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ORIGINAL RESEARCH

Trends in Clinical Practice and Outcomes After Percutaneous Coronary Intervention of Unprotected Left Main Coronary Artery

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BACKGROUND: The use of percutaneous coronary intervention (PCI) to treat unprotected left main coronary artery disease has expanded rapidly in the past decade. We aimed to describe nationwide trends in clinical practice and outcomes after PCI for left main coronary artery disease.

METHODS AND RESULTS: Patients (n=4085) enrolled in the SCAAR (Swedish Coronary Angiography and Angioplasty Registry) as undergoing PCI for left main coronary artery disease from 2005 to 2017 were included. A count regression model was used to analyze time-related differences in procedural characteristics. The 3-year major adverse cardiovascular and cerebrovascular event rate defined as death, myocardial infarction, stroke, and repeat revascularization was calculated with the Kaplan-Meier estimator and Cox proportional hazard model. The number of annual PCI procedures grew from 121 in 2005 to 589 in 2017 (389%). The increase was greater for men (479%) and individuals with diabetes (500%). Periprocedural complications occurred in 7.9%, decreasing from 10% to 6% during the study period. A major adverse cardiovascular and cerebrovascular event occurred in 35.7% of patients, falling from 45.6% to 23.9% (hazard ratio, 0.56; 95% CI, 0.41–0.78; *P*=0.001). Radial artery access rose from 21.5% to 74.2% and intracoronary diagnostic procedures from 14.0% to 53.3%. Use of bare-metal stents and first-generation drug-eluting stents fell from 19.0% and 71.9%, respectively, to 0, with use of new-generation drug-eluting stents increasing to 95.2%.

CONCLUSIONS: Recent changes in clinical practice relating to PCI for left main coronary artery disease are characterized by a 4-fold rise in procedures conducted, increased use of evidence-based adjunctive treatment strategies, intracoronary diagnostics, newer stents, and more favorable outcomes.

Key Words: PCI ■ unprotected left main coronary artery disease

See Editorial by Mukherjee et al.

Treatment of unprotected left main coronary artery disease with percutaneous coronary intervention (PCI-LMCA) has increased rapidly during the past decade, owing to results of randomized trials showing comparable results of PCI and coronary artery bypass grafting (CABG).[1–6] In addition, improvements have been made in the field of coronary intervention. Stents have been refined by a gradual reduction in strut thickness and superior biocompatibility of the drug-carrying polymer, resulting in a decreased incidence of in-stent restenosis and stent thrombosis.[7] Newer bifurcation techniques and the use of intravascular ultrasound as an adjunct

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CLINICAL PERSPECTIVE

What Is New

- In an all-comer nationwide population, the annual number of percutaneous coronary intervention procedures for unprotected left main coronary artery disease increased by ≈400%, while rates of periprocedural complications and major adverse cardiovascular and cerebrovascular events decreased by ≈40%.

What Are the Clinical Implications?

- These findings support the current guideline recommendations endorsing percutaneous coronary intervention as a treatment option in patients with unprotected left main coronary artery disease.

Nonstandard Abbreviations and Acronyms

CCS	chronic coronary syndrome
EXCEL	Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease
KM	Kaplan-Meier
LE MANS	Acute and Late Outcomes of Unprotected Left Main Stenting in Comparison With Surgical Revascularization
MACCE	Major adverse cardiovascular and cerebrovascular event
NOBLE	Percutaneous Coronary Angioplasty Versus Coronary Artery Bypass Grafting in Treatment of Unprotected Left Main Stenosis: A Prospective, Randomised, Open-Label, Non-inferiority Trial
NSTE-ACS	non–ST-segment–elevation acute coronary syndrome
PCI-LMCA	percutaneous coronary intervention of left main coronary artery disease
PRECOMBAT	Randomized Trial of Stents Versus Bypass Surgery for Left Main Coronary Artery Disease
SCAAR	Swedish Coronary Angiography and Angioplasty Registry
SWEDEHEART	Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies
STE-ACS	ST-segment–elevation acute coronary syndrome
SYNTAX	Percutaneous Coronary Intervention Versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease

diagnostic tool for stent sizing and detection of periprocedural complications are increasingly employed,[8–11] as is antithrombotic therapy with modern P2Y12 inhibitors and improved adherence to secondary prophylactic medications. Recent guidelines endorse PCI-LMCA as a treatment option for patients with low anatomic complexity (Class Ia), while maintaining a class IIb and III recommendation for complex anatomies.[12,13]

We aimed to quantify and describe time-related changes in clinical practice and outcomes associated with PCI-LMCA in a real-world all-comer patient population over a 12-year period using the SCAAR (Swedish Coronary Angiography and Angioplasty Registry).

METHODS

Data Sources

The SCAAR registry is part of the nationwide SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry, a national registry of the Swedish health authorities, receiving no commercial funding. The registry records all coronary angiographies and interventions in Sweden and describes each procedure with up to 250 variables. A unique personal identification number allows for longitudinal follow-up of individuals undergoing a repeat angiography at any hospital in Sweden. Data were linked to the National Population Registry and National Patient Registry by the epidemiologic center of the Swedish National Board of Health and Welfare using the personal identification number to obtain censorship dates and death status for each individual. The authors had full access to the data, and the corresponding author takes responsibility for the analyses performed. The data set is legally restricted because of Swedish patient privacy and secrecy laws and the Uppsala University and Uppsala Clinical Research Center legal department. Data are available upon reasonable request to the Data Protection Officer at Uppsala County Council at landstinget@lul.se.

Study Design

The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines and was approved by the Regional Ethical Review Board in Lund. The SCAAR registry as part of the SWEDEHEART

registry is an anonymized quality registry, and patients are informed about their participation and their right to decline participation. Therefore, no informed consent is legally required for patient inclusion. The primary objective was to describe temporal trends of PCI-LMCA in a nationwide all-comer population with respect to angiographic characteristics; periprocedural treatment; use of PCI techniques such as radial versus femoral arterial access; and complete versus incomplete revascularization, intracoronary diagnostic procedures, periprocedural complications, and long-term outcome. All patients with chronic coronary syndrome (CCS) and acute coronary syndrome (ACS) who underwent unprotected PCI-LMCA from 2005 through 2017 were included. Exclusion criteria and flowchart are presented in Figure S1.

Outcomes

The primary outcome was a major adverse cardiovascular and cerebrovascular event (MACCE) within 3 years, defined as death from any cause, first occurrence myocardial infarction regardless of culprit lesion location, stroke, or repeat revascularization (target lesion revascularization with PCI or new CABG). Secondary outcomes were the independent components of the primary outcome along with in-stent restenosis as identified on a subsequent coronary angiography as stenosis in a previously inserted stent. Vital status was obtained from the National Population Registry. Stroke information was obtained from the National Patient Registry and defined by the *International Classification of Diseases Tenth Revision* (*ICD-10*) codes I60, I61, I62, I63, or I64. Target lesion revascularization was defined as repeat PCI in left main coronary artery disease and was assumed in patients undergoing CABG after PCI-LMCA, with date of surgery obtained from the National Patient Registry. Data of target lesion revascularization treated with PCI, in-stent restenosis, and new myocardial infarction were obtained from SCAAR. Myocardial infarction was defined according to the fourth universal definition and verified by coronary angiography. Records of periprocedural complications were obtained from SCAAR and defined as the composite of all complications including hypotension requiring vasoactive drugs, serious arrhythmia, neurological complications, perforation, cardiac tamponade, complications leading to emergency CABG, death in the catheterization lab, procedure-related death, or any complication documented by the PCI operator occurring at the catheterization lab. All outcomes were ascertained up to April 1, 2018.

Statistical Analysis

A Poisson count regression model was used to assess temporal trends in PCI-LMCA using calendar year as categorical variable and annual number of patients as outcome variable in the entire population as well as in selected subgroups. The subgroups of interest were sex, diabetes, age (<75 years versus ≥75 years), stable CCS, non–ST-segment–elevation acute coronary syndrome (NSTE-ACS), and ST-segment–elevation acute coronary syndrome (STE-ACS). Temporal trends in outcome were analyzed by estimating event rates with the Kaplan-Meier (KM) estimator for each year of admission during the study period and hazard ratios with 95% CIs were estimated with Cox proportional hazard models using year of admission as a categorical, independent variable. Analyses were conducted on complete case data. The proportion of missing values is presented in Table S1. For descriptive purposes, patient characteristics were assessed in 2 time periods, before and after 2013. A 2-sided $P<0.05$ was considered significant. All analyses were performed using STATA MP version 16.1 for Macintosh (StataCorp, College Station, TX).

RESULTS

Patient Characteristics and Temporal Trends

A total of 4085 patients with PCI-LMCA were included in the study. The median age of the study population was 74 years (interquartile range, 66–82), and 1165 (28.5%) patients were women (Table). A total of 948 (23.2%) patients presented with CCS; 2266 (55.5%) with NSTE-ACS, and 871 (21.3%) with STE-ACS (Table). A total of 323 patients (10.4%) presented with cardiogenic shock, which decreased from 19.7% before 2013 to 6.2% in 2013 to 2017. The number of patients with PCI-LMCA grew from 121 in 2005 to 589 in 2017, a 386% increase (Figure 1A and Table S2). The increase was greater in men, from 76 to 440 (479%) compared with 45 to 149 (231%) in women (Figure 1A and Table S2); and in patients with diabetes (500%) compared with those without (379%). The increase was less pronounced in patients presenting with STE-ACS (197%) compared with CCS (485%) and NSTE-ACS (447%). No difference in number of procedures in age groups was found (Figure 1B and Table S2). A total of 2217 (54.3%) patients were discussed at a multidisciplinary heart team meeting, among whom 42.8% were declined from CABG before PCI (Table and Figure 1C). In remaining patients who were not declined from CABG, PCI was deemed the preferred option of revascularization. The proportion of patients declined from CABG decreased from 63.2% in 2005 to 31.5% in 2017, whereas the proportion of patients not declined from CABG but in whom PCI is preferred increased from 36.8% to 68.5%. Isolated left main coronary artery lesions were observed in 33% of patients. PCI-LMCA, together with PCI of either proximal left anterior descending artery or circumflex artery, or both, was performed in 48% of patients (Figure 2).

