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FEATURED ARTICLE

Occupational complexity and cognition in the FINGER multidomain intervention trial

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Abstract

Introduction: Lifetime exposure to occupational complexity is linked to late-life cognition, and may affect benefits of preventive interventions.

Methods: In the 2-year multidomain Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER), we investigated, through post hoc

analyses (N = 1026), the association of occupational complexity with cognition. Occupational complexity with data, people, and substantive complexity were classified through the Dictionary of Occupational Titles.

Results: Higher levels of occupational complexity were associated with better baseline cognition. Measures of occupational complexity had no association with intervention effects on cognition, except for occupational complexity with data, which was associated with the degree of intervention-related gains for executive function.

Discussion: In older adults at increased risk for dementia, higher occupational complexity is associated with better cognition. The cognitive benefit of the FINGER intervention did not vary significantly among participants with different levels of occupational complexity. These exploratory findings require further testing in larger studies.

KEYWORDS

Alzheimer's disease, cognitive decline, cognitive reserve, dementia, intelligence, multidomain intervention, occupational complexity, prevention, randomized controlled trials

1 | BACKGROUND

Risk reduction and prevention of Alzheimert's disease (AD) and dementia through lifestyle-based interventions is a growing research area.[1] Among modifiable factors, observational studies have reported a protective role for mentally stimulating activities across the lifespan, including education, occupational complexity (i.e., intellectually demanding jobs), and cognitively stimulating leisure activities.[1,2] Regarding occupation-related mental stimulation, prospective studies have linked higher occupational complexity with better late-life cognition and decreased risk of cognitive impairment, AD, and dementia.[3–9]

In older people at increased risk of or with overt AD dementia, matched for cognitive status, higher occupational attainment has been associated with increased AD neuropathology, and with faster cognitive decline after dementia onset.[10–13]

Although observational studies indicate that lifetime exposure to different levels of occupational complexity is associated with cognition in older adults, there is a lack of data on its association with cognitive trajectories in the context of randomized controlled trials (RCTs) for the prevention of cognitive impairment, AD, and dementia.

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) is a RCT demonstrating that a 2-year multidomain lifestyle intervention consisting of nutritional guidance, exercise, cognitive training, and vascular risk factors management had beneficial effects on cognition in participants at increased risk of dementia.[14]

The present exploratory study investigated the association of occupational complexity with primary (Neuropsychological Test Battery) and secondary cognitive outcomes (executive functioning, processing speed, memory) in the FINGER trial (post hoc analyses).

2 | METHODS

2.1 | The FINGER trial

FINGER is a 24-month, population-based, multicenter, multidomain RCT. The trial protocol, baseline population characteristics, and main results have been previously described in detail.[14–16] FINGER enrolled 1260 participants from previous population-based observational studies, at six different sites across Finland. The eligibility criteria included age 60 to 77 years and Cardiovascular Risk Factors, Aging, and Incidence of Dementia (CAIDE) Risk score ≥6 points, indicating presence of modifiable vascular and lifestyle-related risk factors for dementia.[17] Additionally, participants had to meet at least one of the following criteria: Consortium to Establish a Registry for Alzheimer's Disease (CERAD)[18] word list memory task ≤19 words (maximum score 30), CERAD word list recall ≤75% (maximum 100%), or a Mini-Mental State Examination (MMSE) score of 20 to 26 (maximum score 30).[19] These selection criteria identified older individuals whose cognitive abilities were at the mean level or slightly lower than expected for age according to Finnish population norms.[20] The exclusion criteria were previously diagnosed dementia; suspected dementia at screening visit; conditions affecting the safe participation in the intervention (e.g., malignant tumor, major depression, symptomatic cardiovascular disease, revascularization within 1 year); severe impairment in hearing, vision ,or communication ability, or other conditions preventing cooperation as judged by the study physician; and participation in another trial.[15]

