SUPPLEMENTAL MATERIAL

Risk stratification in patients with ischemic stroke and residual cardiovascular risk with current secondary prevention

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Supplementary Methods.

Definitions of variables in Table 1

Hypertension was defined as self-reported hypertension or use of antihypertensive drugs at admission (Anatomical Therapeutic Chemical Classification System codes (ATC): C03A, C07, C08, C09A/B, C09C/D, C02A, C02C and C02D). Hypercholesterolemia was defined by use of lipid lowering drugs at admission (ATC -code: C10). Previous stroke (before the index event) or transient ischemic attack (TIA) was defined as previous ischemic stroke, TIA, hemorrhagic stroke or stroke of undetermined subtype as reported by doctor (based on review of medical records) / patient. GFR (Glomerular filtration rate) was based on the CKD-EPI equation (based on gender, age and the serum creatinine concentration measured at first day during admission) [1]. Blood tests were taken the first day after admission. Stroke subtype was defined according to the TOAST Trial of ORG 10172 in Acute Stroke Treatment classification [2]. Stroke severity was assessed by National Institutes of Health Stroke Scale (NIHSS). Prestroke cognitive impairment was defined as score ≥ 3 on Global Deterioration Scale assessed by study nurses' interviews of caregivers during hospital stay [1]. Frailty was measured using a modified version of the five-item Fried criteria [1], based on reduced grip strength, slow gait speed, self-reported fatigue, low physical activity and unintentional weight loss, where 3-5 criteria present corresponds to frail. Definitions of variables also included in the SMART-REACH model are described in Table S1.

Registry data

The Norwegian Stroke Registry is a medical quality register where all Norwegian hospitals have been obligated to enter medical data on all residents > 18 years of age admitted to hospital with acute stroke (ICD-10 codes I61, I61 and I64). The Norwegian Stroke Registry had a coverage (completeness) of 87 % in 2018 [3, 4], we therefore also linked Nor-COAST data to the Norwegian Cardiovascular Disease Registry which is more complete [5]. The Norwegian Cardiovascular Disease Registry is an administrative health register based on data from the Norwegian Patient Register, containing information on all admissions to hospital (main and second diagnosis), both private and public, included in the public reimbursement policy in Norway since 2008. For stroke endpoints we restricted analyses to main diagnoses of stroke which give more correct registrations [5]. For myocardial infarction endpoints we used both main and second diagnoses for higher completeness [6]. The Norwegian Causes of Death Registry provided follow-up information on cardiovascular disease as the primary cause of death. All registries are regulated according to the Act relating to Personal Health Data Registries. The quality of information in the registries have previously been described [5, 6].

The use of the SMART-REACH Fine and Gray competing risk model in Nor-COAST

The SMART-REACH risk model is a competing-risk adjusted Fine and Gray model, which can be used for estimation of both 10-year and lifetime risk of major cardiovascular events and non-cardiovascular mortality in patients with clinically manifest vascular disease. The underlying model formulas and methodology were published in the original SMART-REACH publication [7]. With age as underlying timescale, lifetables calculating risks for every 1-year interval are made beginning at the starting age of each individual [7, 8] and repeated up to the maximum age of 90 years. The model was derived using adapted Fine and Gray models to allow for left truncation and right censoring [9].

For better judgement of the calibration, less influenced by arbitrary grouping in comparison to a traditional calibration plot, we showed a flexible calibration curve based on local polynomial regression fitting (*loess*, function R) [10-12]. First, the cohort was divided in 100 quantiles of predicted risk. Then, a local regression was used to smoothly explain the observed cumulative incidence per group by the mean predicted risk per group. The smooth calibration plot and confidence bounds were subsequently predicted from this model over the whole range of relevant predicted risks (cohort predicted risk quantile 0.025 up to 0.975). A curve close to the diagonal indicates that predicted risks correspond well with the observed proportion of events [10].

Recalibration of the model was considered based on the calibration plot and performed using "calibration-in-the-large" by subtracting the expected-observed ratio from the linear predictor for both the CVD hazard function as for the non-CVD mortality function [10, 13]. The expected-observed ratio was calculated by dividing the expected incidence (mean of all predicted 2-year risks) by the observed incidence (cumulative incidence in the study population at 2 years, corrected for competing risks).

Table S1. Definitions of variables included in the SMART-REACH model [7] and sources	
Variable	**Source when used in present study**
Age (years)	As recorded in medical journals
Sex (male/female)	As recorded in medical journals
Current smoking (yes/no)	Patient response to smoking status at 3 months
Diabetes mellitus (yes/no)	Self-reported diabetes or HbA1c ≥ 48 mmol/mol at admission or prescribed antidiabetic drugs at admission or discharge
Congestive heart failure (yes/no)	History of heart failure as reported by doctor (based on review of medical records) / patient
Atrial fibrillation (yes/no)	Self-reported or documented on electrocardiogram or telemetry during admission
Systolic blood pressure (mmHg)	Measured thrice by the same physician at 3 months with one-minute intervals and the average of the second and third measurements was used in the analysis
Creatinine (µmol/L)	Serum concentration at 3 months
Total cholesterol (mmol/L)	Non-fasting serum concentrations from venous blood measured in fresh samples at 3 months
LDL cholesterol (mmol/L)	Non-fasting serum concentrations from venous blood measured in fresh samples at 3 months
History of cerebrovascular disease (yes/no)	All patients were registered with cerebrovascular disease, since stroke was an inclusion criterion in the Nor-COAST study.
History of coronary heart disease (yes/no)	Previous angina pectoris, myocardial infarction or coronary revascularization (coronary bypass surgery or percutaneous coronary intervention) as reported by doctor (based on review of medical records) / patient
History of peripheral artery disease (yes/no)	Symptomatic or documented obstruction of distal arteries of the leg or surgery of the leg or documented surgery of aorta as reported by doctor (based on review of medical records) / patient
Use of antithrombotic drugs (yes/no)	Use of aspirin or equivalent drug belonging to the Anatomical Therapeutic Chemical (ATC) Classification System group B01A at 3 months. As reported by the patient or doctor, if information regarding medications in use were missing, we contacted general practitioners, home care services or used the electronic summary care record for safer healthcare in Norway.

Abbreviations: HbA1c; Hemoglobin A1c. Nor-COAST; Norwegian Cognitive Impairment after Stroke.

