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ORIGINAL ARTICLE
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Risk-stratified analysis of long-term clinical outcomes and cumulative costs in Finnish patients with recent acute coronary syndrome or coronary revascularization: a 5-year real-world study using electronic health records

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Aims

Risk assessment is essential in the prevention of cardiovascular disease. In patients with recent acute coronary syndrome (ACS) or coronary revascularization, risk prediction tools, like the European Society of Cardiology guideline recommended SMART-REACH risk score, are increasingly used to predict the risk of recurrent cardiovascular events enabling risk-based personalized prevention. However, little is known about the association between risk stratification and the social and healthcare costs at a population level. This study evaluated the associations between baseline SMART-REACH risk scores, long-term recurrent clinical events, cumulative costs, and post-index event LDL-C goal attainment in patients with recent ACS and/or revascularization.

Methods and results

This retrospective study used electronic health records and was conducted in the North Karelia region of Finland. The study cohort included all patients aged 45–85 admitted to a hospital for ACS or who underwent percutaneous coronary intervention or coronary artery bypass surgery between 1 January 2017 and 31 December 2021. Patients were divided into quintiles based on their baseline SMART-REACH risk scores to examine the associations between predicted 5-year scores and selected clinical and economic outcomes. In addition, simple age-based stratification was conducted as a sensitivity analysis. The observed 5-year cumulative incidence of recurrent events ranged from 20% in the lowest to 41% in the highest risk quintile, whereas the corresponding predicted risks ranged from 13% to 51%, and cumulative 5-year mean total costs per patient ranged from 15 827 to 46 182€, respectively. Both monitoring and attainment of low LDL-C values were suboptimal.

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Conclusion The use of the SMART-REACH quintiles as a population-level risk stratification tool successfully stratified patients into subgroups with different cumulative numbers of recurrent events and cumulative total costs. However, more research is needed to define clinically and economically optimal threshold values for a population-level stratification.

Keywords Acute coronary syndrome • Risk stratification • Clinical secondary outcomes • Costs

Introduction

Despite advancements in the diagnosis, prevention, and treatment of atherosclerotic cardiovascular disease (ASCVD), cardiovascular diseases (CVDs) remain the leading cause of death in Europe. In particular, coronary artery disease (CAD) accounts for 20% of all deaths,[1,2] and in Finland, it is responsible for approximately every sixth death.[3] Coronary artery disease can lead to acute coronary syndrome (ACS), a life-threatening condition that includes ST elevation myocardial infarction, non-ST elevation myocardial infarction, or unstable angina pectoris.[4] In addition, ACS patients are at risk for recurrent ACS events. Approximately one-third of patients with a recent ACS will have a recurrent ACS event within 3 years after their first ACS event,[5] indicating the need to improve secondary prevention.

The present guidelines for treating ASCVD for secondary prevention[6] define that patients with clinical manifestations of ASCVD fall on average within a general 'very high risk' category. However, clinical risk prediction tools could provide more detailed and reliable way to estimate a patient's individual risk for a recurrent vascular event. For instance, the SMART-REACH risk score, which is advised by the European Society of Cardiology (ESC), can be used to predict the risk of recurrent cardiovascular events.[7] Additionally, it can provide personalized estimates of potential improvements in life expectancy without recurrent cardiovascular incidents for individual patients with CVD.

On a population-wide scale, the implementation of prediction tools like the SMART-REACH has capacity to better strategic planning and resource distribution decisions. For instance, understanding the association between the risk of recurring CVD events and their economic impact at the population level could improve the allocation of resources towards developing risk-based preventive measures. This, in turn, could potentially decrease the number of expensive hospitalizations and emergency department visits. However, currently, there is relatively limited research on how risk stratifications are associated with the use of social and healthcare services and related costs, with some exceptions.[8–12] Therefore, in the present study, we aimed to study the associations between baseline SMART-REACH risk score categories and observed long-term clinical outcomes and cumulative social and healthcare costs in a real-world data set with Finnish patients with a recent ACS and/or coronary revascularization. Furthermore, we assessed the LDL-C goal attainment, as recommended by the ESC guidelines, after the index events across the defined baseline risk categories. This was done to understand how the underlying baseline risk of recurrent cardiovascular events is associated with the observed intensity of post-index event LDL-C treatment in actual clinical practice.

Methods

Study setting

In Finland, healthcare services are mainly produced as public services and are organized by wellbeing services counties. The present study was conducted in the region of North Karelia, Finland, which is one of the 21 wellbeing services counties in Finland. The total population of North Karelia Wellbeing Services County was approximately 164 700 between 2017 and 2021.[13] The North Karelia Wellbeing Services County has provided social and healthcare services for 13 municipalities from the beginning of 2017. All municipalities in the North Karelia region had implemented the same electronic health record (EHR) system in 2010–11. The present study was a retrospective, EHR-based real-world data study. The EHR data include both public primary and specialized healthcare, as well as social care services. Annually, approximately 600–700 new ACS and/or coronary revascularization cases are recorded in the North Karelia Wellbeing Services County.[14]

Study design and data extraction

All patients aged 45–85, who were hospitalized due to ACS (defined as ICD-10 codes I20–I22) or underwent a percutaneous coronary intervention (PCI) or CABG between 1 January 2017 and 31 December 2021 (i.e. an index event), were included in the study cohort. It was defined that the follow-up period started either 7 days after the index event or discharge from hospital, whichever occurred later. Patients were excluded if they died between the index event and the start of the follow-up period. The data for service use, laboratory measurements, and mortality were collected from 1 January 2017 to 30 June 2022, allowing at least a 6-month follow-up related to these outcomes. Comorbidities and other long-term diagnoses were extracted from 1 January 2011 to the index event. The study design is presented schematically in *Figure 1*.

