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Original Study

The Effect of a 2-Year Intervention Consisting of Diet, Physical Exercise, Cognitive Training, and Monitoring of Vascular Risk on Chronic Morbidity—the FINGER Randomized Controlled Trial

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A B S T R A C T

Objective: To verify whether a multidomain intervention lowers the risk of developing new chronic diseases in older adults.
Methods: Multicenter, double-blind randomized controlled trial started in October 2009, with 2-year follow-up. A total of 1260 people aged 60 to 77 years were enrolled in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). Participants were randomly assigned in a 1:1 ratio to a 2-year multidomain intervention (n = 631) (nutritional guidance, exercise, cognitive training, and management of metabolic and vascular risk factors) or a control group (n = 629) (general health advice). Data on most common chronic diseases were collected by a physician at baseline and 2 years later.
Results: At 2-year follow-up, the average number of new chronic diseases was 0.47 [standard deviation (SD) 0.7] in the intervention group and 0.58 (SD 0.8) in the control group ($P < .01$). The incidence rate per

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100 person-years for developing 1+ new disease(s) was 17.4 [95% confidence interval (CI) = 15.1-20.1] in the intervention group and 20.5 (95% CI = 18.0-23.4) in the control group; for developing 2+ new diseases, 4.9 (95% CI = 3.7-6.4) and 6.1 (95% CI = 4.8-7.8); and for 3+ new diseases, 0.7 (95% CI = 0.4-1.5) and 1.8 (95% CI = 1.1-2.8), respectively. After adjustment for age, sex, education, current smoking, alcohol intake, and the number of chronic diseases at baseline, the intervention group had a hazard ratio ranging from 0.80 (0.66-0.98) for developing 1+ new chronic disease(s) to 0.38 (0.16-0.88) for developing 3+ new chronic diseases compared to the control group.

Conclusions: Findings from this randomized controlled trial suggest that a multidomain intervention could reduce the risk of developing new chronic diseases in older people.

Over the past few decades, decreased mortality from illnesses such as cardiovascular diseases[1] and neurodegenerative diseases,[2,3] along with socioeconomic and environmental changes, has increased life expectancy throughout the world.[4] This has led to an increasing number of people affected by chronic diseases that have become a major health and care challenge. Data from the Global Burden of Disease Study show that total global disability-adjusted life years (DALYs, a composite measure of years of life lost and years of life lived with disability) remained largely unchanged from 1990 to 2015, as decreased DALYs due to communicable, neonatal, maternal, and nutritional disease were offset by increased DALYs due to non-communicable diseases.[5]

One of the main causes of disease burden derives from the coexistence of multiple chronic diseases in the same person, so-called multimorbidity.[6] A recent report from our group estimates that 88% of people older than 60 years have at least 2 coexisting diseases, 73% at least 3, and 56% at least 4.[7] Worldwide, health care systems are threatened by the amount and complexity of care necessary for people with multiple chronic diseases and by the consequences of multimorbidity, such as polypharmacy, high health care use and costs, fragmentation of care and resources dispersion, disability, and poor quality of life.[8,9]

Until now, most of the geriatric research has focused on trials to prevent specific chronic diseases or disease-related adverse outcomes.[10,11] Although there is a compelling need to develop programs to prevent comorbid conditions, intervention trials addressing multimorbidity are lacking. Recently, a number of European projects to prevent major chronic conditions such as dementia among older adults have started.[12] Based on the increasing evidence that the most frequent chronic diseases among the elderly people share common but multifactorial risk factors,[13] those projects included multidomain interventions. The first results came from the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER); the intervention was effective in preventing cognitive decline over a 2-year follow-up period.[14]

In the present study, we conducted a secondary analysis of the FINGER data to evaluate whether the multidomain intervention, which included diet, exercise, cognitive training, and vascular risk monitoring, lowered the risk of developing chronic diseases during the 2-year follow-up.

Methods

Study Design and Participants

FINGER was a 2-year population-based multidomain randomized controlled trial conducted at 6 centers in Finland (Helsinki, Vantaa, Kuopio, Oulu, Seinäjoki, and Turku). The study protocol[15] and baseline population characteristics[16] have been published previously. Participants were recruited from earlier population-based noninterventional surveys.[17,18] To be eligible to participate, people had to be 60 to 77 years old and have a Cardiovascular Risk Factors, Aging and Dementia (CAIDE) Risk Score of 6 points or higher.[19] The CAIDE dementia risk score is based on age, sex, education, systolic blood pressure, body mass index (BMI), total cholesterol, and physical activity—total scores ranging from 0 to 15 points. Participants also had to have a cognitive performance equal to or slightly lower than expected for age according to Finnish population norms.[20] Cognitive screening was done with the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological battery.[21] People were excluded from the study if they were previously diagnosed with dementia or if the study physician, after clinical assessment at the screening visit, suspected they might have dementia. They were also excluded if they were participating in another intervention or had any of the following: a Mini-Mental State Examination score of less than 20 points; a disorder that might make it unsafe to participate in the intervention (eg, major depression, revascularization within 1 year previously); severe loss of vision, hearing, or communicative ability; or a disorder that the study physician judged might hamper their ability to cooperate. FINGER was approved by the Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa. Participants provided written informed consent at the screening and baseline visits. Data are anonymized. Additional information is available from the corresponding author by request.

Randomization and Masking

Participants were randomly assigned to the intensive multidomain intervention or regular health advice group (the control group) in a 1:1 ratio. Computer-generated allocation was done in blocks of 4 (2 people randomly allocated to each group) at each site after baseline assessment by the study nurse. Double-blinding was pursued as much as possible: group allocation was not actively disclosed to participants.

Procedures

The control group received regular health advice. All participants (control and intervention group) met the study physician at screening and at 2 years to provide a detailed medical history and undergo physical examination. At baseline, the study nurse gave all participants oral and written information and advice on healthy diet and physical, cognitive, and social activities that can help people manage vascular risk factors and prevent disability. Additionally, the intervention group received 4 intervention components previously described in detail.[15] The nutritional intervention was based on the Finnish Nutrition Recommendations[22] and was conducted by study nutritionists. Participants were advised to consume a diet that consisted of 10% to 20% of daily energy from proteins, 25% to 35% of daily energy from fat [<10% from saturated plus trans fatty acids, 10%-20% from monounsaturated fatty acids, and 5%-10% from polyunsaturated fatty acids (including 2.5-3 g/day of omega-3 fatty acids)], 45% to 55% of daily energy from carbohydrates (<10% from refined sugar), 25 to 35 g/day of dietary fiber, less than 5 g/day of salt, and less than 5% of daily energy from alcohol.

Energy intake that facilitated a 5% to 10% reduction in body weight was recommended only if necessary after taking the BMI, health status, age, and diet of the participant into account. The participants were encouraged to achieve this goal via high consumption of fruit and vegetables, consumption of wholegrain cereal products and low-fat milk and meat products, limitation of sucrose intake to less than 50 g/day, use of vegetable margarine and rapeseed oil instead of butter, and consumption of at least 2 portions of fish per week. The physical exercise program followed international guidelines[23] and was a modified version of the Dose Responses to Exercise Training (DR's EXTRA) study protocol.[24] Training was guided by study physical therapists at the gym and consisted of individually tailored programs to progressively strengthen muscles (1-3 times per week) and aerobic exercise (2-5 times per week). Participants also did exercises to improve postural balance 1 to 3 times per week. Individual aerobic training consisted of activities preferred by each participant. Group aerobic activities were also provided. Cognitive training included group and individual sessions. The 10 group sessions were led by psychologists: 6 sessions with educational content on age-related cognitive changes, memory, and reasoning strategies applied to everyday activities and 4 sessions for checking progress in individual computer-based training plus a visit to the local Alzheimer Association. Individual sessions that consisted of computer-based training at home or at the study site were conducted over 2 periods of 6 months each. Each period included 72 training sessions (3 times per week, 10-15 minutes per session). The training program was a web-based computer program developed in-house that included several executive processing, working memory, episodic memory, and mental speed tasks. 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.[25–27] It included additional meetings with the study nurse (at 3, 9, and 18 months), and the study physician (at 3, 6, and 12 months) to measure blood pressure, weight and BMI, and hip and waist circumference; conduct a physical examination; and provide recommendations on lifestyle management. Study physicians did not prescribe medication but strongly recommended that participants contact their own physician or clinic if needed.

