Healthy ageing through internet counselling in the elderly (HATICE): a multinational, randomised controlled trial

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Summary

Background Although web-based interventions have been promoted for cardiovascular risk management over the past decade, there is limited evidence for effectiveness of these interventions in people older than 65 years. The healthy ageing through internet counselling in the elderly (HATICE) trial aimed to determine whether a coach-supported internet intervention for self-management can reduce cardiovascular risk in community-dwelling older people.

Methods This prospective open-label, blinded endpoint clinical trial among people age 65 years or over at increased risk of cardiovascular disease randomly assigned participants in the Netherlands, Finland, and France to an interactive internet intervention stimulating coach-supported self-management or a control platform. Primary outcome was the difference from baseline to 18 months on a standardised composite score (Z score) of systolic blood pressure, LDL cholesterol, and body-mass index (BMI). Secondary outcomes included individual risk factors and cardiovascular endpoints. This trial is registered with the ISRCTN registry, 48151589, and is closed to accrual.

Findings Among 2724 participants, complete primary outcome data were available for 2398 (88%). After 18 months, the primary outcome improved in the intervention group versus the control group (0·09 *vs* 0·04, respectively; mean difference –0·05, 95% CI –0·08 to –0·01; p=0·008). For individual components of the primary outcome, mean differences (intervention *vs* control) were systolic blood pressure –1·79 mm Hg versus –0·67 mm Hg (–1·12, –2·51 to 0·27); BMI –0·23 kg/m² versus –0·08 kg/m² (–0·15, –0·28 to –0·01); and LDL –0·12 mmol/L versus –0·07 mmol/L (–0·05, –0·11 to 0·01). Cardiovascular disease occurred in 30 (2·2%) of 1382 patients in the intervention versus 32 (2·4%) of 1333 patients in the control group (hazard ratio 0·86, 95% CI 0·52 to 1·43).

Interpretation Coach-supported self-management of cardiovascular risk factors using an interactive internet intervention is feasible in an older population, and leads to a modest improvement of cardiovascular risk profile. When implemented on a large scale this could potentially reduce the burden of cardiovascular disease.

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Introduction

Cardiovascular disease is the leading cause of morbidity and mortality worldwide, and is strongly related to unhealthy behaviours.[1,2] Despite widespread preventive programmes, cardiovascular disease risk factors, including hypertension, hypercholesterolaemia, smoking, diabetes, unhealthy diet, obesity, and physical inactivity, remain highly prevalent.[3,4] Long-term adherence to lifestyle and medication regimens remains a serious challenge and target values for cardiovascular risk management are often not reached because of both patient and doctor factors.[5,6] This gap between evidence and practice leaves room for substantial improvement.[7] Optimisation of cardiovascular risk factors might also contribute to the prevention of cognitive decline and dementia, which can be an extra motivator to increase adherence.[8]

Self-management might empower individuals and improve adherence to lifestyle change and pharmacological prevention programmes to reduce risk of cardiovascular disease.[9] Increasing global access to the internet facilitates delivery of preventive interventions without the need for frequent face-to-face contact, creating the potential for scalability at low cost across a variety of health-care settings.[10]

Previous meta-analyses showed modest, but consistent, beneficial effects of coach-supported (blended) eHealth interventions on individual cardiovascular risk factors, but sustainability over time is an important challenge.[11–13] Because effects of preventive interventions require long-term risk factor improvement, studies evaluating whether effects are sustainable beyond 12 months are needed. Despite rapidly increasing internet use in older populations (ie, >65 years), little is known about the feasibility and effectiveness of eHealth interventions in older people, who are often at increased risk of cardiovascular disease.

In the healthy ageing through internet counselling in the elderly (HATICE) trial we investigated whether a coach-supported interactive internet intervention to

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Research in context

Evidence before this study

In a recent systematic review we concluded that web-based interventions in older people can be moderately effective in reducing individual cardiovascular risk factors, particularly if blended with human support, but that effects decline with time. We updated our systematic review, from inception to July 24, 2019, in MEDLINE, Embase, CINAHL, and the Cochrane Library with search terms designed to capture all systematic reviews and trials using web-based interventions on self-management of cardiovascular risk factors to reduce the risk of cardiovascular disease in older people (>65 years). Search terms included all cardiovascular risk factors (hypertension, glycated haemoglobin A_{1c}, LDL cholesterol, smoking, weight, and physical inactivity), cardiovascular disease and web-based interventions (and synonyms). We found three systematic reviews and meta-analyses, one on hypertension only, and two on primary and secondary prevention of cardiovascular disease. For participants with and without a history of cardiovascular disease, web-based interventions might improve different individual risk factors of people from midlife onwards, but it is not clear whether these effects are sustainable. The evidence for an effect on cardiovascular outcomes is inconsistent. Increasing internet access across the globe has considerable potential for improving cardiovascular risk management to reduce the global burden of cardiovascular disease.

Added value of this study

To the best of our knowledge, this is the largest trial on web-based, multicomponent cardiovascular risk self-management in older people in primary care to date. We show that this type of intervention is feasible in different health-care systems in three European countries. Our intervention had a small but sustained effect on a composite score of systolic blood pressure, LDL, and body-mass index (BMI; primary outcome) over 18 months, with consistent improvements on individual risk factors, although effects were modest and only significant for BMI. Using pre-specified subgroup analyses we identified that the younger age group (65–70 years) and those with the lowest educational attainment might benefit most. Whether these effects will translate into a reduction of incident cardiovascular disease when implemented on a larger scale, over longer periods of time, is unclear.

Implications of all the available evidence

Our study provides evidence that coach-supported self-management of cardiovascular risk using eHealth is feasible in older people and could reduce the risk of cardiovascular disease. This type of intervention might be most effective when targeting people at increased risk, who are not enrolled or insufficiently controlled in existing care programmes.

optimise self-management of cardiovascular risk factors in older individuals can improve cardiovascular risk profiles and reduce the risk of cardiovascular disease and dementia.

Methods

Study design and participants

The HATICE trial was a pragmatic, multinational, multicentre, investigator-initiated, randomised controlled trial using an open-label blinded endpoint design, with 18 months intervention and follow-up. Details of the study design have been published previously.[14] Participants were eligible if they were community dwelling, aged at least 65 years, had two or more cardiovascular risk factors (ie, hypertension, dyslipidaemia, overweight, current smoking, or physical inactivity), or a history of cardiovascular disease (ie, stroke, transient ischemic attack [TIA], myocardial infarction, angina pectoris, or peripheral arterial disease) or diabetes, or both, and had access to the internet using a laptop, desktop computer, or tablet. Exclusion criteria were prevalent dementia, computer illiteracy (operationalised as not able to do a simple internet search or send an email) and any condition expected to hinder successful 18-month follow-up (eg, metastasised malignancy or chronic alcohol abuse; appendix p 2). The full study protocol is provided in the appendix (p 75).

