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Ngandu, Tiia

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Tiia Ngandu[1,2] | Jenni Lehtisalo[1,3] | Saana Korkki[4,5] | Alina Solomon[2,3,6] |
Nicola Coley[7,8] | Riitta Antikainen[9,10] | Lars Bäckman[5] | Tuomo Hänninen[11] |
Jaana Lindström[1] | Tiina Laatikainen[1,12,13] | Teemu Paajanen[14] | Satu Havulinna[15] |
Markku Peltonen[1,2] | Anna Stigsdotter Neely[16,17] | Timo Strandberg[9,18] |
Jaakko Tuomilehto[1,19,20,21] | Hilkka Soininen[3,11] | Miia Kivipelto[1,2,6,12,22]

[1] Department of Public Health and Welfare, Population Health Unit, Finnish Institute for Health and Welfare, Helsinki, Finland

[2] Division of Clinical Geriatrics, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet, Solna, Stockholm, Sweden

[3] Institute of Clinical Medicine/Neurology, University of Eastern Finland, Kuopio, Finland

[4] Department of Psychology, University of Cambridge, Cambridge, UK

[5] Aging Research Center, Department of Neurobiology, Care Sciences and Society, Karolinska Institutet and Stockholm University, Stockholm, Sweden

[6] Ageing Epidemiology Research Unit, School of Public Health, Imperial College London, London, UK

[7] Faculté de Médecine, INSERM-University of Toulouse UMR1295 (CERPOP), Toulouse, France

[8] Department of Epidemiology and Public Health, Toulouse University Hospital, Toulouse, France

[9] Center for Life Course Health Research, University of Oulu, Oulu, Finland

[10] Medical Research Center Oulu, Oulu University Hospital, Oulu, Finland

[11] Neurocenter, Department of Neurology, Kuopio University Hospital, Kuopio, Finland

[12] Institute of Public Health and Clinical Nutrition, University of Eastern Finland, Kuopio, Finland

[13] Joint municipal authority for North Karelia social and health services (Siun sote), Joensuu, Finland

[14] Finnish Institute of Occupational Health, Helsinki, Finland

[15] Department of Public Health and Welfare, Functioning and Service Needs Unit, Finnish Institute for Health and Welfare, Helsinki, Finland

[16] Department of Social Psychological Sciences, Karlstad University, Karlstad, Sweden

[17] Engineering Psychology, Luleå University of Technology, Luleå, Sweden

[18] Department of Medicine, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland

[19] Department of Public Health, University of Helsinki, Helsinki, Finland

[20] Diabetes Research Group, King Abdulaziz University, Jeddah, Saudi Arabia

[21] South Ostrobothnia Central Hospital, Seinäjoki, Finland

[22] Theme Aging, Karolinska University Hospital, Solna, Sweden

Correspondence
Tiia Ngandu, Department of Public Health and Welfare, Population Health Unit, Finnish Institute for Health and Welfare, P.O. Box 30; 00271 Helsinki, Finland.
E-mail: tiia.ngandu@thl.fi

Tiia Ngandu and Jenni Lehtisalo contributed equally to this study.

Abstract

Introduction: Lifestyle interventions may prevent cognitive decline, but the sufficient dose of intervention activities and lifestyle changes is unknown. We investigated how intervention adherence affects cognition in the FINGER trial (pre-specified subgroup analyses).

Methods: FINGER is a multicenter randomized controlled trial examining the efficacy of multidomain lifestyle intervention (ClinicalTrials.gov NCT01041989). A total of 1260 participants aged 60 to 77 with increased dementia risk were randomized to a lifestyle intervention and control groups. Percentage of completed intervention sessions, and change in multidomain lifestyle score (self-reported diet; physical, cognitive, and social activity; vascular risk) were examined in relation to change in Neuropsychological Test Battery (NTB) scores.

Results: Active participation was associated with better trajectories in NTB total and all cognitive subdomains. Improvement in lifestyle was associated with improvement in NTB total and executive function.

Discussion: Multidomain lifestyle changes are beneficial for cognitive functioning, but future interventions should be intensive enough, and supporting adherence is essential.