Assessment of Diseases

Diseases were assessed through a standardized questionnaire, and study physicians interviewed participants at screening and at the 2-year follow-up. The question about diseases was formulated as follows: "Has a physician diagnosed in you or treated you for any of the following diseases during the past year (last 12 months)?" The study physician then read the following list of diseases and procedures: increased blood pressure/hypertension, heart failure, angina pectoris, cancer, asthma, pulmonary emphysema/chronic bronchitis, gallstones/gall bladder inflammation, rheumatoid arthritis, other articular disease, degenerative arthritis of the back/other illness of the back, chronic urethritis/nephritis, cerebrovascular disease, coronary bypass, angioplasty, diabetes, depression, and other psychological illness.

We computed the number of diseases at baseline and follow-up. Each category (n = 17) was considered as one disease.

Outcomes

The outcome of interest in the present study was the new diagnosis of chronic diseases in the same person at the 2-year follow-up.

Statistical Analysis

To calculate the baseline characteristics of the cohort, we performed univariate analyses, using the chi-squared test for categorical data and Student *t* test for continuous data. The incidence rates were estimated as the number of new disease events that occurred during the entire follow-up period divided by person-years of follow-up. Person-years were calculated from baseline assessment (started in October 2009) to the date of follow-up examination (approximately 2 years later) or death, whichever occurred first. Hazard ratios of developing 1+, 2+, and 3+ new chronic diseases and the corresponding 95% confidence intervals (CIs) were derived from Cox proportional hazards regression models. Age, sex, education, current smoking, alcohol intake, and baseline number of chronic diseases were entered in the models as potential confounders. The proportional hazards assumption was assessed by regressing the scaled Schoenfeld residuals against survival time. Results of the analysis stratified according to the number of baseline chronic diseases (0 vs 1+ diseases) is reported. Finally, we calculated the adjusted difference in absolute risk between the intervention and control groups.

There was no difference in the distribution of drop-outs between intervention group and control group ($P = .418$). A multinomial logistic regression was used to compare participants with complete data on diseases with those with missing data and with dropouts. There were no differences in age, sex, education, smoking, alcohol consumption, or number of diseases at baseline between those with complete and missing data on diseases or those who died before the follow-up examination (all P values $>.05$). People who declined to participate in the follow-up examination were older (age, years, odds ratio 1.06, 1.02-1.12) than those who participated.

Although we did not find any difference in sociodemographic characteristics, randomization group, lifestyle factors, or health status between people with and without complete data, we ran a sensitivity analysis with multivariate imputation by chained equations to obtain 5 imputed datasets. We pooled the estimates using the Rubin rule to obtain valid statistical inference (Table S1).

All the statistical analyses were done with Stata, version 14.1 (StataCorp, College Station, TX). This trial is registered with ClinicalTirals.gov, number NCT01041989.

Results

Between September 7, 2009, and November 24, 2011, a total of 2654 people were screened and 1260 randomly assigned to the intervention (n = 631) or control group (n = 629). Eight people in the intervention group (1.3%) and 10 in the control group (1.6%) died during follow-up or soon thereafter and thus did not have follow-up data; they were censored from the study. Fifty-five people in the intervention group (8.7%) and 46 in the control group (7.3%) declined to participate at follow-up. Thirty-six people in the intervention group (5.7%) and 46 in the control group (7.3%) had missing data on 1 or more questions regarding diseases and were excluded from the analyses, which left 532 participants in the intervention group (84.3%) and 527 in the control group (83.8%) with complete disease data at baseline and the 24-month follow-up (Figure 1).

The sociodemographic characteristics of the 2 randomized groups are described in Table 1. There were no differences between the intervention and control groups in age, sex, education, smoking, alcohol habits, or number of chronic diseases at baseline.

The number and percentages of new diseases in the control and intervention group reported at follow-up by baseline morbidity are shown in Table S2. At the 24-month follow-up, the average number of new chronic diseases was 0.47 [standard deviation (SD) 0.7] in the intervention group and 0.58 (SD 0.8) in the control group ($P < .01$).

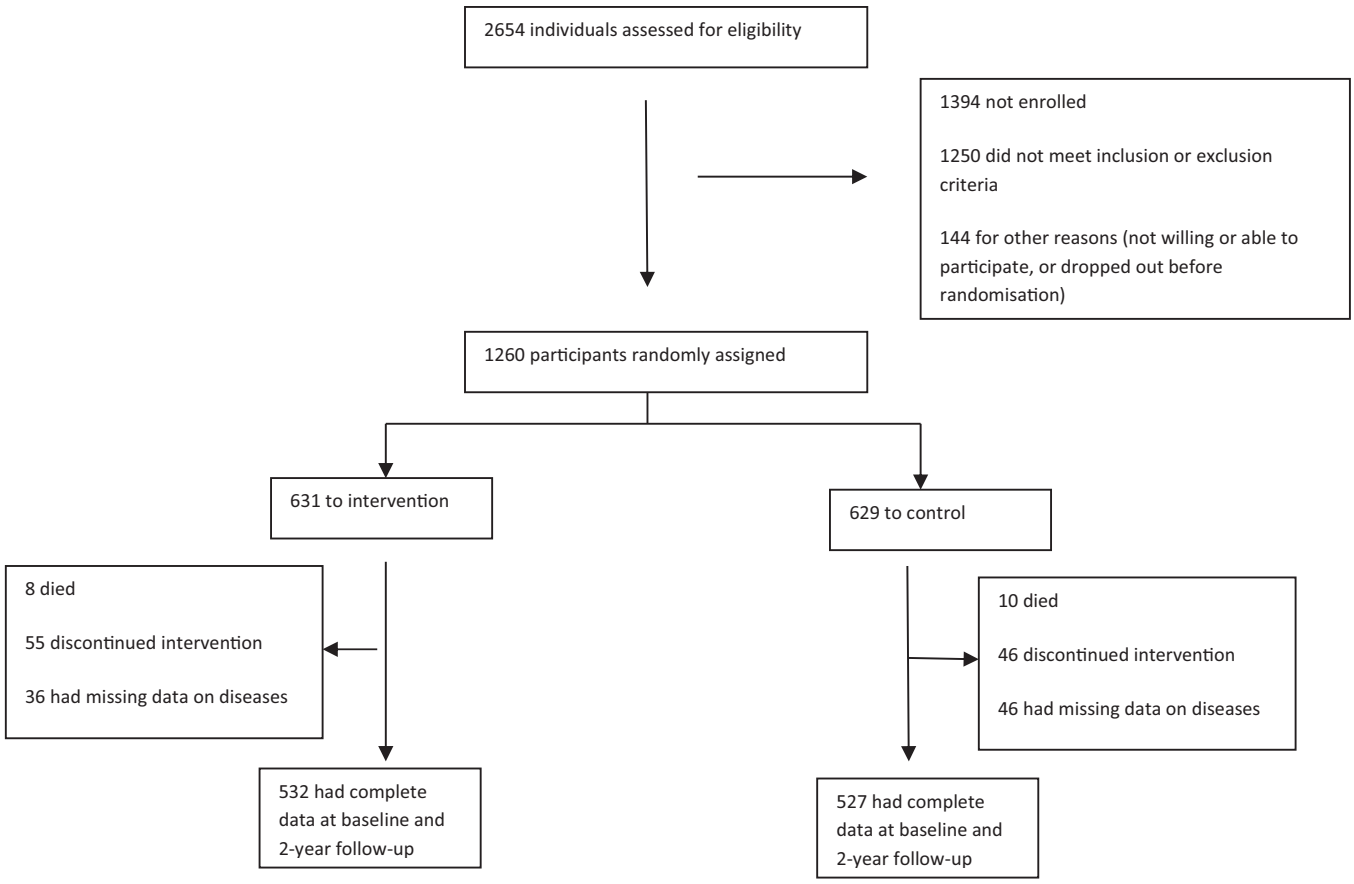

Fig. 1. Trial profile.

