are common sense. They pertain to the (clinical) management of the underlying risk factor, irrespective of the impact on dementia risk; typically, such statements represent situations where WHO guidelines, technical documents and frameworks already exist to prevent, identify and manage respective risk factors. Links and references to relevant WHO resources are provided. Systematic reviews of the evidence were not conducted for such statements.

- **General clinical remarks:** These are statements used in situations where there is no specific generic WHO guidance. The remarks are based on ethical norms, established practices or widely accepted scientific principles rather than on research evidence assessed using GRADE in this guideline update.

2.4.3
Strength of recommendation

The strength of the recommendation was influenced not only by considering the certainty of evidence on benefits and harms and their relative effect, but also by the contextual factors considered in the EtD framework. Each recommendation was classified as strong or conditional, and for or against an intervention, according to the GRADE approach *(18)*.

- **Strong recommendation:** A strong recommendation is one for which the GDG was confident that the desirable effects of adhering to the recommendation outweigh the undesirable effects. A strong recommendation for an intervention indicates that most individuals should receive the intervention and it can be adopted as policy in most circumstances. The same rationale applies in reverse for strong recommendations against an intervention.

- **Conditional recommendation:** A conditional recommendation is one for which the GDG concluded that the desirable effects of adhering to the recommendation probably outweigh the undesirable effects, but the GDG was not confident about these trade-offs or identified specific conditions under which the recommendation applies. A conditional recommendation for an intervention indicates that different choices would be appropriate for different individuals, and policy-making would require substantial debate among different stakeholders. The same rationale applies in reverse for a conditional recommendation against an intervention.

The strength of each recommendation reflects not only the evidence on benefits and harms, but also feasibility, acceptability, equity and resource considerations.

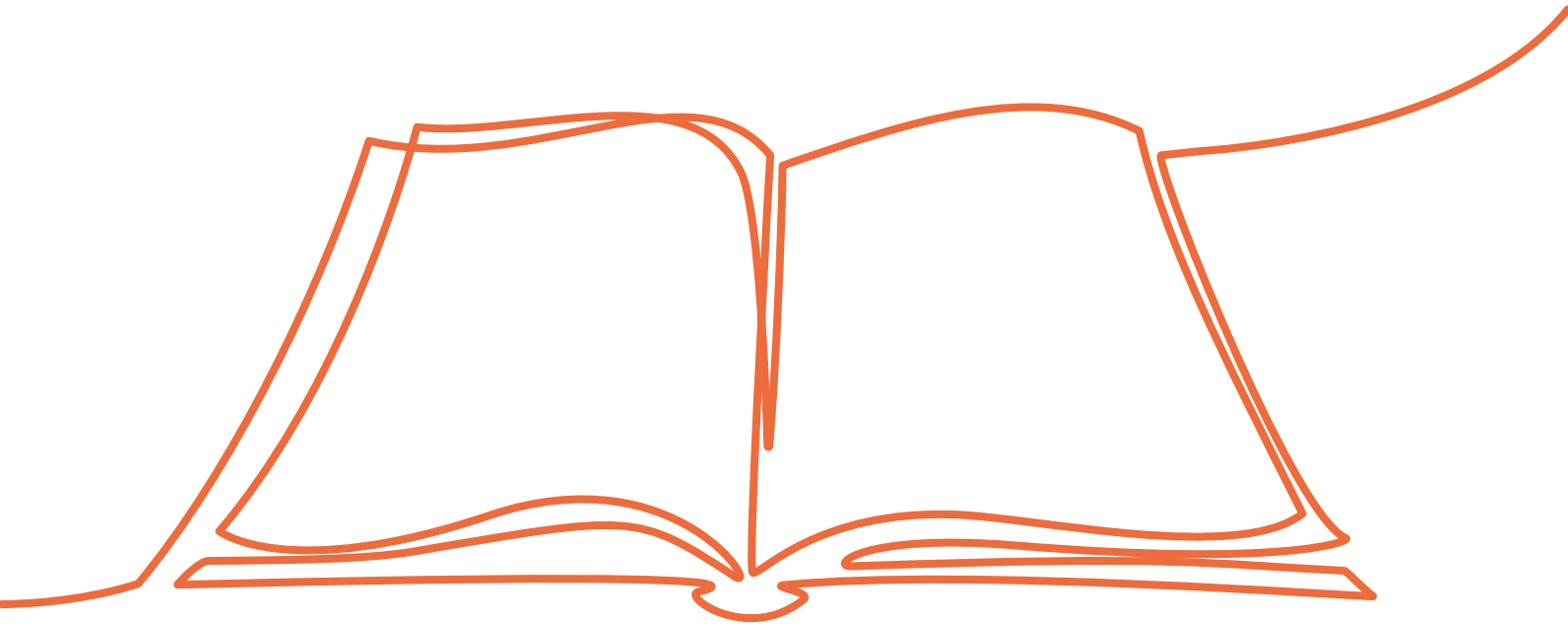
- **Strong recommendations when the evidence is of low or very low certainty.** The GDG used caution and provided thorough justifications when formulating strong recommendations based on low-certainty or very-low-certainty evidence. In accordance with the *WHO handbook for guideline development (14)*, the GDG considered five specific situations in which strong recommendations may be indicated, despite low or very low confidence in effect estimates:
  - life-threatening situations;
  - uncertain benefit, certain harm;
  - potentially equivalent options, one clearly less risky or costly than the other;
  - high confidence in benefits being similar, but one option being potentially more risky or costly than the other; and
  - potential catastrophic harm.

- **Conditional recommendations when the evidence is of low or very low certainty.** The GDG issued conditional (weak) recommendations in situations where the certainty of evidence was limited, but where the anticipated benefits, feasibility, acceptability or equity gains nevertheless justified advising action. In line with the *WHO handbook for guideline development (14)*, the GDG considered that conditional recommendations may be appropriate despite low or very low confidence in effect estimates under the following circumstances:
  - the intervention is low risk, low cost or easily reversible, and therefore unlikely to result in harm even if the estimated benefits are uncertain;
  - the consequences of inaction may be serious, and even small or uncertain benefits may justify recommending the option;
  - stakeholders (including people with lived experience, caregivers and communities) place a high value on the potential benefit, and a lower value on the possible burden or inconvenience;
  - the intervention is feasible and implementable within existing systems, including in low-resource settings, and may reduce inequities in access or outcomes; and
  - the balance of benefits and harms is uncertain, but plausibly favourable, and the intervention aligns with broader public health goals, ethical considerations or programmatic priorities.

2.5
Document preparation and peer review

Following the established processes, the WHO Technical Team circulated consensus recommendations to GDG members and the WHO Steering Group for further input and edits. Based on this feedback, the WHO Technical Team drafted the guideline document, incorporating the final recommendations and supporting evidence. The draft was then shared with independent subject matter experts for external peer review.

Subsequently, the full draft was circulated to the GDG and WHO Steering Group. All comments received from GDG members, the WHO Steering Group and external peer reviewers were compiled and incorporated as appropriate.



3. Recommendations

These updated WHO guidelines on risk reduction of cognitive decline and dementia now include dementia-specific recommendations and generic guidance for 19 potentially modifiable risk factors and multidomain interventions for dementia. Included recommendations focus solely on the effects of risk reduction interventions on cognitive decline and dementia as outcomes.

Interventions are organized into four groups:

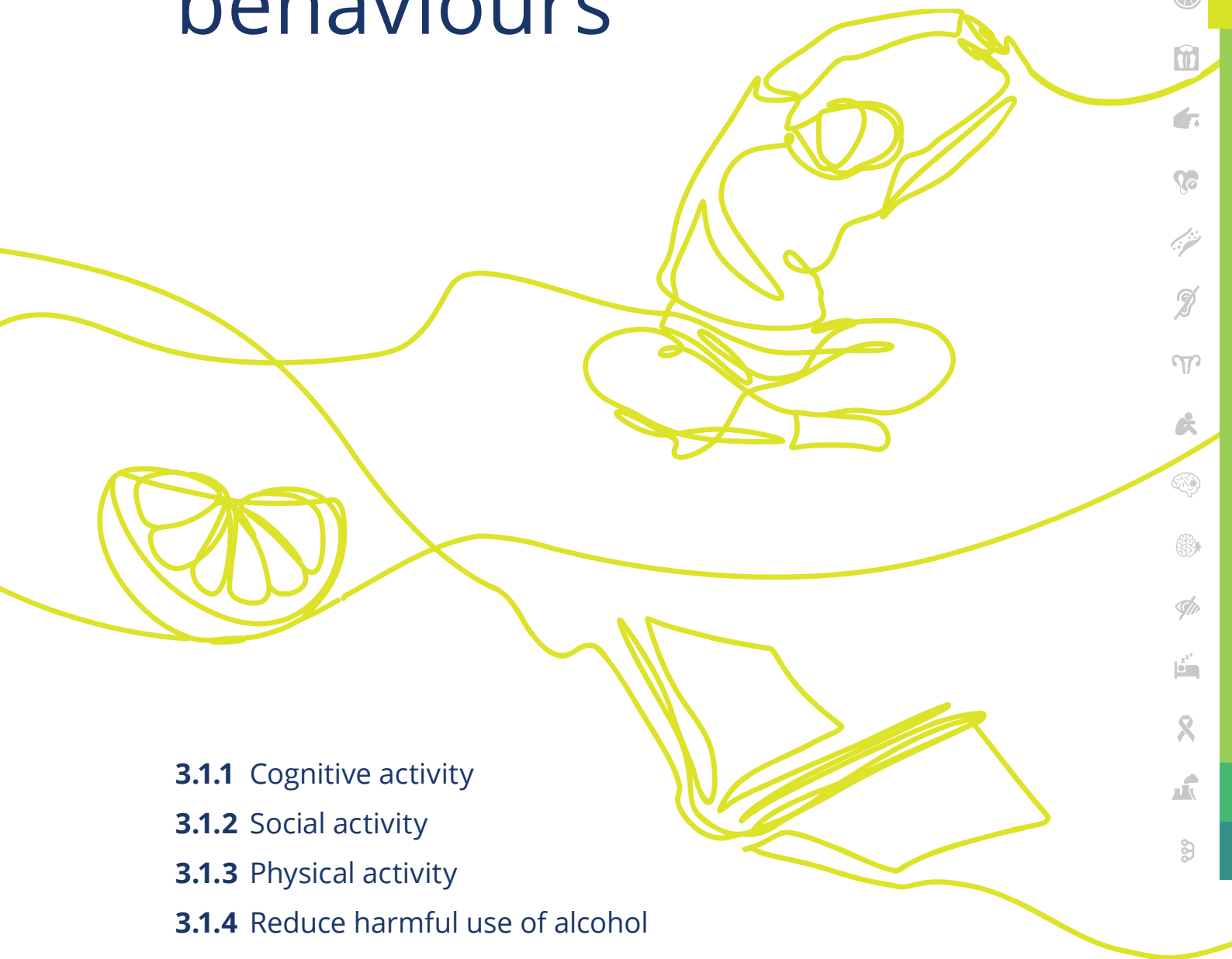
- **interventions promoting healthy behaviours;**
- **interventions to manage physical health conditions or biological states that constitute a dementia risk;**
- **interventions addressing environmental risk factors; and**
- **interventions targeting multiple risk factors.**

In addition, for each risk factor, a summary of existing WHO guidance is provided. The existing guidance is not dementia specific; it is included for context and is unchanged by the evidence syntheses performed as part of this guideline update. For instances where no generic WHO guidance exists, a general clinical remark is provided as a guiding principle.

All recommendations are supported by justifications, key considerations, remarks, identified research gaps and implementation considerations.

The evidence synthesis process for each recommendation is outlined in detailed in the corresponding evidence profile available in the **web annexes**.

3.1 Interventions promoting healthy behaviours



3.1.1 Cognitive activity

Generic WHO guidance on cognitive activity

Lifelong learning through early nurturing interactions, equitable access to quality education, and cognitively stimulating work and environments should be promoted for everyone, to optimize brain health (including cognitive health) across the life course, in line with WHO guidance.

Clinical practice:

- *Integrated care for older people: guidelines on community-level interventions to manage declines in intrinsic capacity (19)*

Service delivery and care pathways:

- *Nurturing care for early childhood development: a framework for helping children survive and thrive to transform health and human potential (20)*
- *Framework to implement a life course approach in practice (21)*
- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (22)*

Public health and policy:

- *Optimizing brain health across the life course: WHO position paper (23)*

PICO: *For adults with normal cognition or MCI, is cognitive stimulation/cognitive stimulating activities or cognitive training more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, cognitive training[a] may be offered to older adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: low

NEW RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, engagement in cognitive stimulation[b] may be encouraged.

Strength of recommendation: conditional

Certainty of evidence: very low

[a] Cognitive training refers to a targeted and repetitive cognitive exercise or task that stimulates specific cognitive domains.

[b] Cognitive stimulation refers to structured activities or programmes in a group or social setting, within a set amount of time, as well as everyday activities that enhance general cognitive function such as reading, storytelling and playing games that individuals can undertake themselves.

Justification

- Individuals with higher levels of education and greater occupational complexity tend to have a lower risk of developing dementia, probably because of the protective effects of enhanced cognitive reserve *(2,24)*[1]. Having less than 10–12 years of education explains about 5% of the risk of dementia *(2)*.

[1] Cognitive reserve is the brain's ability to cope with or compensate for neuropathology or damage.

Cognitively stimulating activities also help to reduce social inactivity, which is itself a risk factor for dementia.

- Engagement in cognitively stimulating activities and cognitive training can build cognitive reserve, which in turn can help to delay the onset of cognitive impairment *(2,25)*. Cognitively stimulating activities also help to reduce social inactivity, which is itself a risk factor for dementia.

- For this guideline update, evidence was extracted and assessed using GRADE from seven systematic reviews *(26-32)*. The extracted data pertained to three intervention types, outlined below:

    - **Cognitive training** – Based on low-to-moderate-certainty evidence, cognitive training in adults with normal cognition or MCI with follow-up of between 1 and 48 weeks may result in small improvement in cognitive function *(26)* (Hedges' g 0.25), but have little to no effect on dementia incidence after 5 years of follow-up (hazard ratio [HR] 1.00).

    - **Cognitive stimulation interventions** – Structured interventions of this type (e.g. tabletop games with follow-up 4–12 weeks) may improve executive function and verbal fluency *(28)* based on low-to-very-low-certainty evidence. Effects on global cognition and working memory were uncertain owing to the very low certainty of evidence. No evidence was found for the impact of cognitive stimulation interventions for dementia or incidence of MCI. Overall effect sizes ranged from standardized mean difference (SMD) 0.04 to 1.36.

    - **Cognitively stimulating activities** – Observational studies suggest that such activities (e.g. reading, playing games, watching television, listening to the radio or playing musical instruments) may be associated with reduced risk of dementia, with follow-up of 3.5–44 years *(29)*, reduced risk of MCI with follow-up of 1.8–16 years, and improved cognitive function with follow-up of 6 years *(30)*. Overall, the certainty of evidence was rated as very low, owing to the observational nature of the evidence, and methodological issues such as imprecision and suspected publication bias, with effect sizes ranging from a relative risk (RR) of 0.69 to 0.95.

The GDG concluded that the desirable effects of the interventions outweighed the undesirable effects, despite the low to very low certainty of evidence, and the lack of RCT evidence and long-term follow-up to determine the lasting impact of cognitive stimulation interventions and cognitive training on cognitive trajectories and dementia risk. Consequently, for cognitive training, the GDG updated the certainty of evidence from the previous guidelines from very low to low and maintained the conditional status of the recommendation.

The GDG introduced a new conditional recommendation for cognitive stimulation, and emphasized that this new recommendation is important because it allows for the inclusion of both structured activities and everyday activities that are culturally appropriate, publicly acceptable and low-cost compared with more formalized interventions (e.g. cognitive training). At this point, the evidence is insufficient to determine the optimal type, frequency, intensity and duration of cognitive training interventions for maintaining or improving cognitive health.

Remarks

- **Cognitive training** is a targeted and repetitive cognitive exercise or task that stimulates specific cognitive domains.
- **Cognitive stimulation** interventions are structured activities or programmes where participants engage in the activities, at times in a group or social setting, within a set amount of time. Such activities have a range of formats, including structured cognitive training (e.g. memory, attention and reasoning), computer-assisted training and informal cognitively stimulating activities (e.g. reading, puzzles and games).
- **Cognitive stimulating activities** are everyday activities that enhance general cognitive function (e.g. reading and playing games), especially if the activities are new and challenging. Such activities also support other dimensions of healthy ageing, including improved mood, enhanced quality of life and increased engagement in other health-promoting behaviours.

Lifelong cognitive activity – including early-life education, ongoing learning opportunities and participation in cognitively engaging pursuits – is a foundational determinant of cognitive health across the life course

- Across different forms of cognitive activity – including cognitive training, cognitive stimulating interventions and cognitive stimulating activities – evidence generally shows improvements in domains such as memory, attention and executive function. Ensuring that cognitive gains translate into real-world functioning is essential for meaningful and sustained impact.
- Lifelong cognitive activity – including early-life education, ongoing learning opportunities and participation in cognitively engaging pursuits – is a foundational determinant of cognitive health across the life course, as highlighted in WHO's position paper on brain health *(23)*.
- In line with existing WHO guidance, cognitive interventions should be offered to older adults living with cognitive decline or dementia *(22,33,34)*.

Research gaps

- There is still little evidence to establish whether cognitive interventions reduce dementia incidence:
  - More RCTs are required that explicitly evaluate whether cognitive training or cognitive stimulation reduces dementia incidence among cognitively healthy individuals and those with MCI.
  - Future observational research should incorporate dementia incidence as an outcome, rather than relying primarily on continuous cognitive measures, to enable more consistent estimation of long-term risk reduction.
  - Research is needed to clarify mechanisms of action, including whether short-term cognitive gains from these interventions lead to durable reductions in dementia risk.

- Current evidence is limited by methodological inconsistencies in intervention design and measurement:
  - Studies should assess differential intervention effects across baseline cognitive status, particularly in distinguishing impacts on cognitively healthy adults versus those with MCI.
  - Harmonized definitions and standardized measurement frameworks for leisure and cognitively stimulating activities are needed, to identify the specific activities that are most effective.
  - Future trials should use factorial or dismantling designs to isolate the independent effect of cognitive training from co-interventions such as physical activity or social engagement.
  - Research should explicitly examine interactions between cognitive interventions and other modifiable risk factors, to understand combined or synergistic effects.
- Evidence is lacking on implementation, feasibility and long-term sustainability:
  - Long-term follow-up studies are needed to determine the durability of effects and the potential for sustained cognitive or functional benefit.
  - Implementation research should evaluate feasibility, acceptability and cost–effectiveness across diverse population groups and real-world service settings.
  - Studies should investigate factors that influence adherence and engagement, to support scalable and sustainable intervention models.
- Evidence gaps limit generalizability and equity of recommendations:
  - Greater investment is needed in studies conducted in LMIC, to ensure that evidence informs globally relevant recommendations.
  - Future research should examine differential effects by sex, age, socioeconomic position and genetic risk, including apolipoprotein E (APOE) status, to ensure that interventions are equitable and appropriately targeted.

Long-term follow-up studies are needed to determine the durability of effects and the potential for sustained cognitive or functional benefit.

Implementation considerations

- Cognitively stimulating activities should be encouraged through public health messaging that highlights the benefits of cognitive stimulation as part of a healthy ageing strategy. Messaging should provide simple, culturally relevant examples of cognitively stimulating activities that older adults can integrate into daily routines.
- Collaboration with community organizations and existing social programmes can help to promote and normalize cognitively stimulating activities across diverse settings.

- Barriers for participation in cognitively stimulating activities (e.g. limited mobility, transportation challenges and economic constraints) could be addressed through local programmes such as the use of libraries, community clubs and learning centres, and by integrating low-cost or no-cost activities into such programmes.
- Special attention should be given to ensuring equity in access, especially among socioeconomically disadvantaged groups, rural populations and individuals with lower educational attainment.
- More formalized cognitive stimulation interventions can be delivered through various modalities including group-based programmes, one-on-one training, community-based workshops and digital platforms, allowing flexibility in implementation. For example, digital tools, including mobile applications and online training platforms, offer scalable and cost-effective delivery options, particularly in remote or underserved regions. However, digital literacy and equitable access must be addressed.
- Cognitive training is adaptable across settings and can be implemented at scale in diverse populations; however, ensuring its relevance and effectiveness requires tailoring both the training and cognitively stimulating activities to local cultural, linguistic and environmental contexts.
- Offering cognitive training within existing health and social care systems (e.g. primary care, community settings or older-adult programmes) can facilitate broader access and uptake. To support programme delivery, particularly in settings with limited expertise in cognitive health promotion, workforce training may be required.

Offering cognitive training within existing health and social care systems (e.g. primary care, community settings or older-adult programmes) can facilitate broader access and uptake.

3.1.2 Social activity

Generic WHO guidance on social activity

Social participation is strongly connected to good health and well-being throughout life, and should be supported over the life course, in line with WHO guidance.

Clinical practice:

- No dedicated WHO clinical guideline

Service delivery and care pathways:

- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (22)*

Public health and policy:

- *From loneliness to social connection: charting a path to healthier societies: report of the WHO Commission on Social Connection (35)*
- *Social isolation and loneliness among older people: advocacy brief (36)*

PICO: *For adults with normal cognition or MCI, is preserving and promoting a high level of social activity and/or preventing social isolation more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, engagement in social activity interventions may be recommended to adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: very low

Justification

- Social disconnection significantly affects the health and well-being of communities *(35)*, with one in four older adults globally reporting feeling socially isolated *(37,38)*. In theory, if social isolation was reduced to zero at the population level, it is estimated that about 5% of dementia cases could be prevented *(2)*.
- Evidence suggests that social connection, such as engaging in social activities, may protect against cognitive decline and dementia *(39,40)* and may delay dementia onset by up to 5 years *(39,40)*. Social connection achieves this by enhancing cognitive reserve, encouraging healthy behaviours and reducing stress *(41)*.
- For this guideline update, evidence was extracted and assessed using GRADE from three systematic reviews *(40,42,43)*, focusing on two types of evidence: social activity interventions, and observational studies comparing individuals with high versus low levels of social engagement:

Social activity interventions may confer small cognitive benefits, particularly in executive function and memory.

- Observational evidence suggests that higher levels of social engagement are associated with a small reduction in dementia risk *(40)*. The certainty of this evidence was rated as low (RR 0.81).
- Evidence from RCTs with follow-up ranging from 6 weeks to 24 months indicates that social activity interventions may lead to small improvements in cognitive functioning among older adults with normal cognition – specifically, small benefits for global cognitive function, memory and executive functioning *(42,43)*. The certainty of this evidence ranges from very low to moderate, with effects ranging from SMD –0.25 to 0.40.
- For individuals with MCI, evidence is limited to a single RCT, which found trivial benefits for global cognition and small benefits for executive function *(42)*. The certainty of this evidence is very low, with effects ranging from Cohen's d 0.04 to 0.24.

In the time since publication of the 2019 guidelines, the evidence base for social activity and dementia risk reduction has expanded. Systematic reviews have reported some small positive effects of the interventions on dementia risk reduction and cognitive function in adults with normal cognition or MCI, albeit with very low overall certainty. The GDG concluded that, although causality cannot be established because of the predominance of observational evidence, consistent findings across study designs and populations establish a lack of social activity as a modifiable risk factor for dementia. In the 2019 guidelines, no recommendation was made owing to insufficient evidence; however, the broader evidence base now indicates that social activity interventions may confer small cognitive benefits, particularly in executive function and memory. In weighing the type and quality of evidence, the GDG emphasized the consistency of observational findings, the feasibility and acceptability of social activity interventions, and the potential of such interventions to improve health equity. Based on this, a conditional recommendation was made to promote social activity for reducing the risk of cognitive decline and dementia.

Remarks

- **Social connection** is an umbrella term that encompasses how individuals relate to and interact with one another. As established by the WHO Commission on Social Connection *(35)*, it encompasses structural (e.g. number and variety of relationships, roles and interactions) and functional aspects (e.g. received and perceived support) and the quality (e.g. positive and negative aspects of relationships and interactions) of those connections *(35,44)*.
  - **Social isolation** and **loneliness** are two types of social disconnection. Social isolation refers to the objective state of having limited social interactions or relationships, whereas loneliness reflects a subjective discrepancy between the desired and actual social connections *(35)*.
  - In contrast, **social activity** – also referred to as social participation or social engagement – is a vital component of successful ageing *(35)*. It includes activities such as meeting friends, volunteering and and attending social events.

There was a considerable variability in how social activity was defined and measured across studies.

- In the studies reviewed, **social activity interventions** included interventions that incorporate social interaction components involving communication or interaction with others (e.g. group recreational activities, volunteering, attending sporting events or online social interactions). There was a considerable variability in how social activity was defined and measured across studies. Indicators included the frequency of interpersonal contact, size of social networks, level of community participation, or subjective feelings of loneliness and emotional support. This variability in operational definitions presents challenges in synthesizing the evidence and standardizing intervention approaches.
- **Social engagement** was also measured differently across studies. Commonly, it was measured using index scores (e.g. regarding participation in social activities), in which the highest category was compared with the reference category.
- WHO's evidence and gap map of digital *(45)* and in-person *(46)* interventions intended to reduce social isolation or loneliness provide examples of available interventions to support social connection throughout the life course.
- WHO is currently in the process of developing guidelines for interventions to reduce social isolation and loneliness, from children to older people.

Research gaps

- Evidence to date relies largely on observational studies, limiting causal inference – there is little evidence from longitudinal interventions studies with extended follow-up to determine whether social activity interventions reduce the incidence of dementia; most available data focus on cognitive function outcomes.
- The optimal type, intensity, frequency and duration of social activity for cognitive health remain unclear, and the interactions with other modifiable risk factors (e.g. depression, physical inactivity and sensory impairments) are poorly understood. In addition, because many interventions combine social, cognitive or physical components, the specific effects of social activity alone are difficult to isolate.
- There is a critical need for the field to adopt consistent and clearly defined terminology related to social activity, social participation, social engagement and social connection. Across studies, these terms are often used interchangeably, despite representing distinct constructs. Future research should employ agreed definitions to strengthen conceptual clarity, and advance the development of frameworks and interventions.
- Most studies are conducted in upper-middle and high-income countries (e.g. China, Finland, Japan, United Kingdom and USA), limiting the generalizability of the findings to LMIC.

- Few studies assess differential effects across subgroups (e.g. age, sex, ethnicity, education and socioeconomic status). Similarly, evidence is concentrated in older adults (aged ≥ 50 years), with limited data on younger populations or life-course effects.
- As digital interactions become increasingly common, further research is needed to understand how digital interactions compare with in person interactions in shaping social connection and social activity.

Implementation considerations

- Programmes to enhance social engagement should be culturally appropriate, inclusive and tailored to the needs and preferences of diverse populations, including older adults and those living in rural or underserved areas.
- Practical approaches include strengthening social infrastructure, intergenerational initiatives, peer support networks and digital platforms that facilitate social interaction.
- Implementation should address key barriers such as limited mobility, transportation challenges, stigma, caregiving responsibilities and digital exclusion, particularly in older age groups. Additionally, culturally adaptability should be carefully considered because programmes developed in one setting may not translate effectively across diverse cultural norms, social structures and expectations for participation.
- Differences between digital and in-person programmes should be considered. Although virtual programmes may reduce barriers to access, they may not fully replicate the social, emotional and cognitive benefits associated with face-to-face interactions.
- Social engagement strategies can be effectively integrated into other health promotion and dementia prevention programmes, including those focused on physical activity, nutrition or mental well-being.
- Primary care can play an important role in implementation through social prescribing – connecting individuals to community-based social activities and supports that align with their preferences, needs and local availability.
- Public awareness campaigns, clinician engagement and multisectoral collaboration (across health, social care, education and community development sectors) are essential to promote participation and scale up sustainable interventions.

Primary care can play an important role in implementation through social prescribing – connecting individuals to community-based social activities and supports that align with their preferences, needs and local availability.

3.1.3 Physical activity

Generic WHO guidance on physical activity

Regular physical activity across all ages and abilities – including aerobic movement, muscle strengthening activities and reduced sedentary behaviour – should be promoted for everyone, in line with WHO guidance.

Clinical practice:

- *WHO guidelines on physical activity and sedentary behaviour (47)*

Service delivery and care pathways:

- *Promoting physical activity through primary health care: a toolkit (48)*
- *Promoting physical activity for older people: a toolkit for action (49)*
- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*

PICO: *For adults with normal cognition or MCI, are physical activity interventions more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline specifically, physical activity should be recommended to adults with normal cognition.

Strength of recommendation: strong

Certainty of evidence: moderate

VALIDATED RECOMMENDATION

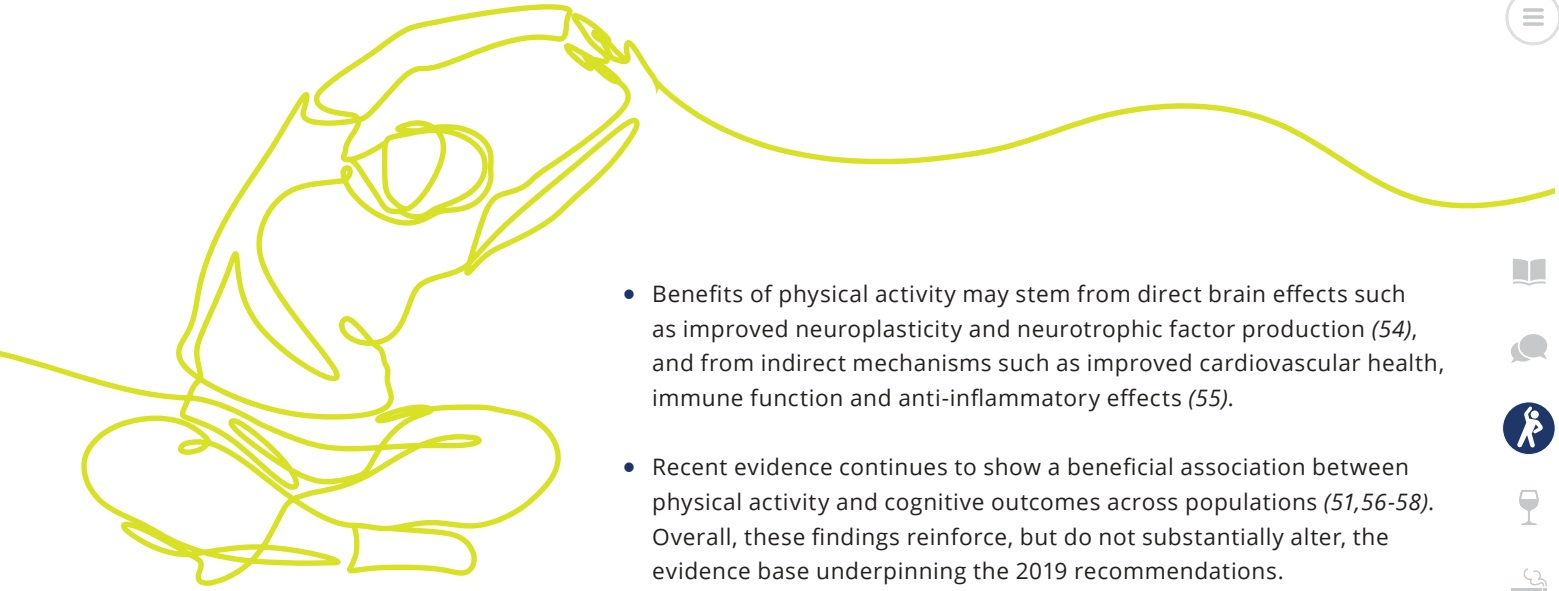
To reduce the risk of cognitive decline specifically, physical activity may be recommended to adults with mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: low

Justification

- A physically active lifestyle is associated with a lower risk of cognitive decline, Alzheimer disease and all-cause dementia, especially when sustained over long durations and at higher levels of intensity *(2,51,52)*.
- If physical inactivity globally continues, almost 500 million preventable NCD cases are expected by 2030, costing about US$ 47.6 billion annually. Although dementia makes up only 3% of these cases, it accounts for 22% of total costs, highlighting the high economic burden of inaction *(53)*. However, in theory, if physical inactivity was reduced to zero at the population level, it is estimated that about 2% of all dementia cases could be prevented *(2)*.