KEYWORDS
cognition, lifestyle, multidomain, prevention

1 | BACKGROUND

Healthy lifestyles are associated with a lower risk of cognitive impairment, including dementia and Alzheimer's disease.[1] Emerging evidence from randomized controlled trials suggests that lifestyle interventions may reduce the risk of cognitive decline.[2] Given the multifactorial nature of old-age cognitive impairment, multidomain interventions are a promising prevention strategy.

Adherence to lifestyle intervention is crucial to have an effect on cognition; not only participation in the proposed activities, but also adopting healthy lifestyles in everyday life. What constitutes a sufficient dose of lifestyle intervention remains unclear. Although some lifestyle trials targeting prevention of cognitive decline have reported attendance to intervention visits[3,4] or change in lifestyle,[5-7] few studies have investigated how adherence impacts cognitive outcomes, with indication of positive association.[8,9] Knowledge of the magnitude of intervention activities needed would improve the efficacy of future trials.

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) was the first large multidomain lifestyle trial reporting beneficial effects on cognitive function among older adults.[10] The aim of the current study is to investigate how intervention adherence explains the observed degree of cognitive change (prespecified subgroup analyses). The analyses examine adherence defined as (1) participation in the intervention activities and (2) achieved changes in lifestyles during the 2-year intervention.

2 | METHODS

2.1 | Setting and population

FINGER is a multidomain lifestyle intervention trial conducted in six areas in Finland (ClinicalTrials.gov NCT01041989).[11] The study comprises a population-based sample aged 60 to 77 years, with an elevated risk for dementia. Persons with CAIDE (Cardiovascular Risk Factors, Aging, and Dementia) risk score[12] ≥6 were invited to a screening visit where they underwent brief neuropsychological testing and a medical examination. They were eligible if free of dementia and conditions affecting safe engagement in the intervention, and with cognitive performance at an average level or slightly below expected.[10] The study was approved by the Coordinating Ethics Committee of Helsinki and Uusimaa Hospital District, and all participants gave written informed consent. The study flowchart is presented as Figure S1 in supporting information. Participants were randomized 1:1 to multidomain lifestyle (intervention) or regular health advice (control) groups using computerized algorithm in blocks of four (two individuals randomly allocated to each group) at each site after baseline by the study nurse. Double-blinding was pursued as much as possible: The outcome assessors were blinded, and the randomization group was not actively told to the participants.

2.2 | Interventions

Participants in the multidomain group received all four intervention components: dietary counseling, exercise training, cognitive training,

and management of cardiovascular and metabolic factors (vascular management).

The dietary intervention was based on national recommendations[13] and included nutrient intake goals operationalized by using food-level recommendations, for example increased consumption of fruits, berries, vegetables, wholegrain cereal, vegetable fats, and fish; individually tailored for each participant. The intervention comprised three individual counseling and six to eight group sessions with a study nutritionist.[6]

The physical exercise intervention followed international guidelines and previous Finnish trials.[14,15] Individually tailored progressive strength training was provided one to three times per week, with exercises for eight main muscle groups and exercises to improve balance. Progression of strength training was based on repetition maximum measurements (4RM). Aerobic exercise (goal 2–5 times per week) included mainly self-guided activities planned with a study physiotherapist.

The cognitive intervention consisted of six group sessions (educational content and guidance to computerized cognitive training program) and individual training with the computer program. The web-based cognitive training program was available at home or at the study site, for two periods of 6 months each with 72 training sessions (three times per week). It included tasks focusing on executive processes, working memory, episodic memory, and mental speed.[16,17]

Intensive management of metabolic and vascular risk factors (vascular intervention) was based on national guidelines aimed at improving blood pressure, lipids, glucose, and body weight with improving lifestyles. Study physicians did not prescribe medication, but strongly recommended contacting local health care if needed. The intervention group met a study nurse (at 3, 9, and 18 months), and the study physician (at 3, 6, and 12 months) for additional measurement and advice.

All participants received mini-intervention with the study nurse at baseline and written feedback on their vascular risk factors.

2.3 | Adherence measures

Adherence to the intervention comprises two aspects: (1) participation in offered activities in the intervention group (prespecified definition) and (2) participants' lifestyle changes in intervention and control groups (details in Supplementary Methods and Table S1 in supporting information).