The incidence rate of a number of diseases was higher in the control than in the intervention group, although the differences were not all statistically significant. These diseases included: heart failure, cerebrovascular diseases, cancer, and articular diseases (Table 2). There were no baseline differences (in age, sex, BMI, smoking or drinking history, cholesterol, or presence of specific diseases, such as hypertension and diabetes) between people in the intervention and control group who developed new chronic diseases and those who did not (data not shown). Overall, participants who developed new cerebrovascular diseases were older at baseline than those who did not (mean age 72.5 years, SD 4.1, vs mean age 69.1 years, SD 4.6; $P < .003$). BMI was higher in people who developed new rheumatoid arthritis (mean BMI 33.4, SD 11.4, vs mean BMI 28.2, SD 4.7; $P < .01$) and new degenerative arthritis of the back (mean BMI 29.7, SD 5.6, vs mean BMI 28.2, SD 4.7; $P < .01$) than in those who did not.

Table 1
Baseline Characteristics of the Intervention and Control Groups

Characteristics at Baseline	Intervention (n = 532)	Control (n = 527)	*P* Value
Age, years, mean (SD)	69.3 (4.6)	68.9 (4.7)	.176
Women, n (%)	239 (44.9)	260 (49.3)	.150
Education, years, mean (SD)	9.9 (3.4)	9.9 (3.4)	.891
Current smokers, n (%)	47 (8.9)	42 (8.0)	.612
Alcohol, at least once per week, n (%)	236 (44.5)	232 (44.4)	.978
Number of chronic diseases, mean (SD)	1.8 (1.4)	1.8 (1.3)	.645
None, n (%)	93 (17.5)	97 (18.4)	.980
One, n (%)	151 (28.4)	148 (28.1)	
Two, n (%)	145 (27.3)	144 (27.3)	
Three or more, n (%)	143 (27.0)	138 (26.2)	

Two participants had missing data on smoking status and education, and 7 on alcohol consumption.

The incidence rate of new diagnoses per 100 person-years was as follows: for 1+ new disease(s), 17.4 (15.1-20.1) in the intervention and 20.5 (18.0-23.4) in the control group; for 2+ new diseases, 4.9 (3.7-6.4) in the intervention and 6.1 (4.8-7.8) in the control group; and 3+ new diseases, 0.7 (0.4-1.5) in the intervention and 1.8 (1.1-2.8) in the control group (Figure 2).

After adjustment for age, sex, education, current smoking, alcohol intake, and baseline number of chronic diseases, people in the intervention group had a hazard ratio ranging from 0.80 (0.66-0.98) for developing 1+ new chronic disease(s) to 0.38 (0.16-0.88) for developing 3+ new chronic diseases compared with the control group (Table 3). The proportional hazard assumption was respected. After stratification by morbidity at baseline, these results remained significant only in people already affected at baseline by at least 1 disease (Table 4). The absolute risk reduction of developing 3+ new chronic diseases was 2.1%, meaning that 2 of 100 have been prevented thanks to the intervention.

Discussion

The findings of the FINGER, a randomized controlled trial, showed that a multidomain intervention may reduce the risk of accumulating new chronic diseases in older people. The effect was greater in participants who already were affected by at least 1 chronic disorder at baseline.

Our aim was not to analyze data on prevention of specific chronic diseases or to study the mechanisms through which any intervention can prevent them. Rather, we wanted to evaluate whether a multidomain lifestyle-based intervention was effective in preventing a number of chronic diseases. However, we might speculate about some

Table 2
Number (n) and 2-Year Cumulative Incidence (2y-CI, per 100 people) and 95% CIs of Newly Developed Diseases During Follow-up in the Intervention and Control Group

New Diseases During 2-Year Follow-up	Intervention (n = 532)		Control (n = 527)	
	n	2y-CI per 100 (95% CI)	n	2y-CI per 100 (95% CI)
Hypertension	36	3.3 (2.4-4.6)	27	2.5 (1.7-3.7)
Diabetes	24	2.2 (1.5-3.3)	23	2.2 (1.4-3.3)
Heart failure	8	0.7 (0.4-1.5)	13	1.2 (0.7-2.1)
Cerebrovascular disease	5	0.5 (0.2-1.1)	12	1.1 (0.6-2.0)
Cancer	16	1.5 (0.9-2.4)	26	2.4 (1.6-3.5)
Angina pectoris, coronary bypass surgery, angioplasty	23	2.1 (1.4-3.2)	31	2.9 (2.1-4.1)
Asthma, pulmonary emphysema, chronic bronchitis	26	2.4 (1.6-3.6)	30	2.8 (2.0-4.0)
Rheumatoid arthritis, other articular diseases, degenerative arthritis of the back	77	7.1 (5.7-8.9)	105	9.8 (8.1-11.8)
Gallstones, gall bladder inflammation	4	0.4 (0.1-1.0)	8	0.7 (0.4-1.5)
Chronic nephritis, urethritis	7	0.6 (0.3-1.4)	8	0.7 (0.4-1.5)
Depression, other psychological illness	15	1.4 (0.8-2.3)	13	1.2 (0.7-2.1)

Information on diseases were collected and analyzed separately through the manuscript. Only in the above table diseases were grouped together according to main organ systems (angina pectoris, coronary bypass surgery, and angioplasty; depression and other psychological illness; asthma and pulmonary emphysema/chronic bronchitis; rheumatoid arthritis, other articular disease, and degenerative arthritis of the back).

of the mechanisms through which such a multidomain intervention could be protective. In the present study, several diseases were newly reported at follow-up, both in the control and the intervention group. Diseases with higher incidence rates in the control group than in the intervention group included heart failure, cerebrovascular diseases, cancer, and diseases of the musculoskeletal system. Some mechanisms could be intervention-specific as FINGER's intervention addressed nutrition, physical activity, vascular control, and cognitive training, as suggested by epidemiologic evidence to reduce the risk of cognitive decline.[15] Although a single component of the intervention, such as physical activity, may have helped to prevent certain diseases such as musculoskeletal disorders, the whole intervention may have decreased the risk of several diseases by acting on common mechanisms such as lowering chronic inflammation. Low-grade chronic inflammation is frequent in older people,[28] especially in those who already have chronic diseases, and the effect of the intervention was especially significant in participants who already had at least 1 disease at baseline. Further, close monitoring of vascular risk factors probably helped in preventing cardiovascular diseases.

