

REVIEW

Open Access



Adherence and intensity in multimodal lifestyle-based interventions for cognitive decline prevention: state-of-the-art and future directions

Natalia Soldevila-Domenech^{1,2}, Amaia Ayala-Garcia¹, Mariagnese Barbera^{3,4}, Jenni Lehtisalo^{3,5}, Laura Forcano^{1,6}, Ana Diaz-Ponce⁷, Marissa Zwan⁸, Wiesje M. van der Flier⁸, Tiia Ngandu^{5,9}, Miia Kivipelto^{4,9,10,11}, Alina Solomon^{3,4,9} and Rafael de la Torre^{1,6,12,13*} 

Abstract

Preventing dementia and Alzheimer's disease (AD) is a global priority. Multimodal interventions targeting several risk factors and disease mechanisms simultaneously are currently being tested worldwide under the World-Wide FINGERS (WW-FINGERS) network of clinical trials. Adherence to these interventions is crucial for their success, yet there is significant heterogeneity in adherence reporting across studies, hindering the understanding of adherence barriers and facilitators. This article is a narrative review of available evidence from multimodal dementia prevention trials. A literature search was conducted using medical databases (MEDLINE via PubMed and SCOPUS) to select relevant studies: nonpharmacological multimodal interventions (i.e., combining three or more intervention domains), targeting individuals without dementia, and using changes in cognitive performance and/or incident mild cognitive impairment or dementia as primary outcomes. Based on the findings, we propose future adherence reporting to encompass both participation (average attendance to each intervention component) and lifestyle change using dementia risk scores (e.g., the LIBRA index). Moreover, we provide an estimation of the expected intensity of multimodal interventions, defined as the ratio of the expected dose (i.e., the overall amount of the intervention offered specified in the trial protocol) to duration (in months). Adjusting the expected dose by average adherence enables estimation of the observed dose and intensity, which could be informative for identifying optimal dosage thresholds that maximize cognitive benefits across different populations. Finally, this article provides an overview of the determinants of adherence to multimodal interventions, emphasizing the need for improved adherence reporting to inform the design and implementation of precision prevention interventions.

Keywords Adherence, Intensity, Lifestyle intervention, Multimodal intervention, Alzheimer's disease, Prevention; review

*Correspondence:
Rafael de la Torre
rtorre2@researchmar.net

Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

Background

Alzheimer's disease (AD), the most prevalent cause of dementia, develops over a long preclinical period and its progression is associated with modifiable lifestyle factors [1, 2]. This offers a window of opportunity for testing early preventive measures. In the last decade, there has been a shift toward multimodal lifestyle-based interventions for dementia prevention (e.g., combining diet, physical activity, cognitive training, vascular risk monitoring, or social interaction), due to the multifactorial nature of this condition [3]. In contrast to interventions targeting one risk factor alone, multimodal interventions target multiple risk factors simultaneously and are expected to generate additive or synergistic preventive effects. However, there is still limited evidence on the effectiveness of multimodal interventions for the prevention of cognitive decline [4]. Additionally, uncertainties persist regarding barriers and facilitators of adherence and response to multimodal interventions, modes of intervention delivery, and the intervention intensity (dose, duration, and adherence) required to influence cognitive performance [5]. Addressing these questions is crucial for advancing and optimizing multimodal interventions for dementia prevention, both at the individual (i.e., personalized prevention), and population levels (i.e., precision prevention) [6, 7].

The effectiveness of a next generation of precision prevention interventions for cognitive decline will rely on how effectively preventive programs are provided to populations of interest, their ability to adhere to such interventions, and the ability of healthcare providers to monitor adherence and adjust the intervention as needed. Adherence is recognized as the strongest predictor of intervention success [8]. However, there is a paucity of studies addressing the determinants of adherence to multimodal interventions [9–14]. This gap in evidence is, in part, attributed to the absence of a gold standard definition of adherence to these complex multimodal interventions. Although a single definition may not universally apply to all studies, the development of consensus-based recommendations for measuring and reporting adherence to multimodal interventions could enhance consistency across studies and thus establish global standards for conducting comparative effectiveness research. This is particularly important in the framework of international collaborative networks conducting multimodal intervention trials aimed at preventing cognitive decline, e.g., the World-Wide FINGERS (WW-FINGERS) network [15]. Harmonizing measures of adherence to multimodal interventions will facilitate pooled analyses, which are crucial for providing robust evidence about adherence profiles and progressing in AD prevention research.

The aim of this narrative review is to provide an overview of the available evidence on adherence and efficacy from multimodal dementia prevention trials.

Main text

Methodology

An English-language literature search was conducted using medical databases (MEDLINE via PubMed and SCOPUS, through November 29th, 2024) and keywords such as “multidomain”, “intervention”, “dementia”, “prevention” and “cognitive decline”. Additional studies were identified through the reference lists of selected publications and the researchers' expertise on WW-FINGERS studies. The search strategy, screening process, and data selection adhered to PRISMA guidelines [16]. The following criteria were used to select relevant studies, including both randomized controlled trials (RCTs) and protocols: nonpharmacological multimodal interventions (defined as combining three or more intervention domains) with a duration of at least 6 months, a target population including individuals without dementia at baseline, and cognitive performance and/or incident mild cognitive impairment (MCI) or dementia as primary or secondary outcomes. This review was not registered in the International Prospective Register of Systematic Reviews (PROSPERO).

During the screening process, two independent reviewers (NS-D and AA-G) assessed eligibility based on titles and abstracts. Data extraction for the narrative review was conducted by one researcher (NS-D), capturing details on study design, multimodal intervention characteristics (e.g., dose, duration, adherence), and primary outcome measures. Quality assessment of the studies included was not conducted.

The database search identified 417 unique articles, with an additional 13 articles retrieved from other sources (Supplementary Fig. 1). After screening, 45 articles were selected for full-text review of clinical trials. Of these, 24 completed clinical trials met the inclusion criteria for analysis, and were distributed geographically as follows: 12 from Asia, 10 from Europe, and 2 from America. Among the excluded articles, 25 protocols of ongoing clinical trials were identified and included in the data synthesis of adherence reporting and assessment of the expected intensity of the multimodal intervention. These protocols were distributed geographically as follows: 8 from Europe, 7 from Asia, 5 from America, 4 from Australia, and 1 from Africa.

Adherence definition in multimodal studies

Adherence is defined as the degree to which the person's behavior corresponds with the agreed-upon recommendations from a healthcare provider [8]. It differs from compliance, which is the extent to which a patient's

Table 1 Reporting of adherence to multimodal interventions for preventing cognitive decline

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
1. Completed studies with published results of adherence			
FINGER (Finland; 2009–2014)	Dietary counseling, exercise and cognitive training, and vascular risk factor monitoring	Simultaneous adherence to all assigned intervention components (CV monitoring, Nutrition, Physical activity, Cognitive training): - 19.0% were adherent to at least 66% of prescribed treatment - 38.9% were adherent to at least 50% of prescribed program (i.e., <i>adherent</i>) - 42% were adherent to less than 50% of prescribed program (i.e., <i>adherent</i> to at least two components; <i>partially adherent</i>) - 21% were adherent to 0% of the prescribed program (i.e., <i>nonadherent</i>)	[9]
		CV monitoring visits: - 94.6% were adherent to at least 50% of prescribed program - 92.9% were adherent to at least 66% of prescribed program	
		Nutrition: - 90.0% were adherent to at least 50% of prescribed program	
		Physical activity: - 60% were adherent to at least 50% of prescribed program	
		Cognitive training (individual + group sessions): - 47.2% were adherent to at least 50% of prescribed program - 24.7% were adherent to at least 66% of prescribed program	
		Cognitive training (only individual sessions): - 63% participated in the cognitive training at least once - 20% completed at least 50% of the training sessions - 12% completed 100% of the training - Mean number of sessions (SD): 45.7 (54.95) - Median number of sessions: 15 (95%CI 6–23)	
		Multidomain sessions: - 53.5% were adherent to at least 75% of prescribed program - 64.4% were adherent to at least 66% of prescribed program	
		Omega-3 capsules: - 71.5% were adherent to at least 75% of prescribed program - 76.1% were adherent to at least 66% of prescribed program	
		Simultaneous adherence to all assigned intervention components (Multidomain sessions and Omega-3 capsules): - 50.7% were adherent to at least 75% of prescribed program - 61.1% were adherent to at least 66% of prescribed program	
		Cardiovascular consultations: - 90.1% for the baseline visit - 71.9% for the 1-year visit - 62.3% for the 2-year visit	
MAPT (France; 2008–2014)	Integrated cognitive training, physical activity, and dietary advice and preventive consultations plus omega-3 PUFAs	Multidomain dose: - Range: 1–37 - Mean number of sessions (SD): 25.86 (9.26)	[9, 42]

Table 1 (continued)

Study (country; start-comple-tion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
eMIND (France; 2017–2019)	Web-based mul-tidomain lifestyle training interven-tion including cognitive training, exercise training, and nutritional advices	Adherence to the MI: Participants accessing all the three interventions (clicking on the multidomain contents in their personal agenda in the web-plat-form) for at least 75% of the requirements were considered adherent - 63.8% of participants adhered to the cognitive training - 60.3% of participants adhered to the nutrition intervention - 5.2% of participants adhered to the physical exercise intervention - 5.2% of participants adhered to all multidomain components - 53.4% of participants followed ≥ 50% of the requested frequency in exercise training (they connected once a week) - 75.8% of participants followed ≥ 50% of the requested frequency in cognitive training - 81% of participants followed ≥ 50% of the requested frequency in nutrition	[63]
preDIVA (The Neth-erlands; 2006–2013)	Multidomain cardiovascular in-tervention (advice)	Multidomain dose: - 22.0% were nonadherent: Participants who on average had received less than 2 out of 3 annual intervention visits (< 66%) upon reaching a study end-point (dementia/death/end of trial)	[14]
HATICE (The Neth-erlands; Finland, France; 2015–2018)	Internet-based platform with remote support from a coach trained in motiva-tional interview-ing and lifestyle behavior advice	Login frequency: - 80% were adhered to the intervention (per-protocol analysis), defined as those who logged onto the platform in at least 12 out of 18 months study participation, and who set at least one goal or entered one or more measurements. - Reasonable uptake: Median of two logins per month in the platform with a wide range and a substantial proportion logging in more than five times a month), almost all participants setting at least one goal (with a considerable proportion up to three goals), and the majority of participants using the platform during the full study period. Number of messages exchanged between coach and participant: - 9.6% of the participants who completed the primary outcome sent 0 messages - 33.9% sent 1–5 messages - 29% sent 6–10 messages - 27.5% sent > 10 messages Number of goals set: - Median of 1 goal (IQR 1–2) - 9.8% set no goal - 47.3% set 1 goal - 34.0% set 2–3 goals - 8.9% set ≥ 4 goals	[26]

Table 1 (continued)

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
MIND-ADmini (Sweden, France, Germany, Finland; 2017–2020)	Nutritional guidance, exercise, cognitive training, vascular/metabolic risk management and social stimulation Medical food	Reporting of adherence to the multimodal intervention Adherence to individual intervention components: - 71.9% of participants adhered to the cognitive training intervention (attendance to 66% of group and individual sessions). - 68.8% of participants adhered to the nutrition intervention (attendance to 66% of sessions). - 81.3% of participants attended both the 3- and 6-month follow-up visits with the study nurse. - 78.1% of participants adhered to the exercise intervention (attendance to 40% of group-based gym sessions). - 87.1% of participants consumed ≥ 60% of medical food product (measured through a study product diary). - 78.1% and 87.1% of participants in the lifestyle and lifestyle + medical food arms were overall adherent, respectively. Overall adherence to the intervention (composite measure of participation in different intervention components): - 78.1% of participants in the lifestyle intervention arm attended a minimum of 40% of sessions per domain, in at least 2/4 domains (exercise, nutrition, cognitive training and monitoring of vascular/metabolic risk factors). - 87.1% of participants in the lifestyle + medical food intervention arm attended a minimum of 40% of sessions per domain, in at least 2/4 domains, and additionally consumed at least 60% of the medical food study product. Overall adherence to healthy lifestyle changes: composite healthy lifestyle score (ranges 0–8 points) based on the FINGER study(64). A score from 0 to 2 was assigned to each tertile of the healthy dietary intake score, physical activity level, cognitive and social activities, and cardiovascular risk burden	[64, 65]
AgeWell.de (Germany; 2018–2022)	Nutritional counseling, enhancement of physical and social activity, cognitive training, and the management of cardiovascular risk factors (overweight, smoking).	Adherence to the MI: it was evaluated by asking to what extent participants were able to reach their goals in the domains of nutrition, physical activity, cognitive activity, and social activity (response options: not at all [0]–absolutely [4]). Adherence to all intervention components was summed across all seven points in time, leading to a score ranging from 0 to 28. Nutrition component (0–4 points): - Mean adherence (SD): 2.80 (0.71) Cognitive activity (0–4 points): - Mean adherence (SD): 2.90 (0.78) Physical activity (0–4 points): - Mean adherence (SD): 2.66 (0.82) Social activity (0–4 points): - Mean adherence (SD): 2.81 (0.76) All components (0–28 points): - Not reported	[25]