Estimation of baseline SMART-REACH risk scores

The SMART-REACH risk score[15] was used to predict the risk of recurrent events after the index event. In the present study, predictions were made for 5 years (due to the timeframe of the study), and the following variables were extracted from the EHRs to estimate 5-year baseline risk scores for the study participants: age at baseline, sex, current smoking, diabetes, systolic blood pressure (mmHg), total cholesterol (mmol/L), creatinine (μmol/L), number of locations of CVD (i.e. CAD, cerebrovascular disease, and peripheral artery disease), history of atrial fibrillation (yes/no), and history of congestive heart failure (yes/no).

Risk stratification based on baseline SMART-REACH risk scores

To study associations between the baseline SMART-REACH risk scores, long-term clinical outcomes and cumulative 5-year social and healthcare costs, as well as post-index event LDL-C goal attainment patients were divided into quintiles based on their baseline SMART-REACH risk scores. SMART-REACH risk scores were calculated without assuming aspirin use, and residence was set to be western Europe. The assumption of no aspirin was done by local clinical experts. The application of this assumption modifies risk scores as adding log(1/0.81) to the linear predictor of the cardiovascular model.[15]

Observed recurrent events and deaths

To study the validity and accuracy of the baseline SMART-REACH risk scores in the Finnish real-world study cohort, the incidence of observed recurrent cardiac events was studied without and with cerebrovascular events (i.e. ischaemic and haemorrhagic strokes) and with/without coronary revascularizations. Therefore, recurrent events were first defined as any hospital admissions due to ACS or any PCI or CABG operations occurring at least 7 days after the index event and not during the index hospitalization or deaths whose causes were indicated by ICD-10 codes I20–I25 [i.e.

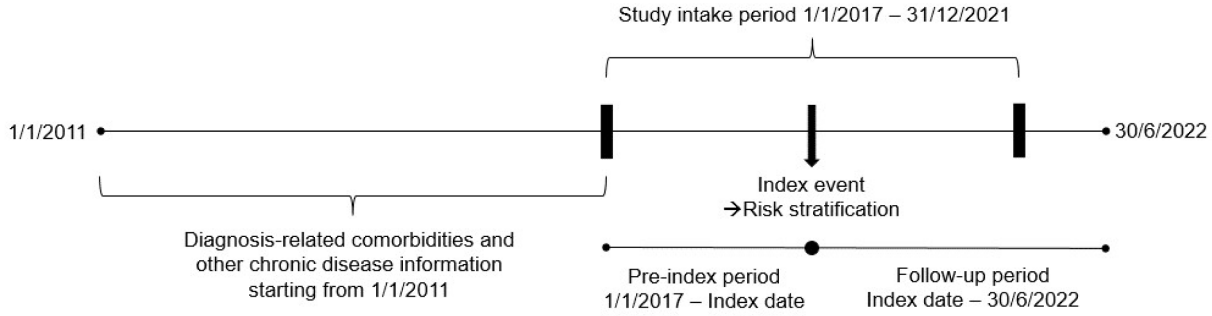

Figure 1 Design of the study.

ischaemic heart diseases (IHDs)]. The time interval between an index event and recurrent event was required to distinguish initial acute care from the follow-up periods. Second, recurrent events were defined to cover also ischaemic and haemorrhagic strokes and exclude coronary revascularizations following the descriptions of the CVD events as defined in the original SMART-REACH study.[16] Non-IHD deaths considered as competing events were defined as death due to other causes or with cause of death missing.

Economic outcomes

For cost analysis, service use related to hospitalizations, days in a primary care health centre ward, secondary and primary outpatient visits, and social service visits (i.e. home care and home nursing care) was collected from EHRs for all patients in the study cohort. Unit costs for these services were collected from the unit cost tariff lists (2022) of North Karelia Wellbeing Services County for social and healthcare services. Estimated social and healthcare costs included all service use, not only ACS-related service use. As a sensitivity analysis, social and healthcare costs were also studied separately, since the use of social care services (i.e. home nursing care and home care services) was expected to be more age dependent than the use of healthcare services, which were expected to be more associated with clinical conditions.

As for sensitivity analysis purposes, the results of SMART-REACH quintiles stratification approach were also compared with stratifying cumulative social and healthcare costs solely based on patients' baseline age quintiles to assess the potential added value of the SMART-REACH quintiles approach in a stratified cost estimation.

LDL-C goal attainment

LDL-C goal attainment stratified by the baseline SMART-REACH risk quintiles was studied as a secondary outcome to assess the current ESC guideline recommended LDL-C goal attainment in the defined baseline SMART-REACH risk quintiles. To enable this assessment, LDL-C levels were extracted from EHRs at baseline and at two time points in the first 14 months after the baseline. Originally, LDL-C laboratory assays (including both fasting and non-fasting measurements) were analysed in the Eastern Finland Laboratory (www.islab.fi), using the photometric direct enzymatic method and standardized to the International Federation of Clinical Chemistry units.