Other large clinical trials based on a multidomain intervention for prevention of chronic diseases are ongoing in Europe; the European Dementia Prevention Initiative (EDPI), an international collaboration, encourages different randomized controlled trials to share data.[29] At the moment, it includes 3 large ongoing European trials: FINGER, Prevention of Dementia by Intensive Vascular Care (preDIVA), and the Multidomain Alzheimer Preventive Trial (MAPT). The EDPI has developed the Healthy Aging Through Internet Counselling in the Elderly (HATICE) program, which, delivered through a coach-supported interactive platform, aims to optimize self-management of cardiovascular risk factors in older people to improve cardiovascular risk profiles and reduce the risk of cardiovascular disease and cognitive decline.[30] Together with FINGER, these projects can become models for trials to prevent multiple chronic diseases. Moreover, secondary analyses of these databases could be used to confirm our preliminary results on prevention of chronic diseases.

This study had several strengths. Older people are often excluded from traditional randomized clinical trials to measure efficacy of medications, mainly because they have multiple diseases. Trials based on nonpharmacologic interventions, such as those in the FINGER, may be more feasible in this part of the population, and their efficacy and effectiveness can be measured with higher external validity than achievable in traditional pharmacologic trials. Additionally, in the present study, participants were included regardless the presence of diseases they had at baseline, dropout rates were low, and adherence to the intervention was high. However, it had limitations as well. First, the FINGER was designed to prevent cognitive impairment and disability. Participants were selected for specific characteristics, that is, cognitive performance and dementia risk. Thus, findings from these analyses can be applied to a large number of the people in this age group[16] but not necessarily to those whose cognitive function is above the mean level and who have no risk factors. Second, the assessment of chronic diseases was done by a physician through a medical questionnaire, so recall bias may have affected participants' answers, but it is unlikely that recall bias differed between the intervention and control group. Although we did not find any difference between people with and without complete data, we ran a sensitivity analysis obtaining similar results. Third, because of the design of the study, we

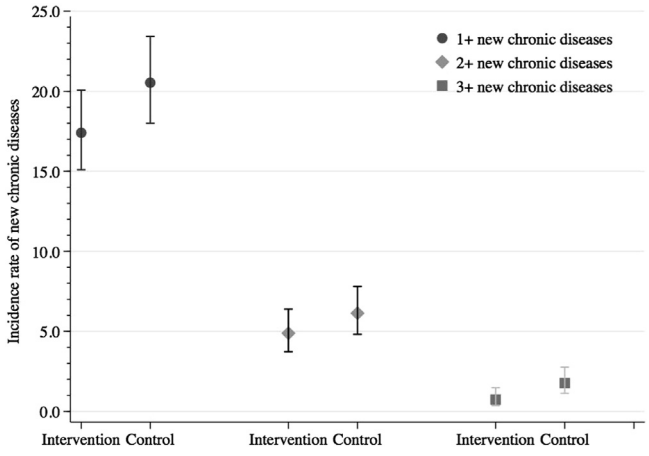

Fig. 2. Incidence rates per 100 person-years of 1+, 2+, and 3+ new chronic diseases in the intervention and control group.

Table 3
Adjusted* HRs (aHRs) and 95% CIs From Cox Regression Models Testing the Effect of the Intervention on the Development of 1+, 2+, and 3+ New Chronic Diseases at Follow-up

	Number of Persons		aHR	95% CI
	Intervention	Control		
Development of 1+ chronic disease(s)	189	221	0.80	0.66-0.98
Development of 2+ chronic diseases	53	66	0.74	0.51-1.06
Development of 3+ chronic diseases	8	19	0.38	0.16-0.88

*Models were adjusted for age, sex, education, smoking status, alcohol consumption, and number of chronic diseases at baseline.

Table 4
Adjusted* HRs (aHR) and 95% CIs From Cox Regression Models Testing the Effect of the Intervention on the Development of 1+, 2+, and 3+ New Chronic Diseases at Follow-up Stratified by Baseline Number of Diseases

Intervention vs Control Group	Subpopulation With No Chronic Diseases		Subpopulation With 1+ Chronic Disease(s)	
	aHR	95% CI	aHR	95% CI
Development of 1+ chronic disease(s)	0.82	0.52-1.29	0.80	0.64 -0.99
Development of 2+ chronic diseases	0.57	0.26-1.27	0.79	0.52-1.19
Development of 3+ chronic diseases	0.64	0.10-3.87	0.33	0.13-0 .87

*Models were adjusted for age, sex, education, smoking status, and alcohol consumption.

cannot ascertain the effect of single domains of the intervention on the development of chronic diseases or evaluate the contribution of each component to the overall effect. Finally, the follow-up period was short, so we cannot rule out the possibility that new diseases were only delayed and not prevented by the intervention. However, delaying the onset of chronic diseases in old age may translate into a compression of morbidity in late life.[31] On the other hand, our estimates of the intervention's effects can be considered conservative for a number of reasons. First, for ethical reasons, advice and feedback on metabolic and vascular risk factors was also provided to the control group. The benefits of the multidomain intervention might have been greater if we had compared the intervention group with a do-nothing control group. Second, cognitive impairment was not included in the list of diseases analyzed in this study because information on the effect of the intervention on cognition has already been published, showing that the intervention helped people to maintain cognitive function.[14] Third, some diseases, such as hypertension, could be overdiagnosed in the intervention group because of more intensive monitoring of vascular risk factors.

During the past 50 years, successful strategies have been developed to prevent infant mortality and infectious diseases and to prevent and treat some highly prevalent and life-threatening chronic diseases, such as cardiovascular diseases.[1] Such lifestyle and medical improvements have increased longevity, but they have also increased the number of people living with multiple chronic diseases.[7] Given the global ageing of the populations, preventing or slowing down the accumulation of multiple chronic disorders will benefit both the single individuals and the society. The FINGER provides a pragmatic model for future trials and integrated intervention programs that could be extended beyond prevention of cognitive impairment to prevention of multiple chronic diseases in various settings and populations. Future studies are needed to confirm these preliminary findings and to evaluate the optimal type and intensity of the multidomain intervention.

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Table S1
Adjusted* HRs (aHRs) and 95% CIs From the Imputation Analysis of the Effect of the Intervention on the Development of 1+, 2+, and 3+ New Chronic Diseases at Follow-up

Intervention vs Control Group	aHR	95% CI
Development of 1+ chronic disease(s)	0.81	0.66-1.00†
Development of 2+ chronic diseases	0.75	0.52-1.09
Development of 3+ chronic diseases	0.41	0.18-0.93

*Models were adjusted for age, sex, education, smoking status, alcohol consumption, and number of chronic diseases at baseline.
†*P* value = .05.

Table S2
Number of New Diseases (%) at Follow-up by the Number of Diseases at Baseline in the Intervention (I) and Control (C) Group

	Number of Diseases at Baseline							
	None (n = 190)		One (n = 299)		Two (n = 289)		Three+ (n = 281)	
	I (n = 93)	C (n = 97)	I (n = 151)	C (n = 148)	I (n = 145)	C (n = 144)	I (n = 143)	C (n = 138)
New diseases at follow-up								
None	58 (62.4)	56 (57.7)	101 (66.9)	80 (54.1)	93 (64.1)	86 (59.7)	91 (63.6)	84 (60.9)
One	25 (26.9)	25 (25.8)	38 (25.2)	49 (33.1)	37 (25.5)	44 (30.6)	36 (25.2)	37 (26.8)
Two	8 (8.6)	13 (13.4)	10 (6.6)	14 (9.5)	14 (9.7)	10 (6.9)	13 (9.1)	10 (7.2)
Three	1 (1.1)	3 (3.1)	1 (0.7)	4 (2.7)	1 (07)	1 (0.7)	3 (2.1)	4 (2.9)
Four	1 (1.1)	0	1 (0.7)	1 (0.7)	0	3 (2.1)	0	3 (2.2)