Table 1 (continued)

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
GOIZ ZAINDU (Spain; 2018–2020)	Nutrition counseling, management of vascular risk factors, physical activity, and individual- and group-based cognitive intervention	Overall adherence to the MI: - 54.7% of participants had high adherence (attendance to all intervention components was higher than 50%) - 17.2% had partial adherence (attendance to at least 30% of activities of all intervention components) - 18.8% had low adherence (attendance to any intervention components was lower than 30%) - 9.4% had very low adherence (attendance to less than 30% to two or more intervention components) Nutrition component: - 73.4% completed at least 2/3 nutrition counseling visits - Mean adherence: 74.5% CV monitoring component: - 67.2% completed at least 2/3 cardiovascular monitoring visits - Mean adherence: 73.44% Individual cognitive training: - 64.1% completed > 50% of the cognitive training individual materials - Mean adherence: 55.47% Group cognitive training: - 70.0% attended > 50% of cognition stimulation workshops - Mean adherence: 54.78% Physical exercise: - > 75% of participants reported practicing physical exercise at least twice a week during the intervention period. - Mean adherence: 76.56%	[18]
ASPIs (Austria; 2010–2014)	Intensive control and motivation for better compliance with prescribed evidence-based medication, regular blood pressure measurements, healthy diet, regular physical activity and cognitive training.	Dietary individual counseling visits (7 in total): - Median (IQR) attendance: 5 (3–5) Dietary group counseling visits (7 in total): - Median (IQR) attendance: 7 (3–7) Physical activity group meetings (9 in total): - Median (IQR) attendance: 8 (4–11) Cognitive group meetings (24 in total): - Median (IQR) attendance: 12 visits (5.5–17)	[66, 67]

Table 1 (continued)

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
StayFitLonger (Switzerland, Canada, Belgium; 2019–2021)	Computerized physical and cognitive training exercises, plus social interactions through access to a moderated Chat Room, psychoeducational content, and gamification elements.	Mean time weekly spent using the program: - 2.6 (SD = 0.3) hours	[68]
SMARRT (USA; 2018–2022)	Multidomain health coaching sessions offered every 4 to 6 weeks	Health contacts: - Mean (SD): 18.8 (5.5) - Range: 1–28	[69]
COCOA (USA; 2018–2022)	Remotely coached multimodal lifestyle intervention	Adherence to the MI: - 86% of participants remained actively engaged with their coach longer than one year - 20.7% of participants remained actively engaged with their coach after two years	[70]
Meng X, et al. 2024 (China; 2017–2017)	Online education, cognitive training and community activities	Adherence to online material (number of times that the participants completed the readings): - Mean adherence: 70% Adherence to computer-based cognitive training (number of times that the participants completed the trainings): - Mean adherence: 26.1% Adherence to face-to-face activities (% of intervention activities attended): - Mean adherence: 65.2%	[71]
J-MINT (Japan; 2019–2022)	Multicomponent intervention including physical exercise, nutrition counseling and cognitive training	Physical activity - Mean adherence: 83% (64.9 ± 15.8 out of 78 sessions) - 84% of participants adhered to ≥ 70% of group-based physical exercise sessions Cognitive training - Mean adherence: 44.4% (69.2 ± 96.9 out of 156 sessions) - 18% of participants adhered to 100% of the cognitive training sessions	[35, 72]
Bae S, et al. 2019 (Japan; 2017–2017)	Multicomponent intervention including physical, cognitive, or social activity sessions	Adherence to the MI: - 70.2% of participants attended to the MI	[73]

Table 1 (continued)

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
SUPERBRAIN (South Korea; 2019–2020)	Vascular risk monitoring and management, cognitive training and social activity, physical exercise, nutritional guidance, and motivational enhancement	- Adherence to the MI: 94.5% (95%CI 91.4, 97.6%) - Vascular and metabolic program: 98.0% - Cognitive training: 97.4% - Social activity: 95.9% - Physical exercise: 91.0% - Nutrition: 94.2% - Motivational enhancement program: 97.7%	[74]
SINGER-Pilot (Singapore; 2018–2020)	Dietary counseling, exercise and cognitive training, and vascular risk factor monitoring	CV monitoring visits: - 100% of participants completed 100% of the sessions Home-based exercise: - 53% of participants completed > 50% of the sessions Food diary completion: - 97% of participants filled the food diary in > 50% of their meals for the three required days at each time point Cognitive training: - 81% of participants completed > 50% of the training	[75]
Ng PEM, et al. 2021 (Singapore; 2018–2020)	Computerized cognitive training, physical-cognitive dual-task exercises (in small group activities) and nutritional guidance (through mobile app)	Physical-cognitive dual task sessions: - Mean adherence (SD): 75.78% (19.13) Small group activities: - Mean adherence (SD): 78.90% (20.25) Computerized cognitive training: - Mean adherence (SD): 70.99% (23.77) Nutritional mobile application: - Used by 15% of participants	[76]
S-FIT (Singapore; 2009–2014)	Cognitive training, physical training, and nutritional intervention (dietary supplement)	Adherence to the MI: measured monthly by estimating the proportion of dietary supplements consumed and training sessions completed. - Mean adherence: 88%	[77]
Ongoing studies within the WW-FINGERS network with prespecified reporting of adherence in the study protocol			

Table 1 (continued)

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
LETHE (Austria, Finland, Italy, Sweden)	Nutritional counseling, exercise, cognitive training, management of vascular/metabolic risk factors, social activity, and sleep and relaxation	Individual components: - Usage of and engagement with the mobile app and smartwatch (frequency and duration of logins). - o During the first 6 months, 50.5% of participants in the intervention group used the full app daily. The median duration of a single session of app usage was 42.1 s in the intervention group. Most participants (98.7%) completed a digital cognitive testing one month after baseline visit. - Participation in study visits and intervention-related activities and meetings.	[31, 78]
		Overall adherence to the intervention: - Adherence to a healthy lifestyle: composite score developed in FINGER, based on self-reported data on exercise, diet, smoking and alcohol, and social and cognitive activity.	
PENSA (Spain)	Nutritional counseling, physical activity, cognitive training, psychoeducation sessions and social stimulation sessions.	Nutrition counseling visits: - Mean percentage of sessions (SD): 90.3% (29.6) - 34.4% were adherent to 100% of sessions - 80.2% were adherent to 89% of sessions (8 out of 9 visits) - 99% were adherent to 78% of sessions (7 out of 9 visits)	[32] (unpublished data)
		Gymnasium classes: - Mean percentage of sessions (SD): 62.1% (38.2) - 45.8% were adherent to ≥ 75% of sessions - 70.0% were adherent to ≥ 50% of sessions	
		Cognitive training: - Mean percentage of sessions (SD): 72.6% (30.8) - 60.4% were adherent to ≥ 75% of sessions - 83.3% were adherent to ≥ 50% of sessions	
		Psychoeducation sessions: - Mean percentage of sessions (SD): 79.0% (40.8) - 75.0% were adherent to ≥ 70% of sessions	
		Ecological Momentary Assessments (EMAs): average weekly adherence, calculated as the number of days that participants completed the dietary EMAs questionnaire divided by 7 days - Mean weekly compliance (SD): 89.0% (17.5) - 93.4% had ≥ 75% of compliance	
		Fitbit: number of complete observations, defined as at least 600 min of valid minute heart rate signal per day (i.e., wear time indicator) - Mean monthly valid data (SD): 84.1% (36.6) - 60.4% had valid data in ≥ 90% of days - 79.2% had valid data in ≥ 75% of days - 92.7% had valid data in ≥ 50% of days	
		Epigallocatechin-3-gallate (EGCG): presence of ≥ 10 ng/mL of EGCG in plasma - 93.5% of compliance at 6 months - 85.1% of compliance at 12 months	

Table 1 (continued)

Study (country; start-completion dates)	Multimodal intervention	Reporting of adherence to the multimodal intervention	Ref
MET-FINGER (UK, Finland, Sweden)	1. Dietary counseling, exercise and cognitive training, and vascular and metabolic risk factor monitoring 2. Metformin when appropriate	Individual components: - Cognitive training: attendance at the cognitive training sessions including automatic recordings of computer program use, and group sessions attendance. - Nutrition: attendance at the 7 group and 3 individual nutrition sessions. - Vascular and metabolic risk factors monitoring: attendance to 6 individual consultations (at least 3 with a study physician). - Physical exercise: participation in group exercise sessions. - Metformin: adherence to target dose and compliance to treatment. Overall adherence to the intervention: calculated through composite measure of participation in different intervention components.	[36]
LatAM-FINGERS (Argentina, Brazil, Bolivia, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Mexico, Paraguay, Peru, Puerto Rico, and Uruguay)	Exercise, diet, cognitive/social stimulation, and cardiovascular health	Implementation: level of fidelity to the intervention protocol estimated on the basis of: - % attendance to team meetings - % physical activity sessions completed - % cognitive training sessions completed - % telephone contacts completed - % health monitoring visits completed - Participant's self-reported adherence to the intervention	[30]
Africa-FINGERS (Kenya and Nigeria)	Exercise, diet, cognitive/social stimulation, and cardiovascular health	Intervention compliance/adherence will be measured via attendance records at group intervention meetings (eg, for physical, social, and cognitive activities), questionnaires on dietary changes/intake, subjective reports of satisfaction with progress to monitor skills/brain training, and regular vascular and metabolic risk monitoring (blood pressure, body mass index, and blood work).	[33]

The studies are sorted by country and continent of origin
CV = cardiovascular. IQR = interquartile range. MI = multimodal intervention. PUFA = polyunsaturated fatty acids