2.3.1 | Participation in intervention activities

The prespecified definition was applied as non-adherent (0 sessions; 0 points), partially adherent (<50% completed; 1 point), or adherent (≥50% completed; 2 points) for each intervention component, summed to reflect multi-participation (range 0–8). In component-specific analyses an alternative categorization for diet (0–50; 51–75; and 76–100%) and vascular (0–75; 76–90; 91–100%) interventions was used, requiring higher participation, due to a small numbers of non-

HIGHLIGHTS

- Active participation in lifestyle intervention was associated with better cognition.
- A 2-year lifestyle intervention resulted in improvements in everyday lifestyles.
- Lifestyle improvements were also associated with better cognitive change.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed literature using PubMed and their own files for trials investigating adherence to lifestyle interventions in relation to cognitive outcomes. While several observational studies have linked lifestyle factors and cognition, there are few large trials investigating the efficacy of lifestyle interventions, and thus limited evidence on how intensive a lifestyle intervention needs to be for achieving cognitive benefits.

2. **Interpretation**: Our results showed that older adults who participated most actively in the intervention activities had better cognitive trajectories compared to the control group. Improvements in everyday lifestyles were more often observed among the most active participants. The lifestyle improvement was also linked to better cognitive outcomes.

3. **Future directions**: The accumulated evidence suggests that even in older age, lifestyle modification is beneficial for cognitive outcomes. Quite an intensive intervention is needed to promote cognitive health, and measures to support adherence are important in future trials and implementation.

adherent participants. Participation was not measured in the control group.

2.3.2 | Lifestyles

Self-reported lifestyles and measured vascular factors were collected annually for both intervention and control groups. Diet score was based on 3-day food records ranging from none to all dietary goals (0–9).[6] Average number of weekly moderate to vigorous physical activity sessions was calculated based on a validated questionnaire.[18] An average number of weekly cognitive and social activities (cognitive activity) was collected with a frequency-based questionnaire. Cardiovascular risk was assessed with the validated Finnish FINRISK score divided

by the score of age- and sex-matched person without vascular risk factors.[19]

Healthy lifestyle pattern at baseline was based on tertiles of each component: 0 points for low (unfavorable), 1 for intermediate, and 2 for upper tertile (favorable); and the healthy multidomain lifestyle composite (multi-lifestyle score) was calculated as the sum (range 0–8). Multi-lifestyle score is used as outcome and predictor in the analyses. Change in each lifestyle was defined as the difference score between baseline and 2-year visit as worsening (0 points), stable (1 point), or improvement (2 points; cut-offs in Table S1). Measure for multi-lifestyle change from worsening in all to improvement in all lifestyle components ranged from 0 to 8.

2.4 | Neuropsychological examination

A trained study psychologist blinded to group allocation administered the Neuropsychological Test Battery (NTB)[10,20] at baseline and annually thereafter. Primary outcome was a composite score reflecting global cognition, calculated as an average of 14 tests standardized to Z scores with higher scores indicating better performance as described. Secondary outcomes included cognitive domain Z scores for executive function, processing speed, and memory.

2.5 | Statistical analyses

Baseline characteristics were compared using t-tests for continuous and Chi^2 tests for categorical variables. Linear mixed modeling was applied with continuous cognitive or lifestyle scores as outcomes and time as a random factor. Predictor variables were: (1) intervention allocation (lifestyle outcome only), (2) participation (within intervention group), (3) participation compared to the control group, (4) baseline lifestyles (cognition outcome only), and (5) change in lifestyles (cognition outcome only). Analyses with lifestyle as predictor included all participants adjusting for the intervention allocation (group x time), and effect modification by the intervention allocation was investigated (group x time x lifestyle). A sensitivity analysis compared the intervention participation groups to control group participants who improved their lifestyle.

All analyses were adjusted for age, education, sex, study area, marital status, systolic blood pressure, total cholesterol, body mass index (BMI), and depressive symptoms at baseline. Missing baseline values were supplemented with values from later years, and depressive symptoms were entered using categories: missing data, no indication of depression (Zung score < 40), and suspected depression (Zung score > = 40).

The change in lifestyle was measurable only for those who completed the study, and the proportion of missing values was relatively high even among completers. For sensitivity analyses, we imputed missing values with maximum likelihood estimation, using the same lifestyle variable from other time points, and other questions that evaluated the same lifestyle, age, education, sex, and marital status. Only statistically significant (P < 0.05) predictors were included. Imputed values were categorized as the observed values. Stata/SE version 16 was used for all analyses.

