

# Characteristics, treatment patterns, and residual cardiovascular risk of patients with a first acute myocardial infarction: A nationwide population-based cohort study in Norway

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## Abstract

There are few nationwide descriptive studies of longitudinal drug use and residual cardiovascular risk in patients with myocardial infarction (MI) in contemporary clinical practice. The objectives of this work were to describe characteristics and longitudinal cardiovascular drug use of patients with a first acute MI in Norway, and to quantify residual risks of cardiovascular events and death. Using nationwide health registries in Norway, we identified 43 750 adults with a first MI (2010 to 2015) and  $\geq 1$  prescription for antiplatelet medication. We described cardiovascular medication post-MI and calculated residual cardiovascular risks. Between 3 months and 13–15 months post MI, medication use dropped from 93.3% to 75.1% for low-dose aspirin, 78.1% to 11.0% for dual antiplatelet therapy, 91.6% to 78.7% for antihypertensives, and 88.0% to 70.7% for lipid-lowering therapy. Incidence rate ratios (IRRs) for recurrent MI were similar between subpopulations at 12 months and notably different at 12–36 months. IRRs (95% CIs) at 12–36 months were 1.52 (1.26–1.82) for 65–74 years, 2.26 (1.88–2.71) for 75–84 years, and 3.97 (3.29–4.79) for  $\geq 85$  years (vs. 18–49 years), 2.42 (2.18–2.69) for those with ischaemic heart disease (IHD), 2.26 (1.97–2.59) for peripheral artery disease (PAD), 2.17 (1.98–2.36) for hypertension, and 1.82 (1.65–2.01) for diabetes. In conclusion, secondary prevention medication use 13–15 months following a first MI is suboptimal among patients in Norway. The elderly and those with IHD, PAD, diabetes, or hypertension are at high-risk for recurrent MI/stroke/death and should be managed closely beyond the first year.

## KEYWORDS

acute myocardial infarction, mortality, peripheral artery disease, pharmacotherapy, residual risks, stroke

**Abbreviations:** CHD, coronary heart disease; CI, confidence interval; DAPT, dual antiplatelet therapy; IRR, incidence rate ratio; ICD-10, International Classification of Diseases, 10th revision; IHD, ischaemic heart disease; MACE, ischaemic stroke, all-cause mortality; MI, myocardial infarction; NPR, Norwegian Patient Register; NorPD, Norwegian Prescription Database; PAD, peripheral artery disease; SD, standard deviation.

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## 1 | INTRODUCTION

Coronary heart disease (CHD) is a leading cause of death in Europe, accounting for 1.8 million deaths each year [1]. While mortality rates of myocardial infarction (MI) have declined significantly in recent decades, one in 10 patients still die in the year after their event, and among those who survive their MI, 20% experience a subsequent cardiovascular event in the first year [2]. Registry data show that, in 2016, 11 401 patients in Norway were admitted to hospital or received outpatient treatment with a primary diagnosis of MI [3]. Population-based surveys from Tromsø, Norway, have shown temporal trends towards a lower proportion of severe infarctions among patients treated for a MI [4], meaning that a higher proportion of these patients are requiring long-term secondary prevention treatment.

Around 1-year of dual antiplatelet therapy (DAPT) with low-dose aspirin and a P2Y<sub>12</sub> receptor inhibitor, and longer-term treatment with aspirin monotherapy and lipid-lowering therapy remains the cornerstone of pharmacotherapy for secondary cardiovascular prevention following MI [5, 6]. Several other secondary prevention drugs are also commonly indicated following MI, including those that effectively manage blood pressure and other key metabolic parameters [2]. Despite the availability and frequent use of these effective preventative treatments, residual cardiovascular risks remain evident. Optimising secondary prevention pharmacotherapy is an essential component in reducing residual risks, and identification of patient groups in whom these risks are greatest would help guide more targeted prevention measures.

There are few nationwide descriptive studies of the broad MI patient population, including longitudinal drug use and residual cardiovascular risks, in contemporary clinical practice. Previous studies on this topic have focused on patients with pre-existing CHD [7], those particularly intensively managed [8], or have evaluated time-trends in drug use [9]. Our present study had two distinct objectives: to describe characteristics and longitudinal cardiovascular drug use patterns of patients with a first MI in Norway, and to quantify long-term residual risks of cardiovascular events and death among this patient population and identify high-risk subgroups.