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Original Study

The Effect of a 2-Year Intervention Consisting of Diet, Physical Exercise, Cognitive Training, and Monitoring of Vascular Risk on Chronic Morbidity—the FINGER Randomized Controlled Trial

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A B S T R A C T

Objective: To verify whether a multidomain intervention lowers the risk of developing new chronic diseases in older adults.
Methods: Multicenter, double-blind randomized controlled trial started in October 2009, with 2-year follow-up. A total of 1260 people aged 60 to 77 years were enrolled in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER). Participants were randomly assigned in a 1:1 ratio to a 2-year multidomain intervention (n = 631) (nutritional guidance, exercise, cognitive training, and management of metabolic and vascular risk factors) or a control group (n = 629) (general health advice). Data on most common chronic diseases were collected by a physician at baseline and 2 years later.
Results: At 2-year follow-up, the average number of new chronic diseases was 0.47 [standard deviation (SD) 0.7] in the intervention group and 0.58 (SD 0.8) in the control group ($P < .01$). The incidence rate per

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100 person-years for developing 1+ new disease(s) was 17.4 [95% confidence interval (CI) = 15.1-20.1] in the intervention group and 20.5 (95% CI = 18.0-23.4) in the control group; for developing 2+ new diseases, 4.9 (95% CI = 3.7-6.4) and 6.1 (95% CI = 4.8-7.8); and for 3+ new diseases, 0.7 (95% CI = 0.4-1.5) and 1.8 (95% CI = 1.1-2.8), respectively. After adjustment for age, sex, education, current smoking, alcohol intake, and the number of chronic diseases at baseline, the intervention group had a hazard ratio ranging from 0.80 (0.66-0.98) for developing 1+ new chronic disease(s) to 0.38 (0.16-0.88) for developing 3+ new chronic diseases compared to the control group.

Conclusions: Findings from this randomized controlled trial suggest that a multidomain intervention could reduce the risk of developing new chronic diseases in older people.

Over the past few decades, decreased mortality from illnesses such as cardiovascular diseases[1] and neurodegenerative diseases,[2,3] along with socioeconomic and environmental changes, has increased life expectancy throughout the world.[4] This has led to an increasing number of people affected by chronic diseases that have become a major health and care challenge. Data from the Global Burden of Disease Study show that total global disability-adjusted life years (DALYs, a composite measure of years of life lost and years of life lived with disability) remained largely unchanged from 1990 to 2015, as decreased DALYs due to communicable, neonatal, maternal, and nutritional disease were offset by increased DALYs due to non-communicable diseases.[5]

One of the main causes of disease burden derives from the coexistence of multiple chronic diseases in the same person, so-called multimorbidity.[6] A recent report from our group estimates that 88% of people older than 60 years have at least 2 coexisting diseases, 73% at least 3, and 56% at least 4.[7] Worldwide, health care systems are threatened by the amount and complexity of care necessary for people with multiple chronic diseases and by the consequences of multimorbidity, such as polypharmacy, high health care use and costs, fragmentation of care and resources dispersion, disability, and poor quality of life.[8,9]

Until now, most of the geriatric research has focused on trials to prevent specific chronic diseases or disease-related adverse outcomes.[10,11] Although there is a compelling need to develop programs to prevent comorbid conditions, intervention trials addressing multimorbidity are lacking. Recently, a number of European projects to prevent major chronic conditions such as dementia among older adults have started.[12] Based on the increasing evidence that the most frequent chronic diseases among the elderly people share common but multifactorial risk factors,[13] those projects included multidomain interventions. The first results came from the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER); the intervention was effective in preventing cognitive decline over a 2-year follow-up period.[14]

In the present study, we conducted a secondary analysis of the FINGER data to evaluate whether the multidomain intervention, which included diet, exercise, cognitive training, and vascular risk monitoring, lowered the risk of developing chronic diseases during the 2-year follow-up.

Methods

Study Design and Participants

FINGER was a 2-year population-based multidomain randomized controlled trial conducted at 6 centers in Finland (Helsinki, Vantaa, Kuopio, Oulu, Seinäjoki, and Turku). The study protocol[15] and baseline population characteristics[16] have been published previously. Participants were recruited from earlier population-based noninterventional surveys.[17,18] To be eligible to participate, people had to be 60 to 77 years old and have a Cardiovascular Risk Factors, Aging and Dementia (CAIDE) Risk Score of 6 points or higher.[19] The CAIDE dementia risk score is based on age, sex, education, systolic blood pressure, body mass index (BMI), total cholesterol, and physical activity—total scores ranging from 0 to 15 points. Participants also had to have a cognitive performance equal to or slightly lower than expected for age according to Finnish population norms.[20] Cognitive screening was done with the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) neuropsychological battery.[21] People were excluded from the study if they were previously diagnosed with dementia or if the study physician, after clinical assessment at the screening visit, suspected they might have dementia. They were also excluded if they were participating in another intervention or had any of the following: a Mini-Mental State Examination score of less than 20 points; a disorder that might make it unsafe to participate in the intervention (eg, major depression, revascularization within 1 year previously); severe loss of vision, hearing, or communicative ability; or a disorder that the study physician judged might hamper their ability to cooperate. FINGER was approved by the Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa. Participants provided written informed consent at the screening and baseline visits. Data are anonymized. Additional information is available from the corresponding author by request.

Randomization and Masking

Participants were randomly assigned to the intensive multidomain intervention or regular health advice group (the control group) in a 1:1 ratio. Computer-generated allocation was done in blocks of 4 (2 people randomly allocated to each group) at each site after baseline assessment by the study nurse. Double-blinding was pursued as much as possible: group allocation was not actively disclosed to participants.

Procedures

The control group received regular health advice. All participants (control and intervention group) met the study physician at screening and at 2 years to provide a detailed medical history and undergo physical examination. At baseline, the study nurse gave all participants oral and written information and advice on healthy diet and physical, cognitive, and social activities that can help people manage vascular risk factors and prevent disability. Additionally, the intervention group received 4 intervention components previously described in detail.[15] The nutritional intervention was based on the Finnish Nutrition Recommendations[22] and was conducted by study nutritionists. Participants were advised to consume a diet that consisted of 10% to 20% of daily energy from proteins, 25% to 35% of daily energy from fat [<10% from saturated plus trans fatty acids, 10%-20% from monounsaturated fatty acids, and 5%-10% from polyunsaturated fatty acids (including 2.5-3 g/day of omega-3 fatty acids)], 45% to 55% of daily energy from carbohydrates (<10% from refined sugar), 25 to 35 g/day of dietary fiber, less than 5 g/day of salt, and less than 5% of daily energy from alcohol.

Energy intake that facilitated a 5% to 10% reduction in body weight was recommended only if necessary after taking the BMI, health status, age, and diet of the participant into account. The participants were encouraged to achieve this goal via high consumption of fruit and vegetables, consumption of wholegrain cereal products and low-fat milk and meat products, limitation of sucrose intake to less than 50 g/day, use of vegetable margarine and rapeseed oil instead of butter, and consumption of at least 2 portions of fish per week. The physical exercise program followed international guidelines[23] and was a modified version of the Dose Responses to Exercise Training (DR's EXTRA) study protocol.[24] Training was guided by study physical therapists at the gym and consisted of individually tailored programs to progressively strengthen muscles (1-3 times per week) and aerobic exercise (2-5 times per week). Participants also did exercises to improve postural balance 1 to 3 times per week. Individual aerobic training consisted of activities preferred by each participant. Group aerobic activities were also provided. Cognitive training included group and individual sessions. The 10 group sessions were led by psychologists: 6 sessions with educational content on age-related cognitive changes, memory, and reasoning strategies applied to everyday activities and 4 sessions for checking progress in individual computer-based training plus a visit to the local Alzheimer Association. Individual sessions that consisted of computer-based training at home or at the study site were conducted over 2 periods of 6 months each. Each period included 72 training sessions (3 times per week, 10-15 minutes per session). The training program was a web-based computer program developed in-house that included several executive processing, working memory, episodic memory, and mental speed tasks. 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.[25–27] It included additional meetings with the study nurse (at 3, 9, and 18 months), and the study physician (at 3, 6, and 12 months) to measure blood pressure, weight and BMI, and hip and waist circumference; conduct a physical examination; and provide recommendations on lifestyle management. Study physicians did not prescribe medication but strongly recommended that participants contact their own physician or clinic if needed.

