ORIGINAL RESEARCH

Socioeconomic Factors, Secondary Prevention Medication, and Long-Term Survival After Coronary Artery Bypass Grafting: A Population-Based Cohort Study From the SWEDEHEART Registry

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Background—Low income and short education have been found to be independently associated with inferior survival after coronary artery bypass grafting (CABG), whereas the use of secondary prevention medications is associated with improved survival. We investigated whether underusage of secondary prevention medications contributes to the inferior long-term survival in CABG patients with a low income and short education.

Methods and Results—Patients who underwent CABG in Sweden between 2006 to 2015 and survived at least 6 months after discharge (n=28 448) were included in a population-based cohort study. Individual patient data from 5 national registries, including the SWEDEHEART (Swedish Web System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry, covering dispensing of secondary prevention medications (statins, platelet inhibitors, β-blockers, and RAAS inhibitors), socioeconomic factors, patient characteristics, comorbidity, and long-term mortaity were merged. All-cause mortality risk was estimated using multivariable Cox regression models adjusted for patient characteristics, baseline comorbidities, time-updated secondary prevention medications, and socioeconomic status. Long-term mortality was higher in patients with a low income and short education. Statins and platelet inhibitors were dispensed less often to patients with a low income, both at baseline and after 8 years. The decline in dispensing over time was steeper for low-income patients. Short education was not associated with reduced dispensing of any secondary prevention medication. Use of statins (adjusted hazard ratio=0.57 [95% CI, 0.53–0.61]), RAAS inhibitors (adjusted hazard ratio=0.78 [0.73–0.84]), and platelet inhibitors (adjusted hazard ratio=0.74 [0.68–0.80]) were associated with reduced long-term mortality irrespective of socioeconomic status.

Conclusions—Secondary prevention medications are dispensed less often after CABG to patients with low income. Underusage of secondary prevention medications after CABG is associated with increased mortality risk independently of income and extent of education. **(*J Am Heart Assoc*. 2020;9:e015491. DOI: 10.1161/JAHA.119.015491.)**

Key Words: coronary artery bypass grafting • medication • mortality • secondary prevention • socioeconomic status

Coronary artery bypass grafting (CABG) reduces symptoms and prolongs life in patients with severe multivessel coronary artery disease.[1] Secondary prevention medications are used after CABG to prevent recurrence of coronary artery disease in native vessels and grafts, and are associated with prolonged survival.[2–4] Current guidelines therefore recommend lifelong treatment with statins and platelet inhibitors for all patients after CABG[5] while renin-angiotensin-aldosterone system (RAAS) inhibitors are recommended for CABG patients with hypertension, diabetes

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Accompanying Tables S1 through S5 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.015491

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Clinical Perspective

What Is New?

- Statins and platelet inhibitors were less often dispensed to coronary artery bypass grafting patients with low income.
- Underusage of secondary prevention medications was associated with inferior survival after coronary artery bypass grafting independently of income and extent of education.

What Are the Clinical Implications?

- Healthcare professionals must be aware of the importance of secondary prevention medications after coronary artery bypass grafting and as far as possible ensure that coronary artery bypass grafting patients with social disadvantages are maintained on treatment.

mellitus, or previous myocardial infarction, and in patients with reduced left ventricular ejection fraction. β-blockers are recommended for patients with previous myocardial infarction and/or reduced ejection fraction.[5,6] The general adherence to these recommendations has been reported to be low,[7–9] and markedly lower after CABG than in coronary artery disease patients treated with percutaneous coronary interventions.[10–12] A recent study by our group, based on the same database as used in the present study, showed that the overall use of secondary prevention medications after CABG was satisfactory early after surgery but decreased significantly over time, especially in older patients.[4]

Some studies have found that low socioeconomic status is associated with increased mortality risk after CABG, even after adjustment for comorbidities.[13,14] The exact reasons for the higher mortality risk in CABG patients with social disadvantages, such as a low income and short education, are not yet clear, but it has been suggested that socioeconomic status-related differences in medical risk profile, medical care, job strain, stress, and lifestyle factors such as smoking habits, diet, and level of physical activity may play a role in other groups of patients with cardiovascular diseases.[15–17] However, it is possible that also underusage of secondary prevention medications in CABG patients with social disadvantages contributes to their higher mortality, but this has not been investigated. The aim of the present study was therefore to investigate whether secondary prevention medications are underused in CABG patients with low socioeconomic status, and whether this has an influence on long-term mortality risk. A secondary aim was to investigate whether there are any interactions between socioeconomic factors and use of secondary prevention medication that might affect long-term mortality risk after CABG.

Methods

The authors declare that all supporting data are available within the article and its online supplementary files.

Study Population

Altogether, 30 952 patients aged >18 years who underwent a first isolated CABG procedure in Sweden in the period January 1, 2006 through July 31, 2015 were considered for inclusion in this population-based cohort study. Since mortality early after surgery is less likely to be preventable by secondary prevention therapy, patients who died during the index hospitalization or within 6 months after discharge (n=806) were excluded. Also, patients with <6 months of follow-up before December 31, 2015 (n=1324), patients who emigrated <6 months after discharge (n=10), and patients with missing values on level of education (n=364) were excluded. In total, this left 28 448 patients for analysis. A flowchart describing inclusion and exclusion is given in Figure 1. Merging of data from different registries was done based on the personal identification number that all Swedish residents are given at birth or shortly after immigration.

Data Sources

The SWEDEHEART Registry

The study population was identified in the Swedish Heart Surgery Registry, which since 2009 has been part of the SWEDEHEART (Swedish Web System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry.[18] The Swedish Heart Surgery Registry has records of all open cardiac operations performed in Sweden since 1992, with baseline variables, operative details, and early complications.[19] The present paper follows the recommendations from the statement of Strengthening the Reporting of Observational Studies In Epidemiology.[20]

Dispensed secondary prevention medications

The Swedish Prescribed Drug Registry contains information on all the medications that have been dispensed at all the pharmacies in Sweden since 2005.[21] The registry was used to obtain information about prescriptions dispensed according to the Anatomical Therapeutic Chemical Classification. Statins were identified using codes C10AA, C10BA02, and C10BX06; β-blockers using C07 (excluding C07AA07); RAAS inhibitors using C09; and platelet inhibitors using B01AC, which includes aspirin, ticagrelor, clopidogrel, and prasugrel. Follow-up for all medications started 6 months after discharge. Exposure status was recorded at baseline and updated every third month during the follow-up, based on the typical package size in Sweden, which covers 90 to 100 daily doses.