## 2 | METHODS

### 2.1 | Study design and data source

We performed a population-based cohort study using linked data from two mandatory nationwide registries—the Norwegian Patient Register (NPR) [10] and the Norwegian Prescription Database (NorPD) [11]. The NPR was established in 2008 and contains all visits

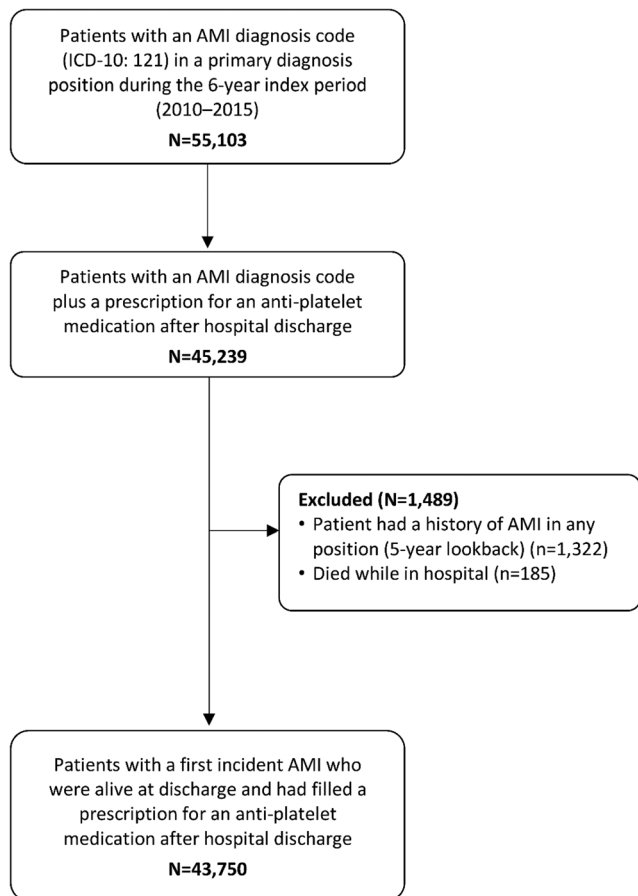
(emergency visits, inpatient hospitalisations, and outpatient ambulatory consultations) from all hospitals in Norway. Diagnoses are coded using the International Classification of Diseases, 10th revision (ICD-10). The NorPD holds data on all prescriptions dispensed at pharmacies nationwide from 1 January 2004. Medications dispensed are coded according to the Anatomical Therapeutic Chemical system, and details are included about the date of drug dispensation, quantity dispensed, and daily dose. Reimbursement codes (based on ICD-10 or the International Classification of Primary Care-2 coding system) are also included for each dispensation, enabling the adjudication of comorbidities that are typically handled in primary care (e.g., hypertension and diabetes). Previous research has shown that the vast majority of patients who are prescribed secondary prevention cardiovascular drugs do go on to collect them from the pharmacy; therefore, the dispensations recorded in NorPD are an accurate reflection of the drugs issued by the prescriber [12]. However, the database does not capture drugs administered during hospitalisation, those used in nursing homes or over-the-counter (OTC) medications. The study protocol was approved by the regional ethics committee on 2 July 2018 (reference number 2018/977/REK sor-ost B).

### 2.2 | MI study cohort

A flowchart depicting identification of the study cohort is shown in Figure 1. We identified all patients aged  $\geq 18$  years with a diagnosis of MI (ICD-10 code I21) in the primary position in the NPR between 1 January 2010 and 31 December 2015, and still alive at hospital discharge. We included patients with a prescription for antiplatelet medication in the NorPD after hospital discharge—this was ascertained in the subsequent 100 days for low-dose aspirin and in the subsequent 30 days for P2Y<sub>12</sub> receptor inhibitors. We excluded patients with a diagnosis of MI in any position (during a 5-year look-back period). The date of the MI was the index date.