The baseline measurement was defined as 365 days before until 14 days after the index event, the first follow-up was captured between 14 days and 5 months after the index event, and the second follow-up between 5 and 14 months, whichever was closest to a 0/3/12-month time point. If no LDL-C value was available from EHRs within a certain period, it was considered as 'not measured'. The LDL-C goal attainment was evaluated using both the ESC guideline recommended LDL-C goal, which is <1.4 mmol/L for CAD patients,[17,18] as well as the previous guideline recommended LDL-C goal, <1.8 mmol/L,[19] which was the target value for most of the patients during the study period.

Statistical analysis

Patient baseline characteristics were reported with descriptive statistics (mean, standard deviation, percentages, median, and interquartile range) by finding the closest measurements to the baseline within 365 days before or 14 days after the index event. Proportions of missing values were calculated and reported. Imputation procedures were performed using single imputation with predictive mean matching, similar to the method used in the derivation of the SMART-REACH algorithm[15] (areglmpute, Hmisc package).

The cumulative incidences of observed recurrent cardiovascular events and non-IHD deaths were estimated with the Aalen–Johansen estimator, a non-parametric model suitable for competing risks, and *P*-values were calculated to compare the subdistributions across risk quintiles. To assess the agreement between predicted and observed events (i.e. calibration), the expected/observed ratios were calculated at 5 years using the means of SMART-REACH risk scores and estimated observed cumulative incidences. Calibration was conducted following the method in Kaasenbrood *et al.*,[15] where log(expected/observed) was subtracted from the linear predictors. In addition, to assess the discrimination of the baseline SMART-REACH risk score in the present data set, the *C*-statistic was calculated with the continuous SMART-REACH 5-year prediction value as the only predictor for the Fine–Gray subdistribution hazard of the recurrent event.

For the estimation of the annual means of accumulative costs starting from the baseline date, Zhao and Tian's estimator[20] (ccostr package) was used, as it allows the estimation of mean costs in situations where some patients may have incomplete cost data due to censoring and distinguishes censoring from death. Confidence intervals (CIs) (95%) for estimated mean costs and differences between risk quintiles were estimated by bootstrapping 1000 samples with replacements. All analyses were performed using R version 4.1.2.[21]

Ethical aspects and analytic environment

The study protocol was approved by the register administrator of the North Karelia Wellbeing Services County (permission ID 2022/26). In the present study, de-identified EHR data were curated, pre-processed, analysed, and reported in a certified cloud-based secure processing environment (SPESiOR® Secure Processing Environment; ESiOR Oy) for sensitive health data, in compliance with both European (General Data Protection Regulation) and Finnish regulations under the Act on the Secondary Use of Health and Social Data (Finlex 552/2019). By law, no written consent from the patients was required for this retrospective, non-interventional, register-based study, and individual patients were not contacted.

Results

Patient characteristics

Baseline characteristics of the study cohort are presented in *Table 1*. A total of 3303 patients were included in the study cohort, with 1923

Table 1 Baseline characteristics stratified by the SMART-REACH quintiles

	Full population (*N* = 3303)	Quintile 1 (*n* = 661)	Quintile 2 (*n* = 660)	Quintile 3 (*n* = 661)	Quintile 4 (*n* = 660)	Quintile 5 (*n* = 661)
Mean age, years (SD)	69.7 (9.2)	59.6 (5.9)	66.0 (7.1)	70.3 (7.1)	75.0 (6.5)	77.5 (6.2)
Sex, male, %	69.1	70.4	70.0	69.7	65.5	70.8
Current smokers, %	18.8	12.1	21.7	22.6	17.5	19.8
BMI (kg/m^2; median, IQR)	28.2 (25.2–31.8)	28.5 (25.8–32.5)	27.8 (24.8–31.2)	28.0 (25.0–31.8)	28.2 (25.2–31.2)	28.4 (25.3–32.5)
Diabetes mellitus, %	30.4	4.5	13.6	28.4	39.2	66.1
Mean systolic blood pressure, mmHg (SD)	143.3 (22.3)	140.8 (17.9)	145.1 (20.7)	145.4 (22.1)	144.5 (23.2)	140.9 (24.9)
Mean total cholesterol, mmol/L (SD)	4.3 (1.2)	4.8 (1.0)	4.6 (1.1)	4.3 (1.2)	4.0 (1.2)	3.6 (1.2)
Mean LDL cholesterol, mmol/L (SD)	2.6 (1.1)	3.0 (1.0)	2.9 (1.1)	2.6 (1.1)	2.4 (1.0)	2.0 (1.0)
Mean creatinine, μmol/L (SD)	89.2 (51.0)	73.1 (15.6)	76.5 (15.7)	82.5 (33.7)	87.8 (34.0)	126.0 (91.8)
Coronary artery disease, %	91.3	90.0	89.1	92.0	92.0	93.5
Cerebrovascular disease, %	6.8	<0.8[a]	1.7	4.4	7.7	19.5
Peripheral artery disease, %	8.1	0.6	1.4	5.1	8.3	25.3
History of atrial fibrillation, %	13.5	2.0	3.2	9.4	18.3	34.3
History of congestive heart failure, %	9.4	0.0	2.0	4.2	9.7	30.9

BMI, body mass index; IQR, interquartile range; SD, standard deviation.
[a]Due to data anonymization requirements, the exact value cannot be reported.

