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ORIGINAL ARTICLE

Clinical and economic outcomes following first-time myocardial infarction: a nationwide cohort study from the SWEDEHEART registry

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Aims This study aimed to estimate consequences of myocardial infarction (MI) on long-term outcomes and resource needs by comparing outcomes, healthcare resource use, and associated costs between first-time MI patients and matched controls.

Methods and results First-time MI patients from the nationwide SWEDEHEART registry, along with matched controls without prior MI (matched by sex, age, and region) 2012–2022, were included. Follow-up continued through November 2024 and assessed major adverse cardiovascular events (MACE), defined as cardiovascular death, MI, ischaemic stroke, acute limb ischaemia, or urgent arterial revascularization, as well as, healthcare resource use and associated costs. Among 118 810 first-time MI patients and 588 687 matched controls, followed for a median (IQR) of 6.6 (4.2–9.4) years, the 10-year MACE probability was 48.5% vs. 21.1% (HR [95% CI] 3.65 [3.61–3.69]), mainly due to higher rate of cardiovascular death (21.7% vs. 11.1%), MI (18.4% vs. 5.9%), and arterial revascularization (22.9% vs. 4.2%). Associations attenuated after adjustment for baseline characteristics but remained significant (MACE: adjHR[95%CI]: 3.18[3.15–3.22]). Cases had twice as many inpatient visits (0.65 vs. 0.32/patient year) and inpatient days (3.05 vs. 1.67/patient year), with nearly double the mean annual total costs (€7266 vs. €3934) when outpatient visits and medication also were included. Differences were greatest in the first year but persisted, especially among females and those with risk factors such as hypertension or diabetes.

Conclusion First-time MI patients have persistently higher risks of cardiovascular death, MI, and ischaemic stroke, along with greater healthcare use and costs, underscoring the need for effective prevention.

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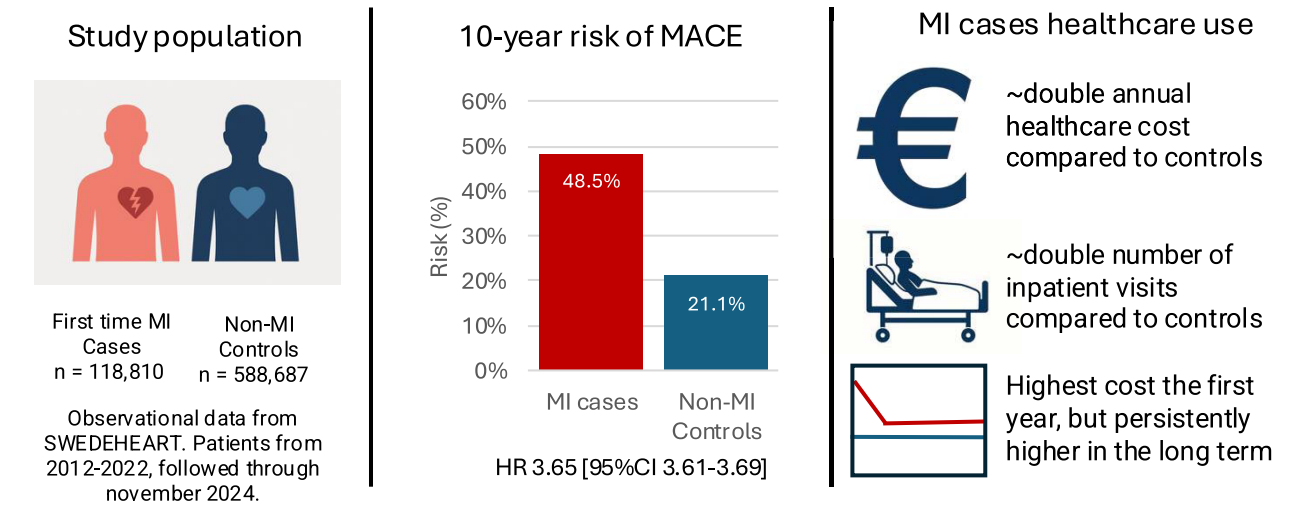
Graphical abstract



Key Question: What are the long-term cardiovascular risks and healthcare resource needs after a first-time myocardial infarction compared with matched controls?
Key Finding: First-time MI patients had a 10-year MACE risk of 48.5% versus 21.1% in controls, with higher cardiovascular death, recurrent MI, and costs nearly double those of controls (MACE HR 3.65 [95% CI 3.61-3.69]).
Take-home Message: First-time MI leads to persistently increased cardiovascular risk and healthcare burden, highlighting the need for effective prevention strategies to reduce disease progression and avoidable healthcare use.

Keywords Myocardial infarction • Prognosis • Health care resource utilization • Costs • Matched controls

Key Learning Points

What is known

- Despite advances in prevention and treatment, atherosclerotic cardiovascular disease (ASCVD) remains a leading cause of morbidity and mortality worldwide.
- ASCVD places a heavy burden on healthcare systems through hospitalizations, procedures, medications, and long-term care, and has been shown to be associated with high healthcare resource use in the short term.