### 2.3 | Patient variables

Information on patient demographics (age at the index date and sex) and comorbidities recorded during the available five-year look-back period were extracted from the NPR focusing on previous cardiovascular disease and its risk factors. Owing to an under-representation of typical primary care diagnoses in the NPR (especially hypertension and diabetes), comorbidities were determined using both ICD-10 codes in the NPR and relevant dispensed treatments from the NorPD. Medication use (based on the NorPD) included antiplatelets (low-dose aspirin, clopidogrel, ticagrelor, and prasugrel),



**FIGURE 1** Flow chart depicting the identification of the AMI study cohort. AMI, acute myocardial infarction

antihypertensives, lipid-modifying drugs, and anti-diabetics. Medication use was assessed at baseline (a prescription during the 120 days before the index date), during the first 3 months after the index date, and for all individuals who did not experience a recurrent MI 12 months after their first incident MI, during 13–15 months after the index date.

## 2.4 | Follow-up and outcome identification

Outcomes of interest were recurrent MI; secondary outcomes were stroke (ischaemic and haemorrhagic), all-cause mortality, and the three-point composite MACE (MI, ischaemic stroke, all-cause mortality). Cohort members were followed from the date of the index MI until the outcome of interest, death or the end of follow-up (31 March 2019), whichever came first, and with separate follow-up conducted for each outcome. In the identification of recurrent MI events, we disregarded cases recorded in the 40 days following the index MI to reduce the risk of misclassification due to these being subsequent entries of the initial event.

## 2.5 | Statistical analysis

Patient demographics, comorbidities and co-medications were described using frequency counts and percentages (all categorical variables), with age also summarised by means with standard deviation (SD). For each outcome during follow-up, crude cumulative incidences at 12 months and 12–36 months were calculated by dividing the number of incident cases by the number of patients at the start of follow-up with 95% confidence intervals (CIs) computed using the binominal distribution, stratified by age at the index MI (18–49, 50–64, 65–74, 75–84 and  $\geq 85$  years). For recurrent MI, we also stratified cumulative incidences by the presence/absence of hypertension, ischaemic heart disease (IHD), diabetes and peripheral artery disease (PAD), and we calculated crude incidence rates of recurrent MI during 12 months' follow-up by dividing the number of incident cases by the total person-years during the respective time periods, with 95% CIs determined using the Poisson distribution, and stratifying by age, sex and the aforementioned comorbidities, with crude incidence rate ratios (IRRs) calculated for each variable. Additionally, in a landmark analysis, we calculated the incidence rates of recurrent MI and associated IRRs during 12–36 months' follow-up restricting to patients who were still alive and had not experienced a MI up to 12 months. The study was designed to be descriptive in nature with no formal statistical hypothesis or standardisation to increase comparability between groups. The SAS software (version 9.4, SAS Institute, Cary, NC) was used for all analyses.

## 3 | RESULTS

### 3.1 | Baseline characteristics

A total of 43 750 patients were identified with a first incident acute MI and a prescription for an anti-platelet in the NorPD following hospital discharge, after applying the exclusion criteria. Baseline characteristics are shown in Table 1 (see Table S1 for comorbidities stratified by age group). Mean age of the cohort was 67.5 years (SD  $\pm$  13.4 years) and over two thirds (67.9%) were men; older patients ( $\geq 75$  years) were mostly men and younger patients were mostly female (Figure S1). The most common comorbidity was hypertension (51.6%), which was more common in women (61.7%) than in men (46.9%), followed by diabetes (14.2%), solid tumours (9.7%), and IHD (9.4%). The most commonly prescribed medications at baseline were antihypertensives (49.2%)—including drugs targeting the renin-angiotensin system (31.5%) and beta-blockers