(58.2%) having been admitted to hospital due to ACS and 1380 (41.8%) having had an elective PCI or CABG as the index event. 38.6% of the patients had a CAD diagnosis and 4.2% had an ACS event before the index event. At the baseline, the mean age of patients was 69.7 years, and most of the patients were men (69.1%).

The data coverage was 87.2% for the calculation of the SMART-REACH risk scores. The proportions of missing values for individual risk factors were 0.2% for creatinine, 24.5% for total cholesterol, 58.3% for smoking status, and 44.8% for systolic blood pressure. The mean follow-up time was 2.9 years.

Predicted and observed event risks by the baseline SMART-REACH quintiles

On average, the predicted 5-year SMART-REACH risk was estimated to be 27.8% (SD 14.4%), whereas the 5-year observed cumulative incidence of recurrent events was 30.1% (95% CI 27.7–32.7) for the whole study cohort. Overall, risk for a recurrent vascular event was highest during the first year after an index event.

For the risk-stratified analysis, the upper cut-off values of the 5-year baseline SMART-REACH quintiles were determined as 15.7%, 21.0%, 28.0%, 38.3%, and 100%. Predicted 5-year risks of recurrent events were 12.8% for the risk Quintile 1, whereas the corresponding figure was 51.4% in the risk Quintile 5. As shown in *Table 1*, patients in the risk Quintile 5 were older than patients in the risk Quintile 1 (i.e. 77.5 vs. 59.6 years, respectively), and the number of comorbidities, such as diabetes, was systematically more common among the patients in higher risk score quintiles.

The cumulative incidences of observed recurrent events (without stroke events) stratified by the baseline SMART-REACH quintiles are presented in *Figure 2*. With the baseline SMART-REACH quintile stratifications, the respective observed cumulative incidences (95% CI) were 19.5% (16.2–23.5), 27.9% (22.8–34.1), 31.4% (25.8–38.2), 30.3% (25.1–36.5), and 41.4% (35.8–48.0; $P < 0.001$ for the difference between the quintiles). When comparing observed and predicted 5-year risk estimates, the observed cumulative incidences of recurrent events were higher than the predicted mean SMART-REACH risk score values in the lowest quintile (observed 19.5% vs. predicted 12.8%; a difference of 6.7 percentage points) and lower in the highest quintile (observed 41.4% vs. predicted 51.4%; a difference of 10.0 percentage points). Overall, the expected/observed ratio was 0.93, indicating that the SMART-REACH risk score slightly underestimated the incidence of these observed recurrent events. The calibration plot is shown in Supplementary material online, *Figure S1*. When the recurrent cardiac events were expanded to also include both ischaemic and haemorrhagic strokes, the expected/observed ratio at 5 years was 1.47 for recurrent cardiovascular events indicating that the baseline SMART-REACH risk score overestimated the incidence of secondary events in this target population (see Supplementary material online, *Figure S2*).

The estimated *C*-statistic for the continuous SMART-REACH risk score values was 0.56 (SE 0.01), considering only recurrent cardiac events excluding stroke events. However, the *C*-statistic showed an improvement to 0.67 (SE 0.01) when the recurrent cardiac events were expanded to also include the stroke events and exclude revascularizations.

The cumulative incidence (95% CI) of non-IHD death, when it was observed as the first event, was estimated to be 8.4% (6.9–10.3) for the whole study cohort, and 1.1% (0.5–2.4), 3.5% (1.9–6.6), 4.3% (2.8–6.8), 14.6% (8.7–24.6), and 19.5% (15.7–24.3) for the SMART-REACH risk score quintiles, $P < 0.001$ for the difference between the quintiles (see Supplementary material online, *Figure S3*). The expected/observed ratio for non-IHD deaths was 1.13 (see Supplementary material online, *Figure S4*), and for non-CVD deaths 1.22 (see Supplementary material online, *Figure S5*).

Cumulative 5-year social and healthcare costs

The estimated mean of total accumulated 5-year costs (including hospitalizations, ward days, secondary and primary outpatient visits, and social care visits) of the whole study cohort was 94.3M€. As shown in *Figure 3*, the total 5-year costs were, on average, 15 827, 20 349, 27 186, 33 206, and 46 182€ per patient for Quintiles 1–5, respectively. In all cost categories, a higher baseline SMART-REACH risk score quintile consistently indicated higher cumulative 5-year costs. This was

