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ORIGINAL ARTICLE
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Achievements of primary prevention targets in individuals with high risk of cardiovascular disease: an 8-year follow-up of the Tromsø study

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Aims To study change over 8 years in cardiovascular risk, achievement of national guideline-based treatment targets of lipids, blood pressure (BP) and smoking in primary prevention of cardiovascular disease (CVD), medication use, and characteristics associated with target achievement among individuals with high CVD risk in a general population.

Methods and results We followed 2524 women and men aged 40–79 years with high risk of CVD attending the population-based Tromsø study in 2007–08 (Tromsø6) to their participation in the next survey in 2015–16 (Tromsø7). We used descriptive statistics and regression models to study change in CVD risk and medication use, and characteristics associated with treatment target achievement. In total, 71.4% reported use of BP- and/or lipid-lowering medication at second screening. Overall, CVD risk decreased during follow-up, with a larger decrease among medication users compared with non-users. Treatment target achievement was 31.0% for total cholesterol <5 mmol/L, 27.3% for LDL cholesterol <3 mmol/L, 43.4% for BP <140/90 (<135/85 if diabetes) mmHg, and 85.4% for non-smoking. A total of 9.8% reached all treatment targets combined. Baseline risk factor levels and current medication use had the strongest associations with treatment target achievement.

Conclusion We found an overall improvement in CVD risk factors among high-risk individuals over 8 years. However, guideline-based treatment target achievement was relatively low for all risk factors except smoking. Medication use was the strongest characteristic associated with achieving treatment targets. This study has demonstrated that primary prevention of CVD continues to remain a major challenge.

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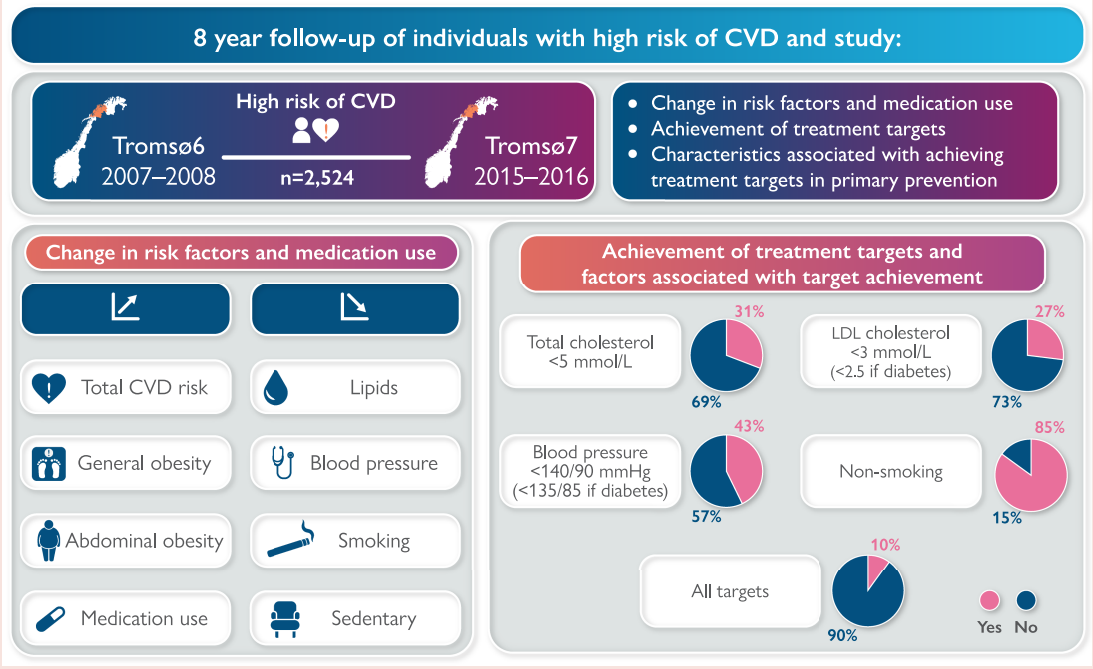
Graphical Abstract



Keywords Cardiovascular disease • Antihypertensives • Lipid-lowering drugs • Primary prevention • Cohort studies

Introduction

Cardiovascular disease (CVD) incidence and mortality rates are declining in many European countries.[1] However, CVD is still a major cause of death and disability and an economic burden for the society, calling for an active preventive approach.[1,2] The main goals of CVD prevention are to delay or prevent the onset of CVD and reduce morbidity and premature mortality.[3] Cardiovascular disease primary prevention guidelines are designed to identify high-risk individuals and highlight the use of cardiovascular risk assessment tools to estimate risk and to guide clinical decision-making on lifestyle interventions and initiating or adjusting medical treatment.[3,4] In Europe, a large proportion of individuals with high CVD risk has an unhealthy lifestyle and there is a discrepancy between evidence-based guidelines and clinical practice.[5,6] We aimed to follow individuals with high risk of CVD from a general population over 8 years to investigate: (i) primary prevention treatment target achievement in lipids, blood pressure (BP), and smoking; (ii) change in cardiovascular risk factors and medication use; and (iii) characteristics associated with achieving primary prevention treatment targets.

Methods

Study design and oversight

The present study followed participants with high risk of CVD attending Tromsø6[7] 2007–08 (attendance 66%) and Tromsø7[8] 2015–16 (attendance 65%). The Tromsø study is a population-based study in the municipality of Tromsø, Norway, and comprising seven surveys conducted between 1974 and 2016 (Tromsø1–Tromsø7). Total birth cohorts and representative population samples have been invited; a total of 45 473 women and men participated in one or more surveys (attendance 65–79%). This study includes data from questionnaires, biological samples, and clinical examinations. We followed high-risk individuals and studied change in CVD risk factors, medication use, treatment targets of lipids, BP, and smoking. Further, we assessed patient characteristics associated with achieving treatment targets in the primary prevention of CVD. The study was approved by the Regional Committee for Medical and Health Research Ethics North (reference 1778/2015).