Table. Patient Characteristics

Baseline table	Total 4085 (100.0%)	Year 2012 or earlier 1584 (38.8%)	Year 2013 or later 2501 (61.2%)
Variable			
Age, y, median (IQR)	74.0 (66.0–82.0)	75.0 (66.0–82.0)	74.0 (67.0–81.0)
Body mass index	25.9 (23.8–28.7)	25.7 (23.7–28.4)	26.1 (23.9–29.0)
Male, n (%)	2920 (71.5)	1111 (70.1)	1809 (72.3)
Female, n (%)	1165 (28.5)	473 (29.9)	692 (27.7)
Smoking status, n (%)			
Never smoked	1695 (46.5)	658 (48.3)	1037 (45.4)
Previous smoker	1445 (39.6)	498 (36.6)	947 (41.5)
Current smoker	505 (13.9)	205 (15.1)	300 (13.1)
Medical history, n (%)			
Diabetes	938 (23.3)	344 (22.3)	594 (23.9)
Hypertension	2847 (71.9)	959 (63.8)	1888 (76.9)
Hyperlipidemia	2481 (62.9)	882 (58.9)	1599 (65.3)
History of myocardial infarction, n (%)	1346 (34.1)	517 (34.6)	829 (33.8)
History of PCI	1166 (28.6)	337 (21.3)	829 (33.1)
Stroke	452 (11.1)	190 (12.0)	262 (10.5)
Chronic heart failure	484 (11.8)	209 (13.2)	275 (11.0)
Renal failure	231 (5.7)	73 (4.6)	158 (6.3)
In-hospital characteristics, median (IQR)			
Creatinine, μmol/L	88.0 (74.0–108.0)	90.0 (75.0–111.0)	87.0 (73.0–107.0)
Estimated glomerular filtration rate–MDRD4, (mL/min per 1.73 m^2	73.3 (56.0–90.0)	71.5 (54.8–87.0)	74.5 (56.9–90.9)
Killip class, n (%)			
Killip I	2458 (79.1)	646 (67.3)	1812 (84.3)
Killip II	222 (7.1)	79 (8.2)	143 (6.7)
Killip III	106 (3.4)	46 (4.8)	60 (2.8)
Killip IV	323 (10.4)	189 (19.7)	134 (6.2)
Indication for angiography, n (%)			
Chronic coronary syndrome	948 (23.2)	306 (19.3)	642 (25.7)
Non–ST-segment–elevation ACS	2266 (55.5)	841 (53.1)	1425 (57.0)
ST-segment–elevation ACS	871 (21.3)	437 (27.6)	434 (17.4)
Office/duty hours—angiography, n (%)			
Planned—office hours	1254 (31.8)	475 (31.1)	779 (32.3)
Acute—office hours	483 (12.2)	272 (17.8)	211 (8.7)
Acute—duty hours	736 (18.7)	325 (21.3)	411 (17.0)
Subacute—office hours	1264 (32.0)	417 (27.3)	847 (35.1)
Subacute—duty hours	207 (5.2)	40 (2.6)	167 (6.9)
Vascular approach, n (%)			
Femoral artery	1500 (36.7)	834 (52.7)	666 (26.6)
Radial artery	2392 (58.6)	685 (43.3)	1707 (68.3)
Combined/other	191 (4.7)	63 (4.0)	128 (5.1)
Treatment before angiography, n (%)			
Clopidogrel/Ticlopidin	1966 (48.2)	1204 (76.2)	762 (30.5)
Prasugrel	49 (1.2)	33 (2.1)	16 (0.6)
Ticagrelor	1350 (33.0)	88 (5.6)	1262 (50.5)
Aspirin	3803 (93.3)	1448 (91.7)	2355 (94.3)
Heparin	3327 (81.4)	1137 (71.8)	2190 (87.6)
Bivalirudin	803 (19.9)	435 (28.2)	368 (14.7)
Glycoprotein IIB/IIIA, within 24 h	448 (11.0)	305 (19.3)	143 (5.7)
Discussed on multidisciplinary heart team	2217 (54.3)	913 (57.6)	1304 (52.1)
Not declined CABG but PCI preferred*	1269 (57.2)	455 (49.8)	814 (62.4)
Declined CABG*	948 (42.8)	458 (50.2)	490 (37.6)
Ad hoc PCI (not discussed)	1471 (36.0)	561 (38.1)	910 (61.9)
Stent diameter, mm	4.0 (3.5–4.0)	3.5 (3.5–4.0)	4.0 (3.5–4.5)
Stent length, mm	16.0 (12.0–23.0)	16.0 (12.0–20.0)	18.0 (14.0–24.0)
Stent pressure inflation, kPa	20.0 (18.0–20.0)	20.0 (18.0–21.0)	20.0 (18.0–20.0)
Number of stents implanted, n (%)			
0	242 (5.9)	126 (8.0)	116 (4.6)
1	1462 (35.8)	626 (39.5)	836 (33.4)
2	1194 (29.2)	464 (29.3)	730 (29.2)
3	636 (15.6)	199 (12.6)	437 (17.5)
≥4	551 (13.5)	169 (10.7)	382 (15.3)

ACS indicates acute coronary syndrome; CABG, coronary artery bypass graft; IQR, interquartile range; MDRD4, Modification of Diet in Renal Disease 4; and PCI, percutaneous coronary intervention.

*Proportion of patients discussed on multidisciplinary heart team.

Periprocedural, Diagnostic, and Therapeutic Procedures

During the study period, treatment with the potent P2Y12 inhibitors ticagrelor/prasugrel became more common and

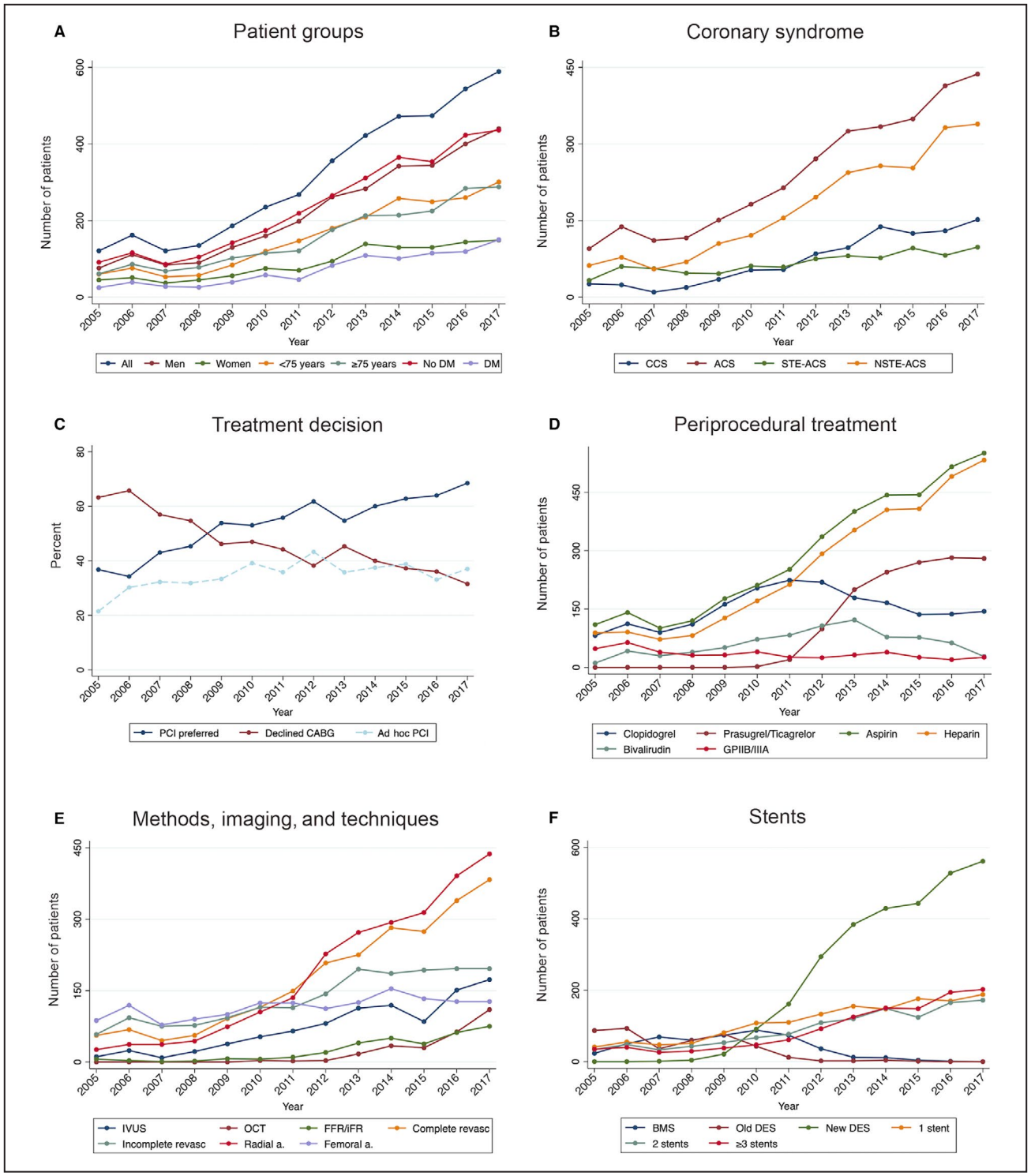

Figure 1. Temporal trends in demographics, clinical presentation, and treatment in patients with LMCA treated with PCI. Temporal trends in PCI-treated unprotected left main coronary artery disease by (**A**) patient characteristics; (**B**) clinical presentation; (**C**) multidisciplinary heart team decision; (**D**) periprocedural treatment; (**E**) PCI techniques and anatomic/physiological diagnostic procedures; and (**F**) stent details. All panels but panel C show absolute number of patients per year. Figure 1C shows the proportion of patients declined from CABG and those that were not declined but in whom PCI was preferred by number of patients discussed at a multidisciplinary heart team meeting, whereas the proportion of patients undergoing ad hoc PCI is presented as a proportion of all PCI-LMCA. BMS indicates bare-metal stent; CCS, chronic coronary syndrome; DES, drug-eluting stent; DM, diabetes mellitus; FFR/iFR, fractional flow reserve/instant wave-free ratio; GPIIB/IIA, glycoprotein IIB/IIA; IVUS, intravascular ultrasonography; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; OCT, optical coherence tomography; PCI-LMCA, percutaneous coronary intervention for unprotected left main coronary artery disease; and STE-ACS, ST-segment–elevation acute coronary syndrome.

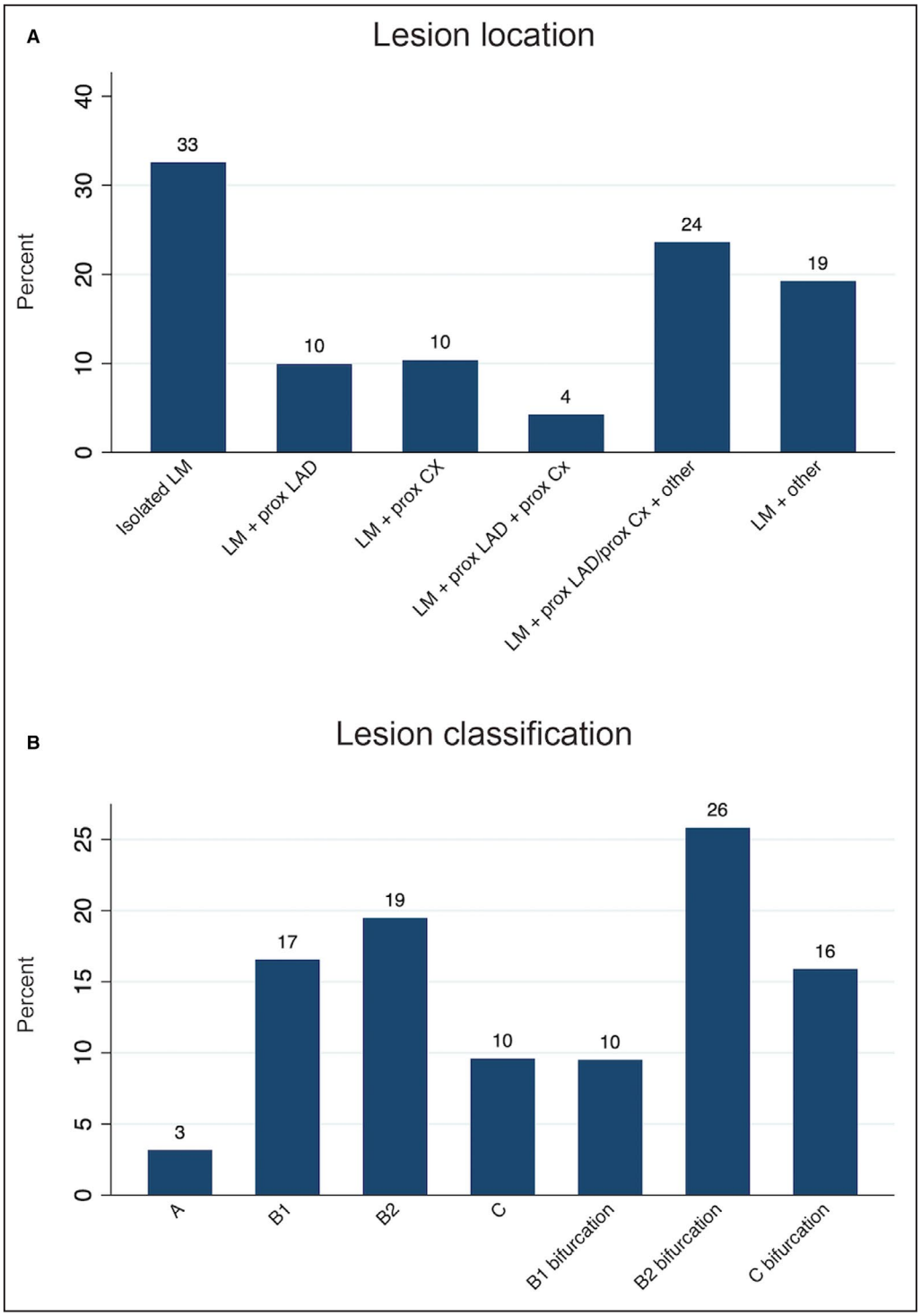

Figure 2. Anatomic pattern of LMCA lesions treated with PCI.
(**A**) Proportion of anatomic locations of coronary artery lesions of the studied cohort and (**B**) their classifications according to American College of Cardiology/American Heart Association. Cx indicates circumflex artery; LAD, left anterior descending artery; LM, left main; LMCA indicates left main coronary artery disease; and PCI, percutaneous coronary intervention.

use of clopidogrel declined (Figure 1D). Periprocedural heparin use increased, while provision of bivalirudin and glycoprotein IIB/IIIA inhibitor remained relatively consistent. The proportion of radial access grew from 21.5% in 2005 to 74.2% in 2017 (Figure 1E). Intracoronary diagnostic procedures (intravascular ultrasound, optical coherence tomography, or instant wave-free ratio/fractional flow reserve) increased from 14.0% in 2005 to 53.3%

in 2017. The use of intravascular ultrasound increased from 9.1% to 29.4%; optical coherence tomography from 1.3% when first introduced in 2010 to 18.7%, and instant wave-free ratio/FFR from 5.0% to 12.8%. Bare-metal stents and first-generation drug-eluting stents, used in 19.0% and 71.9% of cases in 2005, respectively, were phased out by 2017, replaced with new-generation drug-eluting stents (95.2%) (Figure 1F).