- Benefits of physical activity may stem from direct brain effects such as improved neuroplasticity and neurotrophic factor production *(54)*, and from indirect mechanisms such as improved cardiovascular health, immune function and anti-inflammatory effects *(55)*.
- Recent evidence continues to show a beneficial association between physical activity and cognitive outcomes across populations *(51,56-58)*. Overall, these findings reinforce, but do not substantially alter, the evidence base underpinning the 2019 recommendations.

Physical activity remains a broadly beneficial, low-cost and low-risk intervention, with well-established benefits for overall health *(47)*. Although new studies have emerged, the scoping review conducted for this update (Section 2.3.1 and Annex 1) found that the evidence on the effects of physical activity on cognitive outcomes remains largely unchanged, making it unlikely that the strength or direction of the existing recommendations has changed. Given these findings, the GDG decided to validate the existing recommendations.

Remarks

- This recommendation aligns with the *WHO guidelines on physical activity and sedentary behaviour (47)*, and reinforces the value of aerobic and resistance training across the life course.
- One of WHO's recommended 'best buys' for NCD prevention is to implement sustained, population-wide, best-practice communication campaigns to promote physical activity, with links to community-based programmes and environmental improvements to enable and support behaviour change *(5)*.
- This recommendation is also consistent with the strong physical activity recommendation in the WHO mhGAP guideline for people living with dementia, which recommends physical activity three to four times per week, 30–45 minutes per session, for 12 weeks or longer *(33)*.

Research gaps

- Many existing studies use crude or self-reported physical activity measures (e.g. yes/no questions), limiting the precision of dose–response analyses. Future research should employ data from wearable devices; include detailed assessment of duration, intensity and type of physical activity; include baseline cognitive measures; and make individual participant data openly available to improve accuracy and replicability *(51)*.

Evidence remains limited regarding the optimal type, intensity, duration, adherence and setting of physical activity that yield the greatest cognitive benefit.

- Evidence remains limited regarding the optimal type, intensity, duration, adherence and setting of physical activity that yield the greatest cognitive benefit. More long-term RCTs are needed to determine causality and practical implementation pathways *(52)*.
- Further research is needed to clarify the pathways linking physical activity to cognitive health, including its effects on amyloid clearance, cerebral blood flow, inflammation and neurotrophic factors. Understanding these mechanisms is essential for identifying the most effective intervention strategies for dementia risk reduction *(52)*.
- Continued longitudinal research is required to determine whether physical activity enhances cognitive reserve, buffers age-related cognitive decline and delays the onset of dementia, particularly in individuals with early disease markers *(52)*.

Implementation considerations

- Programmes should prioritize aerobic or multimodal exercise, tailored to individual capacity and preference.
- Activities should be integrated into broader community-based or primary care interventions for healthy ageing.
- Local adaptation may be necessary for LMIC, where resource constraints or cultural barriers may affect uptake.
- Social engagement and structured delivery (e.g. group classes and walking groups) may enhance adherence and effectiveness.

3.1.4 Reduce harmful use of alcohol

Generic WHO guidance on alcohol use

Alcohol use is associated with many health risks, owing to its psychoactive, toxic and dependence-producing properties. Hence, alcohol should not be recommended in any amount for health benefits, in line with WHO guidance.

Clinical practice:

- *Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders* – specifically, the module on alcohol use disorders *(33)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *WHO Global strategy to reduce the harmful use of alcohol (59)*
- *Global alcohol action plan 2022–2030 (60)*
- *Global status report on alcohol and health and treatment of substance use disorders (61)*
- *The SAFER technical package: five areas of intervention at national and subnational levels (62)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*
- Alcohol fact sheet *(63)*

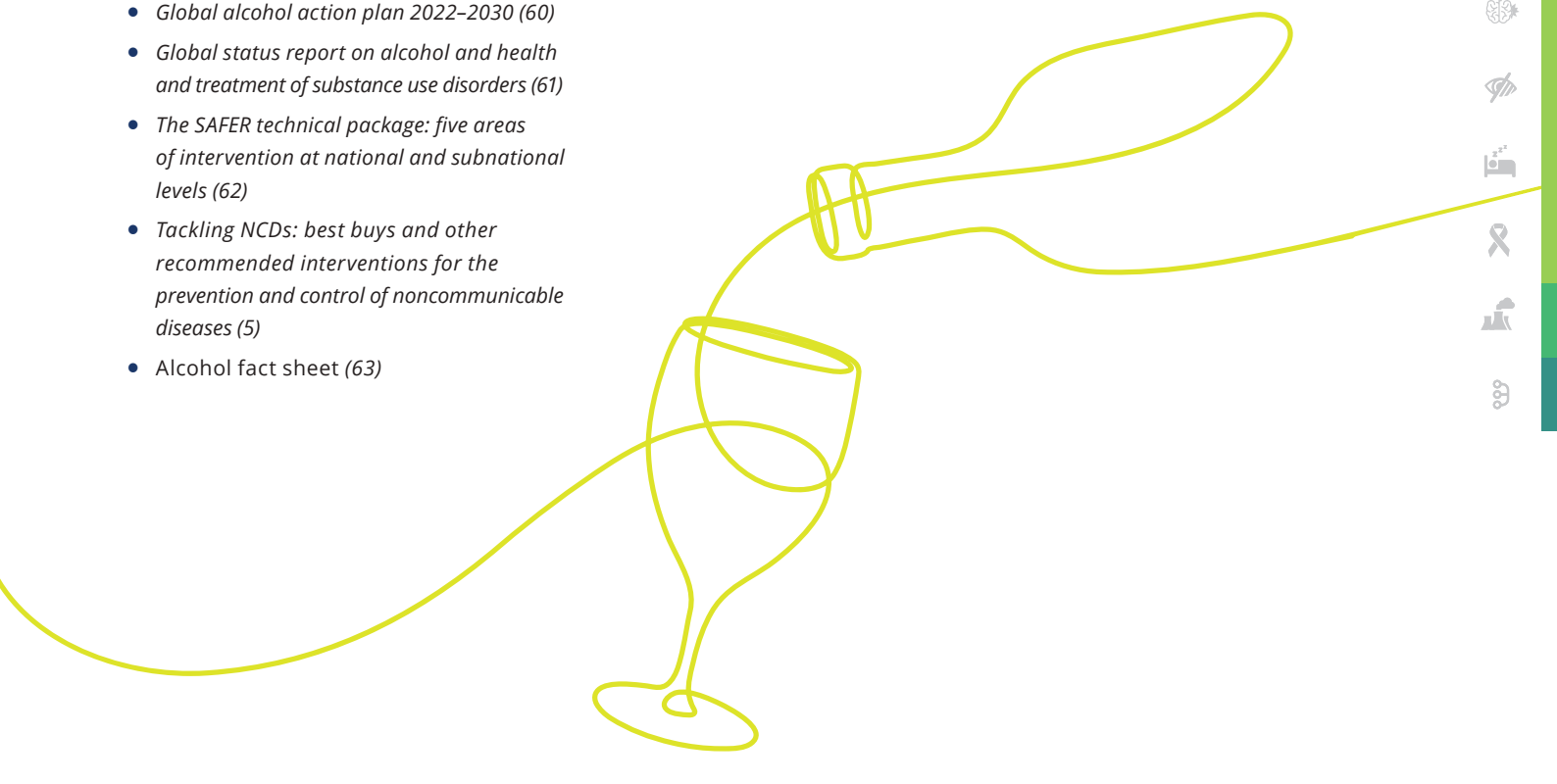
PICO: *For adults with normal cognition or MCI and alcohol use disorders, are behavioural and psychological interventions to treat alcohol use disorders more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, interventions aimed at reducing or ceasing hazardous and harmful drinking (including providing support to people with alcohol dependence) may be offered to adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: moderate



Justification

- Harmful use of alcohol carries a significant global health burden, contributing to 2.6 million deaths globally and being causally linked to over 200 health conditions *(61)*. Adults with a history of alcohol abuse may develop Wernicke's encephalopathy – an acute neuropsychiatric syndrome that can progress to Korsakoff syndrome, a type of secondary dementia *(64)*. A strong body of observational evidence consistently links heavy alcohol use to increased risk of cognitive impairment and dementia *(2,65-69)*. In theory, if harmful use of alcohol was reduced to zero at the population level, it is estimated that about 1% of dementia cases could be prevented *(2)*.

- The commonly cited J-shaped curve for alcohol use and dementia, where light or moderate alcohol use is presented as having a protective effect, is probably the result of methodological bias, including reverse causality and confounding *(70)*. Emerging evidence from broader health research increasingly suggests that there may be no level of alcohol consumption that is risk-free for health *(71)*. Hence, alcohol should not be recommended in any amount for health beneficial effects, including cognitive protection.

Emerging evidence from broader health research increasingly suggests that there may be no level of alcohol consumption that is risk-free for health

- Findings from the scoping review (**Section 2.3.1** and **Annex 1**) indicate that, since the release of the guidelines in 2019, evidence on alcohol as a risk factor for dementia has remained largely unchanged; in addition:
  - reducing alcohol consumption from heavy to moderate levels may be associated with a decreased risk of dementia *(72)*;
  - recovery of multiple cognitive functions (e.g. memory, attention and executive function) can occur with sustained abstinence, typically within 6–12 months *(73)*; and
  - thiamine supplementation in individuals with alcohol use disorder may improve cognitive function *(74)*.

Although the scoping review (Annex 1) identified some new studies published since 2019, the overall evidence on alcohol as a risk factor for dementia has remained largely unchanged, and the additions do not meaningfully shift the certainty or direction of the current recommendation. Emerging findings were deemed to not alter the fundamental evidence base regarding alcohol as a risk factor for cognitive decline and dementia. Thus, the GDG concluded that a full evidence synthesis was not warranted and instead validated the existing 2019 recommendation.

Remarks

- No risk-free level of alcohol use can be recommended for cognitive health. Alcohol is a psychoactive, toxic and dependence-producing substance with well-established harmful effects across multiple organ systems. Even low levels of consumption increase the risk of several major health conditions, including cancer, cardiovascular disease and injuries, and population-level evidence shows no net health benefit

or "protective" effect from light or moderate use *(75)*. Although the specific causal pathways linking alcohol use to dementia are still being clarified, the broader health risks support a precautionary approach.

- Among the most cost-effective strategies to reduce alcohol-related harm are screening, brief interventions and access to a continuum of health services and evidence-based psychosocial and pharmacological interventions through primary care *(76)*. Behavioural interventions are generally more acceptable and safe, with fewer adverse effects than pharmacological treatments *(77)*. Interventions should include both individual-level behavioural strategies and population-level policies (e.g. taxation, advertising bans and reduced availability) *(33,59,60,62)*.

Research gaps

- Most of the existing studies exploring the effects of alcohol use on long-term cognitive outcomes and dementia risk focus on older adults; younger populations and people with heavy drinking patterns or individuals with alcohol use disorders are often excluded or underrepresented. This situation continues to limit the understanding of lifespan risk trajectories and may underestimate the true impact of alcohol on dementia risk. Hospital-based and longitudinal cohort studies with more inclusive sampling are needed *(65)*.

- Large-scale studies, including those cited by the Lancet Commission, suggest that heavy drinking and alcohol use disorders represent significant modifiable risk factors for dementia, yet these risk factors remain under-recognized in public health guidance. Replication of studies across diverse settings is needed to inform screening, early intervention and alcohol policy as components of comprehensive dementia risk reduction strategies *(65)*.

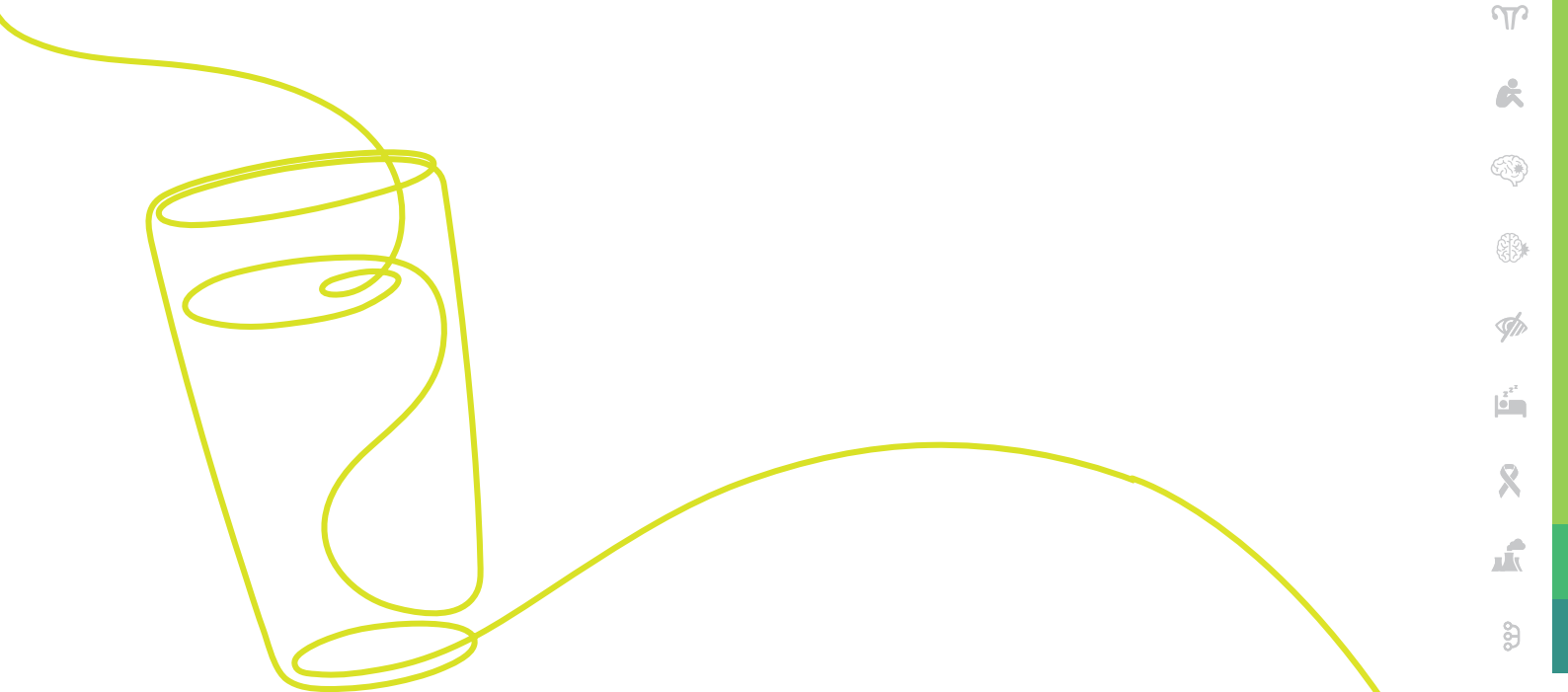
- The causal pathways linking alcohol use to dementia remain unclear. Although Mendelian randomization and twin studies offer useful approaches, current findings are inconclusive owing to inconsistencies in the use of genetic markers and in study designs. Research should aim to clarify whether alcohol's effects are direct, dose dependent or mediated through vascular, inflammatory or neurodegenerative mechanisms *(65)*.

- Most studies rely on self-reported alcohol use, which is prone to underreporting, and they often lack consistent data on beverage type and drinking frequency. Standardized, objective and repeated measures are needed to more accurately capture quantity, pattern and type of alcohol consumption. Similarly, the effects of beverage type (e.g. wine versus spirits, including locally produced alcohol) are highly confounded by sociodemographic factors, and unmeasured variables and healthy survivor bias probably influence findings. Future studies should focus on ethanol exposure itself, and should better control for lifestyle and clinical covariates *(66)*.

Implementation considerations

Access to evidence based treatment options should be increased, and alcohol reduction strategies should be integrated into routine primary care using screening and brief interventions

- Access to evidence-based treatment options should be increased, and alcohol reduction strategies should be integrated into routine primary care using screening and brief interventions, as outlined in WHO's mhGAP guidelines *(33).*
- Efforts focused on the individual (e.g. counselling and motivational interviewing) should be combined with population-level policies (e.g. increased taxation on alcohol, restrictions on alcohol availability and advertising, and enforcement of drink–driving laws, as per the WHO-led SAFER initiative) *(62).*
- Nutritional support (e.g. thiamine) should be included in alcohol treatment protocols to enhance cognitive recovery; also, evidence-based psychosocial and pharmacological treatment should be provided for people with alcohol dependence (e.g. with naltrexone and acamprosate).
- Alcohol reduction interventions, particularly those aimed at middle-aged adults, should be framed within broader healthy lifestyle and dementia prevention strategies.
- In LMIC and under-resourced settings, community health workers and non-specialist providers should be leveraged, to expand the reach of behavioural interventions.



3.1.5 Tobacco cessation

Generic WHO guidance on tobacco

Tobacco use should be avoided entirely. All people who use tobacco should be supported to quit through evidence-based behavioural and pharmacological cessation interventions, and all people should be protected from exposure to tobacco smoke, in line with WHO guidance.

Clinical practice:

- *WHO clinical treatment guideline for tobacco cessation in adults (78)*

Service delivery and care pathways:

- *Strengthening health systems for treating tobacco dependence in primary care to enhance skills and integrate evidence-based cessation practices into routine care (79)*
- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*

PICO: *For adults with normal cognition or MCI who use tobacco, are interventions for tobacco cessation more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline and dementia specifically, interventions for tobacco cessation should be offered to adults who use tobacco.

Strength of recommendation: strong

Certainty of evidence: low

Justification

- Tobacco use is a leading preventable cause of death globally. There are more than 7 million tobacco-attributable deaths per year, contributing substantially to health care costs *(80)*.
- All forms of tobacco use are harmful and there is no safe level of exposure to tobacco, with smoking in midlife as opposed to in later life carrying the greatest risk for developing dementia *(2,81,82)*. In theory, if smoking was reduced to zero at the population level, it is estimated that about 2% of dementia cases could be prevented *(2)*.

There is no safe level of tobacco use in relation to general health or dementia.

- Recent large cohort studies highlight that the time since smoking cessation matters:
  - current smoking and recent cessation (<9 years) are linked to increased dementia risk, whereas never smoking or quitting 9 years or more prior is not *(83)*;
  - among Japanese older adults, those who quit smoking more than 3 years ago had a similar dementia risk to never smokers, suggesting that sustained cessation may reverse the risk *(84)*; and
  - in a Korean cohort of nearly 800 000 adults, smoking cessation lowered dementia risk, whereas both reduction and escalation of smoking were associated with increased risk *(85)*.

Based on the findings of the scoping review (Section 2.3.1 and Annex 1), it was deemed unlikely that the strength of the existing recommendation has changed. Therefore, the GDG decided to validate the existing recommendation.

Remarks

- There is no safe level of tobacco use in relation to general health or dementia.
- Tobacco cessation interventions should align with WHO's clinical treatment guideline for tobacco cessation in adults *(78)* and be embedded in broader population-level strategies and national tobacco control programmes.

Research gaps

- More evidence is needed on how smoking increases dementia risk, whether through vascular pathways, oxidative stress or direct neurodegenerative effects.
- Most studies rely on self-reported or baseline smoking data. To reduce misclassification, future research should include longitudinal tracking, objective measures (e.g. cotinine) and differentiation of current, former and lifetime smoking patterns *(86)*.
- Observed reductions in dementia risk among older smokers probably reflect survival bias and competing mortality risks. Future cohort studies must account for these factors using appropriate statistical methods and life course designs *(85)*.
- Few studies have examined the impact of the timing of smoking cessation or the intensity of reduction in smoking on later dementia risk. Randomized and implementation studies are needed to determine optimal intervention strategies for brain health *(85)*.

- There is a need for further research on the potential risk of dementia associated with the use of new and emerging tobacco and nicotine products, such as vaping, e-cigarettes and heated tobacco products.

Implementation considerations

- Tobacco cessation programmes should be integrated into dementia risk reduction strategies and tailored to primary care settings for maximum impact.
- It is important to build capacity among health care providers by using the WHO training package to enhance skills and integrate evidence-based cessation practices into routine care *(79)*.
- There should be an increase in screening and counselling for tobacco cessation within primary care settings, focusing particularly on adults aged 35–65 years, as part of dementia risk reduction strategies.
- Cessation services should be integrated into NCD and mental health platforms, to enhance accessibility, maximize reach and improve sustainability.
- Implementation should address barriers (e.g. limited provider capacity, lack of awareness and stigma), while ensuring that services are accessible and sustainable.
- Public health messages should be developed that highlight the benefits of early cessation; they should emphasize that quitting sooner provides greater protection against dementia, while reinforcing that cessation at any stage remains beneficial.
- Population-level interventions (e.g. taxation, advertising bans, graphic health warnings, smoke-free laws and public education campaigns) should complement individual-level strategies *(9)*.

Population-level interventions (e.g. taxation, advertising bans, graphic health warnings, smoke-free laws and public education campaigns) should complement individual-level strategies.

3.1.6 Healthy, balanced diet and nutrition

Generic WHO guidance on healthy, balanced diets and nutrition

A healthy, balanced diet should be recommended to all adults, in line with WHO guidance.

Clinical practice:

- *Carbohydrate intake for adults and children: WHO guideline (87, 88)*
- *Guideline: sugars intake for adults and children (89)*
- *Use of non-sugar sweeteners: WHO guideline (90)*
- *Total fat intake for the prevention of unhealthy weight gain in adults and children: WHO guideline (91)*
- *Saturated fatty acid and trans-fatty acid intake for adults and children: WHO guideline (92)*
- *Guideline: sodium intake for adults and children (93,94)*
- *Guideline: potassium intake for adults and children (94)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *Healthy diet (88)*
- *Fiscal policies to promote healthy diets: WHO guideline (95)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*

PICO: *For adults with normal cognition or MCI, are nutritional interventions such as healthy dietary patterns (e.g. the Mediterranean diet) more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, a healthy, balanced dietary pattern[a] may be recommended to adults with normal cognition or mild cognitive impairment.

Strength of recommendation: conditional

Certainty of evidence: moderate

VALIDATED RECOMMENDATION AGAINST

To reduce the risk of cognitive decline and/or dementia specifically, supplemention of vitamins B and E, omega-3 polyunsaturated fatty acids (PUFA) and multivitamins/minerals is not recommended.[b]

Strength of recommendation: strong

Certainty of evidence: moderate

[a] To be healthy, diets need to be (88):

- adequate: providing enough essential nutrients to prevent deficiencies and promote health, without excess;
- balanced: in energy intake and energy sources (i.e. fats, carbohydrates and proteins);
- diverse: including a wide variety of nutritious foods within and across food groups to favour nutrient adequacy and consumption of other health-promoting substances; and
- moderate: in consumption of foods, nutrients or other compounds associated with detrimental health effects.

The exact makeup of a diet will vary depending on individual characteristics, preferences and beliefs, cultural context, locally available foods and dietary customs.

[b] This applies only to individuals without established vitamin deficiencies.

Justification

A healthy diet is essential for overall health and becomes increasingly important with age.

- A healthy diet is essential for overall health and becomes increasingly important with age. Diet quality plays a key role in preventing and managing conditions such as type 2 diabetes and cardiovascular disease *(96,97)*.
- Dietary patterns – for example, the Mediterranean Diet (MeDi), the Dietary Approach to Stop Hypertension (DASH) and the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) – are associated with better cognitive outcomes *(98,99)*. These diets emphasize fruits, vegetables, whole grains, nuts and legumes, while limiting red meat, saturated fats and sugary foods, and are generally compatible with existing WHO recommendations for a healthy and balanced diet.
- Diet may influence dementia risk directly through anti-inflammatory and antioxidant effects and support for brain plasticity *(100)*, and also indirectly by reducing other risk factors such as hypertension and obesity *(101,102)*. Whole-diet approaches are probably more effective than focusing on single nutrients.
- For these guidelines, evidence was extracted and assessed using GRADE from two systematic reviews *(103,104),* pertaining to the impact of a low carbohydrate diet and specific dietary patterns (e.g. MeDi, DASH and MIND) in adults with normal cognition or MCI. Systematic reviews reported some small positive effects of dietary interventions on cognitive function in adults with normal cognition or MCI at a maximum follow-up of between 13 and 37 months; however, the certainty of evidence varied by type of dietary intervention (with effect sizes ranging from SMD 0.05 to 0.30):
    - dietary interventions (i.e. MeDi, DASH and MIND analysed together) may result in a small improvement in global cognition and processing speed but probably have little or no effect on executive function and spatial ability;
    - MeDi interventions (analysed alone) are likely to result in a small improvement in cognition and processing speed, but are likely to have little or no effect on executive function; and
    - the effect of low-carbohydrate diet interventions on executive function and processing speed is uncertain.
- The effects of vitamin and/or mineral supplementation were not reassessed as part of this guideline update (**Annex 1**).

In their deliberations, GDG members noted that the certainty of evidence when all types of interventions identified are combined (e.g. MeDi, DASH, MIND and low-carbohydrate diet) is low to moderate, with moderate-certainty evidence available for MeDi. Moreover, the available evidence is restricted to the effect of dietary pattern interventions on cognitive function outcomes at a maximum follow-up period of 37 months; there is still no available evidence for dementia or MCI as outcomes. The GDG concluded that, at this point, the evidence is insufficient to recommend one specific dietary pattern, and that the benefits of an overall healthy, balanced diet outweigh the harms; therefore, the GDG updated the previous recommendation from focusing on Mediterranean-style diet to a more inclusive focus on healthy, balanced dietary patterns. The strength of the recommendation and the certainty of evidence remained the same.

Previously, the GDG had advised against the supplementation of vitamins B and E, omega-3 polyunsaturated fatty acids (PUFA) and multivitamin/mineral complexes – in the absence of a diagnosed deficiency – for the specific purpose of dementia risk reduction, because of unexpected harmful effects that outweigh any potential benefits. Based on the findings of the scoping review (Section 2.3.1 and Annex 1) it was deemed unlikely that the strength of the existing recommendation against the use of supplements would change. Therefore, the GDG decided to validate the existing recommendation.

Remarks

- According to WHO, a healthy diet is one that provides enough essential nutrients to prevent deficiencies and promote health, without excess; is balanced in energy intake and energy sources (i.e. fats, carbohydrates and proteins); is moderate in consumption of foods, nutrients or other compounds associated with detrimental health effects; and includes a wide variety of nutritious foods within and across food groups to favour nutrient adequacy and consumption of other health-promoting substances. The exact makeup of a diet will vary depending on an individual's characteristics, preferences and beliefs; the cultural context; locally available foods; and dietary customs.

- In the context of dementia risk reduction, the following dietary patterns (all of which are compatible with WHO general guidance) have been studied:

  - **MeDi** emphasizes minimally processed, plant-based foods, with fresh fruits consumed daily and olive oil serving as the primary source of fat. It includes moderate portions of fish, seafood, poultry and dairy products, but limits sugary foods and red meat *(98)*. Although rooted in Mediterranean food traditions, the core principles of MeDi can be adapted to diverse cultural and regional dietary patterns.

  - **DASH** focuses on reducing salt, added sugars and saturated fats, and promotes the eating of plenty of fruits, vegetables, whole grains, legumes, nuts, lean proteins and low-fat dairy products *(105)*.

  - **MIND** – a hybrid dietary approach that integrates principles from both MeDi and DASH – prioritizes the consumption of predominantly plant-based foods while restricting the intake of animal-derived products and items high in saturated fats. A distinctive feature of MIND is its targeted emphasis on the inclusion of berries and green leafy vegetables *(106)*.

- Dietary patterns are complex models that encompass multiple dietary guidelines related to various dietary components. This differs from individual food dietary guidance, such as the WHO nutrition guidelines, which provide advice on the intake of salt, potassium, carbohydrates, saturated fatty acids and trans-fatty acids or the use of non-sugar sweeteners *(87,90,92-94)*, and overall are compatible with WHO recommendations for a healthy and balanced diet. The present review did not identify any evidence for the effects of specific nutrients on the risk of cognitive decline and/or dementia.

- Dietary habits are closely associated with socioeconomic status; thus, it is essential to establish equitable approaches that enable all individuals to access and maintain a healthy diet. Additionally, dietary intake should aim to ensure adequate consumption of nutrients that are of increased importance in older age, such as protein.

- Adherence to a healthy, balanced diet should be supported through fiscal policies *(95)* and by implementing individual dietary guidance *(87,92)*.

- The recommendation against supplementing vitamins B and E, omega-3 PUFA and multivitamin/mineral complexes applies to individuals who do not have a diagnosed nutrient deficiency.

Research gaps

- Most of the evidence identified and reported is based on, and linked to, MeDi interventions. It is crucial to gain more evidence on already established relevant dietary interventions (e.g. DASH, MIND, region-specific or plant-based diets), emerging dietary patterns that have been proposed in the context of specific neurodegenerative disorders (e.g. ketogenic diet), and the implementation of these interventions in different socioeconomic and cultural contexts.

- Identifying and investigating adaptations of healthy dietary patterns (e.g. those that apply the main principles, while adjusting the dietary recommendations based on local resources and habits of particular regions) could be a valuable and equitable approach in countries where resources are limited.

- Most of the available research is based on studies conducted in high-income countries, limiting global applicability. More research is needed in LMIC to ensure equitable and globally relevant recommendations.

- To ensure equitable and globally relevant recommendations, future studies should also explore differential effects by sex, age and genetic predisposition (e.g. APOE status).

Implementation considerations

- Healthy dietary patterns such as MeDi are feasible and adaptable when they are culturally tailored. Programmes should prioritize the adaptation of core principles of these dietary patterns – such as emphasizing vegetables, legumes, whole grains, healthy fats and reduced processed foods – to locally available ingredients and traditional eating practices. This approach supports implementation across diverse cultural, economic and geographical contexts.
- Equity should be central to implementation, especially in low-resource settings where availability and affordability of recommended foods may be limited. Adherence to a healthy diet is not always in the control of the individual; therefore, programmes may need to identify locally accessible, lower cost alternatives that still align with recommended dietary patterns.
- Interventions should emphasize whole-diet approaches rather than focusing on single nutrients, because overall patterns appear to be more relevant for long-term health.
- Longer term interventions and sustained behaviour-change strategies are likely to be more effective, and should be built into programme design and delivery.
- Dietary guidance should balance scientific complexity with practical applicability. In some settings, it may be helpful to translate broader dietary patterns into simple food-based messages.

Adherence to a healthy diet is not always in the control of the individual; therefore, programmes may need to identify locally accessible, lower cost alternatives that still align with recommended dietary patterns.

3.2 Management of health conditions and biological states

For the purpose of these updated guidelines, the term "management" refers to the diagnosis, treatment, care and support for a disease or condition.

3.2.1 Management of obesity

Generic WHO guidance on obesity

Management of obesity should be offered to all adults[a] living with obesity, in line with WHO guidance.

Clinical practice:

- *Guideline on the use of glucagon-like peptide-1 (GLP-1) therapies for the treatment of obesity in adults (107)*

Service delivery and care pathways:

- *Health service delivery framework for prevention and management of obesity (108)*

Public health and policy:

- *WHO acceleration plan to stop obesity: a joint WHO/UNICEF operational model for designing and implementing the response (109,110)*
- *Recommendations for the prevention and management of obesity over the life course (111)*
- *Global action plan for the prevention and control of noncommunicable diseases (112)*

[a] WHO guidance applies to all non-pregnant adults with obesity.

PICO: *For adults with normal cognition or MCI who are overweight or obese, are interventions for weight reduction (or control of obesity) more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, interventions for reducing midlife overweight or obesity may be offered.

Strength of recommendation: conditional

Certainty of evidence: low to moderate

NEW RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, dietary restriction interventions may be offered to adults who are overweight or obese.