What is new

- In a nationwide cohort, nearly 50% of MI cases experienced a MACE within 10 years after a first MI, almost 30 percentage points higher than matched non-MI controls, with excess risk emerging early during follow-up and driven by cardiovascular death, recurrent MI, and urgent revascularization.
- The poor prognosis translates into major healthcare costs. MI patients incurred nearly double hospitalization days, higher outpatient use, 70% higher medication costs, and almost doubled total annual healthcare costs over 10 years (€7266 vs. €3934). The higher resource use persisted over 10 years of follow-up.
- Risk and costs varies by subgroup. Women had a higher excess risk and costs for several ischaemic outcomes compared with men, and patients with diabetes or hypertension showed substantially higher excess events and costs. In contrast, better risk-factor control-particularly >50% LDL reduction-was associated with fewer events, lower resource use, and 24% lower annual total costs.

Introduction

Despite advances in prevention and treatment, atherosclerotic cardiovascular disease (ASCVD) remains a leading cause of morbidity and mortality worldwide—particularly through manifestations such as myocardial infarction (MI) and other serious complications.[1–4]

Beyond its clinical impact, MI places a substantial burden on healthcare systems due to the need for hospitalizations, procedures, medications, and long-term care.[5–7] While short-term costs for individual patients are relatively well studied in clinical trials, those with a history of MI remain at elevated risk for recurrent events and often require ongoing medical care over extended periods. However, the long-term cumulative costs of MI

including inpatient, outpatient, emergency care, and medications are less well described.

To understand long-term prognosis, healthcare resource utilization (HCRU), and associated costs after MI, it is crucial to compare outcomes with those in the general population without prior MI. To date, contemporary large-scale studies comparing clinical outcomes, HCRU, and costs in patients with MI vs. randomly selected, matched individuals without previous MI are scarce.[5]

We hypothesized that individuals with a history of MI have worse clinical outcomes, greater healthcare utilization, and higher costs than matched individuals without MI. The aim of this study was therefore to characterize the clinical and economic burden of MI by comparing outcomes, healthcare use, and costs between individuals with a first time MI and matched controls. We also examined whether these differences varied by sex, the presence of risk factors such as hypertension and diabetes, and the achievement of recommended LDL levels.

Methods

This retrospective longitudinal matched-cohort study was conducted through record linkage between several national Swedish databases: the SWEDEHEART (Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies) registry, the Swedish Patient Register, the Prescribed Drug Register, and the Swedish Population Register. Linkage was enabled using the unique personal identity number assigned to all residents in Sweden. The study received ethical approval from the Swedish Ethical Review Authority (Dnr: 2024-05268-02). Informed consent from individual participants was not required, in accordance with Swedish regulations governing national health data registries. Approval for data linkage was granted by the National Board of Health and Welfare, Statistics Sweden, and the SWEDEHEART steering committee.

The SWEDEHEART registry is a nationwide database including nearly all patients hospitalized with acute MI in Sweden who are admitted to coronary care units or equivalent specialized facilities since 1995. It prospectively collects over 100 variables related to patient demographics, risk factors, medical history, pre-hospital and in-hospital treatments, diagnostic tests, electrocardiographic and biochemical findings, interventions, hospital outcomes, discharge medications, and diagnoses.[8] The registry is regularly monitored with a high agreement between the registry and medical records.[9]

Study population, covariates and intervention

The study population consisted of all adult (≥18 years) patients admitted with a first time ever MI included in the SWEDEHEART registry from January 2012 to January 2022. For each MI case, up to five non-MI controls, were randomly selected from the Swedish Population Registry, exactly matched for sex, year of birth, and geographical location, by Statistics Sweden. Controls with previous MI were excluded. The index date for MI cases was the date of admission because of the initial MI and the index date for non-MI controls was the same as the MI date of the matched MI case. As the registry covers the entire country, a non-MI control could be included in the MI cohort after experiencing an MI episode, but an MI case could never be included as a non-MI control after its MI date, as previous MI was an exclusion criterion for the control group.

Demographic data, including educational level and disposable income (income after taxes and benefits), were obtained from Statistics Sweden. To adjust for inflation, disposable income were divided into tertiles for each year. Information about risk factors and comorbidities was obtained from the national patient registry, which included all ICD codes for all admissions and emergency room visits to Swedish hospitals since 1997 and for all out-patient visits to specialists since 2005. All comorbidities were defined using ICD codes (see Supplementary material online, *Table S1* in the supplemental material). Medical treatment information was obtained from the Swedish prescribed drug registry, which includes all dispensed drugs in Sweden since 2005. Current drug use at baseline was defined as a filled prescription within 6 months before MI or index date. Data regarding anthropometry, lab results and treatment course was only available for MI cases in the SWEDEHEART registry.

Outcomes

Patients were followed from index (i.e. admission) date until November 2024 using data from the Swedish National Cause of Death Register and the Swedish National Patient Register. ASCVD-related clinical endpoints included major adverse clinical event (MACE), which was a composite of cardiovascular death, MI, ischaemic stroke, acute limb ischaemia, or urgent arterial revascularization (coronary, cerebrovascular or peripheral), the individual components of MACE definition, all-cause mortality. The ICD-codes for the endpoints are listed in Supplementary material online, *Table S1* in the supplemental material.