3 | RESULTS

3.1 | Baseline characteristics and lifestyle changes

The mean age of the 1259 participants was 68.9 years, and 54% were men; 12% dropped out.

Most intervention participants met the prespecified definition for adherent participation in diet (n = 557, 88%) and vascular (n = 587, 93%) intervention components; and approximately one half in exercise (n = 361, 57%) and cognitive training (n = 295, 47%) components. Altogether 37% were adherent to all intervention components (adherent multi-participation), 42% at least in two components (partially adherent), and 21% less (non-adherent). The intervention and control groups were similar, but adherent intervention participants were younger, more often married, less often had diabetes, and had fewer depressive symptoms and faster processing speed than non-adherent ones (Table 1), who in turn had several less favorable characteristics than the control group. Compared to the control group, the non-adherent or partially adherent participants in the intervention group had lower multi-lifestyle score at baseline, and adherent participants had higher.

The multi-lifestyle score was available for 1142 (90%) at baseline and 965 (86%) at 2 years, resulting in 899 estimates for lifestyle change (80%). Data were most often missing for exercise (n = 83; 7% at baseline). The multi-lifestyle score improved more in the intervention group (annual improvement 0.24 points, P = < 0.001) than in the control group (annual improvement 0.09 points, P = 0.003), with a significant difference in change (P = 0.002). The participation was unrelated to lifestyle change within the intervention group (annual difference in change between non-adherent vs. adherent at 0.15 points, P = 0.150), but both partially and highly adherent participants improved their lifestyle more than the control group (Figure 1).

3.2 | Change in cognition in relation to multi-participation and multi-lifestyle changes

Adherent multi-participation predicted more improvement in global cognition compared to the non-adherent or the control group (Figure 2) and was related to improvement in all cognitive domains, especially executive function and memory (Table 2). Memory improved less in the non-adherent group than in the control group. Results remained largely unchanged after adjusting for observed lifestyle changes. Adherent multi-participation was related to more improvement in global cognition even compared to the control group participants who improved their lifestyle (n = 214 with imputation; annual difference in change 0.06 points; P = 0.001).

A multi-lifestyle score at baseline predicted improvement in global cognition, processing speed, and memory (Table 3). Healthier lifestyle

TABLE 1 Baseline characteristics of the participants according to intervention allocation and participation activity in the intervention group

|	Control (n = 628)	Intervention (n = 631)	Adherence groups within intervention		
			Non-adherent (n = 132)	Partially adherent (n = 265)	Adherent (n = 234)
Age (years)	68.7 (4.7)	69.0 (4.7)	69.5 (5.0)	69.5 (4.8) †	68.2 (4.3) *
Education (years)	10.0 (3.4)	10.0 (3.5)	10.1 (3.8)	10.1 (3.7)	9.8 (2.9)
Women (n, %)	301 (48%)	286 (45%)	57 (43%)	124 (47%)	105 (45%)
Married or cohabiting (n, %)	473 (76%)	459 (73%)	83 (63%)†	185 (71%)	191 (82%)*,†
APOE ε4 carrier (n, %)	199 (34%)	189 (32%)	40 (33%)	81 (33%)	68 (31%)
Diabetes (n, %)	131 (21%)	132 (21%)	43 (33%)†	52 (20%)*	37 (16%)*
Systolic blood pressure (mmHg)	140 (16)	140 (17)	140 (18)	140 (17)	140 (16)
Total cholesterol (mmol/l)	5.1 (1.0)	5.2 (1.0)	5.2 (1.0)	5.2 (1.0)	5.1 (0.9)
Body mass index (kg/m2)	28.1 (4.9)	28.3 (4.5)	27.8 (4.3)	28.4 (4.7)	28.4 (4.3)
Zung depression score	32.9 (8.3)	32.7 (9.0)	33.6 (9.5)	33.5 (9.1)	31.4 (8.4) *,†
NTB Global cognition	0.02 (0.59)	−0.04 (0.56)	−0.07 (0.58)	−0.02 (0.61)	−0.03 (0.50)
NTB Executive function domain	0.01 (0.69)	−0.04 (0.66)	−0.02 (0.71)	−0.04 (0.70)	−0.04 (0.59)
NTB Processing speed domain	0.03 (0.85)	−0.04 (0.79)	−0.18 (0.84) †	−0.04 (0.80)	0.05 (0.74) *
NTB Memory domain	0.03 (0.66)	−0.03 (0.69)	−0.05 (0.70)	0.00 (0.72)	−0.06 (0.64)
Multi-lifestyle score	4.1 (1.6)	4.0 (1.6)	3.6 (1.7) †	3.9 (1.6) †	4.2 (1.5) *
Diet score (number of goals)	5.0 (1.6)	5.0 (1.5)	4.8 (1.6)	5.0 (1.6)	5.1 (1.5) *
Physical activity (times per week)	4.7 (4.3)	4.3 (3.9)	3.8 (3.5) †	4.2 (3.9)	4.8 (4.1) *
Cognitive activity (activities per week)	16.5 (7.1)	15.8 (7.0)	15.2 (6.9)	15.4 (7.3) †	16.6 (6.6)
Vascular risk score	1.8 (1.2)	1.9 (1.2)	2.3 (1.6) †	1.9 (1.1) *	1.7 (0.9) *