Table 2 Intensity of multimodal intervention studies

Study (country, start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose _{expected} /Length)	Observed intensity (Dose _{observed} /Length)	Main delivery mode	Cognitive outcome results	Ref
Completed studies								
FINGER (Finland; 2009–2014)	N=631 (60–77 years, CAIDE dementia risk score ≥ 6, and cognitive performance at the mean level or slightly lower than expected for age)	24	Expected: 256 sessions in total - 150 Cognitive training (6 group sessions and 144 training exercises) - 88 Physical exercise sessions (80 individual gym training sessions and 8 individual muscle training sessions) - 9 Nutrition counseling visits (3 individual and 6 group sessions) - 9 CV consultations (2 doctor and 7 nurse consultations)	10.6		Structured program	Intervention had beneficial effect on the NTB composite	[9, 10, 24, 62]
MAPT (France; 2008–2014)	N=837 (≥ 70 years, MMSE ≥ 24, with memory complaints, limitation in one IADL or slow gait speed)	36	Expected: 43 sessions in total (38 group sessions + 5 individual interviews) - 14 Multidomain sessions (combined cognitive training, nutrition and physical activity advice) - 14 Cognitive training sessions - 6 Physical activity advice - 3 Nutritional advice - 6 General health advice/Cardiovascular consultations - Omega-3 capsules (2 capsules/day) Observed: 28.86 (mean number of sessions)	1.2	0.8	Structured program	No effect of intervention on global cognition measured with a composite Z score combining four tests. No effect of intervention on other secondary cognitive outcomes.	[9, 42]
eMIND (France; 2017–2019)	N=60 (≥ 65 years, MMSE ≥ 24, with subjective memory complaints)	6	Expected: 117 sessions Participants were requested to follow both exercise and cognitive training twice a week, and nutritional advices every fifteen days;	19.5		Self-guided	No differences on global cognition measured with a composite Z score combining four tests. No effect of intervention on other cognitive outcomes.	[63]
preDIVA (The Netherlands; 2006–2013)	N=1293 (70–78 years without dementia)	72	Expected: 18 visits in total (every 4 months) with practice nurse and general practice where participants were assessed for CV risk factors and blood glucose and lipid concentrations (every two years). On the basis of these assessments, participants received individually tailored lifestyle advice.	0.3		Self-guided	No effect of intervention on dementia incidence.	[14, 61]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
HATICE (The Netherlands, Finland, France; 2015–2018)	N = 1194 (≥ 55 years without dementia, with CV risk factors, history of CVD or diabetes)	18	Expected: 72 logins in total (4 logins per month were expected)	4.0	1.8	Self-guided	No differences between groups in the MMSE or a composite Z score of seven cognitive tests. No effect of the intervention on any of the individual cognitive tests.	[26, 43]
			Observed: 32 logins in total (median of 1.8 logins per month)					
MIND-ADmini (Sweden, France, Germany, Finland; 2017–2020)	N = 63 (60–85 years, prodromal AD)	6	Expected: 106 sessions - 6 nutrition counseling visits (3–4 group and 3 individual sessions) - 48 exercise sessions (2 times/week) - 50 cognitive training sessions (2–3 group sessions and 48 individual training sessions twice a week) - 2 CV risk consultation visits at 3 and 6 months	17.7		Structured program	Not reported	[65]
			Medical food (a 125 ml once-a-day milk-based drink)					
AgeWell.de (Germany; 2018–2022)	N = 546 (60–77 years, CAIDE ≥ 9, without dementia)	24	Expected: 527 in total - 208 Physical activity sessions (exercises for strength/flexibility to be conducted at home twice a week) - 312 Cognitive training sessions (15 min, 3 times per week) - 7 Nutrition counseling visits (2 face-to-face and 5 via telephone) led by study nurses (0, 2, 4, 8, 16 and 20 months) - Management of vascular risk factors and individual goals for social activities in the regular general practitioner (GP) visits	22.0		Self-guided	No effect of intervention on global cognitive performance measured with a composite Z score combining five tests. In sensitivity analyses, beneficial intervention effects were observed on the domain of social cognition.	[25]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
GOIZ ZAINDU (Spain; 2018–2020)	N = 64 (+ 60 years, CAIDE ≥ 6, no dementia, cognitive performance below- than-expected or with MCI)	12	Expected: 156 sessions - 3 cardiovascular risk monitoring visits (month 3, 6, 9) - 5 nutritional visits (month 1, 3, 6, 7, 9) - 13 group-based cognitive stimulation sessions - 135 individual cognitive training sessions (3 times/week for 10 months) - Recommendations to practice 2 to 6 times/week of physical exercise Observed: 99 sessions - 2 cardiovascular visits (3 with 67.2% of average participation) - 3.7 nutritional counseling visits (5 with 73.4% of adherence) - 7.1 group-based cognitive stimulation sessions (13 with 54.8% of adherence) - 86.5 individual cognitive training sessions (135 with 64.1% of adherence) *Self-reported adherence	13	8.3	Structured program	No effect of intervention on global cognition measured with the modified NTB composite (mixed models of repeated measures analyses). However, the intervention reduced the risk of cognitive decline for the NTB executive function score and the NTB processing speed score.	[18]
ASPIS (Austria; 2010–2014)	N = 101 (40–80 years, MMSE ≥ 24, within 3 months after an acute stroke)	24	Expected: 45 sessions - 13 dietary counseling visits (7 group and 6 individual visits) - 8 physical exercise group meetings. - 24 cognitive training group sessions (monthly) Observed: 32 sessions - 12 dietary counseling visits (5 individual and 7 group; median adherence) - 8 physical activity group meetings (median adherence) - 12 cognitive group meetings (median adherence)	1.9	1.3	Structured program	No effect of intervention on global cognition measured with the ADAS-cog. No effect of intervention on cognitive decline or other secondary cognitive outcome variables.	[66, 67]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
StayFitLonger (Switzerland, Canada; Belgium; 2019–2021)	N=59 (≥60 years, MoCA ≥26, and Fried's frailty index <3)	6	Expected: 156 sessions in total During the 26 weeks of intervention, participants were asked to engage in physical exercise 3 days per week for 30–45 min and cognitive exercise for at least three 15-min sessions per week, and through a chat room had opportunities for social and contributing interactions, and psychoeducation content	26.0		Self-guided	In the overall sample, no effect of intervention on global cognition measured with the ZAVEN composite score. No effect of intervention on executive function, processing speed, or memory composites.	[68]
SMARTT (USA; 2018–2022)	N=82 (70–89 years and with ≥2 of 8 targeted risk factors)	24	Expected: 28 health coaching contacts (maximum number of contacts) - Health coaching sessions offered every 4 weeks during the first 3 months, and every 6 weeks for the final 15 months Observed: 18.5 (mean number of contacts)	1.2	0.8	Self-guided	Intervention had beneficial effect on the modified NTB composite	[69, 79]
COCOA (USA; 2018–2022)	N=31 (≥50 years with early AD)	24	Expected: 778 sessions: - 24 calls by a dietitian or nurse. - 24 text or email communications - 730 sessions of cognitive training (30 min/day during the 24 months)	32.4		Self-guided	Intervention had beneficial effect on the Memory Performance Index	[70, 80, 81]
COMBAT (China; 2019–2021)	N=86 (≥60 years at-risk)	9	Expected: 39 sessions in total - Multidomain training program consisting of mindfulness meditation, cognitive training, physical exercise, and nutrition counseling for 9 months, delivered with weekly group sessions at the community hospitals and self-monitoring homework.	4.3		Structured program	Intervention had beneficial effect on global cognition measured with a composite Z score combining seven tests	[82]
Yang Q-h, et al. 2022 (China; 2019–2021)	N=61 (≥65 years with MCI)	6	Expected: 102 sessions - 6 individual nutrition counseling visits. - 44 physical activity sessions (facility based; once/week for the first month and twice/week for months 2–6). - 48 cognitive training sessions (twice/week). - 4 vascular risk monitoring visits.	17.0		Structured program	Intervention had beneficial effect on the MoCA total score	[83, 84]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
Meng X, et al. 2024 (China; 2017–2017)	N=48 (≥ 60 years at risk)	6	Expected: 169 sessions - 153 online educational program, including 27 articles and 126 messages. - 12 cognitive training sessions (1/week, for 12 weeks). - 1 group discussion on dementia-related themes - 3 outdoor aerobic activities - 3 one-to-one voluntary services (only for 11 participants; not considered in the total dose) Observed: 115 sessions - 109 online educational program (70% adherence) - 3 cognitive training sessions (26% adherence) - 1 group discussion (74% adherence) - 2 outdoor aerobic activities (65% adherence)	28.2	19.2	Self-guided	Intervention had beneficial effect on global cognition measured with a composite Z score combining four tests (PACC)	[71]
J-MINT (Japan; 2019–2022)	N=265 (65–85 years with MCI)	18	Expected: 245 sessions - 78 physical exercise sessions in group - 11 nutrition counseling visits (8 telephone and 3 in-person meetings) - 156 cognitive training sessions (9 months of cognitive training at least 4 times/week) Observed: 146 sessions - 64.9 ± 15.8 physical exercise sessions (83% of adherence) - 69.9 ± 96.8 cognitive training sessions - No information on adherence rates to nutrition (11 sessions planned)	13.6	8.1	Structured program	No differences in cognitive performance measured with a composite Z score combining seven tests. Benefits on executive function/processing speed	[35, 72]
J-MIND-Diabetes (Japan; 2019–2022)	N=81 (70–85 years with type 2 diabetes and with MCI to mild dementia)	18	Expected: 48 sessions - 39 group-based physical exercise sessions - 9 individual nutritional counseling sessions (once every two months) - Recommendations to go out at least 3 times/week to promote social participation - Personalized goals for management of diabetes Expected: 48 sessions - Integrated 90-minute multimodal sessions twice weekly for 24 weeks (16 physical activity sessions, 16 cognitive activities sessions, and 16 social activities sessions)	2.7	8.0	Structured program	No differences in cognitive performance measured with a composite Z score combining eight tests	[85]
Bae S, et al. 2019 (Japan; 2017–2017)	N=41 (≥ 60 years with MCI)	6	Expected: 48 sessions - Integrated 90-minute multimodal sessions twice weekly for 24 weeks (16 physical activity sessions, 16 cognitive activities sessions, and 16 social activities sessions)			Structured program	No differences in cognitive performance measured with the MMSE. However, the intervention had beneficial effect on spatial working memory.	[73]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
SUPERBRAIN (South Korea; 2019–2020)	N = 51 (older adults with memory complaints)	6	Expected: 72 sessions in total - Participants visited a study facility three times a week to perform all intervention programs in group or individual sessions (during 24 weeks) Observed: 68 sessions (72 sessions with average adherence of 94.5%)	12	11.3	Structured program	Intervention had beneficial effect on global cognition measured with the RBANS total scale index score.	[74]
Park JE, et al. 2019 (South Korea; 2016–2017)	N = 13 (≥ 60 years, pre-frail/frail)	6	Expected: 13 sessions - 8 MI sessions: 4-week group-based intensive program - 5 Monthly monitoring sessions (20 weeks) during the maintenance program	2.1		Structured program	No differences in global cognitive performance measured with the CERAD-TS battery.	[86]
Ng PEM, et al. 2021 (Singapore; 2018–2020)	N = 96 (≥ 55 years at risk of cognitive impairment)	6	Expected: 48 sessions in total (biweekly sessions) - Cognitive training and physical activity: 31% physical-cognitive dual-task exercises and 69% cognitive sessions, of which 19% were based on small group activities and 50% were computerized cognitive training. Physical training of moderate intensity was conducted in supervised groups of 6 to 10 participants - Nutritional guidance was intended to be on-going via a mobile application throughout the length of the intervention, with one a month face-to-face nutritional talk with a dietitian	8.0		Self-guided	No effect of intervention on global cognition measured with the RBANS total score. No effect of intervention on specific cognitive domains.	[76]
S-FIT (Singapore; 2009–2014)	N = 49 (≥ 65 years, frailty, MMSE > 23)	6	Expected: 48 in total - 24 cognitive training sessions: 2-hour duration weekly group training sessions - 24 physical exercise: Moderate intensity physical exercise on 2 days per week in supervised groups for 12 weeks, followed by 12 weeks of home-based exercises - Daily nutritional supplement Observed: 42 (72 sessions with 88% of adherence)	8	7	Structured program	No effect of intervention on global cognition measured with the RBANS total scale index score. Intervention had beneficial effect on visuospatial construction.	[77]
SINGER-Pilot (Singapore; 2018–2020)	N = 34 (≥ 65 years with mild-to-moderate frailty)	6	Expected: 81 sessions - 4 dietary intervention sessions (2 group, 2 individual) - 3 vascular monitoring visits - 74 cognitive training sessions (72 cognitive training sessions plus 2 memory group talks) - Home-based physical exercise recommendations (twice weekly)	13.5		Structured program	Not reported	[75]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
THISCE (Taiwan; 2014–2016)	N = 549 (≥ 65 years, at risk)	12	Expected: 16 sessions - 16 Multimodal sessions: 4 during the first month, 2 during the second month, and 1 month during months 3–12	1.3		Structured program	No differences in cognitive performance measured with the MoCA test.	[87]
Ongoing studies within the WW-FINGERS network								
PENSA Study (Spain)	N = 104 (60–80 years, APOE-ε4 carriers with subjective cognitive decline)	12	Expected: 245 sessions in total - 144 individual cognitive training sessions (12/month) - 9 individual nutrition counseling visits - 72 group exercise sessions - 10 psychoeducation group sessions - 10 social and cognitive stimulation activities - EGCG intake (1–2 times/day) - Ecological momentary assessments-EMAs (daily) - Activity tracker (daily) Observed: 175 sessions in total - 104 cognitive training sessions (144 with 72.6% average adherence) - 8.1 individual nutrition counseling visits (9 visits with 90.3% of adherence) - 44.7 exercise sessions (72 sessions with 62.1% average adherence) - 7.9 psychoeducation group sessions (10 sessions with 79% of adherence) - 10 social stimulation sessions (no data on compliance)	20.4	14.5	Structured program		[32]
CITA GO-ON (Spain)	N = 547 (60–85 years, CAIDE ≥ 6, nondemented but with low performance in at least one of 3 cognitive tests)	24	Expected: 340 - 6 cardiovascular risk monitoring visits (1 visit every 4 months) - 6 group-based nutrition counseling visits - Recommendations to perform physical activity at home (30 min/day) - 16 group-based cognitive training sessions - 312 individual cognitive training sessions (15–20 min, 3 days/week)	14.1		Structured program		ClinicalTrials.gov Identifier: NCT04840030 [34]

Table 2 (continued)