Non-cost HCRU was measured by identifying inpatient visits (number and length of stay), selected revascularization procedures (number of invasive coronary angiographies and percutaneous coronary interventions), emergency department visits (number), outpatient visits to specialists (number), and dispensed drugs, using SWEDEHEART, the National Patient Registry and the Drug prescription registry.

Hospitalization-related costs were estimated using the National Patient Registry where hospitalization records were matched with diagnosis-related group (DRG) weights, then multiplied by the cost per DRG weight for that year. Examples of hospitalization costs are provided in Supplementary material online, *Table S2* in the supplemental material. Similarly, each outpatient visit was assigned a DRG code, and unit costs were calculated using the same method as for hospitalizations. For the cases, the initial MI hospitalization was not counted, in order for the result to reflect resource use after the MI event. For drug-related costs, price data for each filled prescription was available from the prescription registry, capturing the total cost for each individual, both the patient-paid copayment and the reimbursed portions covered by the healthcare system. All costs were inflation-adjusted using the consumer price index retrieved from Statistics Sweden to reflect costs in 2024 SEK. For presentation, costs were converted to euros (€) using the exchange rate for January 2024 (1 euro = 11.1545 SEK).

Statistical methods

Descriptive analyses of baseline characteristics were conducted to assess balance and standardized mean differences between MI cases and controls. Time to clinical events was assessed using Kaplan Meier and Cox proportional hazards models and reported graphically, as well as with 10-year cumulative probabilities and hazard ratios (HR) with confidence intervals comparing the MI cases and non-MI controls. Given the elevated risk during the acute period following an MI, we performed a 1-year landmark analysis for MACE, all-cause death, and cardiovascular death.

We calculated the cohort-level aggregate HCRU and cost per person-year by dividing total HCRU by total person-time within the MI, and control groups, respectively, along with weighted standard deviations. These cohort-level averages were also calculated annually for each year following the MI or index date.

To model HCRU and costs, we calculated person-level rates by dividing each individual's total HCRU or cost during follow-up by their follow-up time. Given the zero-inflated nature of the data, we used two-part models: a logistic regression model for predicting the probability of any use or cost, and a generalized linear model with a gamma distribution and log link for the positive costs or HCRU. For each cost or HCRU outcome, we calculated unadjusted mean differences between MI cases and non-MI controls. We then fitted multivariable two-part models, adjusting for baseline variables with a standardized mean difference >0.1 between cases and controls. This was repeated within each subgroup to inform subgroup-specific models. We estimated the average treatment effect (ATE) of MI vs. no MI in the study cohort from the combined two-part

model, integrating both parts to account for zero-inflation and skewness. Bootstrap resampling (1000 iterations for the main analyses and 500 for sensitivity analyses) was used to generate 95% confidence intervals for the estimated effects. The results from these models are reported as mean differences, positive value indicates higher cost for cases.

The above analyses were also performed in females and male, those with and without hypertension, those with and without diabetes mellitus (both cases and controls).

To investigate the association between changes in LDL-C and prognosis among MI cases, we compared those who achieved a significant reduction in LDL-cholesterol 6–10 weeks after the index event, defined as a LDL-C reduction ≥50%, to those who did not reach a significant reduction in LDL-C (<50% reduction). A ≥ 50% reduction threshold was selected because it reflects the expected LDL-C decrease with high intensity statin therapy and it was previously observed that achieving this level of LDL-C lowering was associated with a significant reduction in subsequent cardiovascular events.[10]

Results

During the study period, there were 178 547 cases with an acute MI included in the registry. Of these, 124 944 had no prior MI diagnosis, 5914 MI cases could not be matched to a control, and 220 had two registrations the same day, leaving 118 810 patients with a first time MI to be included in the analyses (see Supplementary material online, *Figure S1*). These were matched to 588 687 controls with no prior MI diagnosis. A total of 3.5% of the controls were later included in the SWEDEHEART registry because of a MI event and were therefore also represented in the case population as MI cases. The median (IQR) age of both cases and controls was 71 (62–79) years and 35% were females. Compared with controls, MI cases had a lower income and educational level. They also more often had risk factors such as diabetes mellitus, hypertension and chronic kidney disease, as well as already established ASCVD (*Table 1*). Before the initial MI at baseline, cases were also more often treated with aspirin, beta-blockers and ACE-inhibitors or ARB, whereas the use of statins was similar among the MI and control cohorts. In-hospital characteristics for the MI cases are shown in Supplementary material online, *Table S3* in the supplemental material. Overall, 39% had ST-elevation MI. Percutaneous coronary intervention was performed in 73%, coronary artery by-pass grafting in 5.5%, and 4.5% died during hospitalization. At discharge, 90% were prescribed statins, 79% dual antiplatelet therapy, and 83% beta-blockers.