Methods of data collection

We used questionnaire data to assess diabetes (*Do you have, or have you had diabetes?* yes/no), educational level (*What is the highest level of education you have completed*? primary/secondary school, modern secondary school, technical school, vocational school, senior high school or high school diploma dichotomized to 'lower education' and college/university as 'higher education'), marital status (single, widow/widower, divorced/separated dichotomized to 'single' and married/registered partner as 'married/partner'), smoking status (*Do you/did you smoke daily?* yes now dichotomized to 'smoking', yes previously or never as 'non-smoking'), physical activity level (*Exercise and physical exertion in leisure time the last 12 months?* reading, watching TV or other sedentary activity dichotomized to 'sedentary' and walking, cycling, or other forms of exercise at least 4 h a week, participation in recreational sports, heavy gardening at least 4 h a week, hard training or sports competitions regularly several times a week as 'not sedentary'), psychological distress (Hopkins's symptom checklist-10 summarized with a mean score of $\geq$1.85 previously validated as the cut-off value for psychological distress[9]), self-perceived health (*How do you in general consider your own health to be?* bad, or neither good nor bad dichotomized to 'poor', and good or excellent as 'good'), and family history of coronary heart disease (CHD) (*Have any family members had a heart attack before the age of 60 years?* with alternatives parents, siblings, and/or children). Non-fasting venous blood samples were analysed for total, LDL- and HDL cholesterol within 48 h by enzymatic colorimetric methods (Roche Diagnostics, Mannheim, Germany) at the Department of Laboratory Medicine,

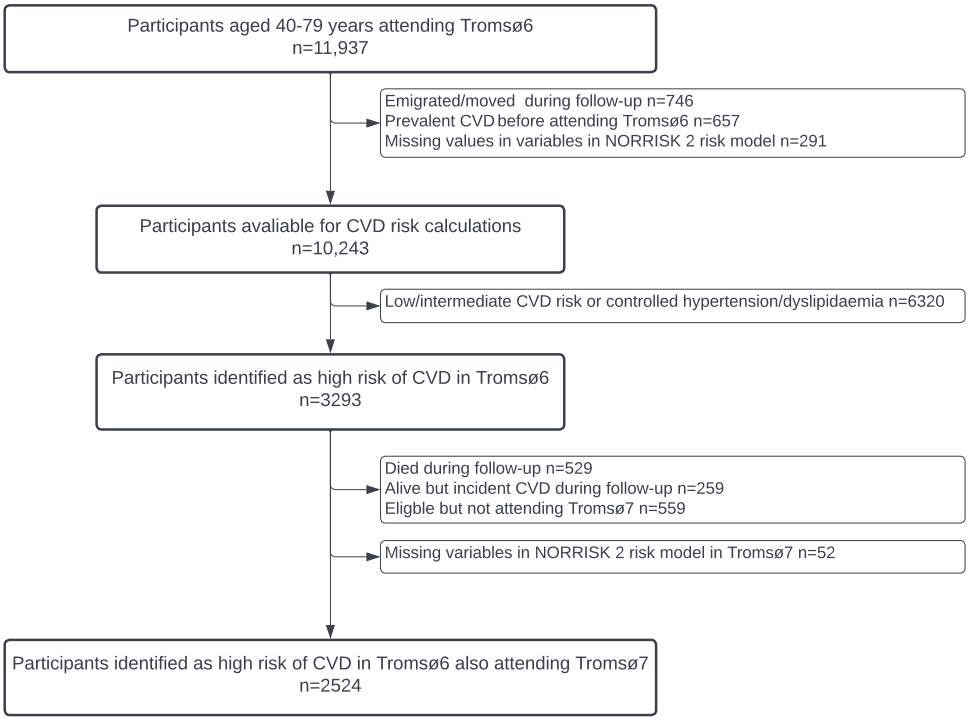


Figure 1 Flowchart of the study. Created in Lucidchart (www.lucidchart.com).

Table 1 Baseline characteristics of the study participants, overall and stratified by sex, the Tromsø Study 2007–08

	Overall ($n = 2524$)	Women ($n = 1094$)	Men ($n = 1430$)
Age, years, mean, SD	60.6 (9.1)	62.1 (8.9)	59.4 (9.1)
Age ≥60 years, % (*n*)	63.7 (1608)	70.3 (769)	58.7 (839)
Diabetes, % (*n*)	8.9 (227)	9.8 (107)	8.4 (120)
Higher education[a], % (*n*)	31.4 (783)	24.8 (268)	36.5 (515)
Married/partner, % (*n*)	66.0 (1666)	60.5 (662)	70.2 (1004)
Psychological distress, % (*n*)	9.9 (251)	15.2 (166)	5.9 (85)
Self-reported health good/very good, % (*n*)	65.1 (1627)	60.2 (652)	68.9 (975)

SD, standard deviation.
[a]Higher education; college/university < and ≥4 years.

University Hospital of North Norway. Blood pressure was measured on the right arm of all participants three times at 1 min intervals after 2 min' seated rest by a Dinamap ProCare 300 monitor (GE Healthcare, Norway), and the mean of the two final readings was used in the analysis. General obesity was defined as body mass index (BMI) ≥30 kg/m^2, calculated as bodyweight in kilograms divided by body height in metres squared. Abdominal obesity was defined as waist circumference ≥88 and ≥102 cm in women and men, respectively, measured to the nearest 0.1 cm with a Seca measurement tape at the level of the umbilicus. Trained personnel performed all measurements. Medication use was defined by a combination of a questionnaire questions (*Do you use blood pressure lowering drugs, Do you use lipid-lowering drugs?* yes now, yes previously, no), and a self-reported written list of brand names of regularly used medication; BP-lowering drugs: ATC-codes C02, C03, C07, C08, C09 and lipid-lowering drugs: ATC-code C10. Current medication use was defined by 'yes now' and/or the ATC-codes.

Study population

We included participants aged 40–79 years identified with high risk of CVD by the risk assessment tool NORRISK 2, elevated single risk factors from the 2017 Norwegian CVD prevention guidelines,[10] or treated but uncontrolled hypertension and/or dyslipidaemia.

We excluded participants with prevalent and incident CVD during follow-up. Cases of first ever myocardial infarction (MI) and cerebral stroke were recorded from the first study entry until 31 December 2014 by the Tromsø Study CVD registry. The national unique 11-digit identification number allowed register-linkage. Cases of MI and ischaemic stroke were identified by linkage to the University Hospital of North Norway's discharge diagnosis registry, the only hospital in the area, with search for International Classification of Diseases, 10th Revision codes. Adjudication of hospitalized and out-of-hospital events was performed by an independent endpoint committee examining medical records, described in detail elsewhere.[11] Due to lack of validated endpoints after 2014, we also used self-reported MI or stroke (yes/no) to exclude participants with CVD after 2014 and before participation in Tromsø7. Emigration from the municipality and/or Norway was identified by linkage to the National Population Register. Death before Tromsø7 was identified by linkage to the Norwegian Cause of Death Registry.