See Online for appendix

Recruitment took place in the Netherlands, Finland, and France from March 9, 2015, to Sept 20, 2016. Detailed recruitment and enrolment procedures in each country are described in the appendix (pp 2–3, 23–24). Medical ethical approval was obtained from the medical ethical committee of the Academic Medical Centre (the Netherlands; June 26, 2014; METC 2014_126), the Northern Savonia Hospital District Research Ethics Committee (Finland; June 10, 2014; 35/2014), and the Comité de Protection des Personnes Sud Ouest et Outre Mer (France; Sept 24, 2014; 2014-A01287–40). All participants gave written informed consent.

Randomisation and masking

After completion of the baseline assessment, participants were individually randomly assigned in a 1:1 ratio using a central, computer-generated sequence, which was linked to the online case record form. In case of spouse or partner participation, both participants were automatically allocated to the same treatment group to prevent contamination. All participants were informed about randomisation to one of two internet platforms, without further details on the contents of the platforms. Complete masking of participants and the coaches delivering the intervention was not possible because of the nature of the intervention. An independent assessor unaware of treatment allocation did the final assessment, including outcome assessment. The primary outcome consisted solely of objectively measurable parameters.

Procedures

Intervention group participants received access to a secure internet-based platform with remote support from a coach trained in motivational interviewing and lifestyle behaviour advice, based on the stages of change model.[15] The platform was designed to facilitate self-management of cardiovascular risk factors by defining health priorities, goal setting, monitoring progress with (graphical) feedback, and a combination of automated and personal feedback from the coach, based on Bandura's social-cognitive theory of self-management and behavioural change, and was described in detail elsewhere (appendix p 4).[16,17] After developing a conceptual framework, the platform was designed in an iterative process engaging end users (target population and nurses), which included an 8-week pilot study with 41 participants (appendix p 4). The main components of the intervention are described in the panel. All advice was according to European and national guidelines for the management of cardiovascular risk factors.[18] Coaches motivated participants via a computer messaging system to set at least one goal to improve a cardiovascular risk factor, encouraged them to interact with the platform, set additional goals over time, and provided motivating feedback. The full coaching protocol is provided in the appendix (p 31). Participants allocated to the control condition had access to a static platform, similar in appearance, with limited general health information only, without interactive components or a remote coach.

After telephone screening, eligible participants were invited in person. During the screening visit, blood pressure and anthropometrics were assessed. Full study logistics and procedures are provided in the appendix (pp 25–26). Medical history and medication use were registered. Mini Mental Status Examination was used to screen for cognitive impairment. Before the baseline assessment, participants were invited to fill out a series of online questionnaires, mainly for secondary outcome assessments. Symptoms of depression were assessed using the 15-item Geriatric Depression Scale, anxiety with the Hospital Anxiety and Depression Scale (anxiety part), diet with the Mediterranean diet adherence screener, disability and functioning with the late-life function and disability instrument, self-efficacy with the Partners in Health questionnaire, and physical activity with the Community Health Activities Model Program for Seniors questionnaire.

Blood was drawn for assessment of lipids, glucose, and glycosylated haemoglobin A_{1c} (HbA_{1c}). 2 weeks after the screening visit, the baseline visit took place, with assessment of physical fitness with the Short Physical Performance Battery and cognitive functioning with the Stroop colour–word test, Trail Making Test A and B, Rey Auditory Verbal Learning test, and semantic fluency test. All measurements were repeated at 18 months. Any finding requiring medical attention, such as an elevated blood pressure, abnormal laboratory values or signs of cognitive impairment or depression led to the advice to visit their general practitioner (GP). Participants in both conditions received a 3-monthly online questionnaire about the occurrence of adverse events and clinical outcomes. At 12 months, a telephone call to all participants was scheduled for assistance with self-reported outcome assessment questionnaires, and in the intervention group only, with a motivational conversation to enhance adherence and address potential challenges with goal-setting and lifestyle improvement.

Panel: Components of the HATICE intervention

Intervention platform

Participant content

- Health priorities*—participants are invited to prioritise up to three health factors; potential health priorities are smoking, blood pressure, cholesterol, diabetes, weight, physical activity, and nutrition; the layout of the homepage changes according to individual chosen priorities
- Goal-setting* according to the SMART principles focusing on their individual health priorities
- Monitoring progress—participants can enter measurements, such as weight, to assess their personal progress, including using graphical and automated feedback
- Messaging system with their personal coach
- Lifestyle groups—group activities in the individual's locality are presented, which participants can join
- Advice and education—static and dynamic information on cardiovascular risk, including peer-to-peer videos and games
- News items related to cardiovascular disease, healthy ageing, or e-health are added regularly

Coach content

- Messaging system with their participants
- Alerts—coaches receive an alert when a participant enters or edits a goal, measurement, or health factor and when a participant does not log in for 3 weeks.
- Overview per participant of their health priorities, goals, measurements, messages, and lifestyle groups

Control platform

Participant content

- Advice and education—general static information on cardiovascular risk

Coach content

- None

*Participants are stimulated to set their first health priorities and goals during the baseline visit. SMART=specific, measurable, assignable, realistic, time related.