Table S2. Guideline recommended targets and effect measures from meta-analyses used when calculating treatment benefits from optimization of risk factors			
Risk factor target	**Guideline defined treatment and target**	**Effect measures and literature references**	**Comments**
Lipid targets	LDL-C ≤ 1.8 mmol/L [14]	A hazard ratio (HR) of 0.78 was assumed per 1.0 mmol/L reduction in LDL-C [15]. Patients who had already achieved the target were modelled with a HR of 1.00, regardless whether this was achieved by lifestyle or medication. LDL-C reduction in mmol/L was defined as the 3-month LDL-C level minus 1.8 mmol/L. We assumed no further risk reduction from lowering LDL-C below 1.8 mmol/L.	We used the effect measure from a meta-analysis with patients from both primary and secondary preventive settings, where subgroup analyses have shown that the relative risk reduction is more or less the same across several groups of patients suggesting broadly generalizable benefits. We therefore assume these effects also are valid in subgroups of stroke patients.
Blood pressure targets	Systolic blood pressure ≤ 140 mmHg [14]	A 10 mmHg reduction in systolic BP was assumed to correspond to a cardiovascular specific HR of 0.80 [16]. Patients who had already achieved this target were modelled with a HR of 1.00, regardless whether this was achieved by lifestyle or medication. BP reduction in mmHg was defined as the 3-month systolic BP minus the target systolic BP of 140. We assumed no further risk reduction from lowering BP below 140 mmHg.	We used the effect measure from a meta-analysis with patients from both primary and secondary preventive settings (including stroke patients), where subgroup analyses have shown that the relative risk reduction is more or less the same across several groups of patients. A HR of 0.80 for the combined endpoint of major cardiovascular events was used. However, the relative effect for stroke separately seems to be larger (HR 0.73) [16].
Antithrombotic treatment	Aspirin or other equivalent antiplatelet drugs. Anticoagulation if non-valvular atrial fibrillation [14]	Estimated risk is based on the assumption that standard care is provided. Such standard care (HR	The HR for long-term aspirin (0.81) monotherapy in secondary preventive setting from the meta-

		1.00) included aspirin or equivalent type of antithrombotic therapy, including vitamin K antagonists or DOACs, regardless of number of antithrombotic drugs in use. We assumed that no use of antithrombotic therapy was associated with the inverse effect of starting (at least) aspirin (i.e., HR 1/0.81 = 1.23) [17].	analysis [17] was used. The estimate is based on 16 secondary preventive trials from whom 10 was in stroke or patients with transient ischemic attack. The benefit of different antithrombotic regimens was not assessed since the proportion not using antithrombotic drugs was low.
Smoking target	Smoking cessation [14]	The effect of smoking cessation was estimated in current smokers and was assumed to reduce the risk of both CVD events and non-CVD mortality. The HR for CVD events for current smokers when converting to ex-smoker was assumed to be 0.60 [18]. The HR for non-CVD mortality for current smokers who are now ex-smokers was assumed to be 0.73 [19].	In absence of evidence from RCTs, the effect of smoking cessation was estimated from observational studies, using the hazard ratio between current and former smoking.

Abbreviations: LDL, Low-density lipoprotein; BP, blood pressure; DOACs, Direct Oral Anticoagulants; RCTs, Randomized Controlled Trials; TIA, Transient ischemic attack

Table S3. Overview of missing values at index stay and 3-month visit (n=465)		
	n (%) missing at index stay	**n (%) missing at 3-month visit**
Age	0	0
Sex	0	0
Current smoking	1 (0.2%)	68 (15%)
Diabetes mellitus	0	0
Systolic blood pressure	34 (7%)	72 (15%)
Total cholesterol	8 (2%)	113 (24%)
HDL cholesterol	12 (3%)	117 (25%)
LDL cholesterol	15 (3%)	115 (25%)
Creatinine	2 (0.4%)	119 (26%)
Coronary artery disease	0	0
Peripheral artery disease (incl. AAA)	0	0
Heart failure	0	0
Atrial fibrillation	0	0
Information about medications	5 (1%)	32 (7%)

Missing values for current smoking, systolic blood pressure, cholesterol, creatinine and information about medications were imputed using single imputation by predictive mean matching for the purpose of CVD risk prediction and assessment of changes in risk factor levels from index stay to 3-months follow-up. With this method, the imputed value is taken randomly from a set of observed values whose predicted values are closest to the predicted value from a specified regression model. For the baseline characteristics age, sex, history of diabetes, coronary artery disease, peripheral artery disease, heart failure and atrial fibrillation, we assumed that registrations at index stay also were valid at the 3-month visit. Abbreviations: eGFR; Estimated glomerular filtration rate. AAA; Abdominal aortic aneurism, HDL; High-density lipoprotein, LDL; Low-density lipoprotein.

Table S4. Cardiovascular medications at discharge from index stay and at 3 months of follow-up for patients with available detailed data on medications in use

	Discharge (n = 460)	3-month visit (n = 433)
Antithrombotic drugs		
No[a]	9 (2%)	8 (2%)
Single antiplatelet therapy	111 (24%)	130 (30%)
Dual antiplatelet therapy	189 (41%)	150 (35%)
Anticoagulation monotherapy	107 (23%)	114 (25%)
Anticoagulation in combination with antiplatelet agent(s)	44 (10%)	31 (7%)
Number of antihypertensive drugs		
0[a]	144 (31%)	118 (27%)
1	167 (36%)	160 (37%)
2	105 (23%)	101 (23%)
3	33 (7%)	43 (10%)
>3	11 (2%)	11 (3%)
Lipid-lowering drugs		
No[a]	45 (10%)	42 (10%)
Any statin monotherapy	407 (88%)	381 (88%)
Low-moderate intensity statin[b]	142 (30%)	133 (31%)
High intensity statin[b]	265 (58%)	248 (57%)
Ezetimibe monotherapy	3 (1%)	6 (1%)
Statin + ezetimibe	5 (1%)	4 (1%)

[a]Of patients with available follow-up information about medications in use at both discharge and 3 months (n=429), 5 out of 8 patients not using (any) antithrombotic drugs (ATC code: B01A) at discharge started antithrombotic treatment between 0 and 3 months, while 4 out of 421 prescribed antithrombotic drugs at discharge discontinued between 0 and 3 months. For antihypertensive drugs (ATC codes: C03A, C07, C08, C09A/B, C09C/D, C02A, C02C and C02D), corresponding numbers were 28 / 133 and 12 / 296. For lipid-lowering drugs (ATC code: C10), corresponding numbers were 12 / 40 and 11 / 389.
[b]High-intensity statin was defined as atorvastatin ≥40 mg/d or other equivalent drug as described previously [1]. Low-moderate intensity statin was defined as <40 mg atorvastatin or other equivalent drug. Abbreviations: ATC, Anatomical Therapeutic Chemical classification system