A total of 2654 individuals were screened and 1260 of them were randomized 1:1 to the multidomain intervention or control group. The outcome assessors were blinded to the group allocation and were not involved in the intervention. The control group received regular health advice.[16] The intervention group received an intensive multidomain lifestyle intervention consisting of four main components: nutritional guidance, physical exercise, cognitive training, and management of vascular risk factors. The dietary intervention was based on the Finnish Nutritional Recommendations and conducted by nutritionists through individual and group sessions.[21] The physical exercise intervention, based on international guidelines,[22] was implemented at the gym with the guidance of physiotherapists, and included aerobic, resistance, and balance training. The cognitive training included psychologist-led group sessions and an individual computer-based training at home or at the study site. The training program was a web-based in-house–developed computer program including several tasks adapted from

protocols previously shown to be effective in shorter-term RCTs.[23] The program focused on the domains of mental speed, executive function, episodic memory, and working memory. Social activities were stimulated through the numerous group meetings of all intervention components. Management of metabolic and vascular risk factors was based on national evidence-based guidelines.[24–26] Study physicians did not prescribe medications, but recommended participants to contact their own physician or clinic when needed.[25]

For this post hoc study we chose three measures of occupational complexity (with data, people, and substantive complexity) that have been associated with late-life cognition and dementia risk in observational studies,[3–5] and the predefined primary and secondary cognitive outcome measures of the FINGER trial.[15] Of all enrolled participants, 1190 (94%) completed at least one assessment of the primary efficacy outcome after the baseline visit.[14] The present exploratory study included 1026 participants (intervention 521; control 505) who had at least one post-baseline assessment (modified intention-to-treat population [mITT]), available data on occupational complexity, and were retired at baseline. People who were still working at the study baseline (n = 118) were excluded from the main analysis, to measure the association of previous (rather than current) occupational complexity (Figure S1 in supporting information).

FINGER (ClinicalTrials.gov identifier: NCT01041989) was approved by the coordinating ethics committee of the Hospital District of Helsinki and Uusimaa in Finland. Participants gave written informed consent at screening and baseline visits.

2.2 | Cognitive outcomes

The cognitive outcome measures were derived using an extended version of the Neuropsychological Test Battery (NTB) and administered by the study psychologists at baseline, 12, and 24 months.[27] The trial primary outcome was the change in the NTB total score, which consisted of combined scores from 14 different tests listed below. The test results were calculated as standardized *z*-scores with higher scores indicating a better performance. The trial secondary outcomes consisted of *z*-scores for the separate domains of executive functioning, processing speed, and memory. Executive functioning domain included Digit Span, Concept Shifting test (Condition C), Trail Making test (shifting score: time in part B – time in part A), Category Fluency test and a 40-item version of the Stroop test (interference score: time in part 3 – time in part 2). The processing speed domain included Letter Digit Substitution, Concept Shifting (condition A), and Stroop (condition 2) test. The memory domain involved Visual Paired Associates test (immediate and delayed recall), Logical Memory test (immediate and delayed recall), and Word List Memory test (learning and delayed recall).

2.3 | Occupational complexity

Information on current or last-held occupation was collected at baseline through a questionnaire, which included a question asking if the participant was still working or retired, and an open-ended question asking the participant to specify the current or (if retired) the last-held job. For the latter question, all answers were written in Finnish. They were translated to English by a native Finnish speaker fluent in English and were then verified by another native Finnish speaker fluent in English. Occupational complexity scores were then assigned using a work complexity matrix that is based on the estimation of more than 12,000 occupations rated during on-site occupational assessments in the United States.[28] These occupational codes from the US Dictionary of Occupational Titles have been previously matched to the 1980 census for Nordic countries (Nordic Occupational Classification, NYK80).[3]

Each occupation was assigned scores reflecting the level of complexity at which a typical worker functions, with higher scores indicating higher complexity. The matrix used included: (1) complexity of work with data, (2) complexity of work with people, (3) complexity of work with things, and (4) substantive complexity.[29] In this study, we measured complexity of work with data, people, and substantive com-

Highlights

- Occupational complexity is linked with better cognition in people at risk of dementia.
- Occupational complexity is not associated with cognitive changes in older adults.
- Lifetime mental stimulation may affect the cognitive benefits of prevention trials.