Clinical events

Patients with MI and controls were followed for a median (IQR) time of 6.6 (4.2–9.4) years (*Figure 1*, *Table 2*). The 10-year cumulative probability of MACE was 48.5% in MI cases and 21.1% in controls (HR[95%CI] 3.65[3.61–3,69]). This was mainly driven by higher risk of cardiovascular death (21.7% vs. 11.1%, HR[95%CI] 2.39[2.35–2.43]), MI (18.4% vs. 5.9%, HR[95%CI] 3.84[3.76–3.91]) and higher need of arterial revascularization (22.9% vs. 4.2%, HR[95%CI] 8.11[7.95–8.27]). Regarding ischaemic stroke (8.7% vs. 6.6%, HR[95%CI] 1.41[1.38–1.45]) and limb ischaemia (3.7% vs. 1.5%, HR[95%CI] 2.61[2.50–2.73]), the absolute differences were small but still statistically significant. After adjusting for differences at baseline, the associations were somewhat attenuated, but remained statistically significant (*Table 2*). The risk of non-cardiovascular death was slightly higher among cases in the unadjusted analysis (HR[95%] 1.05[1.04–1.07]), but was lower among cases after adjustment for baseline characteristics (HR[95%] 0.92[0.90–0.93]). In the adjusted models, the excess risks of MACE in cases were similar in women and men, whereas women with MI had a higher excess risk of new MI, ischaemic stroke and arterial revascularization compared with men with MI (see Supplementary material online, *Table S4*). Cases with diabetes had a higher excess risk of all endpoints, except arterial revascularization, compared with cases without diabetes. A similar pattern was seen for cases with and without hypertension. In a 1-year landmark analysis, MI cases had a significantly higher risk of MACE, all-cause death, and cardiovascular death (HR [95% CI] 1.79 [1.76–1.82], 1.15 [1.13–1.17], and 1.54 [1.51–1.58], respectively) after excluding events from the first year (see Supplementary material online, *Table S9*, Supplementary material online, *Figure S4*).

Healthcare resource utilization and costs

The cohort-level average HCRU and costs per person-year were higher across all measures in the MI group compared with the control group during the study period (*Table 3*). Cases had twice the amount of inpatient visits (0.65 vs. 0.32 per person-year) and inpatient length of stay (3.05 vs. 1.67 days per person-year). They had almost 50% more ED visits, and 7 times more coronary angiographies. The total costs (the sum of inpatient, outpatient and medication costs) was almost double for cases compared to controls (7266 euros vs. 3934 euros). The higher HCRU and costs were most evident the first year after the MI, but large differences between cases and controls persisted throughout the study period (*Figure 2*, Supplementary material online, *Figure S2*).

When modelling the person-level average HCRU per person-year and adjusting for baseline differences in the two-part models, the differences in outcomes persisted, though they were slightly attenuated (see Supplementary material online, *Table S5*).

Subgroup analyses

Cases consistently showed higher HCRU and associated costs than controls in both unadjusted and adjusted analyses. This difference was especially pronounced among females, as well as individuals with hypertension or diabetes mellitus (see Supplementary material online, *Table S6*). When comparing cases who achieved >50% LDL-cholesterol reduction during the first 6–10 weeks after index event with cases who did not, those with >50% LDL-cholesterol reduction had less inpatient visits, inpatient length of stay, and outpatients visit as well as lower inpatient-, outpatient-, medication- and total costs, which could be seen over a long-term period (see Supplementary material online, *Tables S7* and *S8*, Supplementary material online, *Figure S3* in the supplemental material).

Discussion

Among all patients with a first-time MI in an entire country, the 10-year risk of developing a MACE—defined as cardiovascular death, MI, ischaemic stroke, acute limb ischaemia, or urgent coronary arterial revascularization—was nearly 50%, almost 30 percentage points higher than in age- and sex-matched controls without prior MI. The difference in clinical outcomes between MI cases and controls was primarily driven by higher rates of cardiovascular death, recurrent MI, and urgent revascularization. The separation of the event curves occurred mainly during the first three months of follow-up, after which the curves ran more parallel, although continued to diverge among those surviving the initial months.

The observed negative association of non-cardiovascular death among MI cases in the adjusted analysis (HR 0.92, $P < 0.01$) likely reflects competing risks of death, as reflected in