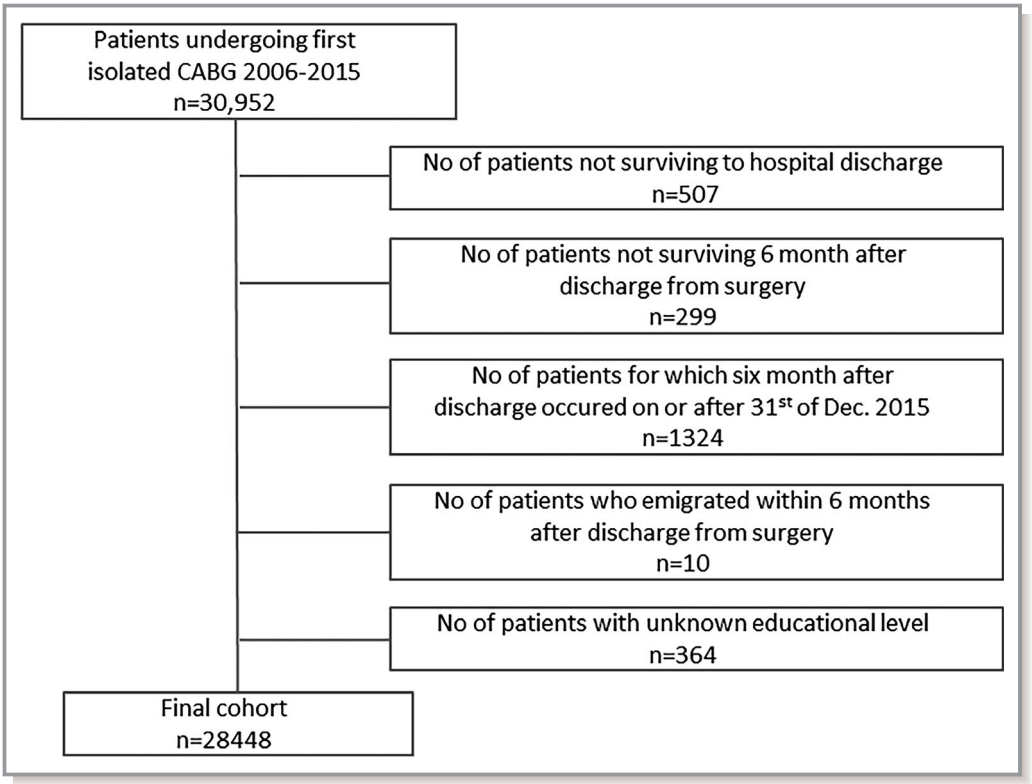

Figure 1. Flowchart describing included and excluded patients. CABG indicates coronary artery bypass grafting.

At least one prescription dispensed during the previous, and the 2 following 3-month periods was defined as the patient being on treatment. If there was no dispensing over 2 consecutive 3-month periods, the patient was classified as being off treatment. Patient exposure status was allowed to change during the follow-up period according to dispensed prescriptions. Information on medications used during hospital admissions was not available for analysis.

Socioeconomic variables

Socioeconomic variables were collected from the LISA (Longitudinal Integration Database for Health Insurance and Labor Market Studies) register held by Statistics Sweden.[22] The registry has collected socioeconomic information annually on all citizens aged >16 years in Sweden since 1990. Income was obtained as household income during the year of surgery. To adjust for inflation rates during the study period, we used the consumer price index according to Statistics Sweden. If income data for the year of surgery were missing, information for the most recent year before surgery was used instead.

Comorbidities

Information on comorbidities was obtained from the NPR (National Patient Registry) and SWEDEHEART. Principal and secondary diagnoses for all hospitalizations in Sweden have been registered in the NPR since 1987, with 85% to 95% validity.[23] The *International Classification of Diseases, Ninth Revision* (*ICD-9*) was used for data collected in the period 1987 to 1997 and *ICD-10* was used for data collected in the period 1997 to 2015. The *ICD* codes used are listed in Table S1. Data on comorbidities were collected before the start of follow-up (ie, 6 months after hospital discharge) for CABG surgery. The following variables pertaining to admission for surgery were obtained from the SWEDEHEART registry: body mass index, left ventricular ejection fraction, and estimated glomerular filtration rate—calculated from serum creatinine using the Chronic Kidney Disease Epidemiology formula.[24]

Statistical Methods

All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc, Cary, NC, USA). Descriptive statistics for baseline data are presented as mean with standard deviation, median with range, or median with interquartile range (IQR) for continuous variables and as frequency with percentage for categorical variables. In calculations with comparison between groups, Fisher exact test was used for dichotomous variables, the Mantel–Haenszel Chi-square test was used for ordered categorical variables, the Chi-square test was used for unordered categorical variables, and the Mann–Whitney *U* test was used for continuous variables. Dispensing of medications over time

has been reported as crude data and the Mantel–Haenszel Chi-square test was used to analyze differences in drug dispensing in different education categories and income categories at baseline, and 4 and 8 years after baseline. Crude event rates per 100 person-years were calculated as the number of events divided by the number of years of follow-up, with 95% CI estimated using exact Poisson limits.

The effect of time-updated secondary prevention medication on all-cause mortality in different socioeconomic subgroups was investigated with Cox regression models and expressed using hazard ratio (HR) and 95% CI. Model 1 was adjusted for age and sex. Model 2 was also adjusted for patient characteristics and comorbidities at baseline that have previously been shown to influence long-term mortality in CABG patients (year of surgery, left ventricular function, body mass index, diabetes mellitus, hypertension, hyperlipidemia, previous stroke, atrial fibrillation, heart failure, peripheral vascular disease, previous myocardial infarction, acute coronary syndrome as indication for surgery, chronic obstructive pulmonary disease, and renal function). Model 3 was also adjusted for the use of all other secondary prevention medications unless it was the main effect variable. Finally, model 4 was also adjusted for (a) length of education ([1] <10 years [primary school]; [2] 10–12 years [secondary school]; or [3] >12 years [university education]); (b) income category [Q1–Q5 {Q1 being the lowest level}] unless this was the main subgrouping variable; and (c) marital status ([1] unmarried; [2] divorced/widowed; or [3] married). If not explicitly stated, the results presented are from model 4.

Using the same methodology, the effect of length of education and income on long-term mortality was studied in 2 models. Model A was adjusted for age, sex, patient characteristics, comorbidities at baseline, marital status, education, and income unless these were the main effect variables. In model B, time-updated secondary prevention medication status was added to model A. Missing data for left ventricular ejection fraction (0.9%), body mass index (8.3%), and estimated glomerular filtration rate (1.6%) were handled as separate categories ("unknown") in the adjustments. All tests were 2-tailed and were interpreted at a significance level of 0.05.

Ethical approval

The study was approved by the Regional Ethics Committee in Gothenburg (registration number 139-16), which waived any requirement for individual patient consent.

Results

Study population

In total, 28 448 CABG patients were included. Mean age was 67.4 years, and there were 5537 women (19.5%) and 22 911 men (80.5%). Patient characteristics are presented in Tables 1 and 2. Mean length of follow-up was 4.9 years (range 0–10). Total follow-up time was 137 475 patient years. During follow-up, 3718 patients died (13.1%). The crude mortality rate was 2.70 (2.62–2.79) deaths per 100 patient years. At baseline, 39.4% of the patients had a duration of education of <10 years, 41.2% had a duration of 10 to 12 years, and 19.4% had a duration of >12 years. In addition, 54.4% of the patients had had a previous myocardial infarction, 70.1% were hypertensive, 30.1% had diabetes mellitus, and 20.8% had had heart failure (Table 2). At baseline, a higher proportion of patients with a short education and a higher proportion of patients with low income were older and were female, and they had a higher prevalence of comorbidities than patients with a long education and high income (Tables 1 and 2).

Socioeconomic Status and Dispensed Medications

Income

The secondary prevention medications dispensed over time in relation to income are presented in Figure 2 and in Table S2. At baseline, statins (91.5% versus 95.2%; $P<0.001$) and platelet inhibitors (92.1% versus 94.9%; $P<0.001$) were dispensed to a lower proportion of patients in the lowest income quintile (Q1) than to patients in the highest income quintile (Q5). The dispensing of RAAS inhibitors at baseline was higher in patients with a low income whereas the dispensing of β-blockers was not significantly different between the income quintiles.

The dispensing of all secondary prevention medications was reduced over time in all income quintiles. The reduction was larger in the lower income quintiles for statins, RAAS inhibitors, and platelet inhibitors (Figure 2). From baseline to 8 years, the dispensing of statins was reduced from 91.5% to 71.0% (relative difference −22.4%) in the lowest quintile and from 95.2% to 81.7% (relative difference −14.2%) in the highest quintile. Dispensing of RAAS inhibitors was reduced from baseline to 8 years, from 74.2% to 63.1% (relative difference −15.0%) in the lowest quintile and from 71.4% to 68.9% (relative difference −3.5%) in the highest quintile. Dispensing of platelet inhibitors was reduced from baseline to 8 years, from 92.1% to 77.6% (relative difference −16.8%) in the lowest quintile and from 94.9% to 81.6% (relative difference −14.0%) in the highest quintile. The reduction in dispensing of β-blockers was comparable in the lowest and highest income quintiles.