Study (country; start- completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose _{expected} / Length)	Observed intensity (Dose _{observed} / Length)	Main delivery mode	Cognitive out- come results	Ref
FINGER-NL (The Netherlands)	N = 603 (60–80 years at risk)	24	Expected: 112 sessions The lifestyle intervention consists of 7 lifestyle domains including physical exercise, cognitive training, management of metabolic and vascular risk factors, nutritional counseling, sleep counseling, stress management, and social activities; and Souvenaid®. - 21 physical activity sessions (9 online group meetings, 7 study- site meetings and 5 personal lifestyle coach sessions). - 21 cognitive training sessions (5 online group meetings, 2 per- sonal lifestyle coach sessions, and 6 individual sessions provided via the digital intervention platform; plus 2 booster sessions during the second year, each including 2 online group meetings and 2 individual sessions). - 11 CV risk management visits (2 online group meeting, 4 at study-site group meetings and 6 personal lifestyle coach sessions) - 34 nutritional counselling visits (5 online group meeting, 1 at study-site group meeting, 24 individual online sessions and 4 personal lifestyle coach sessions) - 5 sleep counselling visits (1 online group meeting, 1 personal lifestyle coach sessions, 2 individual sessions provided via the digital platform; plus 1 booster session that includes an online group meeting) - 12 stress-management visits (7 study-site group meetings, 2 online group meetings and 3 individual online sessions) - 8 social activities (group meetings)	4.7		Mixed		[39, 40]
MET-FINGER (UK, Finland, Sweden)	N = 300 (60–79 years, APOE ε4- enriched population at increased risk of dementia)	24	Expected: 310 sessions - 10 dietary sessions (7 group and 3 individual sessions) - 144 physical activity sessions (92 in a gymnasium and 52 online) - 150 cognitive training sessions (6 in group and 144 indepen- dent training exercises) - 6 CV monitoring sessions (3 practical and 3 medical consultation) Metformin (2 times/day)	12.9		Structured program		[36]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
LETHE (Austria, Finland, Italy, Sweden)	N = 78 (60–77 years with increased dementia risk and sufficient digital readiness)	24	Expected: 532 sessions (approx.) - 5 dietary sessions (3–4 group and 1–2 individual sessions) - 209 physical activity sessions (1 in-person group session plus 1 session/week of independent strength training, and 1–5 sessions/week of independent aerobic training) - 315 cognitive training sessions (3 in group and 312 independent training) - 2–4 CV monitoring sessions	22.2		Mixed		[31]
BRAIN-DIABETES (Ireland)	N = 35 (50+ years with type 2 diabetes)	6	Expected: Not available - 4-month active lifestyle program in the community followed by 2 months of engaging in a self-directed lifestyle program: o 5 diet sessions: 1 online 90-min session with a nutritionist plus 4 online/telephone review meetings o 66 cognitive training sessions (4 individual cognitive training sessions per week for 30 min plus 2 introductory training sessions) o Remotely administered exercise intervention involving 1 online session with an instructor plus personalized recommendations to perform exercises at home that will increase in frequency and intensity over the first 4 weeks (number of sessions not specified) o 3 CV monitoring sessions			Mixed		ClinicalTrials.gov Identifier: NCT05304975 [88]
PDP (Luxembourg)	N = 450 (31–90 years; implementation study targeting individuals with SCD or MCI).		Expected dose: Not available - Voucher system to provide access to the program activities, with a broad range of choices for cognitive training, physical activity, and social activities; individual sessions with a dietitian, and counselling sessions with a psychologist.			Structured program		[89]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
U.S. POINTER (USA)	N = 1000 (at-risk older adults)	24	Expected: 769 sessions - 38 weekly meetings: The structured (STR) program included weekly meetings for the first 4 months, then 2x/month for 2 months, and then monthly, with specific goals for physical activity, diet, cognitive/social challenge and health monitoring. Meetings were performed in groups of 12–15 participants. - 416 physical activity sessions: 4 times/week of physical activity (4 times/week of moderate-to-high intensity aerobic exercise for 30 min, 2 times/week of resistance training with weight for 15–20 min, and 2 times/week of stretching/balancing activities) - 312 Computer-based cognitive training (3 times/week) and home-based cognitively and socially challenging activities (via Team Meetings) - 3 Health coaching visits (participants meet with a study Medical Advisor every 6 months)	32.0		Structured program		[27, 28]
Can Thumbs Up (Canada)	N = 350 (60–85 years, cognitively unimpaired or MCI with at increased risk of dementia)	12	Expected: Not available Fully remote web-based educational intervention (Brain Health Support Program intervention for 45 weeks). The program content is provided progressively to deliver new weekly content of 40 min. Participants are invited to go over the material at their own rate over the week.			Self-guided		[90]
LatAM-FIN- GERS (Argentina, Brazil, Bolivia, Chile, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Mexico, Paraguay, Peru, Puerto Rico, and Uruguay)	N = 600 (60–79 years at risk for dementia)	12	Expected: 364 sessions - 148 physical activity sessions (4 educational meetings + 144 group exercises on a regular basis; flexible protocol including 2–4 times/week sessions) - 4 dietary sessions (4 educational meetings + diet with nutritionist follow-up) - 208 cognitive training sessions (4 weekly sessions) - 4 medical monitoring sessions (4 educational meetings plus individual medical appointments)	30.3		Structured program		[30]
Africa-FINGERS (Kenya and Nigeria)	N = 300 (50–85 years at risk for dementia)	24	Expected: 359 sessions - 10 nutritional counselling visits (3 individual and 7 group sessions) - 312 physical activity sessions (2–4 sessions/week) - 32 cognitive training sessions (8 group sessions and 24 individual sessions performed once/week for ~6 months) - 5 individual cardiovascular monitoring sessions	15.0		Structured program		[33]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
SINGER (Singapore)	N=600 (60–77 years, at risk)	24	Expected: 254 sessions - 9 diet counseling sessions: 6 group-based nutrition advocacy workshops over 12 months plus 3 individual-based nutrition training sessions - 88 physical exercise sessions: once to twice weekly physical activity sessions (modified FINGER exercise program) - 154 cognitive training sessions: 10 cognitive training workshops plus 144 computer-based cognitive training sessions - 3 vascular risk factors management sessions	10.5		Structured program		[37]
MYB-Maintain Your Brain (Australia)	N=4250 (55–77 years with risk factors for dementia)	36	Expected: Not available Online: 4 modules (physical activity, nutrition, peace of mind, and brain training) administered based on individual risk profiles. Participants will complete their assigned modules sequentially, noting that the total number of modules varies depending on the respective individual's risk factors. In practice, this will translate to a minimum of two modules and a maximum of four modules. Each module lasts 10 weeks. Upon completing a module, booster sessions (specific to each module) and ongoing monitoring will then continue for up to three years.			Self-guided		[91]
AU-ARROW (Australia)	N=300 (55–79 years with risk factors for cognitive decline and dementia)	24	Expected: 764 sessions - 16 group education meetings during the first month. - 416 physical exercise sessions in a gymnasium: four times/week (with at least 2 group classes per week). - 23 diet counselling sessions via the group education meetings plus monthly individual follow-up consultations with a dietitian starting at month 2 (phone calls). - 264 computer-based cognitive training sessions. Brain training exercises start at month 3 and are performed at home four times/week. - 3 medical monitoring consultations (every 6 months) - 23 group meetings (1 session/month, starting at month 2) - 19 monthly group meetings to provide further health education and support starting at week 6.	31.8		Structured program		[29]
My-AGELESS (Malaysia)	N=165 (60–80 years with cognitive frailty)	24	Expected: not available - 12 Nutritional guidance sessions: 3 individual and 9 group sessions - Psychosocial interventions (number of sessions not specified) - Physical training sessions: progressively increasing from one to five times a week over a period of 21 weeks - 260 cognitive training sessions (3 times a week for 20 months)			Structured program		[92]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
FINOMAIN (Philippines)	N = 300 (≥ 60 years with type 2 diabetes)	12	Expected: 110 sessions - 104 physical/cognitive exercise: dance called INDAK (Improving Neurocognition through Dance and Kinesthetics): 1 h, twice per week - 3 Nutrition counseling visits (every 3 months) - 3 Vascular risk management (every 3 months) - Vascular care (blood pressure and fasting blood glucose are monitored every 2 months, blood lipids are monitored every 12 months, and group health education is held once every 6 months) - Lifestyle and dietary guidance to improve treatment and control of hypertension, diabetes, and dyslipidemia - Group walking activities (five times a week with each exercise lasting for 20–30 min) - Personalized leisure activities (paper cutting and chess games) - Cognitive training (three times a week, 20 min each time, each time includes 5 games, 4 min/game, and the training is carried out for 6 months each year, a total of 72 times)	9.2		Structured program		[38]
MIND-CHINA (China)	N = 760 (60–79 years)	NA						[93] Chinese Clinical Trial Registry number ChiCTR1800017758
Ongoing studies outside the WW-FINGERS network								
MINE (China)	N = 360 (≥ 50 years; MoCA < 26 points and MMSE > 22 points)	6	Expected: 176 sessions - 72 Exercise training group sessions, 3 times/week - 72 Meditation training (15–20 min after each exercise training session) - 4 Sleep guidance offline session every 1.5 months - 4 Dietary guidance every 1.5 months - 24 Health education: once a week for 6 months, in groups	29.3		Structured program		[41]
The Heritage Study (China)	N = 600 (60–80 years with MCI and modifiable life-style factors)	24	Expected: 316 sessions - 156 cognitive training sessions: 12 structured group guidance cognitive education workshops and 144 individualized cognitive training sessions (3 times/week during the first 12 months) - 144 home-based physical exercise sessions (about 3 times/week during the first 12 months) - 8 nutritional sessions: 6 group nutrition workshops and 2 targeted dietary instruction visits - 4 vascular risks monitoring visits - 4 group psychological counseling sessions	13.2		Mixed		[94]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose expected/Length)	Observed intensity (Dose observed/Length)	Main delivery mode	Cognitive outcome results	Ref
CHINA-IN-MUDI (China)	N = 772 (60–80 years at risk)	24	Expected: 104 sessions - 104 weekly integrated multidomain on-site intervention (lasting 100 min), including group physical training, group cognitive training, medical monitoring, and nutrition and cardiovascular lecture and consultant. - Participants were encouraged to perform at least five weekly sessions at home, with a minimum of 20 min per session	4.3		Structured program		[95]
J-MINT PRIME Tamba (Japan)	N = 100 (65–85 years with DASC-21 between 22–30 points and MMSE ≥ 24)	18	Expected: 78 interventions , delivered as one intervention per week and comprising four domains: - Lifestyle-related diseases management - Physical exercise (90 min per week) - 15 Nutrition counseling (3 times in-person guidance and 12 times telephone follow-up)apple - Cognitive training (4 days a week)	4.3		Structured program		[15]
Brain Boosters (USA)	N = 112 (≥ 65 years with SCD)	6	Expected: 15 sessions - 15 two-hour classes with education about a variety of memory support strategies and healthy lifestyle behaviors, focusing on physical and cognitive activity and stress management - Support in adopting new behaviors and tracking set goals with the Electronic Memory and Management Aid (EMMA) digital application	2.5		Structured program		[96]
The Gray Matters (USA)	N = 104 (40–64 years, at-risk or with MCI)	6	Expected: 39 sessions - 39 MI educational sessions - Social engagement workbook - Smartphone application with tips, feedback and weekly summaries - Personal coach (28 students volunteered to be personal coaches, who provided a weekly email or text message to participants to provide emotional support and encouragement of lifestyle goals)	6.5		Structured program		[97]
APPLE Tree programme (UK)	N = 352 (≥ 60 years with SCD or MCI)	6	Expected: 30 sessions - 20 group sessions during the first 6 months: 10 1-hour group video call sessions every fortnight, and video-call 'tea breaks,' less structured, to facilitate social sessions, in-between intervention sessions, with the same group - 10 individual goal-setting phone calls after each main session (every 2 weeks) during the first 6 months - Access to an online cognitive training platform (the number of sessions is not specified)	5		Structured program		[98]

Table 2 (continued)

Study (country; start-completion dates)	MI population	Length (mo)	Multimodal Dose ¹ (number of visits or sessions)	Expected intensity (Dose _{expected} /Length)	Observed intensity (Dose _{observed} /Length)	Main delivery mode	Cognitive outcome results	Ref
BetterBrains (Australia)	N = 645 (40–70 years; have a family history of dementia, and at least one modifiable risk factor for dementia)	12	Expected: 58 - 6 education and coaching sessions via telehealth during the active intervention phase - Access to psychoeducation material about dementia risk reduction - 52 weekly notifications and reminders to check-in on their recommended intervention.	4.8		Self-guided		[99]
HAPPI MIND (Australia)	N = 250 (45–65 years with ≥ 2 potential dementia risk factors)	24	Expected: 7 - 1 Individualized report with dementia risk based on ANU-ADRI questionnaire - 6 individualized dementia risk reduction motivational interview sessions over 24 months (face-to-face or via telephone or video telehealth) with a trained nurse. Interviews will include education on dementia and dementia risk reduction materials. - Access to the HAPPI-MIND app with support for self-management dementia risk factors at home and track progress against risk reduction goals	0.3		Self-guided		[100]

The studies are sorted by status (completed, ongoing). WW-FINGERS network membership (only for ongoing studies), country and continent of origin

¹The multimodal dose in structured intervention programs only considers the number of guided sessions, except for individual cognitive training sessions that are typically performed at participants' home

AD = Alzheimer's disease. ADAS-cog = Alzheimer disease assessment scale-cognitive. ANU-ADRI = Australian National University–Alzheimer Disease Risk Index. CAIDE = Cardiovascular Risk Factors, Aging, and Incidence of Dementia. CERAD-TS = Consortium to Establish a Registry for Alzheimer Disease neuropsychological battery, total score. CV = cardiovascular. CVD = cardiovascular disease. DASC-21 = the Dementia Assessment Sheet in Community based Integrated Care System-21 items. EGCG = epigallocatechin gallate. EMAS = ecological momentary assessments. GP = general practitioner. IADL = Instrumental Activities of Daily Living. MCI = Mild Cognitive Impairment. MMSE = Mini-Mental State Examination. MO = months. MoCA = Montreal Cognitive Assessment. NTB = neuropsychological test battery. RBANS = Repeatable Battery for the Assessment of Neuropsychological Status. SCD = Subjective Cognitive Decline. ZAVEN = Z-scores of Attention, Verbal fluency, and Episodic memory for Nondemented older adults

behavior matches the prescriber's advice, emphasizing obedience rather than actively choosing to make lifestyle changes. Adherence to multimodal interventions should encompass participation in intervention activities and lifestyle change, as both aspects impact cognitive change and are not directly interrelated [10]. Nonetheless, most studies thus far have focused solely on participation in intervention activities as a measure of adherence [9, 11–14]. Accordingly, good adherence has often been defined as completing at least 66% of prescribed interventions [9], a benchmark often used in behavioral interventions [17]. However, an arbitrary cutoff such as a simple percentage of 66% might not be informative of high adherence, as it depends on the overall amount of the intervention offered.