Table 1 Characteristics

	Cases *n* = 118 810	Controls *n* = 588 687	Standardized mean difference
Demography and socioeconomy			
Age, median (IQR)[a]	71 (62–79)	71 (62–79)	NA
Females, n (%)[a]	41 564 (35)	206 671 (35)	NA
Disposable income[b] strata			**0.11**
Low, n (%)	40 987 (35)	183 442 (31)	
Middle, n (%)	40 789 (34)	193 495 (33)	
High, n (%)	36 793 (31)	210 447 (36)	
Unknown, n (%)	304	1303	
Educational level			
<9 years school, n (%)	27 365 (23)	119 062 (21)	**0.15**
9 years in school, n (%)	12 885 (11)	56 512 (9.8)	
2 years secondary school, n (%)	36 879 (32)	170 269 (29)	
≥3 years secondary school, n (%)	14 458 (12)	74 323 (13)	
<3 years university, n (%)	11 560 (9.9)	66 077 (11)	
≥3 years university, n (%)	12 682 (11)	84 541 (15)	
Doctoral studies, n (%)	1031 (0.9)	7700 (1.3)	
Unknown, n (%)	1950	10 203	
Comorbidities			
Diabetes mellitus, n (%)	19 538 (16)	57 031 (9.7)	**0.20**
Hypertension, n (%)	45 324 (38)	171 256 (29)	**0.19**
Chronic kidney disease, n (%)	4223 (3.6)	10 706 (1.8)	**0.11**
Heart failure, n (%)	8415 (7.1)	29 770 (5.1)	0.08
Chronic pulmonary disease, n (%)	11 002 (9.3)	38 529 (6.5)	**0.10**
Ischaemic heart disease, n (%)	19 182 (16)	49 403 (8.4)	**0.24**
Ischaemic stroke, n (%)	6512 (5.5)	27 980 (4.8)	0.03
Peripheral artery disease, n (%)	7236 (6.1)	18 220 (3.1)	**0.14**
Limb ischaemia, n (%)	3662 (3.1)	7159 (1.2)	**0.13**
Any atherosclerotic CVD, n (%)	25 426 (21)	76 503 (13)	**0.22**
Medications before index date			
Aspirin, n (%)	26 100 (22)	91 264 (16)	**0.17**
P2Y12-rec blockade, n (%)	3960 (3.3)	13 091 (2.2)	0.07
Beta-blockade, n (%)	36 875 (31)	151 858 (26)	**0.12**
ACEI/ARB, n (%)	44 177 (37)	184 915 (31)	**0.12**
Statins, n (%)	28 825 (24)	131 229 (22)	0.05
Ezetimibe	985 (3.4%)	2951 (2.2%)	0.07
PCSK9 Inhibitor	9 (<0.1%)	24 (<0.1%)	0.01
Bile Acid Sequestrants	12 (<0.1%)	34 (<0.1%)	0.01
Statin intolerance, n (%)	15 794 (13)	54 032 (9.2)	**0.13**

Characteristics at baseline for MI cases and controls. Bold figures indicates a standardized mean difference >0.1 between groups.
[a]denotes variables used for matching.
[b]income after taxes and benefits.

the higher cardiovascular and all-cause mortality (HR 1.97, 1.27, $P < 0.01$) among cases, reducing the population at risk of dying from non-cardiovascular causes, and not a protective effect of MI on non-cardiovascular mortality.

The association between MI and outcomes was only slightly attenuated after adjusting for comorbidities, suggesting that comorbidities are not the primary drivers of the poor prognosis in these patients. Overall, this worse prognosis was reflected in nearly twice as many hospitalization days and related costs, more than a 50% increase in outpatient visits and costs, a 70% increase in medication costs, and a rise in mean annual total healthcare costs from €3934 to €7266 during 10 years of follow-up.

Large studies comparing outcomes in MI patients and in randomly selected matched non-MI controls are uncommon.