Strength of recommendation: conditional

Certainty of evidence: low to moderate

Justification

- Obesity is a chronic condition defined by excessive fat deposits that can impair health. It is estimated that 43% of adults globally are overweight and 16% are obese *(113)*.[1] These numbers are expected to continue to increase globally across all age groups, including older adults *(114)*.

[1] Obesity is a chronic, relapsing disease arising from complex interactions between genetics, neurobiology, eating behaviours, access to healthy diet, market forces and the broader environment. For adults, obesity is a body mass index (BMI) greater than or equal to 30.

- In theory, if obesity was reduced to zero at the population level, is it estimated that 1% of dementia cases could be prevented *(2)*, with evidence suggesting that midlife obesity and increased waist circumference are associated with a higher risk of dementia *(115,116)*. Potential mechanisms for obesity to increase the risk of dementia include impaired cerebral perfusion, neurotransmitter dysfunction and reduced β-amyloid clearance *(117-119)*.

- The literature search for this guideline update identified one eligible systematic review *(120)* on dietary restriction interventions, including calorie restriction and intermittent fasting. Although the search also covered other intervention types (e.g. pharmacological and surgical approaches, and other lifestyle interventions), no eligible evidence was identified. The evidence extracted and assessed with GRADE is as follows:

  - For adults with normal cognition, dietary restriction interventions produced small but statistically significant improvements in cognitive outcomes at 6–17 months follow-up, including memory, global cognitive function, attention and composite measures of cognition (combining global function, memory and attention), with effects ranging from SMD 0.18 to 0.35. The certainty of evidence was moderate for memory and overall cognition (composite score), low for global cognitive function and very low for attention. Therefore, dietary restriction interventions may result in a small improvement in global cognitive function and are likely to result in a small improvement in memory and overall cognition, while effects on attention remain uncertain.

- No evidence was identified for the critical outcomes of dementia or MCI incidence, nor was it identified for populations with MCI or for other weight management strategies.

Weight reduction may confer benefits beyond cognition, including improvements in cardiovascular health and hypertension, which are themselves associated with dementia risk.

In their deliberations, the GDG noted the need for a multipronged approach to reducing weight effectively, with guidelines from WHO available to support clinicians and individuals in management. Recommendations included here are only for the added benefit of reducing the risk of cognitive decline and dementia. GDG members noted that weight reduction may confer benefits beyond cognition, including improvements in cardiovascular health and hypertension, which are themselves associated with dementia risk. Sustained weight reduction, however, often requires multidimensional, evidence-based interventions. Although causality has not been established owing to the observational nature of most studies, consistent findings across study designs and populations support addressing midlife overweight and obesity to reduce the risk of cognitive decline, alongside other health benefits. The GDG therefore retained the recommendation from the previous guideline. In addition, low-certainty to moderate-certainty evidence suggests that dietary restriction interventions may offer small cognitive benefits, particularly for memory and overall cognition. In balancing the type and quality of evidence, the GDG emphasized the global prevalence and modifiability of obesity, the potential for broader health benefits and the absence of major harms. Also, the GDG made a new conditional recommendation to offer dietary restriction interventions to reduce the risk of cognitive decline and dementia.

Remarks

Other weight reduction approaches include physical activity programmes, psychological interventions, multidomain lifestyle interventions and pharmacological treatments.

- Conceptualizations of obesity vary across different regions of the world. In many cases, waist-to-hip ratio is considered a more reliable metric than body mass index (BMI) because it better reflects central adiposity, which is more strongly linked to cognitive decline and cardiovascular risk. Individuals with elevated BMI do not necessarily exhibit reduced cognitive function, particularly if they belong to higher socioeconomic groups.
- Dietary restrictions such as calorie restriction and intermittent fasting are not the only interventions available for people living with obesity. Other approaches include physical activity programmes (e.g. resistance training), psychological interventions (e.g. cognitive behavioural therapy), multidomain lifestyle interventions and pharmacological treatments. However, dietary restriction was the only intervention for which new evidence related to dementia risk and cognitive decline was identified as part of this guideline update.
- Weight reduction efforts should be aligned with existing WHO guidance *(107)* and global mandates *(109,111)*. WHO guidance on managing and treating obesity applies to all non-pregnant adults with obesity.

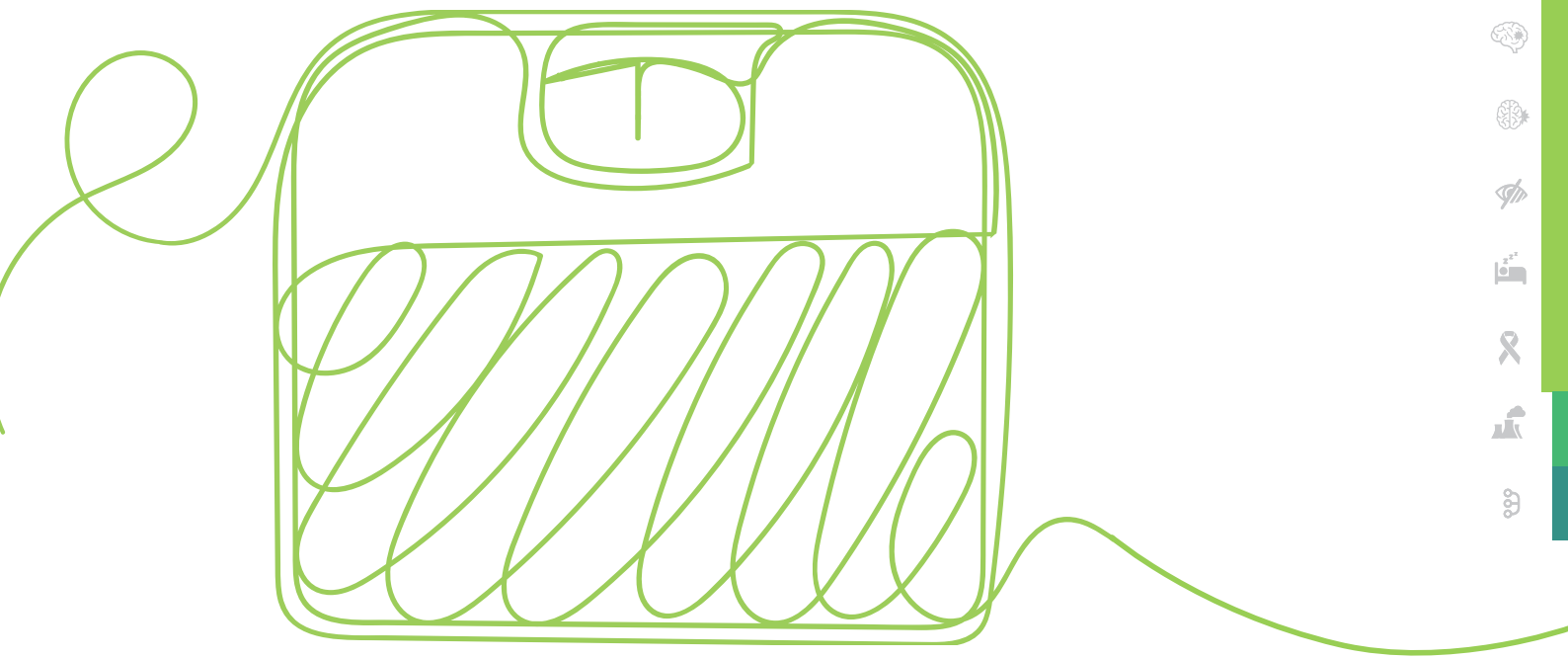
Research gaps

- No systematic reviews were identified that directly assess the impact of weight management interventions on the development of dementia or MCI. Long-term outcomes are difficult to capture in intervention trials owing to extended latency periods, highlighting the need to identify and validate surrogate outcomes (e.g. dementia risk scores) that can be feasibly measured in shorter term studies.
- Current evidence for improving cognition only covers dietary restriction; no systematic reviews were found for other weight management strategies such as physical activity, pharmacological treatments or multidomain interventions.
- No cost–effectiveness data were available, but dietary interventions may offer broader health benefits beyond cognitive outcomes, potentially reducing overall health care costs.
- No evidence was found on the cognitive effects of pharmacological treatments for obesity (e.g. GLP-1 receptor agonists). However, as evidence in this area continues to grow, further research examining the relationship between GLP-1 therapies and dementia risk reduction is needed.
- No age-specific evidence was available, despite known differences in the impact of obesity across midlife and late life. Similarly, no subgroup analyses based on sex, education or socioeconomic status were identified.

Implementation considerations

Dietary restriction interventions are feasible and can be adapted to various settings, but sustainability and accessibility may vary depending on health care infrastructure and cultural norms.

- Health systems should ensure the availability of appropriate, evidence-informed support for weight management (including dietary advice and physical activity components), delivered by trained providers and adapted to local capacity and resources.
- Dietary restriction interventions are feasible and can be adapted to various settings, but sustainability and accessibility may vary depending on health care infrastructure and cultural norms. Additionally, adherence to dietary restrictions may not be in the person's control; therefore, population- and system-level barriers must be identified and addressed.
- Implementation must consider disparities in access to healthy food and health care services, especially in LMIC, where dementia prevalence is rising.
- Dietary restriction should be used cautiously in older adults owing to potential adverse effects; restriction requires ongoing monitoring by health care professionals to ensure that it is safe and appropriate.
- Interventions should be tailored to local cultural contexts to ensure acceptability and effectiveness *(121,122)*.



3.2.2 Management of diabetes

Generic WHO guidance on diabetes

Management of diabetes should be offered to all adults with diabetes, in line with WHO guidance.

Clinical practice:

- *HEARTS D: diagnosis and management of type 2 diabetes (123)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *The WHO Global Diabetes Compact (46)*
- *Global action plan for the prevention and control of noncommunicable diseases 2013–2020 (112)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*

PICO: *In people with diabetes (with normal cognition or MCI), is the treatment of diabetes (i.e. using pharmacological glucose-lowering medicines and/or non-pharmacological interventions such as diet and physical activity/exercise) more effective than placebo or usual care in lowering the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, management of diabetes may be offered to adults with diabetes.

Strength of recommendation: conditional

Certainty of evidence: very low

Justification

- Diabetes is a major and growing global public health concern. Globally, about 830 million people have diabetes, with most of the affected people living in LMIC *(124)*. Among diabetes cases globally, type 2 diabetes (T2D) accounts for over 95% *(125)*.
- Individuals with T2D have a 50–100% increased risk of developing dementia compared with those without the condition *(126)*. In theory, if T2D was reduced to zero at the population level, it is estimated that about 2% of dementia cases could be prevented *(2)*. The mechanisms through which diabetes contributes to an increased risk for dementia are unclear; however, it is believed to be related to metabolic, vascular and neurodegenerative changes that compound over time *(127)*.
- For this guideline update, evidence was extracted and assessed using GRADE from nine systematic reviews on T2D *(128-135)*, pertaining to two main areas: pharmacological treatments using glucose-lowering medicines and lifestyle interventions (including diet and physical exercise). The certainty of evidence varied from very low to moderate.

Diabetes and elevated plasma glucose levels are among the strongest and most consistently identified risk factors for cognitive decline and dementia.

- Exercise-based interventions probably benefit cognitive function in individuals with T2D and MCI, based on moderate-certainty evidence *(135)*. Evidence is less certain for adults with T2D and normal cognition *(133)*. Reported effect sizes ranged from SMD 0.65 to 0.91.
- Based on low-to-moderate-certainty evidence, intensive glucose control probably results in little to no difference in dementia risk (RR 1.27) and cognitive function (β= –0.03) in adults with T2D and normal cognition compared with standard glucose control *(128)*.
- Based on very-low-certainty evidence, dipeptidyl peptidase-4 (DPP-4) inhibitors may provide a small benefit on cognitive function (mean difference [MD] 1.29) in adults with T2D and normal cognition *(129)*, and a large benefit on cognitive function (SMD 0.99) in adults with T2D and MCI *(136)*.
- Similarly, GLP-1 receptor agonists may provide small benefits on cognitive function (HR 0.93), but the certainty of evidence was very low *(130)*.

In its deliberations, the GDG commented on the limited evidence available for WHO recommended pharmacological treatments of T2D (e.g. metformin or second generation sulfonylureas) and their effects on cognition and dementia risk. The GDG noted that diabetes and elevated plasma glucose levels are among the strongest and most consistently identified risk factors for cognitive decline and dementia, making the lack of stronger evidence for intervention effects particularly striking. The GDG emphasized that this gap is probably driven not by an absence of true treatment effect but by methodological limitations, the poor quality of some studies, and the overall lack of long-term trials that are appropriately designed and sufficiently powered.

Given the high prevalence of diabetes, its direct link to cognitive decline and dementia, and the existence of effective treatment options, the GDG proposed no changes to the existing conditional recommendation for the management of diabetes to reduce the risk of cognitive decline and/or dementia. That recommendation currently rests on very-low-certainty evidence owing to the serious risk of bias and imprecision in estimates of effect. Additionally, the GDG underlined the importance of improving access to glucose lowering treatments – including established lifestyle based interventions and pharmacological therapies – for those in need, reaffirming existing WHO guidance.

Remarks

- T2D is widely recognized as being associated with an increased risk of cognitive decline and dementia. Although the condition is chronic, its course and associated risks can be significantly modified through effective management. Management of diabetes includes adherence to a healthy diet, regular physical activity, maintenance of a normal body weight and avoidance of tobacco use *(124)*.
- Effective glycaemic control and comprehensive cardiovascular risk management are central to diabetes care. They align with broader strategies to reduce the risk of cognitive decline and dementia, and offer wide-ranging benefits for metabolic, vascular and brain health.

Research gaps

- There is a paucity of intervention trials specifically designed to evaluate the impact of diabetes treatment – both pharmacological and non-pharmacological – on the incidence and progression of cognitive decline and dementia. For instance, there is limited evidence on the cognitive effects of specific glucose-lowering drugs, including comparisons among agents recommended by WHO (e.g. metformin, gliclazide and insulin). Observational data suggest differential effects across medications (e.g. sodium-glucose cotransporter 2 [SGLT-2] inhibitors and GLP-1 receptor agonists may offer greater cognitive protection); however, these findings require confirmation through high-quality RCTs.

- Notably, there is also a need for clearer guidance on the role of glycaemic targets, treatment intensity, and the potential cognitive benefits or harms of specific glucose-lowering medications. Cumulative exposure to hyperglycaemia and hyperinsulinemia across the life course, in gestational diabetes or in individuals with multiple comorbidities may have important implications for long-term brain health, although this remains an underexplored area.

There is also a need for clearer guidance on the role of glycaemic targets, treatment intensity, and the potential cognitive benefits or harms of specific glucose-lowering medications.

- Similarly, the risks associated with hypoglycaemia for cognitive health may accumulate over time. Research is required to determine the optimal timing (e.g. midlife versus late life), intensity and duration of diabetes interventions for cognitive health benefits.

- Evidence on health behaviour interventions is largely restricted to exercise-based approaches. Broader interventions (e.g. dietary change and weight loss programmes) remain underexplored, despite their relevance for both diabetes and cognitive outcomes.

- A combination of lifestyle interventions (including physical activity and healthy dietary habits), vascular risk factor control and pharmacological interventions is central to the management of diabetes and supporting optimal glycaemic control; these components also align with broader strategies for improving cognitive health. However, more targeted research is needed to clarify the specific contribution of these components to reducing the risk of cognitive decline and dementia.

- Additional research limitations pertain to the following:

  - **outcomes:** most studies focus on cognitive function measures rather than dementia or MCI incidence;

  - **timing:** few trials include individuals with MCI, limiting insights on intervention effectiveness across cognitive stages; and

  - **equity:** evidence largely comes from high-income countries, with minimal research being undertaken in LMIC or diverse populations. Subgroup analyses by age, sex, ethnicity, education and socioeconomic status are rare, hindering tailored prevention strategies for at-risk populations.

Implementation considerations

- In many countries, diabetes prevention and management strategies are already well-integrated into primary care and NCD programmes, providing a strong platform for incorporating dementia risk reduction efforts. Additionally, task-shifting models, such as empowering community health workers to support diabetes education and monitoring, can enhance service delivery in settings with limited health care infrastructure.

- Implementation strategies should prioritize the strengthening of health systems, to ensure consistent access to essential medications, blood glucose monitoring tools and adequately trained health care providers, especially in LMIC. In some settings, digital health tools (including mobile health applications, telemedicine and automated reminders) may support aspects of diabetes self-management, such as medication adherence and blood glucose monitoring.

- Public health messaging should explicitly address the connection between diabetes, hyperinsulinemia and cognitive decline, raising awareness of the cognitive benefits of glycaemic control among both the general public and health care professionals. Integrating diabetes interventions with broader healthy ageing initiatives may enhance efficiency, maximize health gains and support the long-term sustainability of cognitive health programming. Similarly, integrating brain health considerations into diabetes care pathways may enhance outcomes and increase the perceived value of early intervention.

Rather than relying on a one-size-fits-all approach, glycaemic targets should be individualized.

- Rather than relying on a one-size-fits-all approach, glycaemic targets should be individualized, taking into account intrinsic capacity, functional status, comorbidities and life expectancy. In older people, particularly those with significant loss of intrinsic capacity or limited life expectancy, tight glycaemic targets can increase the risk of hypoglycaemia and associated harms (e.g. falls and cognitive decline) without providing meaningful benefits. A person-centred approach is needed, prioritizing safety, quality of life and outcomes that matter to the individual.

- Implementation efforts should be culturally tailored to address beliefs, stigma and barriers to diabetes care (including access to healthier food options); also, they should involve community-based strategies to promote health literacy, self-management and patient engagement.

3.2.3 Management of hypertension

Generic WHO guidance on hypertension

Management of hypertension should be offered to all adults with hypertension, in line with WHO guidance.

Clinical practice:

- *Guideline for the pharmacological treatment of hypertension in adults (137)*
- *HEARTS: technical package for cardiovascular disease management in primary health care (138)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *Global action plan for the prevention and control of noncommunicable diseases 2013–2020 (112)*
- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*

PICO: *For adults with normal cognition or MCI and hypertension, is treatment of hypertension more effective than placebo, no intervention or usual care in reducing the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, management of hypertension may be offered to adults with hypertension.

Strength of recommendation: conditional

Certainty of evidence: very low

Justification

- Hypertension affects about 33% of the global adult population aged 30–79 years, with prevalence increasing significantly with age *(139)*.[1] Two thirds of people with hypertension live in LMIC, where the condition is often underdiagnosed and undertreated.
- Hypertension is a well-established risk factor for dementia, making it a critical target for prevention efforts. In theory, if hypertension was reduced to zero at the population level, about 2% of dementia cases could be prevented *(2)*.

[1] Hypertension (high blood pressure) is when the pressure in the blood vessels is too high: 140/90 mmHg or higher.

At the population level, a considerable treatment gap persists, with only about 44% of adults with hypertension diagnosed and treated, and just 23% achieving control globally.

- For this guideline update, evidence was extracted and assessed using GRADE from two systematic reviews *(140,141)*. The evidence pertained to two areas: pharmacological treatment of hypertension using antihypertensive medications, and intensive blood pressure control compared with standard blood pressure control:
  - Based on low certainty evidence, pharmacological treatment of hypertension in cognitively normal adults may result in little to no effect on incident dementia (effects ranging from odds ratio [OR] 0.87 to 1.01) *(140)* but may result in small improvements in cognitive function (SMD 0.25) based on very-low-certainty evidence *(140)*.
  - Intensive blood pressure control compared with standard control showed uncertain effects on dementia or MCI incidence *(141)* (effects ranging from RR 0.91 to 1.09), based on very-low-certainty evidence. Such control probably results in little to no difference in cognitive function (SMD 0.01) in adults with normal cognition and hypertension *(141)*, based on low certainty evidence.

Hypertension is widely recognized as a key risk factor for cognitive impairment and dementia, and the evidence base for this has grown modestly since 2019; however, GDG members noted that the certainty of evidence on the direct cognitive benefits of hypertension treatment remains very low to low for different methodological reasons. Therefore, the GDG proposed no changes to the existing recommendation. The GDG noted that hypertension management is already strongly recommended for overall health and widely implemented globally. Hence, the GDG emphasized the need to manage hypertension according to existing WHO guidelines *(137)*.

Remarks

- Hypertension is a well-established risk factor for cognitive decline and dementia, including both Alzheimer disease and vascular dementia *(2,142,143)*, and controlling blood pressure during midlife has been shown to provide greater long-term cognitive benefits compared with starting treatment in later life *(2)*.
- Although managing blood pressure supports brain health, its specific effect on dementia outcomes is difficult to isolate because of overlapping risk factors and multimorbidity.
- There is no single optimal blood pressure threshold for cognitive protection. Hence, treatment should be tailored to individual risk profiles, including cardiovascular and metabolic factors.
- Hypertension control is a public health and economic priority, with established treatment pathways and scalable interventions that can reduce dementia-related health care and caregiver burden. Widely available screening tools, treatment protocols and public health guidelines make the management of hypertension both feasible and effective for dementia risk reduction.

- However, at the population level, a considerable treatment gap persists, with only about 44% of adults with hypertension diagnosed and treated, and just 23% achieving control globally *(139)*.
- Hypertension management should follow national and international recommendations *(*137,138*)*.

Research gaps

- Only one RCT was identified that explored the effect of pharmacological treatment of hypertension in individuals with MCI. Further research is needed to determine the effectiveness of pharmacological treatment once blood pressure is adequately controlled.
- More high-quality RCTs and pooled analyses are needed to strengthen conclusions on hypertension and dementia risk, including optimal timing and blood pressure targets (midlife versus late life), intensity (standard versus intensive) and duration of treatment.
- Research is needed into the cognitive effects of different antihypertensive drug classes, particularly their neuroprotective potential.
- There is limited evidence on how hypertension interacts with other risk factors (e.g. diabetes, obesity and dyslipidaemia) in shaping cognitive outcomes.
- Most evidence is derived from older adults (aged 62–84 years), despite hypertension being a midlife risk factor; implementation strategies should prioritize earlier life-course interventions.
- Most available research is based on studies conducted in high-income countries, limiting the global applicability of their findings. More research is needed in LMIC to ensure equitable and globally relevant recommendations.
- To ensure that recommendations are equitable and globally relevant, future studies should also explore differential effects by sex, age and genetic predisposition (e.g. APOE status).
- None of the reviewed studies provided data on the costs of pharmacological or lifestyle-based hypertension treatments in the context of cognitive health or dementia prevention.

Implementation considerations

- Hypertension is strongly linked to cardiovascular and renal complications, including heart attacks, heart failure, stroke and kidney failure *(139)*. Hypertension can be effectively managed through lifestyle changes, such as healthy eating – including low salt intake, physical activity and weight control – as well as antihypertensive medications *(2)*.

- Hypertension control is already embedded in many national NCD programmes; thus, existing infrastructures (especially in primary care) can be leveraged for dementia prevention through routine screening, monitoring, education and referral. For example, integrated approaches that address hypertension alongside other cardiovascular and metabolic risk factors (e.g. diabetes and obesity) are likely to be more sustainable and beneficial for overall brain and heart health.

Integrated approaches that address hypertension alongside other cardiovascular and metabolic risk factors (e.g. diabetes and obesity) are likely to be more sustainable and beneficial for overall brain and heart health.

- In older people, blood pressure targets should be individualized rather than being applied uniformly. Both insufficient and overly intensive blood pressure control may lead to adverse outcomes. Treatment decisions should consider the individual's intrinsic capacity, functional status, orthostatic symptoms and cardiovascular history, acknowledging that the benefit–risk balance of tighter blood pressure control narrows as intrinsic capacity decreases.

- In LMIC, successful implementation requires health system strengthening, including reliable supply chains, access to essential medications and workforce development.

- Culturally tailored education and community-based interventions are needed to reduce stigma, improve adherence and align with local beliefs and behaviours.

- Digital health tools (e.g. mHealth reminders, telemonitoring and decision support systems) can enhance adherence and follow-up, particularly in remote or underserved areas.

- Public health messaging should emphasize the dual benefits of hypertension control for cardiovascular and cognitive health, with a focus on early detection and midlife intervention.

3.2.4 Management of dyslipidaemia

Generic WHO guidance on dyslipidaemia

Management of dyslipidaemia should be offered to all adults with dyslipidaemia, in line with WHO guidance.

Clinical practice:

- *Hearts: technical package for cardiovascular disease management in primary health care: risk-based CVD management (138)*

Service delivery and care pathways:

- *WHO package of essential noncommunicable (PEN) disease interventions for primary health care (50)*

Public health and policy:

- *Global action plan for the prevention and control of noncommunicable diseases (112)*

PICO: *For adults with normal cognition or MCI and dyslipidaemia, is treatment of dyslipidaemia more effective than placebo or no intervention in reducing the risk of cognitive decline and/or dementia?*

VALIDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, management of dyslipidaemia at midlife may be offered.

Strength of recommendation: conditional

Certainty of evidence: low

Justification

- Dyslipidaemia is a metabolic disorder that is characterized by abnormal levels of lipids in the blood. It constitutes a major risk factor for cardiovascular disease, including heart attack and stroke, which are leading causes of death globally *(16)*.
- High levels of cholesterol in the brain have been linked to a greater risk of stroke and the buildup of harmful proteins (e.g. tau and amyloid β), which may explain the connection between low density lipoprotein (LDL) cholesterol and dementia *(144)*. In theory, if dyslipidaemia at midlife was reduced to zero at the population level, it is estimated that about 7% of dementia cases could be prevented *(2)*.
- Statins may help to reduce dementia risk owing to their cholesterol-lowering and anti-inflammatory effects, with observational studies showing a protective association *(145,146)*. However, evidence remains limited since long-term RCTs of statin use to prevent dementia are impractical and unethical *(2)*.

High levels of cholesterol in the brain have been linked to a greater risk of stroke and the buildup of harmful proteins (e.g. tau and amyloid β)

Based on the findings of the scoping review (Annex 1), it was deemed unlikely that any new evidence would alter the strength of the existing recommendation. Therefore, the GDG decided to validate the existing recommendation.

Remarks

- Based on the severity of the dyslipidaemia and overall risk of cardiovascular or cerebrovascular disease, lifestyle or pharmacological approaches can be undertaken to reduce blood cholesterol. The most common and effective lifestyle approaches include weight reduction and decreasing saturated fats in the diet (i.e. decreasing the consumption of food of animal origin). However, dyslipidaemia is often controlled and managed pharmacologically, with statins being the drugs of first choice.
- Although the evidence on how statins influence dementia risk remains limited, statins remain beneficial for cardiovascular health and may be used in line with WHO's guidance *(50)*.
- WHO is currently developing specific guidelines for the treatment and management of dyslipidaemia.

Research gaps

- Evidence on how statins influence dementia risk remains inconclusive. Research is needed to clarify whether potential cognitive effects arise from cholesterol-lowering, vascular protection or direct neurobiological actions (e.g. modulation of inflammation, oxidative stress or synaptic function) *(147)*.
- Most existing research has short follow-up periods, limited participant diversity and inconsistent cognitive measures. Long-term cohort and clinical studies that integrate both new and chronic statin users are needed, to reduce bias and assess causal pathways *(147)*.
- Comparability of studies is limited by heterogeneity in diagnostic criteria, exposure measurement and adjustment for comorbidities, medication use and lifestyle factors. Future research should incorporate standardized dementia definitions and control for 'healthy user' and selection biases *(145)*.

Implementation considerations

- Dyslipidaemia management should be part of integrated midlife cardiovascular prevention strategies, especially in high-risk individuals, with routine cardiovascular risk assessment to support timely diagnosis of dyslipidaemia and early initiation of lipid-lowering therapy if required.
- Although statins should not be initiated solely for dementia prevention in older adults, they may offer cognitive benefits when prescribed for cardiovascular reasons in midlife. It is essential to address patient hesitancy and misconceptions about side-effects through targeted health education on the safety of statins and their role in cardiovascular and cerebrovascular health, and in reducing dementia risk.
- Ensuring affordability and consistent availability of lipid-lowering medicines is crucial for equitable access.

Lifestyle interventions central to dyslipidaemia (e.g. diets low in saturated fats, regular physical activity and weight reduction) remain essential for cholesterol control.

- Lifestyle interventions central to dyslipidaemia (e.g. diets low in saturated fats, regular physical activity and weight reduction) remain essential for cholesterol control. These interventions overlap substantially with recommendations for diabetes prevention and broader dementia risk reduction, although more research is needed to clarify their specific cognitive impact.
- Health systems should prioritize early identification and treatment of dyslipidaemia in midlife, as part of a broader dementia risk reduction strategy.
- In older people, the management of dyslipidaemia should be informed by a comprehensive assessment that includes intrinsic capacity, comorbidities, polypharmacy, life expectancy and individual priorities, rather than by lipid levels alone *(148)*.

3.2.5 Management of hearing loss

Generic WHO guidance on hearing and hearing loss

Prevention, screening and management of hearing loss should be offered, in line with WHO guidance.

Clinical practice:

- *Package of interventions for rehabilitation: module 6: sensory conditions (149)*

Service delivery and care pathways:

- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (22)*

Public health and policy:

- *Hearing screening: considerations for implementation (150)*

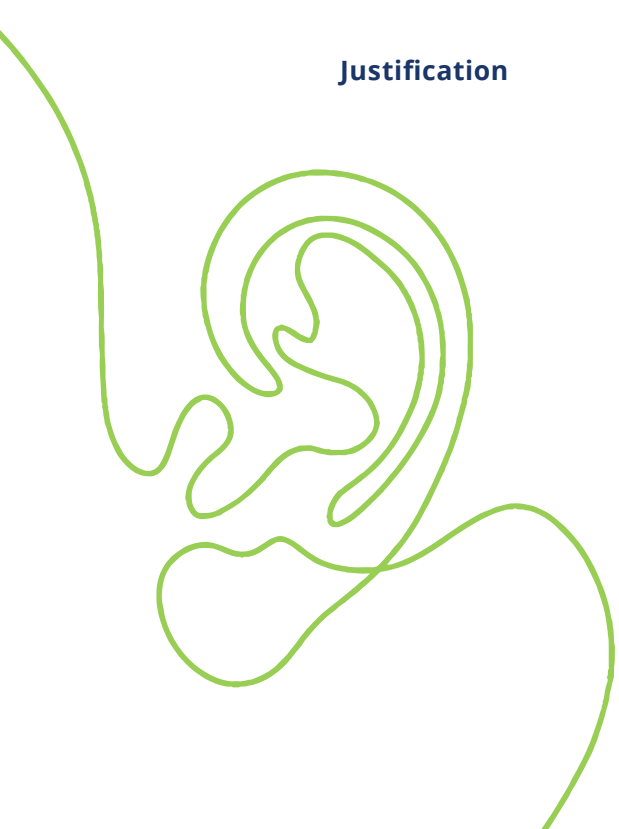
PICO: *For adults with normal cognition or MCI and hearing loss, is treatment of hearing loss more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

UPDATED RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, hearing aids may be offered to adults with hearing loss.

Strength of recommendation: conditional

Certainty of evidence: low



Justification

- Globally, about one in five people experience some form of hearing loss *(151)*, with prevalence rising with age. Despite the availability of effective management options, hearing loss often remains undiagnosed and unaddressed, particularly in older adults *(151)*. Unaddressed hearing loss has widespread impacts on quality of life, relationships and mental health *(152)*; it has also been closely linked to cognitive decline and dementia *(2)*. In theory, if hearing loss was reduced to zero at the population level, it is estimated that about 7% of dementia cases could be prevented *(2)*.
- Mechanisms linking hearing loss to cognitive decline include social isolation, increased cognitive load, cardiovascular pathology and neurobiological changes, all of which may exacerbate the risk of dementia *(2,153)*.

