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FEATURED ARTICLE

Dementia prevention: The potential long-term cost-effectiveness of the FINGER prevention program

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Abstract

Introduction: The aim of this study was to estimate the potential cost-effectiveness of the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) program.

Statement: Informed consent was not necessary because all data are secondary.

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Methods: A life-time Markov model with societal perspective, simulating a cohort of people at risk of dementia reflecting usual care and the FINGER program.

Results: Costs were 1,653,275 and 1,635,346 SEK and quality-adjusted life years (QALYs) were 8.636 and 8.679 for usual care and the FINGER program, respectively, resulting in savings of 16,928 SEK (2023 US$) and 0.043 QALY gains per person, supporting extended dominance for the FINGER program. A total of 1623 dementia cases were avoided with 0.17 fewer person-years living with dementia. The sensitivity analysis confirmed the conclusions in most scenarios.

Discussion: The model provides support that programs like FINGER have the potential to be cost-effective in preventing dementia. Results at the individual level are rather modest, but the societal benefits can be substantial because of the large potential target population.

KEYWORDS
cost effectiveness, costs, dementia, FINGER, health economic simulation, prevention

1 | INTRODUCTION

Dementia disorders affect about 55 million people worldwide[1] with devastating consequences for people living with dementia and their families. Economic consequences are enormous: the global societal costs of dementia in 2019 were estimated to be 1.3 trillion US$.[1] Forecasts provide a challenging scenario, with 75 million people projected to be living with dementia by 2030. The World Health Organization (WHO) stated in 2012 that dementia is a worldwide priority and has subsequently been heavily engaged in dementia issues.[2–5]

About 40% of dementia cases may be potentially preventable by modifying risk factors.[6–8] For example, estimates for the UK suggest that delaying onset by 3 years would reduce costs by 23%.[9] Declining trends in incidence and prevalence of dementia in some high-income countries[10,11] also offer indirect support that prevention may already be happening through better medical and lifestyle risk-factor management, and better education. There is an economic case for addressing mid-life risk factors for dementia,[12] although impacts on dementia prevalence will obviously be slow to emerge.

However, results from intervention studies, preferably randomized controlled trials (RCT), are needed to better understand causality in epidemiological studies. Because single risk-factor interventions have often failed to show significant effects, it has been suggested that multidomain approaches represent the best practice.[13]

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) project is the first RCT to show a statistically significant beneficial effect on cognition of a multidomain lifestyle intervention program for a target population at risk of developing cognitive decline.[14]

Prevention of cardiovascular risk factors in early life may have complex effects in later life:[15] Reduced morbidity results in lower mortality, which affects the risk of developing disorders whose prevalence increases with age.

A hypothetical cost-effectiveness analysis based on the results from the observational Cardiovascular Risk Factors, Aging and Dementia (CAIDE) study in Finland[16] indicated that a primary prevention program targeting dementia risk factors has the potential to be cost-effective.[17]

One key issue in dementia prevention trials is how to quantify the effect of the intervention on dementia risk when the duration of the trial is too short to detect dementia incidence. It is possible to use dementia risk scores that include modifiable factors (e.g., lifestyle, vascular, or metabolic) that are expected to change during the clinical trial to estimate the magnitude of intervention effect on dementia incidence. Several dementia risk scores have already been developed, but very few cover a longer time span to be useful in prevention trials.[18]

The period of cognitive impairment, from the first early signs to end of life with dementia, may last for decades.[6] An important issue for decision makers (budget holders, care planners, policy makers) is therefore whether prevention programs are cost-effective from a societal viewpoint in the long run. The aim of the present study is consequently to explore the potential long-term cost-effectiveness of the FINGER program.