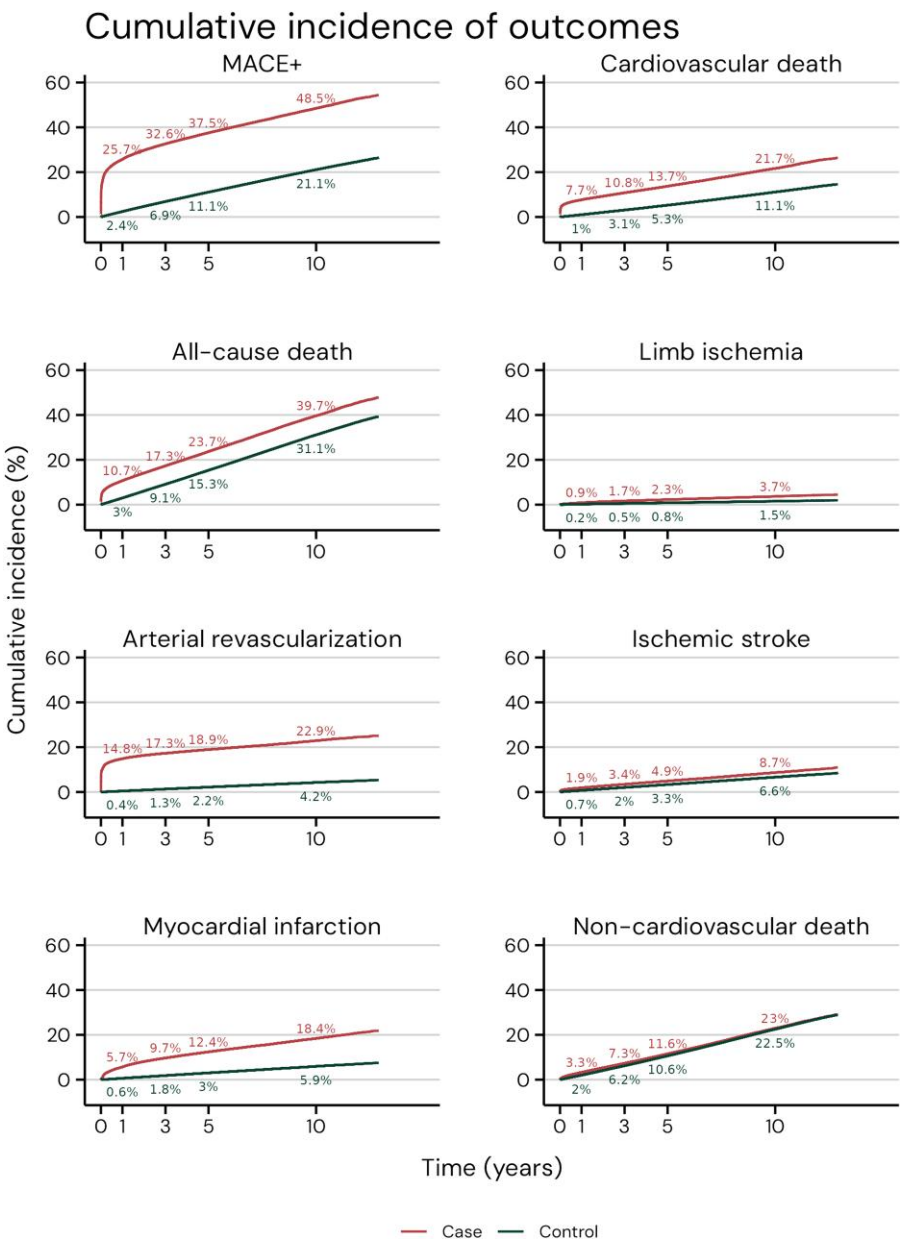


Figure 1 Clinical outcome.

Similar studies have often focused on mortality or have not been able to adjust for differences in comorbidities as in the present study.[11–15] Estimates of health care costs depend on study design, health care setting, and patient selection, making comparisons between studies challenging. In comparison with a Danish study of first-time MIs with a similar age and sex distribution but a shorter follow-up, the total costs during the first year (excluding the index event) for MI cases (€13 000–14 500) and non-MI controls (€4000–5000) were similar,[5] whereas other studies using real-world data have estimated both lower and higher costs.[6,7] In a Swedish study including national data from all patients with MI between 2006 and 2011, hospitalization costs during the first year were similar, whereas costs for subsequent years were lower.[4] Compared with that study, the proportion of outpatient and medical costs relative to the total costs appears to have increased over the years.

The outcomes and healthcare resource utilization patterns observed in our Swedish registry should be interpreted within the context of Sweden's universal healthcare system, where access to guideline-directed therapy is relatively uniform and largely independent of patient demographics or socioeconomic status. Recent international studies show that healthcare system structures and population demographics influence post-MI outcomes and costs. Using the same SWEDEHEART registry as this study, Zwackman *et al.* found that foreign-born MI patients had outcomes as good as or better than native-born patients despite less favourable risk factor profiles, suggesting that equal access to treatments can reduce disparities.[16] In contrast, Dafaalla *et al.* found that more than one-third of STEMI patients with

Table 2 Unadjusted and adjusted associations of MI (vs. controls) with study outcomes

			Unadjusted		Adjusted	
Outcome	IR cases	IR controls	HR	*P*-value	HR	*P*-value
MACE	89.94	23.64	3.65 (3.61–3.69)	<0.01	3.18 (3.15–3.22)	<0.01
All-cause death	53.26	35.91	1.48 (1.47–1.5)	<0.01	1.27 (1.25–1.28)	<0.01
Cardiovascular death	27.55	11.46	2.39 (2.35–2.43)	<0.01	1.97 (1.94–2.01)	<0.01
Limb ischaemia	4.15	1.58	2.61 (2.5–2.73)	<0.01	1.72 (1.64–1.79)	<0.01
Arterial revascularization	38.04	4.35	8.11 (7.95–8.27)	<0.01	7.42 (7.27–7.57)	<0.01
Ischaemic stroke	9.66	6.82	1.41 (1.38–1.45)	<0.01	1.24 (1.21–1.28)	<0.01
Myocardial infarction	23.70	6.11	3.84 (3.76–3.91)	<0.01	3.29 (3.22–3.35)	<0.01
Non-cardiovascular death	25.70	24.45	1.05 (1.04–1.07)	<0.01	0.92 (0.9–0.93)	<0.01

IR, Incidence rate per 1000 person-years; HR, hazard ratio; CI, confidence interval; MACE, major adverse cardiovascular event, defined as the first occurrence of cardiovascular death, limb ischaemia, arterial revascularization, ischaemic stroke, or myocardial infarction. Multivariable models were adjusted for disposable income category, educational level, type 1 and type 2 diabetes, hypertension, chronic kidney disease, peripheral arterial disease, limb ischaemia, ischaemic heart disease, statin intolerance, and use of aspirin, β-blockers, and ACE inhibitors or ARBs within six months before the index date.