Periprocedural Complications and Outcome

Periprocedural complications occurred in 322 (7.9%) patients (Figure 3). The most common complication was death in the catheterization lab, which occurred in 117 (2.9%) patients, with an additional 0.7% procedure-related deaths. The rate of periprocedural complications increased from 10% in 2005 to 16% in 2008 before falling steadily to 6% in 2017 (Figure 3). The 3-year KM event rate for MACCE was 35.7% (1339); death 28.2% (1058); target lesion revascularization with PCI 4.0% (131); new CABG 2.5% (75); stroke 2.2% (66); myocardial infarction 3.5% (110); and in-stent restenosis 1.5% (47) (Figure 4A and Table S3). The MACCE rate was higher in women, 39.3% (429) compared with 34.2% (910) in males (log-rank $P<0.001$) (Figure 4B and Table S3). Patients aged ≥75 years had a significantly higher MACCE event rate of 42.6% (789) compared with 28.8% (550) for <75 (log-rank $P<0.001$) (Figure 4C and Table S3). Similarly, 44.9% (386) of patients with diabetes experienced a MACCE compared with 32.1% (908) of those without diabetes (log-rank $P<0.001$) (Figure 4D and Table S3). The MACCE rate for patients presenting with STE-ACS was 57.9% (487) compared with 34.7% (708) for NSTE-ACS and 17.4% (144) for patients with CCS (log-rank $P<0.001$) (Figure 4E and Table S3). The KM event rate for patients treated with a bare-metal stent was 56.1% (281), 36.9% (153) for old drug-eluting stents, and 30.2% (775) for new-generation drug-eluting stents (log-rank $P<0.001$) (Figure 4F). The KM event rates for 3-year MACCE remained stationary from 2005 to 2010 and fell thereafter from 40.5% (95) in 2010 to 23.9% (114) in 2017 (Figure 5 and Table S4). The overall reduction in MACCE from 2005 to 2017 was 44% (hazard ratio, 0.56; 95% CI, 0.41–0.78; $P=0.001$). Decline in MACCE was observed in all subgroups but was not significant in women (35.8%–32.5%), age ≥75 years (42.8%–29.3%), diabetes (52.9%–29.8%), NSTE-ACS (37.1%–22.6%), or STE-ACS (66.7%–50.2%) (Table S4). Remaining results of the primary outcome are presented in Table S3 and Table S4.

The KM death rate decreased from 36.4% (44) in 2005 to 19.5% (98) in 2017 and was higher in women at 32.2% versus 26.5% in men (Table S3). While the mortality rate decreased significantly for men, from 39.5% in 2005 to 16.8% in 2017, the decline was less pronounced in women, 31.1% to 27.5%. Remaining secondary outcome measures, subgroup analyses, and temporal trends are presented in Table S3 and Table S4. Figure 6 illustrates landmark analysis at 30 days showing that nearly 45% of all MACCE occurred within 30 days of the procedure (570/1339), corresponding to a KM event rate of 14.0%. Figure 7 illustrates outcome by American Heart Association stenosis classification, with MACCE event rates ranging from 28.9% to 44.3%. Lesions classified as C or C bifurcations were associated with worse outcome.

DISCUSSION

In this longitudinal nationwide population-based study, we quantified changes in clinical practice and outcomes in patients with unprotected left main coronary artery disease treated with PCI from 2005 through 2017. The principal finding was a 4-fold increase in PCI-LMCA procedures conducted. This increase was greater in men and in patients with diabetes and was accompanied by a nearly 40% decrease in periprocedural complications and 3-year MACCE risk.

Results of Previous Studies

The use of PCI-LMCA has increased significantly since the introduction of new stents and the publication of the randomized clinical trials PRECOMBAT (Randomized Trial of Stents Versus Bypass Surgery for Left Main Coronary Artery Disease),[1] NOBLE (Percutaneous Coronary Angioplasty Versus Coronary Artery Bypass Grafting in Treatment of Unprotected Left Main Stenosis: A Prospective, Randomised, Open-Label, Non-inferiority Trial),[2] EXCEL (Everolimus-Eluting Stents or Bypass Surgery for Left Main Coronary Artery Disease),[3] SYNTAX (Percutaneous Coronary Intervention Versus Coronary-Artery Bypass Grafting for Severe Coronary Artery Disease),[4] and LE MANS (Acute and Late Outcomes of Unprotected Left Main Stenting in Comparison With Surgical Revascularization).[5] The 5-year MACCE rates found in these trials ranged from 17.5% to 36.9%,[14–17] and the 10-year rate observed in the PRECOMBAT and LE MANS trials ranged from 29.8% to 52.2%.[18,19]

In a real-world setting, we observed a 3-year MACCE event rate of 35.7%, which is higher than that reported in the available randomized studies. This difference can be attributed to several factors; for example, current guidelines recommend PCI as an alternative treatment in patients with low/intermediate lesion complexity. Although the SYNTAX score is not captured in the registry, only 33% of patients in this study exhibited an isolated left main coronary artery

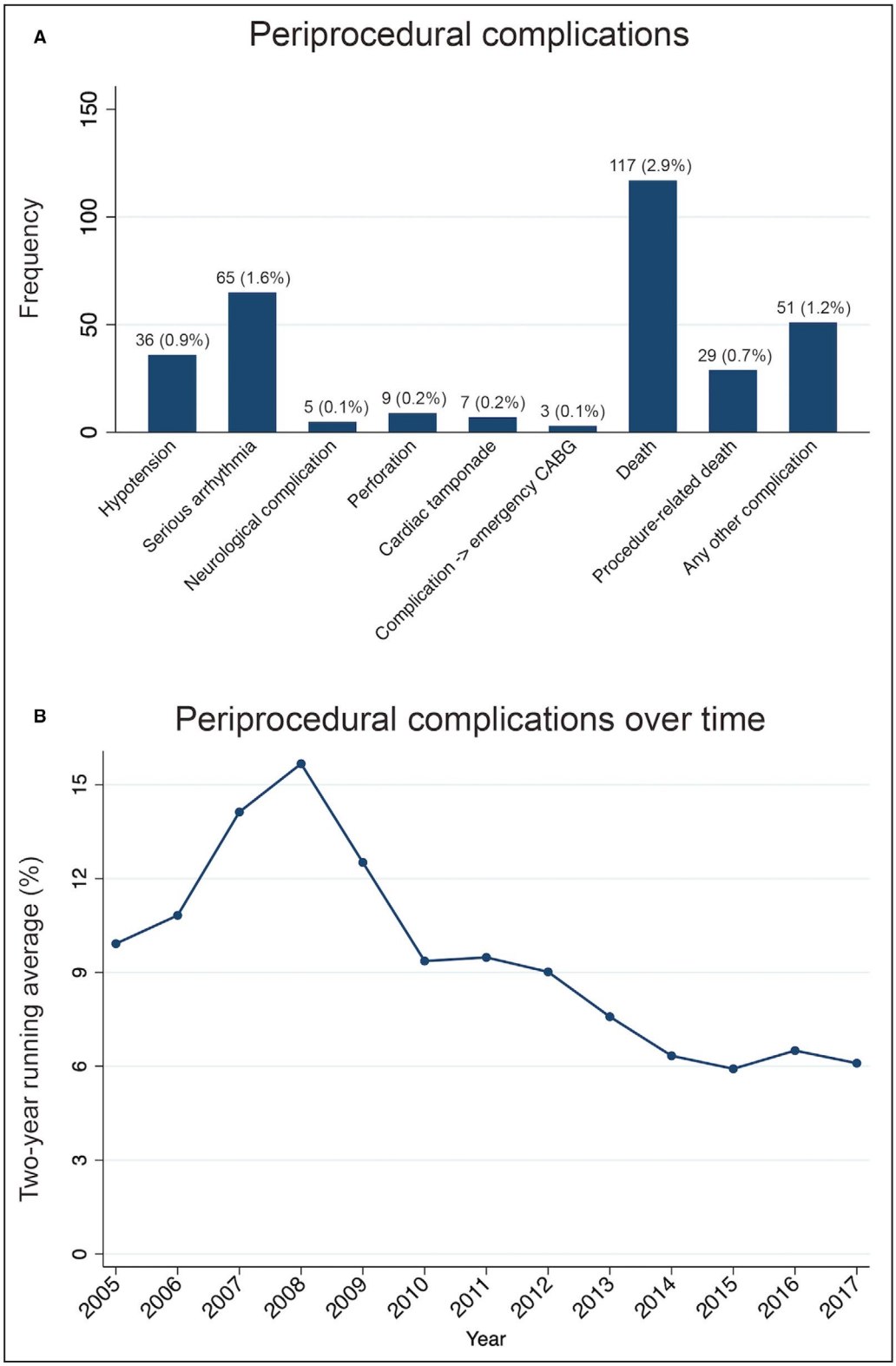

Figure 3. Periprocedural complications in PCI-LMCA.
A, Frequency of periprocedural complications. **B**, Temporal trends in periprocedural complications as 2-year running average. CABG indicates coronary artery bypass grafting; PCI-LMCA, percutaneous coronary intervention for unprotected left main coronary artery disease.