Outcomes

The primary outcome was the change from baseline to 18 months on a composite score of systolic blood pressure, LDL cholesterol, and body-mass index (BMI). For each of the three parameters at baseline and at the 18-month visit, the baseline means and SDs combined were used to calculate Z scores. The Z scores were then averaged for the baseline and the 18-month visit separately, leading to the composite Z score for the respective visits. We decided on this primary outcome on the basis of the following

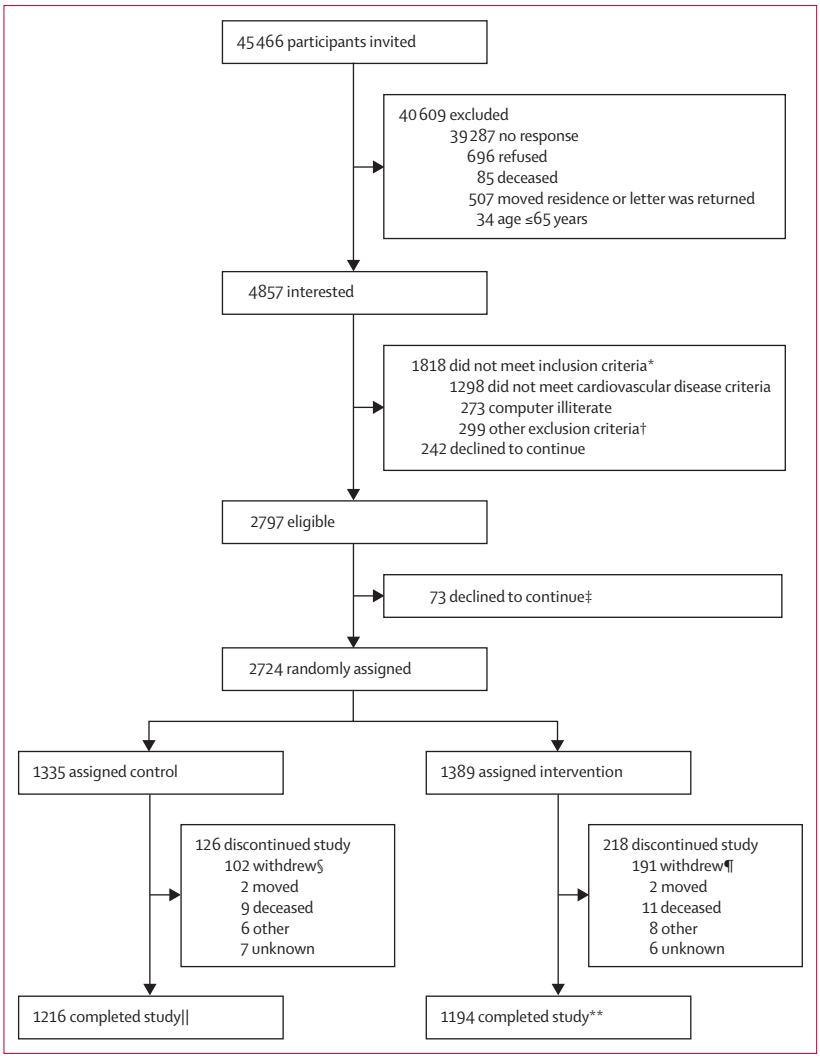

Figure 1: **Trial profile**
*Individual participants could have more than one reason for not meeting inclusion criteria. †Previously diagnosed dementia, any condition expected to limit 18-month compliance and follow-up, severe visual impairment, age <65 years, or participation in another randomised controlled trial. ‡One participant asked for data to be withdrawn. §Seven patients who initially withdrew were retrieved and included in the total. ¶23 patients who initially withdrew were retrieved and included in the total. ||Complete primary outcome in 1209 (99·4%) of 1216 patients in the control group. **Complete primary outcome in 1189 (99·6%) of 1194 patients in the intervention group.

considerations: we deemed a composite outcome appropriate to capture the potential effect of our multidomain intervention; our mixed population of primary and secondary prevention precludes the use of a single existing cardiovascular risk score; including only objectively measurable parameters reduces the risk of reporting bias; and weighing of risk factors was considered not appropriate, because the exact weight of each risk factor was unknown in this population. Full considerations for this primary outcome have been detailed previously.[14]

The main secondary outcomes were the difference at 18 months in systolic blood pressure, LDL cholesterol, BMI, HbA_{1c}, physical activity (hours per week), dietary intake, smoking cessation, estimated 10-year cardiovascular disease risk based on the Framingham cardiovascular disease risk score and the Systematic Coronary Risk Estimation-Older People (SCORE-OP),[19] and dementia risk as measured with the Cardiovascular risk factors, Ageing and Incidence of Dementia (CAIDE) score.[20] Other outcomes reflecting cardiovascular disease risk included difference in level of physical activity, dietary intake, and smoking cessation. Clinical outcomes included disability, physical functioning, cognitive functioning, depression and anxiety, incident cardiovascular disease (stroke, TIA, myocardial infarction, angina pectoris) and mortality. GP consultations, emergency room visits and hospital admissions were registered. Process evaluation outcomes to assess the intervention delivery were determined post hoc and include login frequency, number of messages exchanged between coach and participant and number of goals set. Independent, blinded-outcome adjudication committees in each country evaluated all clinical outcomes on the basis of available clinical information (appendix p 5).

Statistical analysis

We based our sample size calculation on the effect sizes of the HATICE primary outcome as observed in the preDIVA[21] and FINGER[22] trials after 24 months of follow-up. With 80% power, a 0·05 two-sided significance level, accounting for an estimated 14% attrition, an intracluster correlation coefficient of 0·25 for an anticipated 17·5% participants in couples, and an effect size of 0·06 the required sample size was estimated to be 2534 participants.[17] We decided on this target effect size because the difference on this composite outcome after 2 years between those who did and did not develop cardiovascular disease or dementia during a mean of 6·7 years of follow-up in the preDIVA trial was 0·06 (appendix pp 6–8). The statistical analysis plan was completed and published at ISRCTN on June 27, 2017 (appendix pp 6–8) before unblinding of the data on March 31, 2018. All analyses were completed by the study group and verified by an independent epidemiologist.

All analyses were according to the intention-to-treat principle for participants with available data for each outcome. For the primary analysis, we used a general linear model. Accounting for correlations between partners using a random intercept was evaluated, but not included in the final model because this resulted in a worse model fit (higher Akaike information criterion). We additionally did a per-protocol analysis, including only those who logged onto the platform in at least 12 out of 18 months study participation, and who set at least one goal or entered one or more measurements. We did predefined subgroup analyses for country, sex, age group, educational level, prevalent cardiovascular disease and diabetes, or both, partner participation, participation in a cardiovascular risk management programme, and level of self-efficacy. Sensitivity analyses were done excluding 53 participants who did not have a

masked final assessment, excluding those who had switched coach during follow-up, and using multiple imputation by chained equations to evaluate the effects of missing data.

General linear models were also used for analysis of secondary outcomes, both for change scores for continuous or binary outcomes. For parameters assessed at baseline, and months 12 and 18 we used multiple-measurements general linear models. We used standard Cox proportional hazard models with time since inclusion as timescale to analyse the effect on incident cardiovascular disease and mortality, for which participants were censored at time to event or last available follow-up. This trial is registered with the ISRCTN registry, 48151589, and is completed.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the Article. All authors had full access to all data in the study and the corresponding author had final responsibility for the decision to submit for publication.