After exclusions (*Figure 1*), the present study included 2524 participants attending both surveys. All participants gave written informed consent.

Risk calculations and identification of high-risk individuals

In 2017, the current Norwegian national guidelines for CVD prevention and the NORRISK 2 score were introduced to identify individuals with high total CVD risk eligible for intervention.[10,12] NORRISK 2 predicts the 10-year risk (%) of incident non-fatal/fatal MI and stroke combined. The risk estimation is

Table 2 Changes in cardiovascular disease risk factors and medication use among individuals with high risk of cardiovascular disease, overall and stratified by sex, the Tromsø Study 2007–16

	Overall ($n = 2524$)		Women ($n = 1094$)		Men ($n = 1430$)	
	Baseline	Second screening	Baseline	Second screening	Baseline	Second screening
Age, years	60.6 (9.2)	68.6 (9.2)	62.1 (8.9)	70.1 (8.9)	59.4 (9.1)	67.4 (9.1)
Cardiovascular risk factors						
Total CVD risk[a], mean	9.9 (6.1)	13.2 (7.5)	8.3 (5.6)	11.6 (7.1)	11.0 (6.1)	14.2 (7.6)
Total cholesterol, mmol/L	6.0 (1.1)	5.6 (1.2)	6.1 (1.0)	5.7 (1.2)	6.0 (1.1)	5.5 (1.2)
LDL cholesterol, mmol/L	3.9 (0.9)	3.7 (1.1)	3.9 (0.9)	3.7 (1.1)	4.0 (1.0)	3.7 (1.1)
Low HDL cholesterol[b], %	15.5 (390)	13.6 (343)	20.4 (234)	17.6 (192)	11.7 (167)	10.6 (151)
Systolic blood pressure, mmHg	150.3 (21.3)	143.7 (21.2)	153.5 (23.3)	145.6 (23.0)	147.9 (19.4)	142.3 (19.6)
Diastolic blood pressure, mmHg	83.4 (11.0)	77.6 (10.5)	80.4 (10.8)	75.3 (10.3)	85.8 (10.7)	79.3 (10.3)
Smoking, %	21.4 (539)	14.6 (368)	20.8 (227)	14.2 (155)	21.8 (312)	14.9 (213)
General obesity[c], %	27.0 (682)	29.8 (749)	28.3 (309)	31.0 (338)	26.1 (373)	28.8 (411)
Abdominal obesity[d], %	58.8 (1484)	59.6 (1505)	70.6 (772)	71.0 (777)	49.8 (712)	50.9 (728)
Sedentary physical activity level, %	20.6 (481)	18.1 (432)	20.4 (199)	19.6 (196)	20.7 (282)	17.0 (236)
Primary prevention medication use						
Antihypertensives and/or lipid-lowering drugs, %	48.1 (1214)	71.4 (1803)	62.0 (678)	80.1 (876)	37.5 (503)	64.8 (927)
Antihypertensives only, %	26.2 (660)	35.5 (895)	32.9 (360)	38.3 (419)	21.0 (300)	33.3 (476)
Lipid-lowering drugs only, %	8.2 (207)	10.2 (258)	11.7 (128)	11.0 (120)	5.5 (79)	9.7 (138)
Antihypertensives and lipid-lowering drugs, %	13.8 (347)	25.8 (650)	17.4 (190)	30.8 (337)	11.0 (157)	21.9 (313)

Numbers are means (SDs) or proportions (numbers).
[a]Total cardiovascular risk: NORRISK 2 score; 10-year risk of fatal and non-fatal MI or stroke.
[b]Low HDL cholesterol, <1.3 mmol/L women, <1.0 mmol/L men.
[c]Body mass index ≥30 kg/m^2.
[d]Waist circumference men ≥102 cm, women ≥88 cm.

based on age, sex, systolic BP (SBP), total cholesterol, smoking, first-degree family member with premature MI (aged <60 years), low HDL cholesterol (men <1.0 mmol/L, women <1.3 mmol/L), and use of antihypertensive medication (current use increases the score). Selmer *et al.*[12] suggested age-specific thresholds in age groups 45–54, 55–64, and 65–74 years to determine low, medium, or high risk of CVD. Elevated values of single risk factors, i.e. total cholesterol ≥7 mmol/L, LDL cholesterol ≥5 mmol/L (does not apply for women >50 years and men >74 years), SBP ≥160 mmHg or diastolic BP (DBP) ≥100 mmHg identifies individuals eligible for intervention regardless of their NORRISK 2 score.[10] In individuals with diabetes, LDL cholesterol ≥2.5 mmol/L and BP ≥140/90 mmHg indicate intervention.[10] We also identified and included participants with treated but uncontrolled hypertension (BP ≥140/90 mmHg) and/or dyslipidaemia (total cholesterol ≥5 mmol/L and/or LDL cholesterol ≥3 mmol/L).

Outcomes

The outcomes of this study were change in CVD risk factors and primary prevention medication use (antihypertensives and lipid-lowering drugs). Furthermore, the proportion achieving treatment targets for primary prevention defined by the national guidelines: BP <140/90 (<135/85 if diabetes) mmHg, total cholesterol <5 mmol/L, LDL cholesterol <3 (<2.5 if diabetes) mmol/L, and non-smoking. In addition, baseline characteristics, risk factors, and current medication use associated with achieving treatment targets.

Statistics

Means and standard deviations (SDs) were presented for continuous variables, and categorical variables were described as percentages (%). Characteristics at baseline and second screening were presented as appropriate (*Tables 1* and *2*). In separate analyses, we used regression models to compare the study sample with participants lost to follow-up in Tromsø7 due to non-attendance, incident CVD, or death before Tromsø7 (see Supplementary material online, *Table S1*). Regression models were used to present age-adjusted characteristics among non-users and users of medication at second screening, overall and stratified by sex (*Table 3*). We calculated the proportion that achieved the treatment targets at second screening (*Figure 2*), and used multivariable logistic regression with odds ratios (ORs) and 95% confidence intervals (CIs) to identify characteristics associated with treatment target achievement adjusted for age and sex (*Table 4*), adjusted for age, sex, education, and medication use (see Supplementary material online, *Table S2*). *P*-values of <5% were considered statistically significant. Analyses were performed using Stata version 16 (StataCorp. 2019, Stata Statistical Software: StataCorp LLC, College Station, TX, USA).