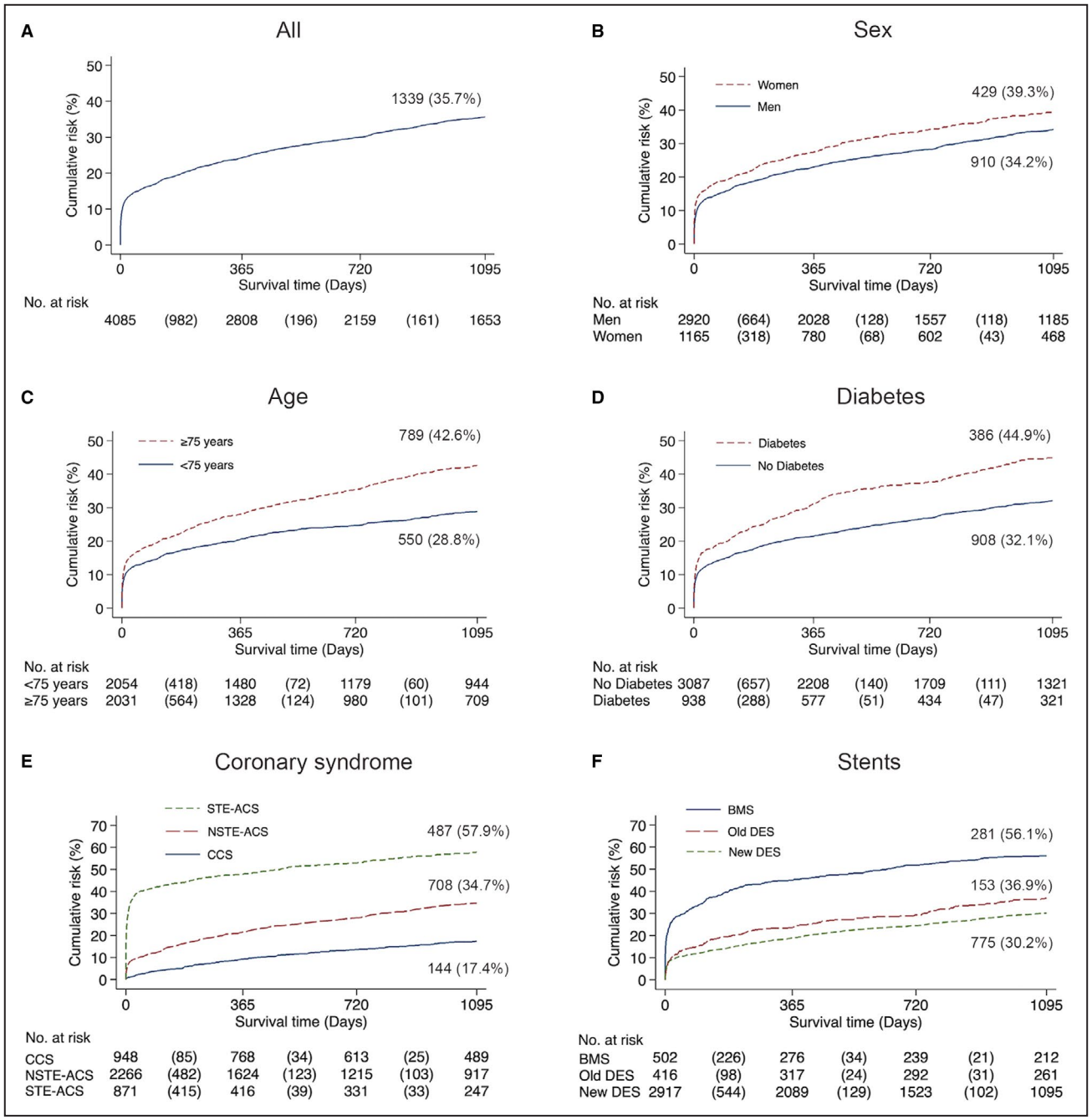

Figure 4. Kaplan-Meier failure estimates of primary end point of PCI-LMCA.
A, Cumulative incidence and Kaplan-Meier event rates of the primary outcome of MACCE within 3 years defined as the first occurrence of all-cause death, repeat revascularization (target lesion revascularization or CABG), stroke, or new myocardial infarction. **B** through **F**, Cumulative incidence of MACCE according to sex, age group, diabetes status, clinical presentation, and stent type. BMS indicates bare-metal stent; CABG, coronary artery bypass grafting; CCS, chronic coronary syndrome; DES, drug-eluting stent; MACCE, major adverse cardiovascular and cerebrovascular event; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; PCI-LMCA, percutaneous coronary intervention for unprotected left main coronary artery disease; and STE-ACS, ST-segment–elevation acute coronary syndrome.

lesion, and nearly 50% presented with a bifurcation lesion or multivessel disease. As we included all consecutively treated patients in Sweden, advanced age and high prevalence of risk factors such as diabetes, hypertension, previous infarct, previous stroke, and previous PCI were common. It is therefore reasonable to assume that a proportion of patients with intermediate and high lesion complexity, likely rejected for surgery because of comorbidity burden, but in whom PCI was considered reasonable, were included. This

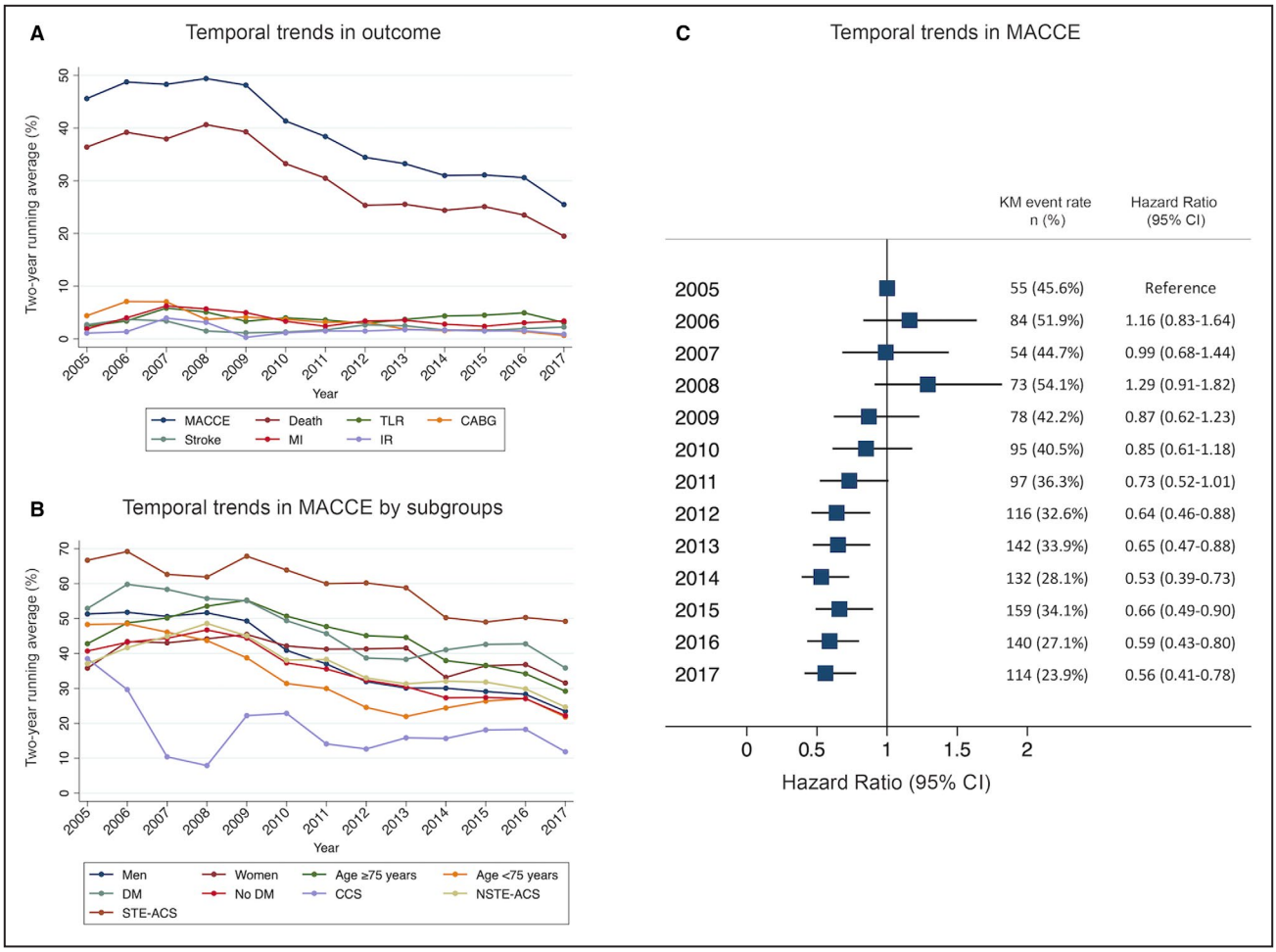

Figure 5. Temporal trends in long-term outcome of PCI-LMCA.
A, Three-year risk of primary and secondary outcomes as 2-year running average of the Kaplan-Meier estimates. **B**, Three-year risk of MACCE over time as 2-year running average of the Kaplan-Meier estimates. **C**, Three-year Kaplan-Meier event rates of the primary outcome together with hazard ratio and 95% CI by year. CCS indicates chronic coronary syndrome; DM, diabetes mellitus; MACCE, major adverse cardiovascular and cerebrovascular event; NSTE-ACS, non–ST-segment–elevation acute coronary syndrome; STE-ACS, ST-segment–elevation acute coronary syndrome; and TLR, target lesion revascularization.

is supported by the high proportion of patients with contraindications to surgery who were declined from CABG by the multidisciplinary heart team. In addition, a high proportion of patients presented with STE-ACS (21.3%) and cardiogenic shock (10.4%), conditions that are associated with markedly higher MACCE rates, likely contributing to the higher rate of adverse outcomes, as patients presenting with these conditions had a MACCE rate approaching 60%.

Observational real-world data of long-term outcome after PCI-LMCA are scarce, with most being limited in sample size or follow-up time. Available studies report a 5-year MACE rate of 34.4% (n=383, age 72.3±9.7 years)[20] and 38.6% (n=421, age 68.4±11.5 years).[21] A large study (n=11 264) reported a 1-year death rate of 11.5%.[9] Lee et al observed a 3-year MACCE rate of 16.0% in 1658 individuals treated with new-generation stents.[22] To the best of our knowledge, the present study is the largest to quantify long-term outcomes after PCI-LMCA and the only conducted in a nationwide population-based setting.

Temporal Trends

Over the course of the study, we observed more PCI-LMCAs conducted, along with a concomitant improvement in outcomes. The more favorable outcomes are multifactorial and relate to progress in several areas associated with an increase in novel evidence-based treatment strategies. The shift to radial artery access has reduced bleeding rates, improving short-term outcome.[23] The more potent P2Y12 blockers prasugrel and ticagrelor as antiplatelet therapy may contribute to the reduced frequency of new myocardial infarction and, together with improved stent design and delivery systems with thinner stent struts, biocompatible polymers,

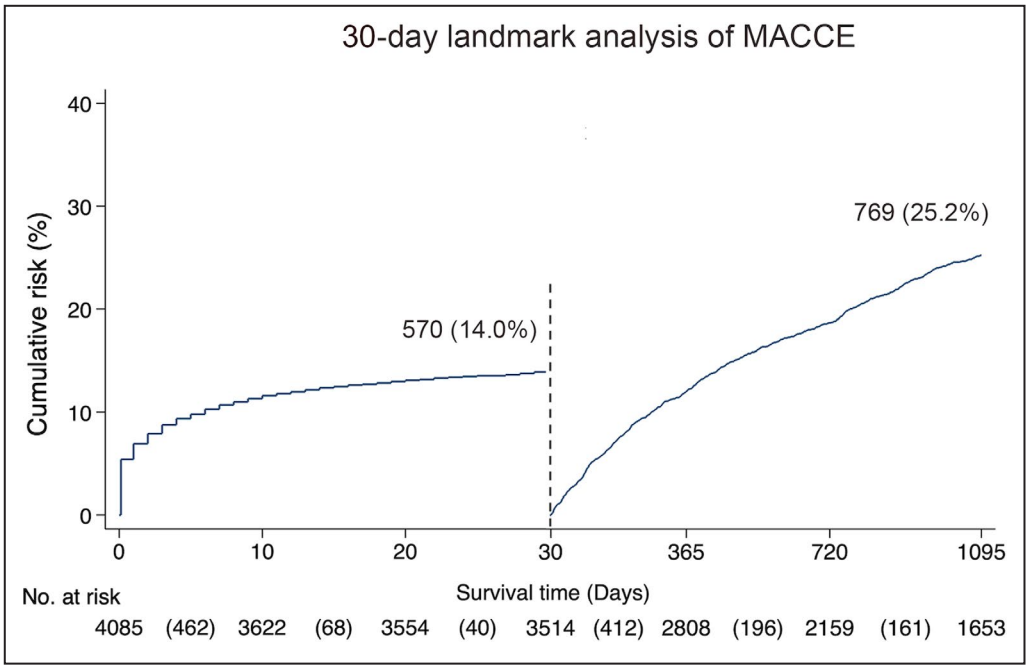

Figure 6. Landmark analysis of MACCE at 30 days after PCI-LMCA.
Cumulative incidence and Kaplan-Meier event rates of the primary outcome major adverse cardiovascular and cerebrovascular event (MACCE) within and after 30 days. PCI-LMCA indicates percutaneous coronary intervention for unprotected left main coronary artery disease.

and more effective drug delivery systems, may explain the low frequency of angiographically verified restenosis and repeat revascularizations.[24–26] The use of intracoronary diagnostic procedures is associated with more accurate stent sizing/apposition and, consequently, better outcomes and reduced incidence of stent thrombosis.[10] Advances in PCI technique (not investigated in this study),[27,28] along with increased skill of PCI operators as a consequence of the expansion in number of procedures performed, could contribute to the reduction in periprocedural complications. Finally, it cannot be ruled out that more favorable outcomes can result from improved risk stratification and selection of patients referred for PCI. Patients treated at the end of the study period tended to have a greater number of comorbidities such as diabetes, hypertension, history of PCI, and renal failure but were generally younger and presented less often with cardiogenic shock, both factors predictive of a better outcome.