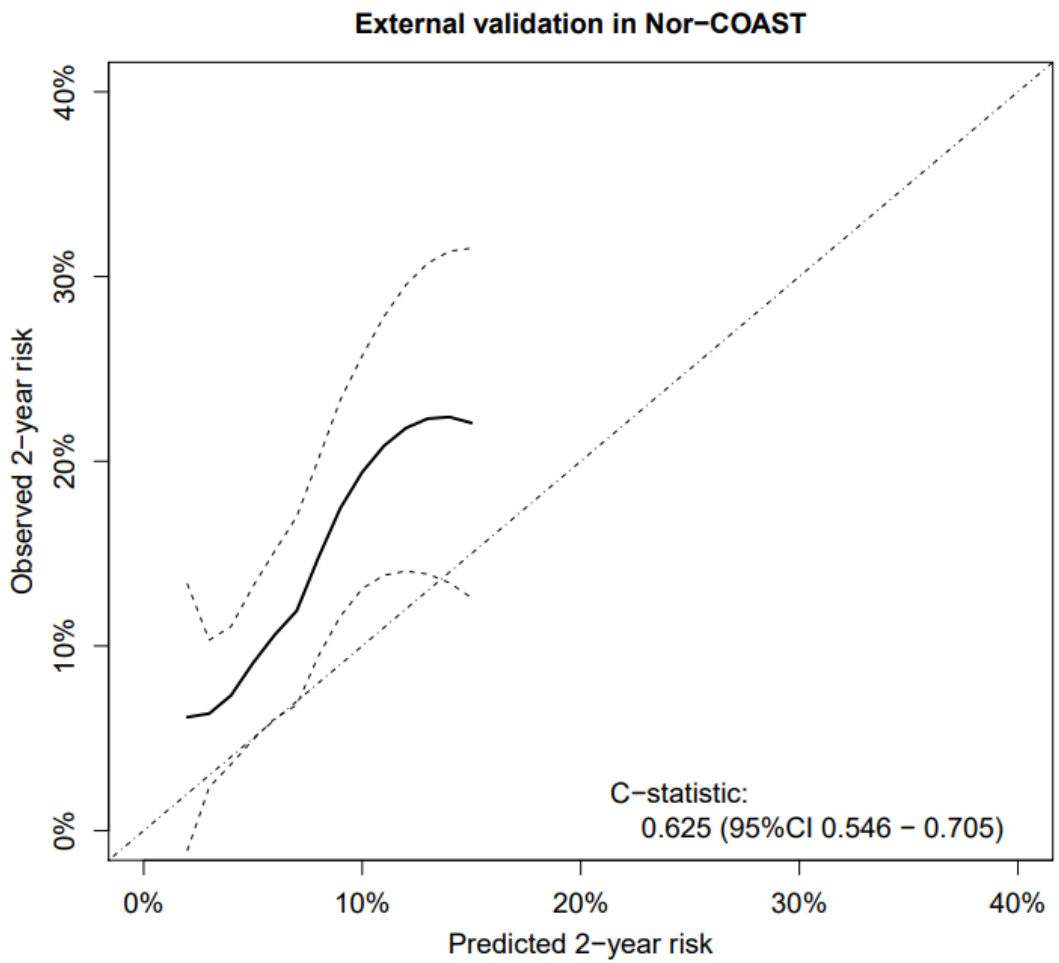


Figure S1. Flexible calibration curve showing the agreement between estimated risk of stroke, myocardial infarction or vascular death by the SMART-REACH model and observed 2-year risk before recalibration

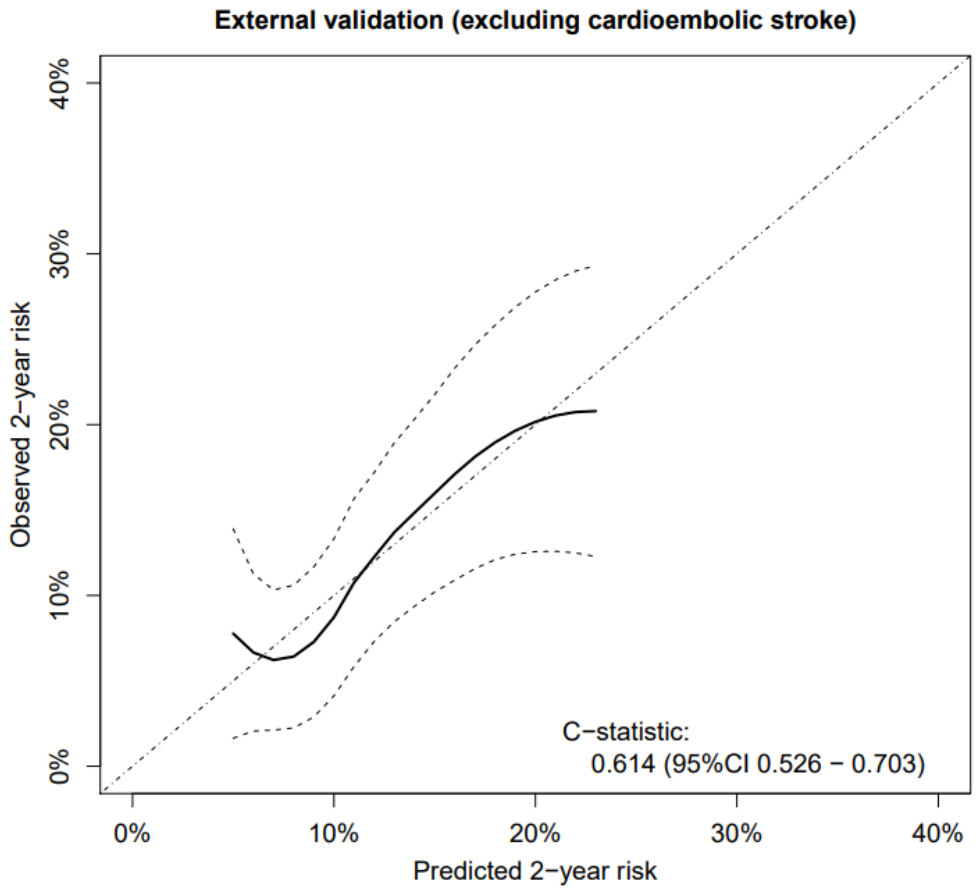


Figure S2. Flexible calibration curve showing the agreement between estimated risk of stroke, myocardial infarction or vascular death by the SMART-REACH model versus observed 2-year risk when excluding patients with cardioembolic stroke etiology according to the TOAST-classification