Abbreviations: APOE, apolipoprotein E; NTB, Neuropsychological Test Battery.

*Statistically significant (P < .05) difference compared to non-adherent participants in the intervention group (within-intervention difference); t-test or Chi^2 test.

†Statistically significant (P < .05) difference compared to the control group (pairwise comparison for each intervention intensity); analysis of variance or Chi^2 test.
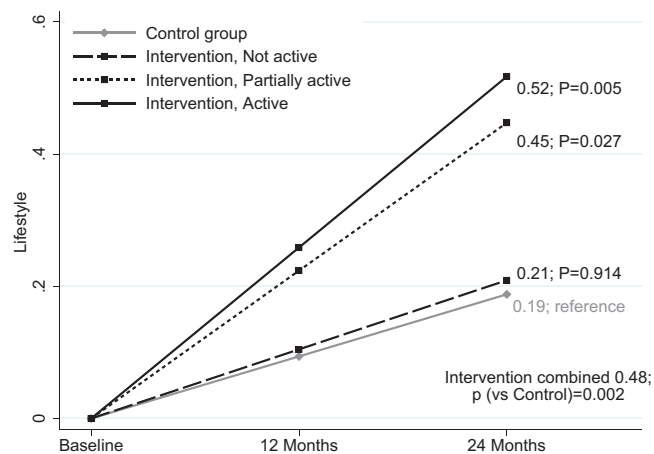
FIGURE 1 Changes in the multi-lifestyle score over 2 years according to the level of participation in intervention activities. Lines represent change in multi-lifestyle score over the 2-year period, estimates obtained from linear mixed model including interaction term participation x time. Model adjusted for baseline age, education, sex, study area, marital status, systolic blood pressure, total cholesterol, body mass index, and Zung depression score
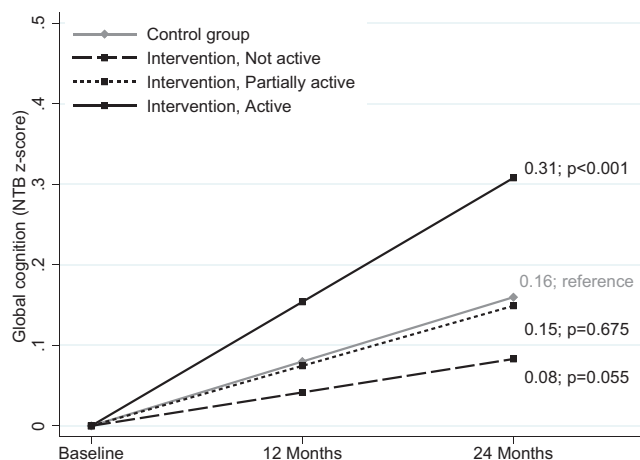
FIGURE 2 Changes in the global cognition over 2 years according to the level of participation in intervention activities. Lines represent change in global cognitive function (Neuropsychological Test Battery [NTB] z-score) over the 2-year period, estimates obtained from linear mixed model including interaction term participation x time. Model adjusted for baseline age, education, sex, study area, marital status, systolic blood pressure, total cholesterol, body mass index, and Zung depression score

TABLE 2 Change in cognitive performance over 2 years according to intervention participation (A) within the intervention group and (B) compared to the control group