2 | METHODS

2.1 | The FINGER project

FINGER is a "proof-of-concept" RCT that targeted people aged 60 to 77 years from the general population considered to be at risk (see below) of cognitive decline. FINGER included a 2-year multidomain

RESEARCH IN CONTEXT

1. **Systematic Review**: A scoping review was conducted to get the inputs needed for the construction of the model, based on a Finnish–Swedish perspective. These inputs constituted the intervention effect, the intervention cost, data on incidence of dementia, disease progression and mortality, costs of care, unit costs, and outcomes.
2. **Interpretation**: The model supports the view that programs like Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) have the potential to be cost-effective for preventing dementia. The results at the individual level are rather modest, but the societal benefits may be substantial because of the large potential target population.
3. **Future Directions**: Better modeling techniques are needed to integrate the complexity of prevention work, such as effects on dementia, but also on other (e.g., cardiovascular) conditions. Also, inputs are needed from other countries/regions to improve generalizability. Future studies as part of the World Wide FINGERS may provide valuable data for these discussions.

lifestyle intervention consisting of exercise, dietary counselling, cognitive training, and cardiovascular risk-factor control.[14] Both groups in the trial were offered six nurse visits, two physician visits, and three psychologist visits for recruitment and outcome assessments. The control group received regular health advice. In addition, the intervention group was offered: three individual sessions and seven to nine group sessions with a nutritionist; group activity at a gym with a physiotherapist (one to three times per week), and independent and guided aerobic exercise (two to five times per week); ten group sessions for cognitive training led by a psychologist, and independent computer-based cognitive training at home or at the study site; and three additional visits with a study nurse and three additional visits with a study physician for the management of metabolic and vascular risk factors.

From the FINGER project, basic model inputs were extracted regarding the intervention effect and the cost of the intervention.

2.2 | Basic model design

A decision-analytic Markov model was developed to simulate 100,000 people at risk of dementia and their progression over their lifetime to reflect usual care (UC) and the effect of the FINGER program (labelled as "prevention"). UC reflects the costs and outcomes related to disease states and disease progression without the added components of FINGER. Assumptions and inputs for the base case are presented in Table S1 in supporting information. The model assumes that no effective disease-modifying drug treatment becomes available. The cohort

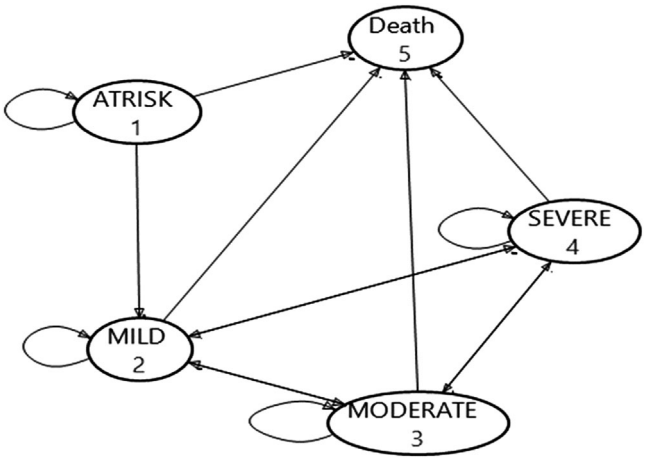

FIGURE 1 The basic structure of the five-state Markov cohort model, starting with 100,000 persons at risk for dementia. Arrows indicate transition directions

state-transition model was chosen for its balance between transparency and possibility to reflect the long-term age-specific natural progression and health-economic outcomes.

Two analytic approaches were applied. In the cost-utility analysis (CUA), the model simulated care costs and quality-adjusted life years (QALYs) to estimate the incremental cost-effectiveness ratio (ICER), incremental net monetary benefits (NMB), and incremental net health benefits (NHB).[19,20] The willingness-to-pay (WTP) threshold was set at 600,000 SEK (Swedish Krona) per additional QALY, which roughly reflects an accepted WTP level in Sweden.[21,22] In the second approach, the cost-effectiveness analysis (CEA), we looked at the number of prevented cases of dementia, the number-needed-to-treat (i.e., number needed to be exposed to the FINGER program) to prevent one case of dementia, the dementia-free life-years saved, and the life-years saved.

The Markov model has five states (Figure 1, Table S4 in supporting information): at risk, mild, moderate, severe dementia, and death. Programming was done with TreeAge® and MS Excel® software. Starting age for modeling was 70 years to reflect the age at which the FINGER program was applied. The model simulated until age 100 years in 30 cycles of 1 year with half-cycle correction. Input parameters for mortality, costs, and QALYs were age-specific (see supporting information).

Because all inputs were not available from Finnish sources, the model is a mix of contexts from Finland and Sweden, aiming to represent care of dementia in a "Northern Europe welfare state."