Results

Of the 45 466 people invited, 4857 were interested and screened for eligibility. 1818 were excluded as ineligible and 242 did not wish to proceed (figure 1). Of the 2797 who were eligible, 72 declined to participate further and one requested for the data to be withdrawn, leaving 2724 participants at baseline. Of these, 1389 (51%) were allocated to the intervention group and 1335 (49%) to the control group. The groups were generally well balanced at baseline (table 1; appendix pp 9–10).

After a mean follow-up of 17·7 months (SD 2·5), data on the primary outcome were available for 2398 (88%) participants (see appendix p 11 for reasons for missing data). Participants not completing the study were slightly older, had lower educational attainment, and more often participated with their partner (appendix pp 12–13). In the intervention group, the composite score of systolic blood pressure, LDL, and BMI improved by 0·09 versus 0·04 in the control group, resulting in a mean difference of –0·05 (95% CI –0·08 to –0·01; p=0·008) in favour of the intervention (figure 2). Prespecified sensitivity analysis showed that the effect was slightly larger in those who were adherent to the intervention (per-protocol analysis) with a mean difference of –0·06 (–0·11 to –0·02; figure 3). Results from prespecified subgroup analyses are shown in figure 3 and show that the effect was largest among participants who were Finnish, younger than age 70 years, and had the lowest education. Results of post-hoc subgroup analyses by country, and by age, education, and cardiovascular risk are provided in the appendix (p 14). The high degree of similarity between those who dropped out in the intervention and control groups (appendix pp 15–16) suggests no selective drop-out occurred. Sensitivity analyses using multiple imputed data did not affect the main finding (–0·04, –0·08 to –0·01; p=0·03; appendix p 17).

	n	All (n=2724)	Control (n=1335)	Intervention (n=1389)
Demographics				
Age, years	2724	69 (67–73)	69 (67–73)	69 (67–73)
Sex				
Female	2724	1297 (47·6%)	639 (47·9%)	658 (47·4%)
Male	2724	1427 (52·4%)	696 (52·1%)	731 (52·6%)
Living alone	2724	725 (26·6%)	353 (26·4%)	372 (26·8%)
Partner participating	2724	436 (16·0%)	203 (15·2%)	233 (16·8%)
Already participating in cardiovascular risk management programme	2722	674 (24·8%)	326 (24·4%)	348 (25·1%)
Educational level				
Basic	2724	781 (28·7%)	364 (27·3%)	417 (30·0%)
Post-secondary non-tertiary	2724	823 (30·2%)	400 (30·0%)	423 (30·5%)
Tertiary	2724	1120 (41·1%)	571 (42·8%)	549 (39·5%)
Race				
White	2700	2639 (97·7%)	1299 (98·2%)	1340 (97·3%)
Other*	2700	61 (2·3%)	24 (1·8%)	37 (2·7%)
Cardiovascular history (self-reported)				
Angina pectoris	2717	342 (12·6%)	159 (11·9%)	183 (13·2%)
Myocardial infarction	2724	305 (11·2%)	152 (11·4%)	153 (11·0%)
Stroke (including TIA)	2717	357 (13·1%)	171 (12·9%)	186 (13·4%)
Any cardiovascular disease†	2711	826 (30·5%)	402 (30·3%)	424 (30·7%)
Cardiovascular risk factors				
Hypertension‡	2679	2244 (83·8%)	1108 (84·2%)	1136 (83·3%)
Dyslipidaemia§	2716	2625 (96·6%)	1291 (96·9%)	1334 (96·4%)
Obesity (body-mass index ≥30 kg/m²)	2723	1016 (37·3%)	487 (36·5%)	529 (38·1%)
Obesity (waist circumference: men >88 cm, women >102 cm)	2723	1835 (67·4%)	889 (66·6%)	946 (68·2%)
Diabetes (self-reported)	2721	602 (22·1%)	306 (23·0%)	296 (21·3%)
Medication use				
Antihypertensive medication	2628	1949 (74·2%)	969 (74·9%)	980 (73·4%)
Lipid-modifying medication	2628	1454 (55·3%)	707 (54·7%)	747 (56·0%)
Blood glucose-lowering medication	2628	514 (19·6%)	256 (19·8%)	258 (19·3%)
Antithrombotic medication	2628	861 (32·8%)	413 (31·9%)	448 (33·6%)

Data are n, median (IQR), or n (%). No statistically significant differences between randomisation groups. TIA=transient ischaemic attack. *Other includes Ghanese, Kurdish, North African, Surinamese (Creole and other), Antillean Arruban, Asian, other African, and other. †Any of angina pectoris, myocardial infarction, or stroke. ‡Either high blood pressure (<80 years, ≥140/90 mm Hg; ≥80 years, ≥160/90 mm Hg), self-reported hypertension diagnosis, or antihypertensive use. §Either LDL of 2·5 or more, total cholesterol of 5 or more, self-reported dyslipidaemia diagnosis, or cholesterol-lowering drugs.

Table 1: **Distribution of screening and baseline characteristics by randomisation group**

The effects of the intervention on secondary outcomes are provided in table 2. Comparing the change in individual components of the primary outcome in the intervention versus the control group, systolic blood pressure declined 1·79 versus 0·67 mm Hg (mean difference –1·12; 95% CI –2·51 to 0·27), BMI declined 0·23 versus 0·08 kg/m² (–0·15, –0·28 to –0·01), and LDL declined 0·12 versus 0·07 mmol/L (mean difference –0·05, 95% CI –0·11 to 0·01; figure 2). The effect on all three components of the primary outcome was largest