	Control (n = 628)	Non-adherent (n = 132)		Partially adherent (n = 265)		Adherent (n = 234)	
		b (SE)	P	b (SE)	P	b (SE)	P
Model A1: Intervention participation							
Global cognition		(ref)		0.03 (0.02)	.111	0.11 (0.02)	<.001
Executive function		(ref)		0.04 (0.03)	.140	0.09 (0.03)	.001
Processing speed		(ref)		−0.03 (0.03)	.324	0.05 (0.03)	.109
Memory		(ref)		0.05 (0.03)	.112	0.16 (0.03)	<.001
Model A2: Intervention participation adjusted for lifestyle change							
Global cognition		(ref)		0.03 (0.02)	.146	0.11 (0.02)	<.001
Executive function		(ref)		0.03 (0.03)	.219	0.08 (0.03)	.006
Processing speed		(ref)		−0.02 (0.03)	.401	0.05 (0.03)	.084
Memory		(ref)		0.05 (0.03)	.139	0.15 (0.03)	<.001
Model B1: Intervention participation compared to the control group							
Global cognition	(ref)	−0.04 (0.02)	.055	−0.01 (0.01)	.675	0.07 (0.01)	<.001
Executive function	(ref)	−0.03 (0.03)	.221	0.01 (0.02)	.539	0.06 (0.02)	<.001
Processing speed	(ref)	0.02 (0.03)	.375	0.00 (0.02)	.784	0.07 (0.02)	<.001
Memory	(ref)	−0.07 (0.03)	.027	−0.02 (0.02)	.380	0.09 (0.02)	<.001
Model B2: Intervention participation compared to the control group adjusted for lifestyle change							
Global cognition	(ref)	−0.04 (0.02)	.061	−0.01 (0.01)	.607	0.07 (0.01)	<.001
Executive function	(ref)	−0.03 (0.03)	.253	0.01 (0.02)	.645	0.05 (0.02)	.002
Processing speed	(ref)	0.02 (0.03)	.393	0.00 (0.02)	.806	0.07 (0.02)	<.001
Memory	(ref)	−0.07 (0.03)	.030	−0.02 (0.02)	.351	0.08 (0.02)	<.001

Note: Coefficient and *P*-values presented for difference in annual rate of cognitive change compared to the reference group (over the 2-year period), obtained from linear mixed models (participation x time interaction). Models adjusted for baseline age, education, sex, study area, marital status, systolic blood pressure, total cholesterol, body mass index, and depression score.

TABLE 3 Change in cognitive performance over 2 years according to baseline lifestyles and lifestyle change (intervention and control groups combined)

	Baseline multi-lifestyle score					Multidomain change				
	Unfavorable	Intermediate		Favorable		Decrease	Stable		Improvement	
		b (SE)	P	b (SE)	P		b (SE)	P	b (SE)	P
Model A: Observed lifestyle assessments										
Global cognition	(ref)	0.01 (0.01)	.620	0.05 (0.02)	.001	(ref)	0.02 (0.01)	.133	0.04 (0.02)	.011
Executive function	(ref)	−0.01 (0.02)	.687	0.01 (0.02)	.453	(ref)	0.04 (0.02)	.007	0.08 (0.02)	<.001
Processing speed	(ref)	0.01 (0.02)	.645	0.06 (0.02)	.003	(ref)	−0.01 (0.02)	.613	0.01 (0.02)	.815
Memory	(ref)	0.01 (0.02)	.505	0.07 (0.02)	.005	(ref)	0.01 (0.02)	.507	0.03 (0.03)	.220
Model B: Imputed lifestyle assessments										
Global cognition	(ref)	0.01 (0.01)	.649	0.04 (0.01)	.003	(ref)	0.01 (0.01)	.264	0.04 (0.01)	.005
Executive function	(ref)	−0.01 (0.01)	.596	0.02 (0.02)	.269	(ref)	0.03 (0.02)	0.032	0.08 (0.02)	<.001
Processing speed	(ref)	0.00 (0.02)	.870	0.04 (0.02)	.024	(ref)	−0.02 (0.02)	0.156	−0.01 (0.02)	.691
Memory	(ref)	0.01 (0.02)	.493	0.06 (0.02)	.013	(ref)	0.02 (0.02)	0.308	0.04 (0.02)	.075