- For this guideline update, evidence was extracted and assessed using GRADE from two systematic reviews *(154,155)*. Only evidence for use of hearing aids was identified; insufficient evidence was available for the use of other hearing interventions such as cochlear implants:
  - Observational data suggest that hearing aid use may be associated with a reduced risk of dementia and MCI *(154)* in adults with normal cognition. The certainty of evidence was rated as very low. Similarly, very-low-certainty evidence suggests that, in adults with MCI, hearing aid use may reduce the risk of progression to dementia *(154)*. Effects ranged from HR 0.73 to 0.83.
  - RCT data indicate that hearing aid use may have a small effect on cognitive function in adults with normal cognition (SMD 0.11) *(155)*. The certainty of evidence was rated very low.

In the 2019 guidelines, no recommendation was made owing to insufficient evidence. The GDG concluded that, although the certainty of evidence is low to very low, the evidence base has increased, and consistent findings across studies suggest that treating hearing loss may reduce the risk of dementia. Given the potential benefits (which probably outweigh the harms), and the global burden of unaddressed hearing loss and its association with dementia risk, the GDG made a conditional recommendation that hearing aids may be offered to adults with hearing loss to reduce the risk of cognitive decline and/or dementia. Additionally, given the widespread impact of hearing loss, the GDG added a reference to existing WHO technical guidance for timely identification and management of hearing loss.

Remarks

- Hearing loss contributes to a cascading effect of decreased social engagement, mental well-being and physical activity, which can increase the risk of cognitive decline and dementia.
- Hearing aids should be used to address hearing loss, not solely for the purpose of preventing dementia.
- The effectiveness of interventions may vary by the type and severity of hearing loss, and the extent to which the device is used. At present, there is insufficient evidence to draw conclusions on the effects of cochlear implants on the risk of dementia.
- Prevention, identification and management of hearing loss should be aligned with national and international guidance *(22,149,150)*.

Hearing loss contributes to a cascading effect of decreased social engagement, mental well-being and physical activity, which can increase the risk of cognitive decline and dementia.

Research gaps

- High-certainty evidence from RCTs on whether addressing hearing loss reduces dementia risk or slows progression is largely lacking or only slowly emerging.
- No randomized or longitudinal studies have reported cognitive or dementia outcomes for cochlear implant users, and no trials have directly compared different hearing interventions (e.g. hearing aids versus cochlear implants versus no intervention or counselling).
- Evidence on hearing interventions in adults with MCI is limited: only one study assessed hearing aid use with dementia as the outcome, and no systematic reviews have evaluated cognition as a primary outcome in this population.
- Existing studies vary widely in sample size and follow-up duration, with most focusing on older adults; evidence on interventions initiated in midlife is limited.
- The influence of hearing loss severity and comorbidities on cognitive outcomes remains unclear.
- It remains uncertain whether cognitive benefits are derived directly from hearing interventions or from related factors such as increased social engagement and health care use.
- Further research is needed to evaluate the long-term cognitive effects of hearing interventions across diverse populations and health system contexts, including how outcomes vary by degree and laterality of hearing loss and timing of onset, and whether hearing loss is measured objectively or self-reported.
- Most available evidence originates from high-income countries; research in LMIC is essential to ensure global applicability.
- Future studies should explore differential effects by sex, age and genetic predisposition (e.g. APOE status) to inform tailored interventions.

Implementation considerations

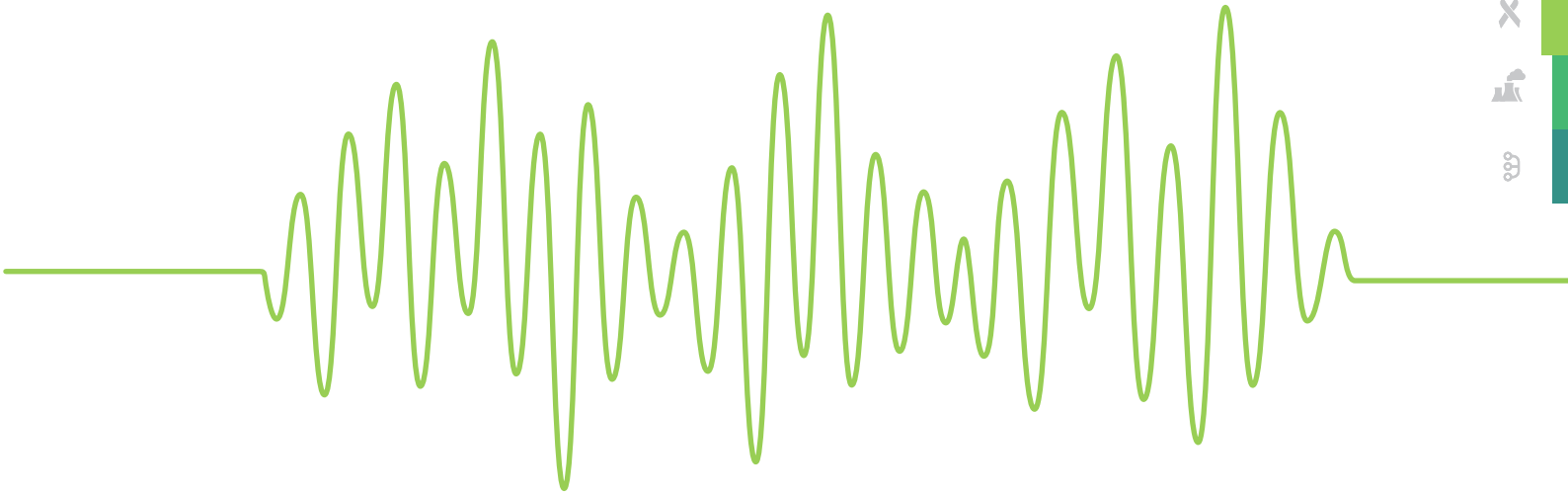
- Over 400 million people with hearing loss could benefit from hearing devices, yet these needs are currently met in only an estimated 17% of those people *(152)*. It is essential to expand access to affordable, culturally appropriate hearing care, especially in LMIC and among high-risk and underserved populations.

- Hearing aids are the most used and widely available assistive technology for hearing loss. They are cost-effective and improve communication and quality of life. However, adherence and sustained use may be challenging, particularly among older adults *(156)*. Barriers include stigma, low awareness, delays in identification and rehabilitation, cost, limited access to hearing care, shortages of trained personnel, and a shortage of infrastructure for fitting and maintaining devices *(152)*. Public health campaigns and capacity-building initiatives (e.g. training audiologists, technicians and other health personnel) are needed to address these challenges.

- WHO guidance calls for systematic screening of adults aged above 50 years, followed by prompt diagnosis and hearing aid fitting through community-based service delivery approaches, to promote access to hearing care in resource-limited settings *(22,150,157)*.

- Integration of hearing care into primary health services, combined with cognitive screening and referral pathways, can enhance feasibility and promote early detection of both hearing loss and cognitive decline. However, context must be considered when selecting screening tools, to ensure cultural appropriateness and relevance.

- In addition to managing hearing loss, primary prevention is essential. Evidence-based measures (e.g. reducing exposure to loud sounds, implementing safe listening practices, preventing and treating childhood ear infections and ensuring vaccination for preventable infectious causes of hearing loss) should be integrated into public health and primary care strategies, to reduce the overall incidence of hearing loss *(152)*.



3.2.6
Use of menopausal hormone therapy

General clinical remark on MHT

MHT is primarily used for symptomatic relief of vasomotor symptoms and genitourinary syndrome of menopause, not for dementia prevention.

PICO: *For women with premature ovarian insufficiency or in early, peri or post-menopause (with normal cognition or MCI), does current or previous menopausal hormone therapy (MHT) use compared to no MHT impact upon the risk of cognitive decline and/or dementia?*

NEW RECOMMENDATION AGAINST ✕

Menopausal hormone therapy is not recommended for specifically reducing the risk of cognitive decline and/or dementia in postmenopausal women aged 65 years and older.

Strength of recommendation: conditional

Certainty of evidence: very low

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For women aged below 65 years – including those experiencing premature ovarian insufficiency, early menopause or perimenopause – and for the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to advise for or against the use of menopausal hormone therapy.

Justification

- Women are more likely than men to develop dementia, even after adjusting for differences in life expectancy *(158)*. Hormonal changes during menopause and the use of MHT may affect dementia risk.
- MHT is widely used for menopausal symptom relief; however, its effect on cognition and dementia risk is uncertain *(2,159)*.

MHT is widely used for menopausal symptom relief; however, its effect on cognition and dementia risk is uncertain.

- For this guideline update, evidence was extracted and assessed using GRADE from 10 primary studies, comprising one RCT and nine observational studies *(160-169)*. A detailed description is given in the **Web Annex H**.
- Based on trial evidence with low to moderate certainty:
  - estrogen-only MHT may result in little to no difference in dementia risk (in women receiving the treatment at age 65 years or above; HR 1.49); and
  - estrogen plus progestogen MHT probably results in little to no difference in dementia risk (in women receiving treatment at age 65 years or above; HR 1.76).
- Based on observational evidence with very low certainty:
  - estrogen-only MHT showed uncertain effects on dementia and Alzheimer disease risk (RR 0.95–1.10); also, irrespective of the duration for which estrogen-only MHT was taken[1] and the age at which the treatment was initiated, effects on dementia and Alzheimer disease risk were uncertain (RR 1.08–1.16; HR 0.93–1.12); and
  - estrogen plus progestogen MHT showed uncertain effects on dementia and Alzheimer disease risk (RR 1.11–1.12); also, irrespective of the duration for which estrogen plus progestogen was taken[2] and the age at which the treatment was initiated, effects on dementia and Alzheimer disease risk were uncertain (RR 1.08–1.16; HR 0.93–1.12).

[1] That is, less than 5 years, 5–10 years or more than 10 years.
[2] That is, less than 5 years, 5–10 years or more than 10 years.

The GDG noted that – given the variability in age at initiation of treatment, hormone type and individual health profiles – a broad recommendation would not adequately address the nuanced clinical decisions required. After reviewing the available evidence, the GDG determined that the only population for which sufficiently robust data existed was postmenopausal women aged 65 years and older. Within this population, evidence consistently demonstrated little to no difference – irrespective of formulation – on reducing the risk of cognitive decline or dementia. The GDG also observed that women aged 65 years and older are not the typical population for whom MHT is clinically indicated, because MHT is generally prescribed for the management of vasomotor or menopausal symptoms, which most commonly occur earlier in the menopausal transition. The GDG therefore considered it inappropriate for clinicians to initiate MHT in older postmenopausal women solely for the purpose of reducing the risk of cognitive decline or dementia. Hence, the GDG made a conditional negative recommendation on MHT (irrespective of type of composition) in postmenopausal women aged 65 years and older for the purpose of reducing the risk of cognitive decline and/or dementia.

No evidence was identified for other subpopulations, including women with premature ovarian insufficiency, those with early menopause and those in the menopausal transition stage (i.e. perimenopause). The GDG concluded that the current evidence base does not allow for a recommendation for or against MHT in these subpopulations, and highlighted the need for further research.

Remarks

- At the time of this guideline update, no dedicated WHO guideline on the management and treatment of menopausal symptoms was available, although development of such guidelines will be initiated soon.
- MHT is used primarily for symptomatic relief (including vasomotor symptoms and genitourinary syndrome of menopause), not for dementia prevention. Initiating MHT more than 10 years after menopause is associated with a less favourable benefit–risk profile compared with earlier initiation. The evidence reviewed for this guideline therefore does not apply to women aged in their 40s and 50s, who represent the typical population seeking treatment for menopausal symptoms.

The negative recommendation in this guideline applies specifically to women aged 65 years and older, irrespective of MHT type.

- The negative recommendation in this guideline applies specifically to women aged 65 years and older, irrespective of MHT type. It reflects the age group for which evidence was available and assessed through the GRADE process (the evidence profile can be found in the **Web Annex H**).
- Evidence considered by the 2024 National Institute for Health and Care Excellence (NICE) Guideline Committee suggests that combined MHT, when initiated after the age of 65 years, may increase the risk of dementia, whereas estrogen-only MHT does not appear to affect dementia risk *(159)*. Accordingly, the NICE guideline recommends that neither combined nor estrogen-only hormone replacement therapy should be offered for the purpose of preventing dementia *(159)*. The NICE guideline also provides detailed evidence on how different types of MHT influence other health outcomes, including breast and ovarian cancer, coronary heart disease and stroke (*159*). Meanwhile, in the USA, the boxed safety warnings for risks associated with MHT products are being updated *(170)*.

Research gaps

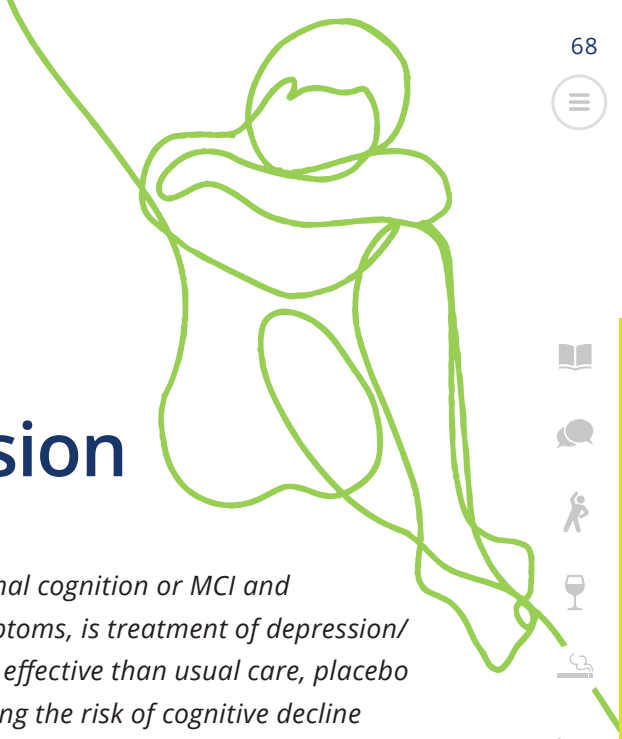
- Most of the available evidence comes from observational studies, with only one RCT included in the GRADE analysis. This RCT, which is from the early 2000s, focused on women aged 65 years and older – an age group that does not reflect typical initiation of MHT – and was terminated early owing to adverse effects. In addition, hormone formulations used in older studies differ from those currently prescribed, which limits the generalizability of findings to present-day clinical practice.
- The long-term effects of MHT, particularly beyond 10 years of use, remain poorly understood, and results vary across different populations and treatment regimens.
- There is considerable variation in how MHT exposure and dementia outcomes are defined and measured across studies, making direct comparison and synthesis of findings challenging.
- Many studies rely on self-reported data or prescription records, without information on adherence; this situation increases the risk of exposure misclassification and recall bias.

- Most studies have been conducted in older postmenopausal women (aged ≥65 years), limiting the applicability to younger women, including those with premature ovarian insufficiency or early menopause.
- The age of menopause varies significantly by region and income level – occurring up to 10 years earlier in LMIC compared with high-income countries – underscoring the need for research across diverse settings.
- Few studies systematically compare estrogen-only versus combined MHT, or differentiate between systemic and vaginal administration, despite potential differences in neurocognitive effects.
- Evidence is lacking on how age at menopause onset, symptom severity and reasons for initiating hormone therapy (symptom relief versus prophylactic use) influence dementia risk.
- There is limited research on how genetic risk factors (e.g. APOE ε4 status), baseline cognitive status and other biomarkers may affect the relationship between MHT and dementia.
- The "critical window" hypothesis – which states that the benefit–risk profile depends on when MHT is initiated in relation to a woman's age or stage of menopause *(171)* – remains unconfirmed, with inconsistent findings and no conclusive evidence to support the hypothesis.

Implementation considerations

In routine practice, women and their health care providers should jointly consider the full balance of benefits and risks of MHT.

- MHT is typically prescribed to manage and relieve current menopausal symptoms, not for the prevention of dementia or other long-term conditions. In routine practice, women and their health care providers should jointly consider the full balance of benefits and risks of MHT. Benefits include effective treatment of hot flushes and night sweats, and prevention of osteoporotic fractures. Depending on the formulation, duration of use and age at initiation, risks may include venous thromboembolism, stroke and certain types of cancer, particularly breast cancer.
- Risks and benefits should be discussed, especially for those initiating MHT at the age of 65 years or older, or those considering long-term use.
- Although the impact of MHT on dementia risk appears to be trivial or uncertain, the risk of serious non-cognitive harms, in particular certain types of cancer, is likely to be clinically significant, particularly with combined estrogen–progestogen therapy.
- No recommendation is made for MHT for the purpose of dementia risk reduction in women aged under 65 years, because there is currently insufficient evidence to advise for or against its use for this purpose. Additional high-quality research is needed in this area.
- MHT is just one component within the broader landscape of women's health. The higher burden of dementia in women reflects the interaction of multiple biological, social and environmental determinants, with MHT representing only one of many modifiable factors.



3.2.7 Management of depression

Generic WHO guidance on depression

Management of depression in the form of psychological interventions and/or antidepressants should be provided to all adults with depression, in line with WHO guidance.

Clinical practice:

- *Mental Health Gap Action Programme (mhGAP) guideline for mental, neurological and substance use disorders (33)*

Service delivery and care pathways:

- *mhGAP intervention guide – Version 2.0 (172)*
- Depression module of the *mhGAP training manuals (173)*
- Depression module of the WHO Academy mhGAP training – *mhGAP: Integrating mental health into primary care (174)*

Public health and policy:

- *Comprehensive mental health action plan 2013–2030 (175)*

PICO: *For adults with normal cognition or MCI and depression/depressive symptoms, is treatment of depression/depressive symptoms more effective than usual care, placebo or no intervention in reducing the risk of cognitive decline and/or dementia?*

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend the management of depression.

Justification

- Depression (including major depressive disorder and dysthymia) is a common and recurrent condition, currently affecting an estimated 332 million people globally; it contributes substantially to disability across the lifespan *(176)*. It is estimated that 5.7% of adults and 5.9% of adults aged 70 years and older experience depression *(176)*.
- Depression has been linked to increased dementia risk, with about 3% of all dementia cases attributable to depression *(2)*. Although the relationship between depression and dementia may be influenced or partially explained by several psychological (e.g. diminished self-care and social isolation) and physiological mechanisms (e.g. elevated cortisol levels that can lead to hippocampal atrophy or brain inflammation) *(2,177)*, the predominantly observational nature of current evidence limits conclusions about causality.

- For this guideline update, evidence was extracted and assessed using GRADE from two systematic reviews *(178,179)* pertaining to pharmacological treatment of depression using antidepressants and non-pharmacological interventions (including cognitive stimulation therapy, psychotherapy and a multidomain intervention), derived primarily from observational studies:
  - for pharmacological treatment, very-low-certainty evidence suggested small negative or no effects of antidepressant use on dementia and MCI in older adults with normal cognition, with effects ranging from RR 1.04 to 1.21; and
  - for non-pharmacological interventions, very-low-certainty evidence suggested small positive or trivial effects on cognitive function in adults with MCI.

Given the very low certainty of the available observational evidence and the absence of RCTs assessing the effect of depression management on dementia or MCI, the GDG concluded that no recommendation could be made at this time. The previous guidelines also refrained from making a recommendation, reflecting the similarly insufficient evidence available at that time. GDG members noted the bidirectional relationship between depression, cognitive function and dementia, as well as the potential for reverse causality. Given the global prevalence and impact of depression, the GDG reaffirmed that managing depression is important for other health benefits, in line with WHO guidelines *(33)*. There is some evidence to suggest that antidepressant use may be associated with an increased risk of dementia in older adults with depression; however, the GDG did not issue a negative recommendation against this intervention, because older adults with depression may still require treatment with antidepressants (these should have a low anticholinergic burden, to minimize potential cognitive adverse effects, as outlined in Box 1).

Remarks

- There are many possible interventions for treating depression, including psychological interventions, affordable generic antidepressants and collaborative care models delivered in primary care and community settings.
- Despite observational evidence, uncertainty persists about any causal relationship between depression and dementia. Research suggests a possible bidirectional relationship, with depression potentially acting both as a risk factor and a symptom of the prodromal phase of dementia *(2)*.

Depression often co-occurs with other modifiable dementia risk factors (e.g. social isolation, sleep disturbances and chronic conditions), amplifying the cumulative risk when left untreated.

- A study that used data from the UK Biobank (not assessed using GRADE) found that individuals in the depression treatment group had a lower risk of dementia *(180)*.
- Depression often co-occurs with other modifiable dementia risk factors (e.g. social isolation, sleep disturbances and chronic conditions), amplifying the cumulative risk when left untreated. Therefore, treating depression may improve quality of life and functional status, even if its effect on reducing dementia incidence is not yet fully established.

- Treatment of depression should be aligned with national and international guidance *(33,175).*

Research gaps

- There is a lack of RCTs directly assessing the impact of depression treatment (whether pharmacological or psychological) on cognitive outcomes or dementia incidence.
- There is limited evidence on whether treating depression in midlife versus late life has different long-term cognitive outcomes.
- Interactions between depression and other modifiable risk factors (e.g. physical inactivity, sleep disorders and social isolation) are poorly understood and require further investigation.
- Studies rarely stratify findings by age, sex, duration of depression or comorbidities, limiting understanding of differential effects.
- Most available evidence originates from high-income countries; research is needed in LMIC to improve global generalizability.

Implementation considerations

- Differentiating depression from cognitive impairment in older adults is complex, owing to overlapping symptoms such as memory impairment, reduced concentration, apathy and social withdrawal. Depression has a more acute onset and fluctuating course, and is potentially reversible with treatment.

Differentiating depression from cognitive impairment in older adults is complex, owing to overlapping symptoms such as memory impairment, reduced concentration, apathy and social withdrawal.

- WHO's mhGAP guidelines for mental, neurological and substance use disorders *(33)* and the ICOPE approach *(22)* provide practical tools that help primary care providers to distinguish between depression and cognitive decline in older adults. These tools emphasize a structured assessment of mood, cognition and functional ability, enabling early detection and appropriate management.
- For older adults with new onset depression, neurological and neuropsychological evaluation should be considered.
- Screening and management of depressive symptoms (using context-specific and validated tools) should be integrated into primary care, especially for older adults and individuals with known dementia risk factors.
- Culturally appropriate and accessible mental health interventions should be prioritized, particularly in LMIC and underserved populations. Although psychological (non-pharmacological) interventions for depression are recommended as first-line treatment, they remain unavailable or inaccessible in many settings.
- Trained non-specialist health workers can support the scalable delivery of psychological interventions in resource-constrained settings.

- Public health messaging should normalize help-seeking for depression, emphasizing its relevance for both emotional well-being and long-term brain health.
- Collaboration among mental health, neurology, primary care, community health and geriatric services may help to improve early detection and intervention for individuals at elevated risk of both depression and dementia.
- When pharmacological treatment is required, preference should be given to antidepressants with a low anticholinergic burden, to minimize potential cognitive adverse effects (see **Box 1**).

Box 1

Caution with pharmacological treatment of depression

Pharmacological management of depression in older people requires a critical evaluation of the anticholinergic burden and the individual's vulnerabilities.

Tricyclic antidepressants (TCAs), such as amitriptyline or clomipramine, have a high anticholinergic burden and should generally be avoided in older people owing to an increased risk of cognitive impairment, delirium, urinary retention, constipation, orthostatic hypotension and falls. Paroxetine, a selective serotonin reuptake inhibitor(SSRI), has high anticholinergic activity and should be avoided when alternatives are available.

When antidepressant medication is indicated, clinicians should select options with lower anticholinergic activity, taking into account local availability. Suitable choices may include sertraline and – depending on local availability – duloxetine or escitalopram, with appropriate monitoring for potential adverse effects such as hyponatremia and QTc prolongation.

Pharmacological treatment should be complemented by regular medication reviews and non-pharmacological interventions.

3.2.8 Management of stroke

Generic WHO guidance on stroke

Management of stroke should be provided to all adults, in line with WHO guidance.

Clinical practice:

- *Package of interventions for rehabilitation: module 3: neurological conditions (34)*

Service delivery and care pathways:

- *Framework for the care of acute coronary syndrome and stroke (181)*

Public health and policy:

- *Tackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)*
- *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (182)*

PICO: *For adults with a history of ischaemic stroke / transient ischaemic attack (TIA), are interventions for treating ischaemia/ stroke, especially those aimed at preventing subsequent/recurrent stroke, effective in reducing the risk of cognitive decline and/or dementia?*

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend pharmacological interventions typically used to reduce the risk of recurrent stroke.

Justification

- Stroke is ranked as the third leading cause of death and disability globally, with an estimated 93.8 million cases in 2021 *(183)*. Most of the global stroke burden is attributable to 10 modifiable risk factors, including high blood pressure, air pollution, dyslipidaemia, excess body weight, physical inactivity and harmful use of alcohol; these risk factors are shared with dementia *(183)*.
- Stroke is a risk factor for dementia, and the risk increases substantially with repeated strokes: individuals who experience recurrent ischaemic stroke have about a 1.5-fold higher incidence of dementia compared with those who have only had a first-ever ischaemic stroke *(184)*, underlying the importance of preventing recurrent strokes as a key strategy for dementia prevention.
- For this guideline update, evidence was extracted and assessed using GRADE from one systematic review *(185)*. The certainty of evidence ranged from very low to high. The evidence focused on blood pressure lowering drugs, antithrombotic drugs and lipid-lowering drugs. Treatment occurred at different times post stroke (details are given in the evidence profile in **Web Annex J**). Results indicated the following:

Effective control of stroke risk factors – including hypertension, diabetes, air pollution, atrial fibrillation and smoking – is crucial for long-term cognitive health.

- Blood pressure lowering treatment makes little to no difference to dementia incidence (OR 0.89–1.08), with small improvements in cognitive function but a probable increase in serious adverse events (SAEs). Compared with standard blood pressure lowering guidelines, stricter guidelines may make little to no difference to cognitive decline, quality of life, activities of daily living (Mini-Mental State Examination [MMSE] differences 1.2 to 4 points lower) and MCI incidence (OR 1.03), with highly uncertain adverse event estimates (OR 0.71–1.41).
- Dual antithrombotic treatments probably make little to no difference to cognitive function (OR 0.90), and to the incidence of dementia, MCI, SAEs and fatal events compared with monotreatment (OR 0.90–1.10).
- Statin treatment after non-cardioembolic ischaemic stroke may make little to no difference to dementia incidence, but probably increases SAEs compared with no statin use (OR 0.97–1.20).
- Stricter versus standard lipid-lowering guidelines in adults with a history of ischaemic or haemorrhagic stroke may make little to no difference to cognitive function and quality of life (MMSE differences 1.9–8.6 points higher), with very uncertain effects on SAEs and fatal events.

In their decision, GDG members acknowledged that stroke is a well-established risk factor for cognitive decline and dementia, particularly vascular dementia. The GDG further noted that dementia risk increases substantially with recurrent stroke, making prevention of subsequent strokes a primary target for dementia risk reduction. Hence, the reviewed evidence focused on pharmacological interventions that aim to prevent recurrent strokes. Nonpharmacological interventions were considered out of scope.

The GDG concluded that current evidence is insufficient to recommend specific interventions for treating ischaemia/stroke for reducing the risk of cognitive decline or dementia. Although some studies showed small or uncertain effects, overall findings were limited by low certainty, small sample sizes and inconsistent results. The GDG acknowledged that although primary prevention of stroke aligns well with broader dementia risk reduction strategies, evidence specific to post-stroke interventions for dementia prevention is limited. Nevertheless, the GDG emphasized that stroke management remains essential and should continue to follow existing clinical guidelines, to support overall vascular health and recovery.

Remarks

- Stroke often leads to long-term cognitive impairment; also, experiencing a second stroke substantially increases the risk of developing dementia. Thus, stroke prevention is one of the most effective public health strategies for reducing the risk of cognitive decline and dementia, particularly given the overlap in vascular and neurodegenerative pathways. Effective control of stroke risk factors – including hypertension, diabetes, air pollution, atrial fibrillation and smoking – is crucial for long-term cognitive health.

- The evidence reviewed for these guidelines focused on pharmacological interventions for preventing recurrent (secondary) stroke; non-pharmacological interventions (e.g. post-stroke cognitive rehabilitation) were not included.
- Timely and evidence-based treatment and management of stroke – including acute care, secondary prevention and rehabilitation – are essential for supporting long-term cognitive outcomes. The core components of WHO guidance on stroke care – interventions such as rapid reperfusion therapies, optimal medical management (e.g. antithrombotic therapy, blood pressure and lipid control) – coupled with structured rehabilitation, contribute to improved functional and cognitive recovery.
- Treating other risk factors (e.g. obstructive sleep apnoea with continuous positive airway pressure [CPAP]) and engaging in physical activity (specifically, aerobic exercise) may further improve post-stroke cognition.

Research gaps

- There is a lack of RCTs evaluating post-stroke interventions designed to reduce the incidence of dementia. Few trials assess cognitive outcomes as primary endpoints, and dementia incidence is often unreported or inconsistently defined.
- There is limited evidence on the impact of multidisciplinary post-stroke rehabilitation programmes including those incorporating cognitive training and psychosocial support on long-term cognitive function and the incidence of dementia.
- The effect of commonly used stroke prevention interventions (e.g. antiplatelet agents, lipid-lowering medications and carotid procedures) on cognitive trajectories remains unclear.
- Research is scarce on long-term cognitive outcomes following different types of stroke (ischaemic versus haemorrhagic) and among subpopulations such as younger age groups.
- The role of imaging markers in predicting dementia risk after stroke requires further investigation.
- Future studies should explore differential effects by sex, age, genetic predisposition (e.g. APOE status) and life-course factors, to inform personalized approaches.
- Most of the available research originates from high-income countries, limiting the global applicability of the findings. More studies are needed in LMIC to ensure equitable and context-appropriate recommendations.

Implementation considerations

- Stroke prevention strategies should be integrated within existing WHO frameworks on NCDs such as the *Global action plan for the prevention and control of noncommunicable diseases 2013–2030 (112)*[1] (including *Appendix 3* of that document) and the *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (182)*, to simultaneously address vascular, brain and cognitive health.
- It is critical to strengthen primary care systems to deliver integrated risk assessments and management for stroke and dementia, especially in LMIC where the burden of stroke is rising but diagnostic and treatment infrastructure may be limited.
- Public health education campaigns should emphasize stroke as both a cause of physical disability and a risk factor for dementia, encouraging preventive health behaviours earlier in life.
- Post-stroke care pathways should be expanded to include cognitive assessments and personalized rehabilitation plans.
- Workforce training in stroke units should incorporate the recognition and management of cognitive impairment and dementia, ensuring continuity of care, early intervention and longer term monitoring.
- Digital health tools and tele-rehabilitation may offer scalable solutions for delivering cognitive follow-up in people with stroke, particularly in rural or underserved settings. Similarly, WHO's iSupport programme can equip those caring for people post stroke who are experiencing cognitive difficulties *(186)*.

It is critical to strengthen primary care systems to deliver integrated risk assessments and management for stroke and dementia, especially in LMIC where the burden of stroke is rising but diagnostic and treatment infrastructure may be limited.

[1] Note, the action plan initially covered the period 2013–2020, but has now been extended to 2030.

3.2.9 Management of TBI

Generic WHO guidance on TBI

Measures to prevent head injuries and traumatic brain injury should be consistently implemented and enforced across all populations. Prevention and management strategies should align with existing WHO guidance:

Clinical practice:

- *Package of interventions for rehabilitation: module 3: neurological conditions (34)*

Service delivery and care pathways:

- *Helmets: a road safety manual for decision-makers and practitioners (187)*
- The global concussion awareness campaign from WHO and the Fédération Internationale de Football Association (FIFA) *(188)*

Public health and policy:

- *Global plan for the decade of action for road safety 2021–2030 (189)*
- *Respect women: preventing violence against women (190)*

PICO: *Are pharmacological and/or non-pharmacological interventions[1] more effective than no intervention or treatment as usual in reducing the risk of cognitive decline and/or dementia after traumatic brain injury?*

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend specific interventions after traumatic brain injury.

[1] Including interventions immediately following TBI to reduce adverse consequences, and interventions to manage longer term post-TBI symptomatology, designed to mitigate adverse consequences and prevent further deterioration.