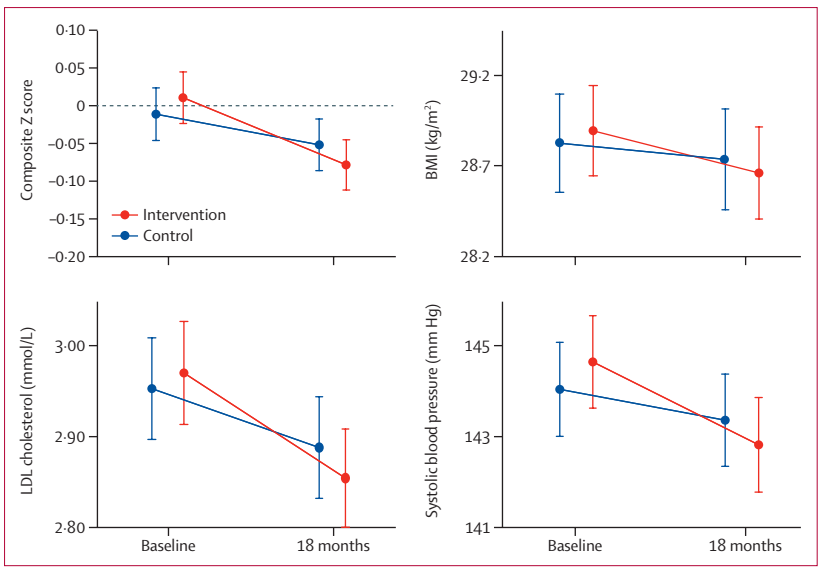

Figure 2: **Treatment effect on primary outcome and individual components of primary outcome**
BMI=body-mass index.

in Finland (appendix p 18). There were no major differences in self-reported lifestyle outcome measures, except for smoking cessation, which was reported by 24 (23·5% of smokers) intervention participants versus 16 (14·2% of smokers) control participants (mean difference 9·4%; 95% CI −1·1 to 19·8). The mean number of risk factors that improved was 2·9 in the intervention group versus 2·7 in the control group (mean difference 0·2, 95% CI 0·1–0·3). The 10-year risk of cardiovascular mortality as expressed by the SCORE-OP was reduced by 0·32% in the intervention versus 0·14% in the control group (mean difference −0·17%; 95% CI −0·38 to 0·04). The 20-year risk of dementia as expressed by the CAIDE score (range 0–15) decreased by 0·19 in the intervention group versus 0·04 in the control group (mean difference −0·15, −0·28 to −0·03). Symptoms of anxiety decreased more in the intervention than the control group (−0·58 versus −0·41; mean difference −0·18, −0·32 to −0·04). There were no significant differences on symptoms of depression, or any of the cognitive tests (table 2; appendix pp 18–19). Stroke incidence was lower in the intervention group versus the control group (four [0·3%] of 1383 versus 13 [1·0%] of 1335; hazard ratio 0·30, 95% CI 0·10–0·93). There were no significant differences in the incidence of other cardiovascular disease, dementia, and mortality (table 3), or in health-care use as measured by hospital visits, hospital admissions, and GP visits (appendix p 20).

The total number of logins was 59 441 in the intervention group versus 17 014 in the control group. The median number of logins in the intervention group was 1·8 times per month (IQR 1·1–2·9), compared with 0·7 times per month (IQR 0·5–0·9) in the control condition (mean difference 1·1, 0·9–1·2; appendix p 28). In the intervention group, 25 356 messages were sent between coaches and participants: 114 (9·6%) of the 1189 participants who completed the primary outcome sent zero messages, 403 (33·9%) sent one to five messages, 345 (29·0%) sent six to ten, and 327 (27·5%) sent more than ten messages. Participants in the intervention group set a median of one goal (IQR 1–2; 117 [9·8%] of 1189 set no goal, 562 [47·3%] set one goal, 404 [34·0%] set two to three goals and 106 [8·9%] set four or more goals). Most goals were set on weight loss (appendix p 21). The effect size of the primary outcome increased with every additional goal set during the study (0·025 per additional goal, 95% CI −0·042 to −0·008; appendix p 22). Participation in lifestyle groups was low in all three countries: 15 of 1471 in the Netherlands, 106 of 885 in Finland, and 23 of 368 in France. In the intervention group, more people started lipid-lowering drugs than in the control group (appendix p 29).

Discussion

Our results show that a coach-supported interactive internet intervention to optimise self-management of cardiovascular risk factors in older individuals is feasible with sustainable engagement, and resulted in a modest reduction of cardiovascular risk after 18 months. This effect was largely driven by a significant reduction in BMI, with point estimates for all components of the primary outcome, and most self-reported lifestyle risk factors also in favour of the intervention. There were consistent small improvements in risk of cardiovascular disease as estimated with the SCORE-OP and risk of dementia as estimated with the CAIDE score. Although this trial was not powered to detect an effect on clinical outcomes, the incidence of stroke was lower in the intervention group than the control group. There was no effect on total cardiovascular disease, and no serious adverse events occurred.

Previous studies have shown beneficial effects of blood pressure treatment in older people.[23] Effects of lifestyle interventions on other risk factors in older people are less consistent, but those targeting physical exercise might be beneficial up to high age.[24] Despite our inclusion criteria, our study population might have had limited room for improvement. The low response rate to the initial invitation and a high percentage already taking statins and antihypertensives is likely to reflect participation of motivated people concerned about their health. Many of the participants had a history of diabetes or cardiovascular disease and these people are more likely to partake in a cardiovascular risk-reduction programme, leaving limited room for further improvement beyond usual clinical care, which has intensified in recent years in most European countries. Therefore, when implemented in a population with higher cardiovascular risk and less access to prevention programmes, the potential beneficial effect might be larger.

The intervention platform was carefully designed using an iterative process involving the end users throughout development, leading to good usability, as confirmed in a