Notes: Coefficient and *P*-values presented for difference in annual rate of cognitive change compared to the reference group (over the 2-year period), obtained from linear mixed models (lifestyle x time interaction). Models adjusted for baseline age, education, sex, study area, marital status, systolic blood pressure, total cholesterol, body mass index, depression score, intervention allocation, and allocation x time interaction.
Abbreviation: SE, standard error.

at baseline also showed cross-sectional association with better global cognition and all cognitive domains (results not shown). Improvement in multi-lifestyle score was associated with improvement in global cognition and executive function. These results were similar in the observed data (Model A) and also imputed data (Model B). Intervention allocation modified the association between lifestyle and executive function (time x group x lifestyle interaction $P = 0.020$ for lifestyle change), but not for other cognitive domains, such that improvement in lifestyles was associated with improvement in executive function in the intervention group only (Figure S2 and Table S2 in supporting information).

3.3 | Change in cognition in relation to participation and changes in different lifestyle components

Adherent participation in each intervention component predicted improvement in global cognition compared to the control group (Table S3 in supporting information). Adherent participation in diet intervention, physical exercise, and cognitive training predicted improvement in all cognitive domains. Adherent participants in the vascular component had more improvement in processing speed, but non-adherent had more negative change in global cognition and executive function than the control group. Participation in lifestyle components was strongly intercorrelated.

The healthiest baseline diet and the lowest vascular risk score predicted improvement in global cognition and memory, and the healthiest diet in processing speed (Table S4 in supporting information). Intermediate baseline cognitive activity was related to cognitive improvement, but the highest activity was not. Increasing cognitive activity in everyday life was associated with more positive change in global cognition and executive function. Improvements in diet and vascular risk were related to improvement in executive function, but change in physical activity showed no associations with cognition. The observed associations remained similar when lifestyle components were adjusted for each other (results not shown).

4 | DISCUSSION

In a 2-year multidomain intervention trial comprising dietary and vascular risk counseling, and exercise and cognitive training, adherent participation resulted in improvement in both cognitive performance and lifestyles. Improved lifestyles were linked to cognitive improvement. Lifestyle changes measured in this study did not, however, explain the participation-related improvement, suggesting that both played a role in the observed cognitive changes. Participation may have benefits beyond the observed measures, for example through social stimulation; and all lifestyle changes induced by the participation may not be captured by these measures.

Several lifestyle interventions have been conducted for the prevention of cognitive impairment,[2,21] but only a few have shown effects on cognitive outcomes,[2] and most have not analyzed cognition in relation to adherence. In earlier analyses of FINGER, adherence to the dietary goals was linked to improvement in executive function.[9] In other trials active memory training was associated with immediate benefits on memory but not on subsequent cognitive trajectories among participants without cognitive impairment,[22] and adherence to physical and cognitive training among persons with mild cognitive impairment was linked to some cognitive improvement.[8] In an uncontrolled clinic-based study, participants with lower or higher adherence to preventive recommendations improved in cognition more than observational controls but did not differ from each other.[23]

Today, it is unclear how intensive an intervention has to be to influence cognitive performance. Two other previous long-term lifestyle trials, the Multidomain Alzheimer Preventive Trial[24] and the Prevention of Dementia by Intensive Vascular Care,[25] both less intensive than FINGER, showed no effect in main analyses, although the latter showed reduced dementia risk among adherent participants with untreated hypertension or no previous cardiovascular disease.[25] In the Finnish Diabetes Prevention study, achieving lifestyle intervention goals was associated with better cognition 9 years after the intervention.[26] Considering the current results showing greatest benefits among those who participated in at least half of all proposed activities, or improved in at least two lifestyle components, evidence suggests quite an intensive program and high adherence. Participants with low adherence differed from those with higher level of adherence in some characteristics, for example they had less favorable lifestyles to begin with. Determinants of adherence to FINGER intervention have been investigated previously.[3,16] Additional tailored support for participants at risk of low adherence may improve intervention outcomes.