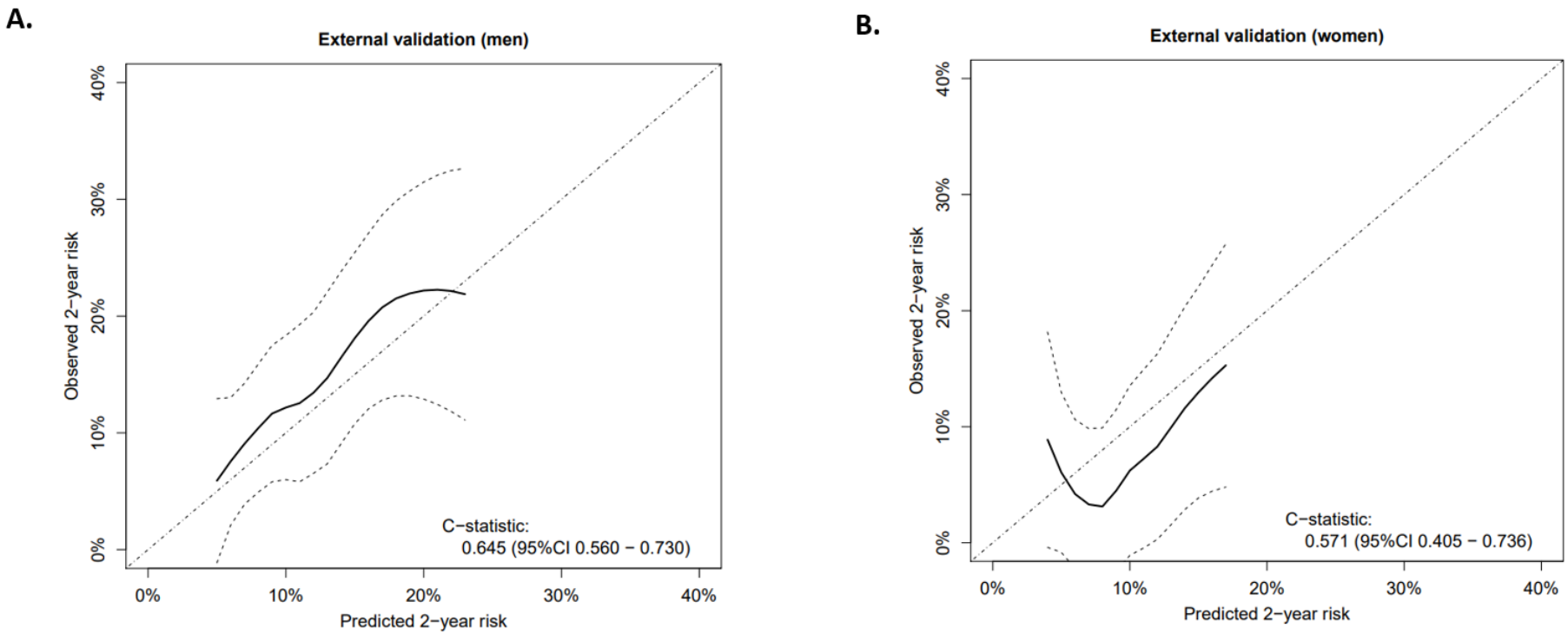
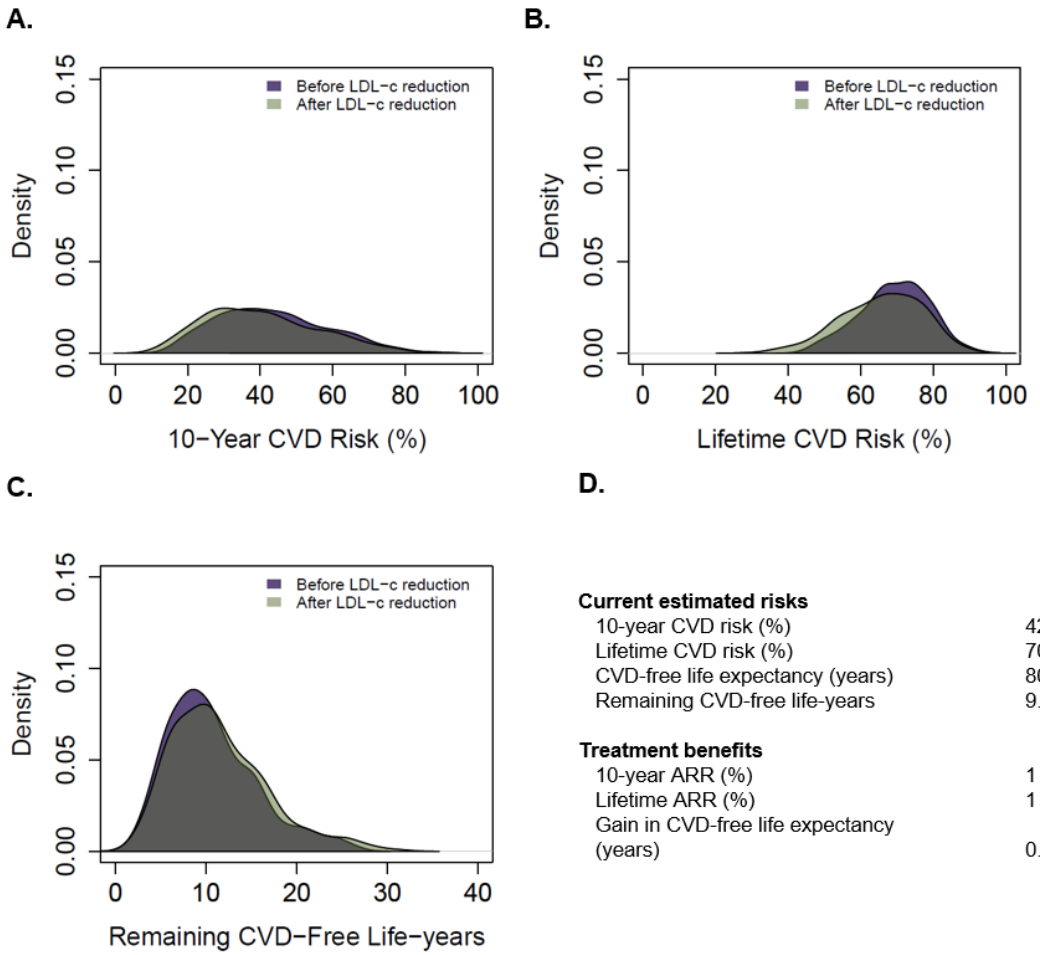


Figure S3. Sex-specific flexible calibration curves showing the agreement between estimated risk of stroke, myocardial infarction or vascular death by the SMART-REACH model versus observed 2-year risk for a) men (n=278) and b) women (n=178).

Notes: Number of CVD events for men and women were n=34 and n=18, respectively. Number of non-CVD related deaths were n=10 and n=5 for men and women respectively.



D.

Current estimated risks	
10-year CVD risk (%)	42 (32 to 54)
Lifetime CVD risk (%)	70 (63 to 76)
CVD-free life expectancy (years)	80.4 (76.4 to 83.5)
Remaining CVD-free life-years	9.9 (7.2 to 13.5)
Treatment benefits	
10-year ARR (%)	1 (0 to 4)
Lifetime ARR (%)	1 (0 to 5)
Gain in CVD-free life expectancy (years)	0.2 (0 to 1)

Figure S4a. Current cardiovascular risk and potential benefit from optimization of LDL-C levels (n = 465)
Distributions of **A.** Ten-year cardiovascular disease risk, **B**. Lifetime CVD risk, **C**. Remaining CVD-free life-years, **D**. Current estimated risks and treatment benefits (median (interquartile range)) from optimization of LDL-C level to ≤1.8 mmol/L in all patients. Abbreviations: LDL-C; Low density lipoprotein cholesterol, CVD; Cardiovascular disease, ARR: Absolute risk reduction