Length of education

The secondary prevention medications dispensed over time in relation to level of education are presented in Figure 3 and Table S3. At baseline, there were no clinically important

Table 1. Descriptive Data of Patient Characteristics by Income Level Among Coronary Artery Bypass Grafting Patients

	Total n (%)	Income Level Q1 (Lowest) n (%)	Income Level Q2 n (%)	Income Level Q3 n (%)	Income Level Q4 n (%)	Income Level Q5 n (%)	*P* Value
No of patients	28 448 (100)	5687 (20.0)	5690 (20.0)	5691 (20.0)	5690 (20.0)	5690 (20.0)	
Baseline characteristics at time of surgery							
Age, mean (SD)	67.4 (9.2)	69.5 (9.4)	69.4 (9.3)	69.3 (8.6)	65.9 (8.3)	63.0 (8.4)	<0.0001
Men	22 911 (80.5)	3673 (64.6)	4525 (79.5)	4720 (82.9)	4910 (86.3)	5083 (89.3)	
Women	5537 (19.5)	2014 (35.4)	1165 (20.5)	971 (17.1)	780 (13.7)	607 (10.7)	<0.0001
Marital status							
Unmarried	3522 (12.4)	1389 (24.4)	920 (16.2)	483 (8.5)	359 (6.3)	371 (6.5)	
Divorced/widowed	7695 (27.0)	3761 (66.1)	1991 (35.0)	900 (15.8)	611 (10.7)	432 (7.6)	
Married	17 231 (60.6)	537 (9.4)	2779 (48.8)	4308 (75.7)	4720 (83.0)	4887 (85.9)	<0.0001
Education category							
<10 y	11 201 (39.4)	2972 (52.3)	2676 (47.0)	2409 (42.3)	1839 (32.3)	1305 (22.9)	
10 to 12 y	11 720 (41.2)	2184 (38.4)	2293 (40.3)	2406 (42.3)	2507 (44.1)	2330 (40.9)	
>12 y	5527 (19.4)	531 (9.3)	721 (12.7)	876 (15.4)	1344 (23.6)	2055 (36.1)	<0.0001
LVEF <50%							
>50%	19 698 (69.2)	3600 (63.3)	3743 (65.8)	3980 (69.9)	4129 (72.6)	4246 (74.6)	
<50%	8507 (29.9)	2044 (35.9)	1898 (33.4)	1669 (29.3)	1510 (26.5)	1386 (24.4)	
Unknown	243 (0.9)	43 (0.8)	49 (0.9%)	42 (0.7%)	51 (0.9%)	58 (1.0%)	<0.0001
BMI, kg/m^2	n=26 096	n=5221	n=5206	n=5213	n=5245	n=5211	0.1080
Mean (SD)	27.4 (4.1)	27.6 (4.4)	27.4 (4.2)	27.3 (3.9)	27.4 (3.9)	27.4 (3.8)	
Unknown	2352 (8.3)	466 (8.2)	484 (8.5)	478 (8.4)	445 (7.8)	479 (8.4)	
eGFR category, mL/min per 1.73 m^2							
≥90	7551 (26.5)	1267 (22.3)	1233 (21.7)	1268 (22.3)	1694 (29.8)	2089 (36.7)	
60 to <90	15 421 (54.2)	2973 (52.3)	3150 (55.4)	3237 (56.9)	3103 (54.5)	2958 (52.0)	
30 to <60	4542 (16.0)	1233 (21.7)	1091 (19.2)	988 (17.4)	726 (12.8)	504 (8.9)	
15 to <30	275 (1.0)	78 (1.4)	80 (1.4)	56 (1.0)	37 (0.7)	24 (0.4)	
<15	195 (0.7)	41 (0.7)	40 (0.7)	40 (0.7)	35 (0.6)	39 (0.7)	
Unknown	464 (1.6)	95 (1.7)	96 (1.7)	102 (1.8)	95 (1.7)	76 (1.3)	<0.0001
Indication for surgery							
Stable angina	11 538 (40.6)	2021 (35.5)	2348 (41.3)	2333 (41.0)	2414 (42.4)	2422 (42.6)	<0.0001
Unstable angina	7814 (27.5)	1543 (27.1)	1508 (26.5)	1589 (27.9)	1560 (27.4)	1614 (28.4)	0.0708
STEMI	7235 (25.4)	1693 (29.8)	1446 (25.4)	1418 (24.9)	1332 (23.4)	1346 (23.7)	<0.0001
NSTEMI	1861 (6.5)	430 (7.6)	388 (6.8)	351 (6.2)	384 (6.7)	308 (5.4)	<0.0001
Medical history 6 mo after surgery at start of follow-up							
Myocardial infarction	15 474 (54.4)	3505 (61.6)	3200 (56.2)	3042 (53.5)	2929 (51.5)	2798 (49.2)	<0.0001
Diabetes mellitus	8576 (30.1)	2004 (35.2)	1795 (31.5)	1730 (30.4)	1619 (28.5)	1428 (25.1)	<0.0001
Hypertension	19 945 (70.1)	4130 (72.6)	4043 (71.1)	4093 (71.9)	3895 (68.5)	3784 (66.5)	<0.0001
Heart failure	5918 (20.8)	1567 (27.6)	1350 (23.7)	1121 (19.7)	1007 (17.7)	873 (15.3)	<0.0001
Atrial fibrillation	7974 (28.0)	1664 (29.3)	1681 (29.5)	1714 (30.1)	1569 (27.6)	1346 (23.7)	<0.0001
Stroke	2501 (8.8)	647 (11.4)	542 (9.5)	523 (9.2)	467 (8.2)	322 (5.7)	<0.0001
Chronic respiratory disease	2737 (9.6)	759 (13.3)	622 (10.9)	518 (9.1)	444 (7.8)	394 (6.9)	<0.0001

Continued

Table 1. Continued

	Total n (%)	Income Level Q1 (Lowest) n (%)	Income Level Q2 n (%)	Income Level Q3 n (%)	Income Level Q4 n (%)	Income Level Q5 n (%)	*P* Value
Renal failure	1394 (4.9)	352 (6.2)	334 (5.9)	275 (4.8)	240 (4.2)	193 (3.4)	<0.0001
Peripheral vascular disease	2695 (9.5)	676 (11.9)	573 (10.1)	593 (10.4)	510 (9.0)	343 (6.0)	<0.0001
History of malignancy	3730 (13.1)	717 (12.6)	810 (14.2)	893 (15.7)	691 (12.1)	619 (10.9)	<0.0001
Hyperlipidemia	14 406 (50.6)	2832 (49.8)	2779 (48.8)	2903 (51.0)	2941 (51.7)	2951 (51.9)	0.0009

BMI indicates body mass index; eGFR, estimated glomerular filtration rate (chronic kidney disease epidemiology); LVEF, left ventricular ejection fraction; NSTEMI, non–ST-segment–elevation myocardial infarction; STEMI, ST-segment–elevation myocardial infarction.

differences in dispensing of statins, platelet inhibitors, or β-blockers to patients with <10 years of education compared with those with 10 to 12 years or >12 years of education. At baseline, however, RAAS inhibitors were dispensed to a higher proportion of patients with <10 years of education than to patients with >12 years of education (74.3% versus 70.1%; *P*<0.001).