Adherence reporting in multimodal studies

As shown in Table 1, there was significant heterogeneity in the reporting of adherence across the completed multimodal intervention studies. Adherence is commonly reported by intervention domain; however, certain studies, such as the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) [9] and the GOIZ-ZAINDU [18], have also assessed simultaneous adherence to all assigned components, albeit with the use of cut-offs. This diversity in adherence reporting makes cross-trial comparisons of adherence to multimodal interventions difficult. This challenge could be improved by reporting average participation (mean (SD), in percentage units) to each intervention component.

On the other hand, ensuring consistency in reporting lifestyle changes across multimodal interventions can be challenging due to the considerable heterogeneity of the assessment tools used to measure lifestyle changes. A solution to this harmonization challenge could be the use of dementia risk scores such as The Cardiovascular Risk Factors, Aging, and Incidence of Dementia (CAIDE) risk score or the Lifestyle for Brain Health (LIBRA) index [19]. These scores can be calculated uniformly across studies irrespective of the various measurement instruments used to evaluate lifestyle or cardiovascular risk factors [20, 21]. Moreover, they have been suggested as surrogate outcomes for lifestyle-based multimodal prevention trials because they may register changes in dementia risk before detectable cognitive changes [22, 23]. However, risk scores often attribute points using categorical scoring systems, which might reduce responsiveness, as large changes in individual risk factors may not be registered if these changes do not cross the categorical cutoff points [22]. To improve their performance, it has been proposed to use continuous scoring systems (crude and weighted z-score versions), taking into account all changes in risk factors, not only those crossing specific cutoff values

[22]. Using this approach, the LIBRA index demonstrated greater responsiveness to change, than did the CAIDE dementia risk score, as it includes a larger number of modifiable risk factors and a broader range of scores [22]. However, risk scores often put very limited weight on the lifestyle changes most frequently targeted in multimodal interventions (e.g., CAIDE has physical activity only, and LIBRA has physical activity, cognitive activity and diet) and contain many factors that cannot be changed (the effect of multimodal interventions on cardiovascular risk factors is modest, particularly when medications are not a part of the program).

Intensity of multimodal interventions

A measure of the intensity of the intervention that combines the dose delivered (i.e., total number of sessions) and the length of the intervention may be more useful for comparing adherence to different multimodal interventions. Among large multimodal intervention studies, the FINGER is the only one that demonstrated benefits on cognition [24]. The Multimodal Alzheimer Preventive Trial (MAPT) [9] and the Prevention of Dementia by Intensive Vascular Care (PreDIVA) [14], for example, reported no intervention effect on their primary cognitive outcomes. In addition to differences in the target population (at-risk individuals in the FINGER, frail individuals with subjective cognitive impairment in the MAPT, and the general population in the PreDIVA), these three studies differed substantially in terms of intervention intensity and delivery mode (structured intervention programs in the FINGER and MAPT, and mainly self-guided intervention in the PreDIVA). The expected intensity of the FINGER study, calculated as the ratio between the prescribed dose (number of prespecified sessions) and the length (months), was 10.6 points. In contrast, the MAPT had an intensity of 1.2 points, and the PreDIVA had an even lower intensity of 0.3 points (Table 2).

As shown in Fig. 1A, structured multimodal intervention programs with expected intensities greater than 10 points are more likely to succeed in terms of improving cognitive performance or meeting primary cognitive outcomes. In turn, mainly self-guided or remote interventions should probably need greater intensities to impact cognition (Fig. 1B), because participants might be less likely to adhere, as evidenced by the AgeWell.de or HATICE results [25, 26]. On the other hand, ongoing studies are mainly framed within the WW-FINGERS network and thus follow the FINGER model of structured multimodal intervention, with expected intensities over 10 points (Fig. 1C). Specifically, the expected intensities ranged from 32 points in the US POINTER [27, 28], 31.8 points in the AU-ARROW [29], 30.3 points in the LatAm-FINGERS [30], 22.2 points in the LETHE trial

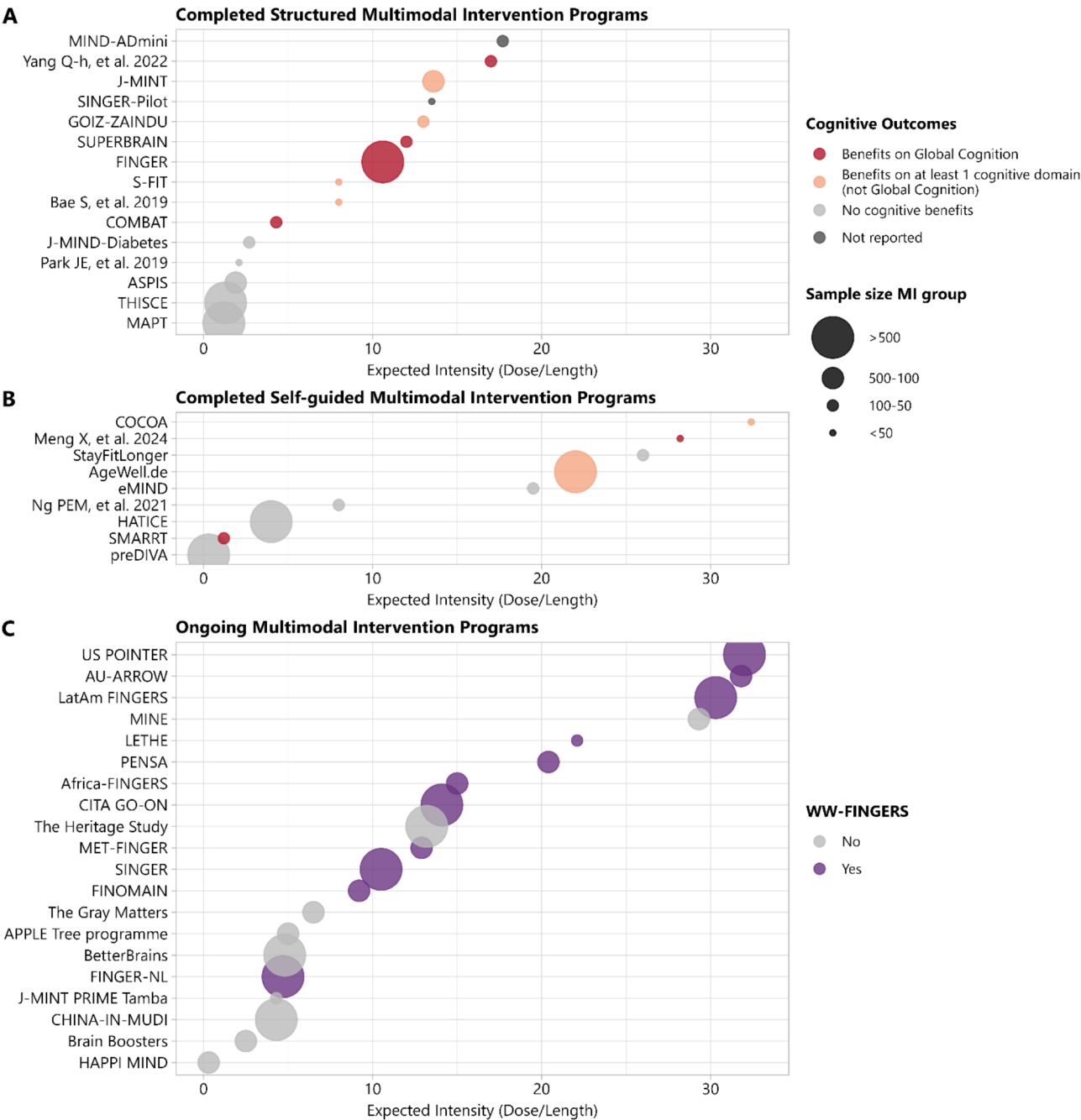


Fig. 1 Intensity of multimodal intervention (MI) studies aimed at preventing cognitive decline, including (A) completed structured intervention programs (A, B) completed predominantly self-guided intervention programs, and (C) ongoing intervention programs categorized by WW-FINGERS network membership. Details of each study are provided in Table 2

[31], 20.4 points in the PENSA Study [32], 15.0 points in the Africa-FINGERS [33], 14.1 points in the CITA GO-ON [34], 12.9 points in the J-MINT and MET-FINGER trials [35, 36], 10.5 points in the SINGER [37], 9.2 points in the FINOMAIN [38], and 4.7 points in the FINGER-NL [39, 40]. Other ongoing multimodal intervention studies that are not members of the WW-FINGERS network usually have lower intensity scores ranging from

0.3 to 6.5 points, except for the MINE trial, which has an expected intensity of 29.3 points [41]. However, it is important to note that the intensity of the intervention is closely affected by the adherence and the content/quality of the intervention (although difficult to quantify). For instance, the observed intensity in the PENSA study after adjusting the expected dose by the average adherence to each intervention component was 14.5 points instead of

Table 3 Overview of determinants of global adherence to multimodal interventions identified in previous studies

Factors associated with poor adherence	Factors associated with good adherence
Lifestyle factors - Current smoking status (9,14)	Sociodemographic factors - Younger age (9,10,12) - Married (10) - Perceived social support (12) - Smaller town (< 200,000) (12) - Education (9)
Psychosocial factors - Depressive symptoms (9–11) - Lower health-related quality of life (9,11) - Higher Impact of memory problems on everyday life (12) - Higher perceived risk of Alzheimer's disease (12) - Lower emotional stability (more anxious) (12) - ≥ 1 Fried frailty criteria (12) - Hopelessness (11) - Nonpositive perception of the study (11)	Cognition - Verbal memory (13) - Processing speed (10) - Global cognition (9,12) - Attention and working memory (9)
Cardiovascular health - Diabetes (9,10,12) - Vascular risk (10) - Obesity, higher body mass index (9,12,14) - History of high blood pressure (9,14)	Lifestyle factors - Healthier lifestyle behaviors (multi-lifestyle score) (10) - Physical activity (12) - Diet score (10) Psychosocial factors - Functionality (14)

20.4 points (30% lower than expected by the design). Similarly, the observed intensity of the MAPT study was 33% lower than that expected by the design [9, 42], and this number was 36% in the GOIZ-ZAINDU study [18], and 55% in the HATICE study [26, 43]. However, the reporting of adherence or participation in intervention activities using cutoffs (e.g., percentage of participants with at least 66% adherence) prevents the assessment of the observed intensity, which requires adjusting the expected intensity by the average adherence to each intervention component. Moreover, information on the duration of cognitive or physical training sessions could allow a more accurate estimation of the intensity, as it could be equivalent to performing, for example, a 60-minute cognitive training session once a week and a 30-minute cognitive training session twice a week. Another aspect that could influence the estimation of the intensity is that the score proposed gives the same weight to all intervention components, although typically cognitive training or physical activity interventions have higher doses (e.g., weekly sessions) than nutrition or cardiovascular risk monitoring interventions (e.g., (bi)monthly visits).

While there is a strong rationale for delivering intensive, high-dose multimodal interventions to promote cognitive improvement or delay the onset of cognitive decline, it is equally crucial to address the challenge of achieving a sustained pattern of lifestyle modification. Striking a balance between intervention intensity, feasibility, cost-effectiveness, and long-term engagement is essential for the success and real-world applicability of these interventions. One potential approach involves a gradual increase in the intervention dose during the first 12–18 months, maintaining this heightened dose until the 2-year mark (in alignment with evidence of efficacy observed in the FINGER study), and thereafter gradually reducing the intervention dose so that the participants are likely to maintain the activities on their own

after the intervention period is over. Another approach is to offer part of the program in a semistructured manner, for example, by using a hybrid intervention design. This approach is currently being tested in FINGER-NL, where part of the intervention program for all lifestyle domains is offered through a digital intervention platform. For example, online exercise instruction videos are made available with options for adapting the intensity of the work-out.

Determinants of adherence

Understanding why individuals engage (or do not engage) in a particular behavior is vital in the context of behavior modification [44]. Moreover, the identification of determinants of adherence is linked to the mechanisms of an intervention as described in, for example, the Medical Research Council guidance regarding complex interventions [45]. Evidence suggests that baseline social and health conditions matter for adherence and efficacy, and interventions that consider psychosocial factors for engaging in a healthy lifestyle (e.g., motivation, environmental adjustment) may achieve better results [46].