Justification

- In 2021, there were about 38 million people living with the lasting effects of a TBI, with an annual incidence of about 21 million *(191)*.
- Meta-analyses of large cohort studies, including sibling-controlled designs, consistently show that TBI increases dementia risk *(192–194)*. Higher risk groups include younger adults, men and former players of contact sports *(144)*. In theory, if TBI was reduced to zero at the population level, it is estimated that 3% of dementia cases could be prevented *(2)*.

Although TBI is associated with an increased risk of dementia, current evidence is insufficient to recommend specific interventions after TBI for reducing the risk of cognitive decline or dementia.

- For this guideline update, evidence was extracted and assessed using GRADE from eight primary studies *(145,146)* that addressed pharmacological and non-pharmacological treatments post-TBI:
  - The use of angiotensin-converting enzyme (ACE) inhibitors, either alone or in combination with statins or metformin, may reduce the risk of dementia following TBI (with effects ranging from RR 0.21 to 0.63), but the certainty of evidence is very low *(195)*.
  - Statins may be associated with a reduced risk of dementia following TBI (with effects ranging from RR 0.63 to 1.32); however, the certainty of this evidence is very low *(195,196)*.
  - Sertraline, primarily prescribed to improve mood and reduce depression or anxiety symptoms after TBI, may have little to no effect on cognitive function in adults with moderate to severe TBI (with effects ranging from SMD −0.03 to 0.17), based on one small RCT *(147)*. The certainty of this evidence was rated as very low.
  - Group-based memory rehabilitation *(147)*, mindfulness training *(197)*, physical exercise *(197)*, computerized cognitive training *(198)* and Tai Chi *(198)* may result in no to small improvements in specific cognitive domains (with effects ranging from SMD −0.01 to 0.43); however, the certainty of evidence overall was rated as very low and effects were often not statistically significant.

The GDG concluded that although TBI is associated with an increased risk of dementia, current evidence is insufficient to recommend specific interventions after TBI for reducing the risk of cognitive decline or dementia. Across all intervention types, effects were small or inconsistent, and the certainty of evidence was very low. The GDG emphasized the need for high-quality long-term studies. The GDG further noted that primary prevention of head injuries and TBI through public health measures should be implemented for all individuals. Preventing TBI is critical to reducing its associated long-term health consequences, including increased dementia risk.

Remarks

- TBI typically results from external forces causing altered brain functions, such as reduced consciousness, memory loss, confusion or neurological deficits. TBI is recognized as both an acute condition and a chronic disease with long-term consequences.
- Common causes of TBI include road traffic accidents, falls, violence and crime, sports injuries and childhood injuries *(151)*.
- Concussion is a form of mild TBI characterized by a temporary loss or diminution of consciousness resulting from direct or indirect force to the head, causing rapid back-and-forth movement that shakes the brain within the skull. It involves temporary impairment of brain function and may include amnesia.

- There is also growing interest in the potential long-term neuropathological consequences of repetitive head impacts, including concussion and subconcussive trauma. In this context, chronic traumatic encephalopathy (CTE) has been described as a neuropathological condition associated with repeated head-impact exposure and linked to cognitive and neuropsychiatric manifestations. At the same time, substantial uncertainties remain regarding its underlying mechanisms, clinical correlates, diagnosis in vivo, and relationship with later cognitive decline and dementia. This area therefore warrants continued monitoring and further research in the context of brain health and dementia prevention.

- TBI disproportionately affects vulnerable populations, including those in LMIC, conflict zones and survivors of gender-based violence.

- Interventions for TBI include primary prevention through policies and legislation (e.g. promoting helmet use, seatbelts, road safety and violence prevention); and secondary and tertiary prevention, which focus on immediate post-injury care to reduce adverse outcomes, and long-term management of symptoms to prevent further deterioration. For instance, pharmacological management may aim to improve cerebral perfusion, reduce inflammation and provide endothelial-mediated neuroprotection.

- Prevention and management strategies should align with existing WHO frameworks and tools *(34,187–190)*.

Research gaps

- Of the studies that were assessed using GRADE, only two reported on dementia and none addressed MCI.

- The biological and psychosocial pathways linking TBI to cognitive decline and dementia remain poorly understood. Questions persist regarding the role of TBI frequency, severity and potential mediating factors (e.g. health, lifestyle and socioeconomic status).

- Few studies explored differences in outcomes based on TBI severity, chronicity or age at injury, despite wide variation in study populations.

- Differences in study design, populations, interventions and outcomes make cross-study comparisons difficult. Additionally, the range of interventions (from pharmacological agents to psychosocial and rehabilitative programmes) complicates synthesis and comparison of evidence.

- Most studies had follow-ups of less than 12 months, which is insufficient to assess long-term cognitive outcomes or dementia risk. Similarly, many RCTs, especially those evaluating psychosocial interventions, lacked adverse event reporting or safety monitoring. Larger, longer term trials with robust safety assessments are needed.

- Several drug classes (see **Web Annex K**) were underrepresented, restricting conclusions about relative efficacy.

- Despite the high burden of TBI from road traffic accidents in LMIC, particularly in South Asia, there is a notable lack of research from these settings. Most of the existing evidence comes from high income countries, limiting the global applicability of the findings; more research in LMIC is needed to ensure equitable and globally relevant recommendations.
- Women are significantly underrepresented in study populations, despite being at higher risk in certain contexts (e.g. intimate partner violence).
- To ensure equitable and globally relevant recommendations, future studies should explore differential effects by sex, age, genetic predisposition (e.g. APOE status) and life-course.

Implementation considerations

- Pharmacological interventions for the treatment and management of TBI are generally considered to be low cost and feasible, whereas non-pharmacological interventions (e.g. cognitive rehabilitation) tend to be more resource-intensive and less accessible, particularly in low-resource settings.
- Surgical interventions are considered high cost and not feasible for widespread use in dementia prevention.
- Ensuring equitable delivery of interventions is essential to reduce health disparities. This includes tailoring services to meet the needs of underserved communities and integrating TBI care into primary health systems, where specialist services may be limited.
- Interventions should be adapted to local health system capabilities, particularly in low-resource settings, where infrastructure and workforce limitations may constrain service delivery.

Preventing TBI at the population level is critical to reducing its incidence and long-term consequences.

- Preventing TBI at the population level is critical to reducing its incidence and long-term consequences. Effective strategies include:
  - **concussion prevention** in sports, through education, protective equipment and adherence to return-to-play protocols;
  - **fall prevention** in older adults, via home safety assessments, strength and balance training, and medication reviews;
  - **road traffic accident reduction**, through enforcement of traffic laws, helmet use, seatbelt campaigns and infrastructure improvements; and
  - **gender-based violence prevention**, by strengthening legal protections, community awareness and support services for survivors.
- To be effective and sustainable, these strategies require multisectoral collaboration across health, education, transport, justice and social protection sectors.

3.2.10 Management of vision impairment

Generic WHO guidance on vision impairment

Screening of suspected vision impairment should be offered to all adults, and management should be offered to those diagnosed with vision impairment, in line with WHO guidance.

Clinical practice:

- *Package of eye care interventions (199)*

Service delivery and care pathways:

- *Vision and eye screening implementation handbook (200)*
- *Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed (22)*

Public health and policy:

- *World report on vision (201)*
- *Eye care in health systems: guide for action (202)*

PICO: *For adults with normal cognition or MCI and vision impairment, is treatment of vision impairment more effective than usual care or no intervention in reducing the risk of cognitive decline and/or dementia?*

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend vision impairment interventions.

Justification

- Vision impairment (including near or distant vision impairment) affects more than 2.2 billion people globally *(155)* with higher prevalence in individuals aged 50 years and older *(203)*.
- Vision impairment is linked to cognitive decline and dementia *(204)*, accounting for about 2% of dementia cases globally *(2)*. Proposed mechanisms include neurodegeneration, reduced sensory input, social isolation and the increased cognitive load required for compensating sensory deficits *(205)*.
- For this guideline update, evidence was extracted and assessed using GRADE from two systematic reviews *(206,207)* pertaining to treatment of vision impairment (specifically, cataract surgery) in adults with normal cognition. Although the systematic reviews reported mostly small positive effects of cataract surgery on dementia risk reduction (HR 0.81) *(206)* and cognitive function in adults with normal cognition (SMD 0.14) *(207)*, the certainty of evidence was very low.

The GDG concluded that although there is a biological and epidemiological rationale for treating vision impairment to potentially reduce dementia risk, the current evidence is insufficient to make a recommendation for or against interventions to treat vision impairment for this purpose. The available evidence is limited to observational studies in adults with normal cognition and is restricted to cataract surgery, with very low certainty. No evidence was identified for individuals with mild cognitive impairment or for other types of vision treatments. The GDG noted the potential public health relevance of vision interventions and emphasized the need for high-quality research to further explore this relationship.

Remarks

- Common causes of vision impairment in older adults include cataracts, diabetic retinopathy, age-related macular degeneration and glaucoma, which together account for a substantial proportion of avoidable vision loss globally.
- In some low- and middle-income settings, avoidable vision loss is linked to infectious eye diseases, with trachoma alone affecting about 1.9 million people and disproportionately affecting poorer and rural communities *(208)*.
- There are effective interventions for over 90% of avoidable vision loss, including cataract surgery, refractive correction and glaucoma treatment. These interventions improve visual function, independence, social participation and quality of life, all of which are relevant to dementia prevention *(22,150,157)*.

Even mild vision impairment can affect everyday functioning, physical well-being, mental health and participation in daily life.

- Even mild vision impairment can affect everyday functioning, physical well-being, mental health and participation in daily life. Although evidence linking treatment of vision impairment to dementia outcomes is lacking (except for cataracts), addressing avoidable vision impairment is essential for maintaining functional ability, participation and well-being *(201)*.
- Various WHO guidelines and technical documents are available to guide the identification, treatment and management of vision impairment *(22,199–202)*.

Research gaps

- There is a lack of high-quality RCTs evaluating whether treatment of vision impairment improves cognitive outcomes or reduces the incidence of dementia.
- No evidence is currently available for adults with MCI or for causes of vision impairment other than cataracts.
- Key outcomes (e.g. quality of life, functional status and adverse events) were not reported in the available evidence syntheses, limiting the ability to fully assess benefits and harms.

- Research from LMIC is scarce, despite the high prevalence of untreated vision impairment and the more limited access to corrective interventions in these settings.
- To ensure globally relevant and equitable recommendations, future studies should assess differential effects by sex, age and genetic factors (e.g. APOE status).
- Although the current evidence base remains limited, emerging data suggest that vision impairment may be an important modifiable risk factor for dementia at the population level. Further research is needed to clarify the causal impact of specific interventions on dementia risk and to guide evidence-based recommendations.

Implementation considerations

- Treatment options such as cataract surgery and corrective lenses are widely available and could offer cognitive benefits through improved sensory input and associated psychosocial engagement. However, despite being modifiable, vision impairment remains underdiagnosed and undertreated globally, particularly in LMIC, where the burden is highest *(209)*.

Health education interventions, screening for vision impairment and referral for treatment should be integrated into routine care for older adults as part of broader ageing and dementia risk reduction strategies.

- Health education interventions, screening for vision impairment and referral for treatment should be integrated into routine care for older adults as part of broader ageing and dementia risk reduction strategies *(22)*. Context must be considered when selecting screening tools, to ensure cultural appropriateness and relevance.
- Any vision-related intervention implemented for dementia risk reduction should also account for coexisting conditions and the potential need for rehabilitation support.
- Public awareness and training of health workers are critical to ensure early detection and management of vision impairment.

3.2.11 Management of sleep

General clinical remark on sleep

Sleep is important for overall health and well-being. Maintaining good sleep – including getting enough hours of sleep, enjoying uninterrupted sleep, and achieving deep, restorative sleep – is advised throughout life.

PICO: *For adults with normal cognition or MCI with sleep–wake disorders, is treatment of sleep–wake disorders more effective than no intervention in reducing the risk of cognitive decline and/or dementia?*

PICO: *For adults with normal cognition or MCI, is improving aspects of sleep[1] (e.g. quality, duration, continuity and depth) more effective than no intervention in reducing the risk of cognitive decline and/or dementia?*

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend interventions to treat sleep–wake disorders.

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend interventions to improve sleep[1] (quality or duration).

[1] Certain aspects of sleep contribute to sleep quality; for example, adequate sleep duration to ensure alertness the following day, continuity through uninterrupted sleep and deep sleep that provides restorative benefits.

Justification

- Sleep problems (including poor sleep quality or duration, adverse sleep patterns and sleep–wake disorders) are highly prevalent among older adults globally, with high rates of obstructive sleep apnoea (46%), poor sleep quality (40%), insomnia (29%) and excessive daytime sleepiness (19%) in adults aged 60 years and older found across 36 countries *(210,211)*.

Certain sleep characteristics as well as specific sleep–wake disorders have been found to increase the risk of cognitive decline and dementia.

- Sleep problems have emerged as a potentially modifiable risk factor for dementia, with certain sleep characteristics as well as specific sleep–wake disorders found to increase the risk of cognitive decline and dementia. Specifically, meta-analytic evidence links insomnia (disorder), short and long sleep duration, poor sleep quality, excessive daytime sleepiness and sleep-disordered breathing – including obstructive sleep apnoea (OSA) – to all-cause dementia and Alzheimer disease *(212,213)*.

- For this guideline update, evidence was extracted and assessed using GRADE from five systematic reviews *(214-218)*, covering five types of intervention: CPAP for OSA, behavioural and medical interventions for sleep dysfunction, pharmacological and non-pharmacological treatments for insomnia, mindfulness-based interventions and acoustic stimulation during sleep:

  - The most robust evidence relates to treatment for insomnia, particularly pharmacological approaches, which may lead to small improvements in cognitive function, with effects ranging from SMD 0.05 to 0.72 *(216)*. However, these effects are limited to cognitive test scores at a maximum follow-up of 6 months and do not extend to dementia or MCI outcomes.

  - Other interventions (e.g. CPAP to treat OSA) may improve executive function in adults with normal cognition with OSA *(214)*, with effects ranging from SMD 0.09 to 0.93, whereas behavioural interventions had no effect on short-term memory *(215)*.

  - No systematic reviews were identified that assessed the impact of sleep interventions on dementia or MCI incidence.

  - Overall, the certainty of evidence across all interventions is low to very low and the observed effects at relatively short follow-up are either inconsistent or trivial in size.

The GDG concluded that although sleep disturbances are consistently associated with cognitive decline, current evidence is insufficient to recommend interventions aimed at treating certain sleep–wake disorders or improving sleep quality or duration for the purpose of reducing the risk of cognitive decline or dementia. Most studies focused on cognitive outcomes at follow-up (ranging from 3 to 128 weeks) rather than dementia or MCI incidence. Although some interventions, particularly for insomnia, showed small cognitive benefits, the certainty of evidence was low to very low. In balancing the type and quality of evidence, the GDG emphasized the need for longer term studies and more practical ways to measure early changes in brain health. Therefore, it was determined that the current body of evidence is insufficient to support a recommendation for interventions aimed at improving sleep specifically for the purpose of reducing dementia risk.

Remarks

- Sleep can be characterized by aspects that contribute to good sleep quality, such as adequate sleep duration to ensure alertness the following day, continuity through uninterrupted sleep and deep sleep that provides restorative benefits. Differences in how individuals respond to, and require, sleep suggest that a universal threshold may not be appropriate, and sleep-related recommendations should be tailored to individual needs.
- Sleep–wake disorders involve various disruptions in sleep patterns, such as difficulty falling or staying asleep (insomnia), excessive daytime sleepiness (hypersomnolence), breathing problems during sleep (sleep-related breathing disorders), irregular sleep schedules (circadian rhythm disorders), abnormal movements during sleep (sleep-related movement disorders), or unusual behaviours and physiological events occurring while falling asleep, during sleep or upon waking (parasomnias) *(64)*.
- Sleep health interacts with other risk factors (e.g. physical inactivity, depression and chronic conditions), warranting integrated prevention approaches.
- Sleep problems may also emerge as early or prodromal symptoms of underlying neurodegenerative processes. Recognizing that some sleep–wake changes may reflect emerging neurodegenerative processes rather than independent risk factors underscores the importance of careful clinical assessment and interpretation.

Research gaps

- Despite observed associations between sleep–wake disorders and dementia risk, there is a lack of large, well-designed RCTs testing whether sleep interventions can reduce dementia incidence. Evidence on causality remains limited, underscoring the need for rigorous intervention studies.
- Existing systematic reviews on improving sleep or treating sleep disorders primarily report cognitive outcomes rather than incident dementia or MCI. Studies directly assessing these endpoints are needed to clarify long-term effects.
- Many available studies include small samples and short follow-up periods, limiting the ability to detect meaningful or sustained changes. Given the slow progression of dementia, longer term follow-up is essential to assess potential protective effects of sleep interventions.
- Since sleep–wake disorders may represent early manifestations of underlying cognitive decline rather than independent risk factors, there is a need for longitudinal studies with extended observation periods to clarify temporal and causal relationships.
- Most GRADE-assessed evidence focuses on narrow or highly specific interventions (e.g. mindfulness-based approaches), which limits generalizability. Broader behavioural, lifestyle and multimodal interventions should be evaluated in diverse populations.

- There is no consensus on optimal sleep duration or sleep quality thresholds for reducing the risk of dementia. Future studies should incorporate objective measurements – including actigraphy and wearable technologies – to strengthen exposure assessment and inform evidence-based recommendations.

Implementation considerations

- Public education campaigns can raise awareness of healthy sleep as a pillar of brain health and encourage early recognition of sleep disturbances.
- Primary care providers should be supported with screening tools to identify individuals at risk and refer them for further sleep assessment and treatment. Context must be considered when selecting screening tools, to ensure cultural appropriateness and relevance.
- Wearable devices to assess sleep health and sleep disorders can be used to assess the relationship between sleep, sleep disorders and cognitive function. Mobile and digital health tools (e.g. apps, short message service [SMS] reminders and online cognitive behavioural therapy [CBT] interventions) can expand access to evidence-based sleep interventions, especially in underserved areas.
- Low-cost strategies such as providing sleep education, improving bedroom environments (reducing noise or light exposure and managing night time heat) and training community health workers to provide advice can be feasible interim solutions for LMIC.
- Implementation strategies should ensure cultural appropriateness, address stigma associated with sleep complaints and integrate with broader dementia prevention frameworks.
- Given that some sleep–wake disturbances may represent early signs of cognitive decline, implementation strategies should ensure clear referral pathways between sleep services and cognitive assessment services (e.g. memory clinics), enabling timely and accurate differentiation between primary sleep–wake disorders and early cognitive changes.

Some sleep–wake disturbances may represent early signs of cognitive decline. Implementation strategies should ensure clear referral pathways between sleep services and cognitive assessment services (e.g. memory clinics).

3.2.12 Management of HIV

Generic WHO guidance on HIV

Antiretroviral therapy should be initiated for all people living with HIV, regardless of WHO clinical stage and CD4 cell count, to achieve and maintain viral suppression; the goal is to reach undetectable levels of HIV. Clinical management of HIV should be in line with WHO guidance.

Clinical practice:

- *WHO updated recommendations on HIV clinical management: recommendations for a public health approach (219)*
- *WHO guidelines on the management of advanced HIV disease (220)*

Service delivery and care pathways:

- *Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach (221)*
- *Consolidated guidelines on differentiated HIV testing services (222)*

Public health and policy:

- *The role of HIV viral suppression in improving individual health and reducing transmission (223)*

PICO: *For adults living with HIV on antiretroviral therapy (ART), are interventions aimed at reducing the risk of cognitive decline and/or dementia or interventions impacting cognition more effective than no intervention?*

INSUFFICIENT EVIDENCE FOR RECOMMENDATION

For the specific purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend one anti-retroviral therapy (ART) combination over another; therefore, ART regimens should be used according to disease control needs and patient preferences.

Justification

- Globally, almost 41 million people live with HIV, with two thirds residing in LMIC (e.g. those in the WHO African Region) and a growing proportion aged 50 years and older *(224)*.
- The introduction and widespread use of combination antiretroviral therapy (ART) have transformed the prognosis of people living with HIV, both improving survival and significantly reducing the incidence of severe neurological complications (including drastically reducing the incidence of HIV-associated dementia). However, cognitive impairment in people living with HIV, including asymptomatic cases, remains common, with an estimated prevalence of 39.6% *(225)*.

- Evidence was extracted and assessed using GRADE from five primary studies *(226–230)* evaluating modifications to ART regimens in adults living with HIV. These were largely limited to ART combinations that are not widely used in clinical practice; for example, protease inhibitor monotherapy, ART simplification, maraviroc intensification, ART intensification (dolutegravir + maraviroc or dolutegravir + placebo) and continuous versus discontinued efavirenz. Notably, no evidence was identified for non-pharmacological interventions or for pharmacological interventions other than ART.

Among the evidence assessed using GRADE studies, maraviroc intensification was the only intervention showing a potentially positive effect on cognitive function in adults living with HIV (effect size: d = 0.55). However, the certainty of this evidence was very low, and maraviroc is not currently recommended in WHO's HIV treatment guidelines owing to its high cost and limited availability *(219, 221)*.

Based on this situation, the GDG concluded that, for the purpose of reducing the risk of cognitive decline and/or dementia, there is currently insufficient evidence to recommend any specific ART combination over another for people living with HIV; the GDG also concluded that there is insufficient evidence (i.e. none identified that meet the criteria) to recommend any other pharmacological or non-pharmacological interventions. GDG members emphasized that effective HIV management requires timely initiation of ART, noting that WHO recommends offering rapid ART initiation to all people living with HIV following confirmed diagnosis and clinical assessment *(221)*. **The GDG further affirmed that, consistent with WHO guidelines, ART should be offered on the same day to people who are ready to start treatment** *(221)*, **and that people living with HIV should be supported to achieve and maintain viral suppression through effective ART, with the goal of reaching undetectable levels of the virus** *(223)*.

Remarks

- It is essential that all people living with HIV receive ART, and that treatment regimens are optimized in line with current WHO recommendations *(219,221)*. Prompt effective ART treatment prevents immune decline (i.e. a low CD4 cell count); such decline strongly correlates with increased morbidity and mortality *(220)*. ART remains the priority for all people living with HIV and it contributes broadly to overall well-being.

- ART is the foundation for safeguarding brain health and reducing dementia risk among people living with HIV. Although ART substantially reduces the risk of HIV-associated dementia, it does not fully prevent milder forms of cognitive impairment. Additional interventions may therefore be required to support cognitive health in this population.

- A key benefit of ART is the suppression of HIV replication within the central nervous system (CNS), which reduces the neuroinflammatory consequences of uncontrolled infection. Evidence suggests that persistent milder cognitive impairment is largely attributable to residual or "legacy" neuronal damage. Ongoing low grade inflammation may further contribute to cognitive decline in some individuals, although the clinical relevance of this process is unclear.

A key benefit of ART is the suppression of HIV replication within the central nervous system (CNS), which reduces the neuroinflammatory consequences of uncontrolled infection.

- Evidence on whether modifying ART regimens improves cognitive outcomes is limited and of low certainty. There is insufficient evidence for any optimal or preferred regimen that specifically affects cognitive outcomes.
- Certain ART medicines (e.g. efavirenz) have been associated with neurotoxic effects that are dose dependent. WHO recommends the 400 mg dose of efavirenz, which has a more favourable side-effect profile, provided there is no pretreatment resistance to non-nucleoside reverse transcriptase inhibitors. The latest guidance on preferred ART regimens can be found in the WHO updated recommendations on HIV clinical management: recommendations for a public health approach *(219).*
- Although pharmacological and non-pharmacological interventions to reduce cognitive decline or dementia risk have been insufficiently studied in people living with HIV, these individuals may still benefit from the generic interventions recommended in these guidelines, regardless of HIV status.
- HIV treatment should follow existing WHO guidance *(219,21).*

Research gaps

- No studies reported outcomes of dementia or MCI incidence among people living with HIV; available evidence focused exclusively on cognitive function outcomes.
- Evidence on other critical outcomes (e.g. quality of life and daily functioning) remains scarce. Only two studies reported functional outcomes, and no studies assessed quality of life or long-term dementia risk.
- No eligible studies on non-pharmacological interventions were identified, leaving a major evidence gap for this population.
- There is a need to evaluate the effectiveness of additional interventions, beyond ART, for improving or preserving cognitive function and reducing dementia risk in people living with HIV.
- Most available studies focused on pharmacological adjustments of ART regimens in high-income countries, limiting the generalizability of the findings for LMIC settings.
- Evidence from studies with follow-up beyond 12 months post-intervention is scarce.
- Meta-analysis and comparability are limited owing to heterogeneity in interventions, small sample sizes and lack of standardized outcome reporting.
- Subgroup analyses of the evidence included in the GRADE assessment (e.g. by age, sex, socioeconomic status, race or comorbid conditions) were not feasible owing to a lack of disaggregated data.

- Advanced HIV disease may result in worse cognitive outcomes; this is an area that requires more research.
- Mechanistic studies exploring neuroinflammation, blood–brain barrier permeability and CNS viral reservoirs in the context of cognitive decline in HIV are needed to guide future pharmacological and non-pharmacological approaches.

Implementation considerations

- Supporting people living with HIV to have viral suppression should be a priority *(223)* and individuals with low CD4 should receive a package of interventions that includes screening, managing and preventing key opportunistic infections and the prompt initiation of ART; these individuals should also be provided with enhanced adherence support, as per WHO guidelines *(220)*.
- Care models should include younger adults with HIV; this population is at risk for cognitive impairment but often excluded from dementia services.
- Greater integration of HIV care and cognitive health services is needed, especially in LMIC, where access to neurological evaluation remains limited.
- Health systems should consider targeted screening for cognitive impairment and cognitive function monitoring as part of standard HIV follow-up, especially in at-risk populations (e.g. older adults, individuals with other comorbidities that increase their dementia risk profile and those presenting with clinical symptoms), with culturally appropriate tools and staff training. When selecting screening tools, it is important to consider the context and ensure cultural appropriateness and relevance.
- Any ART intensification strategy for cognitive benefits must consider patient preferences, polypharmacy risks, potential side-effects and availability of specific ART medications.
- Implementation efforts must address stigma and provide clear communication about cognitive risks to individuals with HIV, fostering engagement with services without exacerbating discrimination.
- People living with HIV should also receive support to implement the broader recommendations on brain health and dementia risk reduction outlined in these guidelines. For example, management of health conditions as well as promoting interventions addressing health-related behaviours should be incorporated into routine HIV care where feasible.

People living with HIV should also receive support to implement the broader recommendations on brain health and dementia risk reduction outlined in these guidelines.

3.3 Interventions addressing environmental risk factors

3.3.1 Reduce exposure to air pollution

3.3.1 Reduce exposure to air pollution

Generic WHO guidance on air pollution

Air pollution is toxic and contributes substantially to the global burden of communicable and noncommunicable diseases, including dementia. Reducing exposure to air pollution, both indoors and outdoors, is critical to improving health and well-being for all people, across the entire life course, in line with guidance from WHO and other organizations:

Public health and policy:

- *WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide, sulfur dioxide and carbon monoxide (231)*
- *Integrated science assessment (ISA) for particulate matter (final report, Dec 2019) (232)*

PICO: *At population level, is a reduction of household air pollution more effective than no reduction of household air pollution in lowering the risk of cognitive decline and/or dementia,*

PICO: *At population level, is a reduction of ambient air pollution (i.e. $PM_{2.5}$, PM_{10}, CO, NO_2, NO_x) more effective than no reduction of ambient air pollution in lowering the risk of cognitive decline and/or dementia.*

NEW RECOMMENDATION

Reducing exposure to household air pollution may reduce the risk or incidence of cognitive decline and/or dementia.

Strength of recommendation: conditional

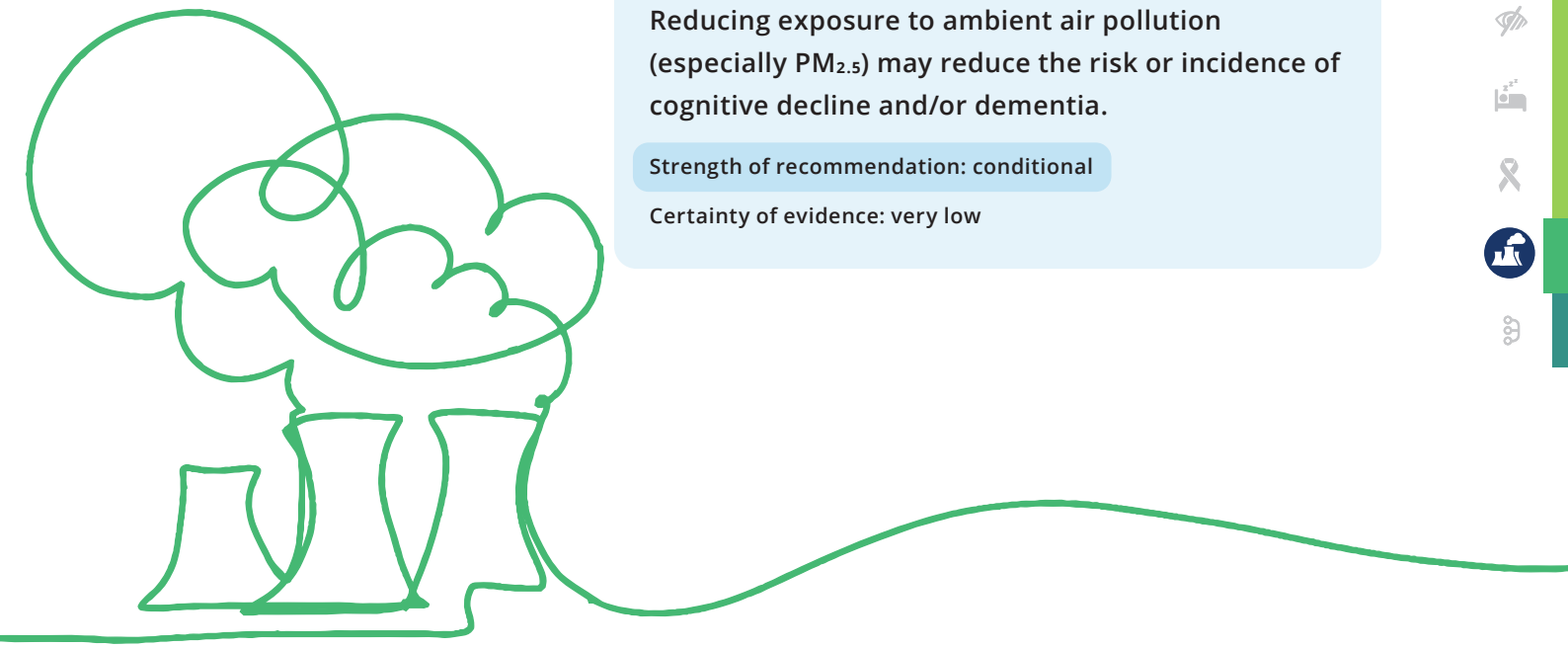
Certainty of evidence: very low

NEW RECOMMENDATION

Reducing exposure to ambient air pollution (especially $PM_{2.5}$) may reduce the risk or incidence of cognitive decline and/or dementia.

Strength of recommendation: conditional

Certainty of evidence: very low



Justification

- Air pollution – for example, particles with a diameter of 2.5 μm or less ($PM_{2.5}$), particles with a diameter of 10 μm or less (PM_{10}), nitrogen dioxide (NO_2), nitrogen oxides (NO_x), carbon monoxide (CO) and ozone (O_3) – in the ambient and household environments, is a global health risk, with both ambient and household air pollutants affecting 99% of the global population *(233)*. In theory, if air pollution was reduced to zero at the population level, it is estimated that about 3% of dementia cases could be prevented *(2)*.

$PM_{2.5}$ can cross the blood–brain barrier and may trigger neuroinflammation and oxidative stress, pathways that are implicated in neurodegeneration.