After the 8-year follow-up, there were no marked differences in dispensing of statins, RAAS inhibitors, or platelet inhibitors to patients with <10 years of education and to those with 10 to 12 years or >12 years of education. However, β-blockers were dispensed to a significantly lower proportion of those with >12 years of education than to those with ≤10 years of education (74.1% versus 77.9%; *P*=0.016).

Socioeconomic Status and Mortality

Hazard ratios for all-cause mortality were higher in all 4 lower income quintiles compared with the highest quintile in the Cox regression model adjusted for age, sex, comorbidities, secondary prevention medications, marital status, and length of education (Table 3). Adjusted hazard ratios for all-cause mortality during follow-up were higher in patients with <10 years of education and in those with 10 to 12 years of education than in those with >12 years of education (Table 3).

Interactions Between Socioeconomic Factors and Mortality Risk

Adjusted interaction analyses between socioeconomic factors and secondary prevention medications are presented in Figure 4 and Tables S4 and S5. Overall, time-updated dispensing of statins (adjusted HR=0.57 [95% CI, 0.53–0.61]), RAAS inhibitors (adjusted HR=0.78 [95% CI, 0.73–0.84]), and platelet inhibitors (adjusted HR=0.74 [95% CI, 0.68–0.80])—but not β-blockers (adjusted HR=0.97 [95% CI, 0.89–1.06])—were found to be associated with reduced mortality risk. Dispensing of statins and platelet inhibitors was associated with lower mortality regardless of socioeconomic subgroup (interaction *P* value: >0.05). However, there were numerical differences in the reductions in mortality ranging from 35% in Q1 to 49% in Q5 for statins, and from 19% in Q1 to 44% in Q5 for platelet inhibitors. For β-blockers, no associations with reduced mortality were observed in any subgroup except in patients with the shortest education (<10 years), where dispensing of β-blockers was associated with reduced mortality (interaction p-value: 0.021). For RAAS inhibitors, there were no significant interactions.

Discussion

The main findings of this large, population-based cohort study were as follows: (1) Patients with a low income were dispensed less statins and platelet inhibitors after CABG. (2) The decline in dispensing of secondary prevention medications over time was steeper in patients with a low income. (3) The extent of a patient's education had no effect on the secondary prevention medications dispensed. (4) Underusage of secondary prevention medications was associated with increased long-term mortality irrespective of income and length of education.

In the present study, dispensing of secondary prevention medications was high early after CABG, regardless of socioeconomic status. At baseline, >90% of the patients were dispensed statins, platelet inhibitors, and β-blockers, and >70% were dispensed RAAS inhibitors, which is comparable to or higher than in most previous reports.[7–11,25] However, at baseline statins and platelet inhibitors were dispensed less in patients with a low income while β-blockers and RAAS inhibitors were dispensed to a higher proportion of patients with short education and a low income. The present study cannot identify the reasons for the lower dispense of statins and antiplatelets in patients with low income. It is plausible that that there is a cost issue for the most vulnerable low-income patients. On the other hand, the costs for statins and most antiplatelets are relatively low in Sweden since generic substances are mainly used. Furthermore, all Swedish citizens are covered by a protection for high medication costs. The maximum annual cost is 2300 SEK (≈240 US$), independently of how many prescriptions that are filled. The higher

Table 2. Descriptive Data of Patient Characteristics by Education Level Among Coronary Artery Bypass Grafting Patients

	All Patients n (%)	Education <10 years n (%)	Education 10 to 12 years n (%)	Education >12 years n (%)	*P* Value
No. of patients	28 448 (100)	11 201 (39.4)	11 720 (41.2)	5527 (19.4)	
Baseline characteristics at time for surgery					
Age, mean (SD)	67.4 (9.2)	69.6 (8.5)	66.0 (9.4)	65.9 (9.0)	<0.0001
Men	22 911 (80.5)	8720 (77.9)	9506 (81.1)	4685 (84.8)	
Women	5537 (19.5)	2481 (22.1)	2214 (18.9)	842 (15.2)	<0.0001
LVEF <50%					
>50%	19 698 (69.2)	7455 (66.6)	8209 (70.0)	4034 (73.0)	
<50%	8507 (29.9)	3654 (32.6)	3407 (29.1)	1446 (26.2)	
Unknown	243 (0.9)	92 (0.8)	104 (0.9)	47 (0.9)	<0.0001
BMI, kg/m^2	n=26 096	n=10 225	n=10 802	n=5069	<0.0001
Mean (SD)	27.4 (4.1)	27.5 (4.1)	27.6 (4.1)	26.9 (3.8)	
Unknown	2352 (8.3)	976 (8.7)	918 (7.8)	458 (8.3)	
eGFR, mL/min per 1.73 m^2					
≥90	7551 (26.5)	2506 (22.4)	3450 (29.4)	1595 (28.9)	
60 to <90	15 421 (54.2)	6174 (55.1)	6184 (52.8)	3063 (55.4)	
30 to <60	4542 (16.0)	2131 (19.0)	1707 (14.6)	704 (12.7)	
15 to <30	275 (1.0)	136 (1.2)	99 (0.8)	40 (0.7)	
<15	195 (0.7)	73 (0.7)	87 (0.7)	35 (0.6)	
Unknown	464 (1.6)	181 (1.6)	193 (1.6)	90 (1.6)	<0.0001
Pulmonary hypertension	202 (0.7)	96 (0.9)	77 (0.7)	29 (0.5)	0.0109
Indication for surgery					
Stable angina	11 538 (40.6)	4348 (38.8)	4816 (41.1)	2374 (43.0)	<0.0001
Unstable angina	7814 (27.5)	3071 (27.4)	3213 (27.4)	1530 (27.7)	0.7534
NSTEMI	7235 (25.4)	3041 (27.1)	2943 (25.1)	1251 (22.6)	<0.0001
STEMI	1861 (6.5)	741 (6.6)	748 (6.4)	372 (6.7)	0.9437
Marital status					
Unmarried	3522 (12.4)	1387 (12.4)	1543 (13.2)	592 (10.7)	
Divorced/widowed	7695 (27.0)	3289 (29.4)	3143 (26.8)	1263 (22.9)	
Married	17 231 (60.6)	6525 (58.3)	7034 (60.0)	3672 (66.4)	<0.0001
Income category					
Q1 (lowest)	5687 (20.0)	2972 (26.5)	2184 (18.6)	531 (9.6)	
Q2	5690 (20.0)	2676 (23.9)	2293 (19.6)	721 (13.0)	
Q3	5691 (20.0)	2409 (21.5)	2406 (20.5)	876 (15.8)	
Q4	5690 (20.0)	1839 (16.4)	2507 (21.4)	1344 (24.3)	
Q5	5690 (20.0)	1305 (11.7)	2330 (19.9)	2055 (37.2)	<0.0001
Medical history 6 mo after surgery at start of follow-up					
Myocardial infarction	15 474 (54.4)	6422 (57.3)	6349 (54.2)	2703 (48.9)	<0.0001
Diabetes mellitus	8576 (30.1)	3541 (31.6)	3589 (30.6)	1446 (26.2)	<0.0001
Hypertension	19 945 (70.1)	8046 (71.8)	8231 (70.2)	3668 (66.4)	<0.0001
Heart failure	5918 (20.8)	2615 (23.3)	2318 (19.8)	985 (17.8)	<0.0001
Atrial fibrillation	7974 (28.0)	3376 (30.1)	3079 (26.3)	1519 (27.5)	<0.0001