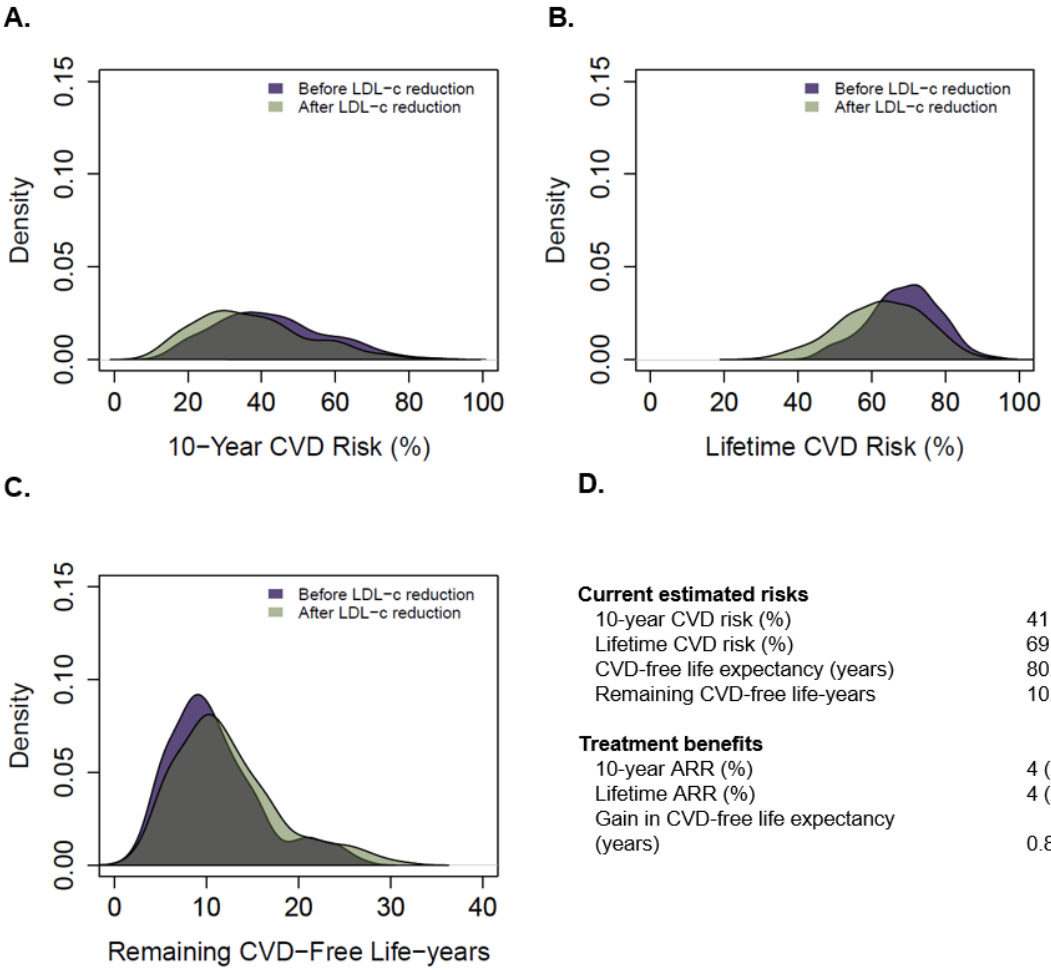
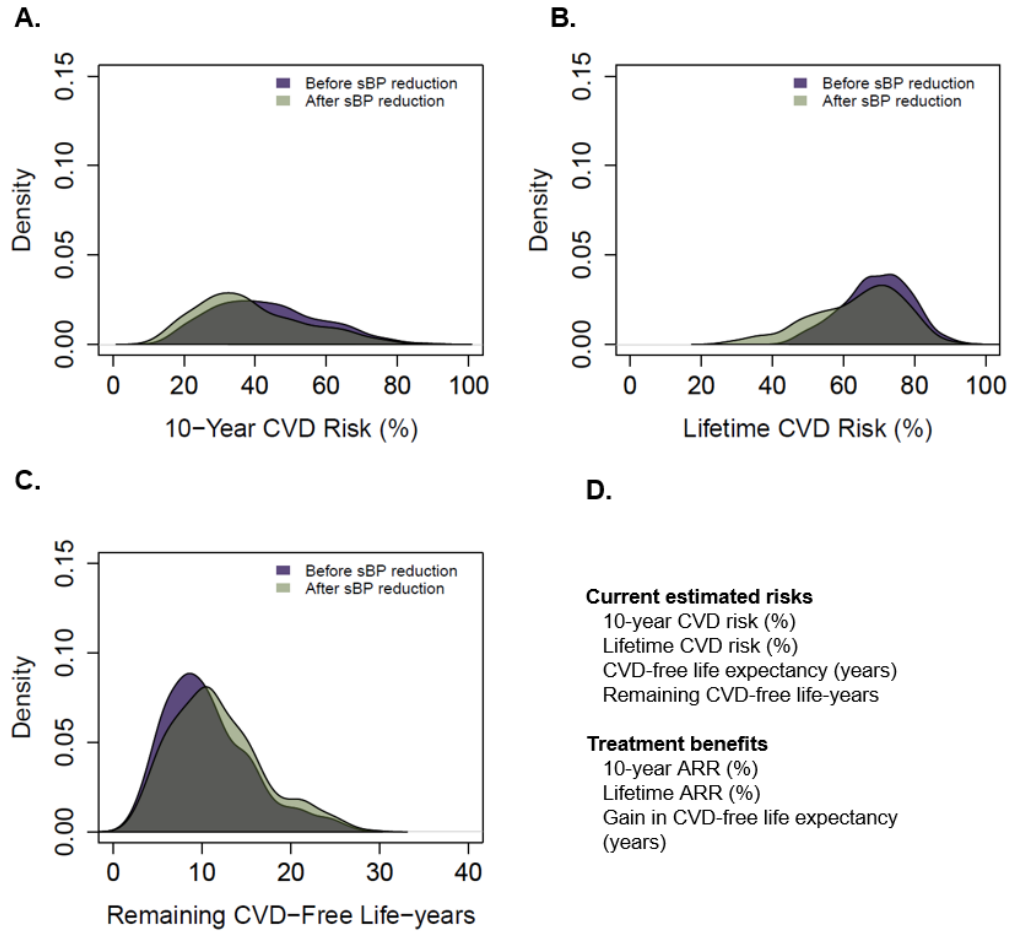


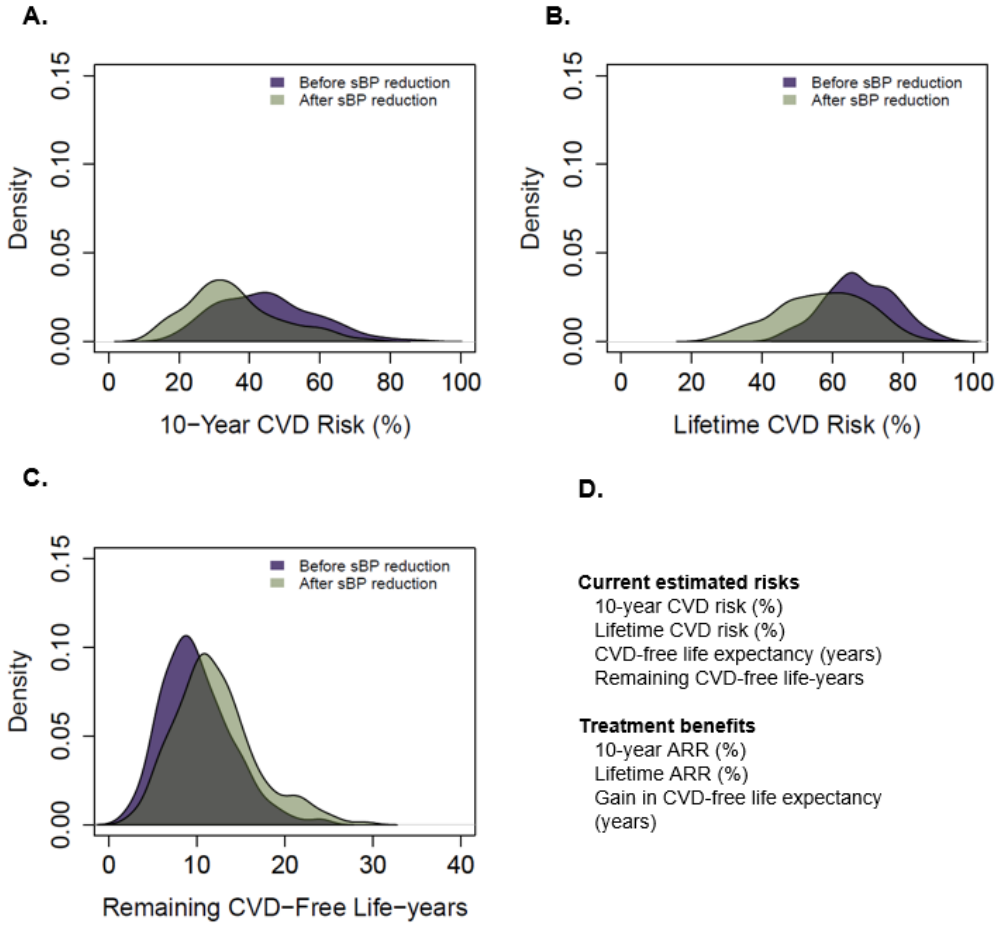
Figure S4b. Current cardiovascular risk and potential benefit from optimization of LDL-C levels in patients with LDL-C > 1.8 mmol/L (n = 265)
Distributions of **A**. Ten-year cardiovascular disease risk, **B**. Lifetime CVD risk, **C.** Remaining CVD-free life-years, **D**. Current estimated risks and treatment benefits (median (interquartile range)) from optimization of LDL-C level to 1.8 mmol/L in patients with LDL-C > 1.8 mmol/L. Abbreviations: LDL-C; Low density lipoprotein cholesterol, CVD; Cardiovascular disease, ARR: Absolute risk reduction



D.