All future costs in the model were discounted at 3% to reflect present value,[23] and expressed as SEK 2016, where 1€ = 9.47 SEK and 1 US$ = 8.56 SEK.[24]

2.3 | Model inputs

A scoping review was conducted to obtain inputs needed for construction of the model, which took a Finnish–Swedish perspective. Inputs

are based on published papers from peer-reviewed journals (including the FINGER trial) or established registries and databases.

2.3.1 | Risk of dementia

Because the FINGER trial does not have data on conversion to dementia, our model used a combination of a fitted Poisson model based on incidence rates in EURODEM at ages 70 to 90+[25] (see supporting information).

The CAIDE risk score provides an estimate of dementia risk based on several risk factors (age, sex, education, systolic blood pressure, total serum cholesterol, obesity, physical inactivity).[26,27] The range is between 0 and 15 points, of which seven points corresponds to modifiable risk factors. A higher score indicates a higher risk of developing dementia. FINGER participants had a mean CAIDE score of 6 and higher, indicating a greater risk compared to a CAIDE score between 0 and 5. Therefore, estimates for the usual care group in EURODEM were multiplied by 2 to reflect a similar population.

2.3.2 | Intervention effect

The intervention effects on the conversion risk to dementia in FINGER have not yet been analyzed due to the relatively short follow-up period and small number of dementia cases accumulated so far. Therefore, the CAIDE risk score was calculated at baseline and at 2 years for both the control and intervention arm. The relative risk reduction corresponding to this score was calculated in several steps using the CAIDE risk model[16] and was estimated to be 6.44%[28] (see supporting information). In the base-case option, the intervention effect was assumed to persist after the end of the 2-year program for the remaining lifetime.

2.3.3 | Disease progression and mortality

To estimate transition probabilities between states, data on disease progression and mortality were derived from the SveDem registry.[29,30] SveDem is a Swedish dementia registry that started in 2007, and now comprises >100,000 people with any type of dementia who are followed annually. Observed transition probabilities were used. Dementia severity was classified as mild (Mini-Mental State Examination [MMSE] score 21–30), moderate (MMSE 10–20), or severe (MMSE 0–9).[31] Figure S2 and Tables S4-S5 in supporting information provide details on dementia disease progression and mortality. All transitions from at risk to dementia were assumed into mild dementia. A transition directly to moderate was regarded as unlikely.

Age-specific mortality for at-risk people was assumed to be the same as for the general population, derived from Statistics Sweden.[32] Mortality in mild, moderate, and severe dementia was estimated by a Cox survival analysis and by applying the hazard ratios to the age-specific mortality rate from Statistics Sweden from the age of 50 until death.

2.3.4 | Costs

Costs were derived from a cross-sectional Swedish population-based costing database, describing resource use and costs in terms of cognitive status age. The database reflects a societal perspective and has been used in several health economic studies.[17,31,33–35] For details, see comments to Figure S3 and Table S6 in supporting information. To reflect the inclusion criteria in FINGER for at-risk people,[14] costs in the costing database were defined as community-living people with MMSE of 26 or less, but not having mild cognitive impairment (MCI) or dementia. Because cost data were skewed, a log-link generalized linear model (GLM) with gamma distribution was used to derive costs in relation to age and level of cognitive impairment.

The net costs of the FINGER program per person were estimated to be 5490 SEK, based on detailed information on the content and actual implementation of the multidomain intervention in FINGER, such as individual and group sessions with various staff categories involved, lengths of sessions, and so on (see Table S7 in supporting information).

2.3.5 | QALYs

Health-related quality of life estimates were obtained from two sources: for the at-risk state, assuming that individuals would be the same as for a normal Swedish population, age-specific QALYs were derived.[36] For the dementia states (mild—moderate–severe) a Swedish study was used[37] (see Table S8 in supporting information). These estimates were based on EQ5D-3L[36] (Swedish tariff). The association by age in the normal population was ad hoc assumed to be applicable to the utilities for the dementia states.

2.4 | Sensitivity analyses

Given the uncertainty in parameters and assumptions, a comprehensive sensitivity analysis was conducted.

2.4.1 | Variation of starting age and model duration

We explored shorter modeling periods (5, 10, and 20 years) and alternative starting ages: at 60 years (modeling 40 cycles) and at 50 years (modeling 50 cycles).