Results

Study sample

At baseline, the mean age was 60.5 years, 63.7% was older than 60 years, 31.4% had higher education, and 8.9% had diabetes (*Table 1*). High-risk individuals not re-attending in Tromsø7 (regardless of cause) were older, had higher mean total CVD risk, a larger proportion had diabetes, low HDL cholesterol, were daily smokers, were sedentary, and had lower educational (see Supplementary material online, *Table S1*).

Change in cardiovascular risk factors and medication use

All CVD risk factors except total CVD risk and obesity improved during follow-up. Change in CVD risk factors was similar among the sexes,

Table 3 Characteristics of non-users and users of antihypertensives and/or lipid-lowering drugs at second screening among individuals with high risk of cardiovascular disease, overall and stratified by sex, the Tromsø Study 2007–16

	Overall ($n = 2524$)			Women ($n = 1094$)			Men ($n = 1430$)		
	Non-user ($n = 721$)	User ($n = 1803$)	*P*-value	Non-user ($n = 218$)	User ($n = 876$)	*P*-value	Non-user ($n = 503$)	User ($n = 927$)	*P*-value
Demographics									
Age, mean	57.4 (56.7, 58.0)	61.9 (61.3, 62.3)	<0.001	58.1 (56.9, 59.2)	63.1 (62.5, 63.7)	<0.001	57.1 (56.2, 57.9)	60.6 (59.9, 61.3)	<0.001
Higher education[a], %	34.8 (31.3, 38.3)	30.0 (27.8, 32.2)	0.021	30.3 (24.3, 36.2)	23.3 (20.8, 26.1)	0.032	37.2 (32.9, 41.5)	36.0 (32.9, 39.2)	0.669
Married/partner, %	65.8 (62.4, 69.3)	66.1 (63.8, 68.2)	0.908	56.4 (49.7, 63.1)	61.5 (58.2, 64.8)	0.177	69.9 (66.1, 73.9)	70.3 (67.4, 73.3)	0.874
Self-reported good/very good health, %	72.9 (69.6, 76.1)	62.0 (59.7, 64.3)	<0.001	68.5 (62.0, 74.2)	58.1 (54.8, 64.2)	0.008	75.0 (71.1, 78.7)	65.4 (62.4, 69.3)	0.001
Psychological distress, %	7.2 (5.3, 9.1)	11.0 (9.6, 12.5)	0.005	10.8 (6.5, 15.0)	16.3 (13.9, 18.9)	0.052	5.4 (3.4.7.4)	6.3 (4.4, 7.9)	0.513
Baseline risk factors									
Total CVD risk[b], mean	11.0 (10.6, 11.3)	9.4 (9.1, 9.6)	<0.001	9.1 (8.6, 9.6)	8.1 (7.8, 8.3)	<0.001	11.7 (11.3, 11.9)	10.6 (10.3, 10.9)	<0.001
Diabetes, %	6.7 (4.8, 8.5)	9.9 (8.4, 11.1)	0.012	12.5 (8.0, 16.9)	9.0 (7.1, 10.9)	0.137	4.2 (2.5, 6.0)	10.8 (8.8, 12.8)	<0.001
Total cholesterol, mmol/L	6.3 (6.2, 6.4)	5.9 (5.8, 5.9)	<0.001	6.4 (6.2, 6.6)	6.0 (5.9, 6.1)	<0.001	6.3 (6.2, 6.4)	5.8 (5.7, 5.9)	<0.001
LDL cholesterol, mmol/L	4.2 (4.1, 4.3)	3.9 (3.7, 3.9)	<0.001	4.1 (4.0, 4.3)	3.8 (3.7, 3.9)	<0.001	4.2 (4.3, 4.3)	3.8 (3.8, 3.9)	<0.001
Low HDL cholesterol[c], %	12.8 (10.5, 15.2)	16.6 (14.6, 18.3)	0.018	18.4 (13.0, 23.3)	20.9 (17.9, 23.7)	0.397	10.3 (7.7, 12.8)	12.3 (10.0, 14.5)	0.205
Systolic blood pressure, mmHg	143.5 (142.0, 144.9)	153.1 (152.2, 154.1)	<0.001	147.0 (144.1, 149.8)	155.1 (153.8, 156.5)	<0.001	141.5 (139.9, 143.1)	151.1 (150.3, 152.6)	<0.001
Diastolic blood pressure, mmHg	80.2 (79.4, 81.0)	84.8 (84.3, 85.3)	<0.001	76.4 (75.0, 77.9)	81.3 (80.7, 82.0)	<0.001	82.1 (81.2, 83.0)	87.8 (87.1, 88.4)	<0.001
Smoking, %	29.5 (26.1, 32.8)	17.8 (15.9, 19.6)	<0.001	25.9 (20.3, 31.7)	19.3 (16.6, 21.9)	0.028	31.2 (27.2, 35.3)	16.5 (13.8, 18.9)	<0.001
General obesity[d], %	16.3 (13.6, 19.0)	31.5 (29.3, 33.7)	<0.001	19.6 (14.3, 24.9)	30.5 (27.6, 33.5)	0.002	15.0 (12.1, 18.3)	32.3 (29.3, 35.4)	0.001
Abdominal obesity[e], %	45.9 (42.2, 49.6)	64.0 (61.7, 66.2)	<0.001	59.0 (52.0, 65.4)	73.4 (70.5, 76.5)	<0.001	39.7 (35.3, 44.0)	55.3 (5.9, 58.5)	<0.001
Sedentary activity level, %	20.5 (17.5, 23.6)	20.6 (18.3, 22.4)	0.955	21.7 (15.8, 27.6)	20.0 (17.1, 22.9)	0.616	20.2 (16.7, 23.7)	21.0 (18.2, 23.7)	0.729
Mean change in risk factors during follow-up									
Total CVD risk[b], mean	+5.7 (5.4, 6.0)	+2.3 (2.1, 2.5)	<0.001	+5.3 (4.7, 5.9)	+2.9 (2.5, 3.1)	<0.001	+5.6 (5.3, 6.2)	+1.9 (1.5, 2.2)	<0.001
Total cholesterol, mmol/L	−0.2 (−0.1,−0.2)	−0.6 (−0.5,−0.7)	<0.001	0.0 (0.0, −0.1)	−0.5 (−0.3, −0.6)	<0.001	−0.2 (−0.1, −0.3)	−0.7 (−0.6, −0.7)	<0.001
LDL cholesterol, mmol/L	+0.1 (0.0, 0.2)	−0.4 (−0.3, −0.4)	<0.001	+0.2 (0.0, 0.3)	−0.3 (−0.2, −0.4)	<0.001	0.0 (−0.1, 0.1)	−0.5 (−0.4, 0.5)	<0.001
Systolic blood pressure, mmHg	+2.4 (0.8, 4.0)	−10.3 (−9.3, −11.4)	<0.001	+1.6 (−1.6, 4.8)	−10.2 (−9.0, 11.8)	<0.001	+2.8 (1.0, 4.5)	−10.3 (−8.9, −11.5)	<0.001
Diastolic blood pressure, mmHg	−1.5 (−0.7, −2.3)	−7.6 (−7.1, −8.2)	<0.001	−0.4 (−1.7, 1.1)	−6.3 (−5.7, −7.1)	<0.001	−2.1 (−1.2, −3.0)	−8.8 (−8.1, −9.5)	<0.001
Daily smoking, %	−6.8 (−4.5, −9.1)	−6.7 (−0.5, −8.1)	0.973	−6.2 (−2.2, −10.2)	−6.7 (−4.5, −8.4)	0.816	−7.2 (−4.3, −10.0)	−6.8 (−4.5, 8.9)	0.843