Research in context

1. **Systematic review**: The authors searched PubMed for studies assessing the association between exposure to mentally stimulating activities (education, occupational complexity, leisure-time activities) and cognition, in non-pharmacological intervention studies for the prevention of cognitive decline. Two randomized controlled trials (RCTs) measured such association using education as indicator of mental stimulation. These studies are appropriately cited.
2. **Interpretation**: In older adults at increased risk for dementia, higher occupational complexity was associated with better cognition, while it was not associated with cognitive changes. However, the possibility that occupational complexity might influence the effect of a multidomain intervention aiming at preventing cognitive impairment could not be excluded.
3. **Future directions**: As most individuals are exposed to mental stimulation during the lifespan, its effect on cognitive changes in the context of preventive RCTs should be assessed, to identify subpopulations of older adults that might respond differently to interventions aiming to prevent cognitive decline and dementia.

plexity. Complexity with things was not used because previous work reported low reliability and predictive ability for this indicator.[30–32]

Complexity of work with data (score range 0–6) measures the level at which a person deals with information in his or her daily work. Complexity with people (score range 0–8) refers to work demands related to interacting and working with other people. Substantive complexity (score range 0–10) reflects general complexity. This measure was derived through a principal component analysis (PCA) of 46 different factors, set to determine characteristics representing general occupational complexity.[28] The PCA identified eight factors representing substantive complexity: general educational development, specific vocational preparation, complexity of work with data, intelligence aptitude, verbal aptitude, numerical aptitude, abstract interest in the job, and temperament for repetitive and continuous processes.[28]

For each occupation, complexity scores were assigned by two raters (AR and ADM) through a consensus discussion. A third opinion was obtained from a senior researcher (IK) when the first two raters were not certain that they had made the optimal coding. Occupational complexity scores could not be assigned to 46 participants, for whom information on occupation was missing or was too general to be coded into complexity (e.g., planner, housewife).

2.4 | Educational attainment

Information on years of formal education was collected through self-reports at baseline.

2.5 | Statistical analysis

For all skewed NTB components, zero-skewness log-transformation was applied, and the *z*-scores for each test at each time point were standardized to the baseline mean and standard deviation. The NTB total score and domain-specific *z*-scores were calculated by averaging *z*-scores of the individual cognitive tests. To calculate NTB total score, a minimum of 8/14 components was required, for processing speed 2/3 tests, memory 3/6 tests, executive functioning 3/5 tests.[14]

All occupational complexity scores were transformed using zero-skewness log-transformation and standardized into *z*-scores to be used in the regression models.

For baseline comparisons between intervention and control groups, and between participants who were retired and those who were still working, *t* test, median test, and Chi-square test were used as appropriate. Spearman rank-order correlation was used to measure the correlation between the measures of occupational complexity and education. Linear regression models were used to estimate the association between occupational complexity and baseline cognitive scores. Mixed-effects regression models with maximum likelihood estimation were used to analyze the association between (1) occupational complexity and change in cognition over time (baseline, 12 months, and 24 months) and (2) occupational complexity, randomization group, and change in cognition over time. The models for the first analysis (1) included occupational complexity (continuous variables), time (continuous variable coded as 0 for baseline, 1 for 12-month visit, and 2 for 24-month visit), their interaction, and randomization group (dichotomous variable coded as 0 for control and 1 for intervention). The second set of analyses (2) included two- and three-way interactions including randomization group (controls vs. intervention), time, and occupational complexity. The three-way interaction randomization group × time × occupational complexity is the interaction of interest when examining potential heterogeneity of intervention effects, according to guidelines for subgroup analyses in RCTs.[33] Each occupational complexity dimension (data, people, and substantive) was tested with each of the four different cognitive outcomes in separate models. All models were adjusted for age, sex, study site, and education. For three-way interactions with *P* values < .10, average marginal intervention effects for different levels of occupational complexity were estimated and presented graphically (Figure 1A-C). Sensitivity analyses were performed on ITT population (all randomized participants), and participants who were still working.

The Stata 15 software package (StataCorp) was used for all analyses.

3 | RESULTS

3.1 | Baseline characteristics

Participants with (n = 1214) and without (n = 46) information on occupational complexity were not significantly different regarding age, sex, and education. There were no significant differences between the intervention and control group regarding age, sex, education, cognition, and occupational complexity scores at baseline (Table 1).

As expected, the three types of occupational complexity scores correlated with each other: substantive complexity with data complexity (Spearman rho = .97, $P < .001$) and with complexity with people (Spearman rho = .68, $P < .001$); data complexity correlated with complexity with people (Spearman rho = .68, $P < .001$). Education correlated with substantive complexity (Spearman rho = .40, $P < .001$), complexity with data (Spearman rho = .35, $P < .001$), and complexity with people (Spearman rho = .41, $P < .001$).

3.2 | Occupational complexity and baseline cognition

Table 2 gives the estimated associations between occupational complexity levels and baseline cognitive performance. For all cognitive outcomes, higher pre-retirement exposures to occupational complexity with data, people, or substantive complexity were associated with higher cognitive performance.