- The biological plausibility of the relationship between long-term exposure to air pollution (particularly $PM_{2.5}$) and cognitive decline and dementia is supported by research indicating that $PM_{2.5}$ can cross the blood–brain barrier and may trigger neuroinflammation and oxidative stress, pathways that are implicated in neurodegeneration *(140,141)*.

- Given its global prevalence, modifiability and substantial contribution to disease burden, air pollution represents an important target for interventions *(234)*, and for reducing cognitive decline and dementia risk.

- For this guideline update, evidence was extracted and assessed using GRADE from 14 systematic reviews, covering both ambient and household air pollution exposures *(235–248)*. Toxicological studies in animals were not considered. Due to ethical and practical constraints, RCTs to study the effects of air pollution interventions on dementia in humans are not feasible. As a result, the best evidence stems from observational studies, which the traditional GRADE approach classifies as low-certainty evidence, disadvantaging domains such as environmental risk factors.

- The strongest evidence pertains to $PM_{2.5}$ exposure, which is associated with increased risk of dementia *(237)* (HR 1.40), and small to moderate effects for decreased cognitive function (OR 1.35) *(244)*. The magnitude of effect varies and is uncertain owing to serious inconsistency and lack of intervention studies. Similarly, NOx exposure is associated with dementia incidence (HR 1.14) but the evidence is uncertain and had to be downgraded for reasons such as serious risk of bias and imprecision *(2,142,143)*. Overall, the GRADE interpretation for ambient air pollution is that a reduction of ambient air pollution, especially of $PM_{2.5}$ and NO_x, may have a beneficial effect on dementia incidence and cognitive function.

- Air pollution arising from the use of solid fuel (e.g. wood, coal, charcoal or dung cake) for cooking in the household is associated with an increased risk of MCI (HR 1.31) and decreased cognitive function (β=−0.73) *(235)*, while switching to clean fuels (e.g. electricity, gas) may yield cognitive benefits (β=−0.71) *(249)*; however, the evidence is of low certainty owing to the observational nature of studies. The GRADE interpretation was that household air pollution generated by using solid fuels for cooking may result in an increased risk of incident MCI, and may have a harmful effect on cognitive function, whereas a reduction in household air pollution achieved by switching to clean fuels from solid fuel use for cooking may have a beneficial effect for cognitive function.

The GDG concluded that – although causality has not been fully established owing to the observational nature of most studies – the coherence of findings across locations, study designs and populations strengthens the case for considering air pollution as a modifiable risk factor for dementia. The evidence is of low to very low certainty owing to the observational nature of the studies, but overall it has shown that reducing exposure to household and ambient air pollution may reduce the risk of cognitive decline and dementia. In balancing the type and quality of evidence, the GDG placed greater emphasis on the consistency of observational findings, the global prevalence and modifiability of air pollution, and the substantial contribution of air pollution to disease burden, and made conditional recommendations for reducing the exposure of household and ambient air pollution for the purpose of reducing dementia risk. The GDG highlighted the urgent need to systematically evaluate the effects on cognitive outcomes and dementia incidence of policy interventions designed to improve air quality (e.g. clean energy policies and traffic emission controls).

Remarks

- Toxicological evaluations provide robust biological evidence that exposure to key ambient air pollutants – particularly $PM_{2.5}$ and O_3 – induces oxidative stress, neuroinflammation, systemic inflammatory responses, vascular dysfunction and disruptions in cardiopulmonary physiology *(232,250).* These mechanistic pathways are consistent with epidemiological findings, and they support the plausibility that long-term exposure to classic air pollutants contributes to increased dementia risk.

- Although everyone can contribute to reducing air pollution, ensuring clean air is ultimately a societal responsibility rather than an individual one. Health workers play a crucial role in educating individuals about the health risks associated with air pollution.

- Interventions to reduce exposure (e.g. improved urban planning, traffic emission controls and clean energy policies) can have widespread impact *(231,251)*. However, owing to ethical and practical concerns, it is not feasible to control environmental exposures in studies, making it challenging to evaluate air pollution reduction interventions through RCTs and thus affecting the certainty of evidence available for decision-makers.

Air pollution disproportionately affects marginalized and low-income populations, who may also be at elevated risk for dementia.

- Air pollution reduction policies offer a win-win for public health and climate change mitigation (in both the short and long term).

- Air pollution disproportionately affects marginalized and low-income populations, who may also be at elevated risk for dementia. However, perceptions of the value of clean air vary globally, influenced by economic, cultural and environmental factors. This underscores the importance of equity considerations when implementing clean air policies and these dementia risk reduction guidelines.

- Risk reduction efforts should be aligned with national and international air quality standards (see **Table 2**), as provided in the *WHO global air quality guidelines (231).*

Table 2. WHO air quality guidelines recommended levels

Pollutant	Air quality guidelines recommended levels
$PM_{2.5}$	Annual mean: 5 µg/m³ 24-hour mean: 15 µg/m³
PM_{10}	Annual mean: 15 µg/m³ 24-hour mean: 45 µg/m³
Ozone (O_3)	Peak season mean: 60 µg/m³ 8-hour mean: 100 µg/m³
Nitrogen dioxide (NO_2)	Annual mean: 10 µg/m³ 24-hour mean: 25 µg/m³
Sulfur dioxide (SO2)	24-hour mean: 40 µg/m³
Carbon monoxide (CO)	24-hour mean: 4 µg/m³

$PM_{2.5}$: particles with a diameter of 2.5 µm or less; PM_{10}: particles with a diameter of 10 µm or less; WHO: World Health Organization.

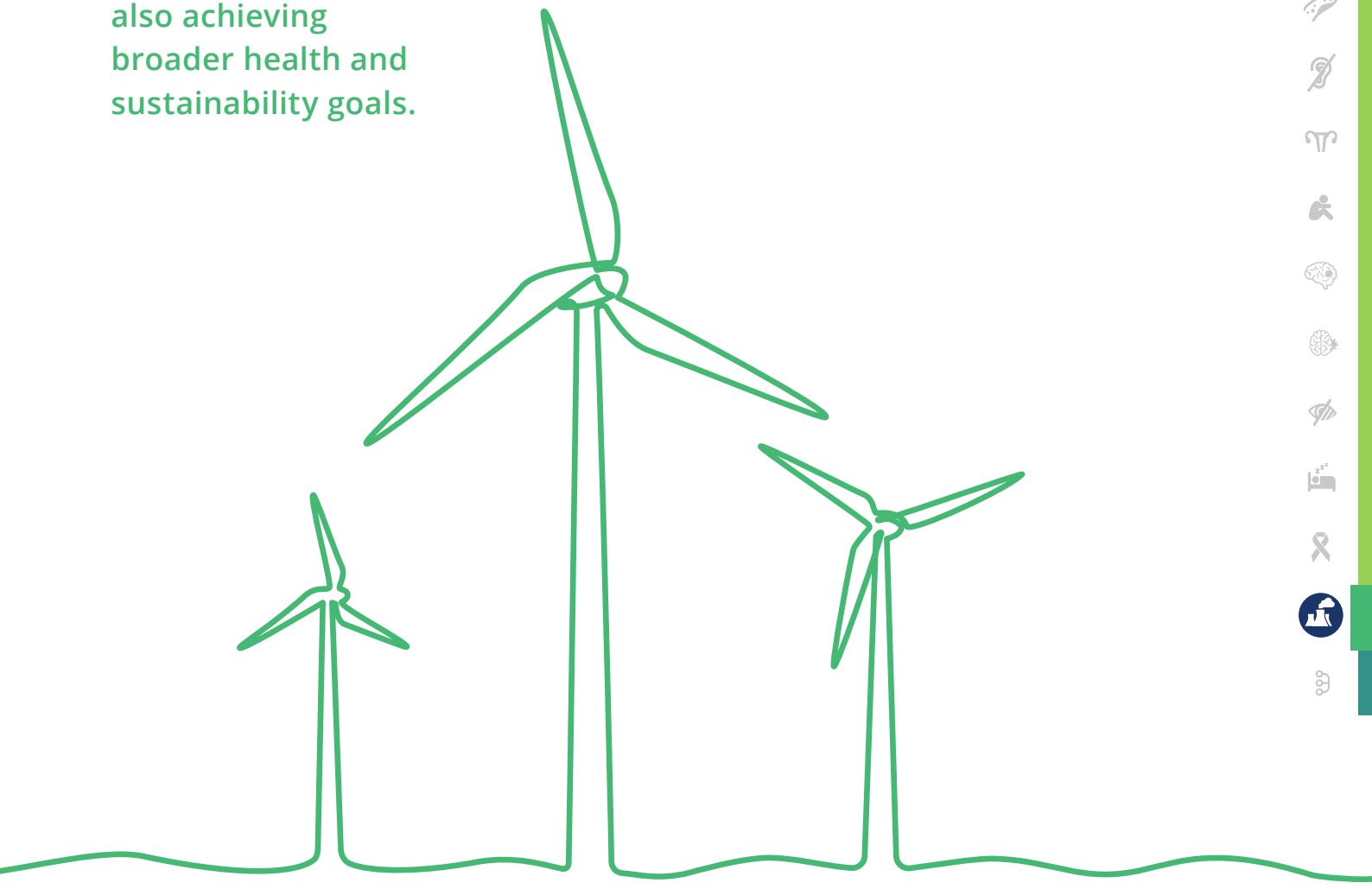
Research gaps

- Associations between air pollution and cognitive decline are well-established in humans; however, there is limited evidence on the extent to which reducing ambient or household air pollution – and to what levels or thresholds – leads to cognitive benefits. Additionally, there have been few studies on the effects of air pollution (both household and ambient) on cognitive outcomes, especially in populations with MCI.
- Most of the available research on humans is observational; intervention studies assessing the impact of air pollution reduction policies on cognitive outcomes in cognitively healthy populations is scarce. Similarly, longitudinal studies assessing cognitive function as a continuous outcome are scarce and inconsistently reported.
- Quasi-experimental and natural experiment designs evaluating changes in cognitive outcomes before and after the implementation of air quality regulations or household fuel transitions are needed, to strengthen causal inference and inform the assessment of policy impacts.
- Most of the available research is based on studies conducted in high-income countries, limiting its global applicability. More research is needed in LMIC to ensure equitable and globally relevant recommendations.
- To ensure that recommendations are equitable and globally relevant, future studies should explore differential effects by sex, age, genetic predisposition (e.g. APOE status) and life-course exposure to air pollution.
- Despite the limitations, the evidence base on the health and economic impacts of air pollution is a dynamic and evolving research area. WHO is making major contributions to this research; for example, through the *Estimating the morbidity from air pollution and its economic costs* (EMAPEC) project *(252)*, which is advancing methodologies to quantify morbidity impacts and estimate their economic costs.

Implementation considerations

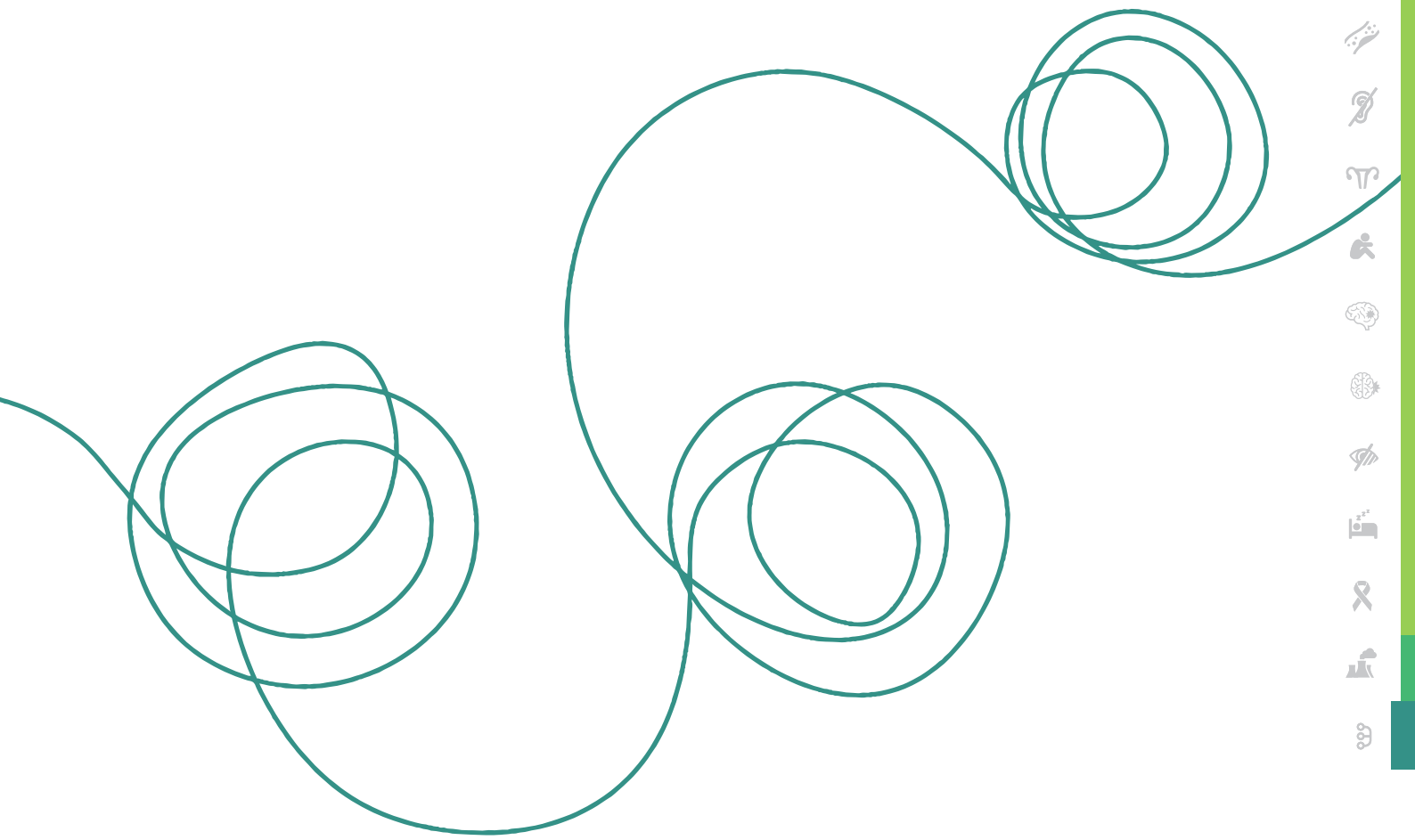
- Effective implementation requires multisectoral collaboration among various sectors: public health, environment, transport and energy. By addressing air pollution through integrated health and environmental policies, significant progress can be made in reducing dementia risk while also achieving broader health and sustainability goals.
- Public education campaigns may increase awareness of cognitive risks related to air pollution and support advocacy for cleaner environments.
- Policy-makers should consider targeted interventions in high-risk areas (e.g. urban centres and regions with industrial emissions) and for vulnerable groups (e.g. older adults and socioeconomically disadvantaged communities).
- Surveillance systems that monitor trends in both air quality and cognitive health may help in evaluating the impact of environmental interventions over time.

By addressing air pollution through integrated health and environmental policies, significant progress can be made in reducing dementia risk while also achieving broader health and sustainability goals.



3.4 Interventions targeting multiple risk factors

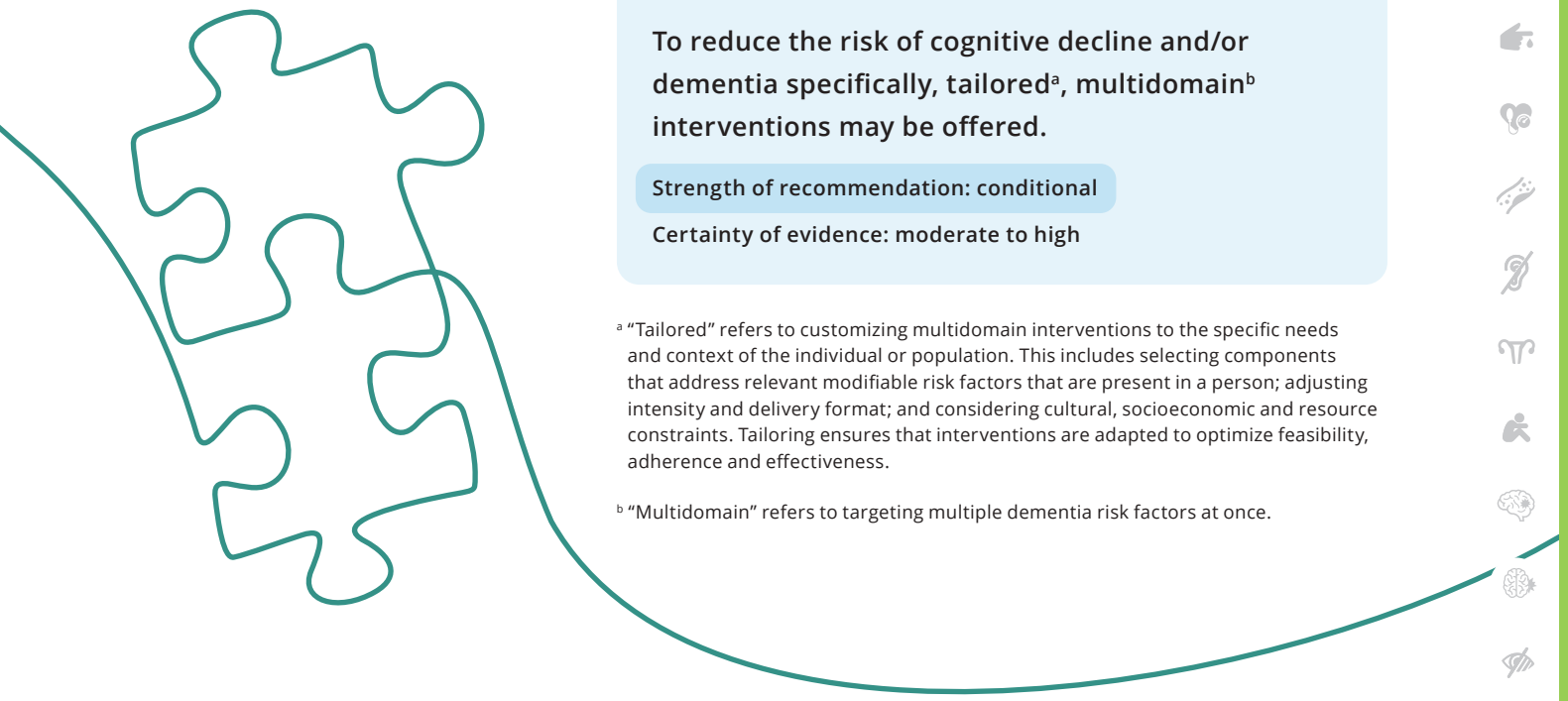
3.4.1 Multidomain interventions



3.4.1 Multidomain interventions

General clinical remark on multidomain interventions

Dementia risk factors should be addressed holistically, because multiple risks often coexist and accumulate over the life course.



PICO: *For adults with normal cognition or MCI, are multidomain interventions (addressing three or more risk factors) more effective than usual care, lower intensity interventions or no intervention in reducing the risk of cognitive decline and/or dementia?*

NEW RECOMMENDATION

To reduce the risk of cognitive decline and/or dementia specifically, tailored[a], multidomain[b] interventions may be offered.

Strength of recommendation: conditional

Certainty of evidence: moderate to high

[a] "Tailored" refers to customizing multidomain interventions to the specific needs and context of the individual or population. This includes selecting components that address relevant modifiable risk factors that are present in a person; adjusting intensity and delivery format; and considering cultural, socioeconomic and resource constraints. Tailoring ensures that interventions are adapted to optimize feasibility, adherence and effectiveness.

[b] "Multidomain" refers to targeting multiple dementia risk factors at once.

Justification

- Multiple risk factors contribute to dementia risk over the life course *(2)*.
- Multidomain interventions target several risk factors simultaneously, offering a tailored and holistic approach to dementia prevention and risk reduction. Multidomain interventions are believed to work through multiple mechanisms; for example, they may improve cardiovascular health, enhance cognitive reserve and reduce inflammation *(2)*.
- For this guideline update, evidence was extracted and assessed using GRADE from a de novo systematic review and meta-analysis of 44 RCTs published between 2012 and 2025 (**Web Annex P**). The multidomain interventions included physical activity, cognitive training and activity, depression management, healthy diet, metabolic and vascular risk monitoring, social activity and tobacco cessation. The extracted data

Dementia risk factors should be addressed holistically, because multiple risks often coexist and accumulate over the life course.

focused on two populations: cognitively healthy or at-risk adults (i.e. adults with normal cognition with or without increased risk of developing dementia/cognitive impairment), and individuals with MCI or prodromal Alzheimer disease:

- For cognitively healthy or at-risk adults, high-certainty evidence suggests that multidomain interventions addressing at least three risk factors (e.g. by combining physical activity, healthy diet and cognitive training) have little or no effect on incident dementia, and consistently positive but very small (i.e. trivial) effects on cognitive function (i.e. global cognition, memory, executive function, processing speed, attention and verbal fluency), with effect sizes ranging from SMD 0.01 to 0.08.

- For individuals with MCI or prodromal Alzheimer disease, evidence indicates that multidomain interventions may confer small to trivial benefits on different measures of cognitive function, including composite scores, with certainty levels ranging from very low to high, and effect sizes ranging from SMD 0.00 to 0.18:

    - small benefits for global cognition using composite scores (low certainty);

    - trivial benefits for memory, processing speed, attention and global cognition using screening tools (high certainty);

    - trivial benefits for executive function, and language or verbal fluency (moderate certainty), and visuospatial abilities (very low certainty); and

    - no effect on clinical dementia rating (CDR) sum of boxes (high certainty).

GDG members noted that – although the magnitude of benefit is very small and may be influenced by variability in intervention modalities and composition, intensity and adherence – overall, multidomain interventions appear to be safe and feasible, with multiple trials having been conducted and published from low-resource settings. The GDG concluded that, despite very small effect sizes, a conditional recommendation was justified owing to the consistent beneficial direction, high certainty of evidence for some outcomes and strong biological rationale. Multidomain interventions also align with broader NCD prevention strategies and may confer additional health benefits beyond cognition.

GDG members emphasized that addressing risk factors together rather than in isolation reflects good clinical and public health practice, because dementia risk factors frequently cluster and interact, amplifying overall risk. Integrated management maximizes efficiency, may improve adherence and leverages cumulative benefits across multiple outcomes, which is consistent with real-world strategies for reducing morbidity and mortality.

Remarks

- Multidomain interventions address three or more risk factors or domains aimed at reducing the risk of cognitive decline and/or dementia. They typically focus on promoting healthy behaviours such as physical activity, cognitive stimulation and dietary improvements; they may also include optimization of pharmacological management for cardiovascular and metabolic risk factors *(253).*
- Although reported effect sizes were very small, even modest improvements can translate to substantial health benefits when implemented at scale.
- People with MCI may benefit the most from multidomain interventions, and although the benefits are modest, they can slow cognitive decline and help individuals to preserve independence for longer.
- Evidence is emerging for structured interventions tailored to individual risk profiles, highlighting the importance of personalization in design and delivery.
- Multidomain interventions should be tailored by adapting components to an individual's risk profile, preferences and local context. This includes selecting the most relevant health-related behaviour targets such as physical activity, diet, cognitive training or management of health conditions (e.g. management of vascular risk) based on a person's health status and needs.
- Health care professionals should provide comprehensive advice and education on how to address multiple risk factors in an integrated manner, promoting holistic health and reducing overall risk beyond cognitive outcomes.

Research gaps

- Few studies have assessed the long-term clinical outcomes of multidomain risk reduction interventions: only two of 44 trials included incident dementia as an outcome, and none evaluated the incidence of MCI.
- Reported small effect sizes may reflect variability in target populations, intervention intensity and adherence. Further research is needed to determine optimal intervention parameters (e.g. duration and frequency) and to develop standardized approaches for measuring adherence.
- Risk scores and blood-based biomarkers are increasingly being explored as surrogate measures to assess the impact of multidomain interventions. Although these approaches show promise for early detection and monitoring, current evidence is limited. Robust, large-scale studies are required to confirm the validity and clinical utility of these approaches.
- Most of the available evidence is derived from studies conducted in high-income countries, limiting its global applicability. Additional research in LMIC is essential to ensure equitable and globally relevant recommendations.

- Future studies should also examine differential effects by sex, age and genetic predisposition (e.g. APOE status), to inform tailored interventions and reduce health inequities.

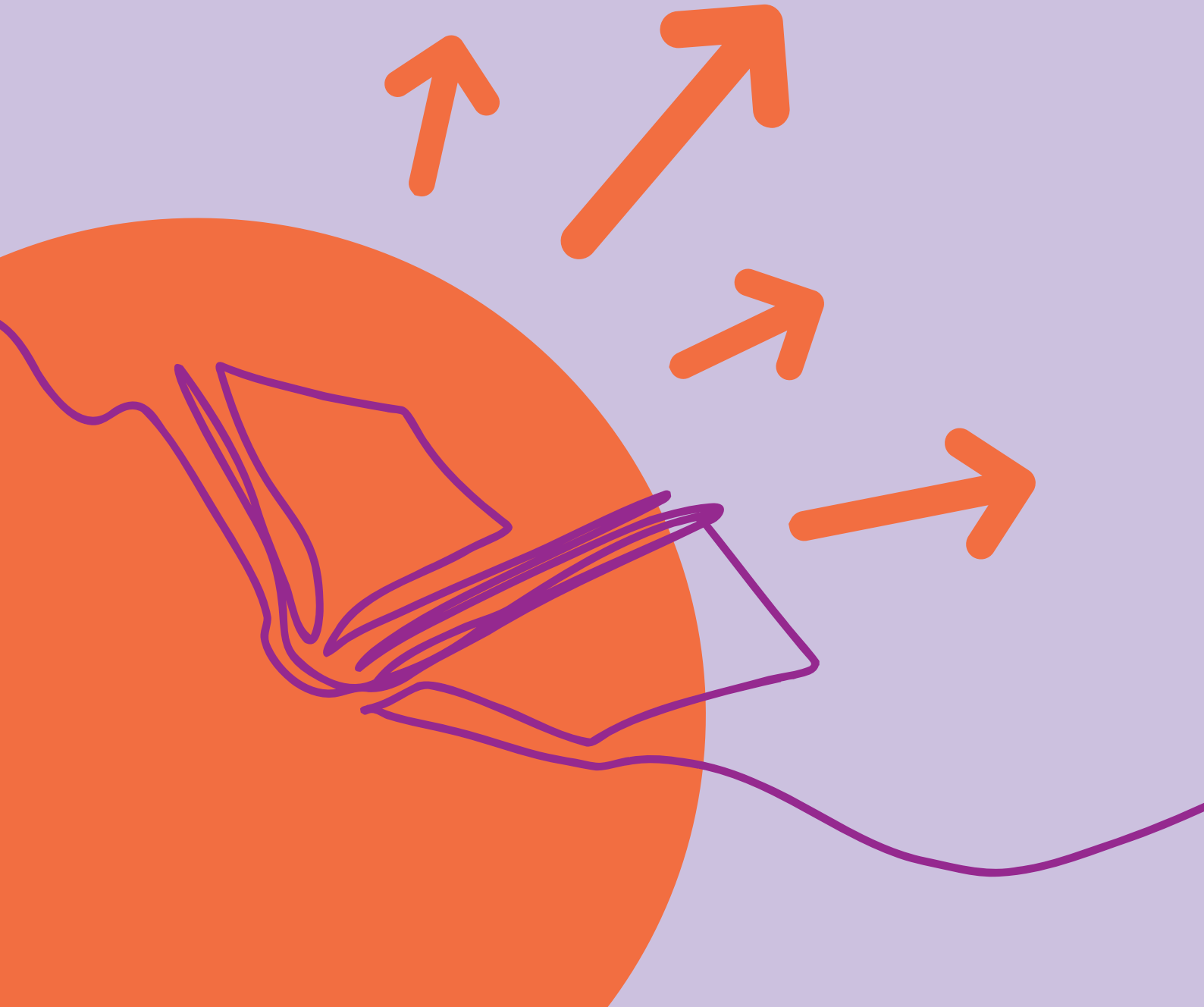
Implementation considerations

- Multidomain interventions can be adapted to different cultural and socioeconomic contexts, but they need to be tailored for feasibility and acceptability. This includes alignment with local context, risk profiles and cultural norms.
- Implementation should prioritize populations with modifiable risk factors and ensure equity in access, particularly in low-resource settings.
- Successful implementation requires adequate training of health care providers and community workers to deliver interventions effectively and consistently, including building capacity for behaviour change strategies to enhance adherence and long-term engagement. Community engagement is critical for sustainability.

Integration into existing health systems and ageing programmes is essential to ensure institutional support and scalability, given the overlap with NCD prevention strategies.

- Integration into existing health systems and ageing programmes is essential to ensure institutional support and scalability, given the overlap with NCD prevention strategies. Intersectoral partnerships across health, social care, education and community sectors are needed to address multiple risk factors comprehensively.
- Digital and hybrid delivery models may improve scalability but they need to address barriers related to digital literacy and access. When using digital tools, compliance with data protection regulations and ethical standards must be ensured.
- Costs vary widely, depending on intervention design and resource intensity; potential cost savings extend beyond dementia prevention to other chronic conditions.
- Creating supportive environments (e.g. safe spaces for physical activity and access to healthy foods) can reinforce individual-level interventions. Policy and financing frameworks should integrate dementia risk reduction into urban planning, clean air initiatives, health promotion, NCD prevention and healthy ageing strategies, to enable sustainable scale-up.

4. Implementation and future directions



4.1 Cross-cutting considerations for implementation

Implementation of dementia risk reduction interventions is influenced by health system, structural and sociocultural factors that frequently lie beyond the control of individuals. Thus, effective and equitable delivery requires actions that extend beyond individual behaviour change. Cross-cutting implementation considerations include the following:

- Addressing structural and policy-level factors (e.g. access to essential medicines and assistive technologies, affordability of healthy foods, availability of safe environments and reduced exposure to air pollution), to ensure that interventions are accessible and sustainable across diverse settings.
- Prioritizing culturally appropriate, context-specific adaptation of interventions, with a focus on underserved groups. Given the diversity of implementation contexts, cultural and contextual adaptation of screening tools, behavioural interventions and community programmes is essential, to ensure relevance and acceptability. When selecting existing screening tools, context must be considered, to ensure cultural appropriateness and relevance.
- Collaborating across sectors and multidisciplinary approaches to ensure coherent, scalable and equitable delivery. Interventions targeting the risk factors included in these guidelines are interconnected, and improvements in one domain often reinforce benefits in others. Addressing multiple risk factors simultaneously within routine care and community-based programmes may yield greater gains than isolated efforts.
- Integrating dementia risk reduction activities into existing health and social care systems (including primary care, NCD programmes, ageing services and community-based platforms), to enhance feasibility, reach and long-term sustainability.
- Using both digital and in-person delivery models to ensure broad accessibility. Although digital tools can expand reach, in-person services remain critical for many interventions and for populations with limited digital access.
- Integrating workforce capacity, public awareness and stigma reduction to support uptake of interventions. Ongoing monitoring and evaluation, including surveillance of environmental exposures, can support continuous improvement of implementation strategies.

Equity considerations apply across all risk factors. Disparities in access to services, digital tools and health-promoting environments have a particularly strong effect on older adults, rural communities, socioeconomically disadvantaged groups and populations in LMICs. Therefore, an equity lens should be applied to all implementation strategies, to ensure that they reach all groups impacted by dementia.

Implementation of dementia risk reduction interventions is influenced by health system, structural and sociocultural factors that frequently lie beyond the control of individuals. Thus, effective and equitable delivery requires actions that extend beyond individual behaviour change.

4.2 Evidence gaps and research needs

Across the risk factors addressed in these guidelines, several common limitations and research gaps were identified:

- Most of the available evidence continues to be derived from observational studies, with relatively few RCTs to establish causality, limiting the certainty of evidence under the GRADE framework to low or very low.
- Dementia or MCI are infrequently used as primary outcomes owing to methodological challenges, and follow-up durations are often short.
- Evidence is predominantly from high-income countries, limiting the generalizability to low- and middle-income settings.
- It is rare for studies to undertake subgroup analyses by age, sex, socioeconomic status and genetic risk.
- Inconsistency in how interventions and outcomes are defined.
- Interactions between multiple risk factors remain underexplored.
- Implementation research on feasibility, scalability and cost–effectiveness is limited.
- There is also a need for validated surrogate outcomes and greater inclusion of underrepresented populations.

