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Research paper

Health-related quality of life in a multidomain intervention trial to prevent cognitive decline (FINGER)

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ABSTRACT

Introduction: The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) successfully demonstrated that multidomain lifestyle intervention can improve or maintain cognitive functioning in at-risk individuals. Health-related quality of life (HRQoL) was a secondary endpoint.

Methods: The intervention (n = 631) aimed at healthy diet, increased physical activity, cognitive training, and vascular risk management. The control group (n = 629) was given general health advice. HRQoL was assessed at baseline, 12, and 24 months using validated RAND-36 (SF-36) instrument with 8 scales.

Results: During the 2-year intervention period, mean scores in all scales decreased in the control group, but increased in the intervention group for vitality (12 months), social function (12 months), and especially general health at both 12 and 24 months. There was a statistically significant beneficial effect of intervention on the change in general health and physical function at 12 and 24 months.

Conclusion: Multidomain lifestyle intervention improved also important dimensions of HRQoL.

1. Introduction

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) is a "proof-of-concept" double-blind, randomized controlled trial, which successfully demonstrated that a 2-year multidomain lifestyle intervention — consisting of exercise, dietary counselling, cognitive training, and cardiovascular risk factor control — can improve or maintain cognitive functioning in older persons at risk of cognitive decline [1]. A further beneficial dimension of the intervention would be its potential effect on health-related quality of life (HRQoL), a clinically important endpoint in outcome research in older people [2]. An improvement in HRQoL could provide added value, and analysis of HRQoL might also help to discern efficient parts of the multidomain intervention. We report here the in-trial changes of HRQoL in the intervention and control groups.

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[7] Sub-cohort leaders (Turku cohort).
[8] Sub-cohort leaders (Seinäjoki cohort).
[9] Statistical analyses.
[10] Intervention supervision (nutrition component).
[11] Intervention supervision (physical exercise component).
[12] Intervention supervision (cognitive component).
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2. Methods

The FINGER study is registered at Clinicaltrials.gov (NCT01041989). FINGER participants were recruited from earlier population-based surveys in Finland, and inclusion criteria were Cardiovascular Risk Factors, Aging and Dementia (CAIDE) Dementia Risk Score at least 6 points and their cognition average or slightly lower than expected for age. Between Sept 7, 2009, and Nov 24, 2011, 2654 individuals were screened and 1260 community-dwelling individuals aged 60 to 77 years were randomly assigned to intervention ($n = 631$) and control ($n = 629$) groups [1]. The two-year intervention aimed at healthy diet, increased physical activity, cognitive training, and evidence-based vascular risk management and monitoring. The control group was given general health advice.

Study participants were not actively told of their group allocation, and the assessors of study outcomes were blinded to group allocation. Analysis was by modified intention to treat (all participants with at least one post-baseline observation). The primary outcome was cognitive performance, change in cognition measured with comprehensive neuropsychological test battery (NTB) Z score, and the results showed a statistically significant between-group difference in the change of NTB total score per year (0.022, 95% CI: 0.002–0.042, $P = 0.030$ [1]). NTB was selected because a sensitive cognitive test was required in this population with MMSE $\geq$ 26 points at baseline.

HRQoL was a pre-specified secondary outcome, and it was measured using the RAND-36 (Medical Outcomes Study 36-Item Short-Form Health Survey; practically identical to Short Form [SF]-36) with its 8 scales: Physical Function (PF), Role Physical (RP), Role mental (RM), Vitality (VT), Mental Health (MH), Social Function (SF), Bodily Pain (BP), and General Health (GH) [3]. HRQoL assessments were performed at baseline, 12, and 24 months. The results of RAND-36 have been validated in the Finnish population, and population standards for the 8 scales are available [4].