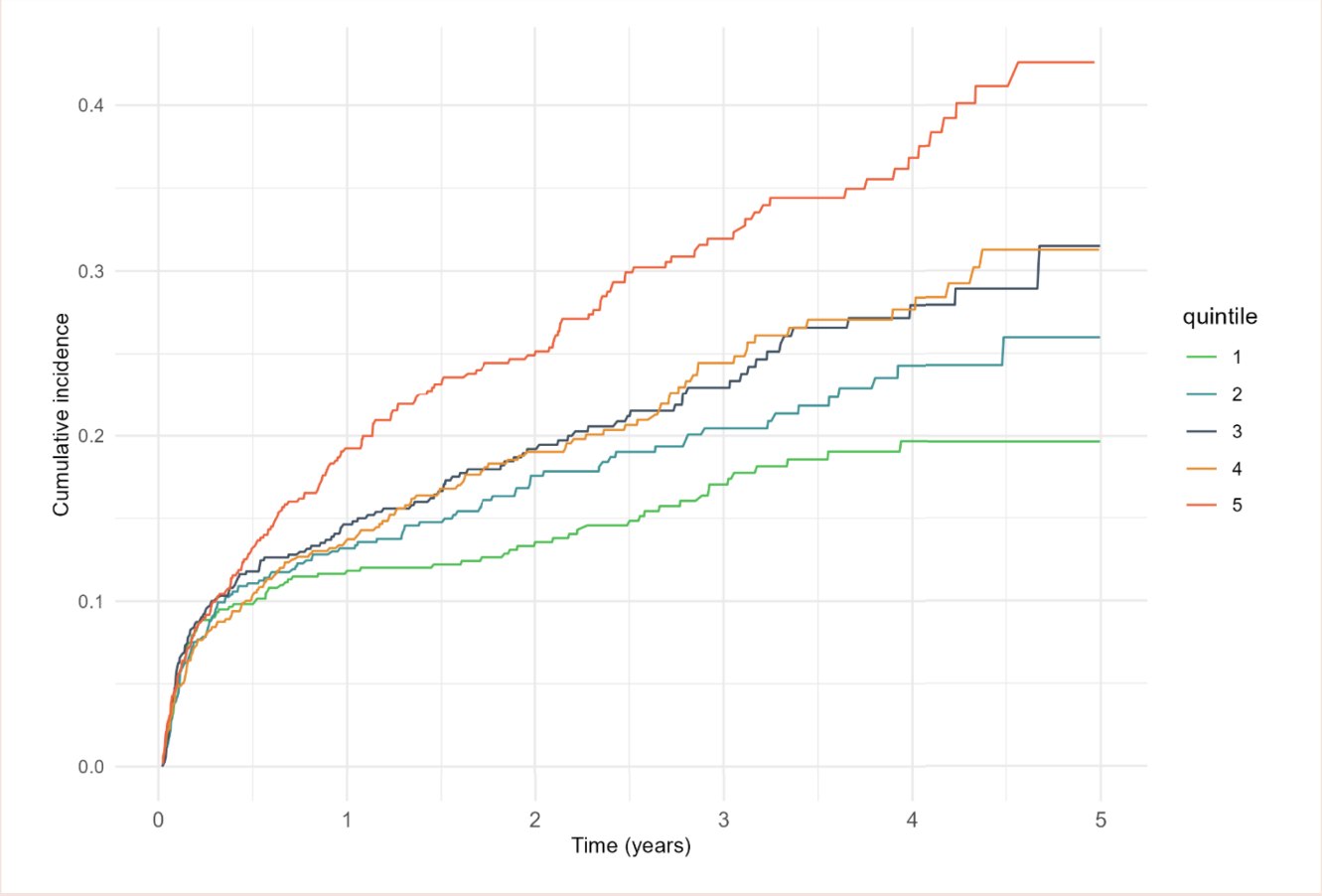

Figure 2 Cumulative incidence of recurrent events (including ischaemic heart diseases death), by SMART-REACH quintiles.

particularly noticeable in the total costs over a 5-year period. The difference between the highest (Quintile 5) and lowest (Quintile 1) quintiles was 29 466€ (95% CI 25 200–34 152€). This suggests that the cumulative costs in Quintile 5 were approximately 1.9 times higher than those in Quintile 1 during the 5-year period (*Table 2*).

When the differences in accumulated 5-year costs were calculated by splitting the population into quintiles based on only baseline age, the risk stratification was more inconsistent compared with the baseline SMART-REACH-based risk stratification (*Table 3*). For example, the cost differences of secondary outpatient visits did not correspond with the age stratification. However, the costs of the social care services were rather similar in the age-based and the risk-based stratification approaches; i.e. the use of those services may be more age-related than the use of overall healthcare services in the target patient population.

LDL-C goal attainment

The achievement of LDL-C treatment goals, broken down by the full population and each quintile of the baseline SMART-REACH risk score, is detailed at each time point in *Table 4*. At baseline, LDL-C values were measured for nearly all patients (95.2%, with a variation of 91.8–96.5 across the baseline SMART-REACH risk quintiles). However, a considerable proportion of patients did not attain the LDL-C treatment goal or undergo follow-ups after the baseline measurement (i.e. the proportions of missing post-index event LDL-C measurements were significant during the follow-up).

Discussion

This study demonstrated that the SMART-REACH risk score, when used as a tool for population-wide risk stratification, effectively divided patients into subgroups after their index events. These subgroups exhibited varying cumulative numbers of recurrent events and total costs. Furthermore, the study revealed a suboptimal level of follow-up and attainment of LDL-C goals in patients who had recently undergone ACS and/or coronary revascularization.

The incidence of ACS and/or coronary revascularization patients was in line with earlier research conducted in the same area.[14] The observed 5-year cumulative incidence of recurrent events, based on the baseline SMART-REACH risk quintiles, varied from 20% to 41%. These results are similar to a previous study in the USA, where the average event rate at the 5-year time point was, on average, 33.4%, but with a slightly different definition of a recurrent event.[22] In addition, the cumulative incidence of non-CVD deaths was, on average, 8.4%, which corresponds well to a previous Finnish registry study,[23] where the proportion of patients dying of causes other than CVDs was around 11.6% over a slightly longer follow-up time of mean 7 years.