Knowledge Gaps

The lack of advancement in outcomes in women and patients of advanced age is of particular concern. Whether this is attributable to more complex lesions, poor risk stratification, or a shorter remaining lifespan warrants further investigation. We observed a significant increase of PCI-LMCA conducted in individuals with diabetes, a subgroup of patients who, in general, benefit more from CABG than from PCI. In this group, the observation of a 50% higher MACCE is worrisome (Table S4, Figure 4 and Figure 5). Whether this may reflect reduced adherence to guideline recommendations or serious comorbidities putting these patients at high or prohibitively high risk in surgery needs to be investigated. Finally, procedures in patients presenting with NSTE-ACS and CCS increased 4- to 5-fold. Only those presenting with CCS showed a convincing trend of improved outcomes during the study. The reason for the static situation in those presenting with ACS warrants investigation. It is possible that patients surviving the procedure succumb to hemodynamic instability (all patients with cardiogenic shock presented with ACS) or, high frailty attributable to more advanced age (median, 76.0 years versus 70.5 years), increasing risk of major complications such as bleeding.

Limitations

We acknowledge some important limitations. The SCAAR does not record SYNTAX scores. Instead, the description of coronary lesions relies on a simple Composite Autonomic Severity Score diagram that records the degree of stenosis and lesion complexity. Lesions were reported as requiring treatment with PCI, bifurcations, and engagement of proximal segments of the left anterior descending artery and circumflex artery. The inability to accurately capture the SYNTAX score in our study, degree of

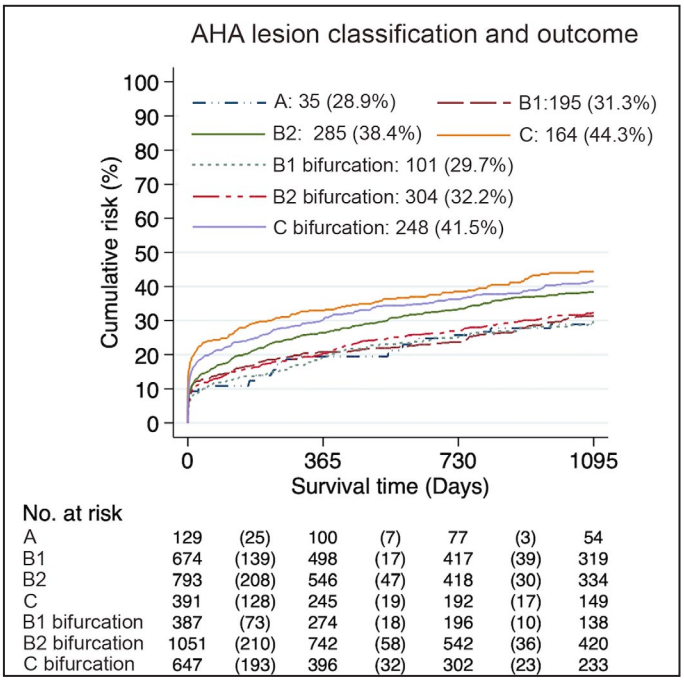

Figure 7. Outcome according to American Heart Association (AHA) lesion complexity.
Lesions classified as C or C bifurcation according to the American Heart Association lesion classification were associated with highest incidence of MACCE within 3 years. MACCE indicates major adverse cardiovascular and cerebrovascular event.

calcification, and Medina classification renders our registry study difficult to directly compare to randomized controlled trials and registry studies using these definitions. In addition, the lack of a SYNTAX score makes it difficult to assess exact reason why PCI was performed as opposed to CABG. Finally, our scope was to investigate temporal trends in patients with PCI-LMCA; hence, patients revascularized with CABG were not included in the analysis. Studies assessing temporal trends in revascularization with CABG could provide further insight into a possible shift in revascularization strategy with respect to patients with left main coronary artery treated with PCI.

CONCLUSIONS

The years 2005 through 2017 saw a 4-fold expansion in PCI-LMCA procedures conducted with an increase in implementation of evidence-based treatment strategies including use of newer stents, recently developed anatomic and physiological diagnostic procedures, and advanced adjunctive pharmacological treatment, accompanied by a concomitant decline in periprocedural complications and improved long-term outcome.

ARTICLE INFORMATION

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Supplemental Material

Tables S1–S5
Figure S1

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Supplemental Material

Table S1. Missing values.

Missing values.

Variable	
Age (years), median (IQR)	0 (0.0%)
Body Mass Index	791 (19.4%)
Men	0 (0.0%)
Women	0 (0.0%)
Smoking status	
Never smoked	440 (10.8%)
Previous-smoker	440 (10.8%)
Current smoker	440 (10.8%)
Past medical history	
Diabetes	60 (1.5%)
Hypertension	126 (3.1%)
Hyperlipidemia	140 (3.4%)
History of myocardial infarction	140 (3.4%)
History of PCI	2 (0.0%)
Stroke	0 (0.0%)
Chronic heart failure	0 (0.0%)
Renal failure	0 (0.0%)
In-hospital Characteristics	
Creatinine (µmol/L)	1067 (26.1%)
Estimated glomerular filtration rate - MDRD4 (mL/min/1.73m2), median (IQR)	1067 (26.1%)
Killip class	
Killip I	976 (23.9%)
Killip II	976 (23.9%)
Killip III	976 (23.9%)
Killip IV	976 (23.9%)
Indication for angio	
Chronic coronary syndrome	0 (0.0%)
Non-ST-elevation ACS	0 (0.0%)
ST-elevation ACS	0 (0.0%)
Office/duty hours - angio	
Planned - Office hours	141 (3.5%)
Acute - Office hours	141 (3.5%)
Acute - Duty hours	141 (3.5%)
Subacute - Office hours	141 (3.5%)
Subacute - Duty hours	141 (3.5%)
Vascular approach	
Femoral artery	2 (0.0%)
Radial artery	2 (0.0%)
Combined/other	2 (0.0%)
Treatment before angiography	
Clopidogrel/Ticlopidin	6 (0.1%)
Prasugrel	0 (0.0%)
Ticagrelor	0 (0.0%)
Aspirin	9 (0.2%)
Heparin	0 (0.0%)
Bivalirudin	43 (1.1%)
GPIIB/IIIA (within 24h)	0 (0.0%)
Stent diameter (mm)	154 (3.8%)
Stent length (mm)	242 (5.9%)
Stent pressure inflation (kPa)	439 (10.7%)
Number of stents implanted	

0	0 (0.0%)
1	0 (0.0%)
2	0 (0.0%)
3	0 (0.0%)
≥4	0 (0.0%)

ACS = acute coronary syndrome; GPIIB/IIIA = glycoprotein IIB/IIIA.

Table S2. Temporal trends in PCI treated LM lesions

Patients		Nr of patients	IRR (95% CI)	P-value
	2005	121	Reference	
	2006	162	1.34 (1.06-1.69)	0.015
	2007	121	1.00 (0.78-1.29)	1.000
	2008	135	1.12 (0.87-1.43)	0.382
	2009	186	1.54 (1.22-1.93)	<0.001
	2010	235	1.94 (1.56-2.42)	<0.001
	2011	268	2.21 (1.79-2.75)	<0.001
	2012	356	2.94 (2.39-3.62)	<0.001
	2013	422	3.49 (2.85-4.27)	<0.001
	2014	472	3.90 (3.19-4.76)	<0.001
	2015	474	3.92 (3.21-4.78)	<0.001
	2016	544	4.50 (3.69-5.47)	<0.001
	2017	589	4.87 (4.00-5.92)	<0.001
Men				
	2005	76	Reference	
	2006	111	1.46 (1.09-1.96)	0.011
	2007	84	1.11 (0.81-1.51)	0.527
	2008	90	1.18 (0.87-1.61)	0.278
	2009	130	1.71 (1.29-2.27)	<0.001
	2010	160	2.11 (1.60-2.77)	<0.001
	2011	198	2.61 (2.00-3.39)	<0.001
	2012	262	3.45 (2.67-4.45)	<0.001
	2013	283	3.72 (2.89-4.80)	<0.001
	2014	342	4.50 (3.51-5.77)	<0.001
	2015	344	4.53 (3.53-5.80)	<0.001
	2016	400	5.26 (4.12-6.73)	<0.001
	2017	440	5.79 (4.54-7.39)	<0.001
Women				
	2005	45	Reference	
	2006	51	1.13 (0.76-1.69)	0.541
	2007	37	0.82 (0.53-1.27)	0.378
	2008	45	1.00 (0.66-1.51)	1.000
	2009	56	1.24 (0.84-1.84)	0.275
	2010	75	1.67 (1.15-2.41)	0.007
	2011	70	1.56 (1.07-2.26)	0.021
	2012	94	2.09 (1.46-2.98)	<0.001
	2013	139	3.09 (2.21-4.32)	<0.001
	2014	130	2.89 (2.06-4.05)	<0.001
	2015	130	2.89 (2.06-4.05)	<0.001
	2016	144	3.20 (2.29-4.47)	<0.001
	2017	149	3.31 (2.37-4.62)	<0.001
Age ≥75 years				
	2005	61	Reference	
	2006	86	1.41 (1.02-1.96)	0.040
	2007	68	1.11 (0.79-1.58)	0.538
	2008	78	1.28 (0.91-1.79)	0.150
	2009	102	1.67 (1.22-2.30)	0.001
	2010	115	1.89 (1.38-2.57)	<0.001
	2011	121	1.98 (1.46-2.70)	<0.001
	2012	176	2.89 (2.16-3.86)	<0.001
	2013	213	3.49 (2.63-4.64)	<0.001
	2014	214	3.51 (2.64-4.66)	<0.001
	2015	225	3.69 (2.78-4.89)	<0.001

	2016	284	4.66 (3.53-6.14)	<0.001
	2017	288	4.72 (3.58-6.22)	<0.001
Age <75 years				
	2005	60	Reference	
	2006	76	1.27 (0.90-1.78)	0.171
	2007	53	0.88 (0.61-1.28)	0.510
	2008	57	0.95 (0.66-1.37)	0.782
	2009	84	1.40 (1.01-1.95)	0.047
	2010	120	2.00 (1.47-2.73)	<0.001
	2011	147	2.45 (1.81-3.31)	<0.001
	2012	180	3.00 (2.24-4.02)	<0.001
	2013	209	3.48 (2.61-4.64)	<0.001
	2014	258	4.30 (3.25-5.69)	<0.001
	2015	249	4.15 (3.13-5.50)	<0.001
	2016	260	4.33 (3.27-5.74)	<0.001
	2017	301	5.02 (3.80-6.62)	<0.001
Diabetes Mellitus				
	2005	25	Reference	
	2006	39	1.56 (0.94-2.58)	0.083
	2007	28	1.12 (0.65-1.92)	0.680
	2008	26	1.04 (0.60-1.80)	0.889
	2009	39	1.56 (0.94-2.58)	0.083
	2010	58	2.32 (1.45-3.71)	<0.001
	2011	46	1.84 (1.13-2.99)	0.014
	2012	83	3.32 (2.12-5.19)	<0.001
	2013	109	4.36 (2.82-6.73)	<0.001
	2014	101	4.04 (2.61-6.26)	<0.001
	2015	115	4.60 (2.98-7.09)	<0.001
	2016	119	4.76 (3.09-7.33)	<0.001
	2017	150	6.00 (3.93-9.16)	<0.001
No Diabetes Mellitus				
	2005	91	Reference	
	2006	116	1.27 (0.97-1.68)	0.083
	2007	86	0.95 (0.70-1.27)	0.707
	2008	105	1.15 (0.87-1.53)	0.318
	2009	142	1.56 (1.20-2.03)	0.001
	2010	174	1.91 (1.48-2.46)	<0.001
	2011	219	2.41 (1.88-3.07)	<0.001
	2012	265	2.91 (2.29-3.70)	<0.001
	2013	311	3.42 (2.71-4.32)	<0.001
	2014	365	4.01 (3.19-5.05)	<0.001
	2015	354	3.89 (3.09-4.90)	<0.001
	2016	423	4.65 (3.71-5.83)	<0.001
	2017	436	4.79 (3.82-6.01)	<0.001
CCS				
	2005	26	Reference	
	2006	24	0.92 (0.53-1.61)	0.777
	2007	10	0.38 (0.19-0.80)	0.010
	2008	19	0.73 (0.40-1.32)	0.299
	2009	35	1.35 (0.81-2.24)	0.251
	2010	53	2.04 (1.27-3.26)	0.003
	2011	54	2.08 (1.30-3.32)	0.002
	2012	85	3.27 (2.11-5.07)	<0.001
	2013	97	3.73 (2.42-5.75)	<0.001
	2014	138	5.31 (3.49-8.07)	<0.001
	2015	125	4.81 (3.15-7.34)	<0.001
	2016	130	5.00 (3.28-7.62)	<0.001