3. Statistical analysis

Mplus (Version 5) was used for fitting Growth mixture models (GMM) with robust maximum likelihood estimation method. Logit link was used to analyze the relationships between categorized scales (RP, RM, SF) and latent growth factors. GMMs are more complex than mixed models used in the cognition report of FINGER [1], since they are based on mixtures of distributions to handle large discrepancies from normal distribution. Estimation of separate mixture distributions is based on latent class analysis in which, as a first step, models with different number of latent classes are estimated (here models with 1–5 latent classes) and the best fitting model was chosen. In-depth information on statistical details can be found in Mplus references [5,6].

Effect size was calculated using Cohen's d formula, i.e. difference score of intervention and control group changes compared to baseline score divided by baseline standard deviation. These values were given separately for 12-month and 24-month effects because non-linear model for change was adopted.

A 2-sided P-value of < 0.05 was considered statistically significant.

4. Results

At baseline, the scores in all RAND-36 scales were considerably higher in FINGER participants compared with the Finnish population of similar age (Table 1). During the 2-year intervention period, mean scores in all scales decreased in the control group, but increased in the intervention group for VT (12 months), SF (12 months), and especially GH at both 12 and 24 months. There was a statistically significant beneficial effect of intervention on the change in GH and PF at 12 and 24 months (Table 2). Effect sizes for most RAND-36 scales were small (0.02–0.08), however higher for GH (0.18–0.20; Table 2).

5. Discussion

In an older population at-risk of dementia, a multidomain intervention to improve or maintain cognitive functioning also had a beneficial effect on several scales of a validated HRQoL instrument, RAND-36 [3], although the effect sizes were not large. However, the net differences in GH scores were greater, between groups they were > 3 points. This is considered clinically meaningful in RAND-36 [3] — and this difference persisted for 2 years. The effect size of GH difference was 0.18–0.20, which is greater than that of cognitive difference (0.13), primary endpoint in FINGER [1]. It is worth noting that the positive effect on GH could

Table 1
Baseline Characteristics of FINGER Participants.

Demographic characteristics	Intervention group ($n = 631$)	Control group ($n = 629$)
Age at baseline visit, mean (SD)	69.5 (4.6)	69.2 (4.7)
Proportion of women, %	45	47
Education, years, mean (SD)	10.0 (3.4)	10.0 (3.4)
MMSE, points, mean (SD)	26.7 (2.0)	26.8 (2.0)

RAND-36 scales[a], age and sex-adjusted	No. of participants with measurement	Intervention group	Control group	Age and sex-adjusted population mean among people aged 65 and over[b]
Physical function	1253	79.0 (0.8)[c]	80.1 (0.8)	60.6
Role physical	1238	73.1 (1.4)	75.7 (1.4)	47.0
Role mental	1232	80.5 (1.3)	80.8 (1.3)	58.8
Vitality	1242	71.0 (0.8)	71.6 (0.8)	60.7
Mental health	1244	81.8 (0.6)	81.1 (0.6)	74.8
Social function	1248	87.8 (0.7)	88.9 (0.7)	77.3
Bodily pain	1249	74.4 (0.9)	74.1 (0.9)	64.2
General health	1251	58.4 (0.7)[d]	61.9 (0.7)	49.0

SD: standard deviation.
[a] The scores of the RAND-36 scales can range from 0 (worst) to 100 (best).
[b] From reference [4].
[c] Mean (SE).
[d] Significantly different from control.

Table 2
Effect of intervention on the change in RAND-36 scales from baseline to 12 and 24 months.