Continued

Table 2. Continued

	All Patients n (%)	Education <10 years n (%)	Education 10 to 12 years n (%)	Education >12 years n (%)	*P* Value
Stroke	2501 (8.8)	1070 (9.6)	1010 (8.6)	421 (7.6)	<0.0001
Chronic respiratory disease	2737 (9.6)	1138 (10.2)	1199 (10.2)	400 (7.2)	<0.0001
Renal failure	1394 (4.9)	580 (5.2)	575 (4.9)	239 (4.3)	0.0195
Peripheral vascular disease	2695 (9.5)	1169 (10.4)	1105 (9.4)	421 (7.6)	<0.0001
History of malignancy	3730 (13.1)	1573 (14.0)	1429 (12.2)	728 (13.2)	0.0165
Hyperlipidemia	14 406 (50.6)	5483 (49.0)	6132 (52.3)	2791 (50.5)	0.0037

BMI indicates body mass index; eGFR, estimated glomerular filtration rate (chronic kidney disease epidemiology); LVEF, left ventricular ejection fraction; NSTEMI, non–ST-segment–elevation myocardial infarction; STEMI, ST-segment–elevation myocardial infarction.

dispensing of β-blockers and RAAS inhibitors in patients with short education and a low income is most likely explained by the higher proportion of patients with previous myocardial infarction, reduced left ventricular ejection fraction, and hypertension in these groups (Tables 1 and 2). Interestingly, it has been reported that stroke patients with higher education are less prone to use statins,[26] and low income has been consistently associated with reduced statin use in non-CABG patients with cardiovascular disease.[27,28]

Although the dispensing of secondary prevention medications was satisfactory early after CABG, it became markedly reduced as time went on, especially in patients with a low income. This is problematic, since there have been no studies supporting discontinuation of the medications in relation to the time elapsed since the operation. In fact, in a previous analysis based on the same database as the present study, a cumulative effect on the association between statins, platelet inhibitors, and RAAS inhibitors on the one hand and reduced mortality risk over time on the other was observed.[4]

The lower use of secondary preventive medications in patients with low income is alarming given the explicit association between the use of statins, RAAS inhibitors, and

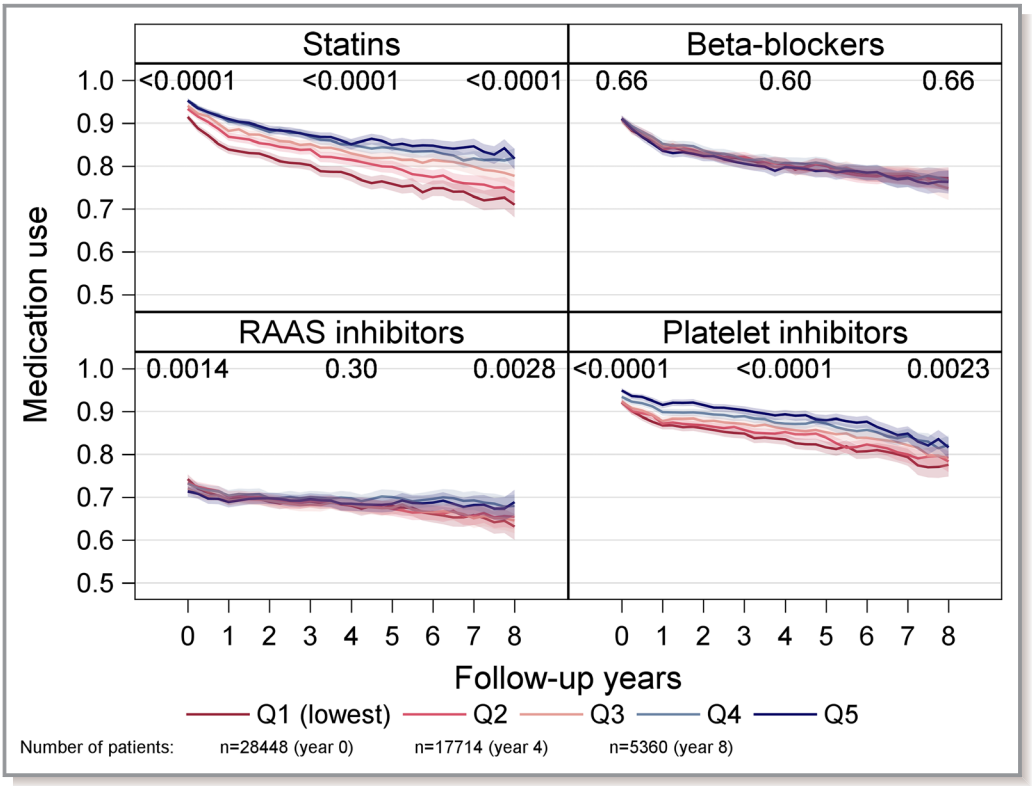

Figure 2. Use of medication over time by income level in coronary artery bypass grafting patients, at baseline, after 4 years and after 8 years. Shaded area represents 95% CIs based on binomial distribution. CABG indicates coronary artery bypass grafting; Q1 to Q5 income quintile (Q1=lowest level); RAAS, renin-angiotensin-aldosterone system.

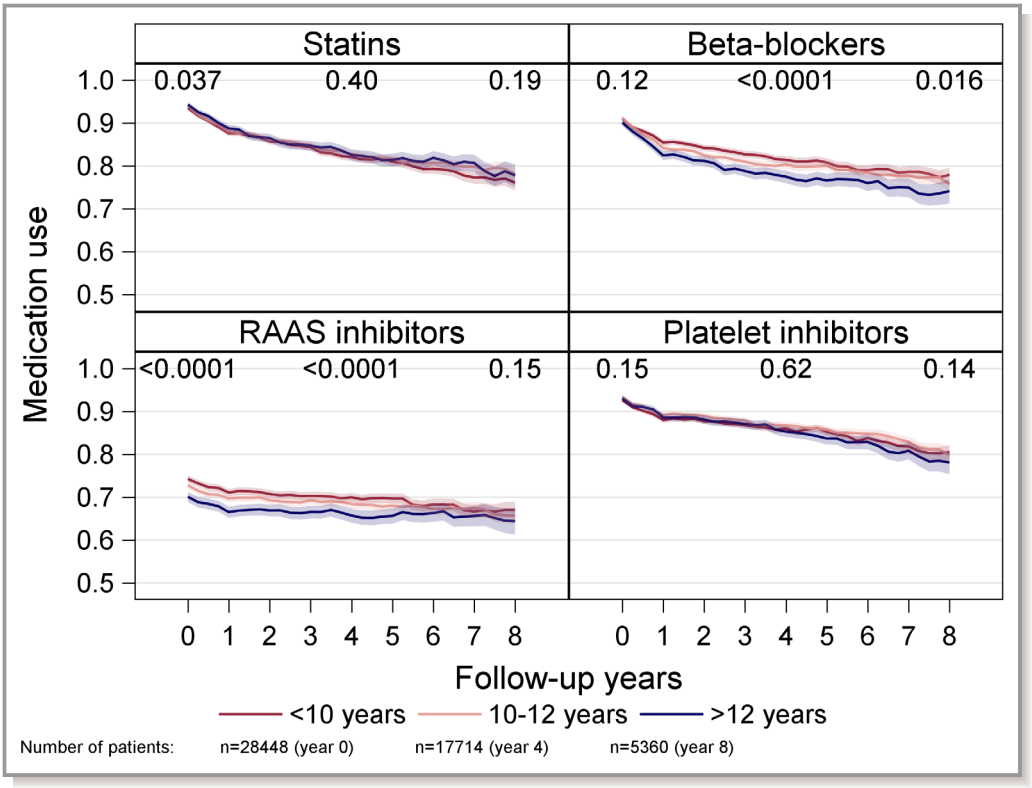

Figure 3. Use of medication over time by education level in coronary artery bypass grafting patients at baseline, after 4 years and after 8 years. Shaded area represents 95% CIs based on binomial distribution. RAAS indicates renin-angiotensin-aldosterone system.

platelet inhibitors on the one hand and reduced long-term mortality risk after CABG in general on the other,[4,7,12] and the increased mortality risk in patients with socioeconomic status disadvantages—as demonstrated in this and previous studies.[13,14] Accordingly, our analyses indicated an increased mortality risk in patients with a low income, because of underusage of secondary prevention medication. However, the difference was limited—that is, only ≈10% of the increased risk in patients with a low income could be explained by the lower dispensing of secondary prevention medications (Table 3). This indicates that other factors that may differ between patients with different incomes—such as smoking habits, diet, level of physical activity, disease progression, and stress—not accounted for in the statistical analyses in the present study, are more important.