In the present study, the cumulative 5-year average total costs per patient ranged from 15 827 to 46 182€, depending on the baseline risk quintiles. The annual costs were highest within 1 year from the index event (excluding social services and primary care outpatient visits), coinciding with the fact that the risk of recurrent events was highest during the first year. In this study, we adopted an all-cause cost estimation approach, rather than limiting our analysis to costs associated

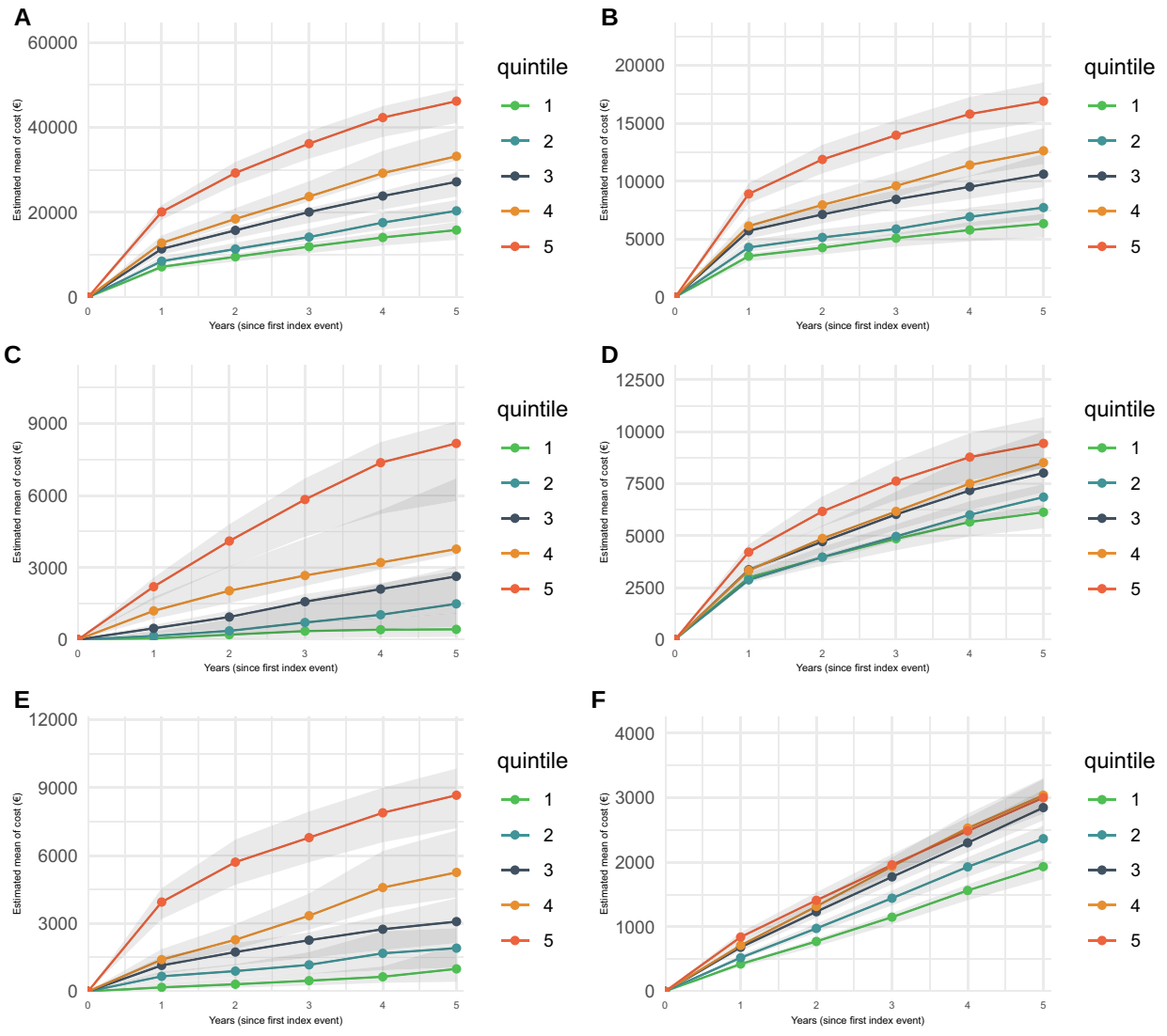

Figure 3 Accumulation of 5-year social and healthcare costs (per a patient), by SMART-REACH quintiles. (*A*) Total cumulative costs. (*B*) Cumulative costs of hospitalizations. (*C*) Cumulative costs of social care services. (*D*) Cumulative costs of secondary care outpatient visits. (*E*) Cumulative costs of health centre ward days. (*F*) Cumulative costs of primary care outpatient visits.

solely with recurrent cardiac events. This approach is supported by a previous study related to diabetes,[24] which revealed that when only diabetes-attributable costs were considered, diabetes-specific costs were underestimated by 14–42%, depending on the type of diabetes and the analytic method employed. It is well established that chronic diseases are interconnected. For example, diabetes is a recognized risk factor for CVD.[6] Moreover, a recent study[25] reported that the average 5-year healthcare costs following ACS index hospitalization amounted to approximately 4000€/year in Italy. This figure aligns closely with our findings, which indicate an annual cost of 5710€, encompassing both social and healthcare costs for the entire population.