Table 3 Annual HCRU and costs

	Case	Control
Inpatient visits	0.65 (1.17)	0.32 (0.62)
Inpatient length of stay (days)	3.05 (7.81)	1.67 (4.81)
Outpatient visits	3.09 (5.54)	2.02 (3.36)
ED visits	0.28 (0.75)	0.15 (0.42)
Coronary angiographies	0.07 (0.19)	0.01 (0.07)
Inpatient cost	4366 (12 606)	2156 (4778)
Outpatient cost	1497 (2774)	955 (1690)
Medication costs	1444 (2819)	856 (2793)
Total cost	7266 (14 198)	3934 (6797)

Cohort-level averages (SD) per patient year, calculated as total cost or HCRU after MI or index date divided by total pooled follow-up time in years. Costs are expressed in 2024 euros.

cancer in the UK received suboptimal care, particularly among ethnic minorities and women.[17] Moledina *et al.* compared young STEMI patients (≤50 years) in the UK and US and found similar demographic changes-more females and ethnic minorities-but different risk factor trends (less smoking in the UK, more in the US) and management patterns (CABG declining only in the US).[18] Similarly, Simonsson *et al.*, also in SWEDEHEART data, observed less smoking but more obesity among Swedish MI patients under age 60.[19] These studies show that post-MI outcomes and healthcare utilization are influenced by both healthcare system structures and changing population risk profiles, which is important to consider when interpreting findings from the Swedish universal healthcare setting.

After adjusting for differences in age and comorbidities, females had a higher excess risk of MI, ischaemic stroke, limb ischaemia and the need for arterial revascularization, which was also reflected in corresponding excess costs. This has also been observed in other studies using matched controls, although focusing on mortality and not adjusting for differences in baseline characteristics.[14,15] One reason is most likely better outcomes in female non-MI controls compared with male non-MI controls. The higher use of angiography in men is most likely explained by the higher prevalence of obstructive coronary artery disease in men with MI.[20]

When comparing outcomes in MI cases and non-MI controls, with and without risk factors, there was a higher excess risk of all endpoints except arterial revascularization in MI patients with diabetes. A similar but less pronounced pattern was observed in patients with hypertension. Previous studies have reported excess mortality in these subgroups, but few have examined outcomes other than mortality using these models.[15] The excess in clinical events could be translated into higher HCRU and costs, with almost 50% higher excess costs in both patients with diabetes and those with hypertension.

Not only the absence of risk factors, but also better control of existing risk factors, was associated with a lower excess risk of cardiovascular events after an MI.

Achieving a significant LDL cholesterol reduction of more than 50% had substantially lower HCRU and 24% lower annual total costs. This is well in line with clinical trials providing evidence for a causal effect of lipid-lowering therapy on costs, as well as real-world data showing an association between lipid-lowering treatment, adherence to therapy, achieving treatment targets, and less need for hospitalizations.[10,21,22]

Strengths and limitations

Strengths of the study include the comprehensive and detailed data, covering almost all first-time MIs in a country, and the long-term follow-up extending up to 10 years. This allows us to show that the excess risk and healthcare burden after a first MI persist well beyond the acute phase, which has not been as clearly demonstrated in prior studies. The excess risk was only modestly attenuated after adjusting for comorbidities, suggesting that the long-term burden is not primarily explained by differences in baseline health status. The results regarding clinical outcomes should be representative for countries with similar cardiovascular risk profiles. However, the cost estimates may not be fully generalizable to other countries, though relative costs between cohorts may be. Sweden's health care system is universal, tax-funded, free at the point of use, and allocates about 10% of its gross domestic product to health. These results should thus be extrapolated with caution in settings with demographic characteristics and healthcare systems