Values are means (95% CI) or percentages (95% CI). All values are age-adjusted using linear and logistic regression models.
P = difference between non-users and users of primary prevention medication.
[a]Higher education; college/university < and ≥4 years.
[b]Total cardiovascular risk: NORRISK 2 score; 10-year risk of fatal and non-fatal MI or stroke.
[c]Low HDL cholesterol, <1.3 mmol/L women, <1.0 mmol/L men.
[d]Body mass index ≥30 kg/m^2.
[e]Waist circumference men ≥102 cm women ≥88 cm.

except for a greater decrease in SBP among women compared with men (*Table 2*). The proportion of participants on medication increased from 48.1 to 71.4%. At both time points, a larger proportion of the study participants used antihypertensives only, followed by antihypertensives and lipid-lowering drugs combined, while the lowest proportion used lipid-lowering drugs only. At both time points, more women than men used medication while men had a higher increase in medication use than women (*Table 2*).

Second screening medication users vs. non-users: characteristics at baseline and follow-up

Users and non-users of medication at second screening differed in characteristics at both time points (*Table 3*). Users were older, had higher educational level, reported poorer self-reported health and more psychological distress, and had less favourable levels at baseline of some of the risk factors, except for total CVD risk and lipid levels, a larger proportion were women, and a lower proportion were daily smokers compared with non-users. Among medication users at second screening, total CVD risk increased less from baseline compared with non-users (*Table 3*). Total cholesterol and DBP decreased in both groups, but users had a larger decrease. Systolic BP and LDL cholesterol decreased in users and increased in non-users.

Treatment target achievement and characteristics associated with reaching targets

At second screening, 31.0% achieved the treatment target for total cholesterol and 27.3% for LDL cholesterol (*Figure 2*). Medication use was the strongest characteristic associated with achieving targets (*Table 4*). Higher values of total CVD risk at baseline were associated with lower odds of reaching the lipid targets, 7 and 6% lower odds per 1% increase in CVD risk, respectively. Higher baseline values of total cholesterol were associated with lower odds of reaching the lipid targets, 54 and 46% reduced odds per 1 mmol/L increase, respectively. Higher baseline values of LDL cholesterol were associated with lower odds of reaching the lipid targets, 52 and 55% reduced odds per 1 mmol/L increase, respectively. Other characteristics associated with reaching lipid targets were male sex (total cholesterol only), age ≥60 years, having diabetes, and poor self-perceived health (*Table 4*). General and abdominal obesity were associated with reaching target for total cholesterol (*Table 4*), but adjusted for education and medication use, the association was no longer statistically significant (see Supplementary material online, *Table S2*).

Overall, 43.4% achieved treatment target for BP (*Figure 2*). Higher baseline total CVD risk were associated with 6% lower odds for reaching target. Higher baseline SBP and DBP were associated with lower odds for reaching the BP target, 32 and 30% reduced odds per 10 mmHg increase, respectively. Further, age <60 years and baseline daily smoking was also associated with reaching BP target. Antihypertensive medication alone was associated with reduced odds of reaching the BP target (*Table 4*), and this was persistent when adjusting for education (see Supplementary material online, *Table S2*). Concomitant use of antihypertensives and lipid-lowering drugs was associated with increased odds of reaching the BP target.

Non-smoking was achieved by 85.4% of the study population (*Figure 2*), and age ≥60 years, having higher education, being married/partner, having obesity, and using medication were all individually associated with reaching the non-smoking target (*Table 4*).

A total of 9.8% reached all treatment targets, where medication use was the strongest characteristic associated with achieving all targets combined. Other significant characteristics were male sex, lower baseline total CVD risk, lipid, and BP levels, having diabetes, and poor self-perceived health. General and abdominal obesity were associated with increased odds of reaching all target (*Table 4*), but when adjusted for education and medication use, this association was no longer significant (see Supplementary material online, *Table S2*).

Discussion

We followed 2524 individuals with high risk of CVD. Despite improvements in risk factor levels, <10% achieved all CVD primary prevention treatment targets combined (i.e. lipids, BP, and smoking status).