To identify determinants of global adherence to multimodal interventions, we conducted a systematic search on PubMed (see details in the introduction section) and employed snowball methods, involving the pursuit of references within references and electronic citation tracking. Table 3 provides a summary of the evidence on the determinants of global adherence in multimodal interventions.

In the recent years, numerous theories, frameworks, and models have emerged within the field of implementation science; however, their application in aging research has been limited [47]. An example of this is the Health Belief Model (HBM), which serves as a framework to explain and predict adherence to health and medical care recommendations. Its main premise lies in the notion

that identifying beliefs and motivations related to health behaviors can inform the development of interventions aimed at increasing desirable health behaviors. This model defines key factors that explain health behaviors, including health knowledge, perceived susceptibility, perceived severity, perceived benefits of action, perceived barriers to action, cues to action, and self-efficacy. Notably, the HBM has been identified as the best-suited model for the development and evaluation of dementia prevention interventions [48]. In the context of the HBM, some studies have investigated the barriers and facilitators to participating in or implementing lifestyle interventions for dementia prevention using qualitative methods, targeting participants [49, 50], healthcare professionals [51] or the general public [52]. Experience with cognitive disorders (through family history or indirectly), motivated attitudes toward prevention and willingness to participate in a prevention trial were found to be facilitators, while beliefs that dementia is part of normal aging and not preventable were found to be barriers to participation. However, barriers to and facilitators of dementia prevention may differ, for example, between different socioeconomic groups, cultures, and genders [53]. Barriers and facilitators of overall participation in a trial may also differ from factors associated with adherence, and they can also differ between the intervention domains.

While HBM factors provide insight into the determinants of adherence, it is unlikely that a single intervention strategy can universally enhance adherence among all participants. The success of lifestyle interventions may depend upon tailoring interventions to the individual characteristics of participants. This is especially relevant in the context of multimodal interventions, which can be burdensome and not universally accepted. Participants may require different focuses on different domains, so tailoring is needed within the intervention. It has been proposed that some people (for example those who are frail or have a lower cognitive reserve) may benefit from higher dose of intervention, while for other people a lower dose might be sufficient [42]. Other factors related to the design of multimodal interventions such as the type, intensity and delivery method, or context (e.g., population, setting, community) may also influence adherence [9]. The adaptation of evidence-based programs to particular settings or populations is thus essential for maximizing their effectiveness [54]. Addressing this evidence-to-practice gap can be facilitated by incorporating implementation science approaches such as Intervention Mapping [55, 56]. These methodologies emphasize the evaluation of context and integrate social determinants of health in the development of interventions. Moreover, they involve program users (implementers, adopters, and maintainers) in the evaluation process [56]. The use of Intervention Mapping or similar methodologies in

the design of dementia prevention studies can enhance their relevance in diverse populations. For instance, the LatAM-FINGERS and the AFRICA-FINGERS initiatives adopted the RE-AIM (reach, effectiveness, adoption, implementation, and maintenance) framework to assess a project's effectiveness, feasibility, and sustainability [30, 33]. This approach has the potential to narrow the gap in dementia prevention research between low and middle-income countries and high-income countries [30, 33].

It is a matter of social justice that accessibility to health services is provided with the principle of equity. Populations with low socioeconomic status (SES) are known to be less likely to access health care and, more importantly, may be more likely to have less healthier lifestyles. Moreover, previous literature has shown a clear relationship between the prevalence of dementia and low SES, measured as annual income, educational level, occupation, and even neighborhood income levels [57]. Another important social determinant of health associated with dementia development is gender. Both a higher prevalence and incidence of dementia have been reported in women than in men, with two-thirds of individuals living with dementia and AD being women [58]. Risk factors associated with gender, which are all interrelated, range from lifestyle and psychosocial factors to cognitive reserve and may also affect participation in and adherence to multimodal interventions [59].

Conclusions

Multimodal interventions for dementia prevention are currently in the trial phase, seeking to prove their efficacy across diverse contexts and target populations and in combination with pharmaceuticals or nutraceuticals. A significant challenge lies in determining the minimum required dose and duration of lifestyle intervention to impact cognition, maintain participant adherence and ensure cost-effectiveness. Ideally, the multimodal intervention dosage should be the minimum required to induce the desired lifestyle changes that, in turn, result in meaningful cognitive benefits [42]. However, it is currently unknown how many metabolic equivalents (METs) of physical activity, or minutes of cognitive training, or the degree of adherence to a healthy diet, are necessary to impact cognition. The room for improving cognition through multimodal interventions in older adults is also unclear, as it is generally assumed that cognition cannot improve ad infinitum, but there is a plateau in which a higher dose does not translate into more cognitive benefits [42, 60]. If this information was available, the intervention dose could be adjusted according to each participant's characteristics. This could entail, for instance, providing fewer physical activity sessions to a participant who already meets physical activity recommendations at baseline; but increasing the number of

sessions if this participant decreased the adherence to such recommendations during the follow-up. This information gap has led to standardizing the dose of lifestyle intervention for all participants. Consequently, the “dose” in multimodal interventions is typically established based on evidence of feasibility and efficacy gathered from prior single-domain or multimodal interventions, considering the necessity for sufficient intensity (as general lifestyle recommendations alone may not be enough to influence cognitive change) [61], while also ensuring that participant motivation is sustained in the long-run.

To better understand the bidirectional relationship between the intervention dose, intensity and adherence, we propose harmonizing the reporting of adherence across multimodal lifestyle-based intervention studies for cognitive decline/dementia prevention, including both participation in intervention activities (average participation in each component) and lifestyle change, using dementia risk scores such as the LIBRA index. The intensity of a multimodal intervention could then be estimated by leveraging the dose, length and observed adherence with each intervention component. Although this intensity score may not encompass all potentially relevant factors (e.g., population or contextual characteristics, intervention quality or duration of sessions), it serves as a preliminary attempt to quantitatively describe this aspect of multimodal interventions. Cross-trial comparisons will be easier across studies, e.g., WW-FINGERS network trials, and others, facilitating an understanding of how intervention observed dose and intensity influence efficacy.

The identification of determinants of adherence to multimodal intervention is important for informing the design and implementation of precision prevention interventions. This article provides an overview of the evidence on the determinants of adherence to multimodal interventions, emphasizing the need to gain knowledge on barriers and facilitators of enrollment, participation, and engagement. The incorporation of implementation science approaches such as Intervention Mapping could enhance the representativeness of the target population, especially including low SES groups, potentially benefiting the most from dementia prevention initiatives. As the field progresses, a commitment to standardized reporting and a nuanced understanding of adherence determinants will be pivotal for advancing dementia prevention research toward meaningful outcomes for diverse populations worldwide.

The topic of adherence may also be quite important to the people participating in these interventions. Additional work should be carried out to understand how this information about adherence should be communicated to participants and to complement the understanding of adherence to multimodal interventions from the

perspective of the participants. This type of work could complement and enrich our understanding of adherence in the short and long term.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13195-025-01691-0>.

Supplementary Material 1

Author contributions

RdIT, NS-D and AA-G conceptualized this paper and drafted the manuscript for intellectual content. MG, JL, LF, AD-P, MZ, WMvdF, TN, MK and AS critically revised the manuscript for intellectual content. All the authors have read and approved the final manuscript.

Funding

EU Joint Program—Neurodegenerative Disease Research (JPND) Multi-MeMo grant (National Institute of Health Carlos III, Spain [Grant AC22/00004]; Research Council of Finland, Finland; The Netherlands Organization for Health Research and Development, Netherlands). RTF led the Consolidated Research Group “Clinical Research Group in Pharmacology and Development of Biomarkers and New Drugs”, a Research Group supported by the Generalitat de Catalunya (2021 SGR 00253). This research was also supported by CIBER—Consorcio Centro de Investigación Biomédica en Red—(CB06/03/0028), Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación and Unión Europea—European Regional Development Fund. FINGER-NL was supported by a Crossover grant (MOCIA 17611) from the Dutch Research Council (NWO). The MOCIA program is a public-private partnership (see <https://mocia.nl/scientific/>). MK received funding from the Alzheimer's Disease Data Initiative (ADDI), Region Stockholm (ALF, Sweden); Center for Innovative Medicine (CIMED) at Karolinska Institute (Sweden); Stiftelsen Stockholms Sjukhem (Sweden); Swedish research council for health, working life and welfare (FORTE). AS was also supported by the European Research Council grant 804371, Alzheimerfonden (Sweden). Grant AC22/00004 funded by Instituto de Salud Carlos III (ISCIII), and by the European Union NextGenerationEU, Mecanismo para la Recuperación y la Resiliencia (MRR). The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Integrative Pharmacology and Systems Neuroscience Research Group, Neuroscience Research Program, Hospital del Mar Research Institute, Dr. Aiguader 88, Barcelona 08003, Spain

²BarcelonaBeta Brain Research Center (BBRC), Pasqual Maragall Foundation, Wellington 30, Barcelona 08003, Spain

³Department of Neurology, Institute of Clinical Medicine, University of Eastern Finland, Yliopistoranta 1C, Kuopio 70211, Finland

⁴The Ageing Epidemiology Research Unit, School of Public Health, Imperial College London, Charing Cross Hospital, St Dunstan's Road, London W6 8RP, UK

⁵Population Health Unit, Finnish Institute for Health and Welfare, Mannerheimintie 166, P.O. Box 30, Helsinki, Finland

⁶CIBER de Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Av. Monforte de Lemos 3-5, Madrid 28029, Spain

⁷Alzheimer Europe,

Sennengerberg Nidderaanwen, Luxembourg City 1736, Luxembourg

⁸Alzheimer Center, Department of Neurology, Neuroscience Campus Amsterdam, VU University Medical Center, De Boelelaan 1117, Amsterdam 1081 HV, Netherlands

⁹Division of Clinical Geriatrics, Center for Alzheimer Research, Department of Neurobiology, Care Sciences and Society, Karolinska Institute, Karolinska Vägen 37A, Solna 171 64, Sweden

¹⁰Medical Unit Aging, Theme Inflammation and Aging, Karolinska University Hospital, Stockholm D1: 04, 171 76, Sweden

¹¹Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Yliopistonrinne 3, Kuopio FI-70211, Finland

¹²Department of Medicine and Life Sciences, Universitat Pompeu Fabra, Dr Aiguader 80, Barcelona 08003, Spain

¹³Neurosciences Research Program, Hospital del Mar Research Institute (HMRI), Dr Aiguader 88, Barcelona 08003, Spain