Evidence on the impact of **policy interventions** to address dementia risk factors remains scarce. Except for air pollution, data on whether policy measures can reduce population-level dementia risk are limited. More quantitative research is urgently needed to evaluate the effectiveness of such policies and to develop tools similar or complementary to WHO's T*ackling NCDs: best buys and other recommended interventions for the prevention and control of noncommunicable diseases (5)* for reducing the risk of dementia.

These research gaps align closely with the WHO publication *A blueprint for dementia research (254)*, particularly the document's Strategic Goals 13–15, which call for improved methodologies, greater diversity and representativeness in study populations, and robust evidence on the efficacy and cost–effectiveness of risk reduction interventions across the life course. Addressing these gaps is essential to inform equitable, effective and context-appropriate dementia prevention strategies; hence, doing so may guide future research priorities and inform the scope of subsequent updates to the guidelines.

More quantitative research is urgently needed to evaluate the effectiveness of policies and to develop tools for reducing the risk of dementia.

The WHO Steering Group will continue to monitor research developments in dementia risk reduction, particularly in areas where evidence is currently limited or of low certainty. New findings may warrant the introduction of additional recommendations or revisions to existing ones. Following the publication and dissemination of these guidelines, any concerns regarding the validity of a recommendation will be promptly communicated to implementers, along with plans for updating the recommendation if necessary.

4.3 Dissemination and derivative products

Although the guidelines were developed in English, the executive summary will be translated into all six official United Nations languages, contingent upon available resources. The guidelines and their accompanying evidence profiles will be made available on the WHO website.

Relevant departments in ministries of health will be notified of the updated guidelines through WHO regional and country offices. A briefing package will be prepared for WHO technical officers outside of WHO headquarters, including an executive summary and a question and answer (Q&A) document related to policy and programme implications. These materials will highlight the major updates and new recommendations introduced in this edition.

Member States will be supported to adapt, use and implement the guidelines through a range of capacity-building activities. These include training of health care personnel, engagement with centres of excellence, and delivery of workshops and learning activities at regional, subregional and national levels. Web based platforms and in person training initiatives will be used to support sustainable implementation and integration into existing health systems.

As part of the scaling-up strategy in countries, derivative products (e.g. campaign posters and job aids) will be developed and updated to reflect the revised recommendations. Existing materials based on the 2019 guidelines will be adapted accordingly to ensure consistency with the current evidence base.

Implementation and dissemination efforts will be aligned with relevant WHO global mandates – *the Global action plan on the public health response to dementia 2017–2025 (3)*, which has been extended to 2031 *(4)*, the *Intersectoral global action plan on epilepsy and other neurological disorders 2022–2031 (182)*, the *Comprehensive mental health action plan 2013–2030 (175)* and the *Global action plan for the prevention and control of noncommunicable diseases 2013–2030 (112)*. This alignment will facilitate the integration of dementia risk reduction into broader health system strengthening and public health initiatives.

4.4 Monitoring and evaluation

After the publication of the updated guidelines, WHO will continue to collect regular feedback from implementation activities, to evaluate their uptake, usefulness and impact. WHO will also continue to collect feedback from international experts and health care providers who have experience in dementia risk reduction. The information gathered will be used to evaluate the effects of the guideline on dementia risk reduction efforts and health outcomes, to ensure the quality of the guidelines and to identify areas where improvement is required. This will draw on existing WHO resources where possible, including:

- the *Global Dementia Observatory (255)* – an online data and knowledge exchange platform for dementia that provides the framework for monitoring implementation of these guidelines; and

- indicators provided as part of implementing the *Global action plan on the public health response to dementia 2017–2025 (3)*, which has been extended to 2031 *(4)*, the *Comprehensive mental health action plan 2013–2030 (175)* and the *Global action plan for the prevention and control of noncommunicable diseases 2013–2030 (112)*.

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Annex 1
Risk reduction of cognitive decline and dementia: scoping review

Introduction

To support the 2026 update of the World Health Organization's (WHO's) guidelines on risk reduction of cognitive decline and dementia, the WHO Secretariat conducted a series of preliminary scoping reviews in 2024. The purpose of these reviews was to determine whether new and relevant evidence had emerged since the publication of the 2019 guidelines *(1)*, and whether full systematic reviews and evidence appraisals were warranted for each of the existing research questions. In addition, the scoping process sought to identify any emerging or previously unconsidered risk factors and target areas for dementia that may require new PICO (population, intervention, comparator and outcome) questions and corresponding recommendations in the updated guidelines.

Methods

Overview of the methodological approach

The WHO Secretariat conducted scoping reviews in 2024 to rapidly assess whether new evidence published since the 2019 WHO guidelines on risk reduction of cognitive decline and dementia *(1)* justified updating existing recommendations or developing new ones. The scoping process followed a structured, multistep methodology consistent with WHO guideline development processes, and focused specifically on identifying changes in the volume, quality and direction of evidence relevant to cognitive decline and dementia prevention. The findings were subsequently presented to the Guideline Development Group (GDG), to support decisions on whether full systematic reviews were required for the guideline update.

Preliminary horizon scanning

An initial horizon scanning exercise was undertaken to map the current evidence landscape, and identify new or emerging modifiable risk factors or target areas that were not included in the 2019 guidelines. This exercise involved reviewing recent comprehensive umbrella reviews, large-scale systematic reviews and meta-analyses, and major policy reports published since 2019. Key resources included recent systematic reviews and scoping overviews on the topic *(2-6)*, as well as the 2024 Lancet Standing Commission report on dementia prevention, intervention and care *(7)*.

This step was also informed by recent guidelines from international bodies, ensuring alignment with global developments in dementia risk reduction. The findings from this mapping exercise informed the consolidated list of risk factors and target areas included in the focused scoping review searches.

Identification of risk factors and target areas for scoping

Risk factors and target areas included in the 2019 guidelines were combined with additional ones identified through the horizon scan described above. Factors and areas were included if they met the following criteria:

- were potentially modifiable (either at the individual or population level);
- had plausible or established associations with cognitive decline or dementia;
- had emerging or evolving intervention-related evidence since 2019; and
- were relevant for potential WHO guidance at the individual or population level.

The resulting consolidated list is presented in **Table A1.1** and formed the basis for the focused scoping review searches.

Table A.1.1. Risk factors and target areas to be included in the guideline update

Factors and areas included in the 2019 guidelines	Proposed new factors and areas
• Cognitive activity	• Air pollution
• Depression[a]	• HIV
• Diabetes	• Menopausal hormone therapy
• Diet and nutrition	• Multidomain interventions
• Dyslipidaemia	• Sleep
• Harmful use of alcohol	• Stroke
• Hearing loss[a]	• Traumatic brain injury
• Hypertension	• Vision impairment
• Obesity	
• Physical activity	
• Social activity[a]	
• Tobacco cessation	

[a] Although the risk factor or areas was included in the 2019 guidelines, there was insufficient evidence at the time to make a recommendation.

Search strategy and eligibility criteria

Focused scoping searches were conducted between July and August 2024 in PubMed and the Cochrane Library. The searches were restricted to systematic reviews and meta-analyses published from January 2019 onwards, consistent with the publication date of the previous WHO guidelines. Search strategies combined keywords for:

- the risk/protective factor (e.g. "physical activity", "diabetes", "air pollution"); AND
- the "intervention" OR "treatment" OR "pharmacological" OR "non-pharmacological" (when applicable); AND
- outcomes related to "cognitive decline" OR "mild cognitive impairment" OR "dementia".

Because these were scoping reviews, searches were restricted to title and abstract, and English language; also, no geographical restrictions were applied.

Articles were included if they met the following criteria:

- systematic reviews or meta-analyses;
- published from 2019 onwards;
- examined the risk factor or target area and the intervention of interest;
- reported outcomes related to cognitive decline, mild cognitive impairment or dementia;
- included human participants of any age or setting; and
- provided sufficient methodological detail to assess reliability.

Primary studies and reviews focusing exclusively on biomarkers or neuropathological outcomes without clinical cognitive measures were excluded. If the described searches did not yield any results, primary evidence from large cohort studies was permissible. Reference lists of included articles were hand searched to include additional articles if relevant.

Data extraction and synthesis

For each search, the WHO Secretariat extracted key information from eligible reviews. Findings were summarized narratively and synthesized into a comparative table listing each risk factor or target area, key evidence identified and initial interpretation of impact on dementia risk. Consistent with the rapid nature of this scoping exercise, summaries did not include formal risk of bias assessments.

The summary of the findings table was first shared with members of the Steering Group for inputs and additional comments, and was supplemented with relevant WHO guidance on individual risk factors and target areas published since 2019. The updated summary table was then shared with the GDG as pre-reading material for the group's meeting in August 2024.

GDG review and decision-making

The results of the scoping review were presented to the GDG during its meeting in August 2024. The GDG considered the strength, direction and potential implications of new evidence for each risk factor or target area, and determined whether a full systematic review and evidence appraisal were warranted. These decisions, along with the corresponding narrative summaries of the scoped literature, are summarized in the Results section below.

Results

The key findings of the scoping review for each risk factor or target area are documented in **Table A.1.2**, together with a summary of the decisions taken by the GDG during its meeting in August 2024.

Table A.1.2

Narrative summary of scoping review findings and GDG decisions

Factor	Summary of scoping review	GDG interpretation and decision
Factors included in the 2019 guidelines (in alphabetical order)		
Cognitive activity	New evidence indicates that cognitive training or cognitive stimulation can lead to immediate improvements in cognitive function, and there is a strong recommendation for adults to engage in mentally stimulating activities to reduce the risk of cognitive decline and dementia *(2)*. However, the evidence remains weak regarding whether these improvements translate into better day-to-day functioning. No evidence was identified during scoping on the persistence of effects after cognitive training *(8-10)*. Available evidence supports the efficacy of cognition-oriented treatments in improving cognitive performance in older adults, but it is unclear whether these changes result in clinically meaningful outcomes *(8)*. Additionally, evidence from a meta-analysis reports significant improvement in cognitive function, particularly memory *(9)*, whereas findings from a Cochrane review suggest only slight improvement in episodic memory, with the clinical importance of these improvements remaining uncertain and no evidence that effects persisted 12 months later *(10)*. Overall, evidence identified during the scoping review suggests that cognition-oriented treatments show immediate but limited durable effects, and there is little evidence on whether benefits translate to everyday functioning. Most studies assessed structured interventions rather than routine cognitively stimulating activities.	Given the limited durability of effects, uncertainty about real-world impact, and the need to consider both interventions and everyday cognitive activities across diverse settings, the GDG recommended a full systematic review.
Depression	Non-pharmacological interventions may offer greater benefits than pharmacological treatments for reducing depressive symptoms and improving cognition in individuals with MCI and AD *(11)*. Evidence from psychosocial interventions indicate improvements in memory, depressive symptoms and activities of daily living among older adults with MCI, although no significant effects were observed for executive function and participants did not have clinical depression *(12)*. Broader evidence shows benefits for mood but no consistent effects on cognition *(13)*. These findings highlight the potential role of non-pharmacological strategies in addressing mood and functional outcomes, while their impact on cognition remains less clear. Large cohort data from the UK Biobank further suggest that effective treatment of depression – pharmacological, psychological or combined – may be associated with reduced dementia risk *(14)*.	Given that the 2019 guidelines did not include a recommendation on depression owing to insufficient evidence, the GDG noted that any potentially relevant new evidence would require a full systematic review. The scoping review identified limited and inconsistent findings that do not fully address the existing PICO. Therefore, the GDG concluded that a comprehensive systematic review is necessary to determine whether a recommendation can now be developed.

Factor	Summary of scoping review	GDG interpretation and decision
Diabetes	Recent systematic reviews highlight new evidence on both pharmacological and non pharmacological interventions for diabetes in relation to cognitive outcomes. Reviews report effects of both pharmacological interventions (including specific agents, intranasal applications and traditional Chinese medicine) and non-pharmacological approaches *(15,16).* Meta analyses indicate that SGLT2 inhibitors, GLP 1 receptor agonists, and DPP 4 inhibitors may offer greater protection against dementia compared with agents such as metformin or sulfonylureas, though results remain mixed *(17,18).* The same meta-analyses also suggest differential effects across racial groups *(17,18)*. Overall, newly available evidence expands and strengthens the evidence base relative to the 2019 guidelines.	The GDG noted that recent evidence represents meaningful advancements compared with the 2019 evidence base, particularly regarding differential effects of specific glucose lowering agent classes. Given the potential implications for recommendations, a full updated systematic review was warranted.
Diet and nutrition	Healthy dietary patterns – characterized by high intake of fruits and vegetables and low consumption of ultra processed foods – are associated with reduced risk of several dementia related risk factors, including obesity, diabetes and hypertension (*19*). Observational evidence suggests that adherence to healthy dietary patterns is linked to a lower risk of dementia and AD *(20)*. Among specific dietary patterns, evidence for the Mediterranean diet indicates potential protective effects on cognitive decline, though results for MCI and AD remain inconsistent across studies *(21,22)*. Cultural specificity, cost and feasibility may also limit the generalizability of Mediterranean style diets in diverse settings. Recent evidence highlights the MIND diet – a combination of Mediterranean and DASH dietary components – as showing dose dependent cognitive benefits and reduced dementia risk *(23,24)*. Cohort data also suggest lower dementia incidence among adults adhering to MIND dietary patterns *(25)*. New reviews on dietary supplements have not altered earlier conclusions, with the overall quality of evidence remaining low to moderate *(26-28)*. Ginkgo biloba was not re examined, because it is already negatively recommended in the mhGAP dementia module.	Given the substantial number of new reviews and meta-analyses published since 2019 on various dietary patterns, the GDG concluded that an updated systematic review is warranted to synthesize the core components of dietary patterns associated with reduced dementia risk.
Dyslipidaemia	A high level of LDL cholesterol in midlife is recognized as a risk factor for dementia and is incorporated in the Lancet dementia risk model *(7)*. Recent evidence has mainly examined the association between lipid lowering therapies – particularly statins – and cognitive outcomes. Meta analyses of observational studies consistently report that statin use is associated with a reduction of about 20% in dementia risk among statin users, with the magnitude of effect varying by statin potency *(29)*. Similarly, Poly et al. (2020) reported a 17% lower risk of dementia among individuals using statins *(30)*, with higher potency statins (e.g. rosuvastatin, atorvastatin and simvastatin) being associated with greater protective effects, whereas standard potency statins (pravastatin, fluvastatin and lovastatin) showed no significant association with reduced dementia risk. Despite the expanding observational evidence, recent research remains limited, and the overall certainty is constrained by the absence of robust RCT data directly assessing cognitive outcomes.	Although recent studies provide additional insights into differential effects of statin potency, the GDG noted that the evidence is still largely observational and does not substantially change the conclusions drawn in 2019. Given the limited new evidence and lack of compelling indications for a revised recommendation, the GDG concluded that an updated systematic review was not warranted.

Factor	Summary of scoping review	GDG interpretation and decision
Harmful use of alcohol	Available epidemiological studies do not provide sufficient support for a protective effect of alcohol on dementia incidence *(31)*. However, some findings indicate that reducing alcohol intake from heavy to moderate levels, as well as initiating mild drinking, may be associated with a decreased risk of dementia *(32)*. Thiamine supplementation in individuals with alcohol use disorder has been linked to improved cognitive function, regardless of the substitution regimen *(33)*. Furthermore, a study assessing neuropsychological recovery following abstinence in individuals with alcohol use disorder found that most cognitive functions, including attention, memory and executive function, showed significant improvement within 6–12 months *(34)*. No recent systematic reviews focusing specifically on alcohol reduction or treatment interventions and cognitive outcomes were identified.	The new evidence does not meaningfully alter the conclusions from 2019 and is unlikely to change existing recommendations; hence, the GDG determined that a full updated review was not warranted.
Hearing loss	Hearing loss has been increasingly recognized as a modifiable risk factor for cognitive decline and dementia. Evidence suggests that the use of hearing aids may improve cognitive function, particularly executive function, in adults without dementia *(35)*. Furthermore, hearing restorative devices (e.g. cochlear implants and hearing aids) have been significantly associated with reduced cognitive decline and improved cognition *(36,37)*.	Because hearing loss was included in the 2019 guidelines but no recommendation was issued owing to insufficient evidence, the GDG determined that newly available studies warrant a full systematic review.
Hypertension	Recent systematic reviews, including a Cochrane review, continue to demonstrate that effective management of hypertension reduces the risk of cognitive decline and dementia *(38-40)*. Evidence shows that individuals treated with antihypertensive medications have a significantly lower risk of developing dementia (*38-40*). Emerging findings also suggest that certain antihypertensive classes – such as angiotensin II receptor blockers and calcium channel blockers – may confer additional protective benefits *(41)*.	Given the availability of new, more specific evidence on antihypertensive treatment classes and dementia risk, the GDG concluded that a full updated systematic review is warranted.
Obesity	Systematic reviews continue to show an association between obesity and increased dementia risk, although most evidence is based on observational studies rather than evaluations of specific weight management interventions. The relationship appears to vary across the life course: midlife overweight and obesity are associated with higher dementia risk, whereas late life underweight also confers increased risk *(42,43)*. Recent evidence suggests maintaining a BMI of between 18.5 and 24.9 in adults aged below 65 years *(2)* and monitoring cognitive function in older adults experiencing unintentional weight loss *(43)*. In contrast, the 2019 recommendation only addressed midlife overweight. Overall, evidence has expanded regarding life course patterns but remains limited on effective interventions.	Given emerging evidence on life-course patterns of body weight and dementia risk, and the limited evidence on specific weight-management interventions, the GDG concluded that a full updated evidence review was warranted to inform more nuanced recommendations, particularly for older adults.

Factor	Summary of scoping review	GDG interpretation and decision
Physical activity	Physical activity is increasingly recognized as a potential strategy for the primary prevention of dementia. Recent evidence continues to support a beneficial association between physical activity and cognitive outcomes. A 2023 guideline review reported that the effectiveness of physical activity for preventing cognitive decline in people with MCI remains uncertain *(44)*. Meta-analytic evidence shows small to moderate cognitive benefits of exercise for adults with normal cognition and for those with MCI, particularly for global cognition and executive function *(45,46)*. Observational studies also indicate that higher levels of physical activity are associated with reduced incidence of all-cause dementia and AD, with long-term protective effects *(47)*. Overall, new findings reinforce but do not substantially change the evidence base considered in 2019.	The GDG noted that recent evidence strengthens but does not change the overall conclusions from 2019. The certainty and direction of findings remain largely the same for both cognitively healthy adults and those with MCI. As a result, an updated systematic review was not deemed necessary.
Social activity	Recent evidence reinforces social activity as a determinant of cognitive health, although overall certainty remains low. Systematic reviews show that participation in formal social activities (e.g. volunteering, clubs or religious and cultural organizations) is associated with reduced likelihood of cognitive decline, albeit with very low certainty evidence *(48)*. Structural and functional aspects of social connection, including small social networks, loneliness and low social support, have been linked to increased risk of cognitive decline *(49)*. The 2024 Lancet Commission report further highlighted the importance of supportive, age friendly environments and community infrastructure to reduce social isolation and promote participation *(7)*.	Because no recommendation was made in the 2019 guidelines owing to insufficient evidence, the GDG noted that any potentially relevant new findings would require a full systematic review. Given the increased volume of evidence and its relevance to dementia prevention and the WHO Commission on Social Connection, the GDG concluded that a comprehensive systematic review is warranted.
Tobacco cessation	Tobacco cessation is associated with reduced risk of dementia. Observational evidence suggests that smoking cessation rather than smoking reduction is associated with a decreased risk of dementia *(50-52)*. These identified studies did not examine specific cessation interventions, only whether individuals stopped smoking, with longer abstinence conferring greater benefit. For example, in a United States cohort of over 13 000 adults aged 52–75 years followed for 12 years, current smokers and those who quit less than 9 years before baseline had a higher risk of dementia than individuals who had never smoked (HR 1.33 and 1.24, respectively), while quitting 9 or more years earlier eliminated excess risk *(50)*. Similarly, a Korean study of 790 000 adults aged 40 years and older found that smoking cessation reduced dementia risk compared with sustained smoking, whereas smoking reduction or increased consumption raised risk *(51)*. Moreover, in a Japanese cohort of 12 000 adults aged 65 years and older, current smokers had an elevated risk of dementia (HR 1.46), whereas quitting more than 3 years prior normalized risk to that of never smokers *(52)*. No systematic reviews or meta-analyses of intervention studies were identified.	Because new evidence reinforces existing conclusions and is unlikely to change recommendations, the GDG determined that a full updated review was not required.

Factor	Summary of scoping review	GDG interpretation and decision
New factors not previously included in the 2019 guidelines (in alphabetical order)		
Air pollution	Systematic reviews and meta-analyses consistently demonstrate a strong association between air pollution and increased dementia risk *(53-55)*. For example, evidence shows an increased risk of cognitive decline when using solid fuels for cooking compared to cleaner well-ventilated cooking stoves *(56)*. Additionally, ambient air pollution, especially PM2.5, seems to be a risk factor for dementia, as well as nitrogen dioxide and nitrogen oxide, although with more limited data *(53)*. Examples of interventions to reduce air pollution may include urban traffic restrictions and postponement of non-essential polluting activities on high-pollution days *(6)*. A quasi-experimental study from China found that implementing clean air policies improved cognitive function and reduced dementia incidence in provinces that implemented the clean air policy *(57)*.	Given the consistent evidence linking air pollution with dementia risk and the growing indications that environmental interventions can reduce cognitive burden, the GDG recommended a full systematic review of the evidence, reflecting its status as a newly considered risk factor.
HIV	Recent studies highlight the nuanced role of ART in managing cognitive impairment in people living with HIV. Evidence indicates that ART improves neurocognitive outcomes – particularly in global cognition, executive function and processing speed – with greater benefits among individuals with advanced immunosuppression *(58)*. However, improvements are not associated with treatment duration, regimen type, CPE scores or conventional biomarkers *(58)*. Similarly, high CPE regimens do not confer additional cognitive benefits and should not be prioritized solely to prevent neurocognitive decline *(59)*. Despite its benefits, ART remains limited in addressing legacy neuronal injury and eliminating peripheral and central viral reservoirs *(60)*.	Given growing recognition of HIV as a potential contributor to cognitive decline, the emerging evidence on ART-related cognitive effects, and the absence of existing WHO recommendations on this topic, the GDG concluded that a full, dedicated systematic review is necessary.
Menopausal hormone therapy	Globally, dementia disproportionately impacts women, both directly and indirectly, as women shoulder a greater disease burden and are commonly the primary caregiver of people living with dementia. Hormonal changes associated with menopause and MHT are thought to contribute to the higher prevalence of dementia in women than men owing to the association between MHT and increased dementia risk *(61)*. The use of MHT to treat menopausal symptoms in women and its effects on cognition remain an area of debate among clinicians owing to potential adverse effects (i.e. malignancies) and conflicting evidence. Estrogen therapy initiated in midlife or before the age of 65 years has been linked to improved verbal memory, whereas estrogen-progestogen therapy started in late life appears to be associated with cognitive decline *(62)*. In midlife, the use of estrogen therapy has been associated with a reduced risk of dementia *(63)*. However, both estrogen therapy and estrogen-progestogen therapy initiated in late life have been linked to an increased dementia risk *(63)*. These findings support the concept of a critical window for therapeutic benefit, suggesting that timing of initiation is key. It is important to note that most of the available evidence is based on observational studies *(63)*.	Given the growing evidence base, heterogeneity of findings and absence of previous WHO guidance on this topic, the GDG recommended a full systematic review to clarify risks, benefits and implications for dementia prevention.

Factor	Summary of scoping review	GDG interpretation and decision
Multidomain interventions	Recent evidence highlights the potential of multidomain interventions in supporting cognitive health among individuals at risk of dementia. For example, interventions combining diet, physical activity and cognitive training have been associated with improvements in cognitive function in adults at risk of dementia *(64)*. A meta-analysis of 28 studies found that multidomain interventions led to greater improvements in global cognition, memory, executive function and verbal fluency in older adults with MCI compared with single-domain interventions *(65)*. However, other meta-analyses report only small effects on dementia risk and composite cognitive scores, with no significant impact on global cognition *(66)*. Similarly, a Cochrane review concluded that while multidomain interventions may have small effects on overall cognition, there is no evidence they can prevent incident dementia (*67)*.	Given the growing evidence base and ongoing global interest in multidomain prevention models, the GDG recommended their inclusion in the guideline update and therefore a full systematic review to clarify effectiveness, feasibility and potential for guideline recommendations.
Sleep	Sleep disturbances – including insomnia, short or long sleep duration, circadian rhythm disruption and OSA – have increasingly been examined as potential contributors to cognitive decline and dementia. Evidence on whether treating sleep problems improves cognition remains limited. The strongest intervention evidence relates to the use of CPAP therapy for OSA. Recent analyses indicate that although CPAP consistently reduces daytime sleepiness, its impact on cognitive outcomes is mixed and inconclusive. A 2023 review highlights that cognitive improvements are not reliably observed across studies *(68)*. In contrast, an observational cohort study reported that CPAP use was associated with a lower incidence of AD and all cause dementia, suggesting possible long term neuroprotective effects *(69)*. When cognitive gains do occur, they appear most evident in attention and are observed particularly in middle aged adults with severe OSA *(70)*. Overall, emerging evidence suggests that CPAP may confer selective cognitive benefits and potentially reduce dementia risk, but findings remain inconsistent and further longitudinal research is needed. Notably, WHO currently has no existing guidelines addressing sleep or sleep disorders in the context of cognitive decline prevention or general health promotion.	Given growing interest in sleep as a potentially modifiable risk factor for cognitive decline, the post-2019 expansion of evidence, and the absence of any existing WHO guidance on this topic, the GDG concluded that a full updated evidence review is warranted.
Stroke	In 2021, stroke was the third leading cause of death and disability globally *(71)*. Dementia incidence is higher in patients with recurrent ischaemic stroke, and a previous stroke increases risk of dementia *(72,73)*. Systematic reviews and meta-analyses indicate that interventions to reduce risk of dementia after stroke include high-dose statins, lipophilic statins, direct oral anticoagulants and aspirin *(74-76)*. Similarly, mechanical thrombectomy *(77)* and antiplatelets therapy may be effective in reducing dementia risk *(78)*.	Given the expanding evidence base and the potential impact of effective secondary prevention strategies, the GDG recommended a full systematic review to evaluate interventions that may reduce dementia risk after stroke.

Factor	Summary of scoping review	GDG interpretation and decision
Traumatic brain injury	TBI is a significant global public health concern, with growing evidence linking it to long-term neurological outcomes, including dementia. In LMIC, TBI most commonly results from road traffic accidents, whereas in high-income countries, falls and violence are leading causes. Sports involving frequent head contact and whiplash events can also result in TBIs. Evidence suggests that TBI increases the risk of dementia, with some studies estimating a nearly 70% increased risk, particularly among younger adults, men and cohorts in Asia, though substantial heterogeneity exists across studies *(79)*. TBI, particularly moderate and severe TBI, may be associated with risk of AD *(80)*. However, another meta-analysis reported that although TBI is linked to an increased risk of dementia, no association was found with AD *(81)*. Systematic reviews of both high- and low-quality evidence indicate that sustaining a TBI increases dementia risk; however, most studies have methodological limitations such as reliance on self-reported TBI and poor case definitions *(82)*. Whether a single TBI or multiple TBIs confer greater risk remains controversial, largely owing to heterogeneity in study design. Although the use of helmets or head protection in contact sports is often proposed in the literature as possible means to reduce dementia risk associated with TBI, formal comprehensive evidence synthesis on the topic is lacking.	Given expanding evidence, persistent methodological gaps and the status of TBI as a newly considered risk factor, the GDG recommended a full systematic review to clarify risk magnitude and assess potential intervention implications for dementia prevention.
Vision impairment	Growing evidence supports an association between untreated vision loss and increased dementia risk, with indications that treatment may modify this risk *(7)*. Specifically, higher dementia risk has been linked to conditions such as cataracts and diabetic retinopathy, but not to glaucoma or age-related macular degeneration *(83)*. The relationship between vision impairment and dementia may reflect underlying illnesses such as diabetes, the direct effects of vision loss (e.g. cataract surgery), or shared neuropathological processes in both the retina and the brain. Evidence suggests that cataract surgery may be associated with a lower risk and incidence of dementia *(84-86)*.	Given growing evidence of an association between vision impairment, its treatment and cognitive outcomes – and its status as a newly considered risk factor – the GDG recommended a full systematic review.

AD: Alzheimer disease; ART: antiretroviral therapy; BMI: body mass index; CPAP: continuous positive airway pressure; CPE: central nervous system penetration effectiveness; DASH: dietary approaches to stop hypertension; GDG: Guideline Development Group; GLP-1: glucagon-like peptide-1; HIV: human immunodeficiency virus; HR: hazard ratio; LDL: low-density lipoprotein; LMIC: low- and middle-income countries; MCI: mild cognitive impairment; mhGAP: WHO Mental Health Gap Action Programme; MHT: menopause hormone therapy; MIND: Mediterranean-DASH Intervention for Neurodegenerative Delay; OSA: obstructive sleep apnoea; PICO: population, intervention, comparator and outcome; PM2.5: particulate matter with a diameter of 2.5 micrometres or less; RCT: randomized controlled trial; SGLT2: sodium-glucose cotransporter 2; TBI: traumatic brain injury; UK: United Kingdom of Great Britain and Northern Ireland; WHO: World Health Organization.

Conclusion

Following the scoping review, the evidence was presented to the GDG at the meeting in August 2024. Based on the evidence presented, the GDG decided to commission full systematic reviews of the intervention-related evidence for the areas listed in **Table A.1.3**, where new or more robust evidence has emerged since 2019 or where no previous recommendation had been made (the risk factors and target areas are listed in alphabetical order).

Table A.1.3. Risk factors and target areas to be updated or newly included in the guideline update

Update	New
• Cognitive activity	• Air pollution
• Depression	• HIV
• Diabetes	• Menopausal hormone therapy
• Diet and nutrition	• Multidomain interventions
• Hearing loss	• Sleep
• Hypertension	• Stroke
• Obesity	• Traumatic brain injury
• Social activity	• Vision impairment

For four risk factors or target areas, the GDG concluded that the newly identified intervention-related evidence did not substantially alter the existing conclusions from the 2019 guidelines and did not justify an updated systematic review. These factors were (in alphabetical order):

- dyslipidaemia
- harmful use of alcohol
- physical activity
- tobacco cessation.

In these areas, existing recommendations – or the rationale for not issuing recommendations – remain valid; therefore, further evidence synthesis was not recommended.

Overall, the scoping review indicated significant progress in the scientific understanding of dementia risk reduction since 2019. The GDG's decisions reflected the need to update recommendations where evidence has evolved, expand the guidelines to incorporate new modifiable factors and ensure alignment with emerging global priorities (e.g. environmental health, sensory impairment, multidomain prevention strategies and women's brain health).

The planned comprehensive evidence reviews will ensure that the updated guidelines are grounded in the most current, rigorous and globally relevant evidence available.