	n	Difference between Z score at baseline and month 18		Mean difference between intervention and control group	$p_{interaction}$
		Control (n=1209)	Intervention (n=1189)	Crude model (95% CI)	
Sensitivity analyses					
Per-protocol analysis	1909	−0·04	−0·11	−0·06 (−0·11 to −0·02)	NA
Blinded end assessment	2345	−0·04	−0·09	−0·05 (−0·08 to −0·01)	NA
Same coach during study	1885	−0·04	−0·09	−0·05 (−0·09 to −0·01)	NA
Subgroup analyses					
Country					
Finland	825	0·04	−0·09	−0·12 (−0·18 to −0·06)	<0·01
France	332	−0·06	−0·07	−0·02 (−0·11 to 0·08)	
The Netherlands	1241	−0·09	−0·09	−0·01 (−0·06 to 0·04)	
Sex					
Male	1258	−0·06	−0·08	−0·03 (−0·07 to 0·02)	0·18
Female	1140	−0·02	−0·10	−0·07 (−0·13 to −0·02)	
Age group, years					
65–70	1360	−0·03	−0·11	−0·07 (−0·12 to −0·02)	0·22
71–75	639	−0·06	−0·09	−0·03 (−0·10 to 0·04)	
>75	399	−0·03	−0·03	0·00 (−0·08 to 0·08)	
Participation with partner					
No	2046	−0·04	−0·09	−0·05 (−0·09 to −0·01)	0·87
Yes	352	−0·03	−0·08	−0·06 (−0·14 to 0·03)	
Already in cardiovascular risk management programme					
No	1804	−0·04	−0·09	−0·06 (−0·13 to 0·01)	0·78
Yes	592	−0·03	−0·09	−0·05 (−0·09 to 0·00)	
Education					
Basic	640	−0·02	−0·12	−0·11 (−0·18 to −0·04)	0·12
Post-secondary and non-tertiary	723	−0·04	−0·08	−0·04 (−0·11 to 0·02)	
Tertiary	1035	−0·05	−0·07	−0·01 (−0·07 to 0·04)	
Previous cardiovascular event					
No	1656	−0·04	−0·10	−0·06 (−0·10 to −0·02)	0·44
Yes	730	−0·03	−0·06	−0·03 (−0·10 to 0·04)	
Diabetes					
No	1877	−0·04	−0·08	−0·04 (−0·08 to 0·00)	0·34
Yes	519	−0·04	−0·12	−0·08 (−0·16 to −0·01)	
Self-efficacy					
Low	1169	−0·07	−0·11	−0·04 (−0·09 to 0·01)	0·60
High	1227	−0·01	−0·07	−0·06 (−0·11 to −0·01)	
All	**2398**	**−0·04**	**−0·09**	**−0·05 (−0·08 to −0·01)**	**NA**

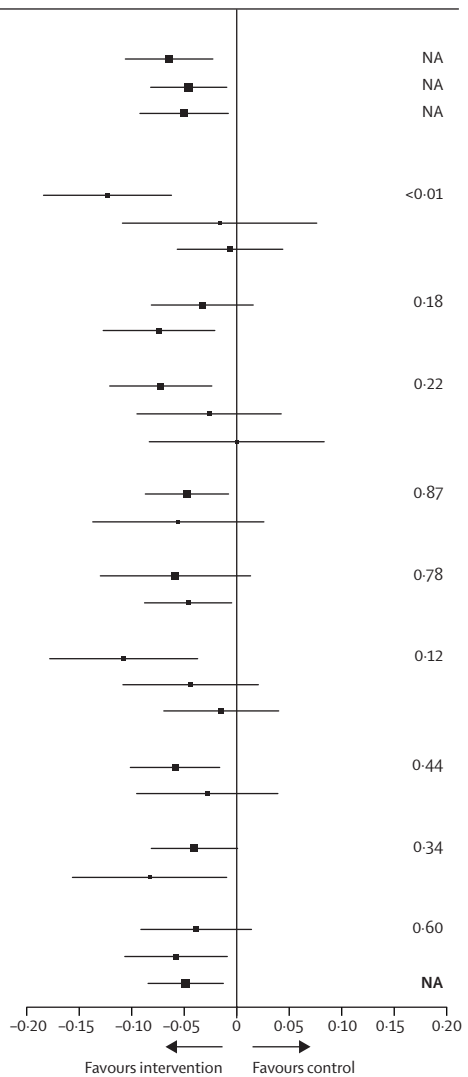

Figure 3: **Forest plot subgroup analyses**
Box sizes are proportional to the number of participants in that specific subgroup analysis. NA=not applicable.

qualitative substudy.[17,18,25] Our pragmatic multicomponent approach makes it difficult to disentangle effects of different components of the intervention, particularly to differentiate between the effects of the application itself and of the coach.

A limitation of our primary outcome is the difficulty to establish its clinical relevance. However, we deemed a composite Z score of three relevant and objectively measurable risk factors most appropriate to reflect the effect of our intervention on overall cardiovascular disease risk in our mixed population of primary and secondary prevention. The observed treatment effect of 0·05 was smaller than the effect size of 0·06 on which our sample size calculation was based, but was nonetheless significant. There could be several reasons for this, including a slightly higher sample size than needed according to the sample size calculation (n=2724 *vs* 2534), lower drop-out rate than expected, and the absence of an anticipated loss of power due to clustering in participating couples. The result is consistent with a modest reduction in cardiovascular disease risk, as measured with the SCORE-OP, and dementia risk, as measured with the CAIDE score, further strengthening the potential relevance of this finding.