Participation in all intervention components contributed to the observed effects on cognition in all cognitive domains, but their relative importance cannot be estimated due to a strong multicollinearity. Actual changes in lifestyle were more independent of each other, and all observed associations remained significant after being included in the same model. Lifestyle changes were linked mainly to changes in executive functioning and global cognition but not to changes in other cognitive domains. Executive functions could be more sensitive for effects of lifestyle modification in early prevention trials as they are suggested to be the first cognitive changes observed in preclinical dementia.[27] Diet, vascular risk control, and cognitive activity, but not physical activity, contributed to associations. Given that physical activity has the strongest previous evidence for beneficial effects,[21] this might indicate that scales used to measure physical activity in the current study were not optimal.

No gold standard for defining adherence to lifestyle intervention has been established, and it is unlikely that one definition would fit all studies. Most often participation in intervention sessions is used,[3,4,28] or sometimes actual lifestyle changes.[5,29] Participation in intervention visits that mainly include counseling is not a direct indicator of targeted behavior change. Therefore, in addition to measuring participation (prespecified analyses), we also investigated the effect of the achieved lifestyle changes. For all intervention components correlations between intervention participation and changes in self-reported

lifestyles were relatively low, indicating that they may represent different aspects of the same lifestyle components. It is plausible that similar lifestyle changes would produce similar effects in both intervention and control groups.

Overall, lifestyles improved in both intervention and control groups, which may be to some extent due to a mini-intervention at the start of the trial or regular monitoring of risk factors and lifestyles during the trial. However, lifestyle changes were larger in the intervention group. Active or partially active intervention group participants showed similar magnitude of lifestyle changes and they did not significantly differ from the non-active participants, which may be due to lack of statistical power, lack of sensitivity in the lifestyle measures used, or the fact that participants even in the non-active group often were active in some of the intervention components. Compared to the control group, the active and partially active intervention groups both improved their lifestyles.

The strengths of this study include the carefully designed and long-term randomized controlled trial, low drop-out rate, careful measurement of standardized cognitive outcomes, and inclusion of a representative sample of older adults at increased risk of dementia.[30] The main limitation is that the trial was not designed to study different intensities of intervention, and thus the groups with different participation rates differed in many characteristics. This may explain the fact that for some cognitive outcomes, the non-adherent intervention group participants had worse trajectories than the control group. Data from drug trials show that adherence to placebo can be associated with better outcomes, supporting the "healthy adherer" effect,[31] and we also detected healthier baseline lifestyle among the adherent people. We adjusted the analyses for several potential confounders but residual confounding is possible. However, cognitive improvement among the adherent intervention participants was greater than for control group participants with the most improvement in lifestyle, who supposedly would be the "healthy adherers" in their group.

The variables for each component were not directly comparable: for diet and vascular risk, the intervention visits were easy to attend, but participation did not automatically mean any improvement in lifestyle, whereas participation in exercise and cognitive training was already an indicator of lifestyle change. Data on lifestyle were all self-reported, and some of the scales were not optimal for measuring changes, for example diet score was based on dichotomous cut-offs, and the cognitive and physical activity scales focused on frequency rather than on changes in content or intensity. The cognitive activity scale did not include activities that were initiated within the intervention. Thus, considering that the intervention group had frequent activities offered by the study, it is possible that they actually had less time for other kinds of activities. The resulting multidomain participation score and lifestyle score are crude measures, aggregating a large set of variables into a single score. However, similar approaches have linked overall healthy lifestyles with dementia[32] and other chronic diseases[33,34] in large epidemiological studies.

Although observational evidence linking lifestyle to cognition is abundant, we are not aware of any previous trials documenting the role of multifactorial lifestyle change in this regard. This is important,

because a single measurement of a lifestyle reflects its presence over many years, even throughout life. To prevent cognitive impairment, it is important to know types of changes and activities provided that are needed to achieve beneficial effects in people at an old age.

Our findings support the multidomain approach to cognition-enhancing intervention, and indicate that both high participation and improvements in everyday lifestyles contribute to the efficacy of the intervention applied in the FINGER. It seems important to offer sufficiently intensive lifestyle interventions, and emphasize measures that support adherence in upcoming trials and implementation activities to promote good cognitive functioning. Newly initiated trials following the FINGER model could investigate the role of adherence in other settings.[35] The long-term follow-up of the FINGER participants will show if the adopted healthier lifestyles will be sustained, and if the adherence affects the longer term outcomes.

CONFLICTS OF INTEREST
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ORCID

Tiia Ngandu https://orcid.org/0000-0002-3698-2021

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SUPPORTING INFORMATION

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