Received: 27 March 2024 / Accepted: 2 February 2025

Published online: 17 March 2025

References

- Stein GL, Cupito AM, Mendez JL, Prandoni J, Huq N, Westerberg D, et al. Pre-clinical Alzheimer's disease: definition, natural history, and diagnostic criteria. *Alzheimer's Dement*. 2016;12(3):292–323.
- Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *Lancet*. 2020;396(10248):413–46.
- Kivipelto M, Mangialasche F, Ngandu T. Lifestyle interventions to prevent cognitive impairment, dementia and Alzheimer disease. *Nat Rev Neurol*. 2018;14(11):653–66.
- Coley N, Giulioi C, Aisen PS, Vellas B, Andrieu S. Randomised controlled trials for the prevention of cognitive decline or dementia: a systematic review. *Ageing Res Rev*. 2022;82(October):101777.
- Röhr S, Kivipelto M, Mangialasche F, Ngandu T, Riedel-Heller SG. Multidomain interventions for risk reduction and prevention of cognitive decline and dementia: current developments. *Curr Opin Psychiatry*. 2022;35(4):285–92.
- van der Flier WM, de Vugt ME, Smets EMA, Blom M, Teunissen CE. Towards a future where Alzheimer's disease pathology is stopped before the onset of dementia. *Nat Aging*. 2023;3(5):494–505.
- Barbera M, Perera D, Matton A, Mangialasche F, Rosenberg A, Middleton L, et al. Multimodal Precision Prevention - A New Direction in Alzheimer's Disease. *J Prev Alzheimer's Disease*. 2023;10(4):718–28.
- World Health Organization. Adherence to Long-Term Therapies: Evidence for action. 2003.
- Coley N, Ngandu T, Lehtisalo J, Soininen H, Vellas B, Richard E, et al. Adherence to multidomain interventions for dementia prevention: data from the FINGER and MAPT trials. *Alzheimer's Dement*. 2019;15(6):729–41.
- Ngandu T, Lehtisalo J, Korkki S, Solomon A, Coley N, Antikainen R, et al. The effect of adherence on cognition in a multidomain lifestyle intervention (FINGER). *Alzheimer's Dement*. 2022;18(7):1325–34.
- Neuvonen E, Lehtisalo J, Solomon A, Antikainen R, Havulinna S, Hänninen T, et al. Psychosocial determinants for adherence to a healthy lifestyle and intervention participation in the FINGER trial: an exploratory analysis of a randomised clinical trial. *Aging Clin Exp Res*. 2022;34(8):1793–805.
- Coley N, Coniasse-Brioude D, Igier V, Fournier T, Poulain JP, Andrieu S, et al. Disparities in the participation and adherence of older adults in lifestyle-based multidomain dementia prevention and the motivational role of perceived disease risk and intervention benefits: an observational ancillary study to a randomised controlled Tr. *Alzheimers Res Ther*. 2021;13(1):1–13.
- Soldevila-Domenech N, Forcano L, Vintrol-Alcaraz C, Cuenca-Royo A, Pintó X, Jiménez-Murcia S, et al. Interplay between cognition and weight reduction in individuals following a Mediterranean Diet: three-year follow-up of the PREDIMED-Plus trial. *Clin Nutr*. 2021;40(9):5221–37.
- Beishuizen CRL, Coley N, van Moll EP, van Gool WA, Richard E, Andrieu S. Determinants of Dropout and Nonadherence in a Dementia Prevention Randomized Controlled Trial: the Prevention of Dementia by Intensive Vascular Care Trial. *J Am Geriatr Soc*. 2017;65(7):1505–13.
- Kivipelto M, Mangialasche F, Snyder HM, Allegri R, Andrieu S, Arai H, et al. World-wide FINGERS Network: a global approach to risk reduction and prevention of dementia. *Alzheimer's Dement*. 2020;16(7):1078–94.
- Moher D, Liberati A, Tetzlaff J, Altman DG, Antes G, Atkins D, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine*. Volume 6. Public Library of Science; 2009.
- García-Pérez LE, Álvarez M, Dilla T, Gil-Guillén V, Orozco-Beltrán D. Adherence to therapies in patients with type 2 diabetes. *Diabetes Therapy*. 2013;4(2):175–94.
- Tainta M, Ecay-Torres M, de Arriba M, Barandarian M, Otaegui-Arrazola A, Iriondo A, et al. GOIZ ZAINDU study: a FINGER-like multidomain lifestyle intervention feasibility randomized trial to prevent dementia in Southern Europe. *Alzheimers Res Ther*. 2024;16(1):1–13.
- Rosenau C, Köhler S, van Boxtel M, Tange H, Deckers K. Validation of the updated 'Lifestyle for BRAin health' (LlBRA) Index in the English Longitudinal Study of Ageing and Maastricht Aging Study. *J Alzheimers Dis*. 2024;101(4):1237–48.
- Tang EYH, Price CI, Robinson L, Exley C, Desmond DW, Köhler S, et al. Assessing the predictive validity of simple dementia risk models in harmonized stroke cohorts. *Stroke*. 2020;51(7):2095–102.
- Huque MH, Kootar S, Kiely KM, Anderson CS, van Boxtel M, Brodaty H, et al. A single risk assessment for the most common diseases of ageing, developed and validated on 10 cohort studies. *BMC Med*. 2024;22(1):501.
- Coley N, Hoevenaer-Blom MP, van Dalen JW, van Moll EP, Kivipelto M, Soininen H, et al. Dementia risk scores as surrogate outcomes for lifestyle-based multidomain prevention trials—rationale, preliminary evidence and challenges. *Alzheimer's Dement*. 2020;16(12):1674–85.
- Anstey KJ, Zheng L, Peters R, Kootar S, Barbera M, Stephen R, et al. Dementia risk scores and their role in the implementation of risk reduction guidelines. *Front Neurol*. 2022;12(January 2022):1–12.
- Ngandu T, Lehtisalo J, Solomon A, Levälahti E, Ahtiluoto S, Antikainen R, et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *Lancet*. 2015;385(9984):2255–63.
- Zülke AE, Seidling H, Bauer A, Pabst A, Lupp A, Roehr S, et al. A multidomain intervention against cognitive decline in an at-risk-population in Germany: results from the cluster-randomized AgeWell.de trial. *Alzheimer's Dement*. 2023;20(1):615–28. <https://doi.org/10.1002/alz.13486>
- Richard E, van Moll EP, Hoevenaer-Blom MP, Coley N, Barbera M, van der Groep A, et al. Healthy ageing through internet counselling in the elderly (HATICE): a multinational, randomised controlled trial. *Lancet Digit Health*. 2019;1(8):e424–34.
- Baker LD, Snyder HM, Espeland MA, Whitmer RA, Kivipelto M, Woolard N et al. Study design and methods: U.S. study to protect brain health through lifestyle intervention to reduce risk (U.S. POINTER). *Alzheimer's and Dementia*. 2023;(October):1–14.
- Katula JA, Ventrelle J, King K, Garcia KR, Graef S, Lovato L, et al. Adherence to in-person vs. virtual delivery of a multi-domain behavioral intervention to prevent cognitive decline: the US POINTER Study. *Alzheimer's & Dementia*. 2022;18(51):1–2.
- Gardener SL, Fuller SJ, Naismith SL, Baker L, Kivipelto M, Villemagne VL et al. The Australian multidomain Approach to reduce dementia risk by protecting brain health with lifestyle intervention study (AU-ARROW): a study protocol for a single-blind, multi-site, randomized controlled trial. *Alzheimer's Dementia: Translational Res Clin Interventions*. 2024;10(2).
- Crivelli L, Calandri IL, Suemoto CK, Salinas RM, Velilla LM, Yassuda MS, et al. Latin American Initiative for Lifestyle Intervention to prevent Cognitive decline (LatAm-FINGERS): study design and harmonization. *Alzheimer's Dement*. 2023;19(9):4046–60.
- Rosenberg A, Untersteiner H, Guazzarini AG, Bödenler M, Bruinsma J, Buchgraber-Schnalzer B et al. A digitally supported multimodal lifestyle program to promote brain health among older adults (the LETHE randomized controlled feasibility trial): study design, progress, and first results. *Alzheimers Res Ther [Internet]*. 2024;16(1):252. Available from: <https://alzres.biomedcentral.com/articles/https://doi.org/10.1186/s13195-024-01615-4>
- Forcano L, Fauria K, Soldevila-Domenech N, Minguiñón C, Lorenzo T, Meneses-Cabral S, et al. Prevention of cognitive decline in subjective cognitive decline APOE-e4 carriers after EGCG and a multimodal intervention (PENSA): study design. Volume 7. *Alzheimer's & Dementia: Translational Research &*; 2021. p. e12155. Clinical Interventions (TRCI). 1.

33. Udeh-Momoh CT, Maina R, Anazodo UC, Akinyemi R, Atwoli L, Baker L, et al. Dementia risk reduction in the African context: multi-national implementation of multimodal strategies to promote healthy brain aging in Africa (the Africa-FINGERS project). *Alzheimer's Dement*. 2024;20(12):8987–9003. <https://doi.org/10.1002/alz.14344>
34. Fundación CITA-A. Cita GO-ON [Internet]. [cited 2024 Mar 7]. Available from: <https://www.cita-alzheimer.org/es/cita-go-on>
35. Sugimoto T, Sakurai T, Akatsu H, Doi T, Fujiwara Y, Hirakawa A, et al. The Japan-Multimodal Intervention Trial for Prevention of Dementia (J-MINT): the study protocol for an 18-Month, Multicenter, Randomized, Controlled Trial. *J Prev Alzheimer's Disease*. 2021;8(4):465–76.
36. Barbera M, Lehtisalo J, Perera D, Aspö M, Cross M, De Jager Loots CA, et al. A multimodal precision-prevention approach combining lifestyle intervention with metformin repurposing to prevent cognitive impairment and disability: the MET-FINGER randomised controlled trial protocol. *Alzheimers Res Ther*. 2024;16(1):1–15.
37. Xu X, Chew KA, Wong ZX, Phua AKS, Chong EJY, Teo CKL, et al. The Singapore GERiatric intervention study to reduce Cognitive decline and physical Frailty (SINGER): Study Design and Protocol. *J Prev Alzheimer's Disease*. 2022;9(1):40–8.
38. Dominguez J, de Guzman MF, Chen SHA, Sano M, Waldemar G, Phung TKT. Filipino Multicomponent intervention to maintain cognitive performance in High-Risk Population (FINOMAIN): study protocol for a Cluster Randomized Controlled Trial. *Front Neurol*. 2021;12(September):1–11.
39. Zwan MD, Deckers K, Claassen JAHR, Oosterman JM, de Heus RAA, van de Rest O, et al. Study design of FINGER-NL: a multidomain lifestyle intervention in Dutch older adults to prevent cognitive decline. *Alzheimer's Dement*. 2021;17:S9.
40. Deckers K, Zwan MD, Soons LM, Waterink L, Beers S, van Houdt S et al. A multidomain lifestyle intervention to maintain optimal cognitive functioning in Dutch older adults—study design and baseline characteristics of the FINGER-NL randomized controlled trial. *Alzheimer's Res Therapy*. 2024;16(1).
41. Wu X, Zhang T, Tu Y, Deng X, Sigén A, Li Y, et al. Multidomain interventions for non-pharmacological enhancement (MINE) program in Chinese older adults with mild cognitive impairment: a multicenter randomized controlled trial protocol. *BMC Neurol*. 2023;23(1):1–16.
42. Belleville S, Cloutier S, Mellah S, Willis S, Vellas B, Andrieu S, et al. Is more always better? Dose effect in a multidomain intervention in older adults at risk of dementia. *Alzheimer's Dement*. 2022;18(9):1700–1. <https://doi.org/10.1002/alz.12693>
43. Barbera M, Mangialasche F, Jongstra S, Guillemont J, Ngandu T, Beishuizen C, et al. Designing an internet-based Multidomain intervention for the Prevention of Cardiovascular Disease and Cognitive Impairment in older adults: the HATICE Trial. *J Alzheimer's Disease*. 2018;62(2):649–63.
44. Kok G, Gottlieb NH, Peters GJY, Mullen PD, Parcel GS, Ruiter RAC, et al. A taxonomy of behaviour change methods: an intervention mapping approach. *Health Psychol Rev*. 2016;10(3):297–312.
45. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM et al. A new framework for developing and evaluating complex interventions: Update of Medical Research Council guidance. *The BMJ*. 2021;374(2018):1–11.
46. Aravena JM. Healthy lifestyle and cognitive aging: what is the gap behind prescribing healthier lifestyle? *Alzheimer's Dement*. 2023;19(7):3233–4.
47. Purtle J, Peters R, Brownson RC. A review of policy dissemination and implementation research funded by the National Institutes of Health, 2007–2014. *Implement Sci*. 2016;11(1):1–8.
48. Kim S, Sargent-Cox K, Cherbuin N, Anstey KJ. Development of the motivation to Change Lifestyle and Health behaviours for Dementia Risk Reduction Scale. *Dement Geriatr Cogn Dis Extra*. 2014;4(2):172–83.
49. Rosenberg A, Coley N, Soulier A, Kulmala J, Soininen H, Andrieu S, et al. Experiences of dementia and attitude towards prevention: a qualitative study among older adults participating in a prevention trial. *BMC Geriatr*. 2020;20(1):1–12.
50. Akenine U, Thunborg C, Kivipelto M, Fallahpour M. Experiences of participation in a Multimodal Preventive Trial MIND-ADMINI among persons with Prodromal Alzheimer's Disease: a qualitative study. *J Multidiscip Healthc*. 2022;15(November 2021):219–34.
51. Kulmala J, Rosenberg A, Ngandu T, Hemio K, Tenkula T, Hyytiä A, et al. Facilitators and barriers to implementing lifestyle intervention programme to prevent cognitive decline. *Eur J Public Health*. 2021;31(4):816–22.
52. Bruinsma J, Heger I, Loukas VS, Kassiotis T, Karanasiou G, Fotiadis DI, et al. Public perspectives on lifestyle-related Behavior Change for Dementia Risk reduction: an exploratory qualitative study in the Netherlands. *J Alzheimer's Disease*. 2023;95:1–8.
53. Eggink E, Hafdi M, Hoevenaer-Blom MP, Richard E, Van Moll EP. Attitudes and views on healthy lifestyle interventions for the prevention of dementia and cardiovascular disease among older people with low socioeconomic status: a qualitative study in the Netherlands. *BMJ Open*. 2022;12(2).
54. Kuroda Y, Fujita K, Sugimoto T, Uchida K, Shimazu T, Saito J, et al. Feasibility of a community-adapted multi-domain intervention for dementia prevention among older adults: a research protocol. *Archives Public Health*. 2023;81(1):1–11.
55. Stensland KD, Sales AE, Damschroder LJ, Skolarus TA. Applying implementation frameworks to the clinical trial context. *Implement Sci Commun*. 2022;3(1):1–13.
56. Fernandez ME, Ruiter RAC, Markham CM, Kok G. Intervention mapping: theory-and evidence-based health promotion program planning: perspective and examples. *Front Public Health*. 2019;7(209):1–8.
57. Fischer C, Yeung E, Hansen T, Gibbons S, Fornazzari L, Ringer L, et al. Impact of socioeconomic status on the prevalence of dementia in an inner city memory disorders clinic. *Int Psychogeriatr*. 2009;21(6):1096–104.
58. Alzheimer's Association. 2023 Alzheimer's Disease Facts and Figures. *Alzheimers Dement*. 2023;19(4).
59. Sindi S, Kåreholt I, Ngandu T, Rosenberg A, Kulmala J, Johansson L, et al. Sex differences in dementia and response to a lifestyle intervention: evidence from nordic population-based studies and a prevention trial. *Alzheimer's Dement*. 2021;17(7):1166–78.
60. Soldevila-Domenech N, De Toma I, Forcano L, Diaz-Pellicer P, Cuenca-Royo A, Fagundo B, et al. Intensive assessment of executive functions derived from performance in cognitive training games. *iScience*. 2023;26(106886):1–26.
61. van Charante EPM, Richard E, Eurelings LS, van Dalen JW, Ligthart SA, van Bussel EF, et al. Effectiveness of a 6-year multidomain vascular care intervention to prevent dementia (preDIVA): a cluster-randomised controlled trial. *Lancet*. 2016;388(10046):797–805.
62. Turunen M, Hokkanen L, Bäckman L, Stigsdotter-Neely A, Hänninen T, Paajanen T, et al. Computer-based cognitive training for older adults: determinants of adherence. *PLoS ONE*. 2019;14(7):1–12.
63. de Souto Barreto P, Pothier K, Soriano G, Lussier M, Bherer L, Guyonnet S, et al. A web-based Multidomain Lifestyle intervention for older adults: the eMIND Randomized Controlled Trial. *J Prev Alzheimer's Disease*. 2021;8(2):142–50.
64. Sindi S, Thunborg C, Rosenberg A, Andersen P, Andrieu S, Broersen LM, et al. Multimodal Preventive Trial for Alzheimer's Disease: MIND-ADMINI Pilot Trial Study Design and Progress. *J Prev Alzheimer's Disease*. 2022;9(1):30–9.
65. Thunborg C, Wang R, Rosenberg A, Sindi S, Andersen P, Andrieu S et al. Integrating a multimodal lifestyle intervention with medical food in prodromal Alzheimer's disease: the MIND-ADMINI randomized controlled trial. *Alzheimer's Res Therapy*. 2024;16(1).
66. Matz K, Teuschl Y, Firlinger B, Dachenhausen A, Keindl M, Seyfang L, et al. Multidomain lifestyle interventions for the prevention of cognitive decline after ischemic stroke randomized trial. *Stroke*. 2015;46(10):2874–80.
67. Brainin M, Matz K, Nemec M, Teuschl Y, Dachenhausen A, Asenbaum-Nan S, et al. Prevention of poststroke cognitive decline: ASPIS - a multicenter, randomized, observer-blind, parallel group clinical trial to evaluate multiple lifestyle interventions - study design and baseline characteristics. *Int J Stroke*. 2015;10(4):627–35.
68. Belleville S, Cuesta M, Bieler-Aeschlimann M, Giacomino K, Widmer A, Mittaz Hager AG, et al. Pre-frail older adults show improved cognition with StayFit-Longer computerized home-based training: a randomized controlled trial. *Geroscience*. 2023;45(2):811–22.
69. Yaffe K, Barnes DE, Rosenberg D, Dublin S, Kaup AR, Ludman EJ, et al. Systematic Multi-domain Alzheimer's risk reduction trial (SMARRT): study protocol. *J Alzheimer's Disease*. 2019;70(s1):S207–20.
70. Roach JC, Rapozo MK, Hara J, Glusman G, Lovejoy J, Shankle WR, et al. A remotely coached Multimodal Lifestyle intervention for Alzheimer's Disease ameliorates functional and cognitive outcomes. *J Alzheimer's Disease*. 2023;96(2):591–607.
71. Meng X, Su J, Gao T, Ma D, Zhao Y, Fang S et al. Multidomain interventions based on a life-course model to prevent dementia in at-risk Chinese older adults: a randomized controlled trial. *Int J Nurs Stud*. 2024;152.
72. Sakurai T, Sugimoto T, Akatsu H, Doi T, Fujiwara Y, Hirakawa A, et al. Japan-Multimodal intervention trial for the Prevention of Dementia: a randomized controlled trial. *Alzheimer's Dement*. 2024;20(6):3918–30.
73. Bae S, Lee S, Lee S, Jung S, Makino K, Harada K, et al. The effect of a multicomponent intervention to promote community activity on cognitive function in