2.4.2 | Variation of risk reduction

The effect of FINGER on the CAIDE score was estimated using an alternative mixed model method,[28] with corresponding relative risk reduction of 6.09% (instead of 6.44%).

The FINGER effect may have been biased by the Hawthorne effect: participants in the control group are also aware of risk factors as a result of being enrolled in a trial.[38] Therefore, the mean risk factor

scores of the FINGER program group at baseline were used instead of the control group at the end of the follow-up period, resulting in a relative risk reduction of 11.8%.

Based on the prevention potential as described by Livingston et al.,[8] two risk-reduction options were applied: 40% as maximum potential risk reduction and 12% based on the population attributable fractions as in the CAIDE score.

The duration and magnitude of the intervention effects are applied in two options: halved intervention effect (3.22%), and an expanded intervention effect applied for transitions both from mild to moderate and from moderate to severe dementia through the modeling period.

Our model only takes the effects on dementia into account. However, it is plausible to assume that the content of FINGER will also influence cardiovascular risks. Based on studies on the effects on prevention programs targeting cardiovascular risk,[39–42] a 10% reduction in mortality in the prevention group in the at-risk and mild states was assumed.

Instead of an "at-risk" population, an option in which the program is applied to a lower risk general population was tested (with dementia risk as in the EURODEM study[25]).

Also, two high-risk scenarios were examined by applying the intervention to a population with a higher risk: one option with start in MCI,[31,43] and another option with a base risk increase by a factor of four instead of two.

2.4.3 | Alternative epidemiologic input

The US National Alzheimer's Coordinating Center (NACC) data[44] on disease progression and mortality were applied as alternative estimates for dementia transition probabilities and survival.

2.4.4 | Alternative discount rates

Discount rates of 1% and 5% were explored.

2.4.5 | Alternative costing inputs

A narrower economic perspective was explored, with only direct medical and social sector costs included (see comments to Figure S3), and costs of informal care excluded.

The intervention costs were also varied: +100%, +50%, −25%, and −50% of the base case.

2.4.6 | Additional intervention program intervals

As the sustainability of the intervention effect (such as life-style changes) over time is unknown, a scenario was examined in which the intervention was repeated at year 5 and then every 10th year at for starting ages of 50, 60, and 70 for those people who remain in the at-risk state.

TABLE 1 Outcomes of the cost-utility analysis (initial hypothetical cohort of 100,000 persons at risk for dementia; base case; costs expressed in SEK 2016)

	Usual care	Prevention	Difference
Cost-utility analysis			
Costs (SEK)/person	1,653,275	1,636,346	−16,928
Effect/QALYs	8.636	8.679	0.043
Incremental C/E (ICER)			<0[a]
Incremental NMB[b]			42,728
Incremental NHB[b]			0.071

Abbreviations: ICER, incremental cost-effectiveness ratio; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year; SEK, Swedish crowns (krona); UC, usual care; WTP, willingness-to-pay.
[a]Extended dominance for the prevention strategy.
[b]Assumption: WTP is 600,000 SEK/QALY.

2.4.7 | Alternative WTP levels

We considered 200,000 400,000 and 1,000,000 SEK per gained QALY.

3 | RESULTS

3.1 | Base case

In the base case of the cost-utility analysis, the prevention program supported extended dominance: there were both cost savings and gains in QALYs compared to UC (Table 1). The threshold for cost neutrality was at an intervention cost of 22,418 SEK.

The mean survival time was about 15 years in both groups (Table 2). The intervention prevented 1623 cases of dementia (out of an initial simulation cohort of 100,000 people) during the simulated period of 30 years. The cumulative risk of developing dementia was 46.3% in the UC group and 44.7% in the prevention group (and the cumulative death risk was almost 100%). There were 12.4 dementia-free years in UC and 12.6 in the prevention group. The number of aggregated prevented cases peaked just before 20 years (Figure 2), where the number needed to treat was 55. After 20 years, greater survival in the prevention group resulted in a larger population at risk of developing dementia, causing somewhat more dementia cases in that group.