Change in cardiovascular risk factors

The observed decrease in single risk factors but increase in total CVD risk could be explained by the impact of age in the NORRISK 2 score, as previously demonstrated.[13] During follow-up, favourable changes were found in lipid and BP levels and smoking status, which are modifiable risk factors with major impact on reducing CVD risk. Previous studies have shown that a reduction of 1 mmol/L in LDL cholesterol is associated with a 22% reduction in CVD events,[14] a 10 mmHg decrease in SBP can reduce risk by 20%,[15] and smoking cessation is associated with 50% risk reduction within 1 year, making smoking cessation the most effective intervention to reduce CVD risk.[16,17] We observed a reduction in the proportion of participants reporting a sedentary physical activity level, but at the same time we observed an increase in both general and abdominal obesity, in line with findings from the general population in Norway[18] as well as worldwide.[19] This is of worry as obesity is associated with development of Type 2 diabetes and CVD.[20]

Medication use in primary prevention

At the second screening, the proportion using primary prevention medication increased from baseline by 23.3% age points to 71.4%. This is lower compared with other studies.[2,5,6] Although medication use increased more in men over time, we found that more women were medication users at baseline as well as at follow-up. A systematic review[21] and meta-analysis of sex differences in medication prescription found statin use was slightly higher among women than men, while the opposite was found for the use of antihypertensives among individuals with a high risk of CVD.

In the present study, users and non-users of medication at second screening differed in several characteristics that may have impacted decision-making in initiation of medical treatment. Compared with medication users at second screening, non-users had lower baseline BP levels, and a significantly larger proportion were daily smokers. In the clinical setting, smoking cessation could be prioritized since it is considered the most cost-effective and important intervention to reduce CVD risk.[22] The decrease in CVD risk factors over time was larger in medication users at second screening compared with non-users. Still, among non-users, the observed decline in total cholesterol, slight increase in LDL cholesterol and SBP, and decrease in DBP may have several explanations. Lifestyle change is key in primary prevention[3] and the relatively stable levels in risk factors could be due to positive lifestyle changes. A substantial decline in lipid and BP levels over time in the general population has been found both in Norway[23,24] and worldwide.[25,26] This has also been shown in the Tromsø study population[27,28] among both medication users and non-users, although more pronounced among users. However, the larger decline in lipid and BP levels among medication users vs. non-users demonstrates the impact of medication treatment.

Treatment target achievement

In our study, 31% achieved the target of total cholesterol <5 mmol/L and 27% for LDL cholesterol <3 mmol/L, while 24% achieved both

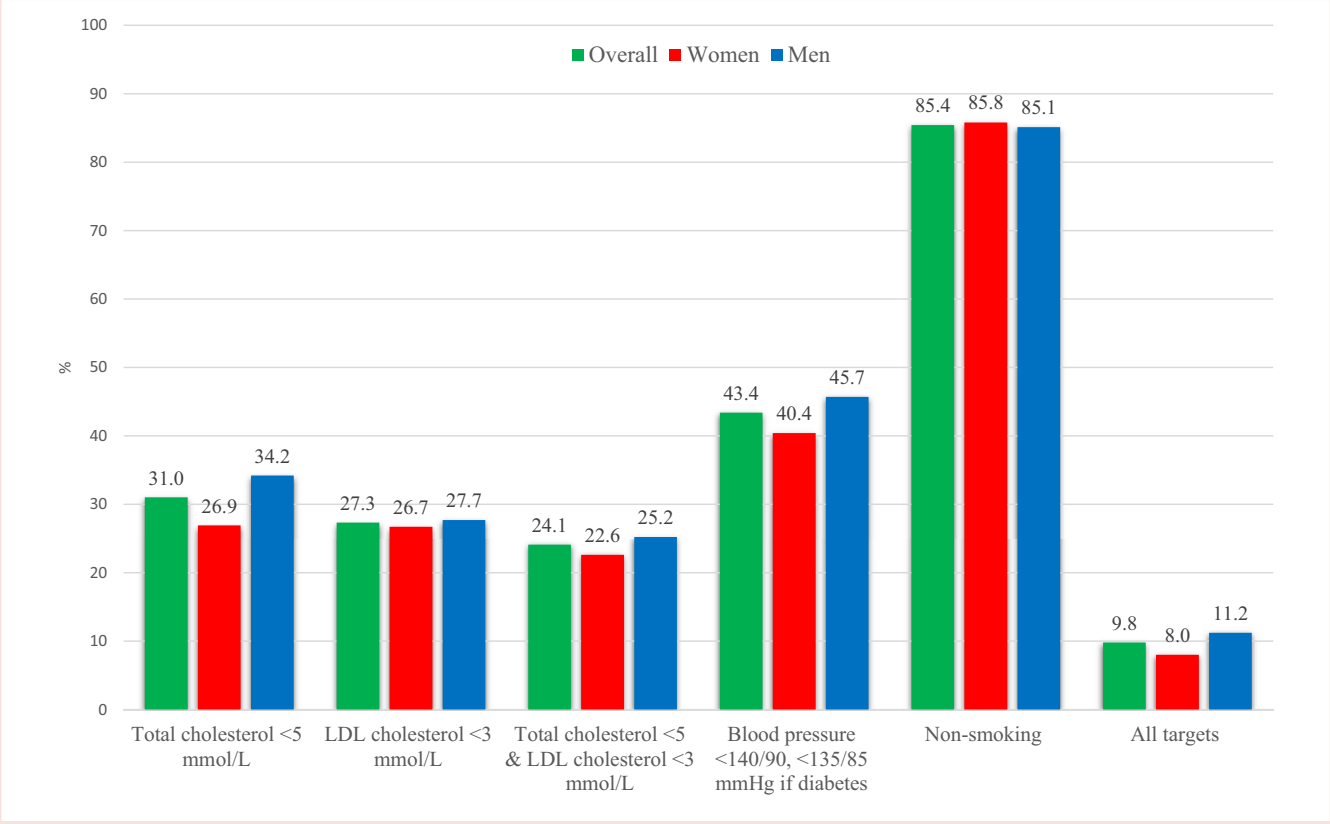


Figure 2 Attained cardiovascular disease primary prevention treatment targets in high-risk individuals, overall and stratified by sex. The Tromsø study 2007–16.

targets. The proportion in our study reaching the lipid targets is lower than in the EURIKA 2009 study, where 43% treated for dyslipidaemia achieved the total cholesterol target, and 41% achieved targets for both total- and LDL cholesterol.[5] In the primary care arm of the EUROASPIRE IV 2014–15 study, 33% of the users of lipid-lowering drugs and 11% of the non-users achieved the LDL target of <2.5 mmol//L.[6] In the more recent EUROASPIRE V 2017–18, 47% of users of lipid-lowering drugs and only 19% of the non-users achieved the LDL target of <2.6 mmol/L.[2]

For BP, we found ~40% achieved the BP target of <140/90 (<135/85 if diabetes) mmHg, comparable to the findings from the EURIKA study, where 39% achieved the BP target,[5] but lower than EUROASPIRE IV where 43% achieved the target,[6] and lower than EUROASPIRE V[2] where 47% achieved the BP target.