Assessment of Diseases

Diseases were assessed through a standardized questionnaire, and study physicians interviewed participants at screening and at the 2-year follow-up. The question about diseases was formulated as follows: "Has a physician diagnosed in you or treated you for any of the following diseases during the past year (last 12 months)?" The study physician then read the following list of diseases and procedures: increased blood pressure/hypertension, heart failure, angina pectoris, cancer, asthma, pulmonary emphysema/chronic bronchitis, gallstones/gall bladder inflammation, rheumatoid arthritis, other articular disease, degenerative arthritis of the back/other illness of the back, chronic urethritis/nephritis, cerebrovascular disease, coronary bypass, angioplasty, diabetes, depression, and other psychological illness.

We computed the number of diseases at baseline and follow-up. Each category (n = 17) was considered as one disease.

Outcomes

The outcome of interest in the present study was the new diagnosis of chronic diseases in the same person at the 2-year follow-up.

Statistical Analysis

To calculate the baseline characteristics of the cohort, we performed univariate analyses, using the chi-squared test for categorical data and Student *t* test for continuous data. The incidence rates were estimated as the number of new disease events that occurred during the entire follow-up period divided by person-years of follow-up. Person-years were calculated from baseline assessment (started in October 2009) to the date of follow-up examination (approximately 2 years later) or death, whichever occurred first. Hazard ratios of developing 1+, 2+, and 3+ new chronic diseases and the corresponding 95% confidence intervals (CIs) were derived from Cox proportional hazards regression models. Age, sex, education, current smoking, alcohol intake, and baseline number of chronic diseases were entered in the models as potential confounders. The proportional hazards assumption was assessed by regressing the scaled Schoenfeld residuals against survival time. Results of the analysis stratified according to the number of baseline chronic diseases (0 vs 1+ diseases) is reported. Finally, we calculated the adjusted difference in absolute risk between the intervention and control groups.

There was no difference in the distribution of drop-outs between intervention group and control group ($P = .418$). A multinomial logistic regression was used to compare participants with complete data on diseases with those with missing data and with dropouts. There were no differences in age, sex, education, smoking, alcohol consumption, or number of diseases at baseline between those with complete and missing data on diseases or those who died before the follow-up examination (all P values $>.05$). People who declined to participate in the follow-up examination were older (age, years, odds ratio 1.06, 1.02-1.12) than those who participated.

Although we did not find any difference in sociodemographic characteristics, randomization group, lifestyle factors, or health status between people with and without complete data, we ran a sensitivity analysis with multivariate imputation by chained equations to obtain 5 imputed datasets. We pooled the estimates using the Rubin rule to obtain valid statistical inference (Table S1).

All the statistical analyses were done with Stata, version 14.1 (StataCorp, College Station, TX). This trial is registered with ClinicalTirals.gov, number NCT01041989.

Results

Between September 7, 2009, and November 24, 2011, a total of 2654 people were screened and 1260 randomly assigned to the intervention (n = 631) or control group (n = 629). Eight people in the intervention group (1.3%) and 10 in the control group (1.6%) died during follow-up or soon thereafter and thus did not have follow-up data; they were censored from the study. Fifty-five people in the intervention group (8.7%) and 46 in the control group (7.3%) declined to participate at follow-up. Thirty-six people in the intervention group (5.7%) and 46 in the control group (7.3%) had missing data on 1 or more questions regarding diseases and were excluded from the analyses, which left 532 participants in the intervention group (84.3%) and 527 in the control group (83.8%) with complete disease data at baseline and the 24-month follow-up (Figure 1).

The sociodemographic characteristics of the 2 randomized groups are described in Table 1. There were no differences between the intervention and control groups in age, sex, education, smoking, alcohol habits, or number of chronic diseases at baseline.

The number and percentages of new diseases in the control and intervention group reported at follow-up by baseline morbidity are shown in Table S2. At the 24-month follow-up, the average number of new chronic diseases was 0.47 [standard deviation (SD) 0.7] in the intervention group and 0.58 (SD 0.8) in the control group ($P < .01$).

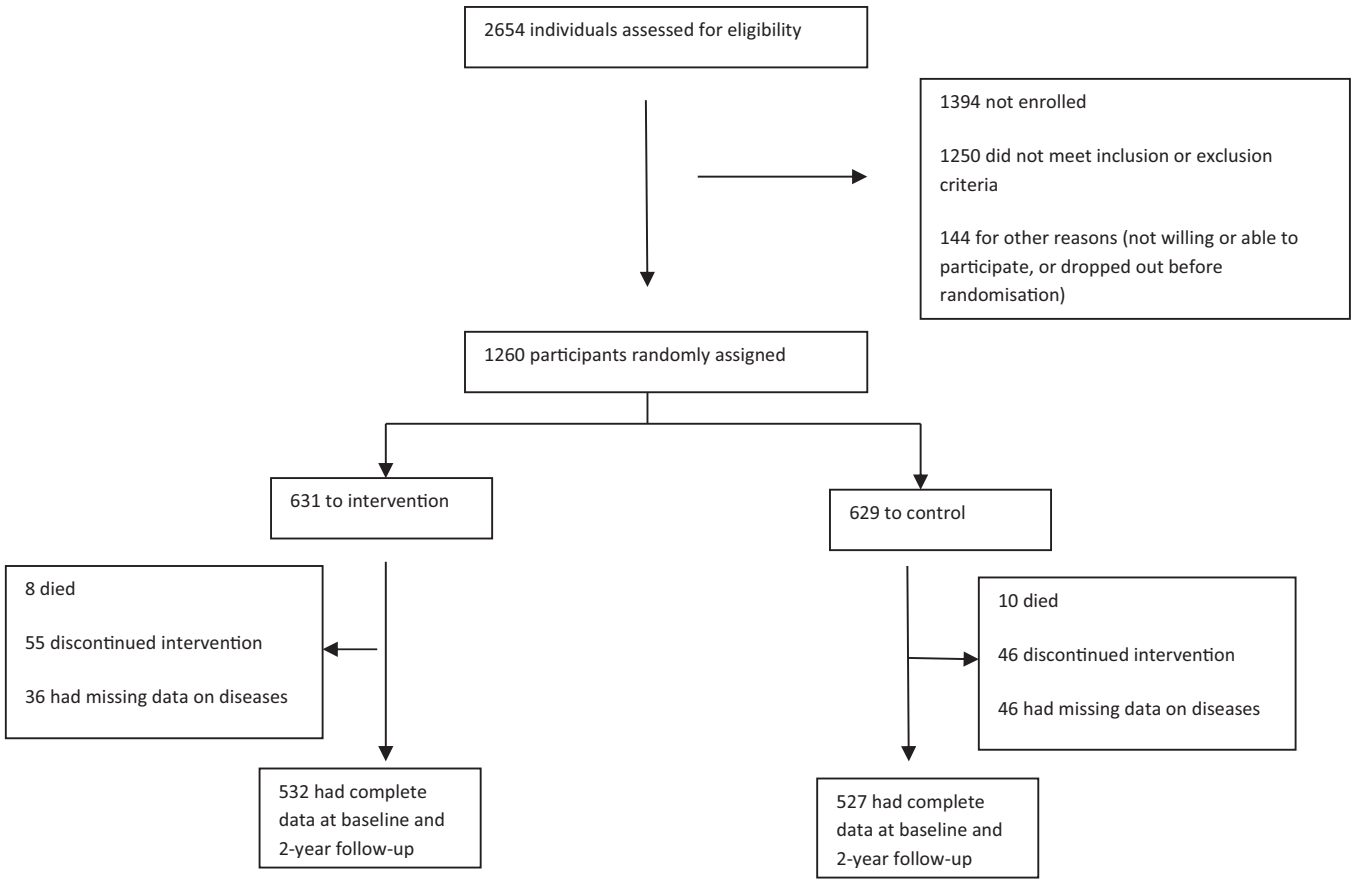

Fig. 1. Trial profile.