The picture is less clear for differences in level of education. While shorter education was evidently associated with increased mortality risk, the medication use at baseline and reduction in medication dispensing over time were comparable in the 3 education groups. Thus, we found no evidence that underusage of secondary medication contributed to the higher long-term mortality in CABG patients with the shortest education.

Our results indicate that the effects of statins and platelet inhibitors were more pronounced in patients with higher income, even though the interaction analyses did not reach statistical significance. This difference is difficult to explain. However, one may speculate that the burden of other risk factors such as smoking and lifestyle factors, not included in the statistical models, may be larger in patients with low income.

The results of the present study suggest that an increased awareness among surgeons, cardiologists and primary care physicians of the importance of maintaining secondary medication in CABG patients with social disadvantages is important. This, potentially in combination with other measures that have been demonstrated to increase adherence to secondary prevention medications, such as a fixed dose combination of cardiovascular medications ("polypill")[29] and full prescription coverage[30] may improve long term outcome after CABG.

The strengths of this study include the large contemporary study population and the complete follow-up on survival. In addition, the Swedish healthcare system—with equal access to medical care for all citizens and a cost ceiling for medical care and medication costs—reduces the risk of bias because of the quality of care provided. On the other hand, the study has the inherent weaknesses of a registry-based retrospective analysis, including selection bias and residual confounders. We could not control for lifestyle variables such as smoking, diet, physical activity, or stress. We used dispensing from a

Table 3. Associations Between Socioeconomic Factors and Long-Term Mortality After Coronary Artery Bypass Grafting With and Without Adjustment for Secondary Prevention Medications

	Model	Comparison	Adjusted Hazard Ratio (95% CI)	*P* Value	Difference After Additionally Adjusting for Secondary Prevention Medication (Model A vs B)
Income	A	Q1 vs Q5	1.54 (1.32–1.79)	<0.0001	…
	B	Q1 vs Q5	1.48 (1.27–1.72)	<0.0001	11.1%
Income	A	Q2 vs Q5	1.39 (1.21–1.59)	<0.0001	…
	B	Q2 vs Q5	1.36 (1.19–1.55)	<0.0001	7.7%
Income	A	Q3 vs Q5	1.20 (1.05–1.37)	0.0089	
	B	Q3 vs Q5	1.20 (1.05–1.37)	0.0086	…
Income	A	Q4 vs Q5	1.25 (1.09–1.43)	0.0018	
	B	Q4 vs Q5	1.25 (1.09–1.44)	0.0013	…
Education	A	<10 vs >12 y	1.21 (1.09–1.34)	0.0004	
	B	<10 vs >12 y	1.24 (1.11–1.37)	<0.0001	…
Education	A	10–12 vs >12 y	1.17 (1.05–1.30)	0.0040	
	B	10–12 vs >12 y	1.18 (1.06–1.31)	0.0029	…

Reference education level= >12 years, Reference income level=Q5 (highest level). Model A: Adjusted for age, sex, body mass index category, diabetes mellitus, hypertension, hyperlipidemia, previous stroke, atrial fibrillation, heart failure, previous myocardial infarction, chronic obstructive pulmonary disease, history of cancer, peripheral arterial disease, pulmonary hypertension, ST-segment–elevation myocardial infarction/non–ST-segment–elevation myocardial infarction/unstable angina as indication for coronary artery bypass grafting, left ventricular ejection fraction categories, chronic kidney disease-stages (Chronic Kidney Disease Epidemiology for estimated glomerular filtration rate), year of surgery, marital status, education (unless main effect variable), and income (unless main effect variable). Model B: Model B additionally adjusted for time-updated secondary prevention (statins, beta blockers, RAAS inhibitors, platelet inhibitors), marital status, education level, and income level.

pharmacy as a measurement of medication use. This measure cannot distinguish whether or not the treating physician has prescribed the medication, or whether or not the patient has chosen not to collect the prescribed medications. Patient adherence to prescribed medications is multifactorial and dependent on factors such as side effects, patients' belief in

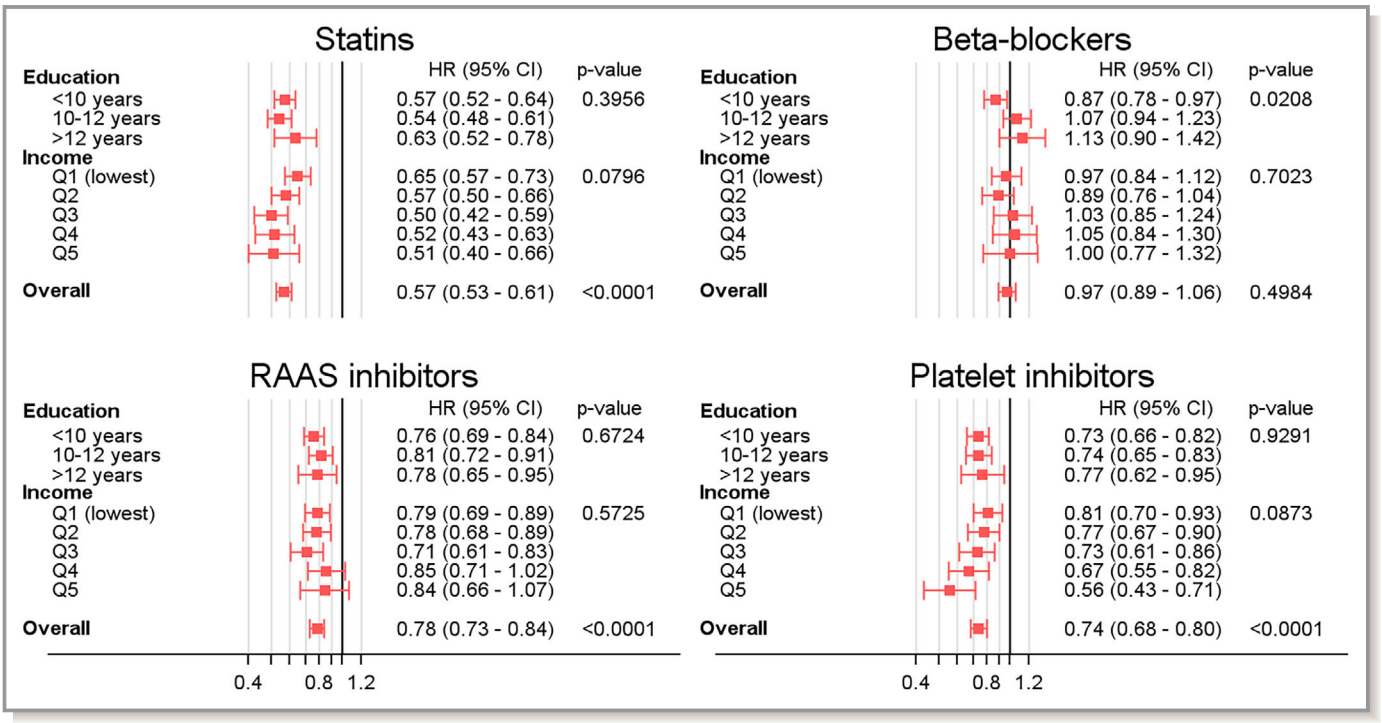

Figure 4. Multi-adjusted effects of time-updated secondary prevention medications on all-cause mortality among coronary artery bypass grafting patients. Hazard ratios for use of time-updated use of medication vs no use of medication (reference) are presented for each socioeconomic status category. HR indicates hazard ratio; Q1 to Q5, income quintiles (Q1=lowest level); RAAS, renin-angiotensin-aldosterone system.

benefit, lack of insight in illness, asymptomatic disease, and costs of medication.[31] There is no consensus as to how drug adherence should be calculated.[32] We used time-updated data on medication dispensing by obtaining individual data from the national Prescribed Drug Registry every third month after discharge. This contrasts with most previous registry-based studies analyzing the effect of secondary prevention medication on outcome after CABG where the medication was registered either only at discharge or at 30 days,[33,34] using long intervals (6 months to several years),[2,10] or using patients' own reports.[35]

Conclusions

Secondary prevention medications are dispensed less often to patients with a low income. Underusage of secondary prevention medications after CABG is associated with increased mortality risk irrespective of income and length of education.