Current estimated risks	
10-year CVD risk (%)	42 (32 to 54)
Lifetime CVD risk (%)	70 (63 to 76)
CVD-free life expectancy (years)	80.4 (76.4 to 83.5)
Remaining CVD-free life-years	9.9 (7.2 to 13.5)
Treatment benefits	
10-year ARR (%)	0 (0 to 7)
Lifetime ARR (%)	0 (0 to 9)
Gain in CVD-free life expectancy (years)	0 (0 to 1.5)

Figure S5a. Current cardiovascular risk and potential benefit from optimization of systolic blood pressure levels (n = 465)
Distributions of **A**. Ten-year cardiovascular disease risk**, B**. Lifetime CVD risk, **C**. Remaining CVD-free life-years, **D.** Current estimated risks and treatment benefits (median (interquartile range)) from optimization of sBP level to ≤140 mmHg in all patients. Abbreviations: sBP; Systolic blood pressure, CVD; Cardiovascular disease, ARR: Absolute risk reduction

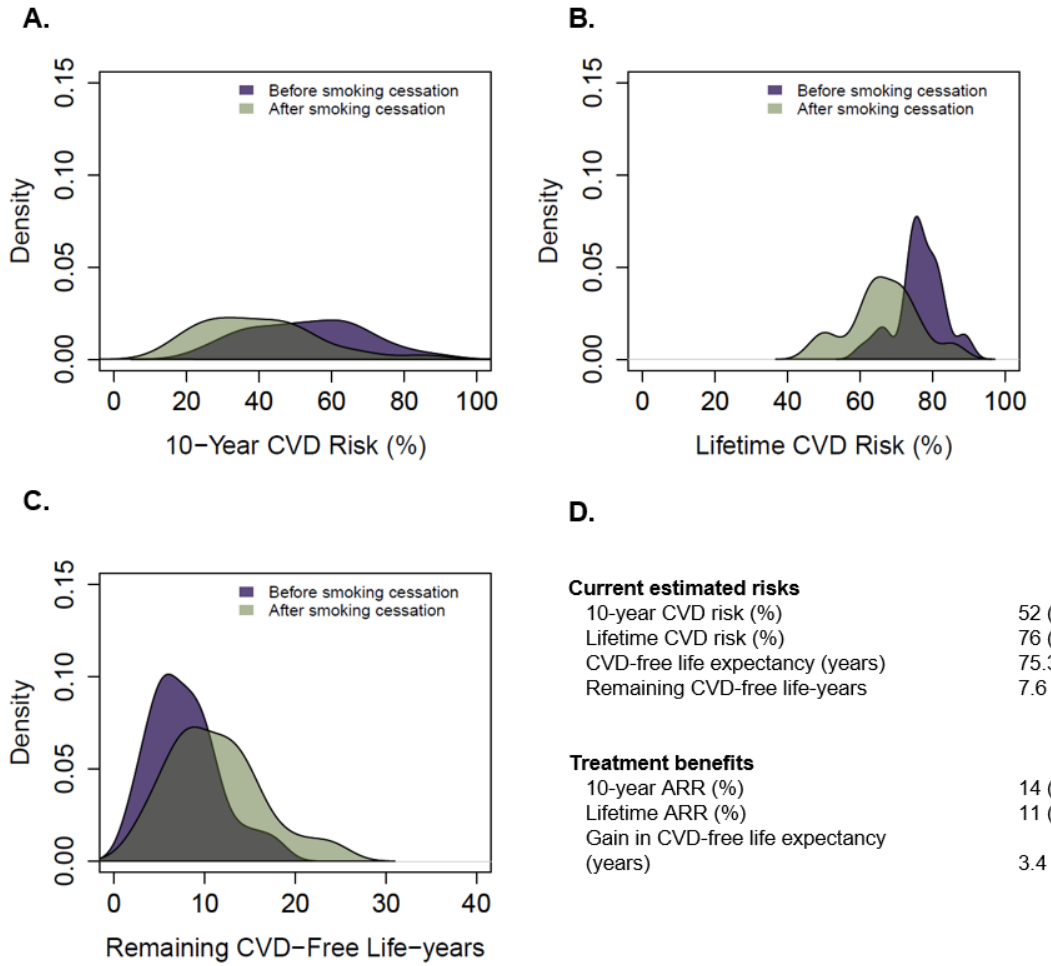


D.

Current estimated risks	
10-year CVD risk (%)	44 (34 to 54)
Lifetime CVD risk (%)	67 (61 to 75)
CVD-free life expectancy (years)	81.8 (78.9 to 84.3)
Remaining CVD-free life-years	9.5 (7.2 to 12.3)
Treatment benefits	
10-year ARR (%)	8 (3 to 14)
Lifetime ARR (%)	9 (3 to 16)
Gain in CVD-free life expectancy (years)	1.6 (0.6 to 3.1)

Figure S5b. Current cardiovascular risk and potential benefit from optimization of systolic blood pressure levels (n = 226) in patients with levels above 140 mmHg.

Distributions of **A**. Ten-year cardiovascular disease risk**, B**. Lifetime CVD risk, **C**. Remaining CVD-free life-years, **D.** Current estimated risks and treatment benefits (median (interquartile range)) from optimization of sBP level to 140 mmHg in patients with sBP > 140 mmHg (n = 226). Abbreviations: sBP; Systolic blood pressure, CVD; Cardiovascular disease, ARR: Absolute risk reduction



D.

Current estimated risks	
10-year CVD risk (%)	52 (39 to 66)
Lifetime CVD risk (%)	76 (74 to 81)
CVD-free life expectancy (years)	75.3 (72.2 to 80.1)
Remaining CVD-free life-years	7.6 (4.8 to 9.9)
Treatment benefits	
10-year ARR (%)	14 (12 to 16)
Lifetime ARR (%)	11 (8 to 13)
Gain in CVD-free life expectancy (years)	3.4 (2.4 to 4.3)

Figure S6: Current cardiovascular risk and potential benefit from smoking cessation in smokers (n = 55)
Distributions of **A**. Ten-year cardiovascular disease risk**, B**. Lifetime CVD risk, **C**. Remaining CVD-free life-years, **D.** Current estimated risks and treatment benefits (median (interquartile range)) from smoking cessation in patients smoking at 3 months. Abbreviations: ARR: Absolute risk reduction, CVD; Cardiovascular disease