The incidence rate of a number of diseases was higher in the control than in the intervention group, although the differences were not all statistically significant. These diseases included: heart failure, cerebrovascular diseases, cancer, and articular diseases (Table 2). There were no baseline differences (in age, sex, BMI, smoking or drinking history, cholesterol, or presence of specific diseases, such as hypertension and diabetes) between people in the intervention and control group who developed new chronic diseases and those who did not (data not shown). Overall, participants who developed new cerebrovascular diseases were older at baseline than those who did not (mean age 72.5 years, SD 4.1, vs mean age 69.1 years, SD 4.6; $P < .003$). BMI was higher in people who developed new rheumatoid arthritis (mean BMI 33.4, SD 11.4, vs mean BMI 28.2, SD 4.7; $P < .01$) and new degenerative arthritis of the back (mean BMI 29.7, SD 5.6, vs mean BMI 28.2, SD 4.7; $P < .01$) than in those who did not.

Table 1
Baseline Characteristics of the Intervention and Control Groups

Characteristics at Baseline	Intervention (n = 532)	Control (n = 527)	*P* Value
Age, years, mean (SD)	69.3 (4.6)	68.9 (4.7)	.176
Women, n (%)	239 (44.9)	260 (49.3)	.150
Education, years, mean (SD)	9.9 (3.4)	9.9 (3.4)	.891
Current smokers, n (%)	47 (8.9)	42 (8.0)	.612
Alcohol, at least once per week, n (%)	236 (44.5)	232 (44.4)	.978
Number of chronic diseases, mean (SD)	1.8 (1.4)	1.8 (1.3)	.645
None, n (%)	93 (17.5)	97 (18.4)	.980
One, n (%)	151 (28.4)	148 (28.1)	
Two, n (%)	145 (27.3)	144 (27.3)	
Three or more, n (%)	143 (27.0)	138 (26.2)	

Two participants had missing data on smoking status and education, and 7 on alcohol consumption.

The incidence rate of new diagnoses per 100 person-years was as follows: for 1+ new disease(s), 17.4 (15.1-20.1) in the intervention and 20.5 (18.0-23.4) in the control group; for 2+ new diseases, 4.9 (3.7-6.4) in the intervention and 6.1 (4.8-7.8) in the control group; and 3+ new diseases, 0.7 (0.4-1.5) in the intervention and 1.8 (1.1-2.8) in the control group (Figure 2).

After adjustment for age, sex, education, current smoking, alcohol intake, and baseline number of chronic diseases, people in the intervention group had a hazard ratio ranging from 0.80 (0.66-0.98) for developing 1+ new chronic disease(s) to 0.38 (0.16-0.88) for developing 3+ new chronic diseases compared with the control group (Table 3). The proportional hazard assumption was respected. After stratification by morbidity at baseline, these results remained significant only in people already affected at baseline by at least 1 disease (Table 4). The absolute risk reduction of developing 3+ new chronic diseases was 2.1%, meaning that 2 of 100 have been prevented thanks to the intervention.

Discussion

The findings of the FINGER, a randomized controlled trial, showed that a multidomain intervention may reduce the risk of accumulating new chronic diseases in older people. The effect was greater in participants who already were affected by at least 1 chronic disorder at baseline.

Our aim was not to analyze data on prevention of specific chronic diseases or to study the mechanisms through which any intervention can prevent them. Rather, we wanted to evaluate whether a multidomain lifestyle-based intervention was effective in preventing a number of chronic diseases. However, we might speculate about some

Table 2
Number (n) and 2-Year Cumulative Incidence (2y-CI, per 100 people) and 95% CIs of Newly Developed Diseases During Follow-up in the Intervention and Control Group

New Diseases During 2-Year Follow-up	Intervention (n = 532)		Control (n = 527)	
	n	2y-CI per 100 (95% CI)	n	2y-CI per 100 (95% CI)
Hypertension	36	3.3 (2.4-4.6)	27	2.5 (1.7-3.7)
Diabetes	24	2.2 (1.5-3.3)	23	2.2 (1.4-3.3)
Heart failure	8	0.7 (0.4-1.5)	13	1.2 (0.7-2.1)
Cerebrovascular disease	5	0.5 (0.2-1.1)	12	1.1 (0.6-2.0)
Cancer	16	1.5 (0.9-2.4)	26	2.4 (1.6-3.5)
Angina pectoris, coronary bypass surgery, angioplasty	23	2.1 (1.4-3.2)	31	2.9 (2.1-4.1)
Asthma, pulmonary emphysema, chronic bronchitis	26	2.4 (1.6-3.6)	30	2.8 (2.0-4.0)
Rheumatoid arthritis, other articular diseases, degenerative arthritis of the back	77	7.1 (5.7-8.9)	105	9.8 (8.1-11.8)
Gallstones, gall bladder inflammation	4	0.4 (0.1-1.0)	8	0.7 (0.4-1.5)
Chronic nephritis, urethritis	7	0.6 (0.3-1.4)	8	0.7 (0.4-1.5)
Depression, other psychological illness	15	1.4 (0.8-2.3)	13	1.2 (0.7-2.1)

Information on diseases were collected and analyzed separately through the manuscript. Only in the above table diseases were grouped together according to main organ systems (angina pectoris, coronary bypass surgery, and angioplasty; depression and other psychological illness; asthma and pulmonary emphysema/chronic bronchitis; rheumatoid arthritis, other articular disease, and degenerative arthritis of the back).

of the mechanisms through which such a multidomain intervention could be protective. In the present study, several diseases were newly reported at follow-up, both in the control and the intervention group. Diseases with higher incidence rates in the control group than in the intervention group included heart failure, cerebrovascular diseases, cancer, and diseases of the musculoskeletal system. Some mechanisms could be intervention-specific as FINGER's intervention addressed nutrition, physical activity, vascular control, and cognitive training, as suggested by epidemiologic evidence to reduce the risk of cognitive decline.[15] Although a single component of the intervention, such as physical activity, may have helped to prevent certain diseases such as musculoskeletal disorders, the whole intervention may have decreased the risk of several diseases by acting on common mechanisms such as lowering chronic inflammation. Low-grade chronic inflammation is frequent in older people,[28] especially in those who already have chronic diseases, and the effect of the intervention was especially significant in participants who already had at least 1 disease at baseline. Further, close monitoring of vascular risk factors probably helped in preventing cardiovascular diseases.