Our finding of a smoking prevalence of 15% at second screening in 2015–16 is similar to or slightly lower than findings from EURIKA and the EUROASPIRE studies, ranging from 17 to 22%.[2,5,6] Differences could be explained by the variation in smoking prevalence over time in European countries included in these studies, as reduction in smoking has occurred at different rates in European populations.[29]

Direct comparisons of target achievement in various studies should be interpreted cautiously due to variation in study populations and time points as well as different thresholds in treatment target. Our result of only 1 in 10 high-risk individuals achieving all targets is worrisome. Achieving treatment targets of lipids and BP is associated with reduced risk of CVD,[30,31] and modifying lipids, BP, and smoking reduces the risk of future CVD events substantially,[14–17] highlighting the importance of efforts in primary prevention of CVD.

Characteristics associated with achieving target

We identified several baseline characteristics associated with achieving primary CVD prevention treatment targets. First, higher levels of total CVD risk were associated with lower odds of reaching targets for lipids, BP, smoking, and all targets combined. Further, we found that higher baseline lipid levels were associated with lower odds of achieving lipid targets and all targets combined, and higher baseline BP was associated with lower odds of achieving treatment goals for BP and all targets combined. This is in line with findings from a study finding total CVD risk as an independent predictor of poor target achievement.[32] Thus, individuals with highest risk of CVD, who will benefit significantly from risk reduction, have the lowest probability of achieving treatment goals.

We found that medication use was the characteristic with the strongest association of achieving lipid targets, smoking cessation, and all targets combined. Previous studies have found that greater proportion of medication users achieve targets compared with non-users.[2,5,6] In our study, antihypertensive medication alone was associated with lower odds of reaching the BP target, while concomitant use of antihypertensives and lipid-lowering drugs was associated with increased odds of reaching the BP target. Although not controlled for in this study, other studies have highlighted the importance of medication non-adherence as a key contributor to uncontrolled hypertension.[33] Further, hypertension control may require use of two or more BP-lowering agents to reach targets, as emphasized in the current European guidelines for primary prevention,[3] making this a complex matter in clinical practice.

Table 4 Odds ratios of cardiovascular disease primary prevention target achievement, adjusted for age and sex, the Tromsø Study 2007–16

	Control of TC		Control of LDL		Control of hypertension		Control of smoking		Control of all targets	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Demographics										
Men vs. women[a]	1.51 (1.3, 1.8)	<0.001	1.14 (0.9, 1.4)	0.146	1.08 (0.9, 1.3)	0.354	1.06 (0.8, 1.3)	0.643	1.46 (1.0, 1.9)	0.007
Age ≥60 vs. <60[b]	1.59 (1.3, 1.9)	<0.001	1.77 (1.5, 2.2)	<0.001	0.43 (0.3, 0.5)	<0.001	1.98 (1.6, 2.5)	<0.001	1.10 (0.8, 1.4)	0.462
Higher vs. lower education[c]	0.83 (0.7, 1.0)	0.054	0.88 (0.7, 1.1)	0.221	1.08 (0.8, 1.3)	0.430	1.75 (1.3, 2.3)	<0.001	0.98 (0.7, 1.3)	0.881
Single/separated vs. married/partner[d]	0.97 (0.8, 1.2)	0.705	0.93 (0.7, 1.1)	0.442	0.92 (0.8, 1.1)	0.370	0.74 (0.6, 0.9)	0.009	1.11 (0.8, 1.4)	0.444
Risk factors at baseline										
Total CVD risk, mean[d,e], %	0.93 (0.9–0.9)	<0.001	0.94 (0.9–0.9)	<0.001	0.94 (0.9–0.9)	<0.001	0.83 (0.9–0.9)	<0.001	0.86 (0.8–0.9)	<0.001
Total cholesterol, mmol/L[d,f]	0.46 (0.4, 0.5)	<0.001	0.54 (0.4, 0.6)	<0.001	1.09 (1.0, 1.2)	0.030	0.95 (0.8, 1.1)	0.275	0.58 (0.5, 0.7)	<0.001
LDL cholesterol, mmol/L[d,f]	0.48 (0.4, 0.5)	<0.001	0.45 (0.4, 0.5)	<0.001	1.08 (0.9, 1.2)	0.076	0.94 (0.8, 1.0)	0.487	0.55 (0.5, 0.6)	<0.001
Systolic BP, mmHg[d,g]	0.98 (0.9, 1.0)	0.385	0.98 (0.9, 1.1)	0.538	0.68 (0.6, 0.7)	<0.001	1.24 (1.2, 1.3)	<0.001	0.84 (0.8, 0.9)	<0.001
Diastolic BP, mmHg[d,g]	1.03 (0.9, 1.1)	0.461	0.99 (0.9, 1.1)	0.822	0.70 (0–6, 0.8)	<0.001	1.37 (1.2, 1.5)	<0.001	0.92 (0.8, 1.1)	0.185
Diabetes vs. no diabetes[d]	3.48 (2.7, 4.6)	<0.001	3.02 (2.3, 4.0)	<0.001	1.23 (0.9, 1.6)	0.151	1.30 (0.8, 1.9)	0.213	2.79 (1.9, 4.0)	<0.001
Smoking vs. non-smoking[d]	0.76 (0.6, 0.9)	0.015	0.84 (0.7, 1.1)	0.123	1.29 (1.0, 1.6)	0.010	—		0.36 (0.2, 0.6)	<0.001
Baseline health factors										
General obesity vs. overweight/normal weight[d,h]	1.40 (1.2, 1.7)	<0.001	1.13 (0.9, 1.4)	0.238	1.19 (0.9, 1.4)	0.063	1.64 (1.2, 2.1)	0.001	1.50 (1.1, 1.9)	0.006
Abdominal obesity vs. normal WC[d,h]	1.33 (1.1, 1.6)	0.002	1.09 (0.9, 1.3)	0.351	1.17 (0.9, 1.4)	0.070	1.58 (1.3, 2.0)	<0.001	1.42 (1.1, 1.9)	0.012
Sedentary vs. physical active at leisure time[d]	1.10 (0.8, 1.4)	0.366	1.10 (0.8, 1.3)	0.392	0.95 (0.8, 1.2)	0.655	0.62 (0.5, 0.8)	0.001	0.96 (0.7, 1.4)	0.819
Poor health vs. good health[d]	1.49 (1.2, 1.8)	<0.001	1.36 (1.1, 1.6)	0.001	1.12 (0.9, 1.3)	0.186	0.68 (0.5, 0.9)	0.001	1.24 (0.9, 1.6)	0.126
Psychological distress vs. no distress[d]	0.94 (0.6, 1.3)	0.683	0.78 (0.5, 1.1)	0.129	1.09 (0.8, 1.4)	0.533	0.73 (0.5, 1.0)	0.080	0.95 (0.6, 1.5)	0.840
Current medication use										
Antihypertensives and/or lipid-lowering drugs[d]	4.95 (3.9, 6.4)	<0.001	5.68 (3.9, 7.0)	<0.001	1.20 (1.0, 1.5)	0.056	2.42 (1.9, 3.1)	<0.001	8.67 (4.9, 15.1)	<0.001
Antihypertensives only[d]	0.35 (0.3, 0.5)	<0.001	0.23 (0.2, 0.3)	<0.001	0.78 (0.7, 0.9)	0.004	2.12 (1.7, 2.9)	<0.001	0.34 (0.3, 0.5)	<0.001
Lipid-lowering drugs only[d]	2.09 (1.7, 2.7)	<0.001	2.62 (2.0, 3.4)	<0.001	1.78 (1.4, 2.3)	<0.001	0.89 (0.6, 1.2)	0.450	2.54 (1.9, 3.7)	<0.001
Antihypertensives and lipid-lowering drugs[d]	7.94 (6.5, 9.8)	<0.001	8.89 (6.9, 10.5)	<0.001	1.22 (0.9, 1.5)	0.034	1.38 (1.0, 1.8)	0.026	5.27 (3.8, 6.9)	<0.001