There are only few publications examining the economic implications of CVD risk profiles, e.g. Zheng *et al.*[26] and Journath *et al.*,[12] and particularly, the population-level economic implications of risk profiles in patients with recent cardiovascular revascularization are very limited.[12] In primary prevention of CVD, a lower CVD risk has been associated with lower annual healthcare costs.[8,9] The cumulative costs of hospitalizations, ward days, and social service visits varied more distinguishably between the baseline SMART-REACH risk score quintiles, whereas the differences in cumulative costs of secondary and primary care outpatient visits between the quintiles were less pronounced because considerable costs were accrued also in the lowest quintiles. In all resource use categories, higher risk quintile constantly indicated higher costs. The similarity in cumulative costs of secondary and primary care outpatient visits between risk quintiles represents the costs of planned follow-ups related to the prevention of CVD and other chronic diseases. Overall, hospitalization costs continue to be the largest component of total 5-year costs highlighting the need for effective prevention measures also in terms of costs.

In the present study, we found that there is still significant room for improvement in the prevention of recurrent cardiac events in the study area (North Karelia, Finland), since only a small proportion of the cohort were below the LDL-C goal value of 1.4 mmol/L as per 2019 ESC guidelines at baseline and during the 14-month follow-up.

Table 2 Differences in accumulated 5-year costs (per a patient) in euros, by SMART-REACH quintiles

Mean differences (Quintile 1 as a reference)	Quintile 2 (95% CI)	Quintile 3 (95% CI)	Quintile 4 (95% CI)	Quintile 5 (95% CI)
Total	4586 (1398– 7995)	10 810 (7412–14 189)	20 175 (16 859–24 431)	29 466 (25 200–34 153)
Hospitalization	1420 (27–2790)	4673 (3007–6491)	6859 (5015–8763)	10 609 (8834–12 576)
Days in health centre ward	709 (−549–1952)	1956 (530–3262)	4485 (2909–6227)	7496 (5885–9031)
Secondary outpatient visits	930 (70–1756)	1874 (967–2824)	3170 (2103–4211)	3499 (2132–4910)
Primary outpatient visits	485 (227–735)	989 (706–1275)	1159 (865–1439)	1120 (817–1450)
Social care visits	1042 (−205–2629)	1318 (358–2403)	4502 (2947–6288)	6805 (5116–8513)

Quintile 1 is applied as a reference category.

Table 3 Differences in accumulated 5-year costs (per a patient) in euros, by age quintiles

Mean differences (Quintile 1 as a reference)	Quintile 2 (95% CI)	Quintile 3 (95% CI)	Quintile 4 (95% CI)	Quintile 5 (95% CI)
Total	5642 (918–10 242)	8729 (4938–12 603)	14 241 (9663–18 747)	19 894 (15 301–24 302)
Hospitalization	2761 (620–4832)	3363 (1660–5048)	5129 (3282–7097)	6054 (4256–7875)
Days in health centre ward	1230 (129–2556)	1745 (891–2651)	3957 (2656–5455)	7754 (6109–9462)
Secondary outpatient visits	−530 (−1993 to 868)	114 (−1433 to 1418)	466 (−1051 to 1908)	−1360 (−2763 to 109)
Primary outpatient visits	716 (427–998)	842 (565–1112)	1243 (910–1572)	771 (492–1058)
Social care visits	1465 (264–3081)	2666 (1329–4253)	3446 (2056–5054)	6674 (5086–8313)

The Quintile 1 is applied as a reference category.

Furthermore, the proportion of patients without LDL-C monitoring was remarkably high and increased over time. Notably, the ESC guideline on the LDL-C goal changed from 1.8 to 1.4 mmol/L during the study period. Even with the higher treatment goal value of 1.8 mmol/L, only around 22% had an LDL-C value below the goal at baseline, and the proportion decreased as well after the 3-month follow-up from 43% to 35% at the 12-month follow-up. These findings corroborate the results of a previous study[27] where only 15% of the patients were on LDL-C treatment goal 1.8 mmol/L at the baseline. The previous study[27] excluded patients who did not have their LDL-C levels measured, whereas our study included those patients as a quality indicator for LDL-C monitoring during the post-index event period.

In the current study, patients were stratified by the risk of a recurrent cardiac event, estimated using the SMART-REACH risk score. The SMART-REACH risk score was shown to be a valid tool in the original SMART-REACH development and validation study[15] and in a Norwegian registry study.[28] The SMART-REACH risk score can potentially be used to identify the high-risk patients who benefit most from more tailored and intensive secondary prevention. The original SMART-REACH risk score estimates the recurrent event risk for all recurrent CVD events.[15] In the present study, we focused primarily on the patients with a recent coronary revascularization, and therefore, the predictions of the SMART-REACH risk score were first compared with recurrent coronary revascularization events. This may partly explain the observed *C*-statistic of 0.56 for these events. However, a higher *C*-statistic of 0.67 was achieved when the observed recurrent events included also cerebrovascular events. This corresponds well with the originally reported *C*-statistics (i.e. 0.68/0.67).[15]

Our study has strengths and limitations. To our knowledge, this is the first real-world EHR data study linking the baseline SMART-REACH risk scores to long-term social and healthcare costs in patients with a recent ACS or coronary revascularization. It demonstrates how the 5-year risk of a recurrent cardiac event stratified into quintiles is significantly associated with the 5-year cumulative social and healthcare costs, adjusting for censoring. Furthermore, we conducted a sensitivity analysis where the differences between costs were assessed by age-based quintiles. With SMART-REACH stratification, the cost increase from a lower to higher risk quintile was consistent in all cost categories, whereas age-