3.2 | Sensitivity analysis

In the sensitivity analysis (Table 3), most alternatives supported cost-effectiveness by reference to the assumed WTP, and most options also confirmed the extended dominance of the FINGER program. Model length is crucial, and 5 years is too short to result in relevant intervention effects on dementia incidence in terms of cost-effectiveness. When the Hawthorne effect was considered, cost savings were about double those found with the base case. A reduction in mortality by 10% in the prevention group resulted in higher costs due to increased

TABLE 2 Outcomes of the cost-effectiveness analysis (initial hypothetical cohort of 100,000 persons at risk for dementia)

	Usual care	Prevention	Difference
Cost effectiveness analysis			
Aggregated outcomes			
Incident cases of dementia after 30 years	46,297	44,674	−1623
Incident cases of dementia after 20 years	40,785	38,966	−1819
Incident cases of dementia after 10 years	16,137	15,179	−957
Deaths after 30 years	99,727	99,699	−28
Mean outcomes per person after 30 years			
Person years alive	15.13	15.18	0.05
Person years without dementia	12.37	12.55	0.17
Person years with dementia	2.76	2.63	−0.12
Person years in mild dementia	1.57	1.50	−0.06
Person years in moderate dementia	1.03	0.97	−0.05
Person years in severe dementia	0.17	0.16	−0.01
Number needed to treat			
To prevent one case of dementia after 10 years			104
To prevent one case of dementia after 20 years			55
To prevent one case of dementia after 30 years			62
To prevent one case of death after 30 years			3619

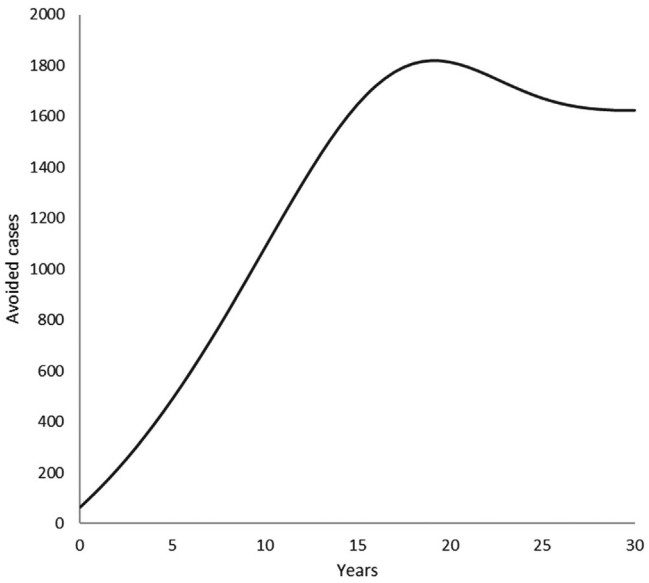

FIGURE 2 Cumulative number of avoided cases during the simulated period of 30 years (initial cohort of 100,000 persons at risk for dementia)

survival, but also greater benefits in terms of QALYs compared to other options. When the program was run on people at greater risk of developing dementia (such as MCI), the cost-effectiveness finding was strengthened per case. When the intervention effect was on a magnitude suggested by Livingston et al.,[8] cost-effectiveness was reinforced. Repeating the intervention program at various intervals resulted in higher incremental costs.

The impact of direct costs is greater than of informal care. Aging and disease progression with associated institutionalization results in a lower impact of informal care as the model runs.

The number of dementia cases due to the intervention (Table 4) varied between 1068 additional cases (cardiovascular risk reduction) and 12,055 avoided cases (40% risk reduction).[8]

4 | DISCUSSION

Based on the simulation described in this paper, FINGER has the potential to be a cost-effective program for preventing or reducing the risk of dementia. Several uncertainties were tested in the sensitivity analyses, and most scenarios resulted in dominance of the FINGER program over UC (i.e., lower costs and better outcomes). However, although supporting cost-effectiveness, the results at the individual level are rather modest, about 17,000 SEK/person (≈2000 US$) or about 600 SEK (≈70 US$) per person and year and relatively small QALY gain of about 0.04 per person. There are several reasons for this finding.