Control of target: TC, total cholesterol <5 mmol/L, LDL <3.0 (2.5 if diabetes) mmol/L, hypertension BP <140/90 (<135/85 if diabetes) mmHg.
[a]Adjusted for age.
[b]Adjusted for sex.
[c]Higher education: College/university < and≥4 years.
[d]Adjusted for age and sex.
[e]Total cardiovascular risk: NORRISK 2 score; 10-year risk of fatal and non-fatal MI or stroke.
[f]Odds ratio per one unit increase (1 mmol/L) in TC and LDL cholesterol.
[g]Odds ratio per 10-unit increase (10 mmHg) in systolic and diastolic BP.
[h]General obesity; BMI ≥30 kg/m^2, abdominal obesity; waist circumference men ≥102 cm women ≥88 cm.

Male sex and age >60 years were associated with reaching target of total cholesterol, in line with findings from other studies.[2,5,6] These studies also found women had higher odds of achieving the BP target,[2,5,6] contrary to our findings. Diabetes was positively associated with achieving target for lipids, and all targets combined; in line with findings from another study demonstrating diabetes to be predictor for reaching lipid targets.[34] This could be explained by the slight difference in cut-off values to be identified as high risk, and the lipid target. Further, diabetics should receive regular follow-up including monitoring of lipid and BP levels. This is an opportunity to initiate or adjust medical treatment and to provide lifestyle advice that could lead to increased risk awareness. Age <60 years, lower education, and being single were associated with lower odds of being a non-smoker, in line with findings from other studies.[5,6,35]

Potential explanations for not achieving treatment targets

The low proportion of reaching treatment targets in our study can be explained by several factors such as 'clinical inertia' (i.e. the failure of clinicians to initiate or intensify therapy when therapeutic targets are not reached)[36] dose prescriptions, not up-titrated doses, poor patient adherence, and barriers within the healthcare system to follow up high-risk individuals.[37] Another study found that high-risk individuals without previous CVD had lower adherence to medication and more uncontrolled risk factors than those with established CHD.[35] Therefore, clinically oriented counselling is suggested as a key component. Counselling should not only focus on biomedical risk factors, but also address psychosocial and economic factors as underlying causes of risk.[35]

Strengths and limitations

A strength of this study is the use of data from a population-based longitudinal study allowing follow-up of high-risk individuals from the general population, as previous studies were based on cross-sectional analyses of patients from clinical settings.[2,5,6] Another strength is the use of validated measurements by trained personnel using standardized protocols, and self-reported medication use which has shown high validity compared with dispensing data.[38] A study limitation is survivor bias, a form of selection bias,[39] as we included high-risk participants in Tromsø6 who met for second screening in Tromsø7. This means that those who died, experienced MI/stroke during follow-up or did not re-attend due to other causes were lost to-follow-up. In addition, all participants received standardized letters with information about selected measurements. Additional feedback was given to participants (<80 years) above thresholds with a recommendation to see their general practitioner. The thresholds were SBP $145.8 + 0.68 \times$ age or ≥170 mmHg. DBP $94.2 + 0.32 \times$ age or ≥100 mmHg. Total cholesterol (mmol/L) in women ≥6.78–8, in men ≥6.26–8.00, and all ≥8.00. Thus, attendance in the Tromsø study could influence attitudes and behaviours. Survivor bias and attendance can lead to overly optimistic interpretation and overestimation of change in risk factors and treatment target achievement. Another limitation is the application of NORRISK 2 and 2017 guidelines in a time-period when this tool and guidelines did not exist, which can introduce bias in the study sample.

Conclusions

We found favourable changes in most CVD risk factors. However, the majority of high-risk individuals did not achieve treatment targets for lipids and BP, <10% achieved all primary prevention targets combined. We also showed the impact of medication use, the strongest characteristic associated with achieving targets. In line with previous studies, our study has demonstrated a great potential for improvement in the primary prevention of CVD.

Authors contributions

A.N.H., I.A., and L.A.H. contributed to the conception and design of the work. A.E.E., M.-L.L., I.N., and T.W. contributed to data acquisition. A.N.H. and T.W. contributed to the data analysis, and all authors contributed to the interpretation of the work. A.N.H. drafted the manuscript. All critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work ensuring integrity and accuracy.

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Data availability

All data are incorporated into the article and its Supplementary material online.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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