Table 4 LDL-C treatment goal attainment with LDL-C target values 1.4 and 1.8 mmol/L, for the full population and stratified by the SMART-REACH quintiles

	Baseline	First follow-up (around 3 months)	Second follow-up (around 12 months)
On treatment goal, LDL-C <1.4 or <1.8 mmol/L, % of patients still in follow-up			
Whole population	9.7/22.4	22.4/42.9	18.3/34.7
Quintile 1	2.6/7.3	20.2/41.9	14.8/31.3
Quintile 2	3.6/12.9	20.8/44.1	17.0/33.6
Quintile 3	7.9/21.0	24.7/46.8	19.3/35.7
Quintile 4	11.4/28.6	24.4/41.1	20.2/37.8
Quintile 5	23.0/42.2	22.1/40.3	20.5/35.7
Above treatment goal, LDL-C ≥1.4 or ≥1.8 mmol/L, % of patients still in follow-up			
Whole population	85.5/72.8	49.4/29.1	38.4/22.0
Quintile 1	93.9/89.3	55.4/33.7	38.9/22.3
Quintile 2	92.0/82.7	56.7/33.4	40.0/23.4
Quintile 3	88.4/75.3	50.4/28.3	39.2/22.9
Quintile 4	84.5/67.3	44.0/27.4	39.6/21.9
Quintile 5	68.8/49.6	40.1/22.0	34.2/19.0
Not measured, % of patients still in follow-up			
Whole population	4.8	28.2	43.3
Quintile 1	3.5	24.5	46.4
Quintile 2	4.4	22.4	43.0
Quintile 3	3.8	25.0	41.5
Quintile 4	4.1	31.5	40.2
Quintile 5	8.2	37.8	45.2
Dead, % of baseline			
Whole population	0.0	2.0	4.0
Quintile 1	0.0	<0.8	0.8
Quintile 2	0.0	1.1	1.7
Quintile 3	0.0	1.2	2.7
Quintile 4	0.0	2.2	3.9
Quintile 5	0.0	5.0	10.9
End of follow-up (censoring), % of baseline			
Whole population	0.0	0.0	7.0
Quintile 1	0.0	0.0	7.6
Quintile 2	0.0	0.0	6.5
Quintile 3	0.0	0.0	8.6
Quintile 4	0.0	0.0	7.1
Quintile 5	0.0	0.0	5.1

based stratification did not lead to consistent result e.g. in the case of outpatient visits in primary and secondary care. This indicates that in patients with a recent coronary revascularization, baseline age alone does not predict the social and healthcare costs as well as risk-based stratification. In addition, EHR data are not prone to non-responsiveness or recall bias.

Naturally, our study also has limitations. First, our study did not consider private healthcare services and occupational health services due to data availability limitations, which might lead to an underestimation of long-term costs. However, the role of private healthcare services and occupational health services could be expected to be limited given the old age of the patient group. Second, as in all studies using real-world EHR data, data quality depends on care and recording practices. The proportions of missing data for different variables varied significantly, and therefore, data imputation methods were applied to risk predictors to improve the comprehensiveness of data. Third, in the present study, we were not able to consider medication data due to data limitations, potentially causing bias in our analysis. Omitting the costs of medications could underestimate actual total costs. Instead, we evaluated compliance with guidelines using the real-world attainment of the LDL-C treatment goals as an indicator. Fourth, one limitation relates to the representativeness of our study findings as our data were limited to one region of Finland. However, we believe that the findings would be similar in other areas of Finland since the corresponding baseline characteristics of our study are in line with the previous Finnish registry studies[5,27] mentioned above. Finally, the study period of the present study overlaps with the period of COVID-19 pandemic, which might have affected patients managing their care adequately. For example, the results of a previous study[29] from the same area as our present study showed that the COVID-19 lockdown decreased the frequency of monitoring, but monthly average LDL had a steadily improving pattern in coronary heart disease patients at the time of the lockdown. Thus, the lockdown may have introduced selection in patients who had their treatment outcomes monitored. However, better self-management of risk factors could also explain this observed phenomenon.

Conclusions

The use of the baseline SMART-REACH risk score quintiles as a risk stratification tool managed to stratify patients into subgroups with different risks of recurrent events and cumulative 5-year total costs. Thus, the use of the SMART-REACH quintiles may provide a practical tool to recognize those patients with a recent ACS and/or coronary revascularization, who are at a particularly high (or low) risk for a recurrent event. In addition, the wider use of prediction tools like SMART-REACH has the potential to enhance population-level treatment planning and resource distribution decisions by providing a deeper understanding of the association between the risk of recurring CVD events and the long-term healthcare needs, as well as costs of patients. However, more research is currently needed to define clinically and economically optimal threshold values for stratification.

Lead author biography

Minna Oksanen, MSc, is a data scientist at ESiOR Ltd in Finland. She completed her master's degree in bioinformatics at Aalto University and specializes in real-world data analysis within the healthcare sector.

Data availability

Data analysed in the study are pseudonymized patient information, which was collected from EHRs, and it cannot be shared for privacy reasons.

Supplementary material

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

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Conflict of interest: M.O. and C.A. are employees of ESiOR Oy. At the time of writing, J.P. was an employee of ESiOR Oy. J.P. is no longer an employee of ESiOR Oy. J.M. is a founding partner and shareholder of ESiOR Oy. A.K. is an employee of Novartis. Other declare no competing interest to the current study.

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