First, while FINGER participants were "at risk," the absolute risk of developing dementia is still relatively low, and thus the potential benefits at the individual level are relatively small as well. Nevertheless, the potential target population for a program with similar risk profiles is likely to be large,[45] indicating that the societal benefits may be substantial if FINGER is implemented at large scale. In prevention work, there are often trade-offs between, on the one hand, low-cost programs targeting large groups with rather small intervention effects, and on the other, expensive programs targeting small high-risk groups with large

TABLE 3 Results of the one-way sensitivity analyses of the cost-utility analysis (SEK 2016)

	Incremental costs	Incremental QALYs	ICER	NMB[a]	NHB[a]
Base case	−16,928	0.043	<0[b]	42,728	0.071
1. Variation of start-age and model duration					
Model length 5 years	3290	0.002	2,122,623	−2,090	−0.003
Model length 10 years	−3692	0.008	<0	8,492	0.014
Model length 20 years	−18,105	0.033	<0	37,905	0.063
Start-age 60, 40 cycles	−16,402	0.040	<0	40,402	0.067
Start-age 50, 50 cycles	−12,913	0.033	<0	20,160	0.034
2. Variation of risk reduction					
6.09% risk reduction (alternative method)[28]	−15,693	0.041	<0	56,693	0.057
11.8% risk reduction (Hawthorne effect)	−36,083	0.080	<0	84,083	0.14
40% risk reduction (Livingston et al.[8])	−145,236	0.293	<0	321,036	0.54
12% risk reduction (Livingston et al.[8])	−36,806	0.082	<0	86,006	0.14
3.22% risk reduction	−5640	0.021	<0	8,240	0.030
Effect in mild and moderate states	−10,434	0.060	<0	46,434	0.077
Cardiovascular effect: a 10% reduction in mortality in the model states of at-risk and mild dementia	99,524	0.30	332,671	80,476	0.13
Low risk: general population	−8722	0.028	<0	25,522	0.043
High risk: start in MCI	−46,072	0.093	<0	101,872	0.17
Base risk 4× instead of 2×	−25,978	0.058	<0	60,778	0.10
3. Alternative epidemiologic input					
NACC data progression & mortality	−8629	0.047	<0	36,829	0.061
4. Alternative discount rates					
Discount rate 1%	−22,041	0.059	<0	57,441	0.096
Discount rate 5%	−12,884	0.032	<0	32,084	0.053
5. Alternative costing inputs					
Analyze only direct costs	−16,223	0.043	<0	42,033	0.070
Intervention cost +100%	−11,438	0.043	<0	37,238	0.062
Intervention cost +50%	−14,183	0.043	<0	39,983	0.067
Intervention cost −25%	−18,300	0.043	<0	44,100	0.074
Intervention cost −50%%	−19,673	0.043	<0	45,473	0.076
6. Alternative intervention program intervals					
Repeat intervention at 5, 15, and 25 years	−11,509	0.043	<0	37,309	0.062
Start age 60 + Repeat intervention at 5, 15, 25, and 35 years	−8367	0.040	<0	32,167	0.054
Start age 50 + repeat intervention at 5, 15, 25, 35, and 45 years	−2516	0.033	<0	22,316	0.037
7. Alternative WTP levels					
WTP 200,000	−16,928	0.043	<0	25,528	0.13
WTP 400,000	−16,928	0.043	<0	34,128	0.085
WTP 1,000,000	−16,928	0.043	<0	59,928	0.060

Abbreviations: ICER, incremental cost-effectiveness ratio; NACC, National Alzheimer's Coordinating Center; NHB, net health benefit; NMB, net monetary benefit; QALY, quality-adjusted life year; SEK, Swedish crowns (krona); UC, usual care; WTP, willingness-to-pay.

[a]Based on a WTP of 600,000 SEK/QALY (except for the last three lines).

[b]ICER < 0 indicates extended dominance for the intervention (both cost saving and QALY gain).