	2017	152	5.85 (3.86-8.86)	<0.001
NSTE-ACS				
	2005	62	Reference	
	2006	78	1.26 (0.90-1.76)	0.177
	2007	55	0.89 (0.62-1.28)	0.518
	2008	69	1.11 (0.79-1.57)	0.541
	2009	105	1.69 (1.24-2.32)	0.001
	2010	121	1.95 (1.44-2.65)	<0.001
	2011	155	2.50 (1.86-3.36)	<0.001
	2012	196	3.16 (2.38-4.21)	<0.001
	2013	244	3.94 (2.98-5.20)	<0.001
	2014	257	4.15 (3.14-5.47)	<0.001
	2015	253	4.08 (3.09-5.39)	<0.001
	2016	332	5.35 (4.08-7.02)	<0.001
	2017	339	5.47 (4.17-7.17)	<0.001
STE-ACS				
	2005	33	Reference	
	2006	60	1.82 (1.19-2.78)	0.006
	2007	56	1.70 (1.10-2.61)	0.016
	2008	47	1.42 (0.91-2.22)	0.119
	2009	46	1.39 (0.89-2.18)	0.145
	2010	61	1.85 (1.21-2.82)	0.004
	2011	59	1.79 (1.17-2.74)	0.008
	2012	75	2.27 (1.51-3.42)	<0.001
	2013	81	2.45 (1.64-3.68)	<0.001
	2014	77	2.33 (1.55-3.51)	<0.001
	2015	96	2.91 (1.96-4.32)	<0.001
	2016	82	2.48 (1.66-3.72)	<0.001
	2017	98	2.97 (2.00-4.41)	<0.001

ACS = acute coronary syndrome; CCS = chronic coronary syndrome.

Table S3. Kaplan-Meier event rates for primary and secondary outcome.

Subgroups	Number of patients	Major adverse cardiovascular and cerebrovascular events	Death	Target Lesion Revascularization	Coronary artery bypass graft	Stroke	Myocardial Infarction	In-stent restenosis
All patients	4085	1339 (35.7%)	1058 (28.2%)	131 (4.0%)	75 (2.5%)	66 (2.2%)	110 (3.5%)	47 (1.5%)
Men	2920	910 (34.2%)	707 (26.5%)	95 (4.0%)	57 (2.6%)	39 (1.9%)	78 (3.4%)	34 (1.5%)
Women	1165	429 (39.3%)	351 (32.2%)	36 (3.9%)	18 (2.2%)	27 (3.0%)	32 (3.6%)	13 (1.5%)
Age ≥75 years	2031	789 (42.6%)	668 (36.2%)	57 (3.6%)	20 (1.3%)	45 (3.2%)	59 (4.0%)	22 (1.4%)
Age <75 years	2054	550 (28.8%)	390 (20.3%)	74 (4.4%)	55 (3.5%)	21 (1.3%)	51 (3.1%)	25 (1.5%)
Diabetes Mellitus	938	386 (44.9%)	320 (37.2%)	38 (5.5%)	17 (2.7%)	16 (2.3%)	36 (5.5%)	16 (2.3%)
No Diabetes Mellitus	3087	908 (32.1%)	695 (24.5%)	93 (3.6%)	57 (2.4%)	48 (2.1%)	74 (3.0%)	31 (1.3%)
CCS	948	144 (17.4%)	90 (11.2%)	34 (4.0%)	20 (2.5%)	11 (1.4%)	0 (0.0%)	12 (1.4%)
NSTE-ACS	2266	708 (34.7%)	551 (27.1%)	76 (4.0%)	32 (1.8%)	37 (2.2%)	74 (4.0%)	32 (1.8%)
STE-ACS	871	487 (57.9%)	417 (49.2%)	21 (3.8%)	23 (4.7%)	18 (3.3%)	36 (7.1%)	3 (0.6%)

ACS = acute coronary syndrome; CCS = chronic coronary syndrome.

Table S4. Temporal trends in primary outcome major adverse cardiovascular and cerebrovascular events.

All patients	Nr of patients	KM event-rate n (%)	Hazard Ratio (95% CI)	P-value
2005	121	55 (45.6%)	Reference	
2006	162	84 (51.9%)	1.16 (0.83-1.64)	0.382
2007	121	54 (44.7%)	0.99 (0.68-1.44)	0.959
2008	135	73 (54.1%)	1.29 (0.91-1.82)	0.159
2009	186	78 (42.2%)	0.87 (0.62-1.23)	0.428
2010	235	95 (40.5%)	0.85 (0.61-1.18)	0.333
2011	268	97 (36.3%)	0.73 (0.52-1.01)	0.059
2012	356	116 (32.6%)	0.64 (0.46-0.88)	0.006
2013	422	142 (33.9%)	0.65 (0.47-0.88)	0.006
2014	472	132 (28.1%)	0.53 (0.39-0.73)	0.000
2015	474	159 (34.1%)	0.66 (0.49-0.90)	0.009
2016	544	140 (27.1%)	0.59 (0.43-0.80)	0.001
2017	589	114 (23.9%)	0.56 (0.41-0.78)	0.001
Men				
2005	76	39 (51.3%)	Reference	
2006	111	58 (52.3%)	0.99 (0.66-1.48)	0.949
2007	84	41 (48.9%)	0.95 (0.61-1.47)	0.805
2008	90	49 (54.4%)	1.05 (0.69-1.60)	0.825
2009	130	57 (44.2%)	0.79 (0.52-1.18)	0.245
2010	160	60 (37.6%)	0.64 (0.43-0.96)	0.030
2011	198	72 (36.4%)	0.62 (0.42-0.91)	0.015
2012	262	72 (27.5%)	0.43 (0.29-0.64)	0.000
2013	283	92 (32.7%)	0.52 (0.36-0.75)	0.001
2014	342	93 (27.4%)	0.43 (0.30-0.63)	0.000
2015	344	104 (30.8%)	0.49 (0.34-0.71)	0.000
2016	400	98 (25.8%)	0.47 (0.32-0.68)	0.000
2017	440	75 (21.1%)	0.41 (0.28-0.61)	0.000
Women				
2005	45	16 (35.8%)	Reference	
2006	51	26 (51.0%)	1.58 (0.85-2.94)	0.151
2007	37	13 (35.1%)	1.00 (0.48-2.07)	0.992
2008	45	24 (53.3%)	1.89 (1.01-3.56)	0.048
2009	56	21 (37.6%)	1.02 (0.53-1.95)	0.962
2010	75	35 (46.7%)	1.46 (0.81-2.64)	0.209
2011	70	25 (35.8%)	0.98 (0.52-1.83)	0.943
2012	94	44 (46.8%)	1.44 (0.81-2.56)	0.208
2013	139	50 (36.3%)	0.99 (0.56-1.74)	0.967
2014	130	39 (30.0%)	0.79 (0.44-1.42)	0.436
2015	130	55 (43.0%)	1.22 (0.70-2.14)	0.478
2016	144	42 (30.6%)	0.92 (0.52-1.64)	0.778
2017	149	39 (32.5%)	1.11 (0.62-2.00)	0.724
Age ≥75 years				
2005	61	26 (42.8%)	Reference	
2006	86	47 (54.7%)	1.33 (0.82-2.15)	0.243
2007	68	31 (45.6%)	1.10 (0.65-1.85)	0.730
2008	78	48 (61.5%)	1.65 (1.02-2.66)	0.040
2009	102	50 (49.0%)	1.13 (0.70-1.81)	0.623
2010	115	60 (52.4%)	1.28 (0.81-2.03)	0.292
2011	121	52 (43.0%)	0.96 (0.60-1.53)	0.858
2012	176	83 (47.2%)	1.09 (0.70-1.70)	0.694
2013	213	89 (42.0%)	0.91 (0.59-1.42)	0.688
2014	214	72 (33.9%)	0.72 (0.46-1.13)	0.151
2015	225	87 (39.3%)	0.84 (0.54-1.31)	0.447

2016	284	77 (29.1%)	0.69 (0.44-1.08)	0.104
2017	288	67 (29.3%)	0.79 (0.50-1.24)	0.301
Age <75 years				
2005	60	29 (48.3%)	Reference	
2006	76	37 (48.7%)	1.02 (0.63-1.66)	0.941
2007	53	23 (43.5%)	0.90 (0.52-1.55)	0.696
2008	57	25 (43.9%)	0.93 (0.54-1.59)	0.790
2009	84	28 (33.6%)	0.63 (0.37-1.06)	0.080
2010	120	35 (29.2%)	0.54 (0.33-0.88)	0.013
2011	147	45 (30.7%)	0.56 (0.35-0.90)	0.016
2012	180	33 (18.4%)	0.31 (0.19-0.52)	0.000
2013	209	53 (25.5%)	0.44 (0.28-0.69)	0.000
2014	258	60 (23.3%)	0.40 (0.26-0.62)	0.000
2015	249	72 (29.4%)	0.53 (0.34-0.81)	0.004
2016	260	63 (24.8%)	0.50 (0.32-0.77)	0.002
2017	301	47 (18.8%)	0.40 (0.25-0.63)	0.000
Diabetes Mellitus				
2005	25	13 (52.9%)	Reference	
2006	39	26 (66.7%)	1.54 (0.79-3.00)	0.202
2007	28	14 (50.0%)	0.92 (0.43-1.95)	0.824
2008	26	16 (61.5%)	1.30 (0.62-2.69)	0.489
2009	39	19 (48.7%)	0.90 (0.45-1.82)	0.772
2010	58	29 (50.1%)	0.97 (0.50-1.86)	0.924
2011	46	19 (41.3%)	0.77 (0.38-1.56)	0.469
2012	83	30 (36.1%)	0.62 (0.32-1.18)	0.144
2013	109	44 (40.5%)	0.73 (0.39-1.35)	0.315
2014	101	42 (41.6%)	0.75 (0.40-1.39)	0.356
2015	115	49 (43.6%)	0.80 (0.44-1.48)	0.485
2016	119	48 (41.9%)	0.89 (0.48-1.65)	0.716
2017	150	37 (29.8%)	0.68 (0.36-1.28)	0.229
No Diabetes Mellitus				
2005	91	37 (40.7%)	Reference	
2006	116	53 (45.7%)	1.12 (0.74-1.70)	0.599
2007	86	37 (43.0%)	1.12 (0.71-1.77)	0.613
2008	105	53 (50.5%)	1.36 (0.89-2.06)	0.155
2009	142	54 (38.3%)	0.89 (0.59-1.36)	0.602
2010	174	63 (36.3%)	0.86 (0.57-1.29)	0.465
2011	219	76 (34.8%)	0.80 (0.54-1.18)	0.259
2012	265	79 (29.9%)	0.67 (0.46-0.99)	0.046
2013	311	96 (31.1%)	0.68 (0.46-0.99)	0.042
2014	365	85 (23.5%)	0.50 (0.34-0.74)	0.000
2015	354	109 (31.3%)	0.70 (0.48-1.01)	0.056
2016	423	91 (22.8%)	0.56 (0.38-0.82)	0.003
2017	436	75 (21.6%)	0.58 (0.39-0.86)	0.007
CCS				
2005	26	10 (38.5%)	Reference	
2006	24	5 (20.8%)	0.50 (0.17-1.46)	0.202
2007	10	0 (0.0%)	0.00 (0.00-)	1.000
2008	19	3 (15.8%)	0.37 (0.10-1.35)	0.131
2009	35	10 (28.6%)	0.73 (0.30-1.75)	0.475
2010	53	9 (17.1%)	0.40 (0.16-0.99)	0.047
2011	54	6 (11.1%)	0.25 (0.09-0.69)	0.007
2012	85	12 (14.2%)	0.33 (0.14-0.78)	0.011
2013	97	17 (17.5%)	0.41 (0.19-0.89)	0.025
2014	138	19 (13.8%)	0.32 (0.15-0.69)	0.004
2015	125	27 (22.4%)	0.54 (0.26-1.11)	0.092
2016	130	18 (14.1%)	0.43 (0.20-0.94)	0.035