Other large clinical trials based on a multidomain intervention for prevention of chronic diseases are ongoing in Europe; the European Dementia Prevention Initiative (EDPI), an international collaboration, encourages different randomized controlled trials to share data.[29] At the moment, it includes 3 large ongoing European trials: FINGER, Prevention of Dementia by Intensive Vascular Care (preDIVA), and the Multidomain Alzheimer Preventive Trial (MAPT). The EDPI has developed the Healthy Aging Through Internet Counselling in the Elderly (HATICE) program, which, delivered through a coach-supported interactive platform, aims to optimize self-management of cardiovascular risk factors in older people to improve cardiovascular risk profiles and reduce the risk of cardiovascular disease and cognitive decline.[30] Together with FINGER, these projects can become models for trials to prevent multiple chronic diseases. Moreover, secondary analyses of these databases could be used to confirm our preliminary results on prevention of chronic diseases.

This study had several strengths. Older people are often excluded from traditional randomized clinical trials to measure efficacy of medications, mainly because they have multiple diseases. Trials based on nonpharmacologic interventions, such as those in the FINGER, may be more feasible in this part of the population, and their efficacy and effectiveness can be measured with higher external validity than achievable in traditional pharmacologic trials. Additionally, in the present study, participants were included regardless the presence of diseases they had at baseline, dropout rates were low, and adherence to the intervention was high. However, it had limitations as well. First, the FINGER was designed to prevent cognitive impairment and disability. Participants were selected for specific characteristics, that is, cognitive performance and dementia risk. Thus, findings from these analyses can be applied to a large number of the people in this age group[16] but not necessarily to those whose cognitive function is above the mean level and who have no risk factors. Second, the assessment of chronic diseases was done by a physician through a medical questionnaire, so recall bias may have affected participants' answers, but it is unlikely that recall bias differed between the intervention and control group. Although we did not find any difference between people with and without complete data, we ran a sensitivity analysis obtaining similar results. Third, because of the design of the study, we

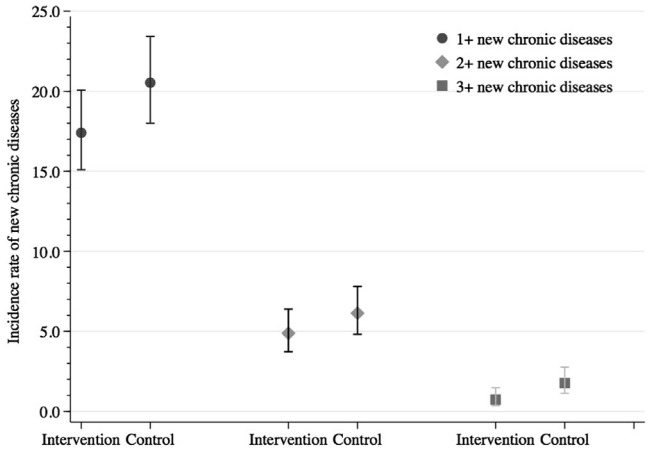

Fig. 2. Incidence rates per 100 person-years of 1+, 2+, and 3+ new chronic diseases in the intervention and control group.

Table 3
Adjusted* HRs (aHRs) and 95% CIs From Cox Regression Models Testing the Effect of the Intervention on the Development of 1+, 2+, and 3+ New Chronic Diseases at Follow-up

	Number of Persons		aHR	95% CI
	Intervention	Control		
Development of 1+ chronic disease(s)	189	221	0.80	0.66-0.98
Development of 2+ chronic diseases	53	66	0.74	0.51-1.06
Development of 3+ chronic diseases	8	19	0.38	0.16-0.88

*Models were adjusted for age, sex, education, smoking status, alcohol consumption, and number of chronic diseases at baseline.

Table 4
Adjusted* HRs (aHR) and 95% CIs From Cox Regression Models Testing the Effect of the Intervention on the Development of 1+, 2+, and 3+ New Chronic Diseases at Follow-up Stratified by Baseline Number of Diseases

Intervention vs Control Group	Subpopulation With No Chronic Diseases		Subpopulation With 1+ Chronic Disease(s)	
	aHR	95% CI	aHR	95% CI
Development of 1+ chronic disease(s)	0.82	0.52-1.29	0.80	0.64 -0.99
Development of 2+ chronic diseases	0.57	0.26-1.27	0.79	0.52-1.19
Development of 3+ chronic diseases	0.64	0.10-3.87	0.33	0.13-0 .87

*Models were adjusted for age, sex, education, smoking status, and alcohol consumption.

cannot ascertain the effect of single domains of the intervention on the development of chronic diseases or evaluate the contribution of each component to the overall effect. Finally, the follow-up period was short, so we cannot rule out the possibility that new diseases were only delayed and not prevented by the intervention. However, delaying the onset of chronic diseases in old age may translate into a compression of morbidity in late life.[31] On the other hand, our estimates of the intervention's effects can be considered conservative for a number of reasons. First, for ethical reasons, advice and feedback on metabolic and vascular risk factors was also provided to the control group. The benefits of the multidomain intervention might have been greater if we had compared the intervention group with a do-nothing control group. Second, cognitive impairment was not included in the list of diseases analyzed in this study because information on the effect of the intervention on cognition has already been published, showing that the intervention helped people to maintain cognitive function.[14] Third, some diseases, such as hypertension, could be overdiagnosed in the intervention group because of more intensive monitoring of vascular risk factors.

During the past 50 years, successful strategies have been developed to prevent infant mortality and infectious diseases and to prevent and treat some highly prevalent and life-threatening chronic diseases, such as cardiovascular diseases.[1] Such lifestyle and medical improvements have increased longevity, but they have also increased the number of people living with multiple chronic diseases.[7] Given the global ageing of the populations, preventing or slowing down the accumulation of multiple chronic disorders will benefit both the single individuals and the society. The FINGER provides a pragmatic model for future trials and integrated intervention programs that could be extended beyond prevention of cognitive impairment to prevention of multiple chronic diseases in various settings and populations. Future studies are needed to confirm these preliminary findings and to evaluate the optimal type and intensity of the multidomain intervention.

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Table S1
Adjusted* HRs (aHRs) and 95% CIs From the Imputation Analysis of the Effect of the Intervention on the Development of 1+, 2+, and 3+ New Chronic Diseases at Follow-up

Intervention vs Control Group	aHR	95% CI
Development of 1+ chronic disease(s)	0.81	0.66-1.00†
Development of 2+ chronic diseases	0.75	0.52-1.09
Development of 3+ chronic diseases	0.41	0.18-0.93

*Models were adjusted for age, sex, education, smoking status, alcohol consumption, and number of chronic diseases at baseline.
†*P* value = .05.

Table S2
Number of New Diseases (%) at Follow-up by the Number of Diseases at Baseline in the Intervention (I) and Control (C) Group

	Number of Diseases at Baseline							
	None (n = 190)		One (n = 299)		Two (n = 289)		Three+ (n = 281)	
	I (n = 93)	C (n = 97)	I (n = 151)	C (n = 148)	I (n = 145)	C (n = 144)	I (n = 143)	C (n = 138)
New diseases at follow-up								
None	58 (62.4)	56 (57.7)	101 (66.9)	80 (54.1)	93 (64.1)	86 (59.7)	91 (63.6)	84 (60.9)
One	25 (26.9)	25 (25.8)	38 (25.2)	49 (33.1)	37 (25.5)	44 (30.6)	36 (25.2)	37 (26.8)
Two	8 (8.6)	13 (13.4)	10 (6.6)	14 (9.5)	14 (9.7)	10 (6.9)	13 (9.1)	10 (7.2)
Three	1 (1.1)	3 (3.1)	1 (0.7)	4 (2.7)	1 (07)	1 (0.7)	3 (2.1)	4 (2.9)
Four	1 (1.1)	0	1 (0.7)	1 (0.7)	0	3 (2.1)	0	3 (2.2)