	n		Baseline		Follow-up		Mean difference in change (intervention *vs* control)	p value
	Control	Intervention	Control	Intervention	Control	Intervention		
Cardiovascular risk factors*								
LDL cholesterol (mmol/L)	1215	1195	2·96 (1·00)	2·97 (1·00)	2·89 (0·99)	2·85 (0·95)	−0·05 (−0·11 to 0·01)	0·11
Z score	1215	1195	−0·01 (1·00)	0·01 (1·00)	−0·07 (1·00)	−0·11 (0·96)	−0·05 (−0·11 to 0·01)	0·11
Body-mass index (kg/m²)	1216	1191	28·8 (4·8)	28·9 (4·4)	28·7 (4·9)	28·7 (4·5)	−0·15 (−0·28 to −0·01)	0·04
Z score	1216	1191	−0·01 (1·04)	0·01 (0·95)	−0·03 (1·07)	−0·04 (0·97)	−0·03 (−0·06 to −0·00)	0·04
SBP (mm Hg)	1216	1192	144·1 (18·5)	144·6 (18·0)	143·4 (18·1)	142·8 (18·4)	−1·12 (−2·51 to 0·27)	0·11
Z score	1216	1192	−0·02 (1·01)	0·02 (0·99)	−0·05 (0·99)	−0·08 (1·01)	−0·06 (−0·14 to 0·01)	0·11
HbA_{1c}, all	1188	1172	41·5 (8·0)	41·2 (7·5)	41·6 (8·3)	40·9 (7·7)	−0·4 (−0·7 to 0·0)	0·054
HbA_{1c}, diabetes only	276	239	50·3 (10·6)	50·3 (10·5)	51·0 (10·2)	50·3 (10·4)	−0·7 (−2·1 to 0·7)	0·33
SCORE OP, all†	1198	1178	10·3% (11·0)	10·4% (12·1)	10·1% (11·0)	10·1% (11·5)	−0·17 (−0·38 to 0·04)	0·10
SCORE OP, without cardiovascular disease†	837	806	9·2% (9·2)	9·9% (12·4)	9·1% (9·5)	9·6% (11·4)	−0·20 (−0·45 to 0·05)	0·12
Lifestyle factors								
Moderate to high intense physical activity (h/week)†	1244	1207	6·0 (5·6)	6·0 (5·5)	5·5 (5·4)‡	5·9 (5·7)‡	0·30 (−0·06 to 0·66)	0·11
Physical activity (adherent to WHO guidelines)§	1244	1207	67·3% (64·7 to 69·9)	68·0% (65·3 to 70·6)	63·8% (61·8 to 65·7)‡	65·8% (63·8 to 67·7)‡	1·7 (−1·8 to 5·1)	0·34
Physical fitness (SPPB, range 0–12)*	1228	1206	10·7 (1·6)	10·9 (1·9)	10·3 (2·1)	10·3 (2·1)	−0·06 (−0·21 to 0·08)	0·41
Diet (MEDAS score, range 0–14)§	1305	1303	6·0 (1·9)	6·1 (2·0)	5·9 (2·1)‡	5·9 (2·1)‡	0·02 (−0·12 to 0·16)	0·81
Smoking (yes)*	1205	1183	8·8% (7·3 to 10·5)	8·1% (6·7 to 9·8)	8·0% (6·6 to 9·7)‡	6·6% (5·3 to 8·2)‡	−0·8 (−2·0 to 0·4)	0·21
Quit smoking (yes)¶	113	102	NA	NA	14·2% (8·9 to 21·8)‡	2·4% (16·4 to 32·6)‡	9·4 (−1·1 to 19·8)	0·08
Number of improved risk factors‖	1144	1117	NA	NA	2·7 (1·3)	2·9 (1·4)	0·2 (0·1–0·3)	<0·0001
Disability (LLFDI, range 16–90)§**	809	800	71·5 (9·0)	72·2 (8·4)	71·6 (10·3)	71·7 (11·6)	−0·52 (−1·29 to 0·26)	0·19
Dementia risk score (CAIDE, range 0–15)*	1175	1139	9·2 (2·2)	9·3 (2·1)	9·2 (2·1)	9·1 (2·0)	−0·15 (−0·28 to −0·03)	0·02
Self-efficacy (PIH, range 0–96)‡	1228	1201	84·6 (9·8)	85·1 (8·7)	85·5 (9·6)‡	85·5 (11·2)‡	−0·68 (−1·37 to 0·01)	0·05
Cognitive functioning*								
Global (MMSE, range 0–30)	1215	1194	28·5 (1·5)	28·6 (1·4)	28·6 (1·7)	28·5 (1·82)	−0·05 (−0·18 to 0·09)	0·49
Composite Z score of seven cognitive tests††	1156	1127	0·00 (0·61)	0·00 (0·62)	−0·02 (0·64)	0·00 (0·66)	0·01 (−0·02 to 0·04)	0·44
Mood§								
Depressive symptoms (GDS, range 0–15)	1233	1203	2·0 (2·4)	1·9 (2·2)	1·9 (2·3)	1·8 (2·2)	−0·10 (−0·24 to 0·03)	0·12
Anxiety (HADS, range 0–42)	1233	1198	4·1 (2·8)	4·2 2·7)	3·7 (2·7)	3·5 (2·6)	−0·18 (−0·32 to −0·04)	0·01

Data are n, mean (SD), and mean difference in change (95% CI). SBP=systolic blood pressure. HbA_{1c}=glycated haemoglobin A_{1c}. SCORE-OP=systematic coronary risk estimation-older people. SPPB=short physical performance battery. MEDAS=Mediterranean Diet Adherence Screener. NA=not applicable. LLFDI=late life function and disability instrument. CAIDE=cardiovascular risk factors, ageing and incidence of dementia. PIH=partners in health. MMSE=mini mental status examination. GDS=geriatric depression scale. HADS=hospital anxiety and depression scale. *Measured at baseline and 18 months. †For SCORE-OP at 18 months, the baseline age was used. ‡Based on number of observations in number of individuals in intervention *vs* control: physical activity (h/week) 2347/1244 *vs* 2254/1207; physical activity (% adherent to WHO) 2347/1244 *vs* 2254/1207; MEDAS score 2573/1305 *vs* 2532/1303; LLFDI score 1483/809 *vs* 1450/800; PIH score 2280/1228 *vs* 2221/1201; GDS score 2276/1233 *vs* 2215/1203; HADS score 2296/1233 *vs* 2217/1198. §Measured at baseline, 12 months, and 18 months. Difference between baseline and follow-up is mean difference between baseline and 12-month measurement and between baseline and 18-month measurement. Difference between intervention and control group is analysed with the previous model and a random intercept for individual (adding random slope for individual did not improve the model), with time by treatment interaction in years. ¶Reference group is smokers at baseline. ‖The number of improved risk factors was defined as the total number of risk factors that showed a beneficial difference between baseline and month 18 for each participant for the following six risk factors: blood pressure, body-mass index, LDL cholesterol, HbA_{1c}, moderate to high intense physical activity, or diet (MEDAS score). **LLFDI was not measured in Finland. ††There was no effect of the intervention on any of the individual cognitive tests (MMSE, Stroop 1–3, Rey Recall, Rey Recognition and Verbal fluency; appendix p 19).

Table 2: **Effect of the intervention on secondary outcomes**

Uptake of the intervention was reasonable, with a median of almost two logins per month (with a wide range and a substantial proportion logging in more than five times a month), almost all participants setting at least one goal (with a considerable proportion up to three goals), and the majority of participants using the platform

during the full study period. The increasing effect size with every additional goal set during the study supports the notion of a dosage–effect relationship and the additional potential for a larger effect if the participant had interacted more frequently with the application and the coach. An embedded qualitative study[25] indicated that interaction with the coach in person at baseline and during the study was pivotal. This is in line with previous reports suggesting intensive counselling interventions can be effective in reducing cardiovascular risk and disease,[26,27] whereas less intensive interventions are not.[28] Estimation of the potential effect of this intervention in other settings and countries might depend on contextual information, including cultural aspects and the fit of the intervention with the local health-care system. The slightly higher drop-out in the intervention group needs further exploration, because it might suggest burden associated with the intervention, although those who dropped out in the intervention group hardly differed from those in the control group at baseline (appendix p 15) and multiple imputation of missing values did not change the results (appendix p 17).

The contrast between intervention and control group was largest in Finland. In the Netherlands and France, a combination of Hawthorne effects and the initiation of treatment by the GP in response to baseline measurements could have led to improvements in the control group, limiting overall study contrast. The lower frequency of GP visits and higher frequency of emergency room visits in Finland might reflect a different health-care structure and could explain the lack of improvement in the control group.