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Annex 2
Guideline development teams

Steering Group

World Health Organization (WHO) headquarters

Kouamivi Agboyibor	Department of Noncommunicable Diseases and Mental Health
Avni Amin	Department of Sexual, Reproductive, Maternal, Child, and Adolescent Health and Ageing
Francesca Celletti	Department of Noncommunicable Diseases and Mental Health
Matteo Cesari	Department of Sexual, Reproductive, Maternal, Child, and Adolescent Health and Ageing
Shelly Chadha	Department of Noncommunicable Diseases and Mental Health
Neerja Chowdhary	Department of Noncommunicable Diseases and Mental Health
Laura García Diaz	Department of Noncommunicable Diseases and Mental Health
Tarun Dua	Department of Noncommunicable Diseases and Mental Health
Bianca Hemmingsen	Department of Noncommunicable Diseases and Mental Health
Stuart Keel	Department of Noncommunicable Diseases and Mental Health
Dzmitry Krupchanka	Department of Noncommunicable Diseases and Mental Health
Christopher Mikton	Department of Health Determinants, Promotion and Prevention
Manjulaa Narasimhan	Department of Sexual, Reproductive, Maternal, Child, and Adolescent Health and Ageing
Primrose Nyamayaro	Department of Noncommunicable Diseases and Mental Health
Alana Officer	Department of Health Determinants, Promotion and Prevention
Vinayak Prasad	Department of Health Determinants, Promotion and Prevention
Ajay Rangaraj	Department of HIV, TB, Hepatitis and Sexually Transmitted Infections
Heather Adair-Rohani	Department of Environment, Climate Change, One Health and Migration
Ritu Sadana	Department of Sexual, Reproductive, Maternal, Child, and Adolescent Health and Ageing
Kuntal Saha	Department of Nutrition and Food Safety
Nicoline Schiess	Department of Noncommunicable Diseases and Mental Health
Kerstin Schotte	Department of Health Determinants, Promotion and Prevention
Katrin Seeher	Department of Noncommunicable Diseases and Mental Health
Nhan Tran	Department of Health Determinants, Promotion and Prevention
Inka Weissbecker	Department of Noncommunicable Diseases and Mental Health
Juana Willumsen	Department of Health Determinants, Promotion and Prevention
Kazuki Yamada	Department of Health Determinants, Promotion and Prevention

WHO regional offices

Andrea Bruni	Regional Office for South-East Asia: Department of Healthier Populations and Noncommunicable Diseases
Ledia Lazeri	Regional Office for Europe: Department of Mental Health and Well-being
Renato Oliveira e Souza	Regional Office for the Americas: Department of Noncommunicable Diseases and Mental Health
Chido Rwafa- Madzvamutse	Regional Office for Africa: Department of Mental Health and Substance Use
Khalid Saeed	Regional Office for the Eastern Mediterranean: Department of Mental Health, Neurological and Substance Use Disorders
Atsuro Tsutsumi	Regional Office for the Western Pacific: Prevention and Management of Noncommunicable Diseases and Mental Health

Guideline Development Group

Name and affiliation	WHO region	Area of expertise
Hanadi Al Hamad Hamad Medical Corporation Doha, Qatar	Eastern Mediterranean	Geriatric medicine, hypertension and diabetes
Charles Alessi Nightingale Health Helsinki, Finland	European	Public health research into dementia risk reduction and multidomain interventions for dementia
Kaarin Anstey University of New South Wales Sydney, Australia	Western Pacific	Dementia risk reduction and research into socioeconomic, environmental and metabolic risk factors of dementia
Abolfazl Avan Western University London, Canada	Eastern Mediterranean	Public health policy and dementia risk reduction
Claudio Bassetti University of Bern Bern, Switzerland	European	Neurology, sleep
Cleusa Ferri Universidade Federal de Sao Paulo Sao Paulo, Brazil	Americas	Psychiatry, epidemiology of dementia, late-life mental disorders
Hany Ibrahim Ain Shams University Cairo, Egypt	Eastern Mediterranean	Geriatric medicine, cognitive training
Sonali Jhanjee All India Institute of Medical Sciences New Delhi, India	South-East Asia	Psychiatry, tobacco cessation
John Joska University of Cape Town Cape Town, South Africa	African	Psychiatry, HIV
Miia Kivipelto Karolinska Institutet Stockholm, Sweden	European	Geriatric medicine and prevention, early diagnosis and treatment of cognitive impairment and dementia
Sebastian Köhler Maastricht University Maastricht, Kingdom of the Netherlands	European	Neuroepidemiology, population research and dementia risk reduction
Tiina Laatikainen University of Eastern Finland Kuopio, Finland	European	Noncommunicable diseases, evidence-based lifestyle interventions
Emily Ong Singapore	Western Pacific	Lived experience
Chris Roberts Wales, United Kingdom	European	Lived experience perspective
Jane Rylett Canadian Institutes of Health Research Ottawa, Canada	Americas	Neurobiology
Palanimuthu Thangaraju Sivakumar National Institute of Mental Health and Neuro Sciences Bengaluru, India	South-East Asia	Psychiatrist with expertise in late-life social connection

Name and affiliation	WHO region	Area of expertise
Jaimie Steinmetz Institute for Health Metrics and Evaluation Seattle, USA	Americas	Sensory and neurological disorders, public health
Kusumadewi (DY) Suharya Alzheimer's Disease International Jakarta, Indonesia	Western Pacific	Sensory and neurological disorders, public health
Shyh Poh Teo RIPAS Hospital Universiti Brunei Darussalam Bandar Seri Begawan, Brunei Darussalam	Western Pacific	Geriatric medicine, hypertension and physical activity
Chinedu T Udeh-Momoh Wake Forest University School of Medicine North Carolina, USA	Americas	Neuroscience, dementia prediction and prevention, women's health, menopause, brain health disparities
Huali Wang Peking University Institute of Mental Health Beijing, China	Western Pacific	Psychiatry, late-life dementia, policy advocacy
Stephen Watiti Lived experience Kampala, Uganda	African	Public health, lived experience
Shehan Williams University of Kelaniya Colombo, Sri Lanka	South-East Asia	Psychiatry, depression

Declarations of interest

In total, 18 experts declared interests. The kind and nature of these declared interests as well as the WHO Secretariat's decision to mitigate risks for bias arising from potential conflicts of interest are summarized below for each expert (in alphabetical order).

1. **AL HAMAD, Hanadi (Hamad Medical Corporation, Qatar)** declared significant government research funding from Hamad Medical Corporation, the main provider of secondary and tertiary health care in the State of Qatar for several research projects on physical activity, dementia risk reduction, depression and developing a national dementia registry. **Although the research is related to the guidelines, it was decided that research support from this government institution would be unlikely to affect Dr Al Hamad's judgement and therefore does not preclude Guideline Development Group (GDG) participation. No further action was deemed necessary.**

2. **ALESSI, Charles (Nightingale Health, Finland)** declared royalties received from his book *Increase your brainability and reduce your risk of dementia* published by Oxford University Press in 2021. In the last financial year, royalties were less than US$ 1000 and have not exceeded US$ 1000 since the book was published. **These royalties were deemed nominal and do not constitute a conflict of interest. No further action was deemed necessary.**

3. **ANSTEY, Kaarin (University of New South Wales, Australia)** previously provided paid consulting services to AARP (formerly the American Association of Retired Persons) for the Staying Sharp Brain Health platform; consulting ceased in 2021. She also received travel reimbursements for meetings and speaker honoraria less than US$ 6000 in total from different entities (Roche, Nutricia, University of British Columbia, Asia-Pacific Economic Forum, Conference of Major Superannuation Funds), with individual amounts ranging from US$ 335 to US$ 3000. She declared membership of international councils and committees (e.g. World Dementia Council, Governance Committee of the Global Council of Brain Health). Further, she has declared significant research support focusing on dementia risk reduction that goes to her institution from government funders (Australian Medical Research Future Fund, National Health and Medical Research Council). **While the declared interests are relevant to these guidelines, consulting for AARP, which is a non-profit entity, would be unlikely to affect Dr Anstey's judgement and was deemed not to constitute a conflict of interest. Research support from governmental agencies going to her institution for research on dementia prevention (while relevant to these guidelines) was deemed unlikely to affect Dr Anstey's judgement, but rather demonstrates her expertise in the area. Furthermore, membership of councils and ceased speaker honoraria or travel reimbursement to attend meetings on the topic of dementia, of which none were more than US$ 3000, were deemed unlikely to affect Dr Anstey's judgement and therefore do not preclude GDG membership. No further action was deemed necessary.**

4. **FERRI, Cleusa (Universidade Federal de Sao Paulo, Brazil)** declared research support from internal university funds (for research on cognitive stimulation therapy, Strengthening responses to dementia in developing countries – STRiDE) and the Ministry of Health in Brazil (for a national dementia report). Dr Ferri has also been a co-author of the recently updated Lancet Commission report on dementia prevention, treatment and care. **While the declared interests are related to the topic of these guidelines, internal university funds and government research funding and membership of the Lancet Commission on dementia risk reduction were deemed unlikely to affect Dr Ferri's judgement, but rather speak to her expertise, and therefore do not constitute a conflict of interest for the purpose of the guideline update. No further action was deemed necessary.**

5. **JHANJEE, Sonali (All India Institute of Medical Sciences, India)** declared research support from the WHO Regional Office for South-East Asia and less than US$ 100 speaking fees for presentations on tobacco cessation and deadly effects of tobacco from Maulana Azad Institute of Dental Sciences and News Services Division of All India Radio. **It was discussed that research support from WHO internal sources and nominal amounts for speaking engagements did not constitute a conflict of interest. No further action was deemed necessary.**

6. **JOSKA, John (University of Cape Town, South Africa)** declared receiving significant research grants from government funding (US National Institutes of Health [NIH], National Institute of Mental Health). These grants focus on interventions for sexual trauma in women living with HIV, antiretroviral therapy adherence and smoking cessation in HIV/tuberculosis (TB) care; a longitudinal study on health, aging and dementia in South Africa; and a training development plan for HIV-associated behavioural medicine. Dr Joska also declared receiving less than US$ 1000 in speaking fees at an HIV–central

nervous system (CNS) meeting in the United Kingdom in 2022. **While his research is in parts related to these guidelines, it was decided that research support from these government institutions was unlikely to affect Dr Joska's judgement and therefore did not preclude GDG membership. Furthermore, a one-time ceased speaker honorarium on the topic of HIV and CNS of nominal amount was deemed to constitute no conflict of interest in the context of these guidelines. No further action was deemed necessary.**

7. **KIVIPELTO, Miia (Karolinska Institutet, Sweden)** declared being the Director of Research and Development, Karolinska University Hospital Unit of Clinical Trials, and the Scientific Lead for the World Wide FINGERS network with several ongoing multidomain lifestyle interventions. Dr Kivipelto further declared significant research funding (going to her institution) as Primary Investigator for research related to dementia risk reduction from government funders (Swedish Research Council, Joint Programme – Neurodegenerative Disease Research [JPND], Horizon 2020, NordForsk, European Union [EU] Innovative Health Initiative, EU Innovative Medicines Initiative 2 [IMI2] project), non-profit organizations and public–private foundations (Hjärnfonden [Swedish Brain Foundation], Gates Ventures/Alzheimer's Disease Data Initiative, af Jochnick Foundation, Davos Alzheimer's Collaborative, Center for Innovative Medicine [CIMED] at Johns Hopkins Medicine, Alzheimer's Drug Discovery Foundation, Karolinska Institute–Janssen strategic collaboration), and regional hospital grants (ALF grants). Dr Kivipelto also received competitive grants supporting her professorship from Wallenberg Clinical Scholars and Stockholms Sjukhem covering her salary as Professor for 2016 to 2026. Non-profit organizations, foundations and public–private partnerships have been reviewed, due diligence performed and assessment made in view of the nature of specific research projects being funded, and the real or perceived risk of these grants affecting Dr Kivipelto's judgement. **The received research support from government funders, non-profit organizations/charities and hospital internal funds was deemed to reflect Dr Kivipelto's expertise in the area. Funding received from government and public–private partnerships especially for research involving effects of metformin and multidomain risk reduction interventions potentially constitute actual or perceived conflicts of interest. To manage potential risks of biased judgement, the WHO Secretariat decided to allow Dr Kivipelto to participate in the discussions of the GDG (fully disclosing conflicts to other GDG members) but asked her to recuse herself from voting in the decision-making process around PICOs directly related to metformin and multidomain interventions.**

8. **KÖHLER, Sebastian (Maastricht University, Kingdom of the Netherlands)** declared significant research funding for dementia prevention from government funders (ZonMw, TKI Health Holland, NWO/Dutch Science Organization), non-profit organizations and charities (Alzheimer's Association and Alzheimer Nederland, Gieskes-Strijbis Fonds, Landelijk Kenniscentrum Dementie op Jonge Leeftijd, Hersenstichting [Brain Foundation]) and internal university funds (Maastricht UMC, Mental Health and Neuroscience Research Institute [MHeNs]), all going to his institution. All non-profit organizations and charities have been reviewed, due diligence performed and no potential issues identified. **While the funded research projects are directly related to these guidelines, research support provided to Dr Köhler's institution from government funders, non-profit organizations/charities and university internal funds was deemed unlikely to affect his judgement, but rather demonstrates his expertise in the area. It was therefore deemed not to constitute a conflict of interest for the purpose of these guidelines. No further action was deemed necessary.**

9. **LAATIKAINEN, Tiina (University of Eastern Finland, Finland)** declared significant research support on cardiovascular disease and diabetes from Horizon 2020, State Research Funding (Finland) and the Heart Research Foundation. **While this research content is related to these guidelines, it was decided that research support from these government and non-profit institutions going directly to Dr Laatikainen's institution would be unlikely to affect her judgement and does not constitute a conflict of interest. No further action was deemed necessary.**

10. **ONG, Emily (Singapore)** declared providing expertise and testimony on the subject matter of the meeting from her perspective as someone with lived experience at several international conferences. She also declared being a current board member of Alzheimer's Disease International and a former board member of Dementia Alliance International. She declared receiving an honorarium for speaking at a conference and payment for a manuscript to be published in BMJ. **While relevant to the topic of these guidelines, this was deemed not to constitute a conflict of interest as Ms Ong will be speaking from her perspective as someone with lived experience. No further action was deemed necessary.**

11. **ROBERTS, Chris (United Kingdom)** declared being the Chairperson of the European Working Group of People with Dementia (EWGPWD) (ceased earlier in 2024) and an ex-officio member of the Board of Alzheimer Europe, with full voting rights as a person with lived experience. **While related to the topic of these guidelines, this does not constitute a conflict of interest as Mr Roberts will be speaking from his perspective as someone with lived experience. No further action was deemed necessary.**

12. **RYLETT, Jane (Canadian Institutes of Health Research, Canada)** received a research grant on human choline acetyltransferase from the Canadian Institutes of Health Research. Dr Rylett is also an ad hoc member of the Ministerial Advisory Board on Dementia in her capacity as Scientific Director for the Canadian Institutes of Health Research. **Research on this particular topic is not directly linked to the guidelines. It was decided that Dr Rylett's advisory role to the ministry does not constitute a conflict of interest for the purpose of this guideline update. No further action was deemed necessary.**

13. **SIVAKUMAR, Palanimuthu Thangaraju (National Institute of Mental Health and Neuro Sciences, India)** receives salary support from the Government of India. Dr Sivakumar also declared being an unpaid advisor on dementia risk reduction for a charity (Dementia Alliance) and being involved in research grants funded by government (US NIH and Government of India) on risk factors for Alzheimer disease. **While the research content is related to the topic of these guidelines, it was decided that research support from NIH and the Government of India was unlikely to affect Dr Sivakumar's judgement and therefore does not constitute a conflict of interest for the purpose of these guidelines. Similarly, his involvement with the non-profit entity was deemed unlikely to affect his judgement and does not preclude GDG membership. No further action was deemed necessary.**

14. **STEINMETZ, Jaimie (Institute for Health Metrics and Evaluation [IHME], USA)** declared that her salary at IHME is supported by a grant from the Bill & Melinda Gates Foundation for the Global Burden of Disease (GBD) study. **As only tangibly related to the main focus of these guidelines (risk factors are being modelled as part of GBD, but intervention effects are not established), receiving salary support from this donor was deemed unlikely to affect Dr Steinmetz' judgement and therefore does not constitute a conflict of interest for the purpose of these guidelines. No further action was deemed necessary.**

15. **TEO, Shyh Poh (RIPAS Hospital, Universiti Brunei Darussalam, Brunei)** declared research support for community dementia screening with cognitive tests (not related to these guidelines) and travel and accommodation paid by Dementia Brunei (a non-profit institution) to attend Alzheimer's Disease International Asia-Pacific Regional Conference 2022 in Taiwan, China. **As the research is not directly related to the scope of these guidelines and travel support received by a non-profit organization to attend a conference is nominal, it was deemed that the declared interests were unlikely to affect Dr Teo's judgement and therefore do not constitute a conflict of interest for the purpose of these guidelines. No further action was deemed necessary.**

16. **UDEH-MOMOH, Chinedu T (Wake Forest University School of Medicine, USA)** declared salary support from Wake Forest University School of Medicine in the USA and payment of consultancy services from Aga Khan University in Kenya. She declared significant research support going to her institution focusing on biomarkers and dementia prevention from government agencies (UK Research and Innovation Medical Research Council, UK Defence and Security Accelerator) and non-profit organizations/foundations (Wellcome Trust, US Alzheimer's Association, US Davos Alzheimer's Collaborative, Global Brain Health Institute, Rosetrees Foundation). All non-profit organizations and foundations have been reviewed, due diligence performed and no issues identified. Dr Udeh-Momoh also received travel fellowships from the US Alzheimer's Association and US National Academies of Sciences, Engineering, and Medicine to present her work at meetings and participated as an unpaid expert in the following committees: NIH-sponsored committee on Alzheimer Disease and Related Dementias, British Society for Neuroendocrinology, Alzheimer's Association ISTAART Biofluid Based Biomarker PIA, and FINGERS Brain Health Institute (as a fluid biomarker specialist). **Receiving salary support research grants from government agencies and non-profit organizations/ foundations or travel fellowships for research on biomarkers (not relevant to these guidelines) and dementia prevention (relevant to these guidelines) was deemed to demonstrate Dr Udeh-Momoh's expertise in the area and unlikely to affect her judgement overall. Her committee memberships primarily relate to biomarkers (outside the scope of these guidelines) and are unlikely to affect her judgement. Overall, it was decided that none of the declared interests preclude the expert from participating in the GDG. No further action was deemed necessary.**

17. **WANG, Huali (Peking University Institute of Mental Health, China)** declared nominal reimbursement for committee membership from a pharmaceutical company (Eisai) not exceeding US$ 500. **This nominal amount was deemed unlikely to affect Dr Wang's judgement and therefore constitutes no conflict of interest. No further action was deemed necessary.**

18. **WATITI, Stephen (National Forum of PLHIV Networks in Uganda, Watiti Foundation, Uganda)** declared relevant interests in the topic because of his lived experience of HIV, diabetes and hypertension. **While related to the topic of these guidelines, this does not constitute a conflict of interest as Dr Watiti will be speaking from his perspective as someone with lived experience. No further action was deemed necessary.**

Experts who did not declare any conflicts were:

1. AVAN, Abolfazl
2. BASSETTI, Claudio
3. IBRAHIM, Hany
4. SUHARYA, Kusumadewi (DY)
5. WILLIAMS, Shehan

Conclusion

Among the 24 experts contacted, a total of 18 declared some kind of interest. All interests were analysed by members of the WHO Secretariat and duly evaluated according to the WHO guidance on conflict of interest. Overall, declared interests were found to be relatively minor and unlikely to affect the experts' judgement in the proposed activities. Although some of the research grants declared by the experts are related to the subject of the guideline update, they were deemed to pose minimal or no risk of conflict of interest. Some activities performed by the experts were tangentially related to the scope of the guideline update and resulted in nominal payments or reimbursements for experts. These were deemed inconsequential in importance, or they had ceased and were therefore unlikely to affect current behaviour. One expert declared research support from public–private partnerships for research directly related to the effects of metformin in combination with multidomain risk reduction interventions, which may affect judgement or be perceived as a conflict of interest. The expert was invited to participate in the GDG but she was asked to recuse herself from voting or decision-making processes related to PICOs directly concerning metformin and multidomain interventions.

Further, as a precaution, it was decided that if the issue to be voted upon involved primary research or systematic reviews conducted by any of the participants (who had declared an academic conflict of interest), the participants in question would be allowed to partake in the discussion but not in related voting.

Overall, with one expert having declined participation and none of the remaining experts found to have a conflict of interest that would preclude GDG membership, the GDG comprised 23 experts.

Peer-reviewers

Declarations of interest

In total, 12 experts declared interests. The kind and nature of these declared interests as well as the WHO Secretariat's decision to mitigate risks for bias arising from potential conflicts of interest are summarized below for each expert (in alphabetical order).

1. **AKINYEMI, Rufus (University of Ibadan, Nigeria)** declared research support from government funding, specifically US NIH. **While Dr Akinyemi's research is related to these guidelines, it was decided that research support from this government institution that goes to his institution will be unlikely to affect his judgement and therefore does not preclude contribution as an expert reviewer. No further action was deemed necessary.**

2. **ALLADI, Suvarna (National Institute of Mental Health and Neuro Sciences, India)** declared dementia research support from government funding, including Indian Council of Medical Research, Government of Karnataka, US NIH, non-profit organizations and private organizations including Wellcome and Lowe's Services India. She also declared receiving a travel grant as an invited plenary speaker at the AAIC. **While Dr Alladi's research is related to these guidelines, it was decided that research support from government institutions and non-profit organizations that goes to her institution will be unlikely to affect her judgement and therefore does not preclude contribution as an expert reviewer. The funding from Lowe's Services India is for a project unrelated to dementia risk reduction. No further action was deemed necessary.**

3. **ALLEGRI, Ricardo (Institute for Neurological Research – FLENI, Argentina)** declared research support from a non-profit organization, Alzheimer's Association, for the Latin American Initiative for Lifestyle Intervention to Prevent Cognitive Decline (LatAm FINGERS). **While the declared interests are related to the topic of these guidelines, the declared non-profit research funding go to Dr Allegri's institution and therefore was deemed unlikely to affect his judgement, but rather speaks to his expertise. No further action was deemed necessary.**

4. **BAUMGART, Matthew (Alzheimer's Association, USA)** declared employment with Alzheimer's Association USA. He is the Vice President of Health Policy, Alzheimer's Association. **This interest was deemed insignificant or minimal and unlikely to affect, or be reasonably perceived to affect, Mr Baumgart's judgement in the review of the guidelines. He is deemed to be participating in the external peer review process in an individual capacity and not representing any organization. No further action was deemed necessary.**

5. **BRAYNE, Carol (University of Cambridge, United Kingdom)** declared research support on epidemiological studies of dementia from Alzheimer's Society, a non-profit organization, as well as government funding from UK Research and Innovation, and National Institute for Health and Care Research. **While the declared interests are related to the topic of these guidelines, the declared government and non-profit research funding goes to Dr Brayne's institution and therefore was deemed unlikely to affect her judgement, but rather speaks to her expertise. No further action was deemed necessary.**

6. **BRODATY, Henry (University of New South Wales, Australia)** declared dementia research support from government funding, specifically National Health and Medical Research Council, Medical Research Future Fund and NIH. He also declared that he is on advisory boards for pharmaceutical companies for which he receives compensation for meetings, specifically Eisai Australia, Eli Lilly Australia, Medicines Australia, Roche Australia and Novo Nordisk Australia. **While the declared interests are related to the topic of these guidelines, the declared government funding goes to Dr Brodaty's institution and therefore was deemed unlikely to affect his judgement, but rather speaks to his expertise. His advisory roles were deemed to demonstrate his expertise, and he is deemed to be participating in the peer review process in an individual capacity and not representing any organization. No further action was deemed necessary.**

7. **DEBETTE, Stéphanie (Paris Brain Institute, France)** declared that she is on advisory boards of public institutions, specifically the German Center for Neurodegenerative Diseases (DZNE), Ludwig-Maximilians-Universität München (University of Munich), and British Heart Foundation (BHF) Centre of Research Excellence on vascular brain diseases in

Edinburgh, the United Kingdom. No compensation is received. She also declared previously holding the position of Director of the Vascular Brain Health Institute (VBHI) and the Bordeaux Population Health Research Center at the University of Bordeaux. Dr Debette declared serving as the referent for omics studies at the VBHI. Dr Debette also serves on the research steering committee of the CHARGE (Cohorts for Heart and Aging Research in Genomic Epidemiology) consortium and has previously served on the International Stroke Genetics Consortium steering committee. She has also been on the Data Safety Monitoring Board of the CASES clinical trial (NCT06511089) sponsored by University Medical Center Groningen without compensation. Dr Debette has received compensation (<€1000) for presentations at the European Stroke Organization Conference (ESOC) and the Japanese Stroke Conference. Dr Debette also declared being a co-applicant on a patent that has been filed on a putative therapeutic target for cerebral small vessel disease. **Dr Debette's advisory roles, committee memberships and previous director roles were deemed to demonstrate her expertise and be unlikely to affect her judgement overall. She is deemed to be participating in the peer review process in an individual capacity and not representing any organization. The patent that was declared is outside the scope of these guidelines. Overall, it was decided that none of the declared interests preclude Dr Debette from participating as a peer reviewer. No further action was deemed necessary.**

8. **IBÁÑEZ, Agustín (Latin American Brain Health Institute, Chile, and Global Brain Health Institute, Trinity College Dublin, Ireland)** declared research support from government funders including US NIH, Ministry of Education Argentina, Government of Chile and Horizon 2020 (EU). Dr Ibáñez declared research support from non-profit organizations including Wellcome, Atlantic Institute and Global Brain Health Institute. He also declared research support from pharmaceutical companies Takeda and Alector Inc. Due diligence was performed and assessed in view of the nature of specific research projects being funded and the real or perceived risk of these grants affecting Dr Ibáñez's judgement. **Receiving research grants for dementia research that go to Dr Ibáñez's institution from government agencies and non-profit organizations was deemed to demonstrate his expertise in the area and be unlikely to affect his judgement overall. The research support from pharmaceutical companies does not go directly to Dr Ibáñez but to his institution and relates to electroencephalographic (EEG) biomarkers and genetic screening (outside the scope of these guidelines) and is unlikely to affect his judgement. Overall, it was decided that none of the declared interests preclude Dr Ibáñez from participating as an external peer reviewer of the guidelines. No further action was deemed necessary.**

9. **LEVINSON, Anthony (McMaster University, Canada)** declared public research grants on dementia prevention from the Public Health Agency of Canada. He also declared intellectual property – specifically, shared copyright – in DementiaRisk.ca e-learning, a free public resource with no associated costs or royalties. This is co-owned with McMaster University. Dr Levinson does not receive any income or royalties for this. **While the research content is related to the topic of these guidelines, it was decided that research support from the Public Health Agency of Canada that goes to his institution would be unlikely to affect Dr Levinson's judgement and therefore does not constitute a conflict of interest for the purpose of these guidelines. The intellectual property declared was deemed not to constitute a conflict of interest. No further action was deemed necessary.**

10. **LIVINGSTON, Gill (University College London, United Kingdom)** has declared research support on dementia prevention from UK Research and Innovation, National Institute for Health and Care Research and non-profit organizations, specifically Wellcome and Alzheimer's Society. Dr Livingston leads the Lancet Standing Commission on Dementia Prevention, Intervention and Care, which published reports in 2017, 2020 and 2024. **While the research content is related to the topic of these guidelines, it was decided that research support from government institutions and non-profit organizations that goes to Dr Livingston's institution would be unlikely to affect her judgement and therefore does not constitute a conflict of interest for the purpose of these guidelines. Leading the Lancet Standing Commission was deemed to demonstrate Dr Livingston's expertise, and she is deemed to be participating in the peer review process in an individual capacity and not representing any organization. No further action was deemed necessary.**

11. **MA'U Etuini (University of Auckland, New Zealand)** declared research support for a clinical training fellowship on dementia prevention from the Health Research Council of New Zealand. **While Dr Ma'u's research is related to these guidelines, it was decided that research support from this government institution will be unlikely to affect his judgement and therefore does not preclude contribution as an expert reviewer. No further action was deemed necessary.**

12. **STEPHAN, Blossom (Curtin University, Australia)** declared receiving dementia research grants as lead investigator from government funding, specifically National Institute for Health and Care Research, UK Research and Innovation, and Western Australia cohort studies research support program. Dr Stephan declared support from the Academy of Medical Sciences, a non-profit organization in the United Kingdom. She also declared being a board member of the Dementia Australia Research Foundation. **While Dr Stephan's research is in parts related to these guidelines, it was decided that research support from government institutions that goes to her institution is unlikely to affect her judgement and therefore does not preclude contribution as an expert reviewer. Her board membership was deemed to speak to her expertise. No further action was deemed necessary.**

Experts who did not declare any conflicts were:

1. ALBANESE, Emiliano
2. BROULÍKOVÁ, Hana
3. CHARWAY-FELLI, Augustina
4. DURRANI, Abida
5. GOUIDER, Riadh
6. GUEKHT, Alla
7. HOLTZHAUSEN, Berrie
8. IKIZ, Burcin
9. MICHALSKA, Malgorzata
10. PAGAN, John-Richard
11. QASSEM, Tarik
12. ROCHFORD-BRENNAN, Helen
13. SHAHUZA, Aminath
14. SUHRAWARDY, Rashed
15. WATTANAVITUKUL, Peach
16. YEATES, Bill

Conclusion

A total of 38 external experts were invited to provide peer review of the guideline update. Of these, 28 completed the review. Five experts did not respond to the invitation, one declined to participate, and four did not complete the review process. Among the 28 experts who completed the peer review, 12 declared some kind of interest. All interests were analysed by members of the WHO Neurological, Sensory and Oral Conditions Unit, and were duly evaluated according to the WHO guidance on conflict of interest. Overall, declared interests were found to be relatively minor and unlikely to affect the experts' judgement in the proposed activities.

Although some of the research grants declared by the experts are related to the subject of the guideline update, they were deemed to pose minimal or no risk of conflict of interest. Some activities performed by the experts were tangentially related to the scope of the guideline update and resulted in nominal payments or reimbursements for experts. These were deemed inconsequential in importance or had ceased and were therefore unlikely to affect current behaviour.

Web annexes

Web Annex A
Evidence profile and evidence-to-decision table for cognitive activity
(https://doi.org/10.2471/B09793)

Web Annex B
Evidence profile and evidence-to-decision table for social activity
(https://doi.org/10.2471/B09795)

Web Annex C
Evidence profile and evidence-to-decision table for healthy balanced diet and nutrition
(https://doi.org/10.2471/B09796)

Web Annex D
Evidence profile and evidence-to-decision table for management of obesity
(https://doi.org/10.2471/B09797)

Web Annex E
Evidence profile and evidence-to-decision table for management of diabetes
(https://doi.org/10.2471/B09798)

Web Annex F
Evidence profile and evidence-to-decision table for management of hypertension
(https://doi.org/10.2471/B09799)

Web Annex G
Evidence profile and evidence-to-decision table for management of hearing loss
(https://doi.org/10.2471/B09800)

Web Annex H
Evidence profile and evidence-to-decision table for use of menopausal hormone therapy
(https://doi.org/10.2471/B09801)

Web Annex I
Evidence profile and evidence-to-decision table for management of depression
(https://doi.org/10.2471/B09802)

Web Annex J
Evidence profile and evidence-to-decision table for management of stroke
(https://doi.org/10.2471/B09803)

Web Annex K
Evidence profile and evidence-to-decision table for management of traumatic brain injury
(https://doi.org/10.2471/B09804)

Web Annex L
Evidence profile and evidence-to-decision table for management of vision impairment
(https://doi.org/10.2471/B09805)

Web Annex M
Evidence profile and evidence-to-decision table for management of sleep
(https://doi.org/10.2471/B09806)

Web Annex N
Evidence profile and evidence-to-decision table for management of HIV
(https://doi.org/10.2471/B09807)

Web Annex O
Evidence profile and evidence-to-decision table for reducing air pollution
(https://doi.org/10.2471/B09808)

Web Annex P
Evidence profile and evidence-to-decision table for multidomain interventions
(https://doi.org/10.2471/B09809)

For more information,
please contact:

Department of Noncommunicable Diseases
and Mental Health

World Health Organization
Avenue Appia 20
CH-1211 Geneva 27
Switzerland

E-mail: whodementia@who.int
https://www.who.int/health-topics/dementia