3.3 | Occupational complexity and cognitive changes

The previously published main results of the FINGER trial showed that most participants improved their cognitive performance over time (primary and secondary cognitive outcomes), and improvement on NTB

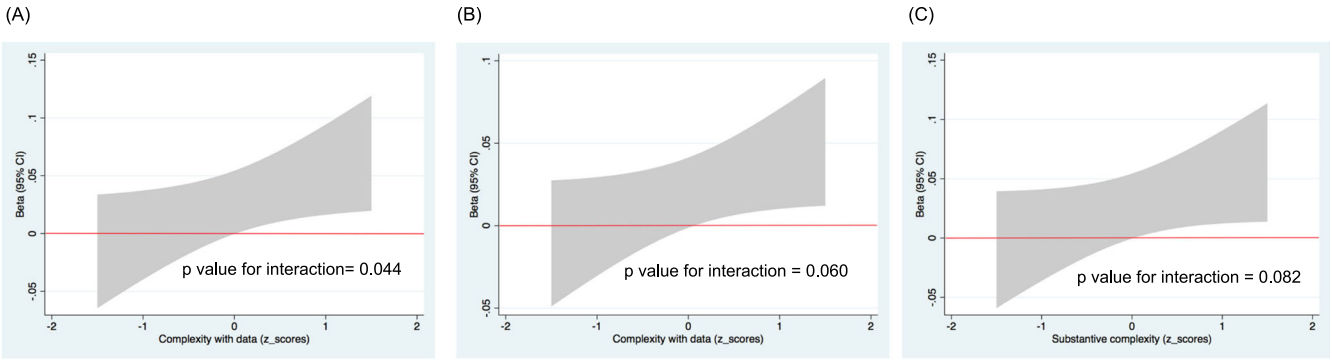

FIGURE 1 In each figure (A: executive function and complexity with data; B: Neuropsychological Test Battery [NTB] total and complexity with data; C: executive function and substantive complexity), the Y-axis shows the difference between intervention and control groups in yearly change on cognition for people with different levels of occupational complexity (positive values indicate effect in favor of the intervention). The shaded area represents the 95% confidence interval (CI) for the regression coefficient. Significant associations between the intervention allocation and yearly change on cognition are found in the occupational complexity levels when the shaded area (CI) does not overlap with zero. Average marginal effects were estimated from mixed-model repeated-measures analyses, including randomization group, time, occupational complexity, interactions group x time, group x occupational complexity, time x occupational complexity, and the three-way interaction group x time x occupational complexity, age, sex, study site, education. *P* values are shown for the group x time x occupational complexity interaction. Marginal effects were estimated only for parameters in which the 3-way interaction had level of significance $P < .10$. Data are based on all participants with at least one post-baseline measurement of the primary efficacy endpoint (modified intention-to-treat population) and who were retired at baseline

TABLE 1 Baseline characteristics of FINGER participants

Characteristic	Participants with information available	Control group (N = 505)	Intervention group (N = 521)
Age at baseline, years	1026	69.8 (4.44)	70.0 (4.36)
Number of women (%)	1026	251 (49.7%)	242 (46.4%)
Education, years	1026	9.0 [3.0]	9.0 [3.0]
Occupational complexity			
Complexity with data	1026	3.0 [2.6]	3.1 [3.2]
Complexity with people	1026	1.8 [1.7]	1.8 [1.5]
Substantive complexity	1026	4.5 [3.3]	4.5 [3.9]
Cognition			
NTB total	1026	−.01 (.58)	−.05 (.55)
Executive function	1025	−.02 (.67)	−.07 (.66)
Memory function	1026	.00 (.66)	−.04 (.68)
Processing speed	1026	−.02 (.82)	−.06 (.76)
MMSE	1023	26.7 (2.05)	26.6 (2.10)

Notes: Baseline characteristics are shown for the modified intention-to-treat population (mITT: participants who underwent at least one post-baseline evaluation of the primary efficacy endpoint) and including only participants who were retired.
Data are reported as number (N); mean and standard deviation (SD); median and interquartile [IQR] range. Scores on the NTB total score, executive functioning, processing speed, and memory are mean values of *z*-scores of the cognitive tests included in each cognitive outcome, with higher scores suggesting better performance. All comparisons ns.
Abbreviations: FINGER, Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability; MMSE, Mini Mental State Examination; NTB, Neuropsychological Test Battery.

total score, executive function, and processing speed was significantly higher in the intervention than in the control group.[14] Table S2 in supporting information shows that occupational complexity was not associated with cognitive changes during the 2-year study period in the entire study population, except for complexity with people. While most participants improved in all cognitive outcomes, irrespective of randomization group and of occupational complexity levels, individuals with higher occupational complexity with people improved less in the domain of processing speed, compared to those with lower occupational complexity with people (Table S2).