2017	152	8 (9.6%)	0.26 (0.10-0.66)	0.005
NSTEACS				
2005	62	23 (37.1%)	Reference	
2006	78	36 (46.2%)	1.27 (0.75-2.14)	0.378
2007	55	24 (43.6%)	1.21 (0.68-2.14)	0.516
2008	69	37 (53.6%)	1.55 (0.92-2.62)	0.097
2009	105	38 (36.5%)	0.96 (0.57-1.61)	0.880
2010	121	48 (39.7%)	1.07 (0.65-1.76)	0.795
2011	155	57 (36.9%)	0.99 (0.61-1.60)	0.962
2012	196	57 (29.1%)	0.73 (0.45-1.18)	0.202
2013	244	81 (33.5%)	0.86 (0.54-1.36)	0.512
2014	257	78 (30.6%)	0.77 (0.48-1.23)	0.273
2015	253	82 (33.0%)	0.85 (0.54-1.35)	0.492
2016	332	85 (26.7%)	0.82 (0.51-1.29)	0.388
2017	339	62 (22.6%)	0.78 (0.48-1.27)	0.323
STE-ACS				
2005	33	22 (66.7%)	Reference	
2006	60	43 (71.7%)	0.98 (0.59-1.64)	0.948
2007	56	30 (53.6%)	0.67 (0.38-1.16)	0.150
2008	47	33 (70.2%)	1.13 (0.66-1.95)	0.647
2009	46	30 (65.5%)	0.83 (0.48-1.43)	0.495
2010	61	38 (62.3%)	0.85 (0.50-1.44)	0.548
2011	59	34 (57.7%)	0.71 (0.42-1.22)	0.213
2012	75	47 (62.7%)	0.79 (0.48-1.31)	0.361
2013	81	44 (54.9%)	0.60 (0.36-1.00)	0.048
2014	77	35 (45.6%)	0.53 (0.31-0.90)	0.019
2015	96	50 (52.4%)	0.61 (0.37-1.00)	0.052
2016	82	37 (48.2%)	0.55 (0.33-0.94)	0.028
2017	98	44 (50.2%)	0.65 (0.39-1.08)	0.097

ACS = acute coronary syndrome; CCS = chronic coronary syndrome.

Table S5. Temporal trends in secondary outcomes.

All patients	Nr of patients	Death	Target Lesion Revascularization	Coronary artery bypass graft	Stroke	Myocardial Infarction	In-stent restenosis
2005	121	44 (36.4%)	2 (2.4%)	4 (4.4%)	2 (2.7%)	2 (1.9%)	1 (1.1%)
2006	162	68 (42.0%)	5 (4.4%)	11 (9.8%)	6 (4.7%)	7 (6.1%)	2 (1.6%)
2007	121	41 (33.9%)	7 (7.3%)	4 (4.3%)	2 (2.1%)	6 (6.4%)	6 (6.3%)
2008	135	64 (47.4%)	3 (2.9%)	3 (3.1%)	1 (0.9%)	5 (5.0%)	0 (0.0%)
2009	186	58 (31.2%)	6 (3.8%)	8 (5.2%)	2 (1.4%)	8 (5.0%)	1 (0.6%)
2010	235	83 (35.3%)	8 (4.2%)	4 (2.2%)	2 (1.2%)	3 (1.7%)	3 (1.7%)
2011	268	69 (25.7%)	7 (3.0%)	9 (4.1%)	5 (2.2%)	7 (3.1%)	3 (1.3%)
2012	356	89 (25.0%)	9 (2.9%)	7 (2.3%)	9 (3.1%)	11 (3.7%)	5 (1.7%)
2013	422	110 (26.1%)	16 (4.5%)	5 (1.4%)	7 (1.9%)	12 (3.4%)	6 (1.8%)
2014	472	107 (22.7%)	17 (4.2%)	7 (1.7%)	6 (1.5%)	9 (2.2%)	6 (1.5%)
2015	474	128 (27.5%)	20 (4.8%)	7 (1.8%)	7 (1.7%)	11 (2.6%)	6 (1.5%)
2016	544	99 (19.5%)	25 (5.1%)	5 (1.0%)	10 (2.2%)	17 (3.5%)	7 (1.6%)
2017	589	98 (19.5%)	6 (1.1%)	1 (0.3%)	7 (2.3%)	12 (3.3%)	1 (0.2%)
Men							
2005	76	30 (39.5%)	2 (4.0%)	4 (7.3%)	1 (2.2%)	2 (3.0%)	1 (1.8%)
2006	111	47 (42.3%)	4 (5.2%)	9 (11.5%)	1 (1.3%)	5 (6.6%)	1 (1.2%)
2007	84	32 (38.1%)	4 (6.0%)	3 (4.8%)	2 (3.1%)	5 (8.0%)	4 (6.0%)
2008	90	42 (46.7%)	3 (4.1%)	1 (1.4%)	0 (0.0%)	5 (7.0%)	0 (0.0%)
2009	130	43 (33.1%)	4 (3.7%)	7 (6.4%)	0 (0.0%)	7 (6.2%)	1 (0.9%)
2010	160	53 (33.1%)	5 (3.8%)	1 (0.8%)	1 (0.9%)	1 (0.8%)	2 (1.6%)
2011	198	51 (25.8%)	5 (2.9%)	8 (4.9%)	4 (2.5%)	5 (3.0%)	2 (1.2%)
2012	262	52 (19.8%)	5 (2.2%)	6 (2.6%)	5 (2.2%)	7 (3.1%)	3 (1.3%)
2013	283	71 (25.1%)	10 (4.2%)	3 (1.3%)	4 (1.7%)	10 (4.2%)	4 (1.8%)
2014	342	72 (21.1%)	13 (4.4%)	5 (1.7%)	6 (2.1%)	6 (2.0%)	4 (1.4%)
2015	344	83 (24.6%)	15 (4.9%)	5 (1.8%)	3 (1.0%)	7 (2.3%)	5 (1.7%)
2016	400	67 (17.9%)	21 (5.9%)	4 (1.1%)	8 (2.2%)	10 (2.8%)	6 (1.8%)
2017	440	64 (16.8%)	4 (1.0%)	1 (0.3%)	4 (2.1%)	8 (2.8%)	1 (0.3%)
Women							
2005	45	14 (31.1%)	0 (0.0%)	0 (0.0%)	1 (3.4%)	0 (0.0%)	0 (0.0%)
2006	51	21 (41.2%)	1 (2.4%)	2 (5.9%)	5 (11.6%)	2 (4.9%)	1 (2.4%)
2007	37	9 (24.3%)	3 (9.8%)	1 (3.3%)	0 (0.0%)	1 (3.2%)	2 (6.8%)
2008	45	22 (48.9%)	0 (0.0%)	2 (7.6%)	1 (3.0%)	0 (0.0%)	0 (0.0%)
2009	56	15 (26.8%)	2 (4.3%)	1 (2.4%)	2 (4.4%)	1 (2.4%)	0 (0.0%)
2010	75	30 (40.0%)	3 (5.3%)	3 (5.8%)	1 (1.9%)	2 (3.7%)	1 (2.0%)
2011	70	18 (25.7%)	2 (3.2%)	1 (1.8%)	1 (1.5%)	2 (3.3%)	1 (1.7%)
2012	94	37 (39.4%)	4 (5.4%)	1 (1.5%)	4 (5.9%)	4 (6.2%)	2 (3.0%)
2013	139	39 (28.1%)	6 (5.3%)	2 (1.7%)	3 (2.3%)	2 (1.6%)	2 (1.8%)
2014	130	35 (26.9%)	4 (3.6%)	2 (1.8%)	0 (0.0%)	3 (2.7%)	2 (1.9%)
2015	130	45 (35.2%)	5 (4.4%)	2 (1.9%)	4 (3.7%)	4 (3.5%)	1 (1.0%)
2016	144	32 (23.8%)	4 (3.0%)	1 (0.8%)	2 (2.0%)	7 (5.8%)	1 (0.8%)
2017	149	34 (27.5%)	2 (1.4%)	0 (0.0%)	3 (2.7%)	4 (4.9%)	0 (0.0%)
Age ≥75 years							
2005	61	23 (37.7%)	0 (0.0%)	0 (0.0%)	1 (2.8%)	2 (3.8%)	0 (0.0%)
2006	86	38 (44.2%)	4 (6.7%)	4 (6.5%)	5 (7.8%)	4 (6.5%)	1 (1.4%)
2007	68	25 (36.8%)	4 (7.5%)	2 (3.8%)	1 (1.9%)	4 (7.2%)	3 (5.8%)
2008	78	42 (53.8%)	2 (3.2%)	1 (1.7%)	1 (1.5%)	4 (6.8%)	0 (0.0%)
2009	102	38 (37.3%)	4 (4.8%)	2 (2.3%)	2 (2.7%)	6 (7.1%)	1 (1.1%)
2010	115	53 (46.1%)	6 (6.7%)	2 (2.3%)	2 (2.8%)	3 (3.7%)	2 (2.5%)
2011	121	38 (31.4%)	3 (3.0%)	2 (2.1%)	3 (3.0%)	4 (3.9%)	1 (1.0%)
2012	176	70 (39.8%)	5 (3.6%)	1 (0.7%)	8 (6.3%)	6 (5.0%)	3 (2.2%)
2013	213	72 (33.8%)	7 (4.3%)	2 (1.3%)	5 (3.0%)	6 (3.6%)	4 (2.5%)
2014	214	68 (31.8%)	5 (2.8%)	3 (1.6%)	2 (1.1%)	3 (1.8%)	2 (1.1%)