TABLE 4 Results of the one-way sensitivity analysis of the outcomes in the cost-effectiveness analysis

	Prevented cases	NNT to prevent 1 case of dementia	Saved PYs without dementia
Base case	1623	62	0.17
Start age 60	1583	63	0.20
Start age 50	1562	64	0.21
Model length 10 years	957	104	0.04
Model length 20 years	1819	55	0.14
11.8% risk reduction (Hawthorne effect)	3053	33	0.32
40% risk reduction[8]	12,055	8	1.20
12% risk reduction[8]	3108	32	0.33
3.22% risk reduction	799	125	0.09
Base risk 4× instead of 2×	1522	66	0.22
Cardiovascular effect: 10% mortality reduction in at risk and mild dementia	−1068	Na[a]	0.48
Low risk: general population	1379	73	0.12
High risk: start in MCI	1937	41	0.32

Abbreviation: MCI, mild cognitive impairment; NNT, number needed to treat; PY, person year.
[a]No reduction in dementia cases.

individual effects. This is the familiar "prevention paradox" suggested by Rose.[46] The cost-effectiveness appears to be better with an MCI population than with the "at-risk population" (see sensitivity analysis), but we know little about lifestyle prevention in people with MCI. Thus, the FINGER trial and our findings here can be used to discuss the identification of target risk groups for prevention.[47] Furthermore, because the target population is also much greater for those "at risk" than for MCI, the aggregated societal benefits are larger for "at risk."

Second, lifestyle and cardiovascular treatment programs are already well-implemented in Finland, Sweden, and several other high-income countries. The control group in the FINGER study received regular measurements and feedback on their vascular risk-factors during the trial. By controlling for the Hawthorne effect, we compensated for that in the sensitivity analysis.

Third, the model did not reach the magnitude of the potential prevention effect that has been suggested.[8] However, our results reflect the potential of a real-world prevention program rather than hypothesized effects.

5 | LIMITATIONS

Any model in this area aims to reflect the biological and socioeconomic pathway and progression of a disorder. However, to do so, simplifications and assumptions are needed, causing limitations.

First, the most important limitation was the use of an indirect method to estimate the risk of conversion from "at risk" to dementia (i.e., the CAIDE score), given the assumption on causality in reducing dementia incidence. Conversion to dementia was not a primary outcome in FINGER. Longer-term follow-up data are expected, which could provide empirical evidence on the risk of conversion to dementia. The magnitude of the effect is also likely to be an underestimate given that it is based on the CAIDE score that does not include several other important risk factors such as diet, smoking, diabetes, depression, and cognitive activity. However, reality is not as simple as in a risk equation, so "real-world" data of conversion would catch the complexity of risks much better, particularly in combination with a rather long time horizon as in our model.

Second, the model duration was 30 to 50 years. By using such a long simulation period, the estimates for costs and outcomes later in the period may be incorrect.

Third, the incidence data are not recent. There are relatively strong recent indications of a lowering in age-specific incidence of dementia, at least in some population subgroups such as highly educated people in high-income countries.[10,11]

Fourth, several components in the FINGER program are similar to cardiovascular prevention programs that can be expected to have an impact on cardiovascular morbidity and mortality. The base case in our model did not take such effects into consideration. However, because it is expected that the FINGER program has the potential also to affect cardiovascular risks, and it has reduced the incidence of chronic diseases,[48] we included a hypothetical alternative in the sensitivity analysis with a 10% reduction in mortality. In this analysis, there were obviously stronger effects on survival, resulting in more persons with dementia, and thereby increased costs due to a prolonged survival compared to the base case—the "prevention paradox"—and better outcomes in terms of gained QALYs. Thus, the results of the simulation in the base case can be regarded as the added value of dementia prevention to public health programs focusing on cardiovascular risk. However, this option did not take into account the potential of reduced cost of cardiovascular disorders, only a reduction in mortality.

Fifth, with many input sources, the impact on missing data may be substantial. However, for the most important input, the FINGER trial, the level of drop-outs was low (12%) and missing data was 2%.[14] The management of missing data in SveDem has been discussed in a specific paper.[30]

Although for each limitation one could predict the direction of possible bias, it is difficult to predict the combined effects on the findings. Therefore, we argue for improved empirical estimates and more detailed uncertainty analyses. We took into account not only parameter uncertainties but also the model's structural uncertainties such as the impact of cardiovascular effects. Alternative modeling approaches may be explored, such as general health models in which multimorbidity conditions are examined.[49,50]

6 | CONCLUSIONS

The model suggests that programs like FINGER have the potential to be cost-effective for preventing dementia. The results at the individual level are rather modest, but the societal benefits may be substantial because the potential target population is large. Better modeling techniques are needed to integrate the complexity of prevention work, such as effects on dementia, but also on other (e.g., cardiovascular) conditions.

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CONFLICTS OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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