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SUPPLEMENTAL MATERIAL

Table S1. Classification of comorbidities according to International Classification system 9 and 10.

Diagnosis	ICD 9	ICD 10
Myocardial infarction	410	I21.0-I21.4
Diabetes	250	E10-E14
Hypertension	401-405	I10-I15
Heart failure	428	I50 I42-143.8, I11.0, I13.0, I13.2 I50, I25.5
Atrial fibrillation	427D	I48
Stroke	431-434, 436	I61-I64, I69
Chronic respiratory disease	490-496	J40-J47
Peripheral vascular disease	440, 441, 442, 443, 443X, 444, 447	I65-I65.9, I70 -174, I77
Renal failure	584-586	N17-N19
Hyperlipidemia	272.0, 272.01, 272.09	E78
Malignancy	140-208	C00-C97
N-STEMI	410B	I21.4
STEMI	410A	I21.0, I21,1, I21.2, I21.3
Unstable Angina	411B	120.0, I20.1
Stable Angina	413	I22.1, I22.8, I22.9

Table S2. Medication use over time by income level in CABG patients.

Years		Income level					
		Q1 (lowest)	**Q2**	**Q3**	**Q4**	**Q5**	
		n (%)	**n (%)**	**n (%)**	**n (%)**	**(n=114331)**	**p-value**
0 y	**No of patients**	**5687**	**5690**	**5691**	**5690**	**5690**	
	Statins	5201 (91.5)	5313 (93.4)	5355 (94.1)	5422 (95.3)	5419 (95.2)	<.0001
	RAAS-inhibitors	4222 (74.2)	4175 (73.4)	4100 (72.0)	4164 (73.2)	4060 (71.4)	0.0014
	β-blockers	5162 (90.8)	5182 (91.1)	5163 (90.7)	5184 (91.1)	5179 (91.0)	0.6555
	Platelet inhibitors	5239 (92.1)	5254 (92.3)	5254 (92.3)	5313 (93.4)	5400 (94.9)	<.0001
	All four medication groups	3417 (60.1)	3435 (60.4)	3310 (58.2%)	3482 (61.2%)	3453 (60.7)	0.3232
4 y	**No of patients**	**3504**	**3703**	**3542**	**3606**	**3359**	
	Statins	2729 (77.9)	3016 (81.4)	2938 (82.9)	3066 (85.0)	2859 (85.1)	<.0001
	RAAS-inhibitors	2383 (68.0)	2525 (68.2)	2418 (68.3)	2515 (69.7)	2300 (68.5)	0.3026

	β-blockers	2821 (80.5)	2978 (80.4)	2825 (79.8)	2912 (80.8)	2679 (79.8)	0.5951
	Platelet inhibitors	2926 (83.5)	3154 (85.2)	3044 (85.9)	3143 (87.2)	3000 (89.3)	<.0001
	All four medication groups	1515 (43.2)	1641 (44.3)	1554 (43.9)	1715 (47.6)	1569 (46.7)	0.0001
8 y	**No of patients**	**1003**	**1140**	**1089**	**1123**	**1005**	
	Statins	712 (71.0)	842 (73.9)	846 (77.7)	920 (81.9)	821 (81.7)	<.0001
	RAAS-inhibitors	633 (63.1)	746 (65.4)	703 (64.6)	763 (67.9)	692 (68.9)	0.0028
	β-blockers	774 (77.2)	875 (76.8)	815 (74.8)	860 (76.6)	767 (76.3)	0.6583
	Platelet inhibitors	778 (77.6)	893 (78.3)	862 (79.2)	923 (82.2)	820 (81.6)	0.0023
	All four medication groups	341 (34.0)	403 (35.4)	379 (34.8)	455 (40.5)	418 (41.6)	<.0001

Platelet inhibitors: ASA, Clopidogrel, Ticagrelor, Prasugrel. All four medications: Statins, RAAS inhibitors, β-blockers, Platelet inhibitors

Table S3. Medication use over time by education levels among CABG patients.

Year		Educational level <10 years n (%)	10-12 years n (%)	>12 years n (%)	p-value
	No of patients	**11201**	**11720**	**5527**	
0 y	Statins	10476 (93.5)	11023 (94.1)	5211 (94.3)	0.0371
	RAAS-inhibitors	8319 (74.3)	8529 (72.8)	3873 (70.1)	<.0001
	β-blockers	10197 (91.0)	10691 (91.2)	4982 (90.1)	0.1237
	Platelet inhibitors	10374 (92.6)	10944 (93.4)	5142 (93.0)	0.1531
	All four medication groups	6785 (60.6)	7116 (60.7)	3196 (57.8)	0.0034
4 y					
	No of patients	**7205**	**7189**	**3320**	
	Statins	5914 (82.1)	5952 (82.8)	2742 (82.6)	0.3952
	RAAS-inhibitors	5040 (70.0)	4919 (68.4)	2182 (65.7)	<.0001
	β-blockers	5865 (81.4)	5777 (80.4)	2573 (77.5)	<.0001
	Platelet inhibitors	6197 (86.0)	6238 (86.8)	2832 (85.3)	0.6233
	All four medication groups	3320 (46.1)	3264 (45.4)	1410 (42.5)	0.0014
8 y	**No of patients**	**2149**	**2252**	**959**	
	Statins	1636 (76.1)	1759 (78.1)	746 (77.8)	0.1890

RAAS-inhibitors	1440 (67.0)	1479 (65.7)	618 (64.4)	0.1460
β-blockers	1674 (77.9)	1706 (75.8)	711 (74.1)	0.0158
Platelet inhibitors	1730 (80.5)	1797 (79.8)	749 (78.1)	0.1394
All four medication groups	812 (37.8)	841 (37.3)	343 (35.8)	0.3159

Platelet inhibitors: ASA, Clopidogrel, Ticagrelor, Prasugrel. All four medications: Statins, RAAS inhibitors, β-blockers, Platelet inhibitors

Table S4. Adjusted effects of time-updated secondary prevention on all-cause mortality among CABG patients.