TABLE 2 Associations between occupational complexity and baseline cognition in the FINGER trial

	Occupational complexity								
	Complexity with data			Complexity with people			Substantive complexity		
Cognition	ß	SE	*P*	ß	SE	*P*	ß	SE	*P*
NTB total	.106	.017	<.001	.127	.017	<.001	.109	.017	<.001
Executive function	.119	.020	<.001	.127	.020	<.001	.123	.021	<.001
Memory	.076	.021	<.001	.103	.021	<.001	.075	.021	.001
Processing speed	.147	.025	<.001	.176	.025	<.001	.155	.026	<.001

Notes: Linear regression models were used to estimate the association between occupational complexity and baseline cognitive scores. All models were adjusted for age, sex, study site, and education. Data are based on all participants with at least one post-baseline measurement of the primary efficacy endpoint (mITT population) and who were retired at baseline.
The table shows the ß coefficients, SE, and *P* values for the association between occupational complexity scores and baseline cognitive scores. A positive ß value indicates that higher scores in occupational complexity are associated with better cognitive scores.
Abbreviations: ß, standardized beta coefficient; FINGER, Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability; mITT, modified intention-to-treat; NTB, Neuropsychological Test Battery; SE, standard error.

TABLE 3 Associations of occupational complexity with intervention effects on primary and secondary cognitive outcomes in the FINGER trial

	Occupational complexity								
	Complexity with data			Complexity with people			Substantive complexity		
Cognition	ß	SE	*P*	ß	SE	*P*	ß	SE	*P*
NTB total	.021	.011	.060	.007	.011	.505	.016	.011	.134
Executive function	.028	.014	.044	.013	.014	.377	.025	.014	.082
Memory	.021	.018	.238	.004	.018	.831	.017	.018	.356
Processing speed	-.001	.015	.940	-.006	.015	.682	-.007	.015	.663

Notes: Mixed-model repeated-measures analyses with maximum likelihood estimation were used to estimate the change in cognitive scores as a function of randomization group, time, baseline occupational complexity, interactions group x time, group x occupational complexity, time x occupational complexity, and the three-way interaction: group x time x occupational complexity. All models were adjusted for age, sex, study site, and education. Data are based on all participants with at least one post-baseline measurement of the primary efficacy endpoint (mITT population) and who were retired at baseline. The table shows the ß coefficients, SE, and *P* values for the three-way interaction: time x randomization group x occupational complexity. A positive ß value indicates that higher scores in occupational complexity are associated with effect on cognition favoring intervention group. Significant *P* values for interaction ($P < .05$) indicate that the intervention effects on cognition vary significantly by baseline occupational complexity. NTB total is the FINGER primary outcome; executive function, memory, and processing speed are secondary outcomes.
Abbreviations: ß, standardized beta coefficient; FINGER, Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability; mITT, modified intention-to-treat; NTB, Neuropsychological Test Battery; SE, standard error.

The association of occupational complexity with the intervention effects on the cognitive outcomes is shown in Table 3 with beta coefficients (standard errors and *P* values) for the randomization group x time x occupational complexity interaction as the main result (i.e., the estimated difference in intervention effects per year, for one standard deviation unit of increase in occupational complexity). Table 3 shows that participants with a pre-retirement exposure to higher occupational complexity with data had a more pronounced beneficial intervention effect in the executive function outcome (ß[SE]: .028[.014], $P = .044$), compared to those with lower occupational complexity with data. No other significant differences in intervention effects were found. The average marginal effects of the intervention for increasing levels of occupational complexity are reported in Figure 1. The intervention benefits on executive functions was significant only for participants with higher levels of occupational complexity with data (Figure 1A).