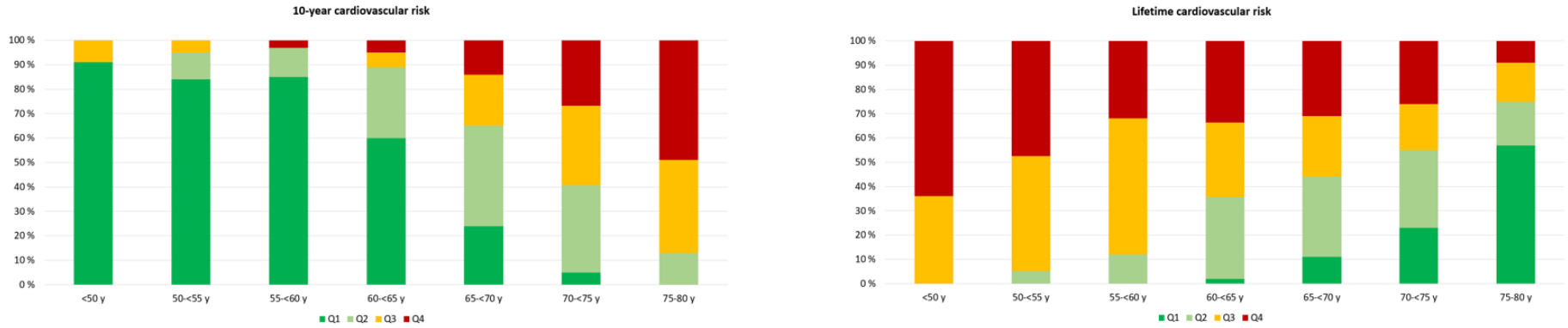


Figure S7. Age-specific subgroups of estimated 10-year and lifetime risk of a recurrent vascular event by the SMART REACH model in patients with ischemic stroke in the Nor-COAST study. Data are shown as quartiles of risk where Q1 corresponds to lowest risk quartile and Q4 the highest risk quartile.

Table S5. Patient characteristics stratified by quartiles (Q1 – Q4) of estimated 10-year risk of recurrent vascular events and mortality

	10-year CVD risk			
	Q1 (n = 117)	**Q2 (n = 116)**	**Q3 (n = 116)**	**Q4 (n = 116)**
Median (IQR) estimated 10-year risk, %	26 (21 to 29)	37 (34 to 39)	48 (44 to 50)	66 (58 to 68)
Age, y	59.5 (6.2)	68.8 (5.6)	73.0 (5.6)	74.9 (4.5)
Female sex	46 (39%)	49 (42%)	45 (39%)	38 (33%)
Atrial fibrillation	7 (6%)	14 (12%)	30 (26%)	50 (43%)
Diabetes mellitus	2 (2%)	13 (11%)	19 (16%)	58 (50%)
≥ 2 vascular areas[a] affected	2 (2%)	9 (8%)	20 (17%)	65 (56%)
Current smoker[b]	5 (5%)	11 (10%)	13 (11%)	26 (22%)
Systolic blood pressure (mmHg)[b]	137 (16)	139 (15)	144 (18)	140 (25)
Total cholesterol[b], mmol/L	4.0 (0.8)	4.1 (1.0)	4.1 (1.0)	3.9 (0.8)
LDL cholesterol[b], mmol/L	2.1 (0.8)	2.2 (0.8)	2.1 (0.8)	2.0 (0.7)
eGFR (ml/min/1.73 m²)[b, c]	87 (12)	81 (13)	75 (15)	65 (18)
Frail[d]	3 (3%)	6 (5%)	9 (8%)	16 (14%)
Prestroke dementia[e]	0 (0%)	1 (1%)	3 (3%)	9 (8%)

Values are n / N (%) or mean (standard deviation) if other not specified. [a]Number of vascular areas were one if only stroke, two if combined with either coronary artery disease or peripheral artery disease, and three if all three areas were affected. [b]Measured at 3 months follow-up. [c]CKD-EPI equation. [d]Frailty measured by 5-item Fried frailty criteria. [e]Cognitive impairment defined as score ≥ 3 on Global Deterioration Scale. Abbreviations: CVD, Cardiovascular disease; IQR, Interquartile range; LDL, Low density lipoprotein; eGFR, Estimated Glomerular Filtration Rate.

Table S6. Patient characteristics stratified by quartiles (Q1 – Q4) of estimated lifetime risk of recurrent vascular events and mortality

	Lifetime CVD risk			
	Q1 (n = 117)	**Q2 (n = 116)**	**Q3 (n = 116)**	**Q4 (n = 116)**
Median (IQR) estimated life-time risk, %	58 (54 to 61)	67 (65 to 68)	73 (71 to 74)	80 (78 to 83)
Age, y	75.6 (3.7)	69.9 (5.9)	65.7 (8.6)	64.8 (8.8)
Female sex	67 (57%)	49 (42%)	32 (28%)	30 (26%)
Atrial fibrillation	18 (15%)	28 (24%)	23 (20%)	32 (28%)
Diabetes mellitus	0 (0%)	9 (8%)	29 (25%)	55 (47%)
≥ 2 vascular areas[a] affected	6 (6%)	17 (14%)	26 (23%)	47 (41%)
Current smoker[b]	2 (2%)	6 (5%)	18 (16%)	29 (25%)
Systolic blood pressure (mmHg)[b]	144 (16)	142 (19)	136 (18)	138 (23)
Total cholesterol[b], mmol/L	4.2 (0.8)	4.2 (1.0)	4.0 (0.9)	3.8 (0.9)
LDL cholesterol[b], mmol/L	2.2 (0.8)	2.2 (0.8)	2.1 (0.8)	2.0 (0.7)
eGFR (ml/min/1.73 m²)[b, c]	77 (12)	79 (15)	81 (15)	71 (22)
Frail[d]	11 (9%)	10 (9%)	4 (3%)	9 (8%)
Prestroke dementia[e]	5 (4%)	4 (4%)	0 (0%)	4 (4%)

Values are n / N (%) or mean (standard deviation) if other not specified. [a]Number of vascular areas were one if only stroke, two if combined with either coronary artery disease or peripheral artery disease, and three if all three areas were affected. [b]Measured at 3 months follow-up. [c]CKD-EPI equation. [d]Frailty measured by 5-item Fried frailty criteria. [e]Cognitive impairment defined as score ≥ 3 on Global Deterioration Scale. Abbreviations: CVD, Cardiovascular disease; IQR, Interquartile range; LDL, Low density lipoprotein; eGFR, Estimated Glomerular Filtration Rate.

Table S7. Patient characteristics stratified by quartiles (Q1 – Q4) of estimated 10-year ARR of recurrent vascular events and mortality				
	10-year ARR			
	Q1 (n = 117)	**Q2 (n = 116)**	**Q3 (n = 116)**	**Q4 (n = 116)**
Median (IQR) estimated 10-year ARR, %	0% (0 to 0)	3% (2 to 4)	10% (8 to 12)	21% (16 to 27)
Age, y	67.4 (8.5)	67.5 (8.8)	69.4 (7.5)	71.7 (6.8)
Female sex	42 (36%)	42 (36%)	41 (35%)	53 (46%)
Atrial fibrillation	31 (27%)	22 (19%)	22 (19%)	26 (22%)
Diabetes mellitus	17 (15%)	21 (18%)	23 (20%)	31 (27%)
≥ 2 vascular areas[a] affected	18 (16%)	27 (23%)	20 (17%)	31 (27%)
Current smoker[b]	0 (0%)	1 (1%)	8 (7%)	46 (40%)
Systolic blood pressure (mmHg)[b]	128 (10)	132 (12)	146 (13)	155 (23)
Total cholesterol[b], mmol/L	3.4 (0.6)	3.9 (0.5)	4.3 (0.8)	4.5 (1.2)
LDL cholesterol[b], mmol/L	1.6 (0.3)	2.1 (0.4)	2.3 (0.8)	2.6 (1.0)
eGFR (ml/min/1.73 m²)[b, c]	80 (14)	77 (18)	77 (16)	75 (17)
Frail[d]	6 (5%)	7 (6%)	7 (6%)	14 (12%)
Prestroke dementia[e]	2 (2%)	5 (4%)	2 (2%)	4 (4%)

Values are n / N (%) or mean (standard deviation) if other not specified. [a]Number of vascular areas were one if only stroke, two if combined with either coronary artery disease or peripheral artery disease, and three if all three areas were affected. [b]Measured at 3 months follow-up. [c]CKD-EPI equation. [d]Frailty measured by 5-item Fried frailty criteria. [e]Cognitive impairment defined as score ≥ 3 on Global Deterioration Scale. Abbreviations: IQR, Interquartile range; ARR, Absolute risk reduction; LDL, Low density lipoprotein; eGFR, Estimated Glomerular Filtration Rate.