RAND-36 scales		Estimated mean change (intervention/control) in domains during intervention period[a]							
		12 months		*P*-value for difference between groups	Effect size[b]	24 months		*P*-value for difference between groups	Effect size
		Intervention (*P*-value for change)	Control (*P*-value for change)			Intervention (*P*-value for change)	Control (*P*-value for change)		
Physical function	1253	−1.2 (0.003)	−2.5 (<0.001)	0.045	0.06	−2.3 (<0.001)	−4.0 (<0.001)	0.013	0.08
Role physical	1238	−1.6 (0.27)	−4.5 (0.014)	0.29	0.08	−1.7 (0.43)	−4.7 (0.004)	0.11	0.08
Role mental	1232	−0.1 (0.95)	−0.9 (0.51)	0.57	0.02	−0.1 (0.95	−1.7 (0.29)	0.41	0.05
Vitality	1242	0.7 (0.20)	−0.7 (0.34)	0.11	0.07	−0.3 (0.64)	−0.9 (0.026)	0.49	0.03
Mental health	1244	−0.3 (0.40)	−0.3 (0.48)	0.97	0.0	−0.6 (0.17)	−0.9 (0.061)	0.56	0.02
Social function	1248	0.5 (0.38)	−0.5 (0.39)	0.21	0.06	−0.8 (0.057)	−1.2 (0.043	0.53	0.02
Bodily pain	1249	−1.3 (0.07)	−1.1 (0.52)	0.87	0.01	−2.4 (0.086	−2.1 (0.099)	0.89	0.01
General health	1251	1.6 (0.026)	−1.8 (0.004)	<0.001	0.20	1.5 (0.003)	−1.6 (0.050)	<0.001	0.18

[a] Mean values are estimated based on the growth mixture models adjusted for age, sex, education years, and points of Mini Mental State Examination (MMSE) at baseline.
[b] Effect size was calculated as described in Methods.

be demonstrated in the intervention group compared to the control group, even though FINGER participants had a relatively good HRQoL at baseline as compared to population standards [4]. Even though the FINGER participants were population-driven, common experience is that voluntary participants in trials may differ in various ways from non-participants [7].

The results on GH are especially interesting, because self-rated health ("self-perceived health" [SRH]), one component of the GH scale in RAND-36, has been repeatedly shown to be associated with important clinical outcomes including mortality, disability, and use of social insurance facilities and health care services [8–13], independently of conventional risk factors. Recently, SRH has also been shown to predict the development of old age frailty during long-term in clinically healthy middle-aged men [14]. SRH is considered to represent a global perception of an individual's current state of health, which is not necessarily identical with objective state of health.

Conseptualizing SRH is challenging, both biology and culture are involved [15], but among the SF-36/RAND-36 scales it is more strongly related to physical functioning than dimensions of mental health and social functioning [16]. Nevertheless, improvement in GH and SRH may also represent better stress-handling ability and coping [10]. The effects of the FINGER intervention on HRQoL therefore complement the beneficial effects of the intervention on the primary outcome, cognition, and present a potential of the multidomain intervention to improve overall health and well-being of older individuals.

The present results may also hint how various parts of the multidomain intervention contributed to the clinical results of the trial. Physical exercise is interesting here because PF was improved in the intervention group, and physical function is also an important determinant of SRH [16]. However, a recent systematic review could not establish evidence that aerobic physical exercise alone would have cognitive benefit in cognitively healthy older people [17]. On the other hand, in the randomized Finnish Alzheimer disease exercise trial (FINALEX) physical exercise alone improved physical function [18], but had limited effect on cognition (only executive function) in established memory disease [19]. FINGER participants differed from those studies, because their cognition was average or slightly below average and they received multidomain intervention. Forthcoming analyses of adherence during FINGER intervention period will give more data on the issue of how various components of the multidomain intervention were associated with changes in cognition.

Strengths of the present study include the randomized, controlled design, low drop-out rate, and use of generic and validated HRQoL instrument. Limitations include the small effect sizes between groups and potential presence of the regression to the mean phenomenon. Also, it is impossible to conclusively mask the study group membership in this type of study and this may affect self-reported data, such as HRQoL. Finally, long-term effects and sustainability of the beneficial effects are not known.

Ethical statement

The FINGER study is registered at Clinicaltrials.gov (NCT01041989). All participants gave informed consent and the study was approved by appropriate ethical committees.

Disclosure of interest

The authors declare that they have no competing interest.

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