3.4 | Sensitivity analyses

The participants who were still working were excluded from the main analysis. Compared to the retired participants, those who were still working were younger, more likely to be male, had higher education and occupational complexity, and higher scores in the cognitive measures (Table S1 in supporting information). Sensitivity analyses were conducted including participants still working (n = 1144) and considering the ITT population (n = 1091). In both sets of analyses, no significant differences between the intervention and control group regarding age, sex, education, nor for cognitive and occupational complexity scores were seen. These additional analyses produced results similar to the main analysis, in terms of associations between occupational complexity levels and baseline cognitive performance, and heterogeneity of intervention effects due to occupational complexity levels (Tables S3-6 in supporting information).

4 | DISCUSSION

In the FINGER multidomain RCT, occupational complexity was associated with baseline cognition, while it had no association with longitudinal cognitive changes, except for the processing speed outcome. The beneficial effect of the multidomain intervention on cognition did not differ across levels of occupational complexity, except for the executive function outcome.

4.1 | Occupational complexity and baseline cognition

At the start of the trial, participants who had higher occupational complexity with data, people, and substantive complexity had better cognition, both in overall performance and specific cognitive domains—executive function, processing speed, memory—all of which are essential for daily functioning and susceptible to age-related decline.[34] The associations between occupational complexity and cognitive measures were independent of educational attainment. This observation confirms findings from previous observational studies showing that, although education and occupation are closely related they can still have independent associations with cognitive functioning and dementia risk.[3,9,32,35]

Our results are consistent with prospective studies reporting an association between intellectually demanding occupations and better late-life cognition,[5,36,37] including studies investigating occupational complexity and cognitive performance among retired individuals[38,39] and recent multicohort studies on work-related cognitive stimulation and dementia risk.[9] Findings from observational studies suggest that lifetime intellectual enrichment can differentially affect cognition in older adults across the cognitive continuum: higher mental stimulation has been related to better cognition in late-life, but may be linked to accelerated cognitive decline after the onset of dementia.[13] Not much is known about these associations among people who are in at-risk asymptomatic stages of dementia and AD. These individuals are the focus of preventive interventions such as the FINGER trial. This study adds to the existing literature by characterizing the associations of three dimensions of occupational complexity—with data, with people, and substantive complexity—in older people at increased risk for dementia identified through a validated dementia risk score.[17]

Our findings can be appraised within the theories of cognitive reserve—related to the adaptability of cognitive processes—and brain maintenance related to brain structure and function related. These concepts have been proposed to explain how lifetime exposure to mental stimulation might contribute to inter-individual variability in late-life cognition, although the underlying mechanisms are not fully understood.[40] Recently, the definitions of resistance and resilience to AD have been proposed for factors linked to slower accumulation of AD pathology (resistance) or the ability to cope with it and maintain better-than-expected cognition (resilience). In this framework, the "resistance *versus* resilience" terms can be extended to neuropathologies other than AD.[41] Lifetime intellectual enrichment, including occupational complexity, has been linked to both improved resistance and resilience.[12,42]

The association of occupational complexity with late-life cognition might be partially accounted for by cognitive abilities in childhood and early adulthood, as people with higher cognitive abilities may be more likely to attain higher levels of education, as well as jobs with higher occupational complexity.[6] Data on early-life cognitive abilities were not available for FINGER participants, and this might have led to an overestimation of the association between occupational complexity and baseline cognition. Studies analyzing the association between early-life cognitive abilities, occupational complexity, and late-life cognition have yielded mixed results. Heterogeneity of findings could stem from methodological differences in those studies, including variation among the cohorts examined, and differences in methods to assess cognition and occupational complexity. One study found that occupational complexity explained less than 1% of the variance in late-life cognition, when adjusting for childhood cognitive abilities.[43] Other studies reported that the association between occupational complexity and late-life cognition or dementia risk was reduced, but not eliminated, when adjusting for childhood cognitive abilities.[4,6,44]

4.2 | Occupational complexity and cognitive changes

In the FINGER trial, cognition improved after 2 years for most of the participants, in the primary and secondary outcomes.[14] In this study, we found that occupational complexity levels were not associated with cognitive changes during the 2-year study period in the whole study population, except for complexity with people. Higher occupational complexity with people was associated with less improvement in processing speed, irrespective of randomization group, likely due to better baseline cognition. Conceivably, effects of repeated cognitive testing[45] might partially account for improvements in both the intervention and control groups. However, as previously reported by Ngandu et al.,[14] for the primary (overall cognition) and secondary outcomes (executive function, processing speed) the improvement in the intervention group was significantly greater than in the control group, suggesting cognitive benefits beyond practice effects.