Table S8. Patient characteristics stratified by quartiles (Q1 – Q4) of lifetime benefit from optimization of risk factors				
	Gain in CVD-free life years			
	Q1 (n = 122)	**Q2 (n = 117)**	**Q3 (n = 113)**	**Q4 (n = 113)**
Median (IQR) lifetime benefit (in terms of CVD-free life years)	0 (0 to 0)	0.6 (0.4 to 1.0)	2.3 (1.8 to 2.8)	5.3 (4.3 to 7.1)
Age, y	68.6 (8.2)	69.2 (7.9)	71.2 (7.1)	66.0 (8.7)
Female sex	41 (34%)	43 (37%)	43 (38%)	51 (45%)
Atrial fibrillation	34 (28%)	23 (20%)	25 (22%)	19 (17%)
Diabetes mellitus	22 (18%)	24 (21%)	25 (22%)	21 (19%)
≥ 2 vascular areas[a] affected	25 (20%)	29 (25%)	22 (19%)	20 (18%)
Current smoker[b]	0 (0%)	2 (2%)	16 (14%)	37 (33%)
Systolic blood pressure (mmHg)[b]	128 (10)	133 (14)	143 (17)	157 (19)
Total cholesterol[b], mmol/L	3.4 (0.6)	3.9 (0.6)	4.2 (0.8)	4.6 (1.1)
LDL cholesterol[b], mmol/L	1.6 (0.3)	2.0 (0.4)	2.3 (0.7)	2.7 (1.0)
eGFR (ml/min/1.73 m²)[b, c]	78 (15)	73 (19)	78 (13)	79 (19)
Frail[d]	8 (7%)	8 (7%)	8 (7%)	10 (9%)
Prestroke dementia[e]	2 (2%)	6 (5%)	4 (4%)	1 (1%)

Values are n / N (%) or mean (standard deviation) if other not specified. [a]Number of vascular areas were one if only stroke, two if combined with either coronary artery disease or peripheral artery disease, and three if all three areas were affected. [b]Measured at 3 months follow-up. [c]CKD-EPI equation. [d]Frailty measured by 5-item Fried frailty criteria. [e]Cognitive impairment defined as score ≥ 3 on Global Deterioration Scale. Abbreviations: CVD, Cardiovascular disease; IQR, Interquartile range; LDL, Low density lipoprotein; eGFR, Estimated Glomerular Filtration Rate.

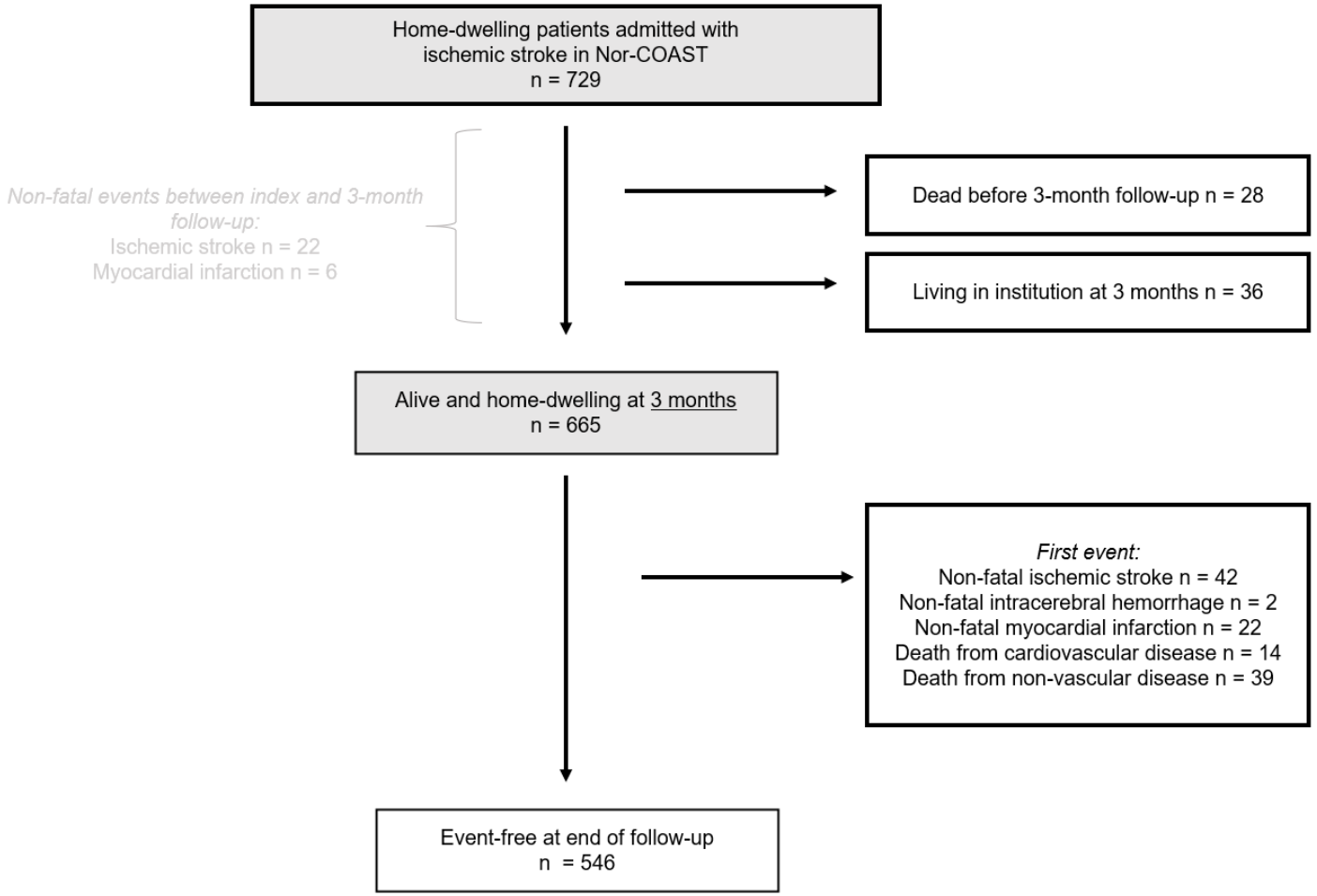


Figure S8. Recurrent stroke, myocardial infarction and death in home-dwelling patients with ischemic stroke in Nor-COAST regardless of age.

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