- older adults with mild cognitive impairment: a randomized controlled trial. *Complement Ther Med*. 2019;42:164–9.
74. Moon SY, Hong CH, Jeong JH, Park YK, Na HR, Song HS, et al. Facility-based and home-based multidomain interventions including cognitive training, Exercise, Diet, vascular risk management, and motivation for older adults: a randomized controlled feasibility trial. *Aging*. 2021;13(12):15898–916.
75. Chew KA, Xu X, Siongco P, Villaraza S, Phua AKS, Wong ZX, et al. SINGapore GERiatric intervention study to reduce physical frailty and cognitive decline (SINGER)—pilot: a feasibility study. *Alzheimer's Dementia: Translational Res Clin Interventions*. 2021;7(1):1–10.
76. Ng PEM, Nicholas SO, Wee SL, Yau TY, Chan A, Chng I, et al. Implementation and effectiveness of a multi-domain program for older adults at risk of cognitive impairment at neighborhood senior centres. *Sci Rep*. 2021;11(1):1–11.
77. Ng TP, Ling LHA, Feng L, Nyunt MSZ, Feng L, Niti M, et al. Cognitive effects of multi-domain interventions among pre-frail and frail community-living older persons: randomized controlled trial. *J Gerontol Series A Biol Sci Med Sci*. 2018;73(6):806–12. <https://doi.org/10.1093/gerona/glx207>
78. Barbera M, Lehtisalo J, Rissanen H, Hannukkala R, Ngandu T, Solomon A, et al. Development of a healthy lifestyle index within a multidomain intervention aimed at prevention of cognitive impairment and dementia, and its association with cognition: results from the FINGER trial. *Alzheimer's Dement*. 2021;17:S10.
79. Yaffe K, Vittinghoff E, Dublin S, Peltz CB, Fleckenstein LE, Rosenberg DE, et al. Effect of personalized risk-reduction strategies on Cognition and Dementia Risk Profile among older adults. The SMARRT Randomized Clinical Trial. *JAMA Intern Med*. 2023;94143(1):54–62.
80. Roach JC, Hara J, Fridman D, Lovejoy JC, Jade K, Heim L, et al. The coaching for Cognition in Alzheimer's (COCOA) trial: study design. *Alzheimer's Dementia: Translational Res Clin Interventions*. 2022;8(1):1–12.
81. Roach JC, Edens L, Markewych DR, Rapozo MK, Hara J, Glusman G et al. A multimodal intervention for Alzheimer's disease results in multifaceted systemic effects reflected in blood and ameliorates functional and cognitive outcomes. *medRxiv [Internet]*. 2022; Available from: <https://doi.org/10.1101/2022.09.27.22280385>
82. Liu X, Ma Z, Zhu X, Zheng Z, Li J, Fu J, et al. Cognitive benefit of a Multidomain intervention for older adults at risk of Cognitive decline: a cluster-randomized controlled trial. *Am J Geriatric Psychiatry*. 2023;31(3):197–209.
83. Lyu Q, Cheung DSK, Lai H, Wang X, Qiu J, Huang Y, et al. A multicomponent integrative intervention to slow down the progression of mild cognitive impairment: a protocol for a randomized controlled trial. *Res Nurs Health*. 2020;43(4):307–16.
84. Yang Qhong, Lyu X, Lin Q, ran, Wang Z wen, Tang L, Zhao Y et al. Effects of a multicomponent intervention to slow mild cognitive impairment progression: A randomized controlled trial. *Int J Nurs Stud*. 2022;125:104110.
85. Sugimoto T, Araki A, Fujita H, Fujita K, Honda K, Inagaki N, et al. Multidomain intervention trial for preventing Cognitive decline among older adults with type 2 diabetes: J-MIND-Diabetes. *Journal of Prevention of Alzheimer's Disease*; 2024.
86. Park JE, Jeon SY, Kim SA, Kim JH, Kim SH, Lee KW, et al. A Multidomain intervention for modifying Lifestyle habits reduces the dementia risk in Community-Dwelling older adults: a single-blinded Randomized Controlled Pilot Study. *J Alzheimer's Disease*. 2019;70(1):51–60.
87. Chen LK, Hwang AC, Lee WJ, Peng LN, Lin MH, Neil DL, et al. Efficacy of multidomain interventions to improve physical frailty, depression and cognition: data from cluster-randomized controlled trials. *J Cachexia Sarcopenia Muscle*. 2020;11(3):650–62.
88. McEvoy CT, Regan-Moriarty J, Dolan C, Bradshaw C, Mortland V, McCallion M et al. A qualitative study to inform adaptations to a brain health intervention for older adults with type 2 diabetes living in rural regions of Ireland. *Diabet Med*. 2023;40(4).
89. Schröder VE, Skrozic A, Erz D, Kaysen A, Fritz JV, Loureiro JM, et al. Programme Dementia Prevention (pdp): a Nationwide Program for Personalized Prevention in Luxembourg. *J Alzheimer's Disease*. 2024;97(2):791–804.
90. Feldman HH, Belleville S, Nygaard HB, Montero-Odasso M, Durant J, Lupo JL, et al. Protocol for the Brain Health Support Program Study of the Canadian Therapeutic Platform Trial for Multidomain Interventions To Prevent Dementia (CAN-THUMBS UP): a prospective 12-Month intervention study. *J Prev Alzheimer's Disease*. 2023;10(4):875–85.
91. Heffernan M, Andrews G, Fiatarone Singh MA, Valenzuela M, Anstey KJ, Maeder AJ, et al. Maintain your brain: protocol of a 3-Year randomized controlled trial of a personalized Multi-modal Digital Health Intervention to prevent Cognitive decline among Community Dwelling 55 to 77 Year Olds. *J Alzheimer's Disease*. 2019;70(s1):S221–37.
92. Ponvel P, Shahar S, Singh DKA, Ludin AFM, Rajikan R, Rajab NF, et al. Multidomain intervention for reversal of cognitive Frailty, towards a Personalized Approach (AGELESS Trial): Study Design. *J Alzheimer's Disease*. 2021;82(2):673–87.
93. Wang Y, Han X, Zhang X, Zhang Z, Cong L, Tang S, et al. Health status and risk profiles for brain aging of rural-dwelling older adults: data from the interdisciplinary baseline assessments in MIND-China. *Alzheimer's Dementia: Translational Res Clin Interventions*. 2022;8(1):1–13.
94. Xu X, Pang T, Zhou Y, Zhang H, Ma A, Yuan C, et al. The multi-domain lifestyle intervention for cognitive impairment in Community-Dwelling older adults in Hangzhou (the Heritage Study): Study Design and Protocol. *J Prev Alzheimer's Disease*. 2024;11(3):601–11.
95. Li SY, Xie XY, Liu D, Cheng GR, Hu FF, Zeng DY, et al. China Initiative for Multi-domain intervention (CHINA-IN-MUDI) to prevent Cognitive decline: Study Design and Progress. *J Prev Alzheimer's Disease*. 2024;11(3):589–600.
96. Tomaszewski Farias S, Fox J, Dulaney H, Chan M, Namboodiri S, Harvey DJ, et al. Memory support training and lifestyle modifications to promote healthy aging in persons at risk for Alzheimer's disease: a digital application supported intervention (brain boosters). *BMC Geriatr*. 2023;23(1):1–12.
97. Norton MC, Clark CJ, Tschanz JAT, Hartin P, Fauth EB, Gast JA, et al. The design and progress of a multidomain lifestyle intervention to improve brain health in middle-aged persons to reduce later Alzheimer's disease risk: the Gray matters randomized trial. *Alzheimer's Dementia: Translational Res Clin Interventions*. 2015;1(1):53–62.
98. Poppe M, Duffy L, Marchant NL, Barber JA, Hunter R, Bass N, et al. The APPLE Tree programme: active Prevention in people at risk of dementia through Lifestyle, bEhaviour change and technology to build REsilience—randomised controlled trial. *Trials*. 2022;23(1):1–14.
99. Lim YY, Ayton D, Perin S, Lavale A, Yassi N, Buckley R, et al. An online, Person-Centered, Risk Factor Management Program to prevent Cognitive decline: protocol for a prospective behavior-modification Blinded Endpoint Randomized Controlled Trial. *J Alzheimer's Disease*. 2021;83(4):1603–22.
100. Cross AJ, Geethadevi GM, Magin P, Baker AL, Bonevski B, Godbee K, et al. A novel, multidomain, primary care nurse-led and mhealth-assisted intervention for dementia risk reduction in middle-aged adults (HAPPI MIND): study protocol for a cluster randomised controlled trial. *BMJ Open*. 2023;13(12):1–14.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.