2015	225	79 (35.7%)	7 (3.6%)	0 (0.0%)	4 (2.3%)	2 (1.0%)	4 (2.1%)
2016	284	62 (23.8%)	7 (2.8%)	1 (0.4%)	7 (3.0%)	10 (4.1%)	0 (0.0%)
2017	288	60 (25.4%)	3 (1.1%)	0 (0.0%)	4 (1.7%)	5 (3.9%)	1 (0.4%)
Age <75 years							
2005	60	21 (35.0%)	2 (4.8%)	4 (9.1%)	1 (2.6%)	0 (0.0%)	1 (2.2%)
2006	76	30 (39.5%)	1 (1.8%)	7 (13.5%)	1 (1.3%)	3 (5.7%)	1 (1.8%)
2007	53	16 (30.2%)	3 (7.1%)	2 (5.0%)	1 (2.4%)	2 (5.3%)	3 (7.1%)
2008	57	22 (38.6%)	1 (2.4%)	2 (5.0%)	0 (0.0%)	1 (2.5%)	0 (0.0%)
2009	84	20 (23.8%)	2 (2.7%)	6 (8.4%)	0 (0.0%)	2 (2.7%)	0 (0.0%)
2010	120	30 (25.0%)	2 (2.0%)	2 (2.1%)	0 (0.0%)	0 (0.0%)	1 (1.1%)
2011	147	31 (21.1%)	4 (3.0%)	7 (5.7%)	2 (1.6%)	3 (2.4%)	2 (1.6%)
2012	180	19 (10.6%)	4 (2.4%)	6 (3.6%)	1 (0.6%)	5 (3.0%)	2 (1.2%)
2013	209	38 (18.2%)	9 (4.8%)	3 (1.6%)	2 (1.0%)	6 (3.2%)	2 (1.1%)
2014	258	39 (15.1%)	12 (5.2%)	4 (1.8%)	4 (1.8%)	6 (2.6%)	4 (1.8%)
2015	249	49 (20.1%)	13 (5.8%)	7 (3.3%)	3 (1.3%)	9 (4.0%)	2 (1.0%)
2016	260	37 (14.6%)	18 (7.6%)	4 (1.7%)	3 (1.3%)	7 (3.0%)	7 (3.2%)
2017	301	38 (13.9%)	3 (1.0%)	1 (0.5%)	3 (2.7%)	7 (2.9%)	0 (0.0%)
Diabetes Mellitus							
2005	25	11 (44.0%)	0 (0.0%)	1 (5.0%)	1 (7.7%)	0 (0.0%)	0 (0.0%)
2006	39	24 (61.5%)	1 (5.3%)	2 (9.8%)	2 (7.3%)	2 (9.5%)	0 (0.0%)
2007	28	11 (39.3%)	2 (8.4%)	1 (4.0%)	1 (4.0%)	2 (9.7%)	2 (8.4%)
2008	26	14 (53.8%)	0 (0.0%)	2 (10.6%)	0 (0.0%)	2 (10.5%)	0 (0.0%)
2009	39	16 (41.0%)	2 (6.1%)	1 (3.1%)	1 (3.3%)	2 (5.9%)	0 (0.0%)
2010	58	25 (43.1%)	2 (4.6%)	2 (5.0%)	0 (0.0%)	0 (0.0%)	2 (4.6%)
2011	46	14 (30.4%)	1 (2.7%)	1 (2.8%)	0 (0.0%)	2 (5.6%)	0 (0.0%)
2012	83	27 (32.5%)	4 (5.4%)	0 (0.0%)	4 (5.4%)	2 (3.1%)	2 (2.6%)
2013	109	35 (32.1%)	4 (5.0%)	1 (1.1%)	0 (0.0%)	3 (3.8%)	2 (2.5%)
2014	101	30 (29.7%)	10 (11.8%)	3 (3.7%)	1 (1.1%)	5 (6.0%)	4 (4.9%)
2015	115	43 (38.5%)	5 (5.4%)	2 (2.4%)	3 (3.3%)	2 (2.1%)	1 (1.1%)
2016	119	37 (32.8%)	5 (5.5%)	1 (1.1%)	2 (2.0%)	8 (8.6%)	2 (2.5%)
2017	150	33 (24.2%)	2 (1.5%)	0 (0.0%)	1 (0.7%)	6 (8.3%)	1 (0.8%)
No Diabetes Mellitus							
2005	91	28 (30.8%)	2 (3.0%)	3 (4.3%)	1 (1.6%)	2 (2.4%)	1 (1.4%)
2006	116	39 (33.6%)	4 (4.4%)	9 (10.1%)	3 (3.3%)	5 (5.5%)	2 (2.1%)
2007	86	27 (31.4%)	5 (7.3%)	3 (4.7%)	1 (1.5%)	4 (5.9%)	4 (5.9%)
2008	105	46 (43.8%)	3 (3.6%)	1 (1.2%)	1 (1.1%)	3 (3.7%)	0 (0.0%)
2009	142	37 (26.1%)	4 (3.2%)	7 (5.7%)	1 (0.9%)	6 (4.8%)	1 (0.8%)
2010	174	55 (31.6%)	6 (4.1%)	2 (1.4%)	2 (1.6%)	3 (2.2%)	1 (0.8%)
2011	219	53 (24.2%)	6 (3.0%)	8 (4.4%)	5 (2.7%)	5 (2.6%)	3 (1.6%)
2012	265	57 (21.5%)	5 (2.2%)	6 (2.7%)	5 (2.3%)	9 (4.0%)	3 (1.4%)
2013	311	73 (23.5%)	12 (4.4%)	4 (1.5%)	7 (2.6%)	9 (3.3%)	4 (1.5%)
2014	365	72 (19.7%)	7 (2.2%)	4 (1.2%)	5 (1.6%)	4 (1.2%)	2 (0.6%)
2015	354	84 (24.1%)	15 (4.7%)	5 (1.7%)	4 (1.3%)	9 (2.8%)	5 (1.6%)
2016	423	61 (15.6%)	20 (5.1%)	4 (1.0%)	8 (2.2%)	9 (2.3%)	5 (1.4%)
2017	436	63 (17.5%)	4 (0.9%)	1 (0.3%)	5 (2.5%)	6 (1.9%)	0 (0.0%)
CCS							
2005	26	6 (23.1%)	1 (5.0%)	3 (12.0%)	1 (4.8%)	0 (0.0%)	0 (0.0%)
2006	24	4 (16.7%)	2 (8.3%)	0 (0.0%)	1 (4.2%)	0 (0.0%)	1 (4.2%)
2007	10	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2008	19	2 (10.5%)	0 (0.0%)	1 (5.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2009	35	7 (20.0%)	1 (2.9%)	3 (9.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2010	53	4 (7.5%)	2 (3.8%)	1 (1.9%)	1 (2.1%)	0 (0.0%)	1 (2.0%)
2011	54	2 (3.7%)	1 (1.9%)	3 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2012	85	10 (11.8%)	1 (1.2%)	2 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2013	97	12 (12.4%)	3 (3.2%)	2 (2.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2014	138	12 (8.7%)	5 (3.8%)	2 (1.5%)	1 (0.8%)	0 (0.0%)	1 (0.8%)
2015	125	17 (14.3%)	9 (7.4%)	3 (2.6%)	0 (0.0%)	0 (0.0%)	4 (3.4%)

2016	130	9 (6.9%)	8 (6.5%)	0 (0.0%)	5 (4.0%)	0 (0.0%)	5 (4.3%)
2017	152	5 (5.1%)	1 (0.7%)	0 (0.0%)	2 (4.0%)	0 (0.0%)	0 (0.0%)
NSTE-ACS							
2005	62	18 (29.0%)	1 (1.9%)	0 (0.0%)	1 (2.4%)	1 (1.7%)	1 (1.9%)
2006	78	26 (33.3%)	2 (3.3%)	5 (8.7%)	2 (3.4%)	3 (5.1%)	1 (1.4%)
2007	55	16 (29.1%)	6 (11.9%)	3 (6.0%)	1 (2.0%)	4 (8.3%)	5 (10.1%)
2008	69	32 (46.4%)	2 (3.2%)	1 (1.9%)	0 (0.0%)	5 (8.3%)	0 (0.0%)
2009	105	29 (27.6%)	4 (4.3%)	3 (3.1%)	2 (2.3%)	4 (4.3%)	1 (1.0%)
2010	121	43 (35.5%)	3 (2.9%)	2 (2.1%)	1 (1.0%)	3 (3.1%)	2 (2.0%)
2011	155	41 (26.5%)	5 (3.6%)	2 (1.5%)	2 (1.4%)	7 (5.2%)	3 (2.2%)
2012	196	45 (23.0%)	7 (4.0%)	2 (1.2%)	6 (3.6%)	4 (2.3%)	4 (2.3%)
2013	244	64 (26.2%)	7 (3.5%)	1 (0.5%)	4 (2.0%)	6 (2.9%)	5 (2.5%)
2014	257	61 (23.7%)	12 (5.3%)	5 (2.2%)	5 (2.3%)	8 (3.5%)	5 (2.3%)
2015	253	69 (27.8%)	8 (3.5%)	2 (1.0%)	4 (1.9%)	5 (2.2%)	2 (0.9%)
2016	332	57 (18.2%)	14 (4.6%)	5 (1.7%)	5 (1.8%)	14 (4.7%)	2 (0.7%)
2017	339	50 (17.5%)	5 (1.5%)	1 (0.4%)	4 (1.4%)	10 (4.8%)	1 (0.3%)
STE-ACS							
2005	33	20 (60.6%)	0 (0.0%)	1 (7.7%)	0 (0.0%)	1 (4.5%)	0 (0.0%)
2006	60	38 (63.3%)	1 (3.7%)	6 (20.2%)	3 (6.9%)	4 (13.4%)	0 (0.0%)
2007	56	25 (44.6%)	1 (2.9%)	1 (3.0%)	1 (2.9%)	2 (6.0%)	1 (2.9%)
2008	47	30 (63.8%)	1 (5.0%)	1 (5.0%)	1 (3.8%)	0 (0.0%)	0 (0.0%)
2009	46	22 (47.8%)	1 (3.3%)	2 (6.7%)	0 (0.0%)	4 (13.0%)	0 (0.0%)
2010	61	36 (59.0%)	3 (8.7%)	1 (3.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
2011	59	26 (44.1%)	1 (2.3%)	4 (10.9%)	3 (8.0%)	0 (0.0%)	0 (0.0%)
2012	75	34 (45.3%)	1 (2.1%)	3 (6.8%)	3 (6.6%)	7 (15.6%)	1 (2.1%)
2013	81	34 (42.0%)	6 (10.0%)	2 (3.3%)	3 (4.6%)	6 (10.3%)	1 (1.9%)
2014	77	34 (44.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)
2015	96	42 (44.1%)	3 (4.0%)	2 (3.2%)	3 (4.5%)	6 (8.6%)	0 (0.0%)
2016	82	33 (43.3%)	3 (5.0%)	0 (0.0%)	0 (0.0%)	3 (5.4%)	0 (0.0%)
2017	98	43 (49.0%)	0 (0.0%)	0 (0.0%)	1 (1.4%)	2 (2.6%)	0 (0.0%)

ACS = acute coronary syndrome; CCS = chronic coronary syndrome.

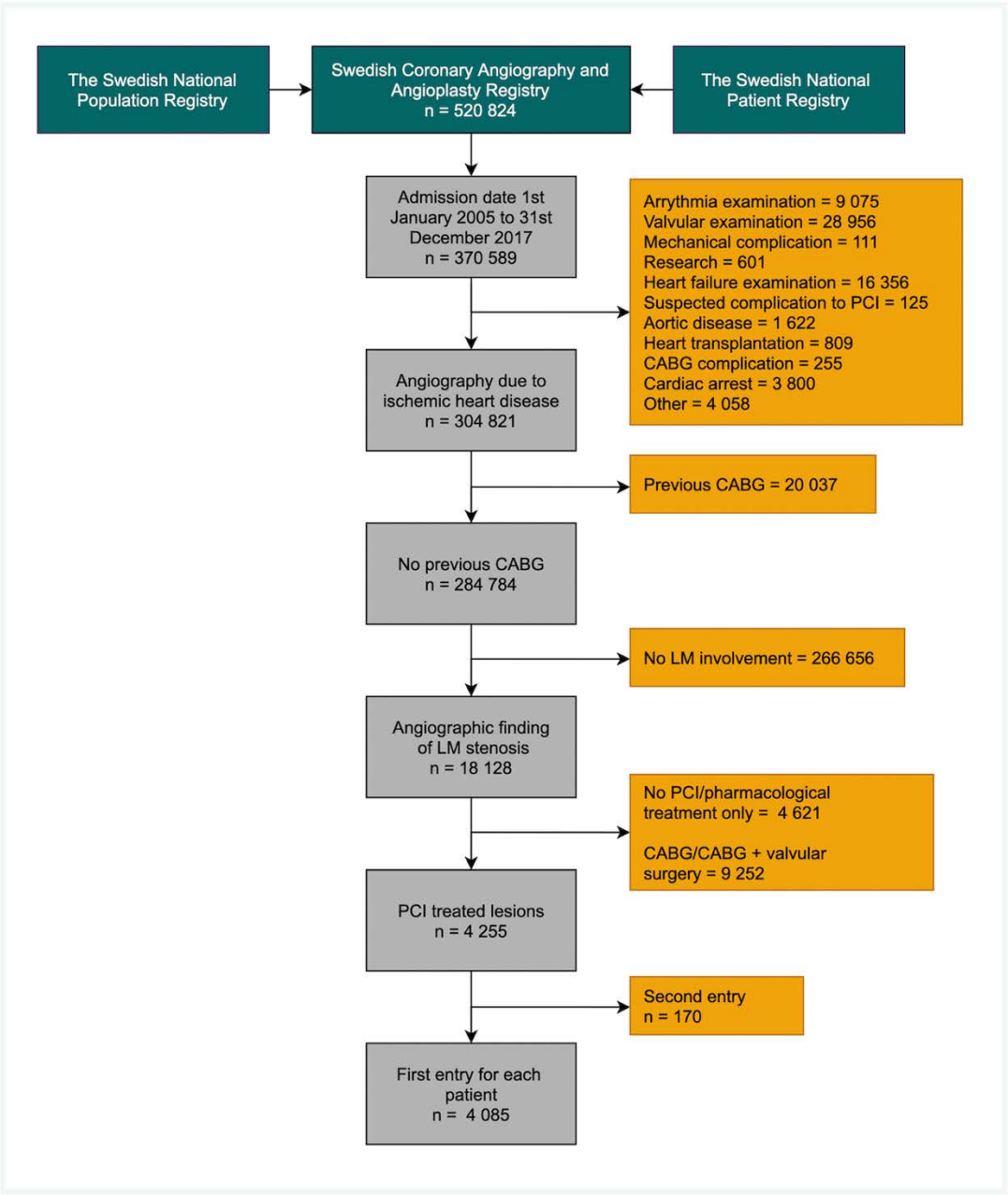

Figure S1. Patient flowchart

Number of patients remaining in the analyses after applying inclusion and exclusion criteria.
CABG = coronary artery bypass grafting; LM = left main.