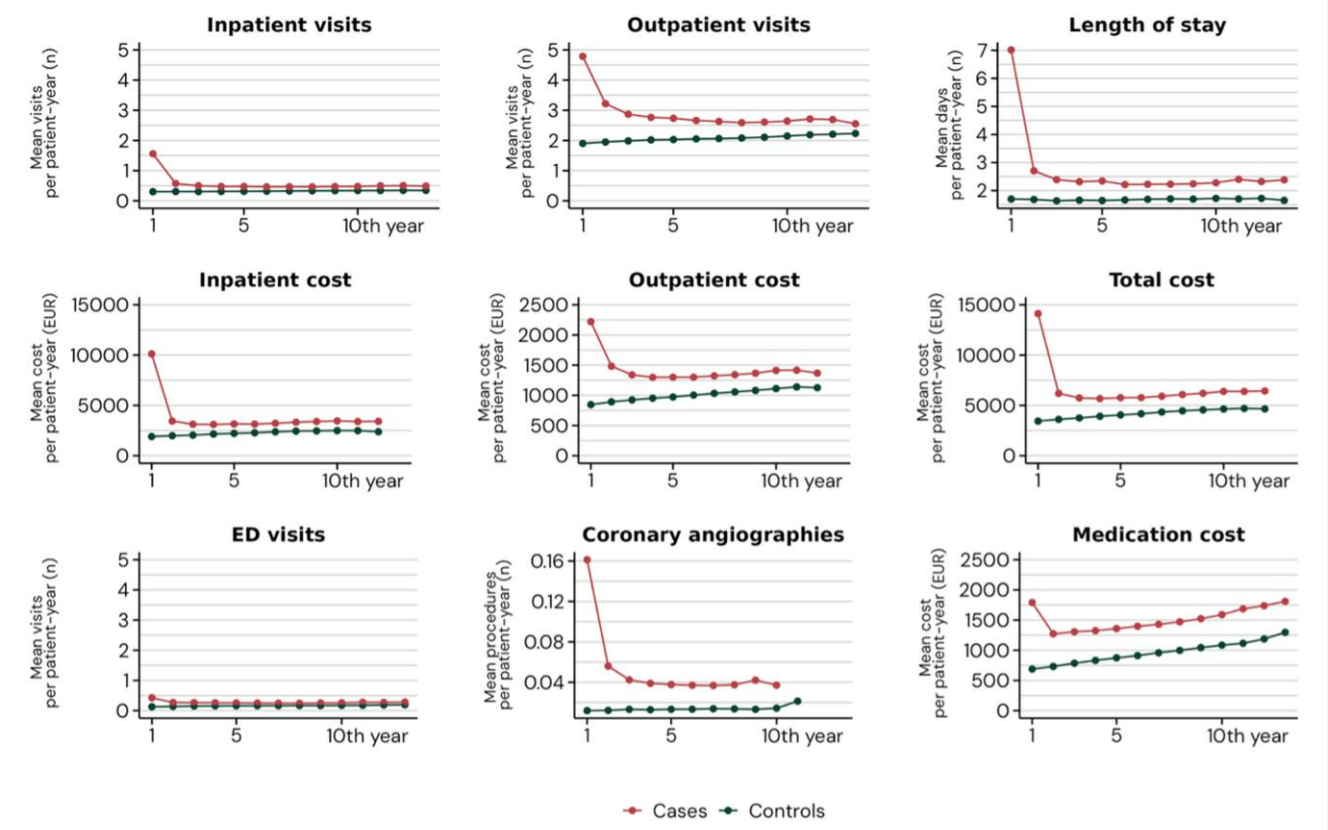


Figure 2 Average healthcare resource utilization (HCRU) for each consecutive year after index date, stratified by group. Costs are presented in 2024 euros. Visit-related measures reflect the number of visits per person per year, and inpatient length of stay is reported in days. Cost estimates represent the cohort-level averages (total cost divided by total person-time) for each year.

that differ from Sweden's. Detailed data on mean resource use are also provided, enabling estimation of how cost results might change if different unit costs are applied. Another limitation with the study is the lack of primary-care data, leading to an underestimation of the outpatient costs, especially the long-term costs. Diagnoses and costs were identified using ICD and DRG codes, which may not fully capture the actual clinical picture, including disease severity or the total cost of care. Additionally, morbidity is associated with secondary costs such as sick leave and insurance costs. Although this is largely an older population, caretaker burden and decreased productivity costs to the society are not accounted for as we here focus on healthcare resource use only. Estimates here are therefore conservative; additional data would be of interest to policy makers, public health agencies, employers, insurers, patients and families. We did not distinguish between MI-related costs and costs from other causes. However, by comparing with matched controls and adjusting for differences in baseline characteristics, the observed differences in outcomes should be attributable to the MI itself. This is an observational study, and as such there will always be a risk of residual confounding and confident conclusions regarding causality cannot be made.

Conclusions

In conclusion, first-time MI patients have a substantially higher risk of cardiovascular events—including cardiovascular death, MI, and stroke—than matched non-MI controls, even after adjusting for comorbidities. These risks are accompanied by higher HCRU and costs, underscoring the need for effective prevention strategies to reduce disease progression and avoidable healthcare use.

Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

Author contributions

Christian Reitan (Conceptualization, Investigation, Methodology, Writing—original draft, Writing—review & editing [equal], Data curation, Formal analysis, Project administration, Visualization [lead]), Alexandre H. Watanabe (Conceptualization, Methodology, Project administration, Resources, Writing—review & editing [equal], Visualization [supporting]), Lori D. Bash (Conceptualization, Methodology, Resources, Writing—review & editing [equal], Supervision, Visualization [supporting]), Thibaut Galvain [Conceptualization, Methodology, Writing—review & editing (equal)], Urs Arnet [Conceptualization, Methodology, Writing—review & editing (equal)], and Tomas Jernberg (Conceptualization, Investigation, Methodology, Project administration, Resources, Writing—review & editing [equal], Funding acquisition, Supervision, Writing—original draft [lead])

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Conflict of interest: CR reports institutional grant from MSD during the conduct of this study and has previously acted as local PI for a study sponsored by AstraZeneca. AHW and LDB are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. TG, and UA are employees of MSD Switzerland, who may own stock and/or hold stock options in Merck & Co., Inc., Rahway, NJ, USA. TJ reports institutional grant from MSD during the conduct of this study.

Data availability

The data underlying this article cannot be shared publicly due to data protection regulations and ethical restrictions, as they contain sensitive individual-level health information. Access to the data may be granted on reasonable request to the corresponding author, subject to approval by the relevant data custodians and ethical review boards.

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