		Statins		β-blockers		RAAS inhibitors		Platelet inhibitors	
		HR (95% CI)	p-value*	HR (95% CI)	p-value*	HR (95% CI)	p-value*	HR (95% CI)	p-value*
Education									
Model 1	<10 y	0.50 (0.45-0.55)	0.4481	0.78 (0.70-0.88)	0.0034	0.82 (0.74-0.90)	0.2846	0.55 (0.49-0.61)	0.6989
	10-12 y	0.46 (0.41-0.51)		1.02 (0.89-1.17)		0.92 (0.82-1.03)		0.53 (0.47-0.60)	
	>12 y	0.51 (0.42-0.62)		1.05 (0.84-1.31)		0.86 (0.71-1.03)		0.59 (0.48-0.73)	
Model 2	<10 y	0.52 (0.47-0.57)	0.3902	0.74 (0.66-0.82)	0.0316	0.68 (0.61-0.75)	0.6789	0.65 (0.58-0.73)	0.9448
	10-12 y	0.49 (0.43-0.55)		0.90 (0.78-1.03)		0.72 (0.64-0.81)		0.66 (0.58-0.75)	
	>12 y	0.57 (0.47-0.70)		0.94 (0.75-1.18)		0.69 (0.57-0.83)		0.68 (0.55-0.84)	
Model 3	<10 y	0.56 (0.51-0.62)	0.3795	0.88 (0.78-0.98)	0.0290	0.76 (0.68-0.83)	0.7041	0.73 (0.65-0.81)	0.9084
	10-12 y	0.53 (0.47-0.59)		1.07 (0.93-1.22)		0.80 (0.72-0.90)		0.73 (0.64-0.83)	

	>12 y	0.62 (0.51-0.76)		1.14 (0.91-1.42)		0.77 (0.64-0.93)		0.76 (0.62-0.94)	
Model 4	<10 y	0.57 (0.52-0.64)	0.3956	0.87 (0.78-0.97)	0.0208	0.76 (0.69-0.84)	0.6724	0.73 (0.66-0.82)	0.9291
	10-12 y	0.54 (0.48-0.61)		1.07 (0.94-1.23)		0.81 (0.72-0.91)		0.74 (0.65-0.83)	
	>12 y	0.63 (0.52-0.78)		1.13 (0.90-1.42)		0.78 (0.65-0.95)		0.77 (0.62-0.95)	
Income									
Model 1	Q1 (lowest)	0.55 (0.49-0.63)	0.2519	0.85 (0.74-0.98)	0.2626	0.84 (0.75-0.95)	0.8386	0.60 (0.52-0.68)	0.0460
	Q2	0.50 (0.44-0.57)		0.82 (0.70-0.95)		0.85 (0.75-0.97)		0.60 (0.52-0.70)	
	Q3	0.47 (0.40-0.55)		1.06 (0.88-1.27)		0.86 (0.74-1.00)		0.54 (0.46-0.64)	
	Q4	0.46 (0.3 -0.56)		0.96 (0.77-1.18)		0.90 (0.76-1.08)		0.52 (0.43-0.64)	
	Q5	0.43 (0.34-0.55)		0.93 (0.71-1.22)		0.97 (0.77-1.23)		0.40 (0.31-0.51)	
Model 2	Q1 (lowest)	0.59 (0.52-0.66)	0.1325	0.78 (0.67-0.89)	0.3989	0.68 (0.60-0.77)	0.6693	0.70 (0.61-0.81)	0.1203
	Q2	0.54 (0.47-0.61)		0.75 (0.65-0.87)		0.71 (0.62-0.81)		0.71 (0.61-0.82)	
	Q3	0.47 (0.40-0.55)		0.91 (0.76-1.10)		0.66 (0.56-0.77)		0.67 (0.57-0.80)	
	Q4	0.48 (0.39-0.58)		0.90 (0.72-1.11)		0.76 (0.63-0.91)		0.60 (0.50-0.74)	

	Q5	0.47 (0.37-0.60)		0.88 (0.67-1.15)		0.78 (0.61-0.98)		0.50 (0.39-0.64)	
Model 3	Q1 (lowest)	0.65 (0.57-0.73)	0.0842	0.97 (0.84-1.13)	0.7094	0.78 (0.69-0.89)	0.5781	0.80 (0.70-0.92)	0.0908
	Q2	0.58 (0.50-0.66)		0.90 (0.77-1.04)		0.78 (0.68-0.89)		0.78 (0.67-0.90)	
	Q3	0.50 (0.42-0.59)		1.04 (0.86-1.25)		0.71 (0.61-0.83)		0.73 (0.61-0.86)	
	Q4	0.52 (0.43-0.63)		1.05 (0.85-1.30)		0.86 (0.71-1.03)		0.67 (0.55-0.82)	
	Q5	0.51 (0.40-0.65)		1.00 (0.77-1.32)		0.84 (0.66-1.07)		0.55 (0.43-0.71)	
Model 4	Q1 (lowest)	0.65 (0.57-0.73)	0.0796	0.97 (0.84-1.12)	0.7023	0.79 (0.69-0.89)	0.5725	0.81 (0.70-0.93)	0.0873
	Q2	0.57 (0.50-0.66)		0.89 (0.76-1.04)		0.78 (0.68-0.89)		0.77 (0.67-0.90)	
	Q3	0.50 (0.42-0.59)		1.03 (0.85-1.24)		0.71 (0.61-0.83)		0.73 (0.61-0.86)	
	Q4	0.52 (0.43-0.63)		1.05 (0.84-1.30)		0.85 (0.71-1.02)		0.67 (0.55-0.82)	
	Q5	0.51 (0.40-0.66)		1.00 (0.77-1.32)		0.84 (0.66-1.07)		0.56 (0.43-0.71)	

Model 1, adjusted for age and sex; Model 2, additionally adjusted for BMI (categories; <18.5, 18.5-25, >25-30, >30-35, >35 kg/m^2), diabetes, hypertension, hyperlipidemia, previous stroke, atrial fibrillation, heart failure, previous myocardial infarction, chronic respiratory disease, malignancy, peripheral vascular disease, pulmonary hypertension, STEMI, NSTEMI, unstable angina, left ventricular function (>50%, <50%),

CKD-stages (CKD-EPI for eGFR (ml/min/1.73m^2; ≥90, 60-<90, 30-60, 15-30, <15), year of CABG; Model 3, additionally adjusted for: all other time-updated secondary prevention medications unless main effect variable; Model 4, additionally adjusted for all other SES variables.

*p-value for interaction

Table S5. Adjusted overall effects of time-updated secondary prevention on All-cause mortality among CABG patients.

	Statins		β-blockers		RAAS inhibitors		Platelet inhibitors	
	HR (95% CI)	**p-value***	**HR (95% CI)**	**p-value***	**HR (95% CI)**	**p-value***	**HR (95% CI)**	**p-value***
Model 1	0.48 (0.45 - 0.52)	<.0001	0.91 (0.84 - 0.98)	0.0146	0.86 (0.81 - 0.92)	<.0001	0.55 (0.51 - 0.59)	<.0001
Model 2	0.51 (0.48 - 0.55)	<.0001	0.82 (0.76 - 0.89)	<.0001	0.69 (0.65 - 0.75)	<.0001	0.66 (0.61 - 0.72)	<.0001
Model 3	0.56 (0.52 - 0.60)	<.0001	0.98 (0.90 - 1.06)	0.6053	0.77 (0.72 - 0.83)	<.0001	0.73 (0.68 - 0.80)	<.0001
Model 4	0.57 (0.53 - 0.61)	<.0001	0.97 (0.89 - 1.06)	0.4984	0.78 (0.73 - 0.84)	<.0001	0.74 (0.68 - 0.80)	<.0001

Model 1, adjusted for age and sex; Model 2, additionally adjusted for BMI (categories; <18.5, 18.5-25, >25-30, >30-35, >35 kg/m^2), diabetes, hypertension, hyperlipidemia, previous stroke, atrial fibrillation, heart failure, previous myocardial infarction, chronic respiratory disease, malignancy, peripheral vascular disease, pulmonary hypertension, STEMI, NSTEMI, unstable angina, left ventricular function (>50%, <50%), CKD-stages (CKD-EPI for eGFR (ml/min/1.73m^2; ≥90.60-<90, 30-60, 15-<30, 15), year of CABG; Model 3, additionally adjusted for: all other time-updated secondary prevention medications unless main effect variable; Model 4, additionally adjusted for all other SES variables.

*p-value for interaction