Occupational complexity was not associated with the beneficial effects of the multidomain intervention, exception for executive function. Higher pre-retirement levels of occupational complexity with data were associated with greater benefit from the intervention in terms of executive function. As observational studies have reported an effect of lifetime mentally stimulating activities on late-life cognitive trajectories,[30,46] it is conceivable that levels of occupational complexity might have an effect on cognitive changes in the context of interventions aiming at preventing or delaying cognitive impairment in older adults. Few studies have measured the effect of lifetime exposure to mental stimulation on the cognitive response to non-pharmacological interventions. In the FINGER, prespecified subgroup analyses have shown that intervention effects were not significantly different across several baseline characteristics, including baseline cognition (measured with MMSE), apolipoprotein E (*APOE*) allele

status, and education. However, there was some indication that participants with higher education (≥9 years) might have been more responsive to the multidomain intervention, in terms of improvement in the NTB total score and executive functions.[47,48] The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) trial tested three types of cognitive training in 2800 dementia-free participants with age ≥65 years. Secondary analyses found that participants with higher education were more likely to improve their performance in measures of episodic memory.[49] Another analysis in the same RCT found that participants with education < 12 years responded better to the processing speed training, compared to those with education ≥16 years.[50]

The performance of occupational-related tasks involving data relies significantly on executive functions.[51] Although our analysis is exploratory and data must be interpreted cautiously, it is possible that previous occupational exposure to tasks high on data complexity might give an advantage for improvement in executive functions in the context of an intervention aiming to improve cognition.

4.3 | Strengths and limitations

This study has several strengths. Occupational complexity was assessed using a well-validated method, applied to the FINGER trial, which had a larger sample size and longer duration than in most dementia prevention RCTs. Thorough randomization and blinding, detailed outcome assessments, and high-quality data collection were also implemented in FINGER.

Limitations include the exploratory study design: all analyses were post hoc, thus our findings need to be verified in larger studies. We performed between-group comparisons to test heterogeneity of intervention effects. However, the FINGER trial might not be powered to detect subgroup effects reliably.[33] Subgroup–treatment interactions were statistically non-significant, although significant estimates for differences between intervention and control groups were observed for the higher levels of occupational complexity with data and substantive complexity, suggesting that while the intervention benefits the elderly population in general, subgroups of individuals with higher levels of occupational complexity might be more responsive. This hypothesis is consistent with observational studies supporting a protective role of lifetime intellectual enrichment in late-life cognitive decline and dementia risk, and should be further tested in prevention RCTs.[5,30]

Another limitation is that occupational complexity was assessed using information from the last-held job, which might not reflect overall level of complexity during a person's working life. However, previous studies comparing scores of occupational complexity derived from the last-held job or multiple jobs found negligible differences.[52] Due to the small number of participants who were still working at the start of the trial, the effect of retirement on cognitive changes and intervention effect was not investigated.

The FINGER population is representative of older Finnish individuals with multiple risk factors for dementia in the absence of pronounced cognitive impairment, so the results cannot be generalized to individuals who already have substantial cognitive impairment, because they were excluded from the trial. Similarly, results should not be generalized to older adults with high cognitive performance, as they were not included in FINGER.[15]

5 | CONCLUSIONS

This study adds to an increasing body of work indicating that the FINGER model is beneficial to a considerable portion of the elderly population at risk for cognitive decline and dementia, including those with genetic risk factors for sporadic AD (*APOE* ε4) and lower educational attainment.[47,48] At the same time, tailored interventions for populations with different risk profiles are needed for optimal prevention effects on a larger scale. Our findings cannot rule out the possibility that some dimensions of occupational complexity might affect cognitive changes in the context of RCTs aiming at preventing or delaying cognitive impairment in older adults. Most individuals are exposed to occupation-related mental stimulation for several decades during adulthood. Evaluation of its role, as well as possible effects of related retirement, might be relevant to the RCTs' design and data interpretation, to identify subpopulations of older adults that might respond differently to preventive interventions.

The FINGER model is being tested and adapted in different populations within the World-Wide FINGERS Network,[53] enabling joint analyses (i.e., larger samples) on the effect of occupational complexity in the context of prevention trials, moving toward the identification of precision prevention strategies for cognitive decline.

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CONFLICTS OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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