Previous research showed that there seems to be little room for improvement in high-income settings with a digital approach in patients with a high cardiovascular disease risk, even with good uptake, because most people already participate in cardiovascular disease prevention programmes.[29] Especially in old age, achieving further lifestyle changes might be challenging. Prespecified subgroup analyses in our study suggest the largest effect in the younger age group (65–70 years) and in those with the lowest level of education. These groups had a higher baseline risk, yielding a larger room for improvement. The effect size was also larger in those who were adherent to the intervention. Taken together, this suggests that targeting high-risk populations with more efforts to stimulate engagement might be effective and needs testing. Absence of clinical effects on cognition or depressive symptoms does not preclude potential long-term effects on these parameters. This is supported by the significant reduction on the CAIDE risk score. The effect of the intervention on incident stroke should be interpreted with caution because absolute numbers are small and this was a secondary outcome.

We decided to design a generic, scalable, and cheap intervention, implementable across a range of health-care settings. With rapidly increasing internet literacy in most parts of the world, including in older people, an eHealth approach is likely to become less of a barrier in the near future. A potential limitation of our approach is that it was not embedded in, or aligned with, the local primary care systems. For example, in the TASMINH4 study,[30] in which GPs were actively involved in the intervention, self-monitoring of blood pressure with and without telemonitoring was more effective, with substantially decreased systolic blood pressure values after 12 months. Furthermore, this study used more frequent measurements and reminders, which might have additionally stimulated engagement and adherence. However, such a study design might not be feasible in large parts of the world with underdeveloped primary care systems.

Major strengths of our study are the large sample size, the blinded outcome assessment, the multicomponent approach including several modifiable risk factors, and considerable study duration for an eHealth study, documenting sustained engagement with the intervention. The low overall drop-out and the high level of complete data collection further increase the robustness of our findings, while execution in three countries improves the generalisability of its results. Small but sustained improvements of common risk factors over 18 months, such as those detected in our study, might favourably affect the rate of incident cardiovascular disease at the population level long term. Further development of eHealth and mobile health applications could offer opportunities for broad implementation at low cost in a variety of settings, including low-income and middle-income countries, where internet access is rapidly increasing. Embedding interventions in local health-care infrastructures might enhance adoption and effectiveness. eHealth interventions offer the opportunity to scale up and do larger implementation trials with clinical outcomes, including incident cardiovascular disease, cognitive decline, and mortality.

Coach-supported self-management of cardiovascular risk factors using an interactive internet-based intervention is feasible in an older population at increased risk of cardiovascular disease and was associated with a modest

	Control	Intervention	Hazard ratio (95% CI)
Poor clinical outcome*	40/1333 (3·0%)	37/1382 (2·7%)	0·87 (0·55–1·37)
All-cause mortality	9/1333 (0·7%)	11/1388 (0·8%)	1·01 (0·40–2·54)
Cardiovascular mortality	1/1333 (0·1%)	4/1388 (0·3%)	2·02 (0·18–22·5)
Total cardiovascular disease†	32/1333 (2·4%)	30/1382 (2·2%)	0·86 (0·52–1·43)
Total stroke	13/1335 (1·0%)	4/1383 (0·3%)	0·30 (0·10–0·93)
Ischaemic stroke	11/1335 (0·8%)	3/1383 (0·2%)	0·27 (0·08–0·97)
Transient ischaemic attack	3/1335 (0·2%)	6/1383 (0·4%)	1·98 (0·49–7·90)
Myocardial infarction	6/1335 (0·4%)	6/1383 (0·4%)	0·99 (0·32–3·07)
Angina pectoris	10/1335 (0·7%)	10/1383 (0·7%)	0·99 (0·41–2·37)

Data are n/N (%). *Mortality, dementia, or cardiovascular disease. †Stroke, transient ischaemic attack, myocardial infarction, or angina pectoris, morbidity, and mortality combined.

Table 3: **Effect of the intervention on clinical outcomes**

improvement of cardiovascular risk profile without any indication of adverse events. When implemented at the population level, this could provide a low-cost way of reducing the burden of cardiovascular disease. The effect might be largest in those with considerable room for improvement and who actively engage in self-management. Large-scale implementation research and adaptation to different high-risk populations is warranted to confirm sustainability and effects on clinical outcomes including cardiovascular disease, dementia, and mortality.

Contributors

ER and EPMvC contributed to the concept, design, data collection, data interpretation, writing of the Article, and coordination of the trial. MPH-B contributed to data collection, data cleaning, data analysis, interpretation, tables, figures, and revising the Article. NC and MB contributed to the design, data collection, data interpretation, and revising the Article. AVdG and YM contributed to concept, design, software development, interpretation, and revising the Article. FM contributed to design, data interpretation, and revising the Article. CBB, SJ, and TvM contributed to concept, design, data collection, data cleaning, and revising the Article. LLVW contributed to data collection, data analysis, interpretation, figures, and revising the Article. TN contributed to design, data collection, data interpretation, and revising the Article. JG contributed to design, data collection, and revising the Article. SA, CB, MK, and HS contributed to concept, design, data interpretation, and revising the Article. WAVG contributed to concept, design, data interpretation, writing of the Article, and coordination of the trial.

Declaration of interests

MK receives funding for multimodal preventive trials for Alzheimer's disease from the Joint Programming for Neurodegenerative Diseases, the Academy of Finland, the Swedish research council, state research funding from Kuopio University Hospital, and Wallenberg Clinical Scholars; and holds the Stiftelse Stockholms Sjukhem donation professor post. All other authors declare no competing interests.

Data sharing

The HATICE consortium is in principle inclined to share data collected in the HATICE trial with external researchers. This will concern the data dictionary and de-identified data only. The study protocol and the statistical analysis plan are published in the appendix. Data will not be made available to any commercial party. Researchers from academic institutions interested in the use of the data of HATICE, will be asked to write a short study protocol, including the research question, the planned analysis and the data required. The scientific committee of the HATICE consortium will then evaluate the relevance of the research question, the suitability of the data, and the quality of the proposed analysis. Based on this, the committee will provide the data or reject the request. Analysis will then be done in collaboration with and on behalf of the HATICE consortium. A data access agreement will be prepared and signed by both parties. Any analysis proposed which is already in the HATICE analysis plan and planned to be done by members of the HATICE consortium will either be rejected, or proposed to be done as a collaborative effort, to be determined on a case-by-case basis.

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For more on **HATICE** see www.hatice.eu

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