**TABLE 1** Baseline characteristics of the AMI study cohort

	Male <i>N</i> = 29 715 <i>n</i> (%)	Female <i>N</i> = 14 035 <i>n</i> (%)	All <i>N</i> = 43 750 <i>n</i> (%)
<b>Age (years)</b>			
18–49	3412 (11.5)	764 (5.4)	4176 (9.5)
50–64	11 282 (38.0)	2948 (21.0)	14 230 (32.5)
65–74	7820 (26.3)	3430 (24.4)	11 250 (25.7)
75–84	5019 (16.9)	3774 (26.9)	8793 (20.1)
≥85	2182 (7.3)	3119 (22.2)	5301 (12.1)
Mean (SD)	65.0 (12.7)	72.9 (13.3)	67.5 (13.4)
<b>Comorbidities<sup>a</sup></b>			
Hypertension	13 924 (46.9)	8654 (61.7)	22 578 (51.6)
Diabetes	4028 (13.6)	2185 (15.6)	6213 (14.2)
Solid tumour	2900 (9.8)	1351 (9.6)	4251 (9.7)
Ischaemic heart disease	3049 (10.3)	1065 (7.6)	4114 (9.4)
Atrial fibrillation	1669 (5.6)	965 (6.9)	2634 (6.0)
PAD	1525 (5.1)	866 (6.2)	2391 (5.5)
COPD	1378 (4.6)	1018 (7.3)	2396 (5.5)
Kidney disease	1323 (4.5)	721 (5.1)	2044 (4.7)
Congestive heart failure	1023 (3.4)	724 (5.2)	1747 (4.0)
Stroke	744 (2.5)	416 (3.0)	1160 (2.7)
<b>Medications<sup>b</sup></b>			
Antiplatelets	7615 (25.6)	4308 (30.7)	11 923 (27.3)
DAPT	151 (0.5)	55 (0.4)	206 (0.5)
Low-dose aspirin	7169 (24.1)	4044 (28.8)	11 213 (25.6)
P2Y-12 inhibitors	293 (1.0)	133 (0.9)	426 (1.0)
Clopidogrel	272 (0.9)	132 (0.9)	404 (0.9)
Ticagrelor	17 (0.1)	1 (0)	18 (0)
Prasugrel	4 (0)	0 (0)	4 (0)
Antihypertensives	13 246 (44.6)	8272 (58.9)	21 518 (49.2)
Diuretics	2656 (8.9)	2737 (19.5)	5393 (12.3)
Beta-blockers	6249 (21.0)	3958 (28.2)	10 207 (23.3)
Peripheral vasodilators	20 (0.1)	14 (0.1)	34 (0.1)
Calcium antagonists	4203 (14.1)	2462 (17.5)	6665 (15.2)
Renin-angiotensin system drugs	8705 (29.3)	5080 (36.2)	13 785 (31.5)
Other	478 (1.6)	140 (1.0)	618 (1.4)
Lipid-modifying drugs	7369 (24.8)	3732 (26.6)	11 101 (25.4)
Nitrates	2095 (7.1)	1300 (9.3)	3395 (7.8)
Antidiabetic drugs	3286 (11.1)	1756 (12.5)	5042 (11.5)
Insulin	1111 (3.7)	637 (4.5)	1748 (4)
NSAIDs	3739 (12.6)	2283 (16.3)	6022 (13.8)
Acid secretory drugs	4171 (14.0)	2853 (20.3)	7024 (16.1)

<sup>a</sup>During a 5-year look-back period.<sup>b</sup>During the 120 days before the index date.

Abbreviations: ASA, acetylsalicylic acid; ATC, Anatomical Therapeutic Chemical; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; ICD, International Classification of Diseases; NSAID, nonsteroidal anti-inflammatory drug; PAD, peripheral artery disease; SD, standard deviation.

(23.3%)—lipid-modifying drugs (25.4%), and low-dose aspirin (25.6%). A quarter (24.8%) of patients died over the whole follow-up period (mean 2.8, SD ± 0.7 years; maximum 9.3 years), 34% of

females and 20.5% of males. Deaths in the older age groups (≥75 years) were slightly more likely to be male, while deaths in those aged <75 years were slightly more likely to be female (Figure S2).

## 3.2 | Medication use following the index MI

Medication use in the 3 months post index date, and in the 13–15 months post index date for patients who did not experience a recurrent MI in the first 12 months' follow-up, is shown in Table 2. The vast majority of patients had a dispensation for low-dose aspirin (93.3%), a P2Y12 inhibitor (84.4%) or DAPT (78.1%) at 3 months (acute treatment phase). These proportions dropped to 75.1% (low-dose aspirin), 13.6% (P2Y12 inhibitors), and 11.0% (DAPT) at 13–15 months. At 3 months, most patients were dispensed an antihypertensive (91.6%) and a lipid-lowering drug (88.0%); at 13–15 months, these proportions dropped to 78.7% and 70.7%, respectively.

## 3.3 | Residual risks

### 3.3.1 | Incidence rates and rate ratios of recurrent MI

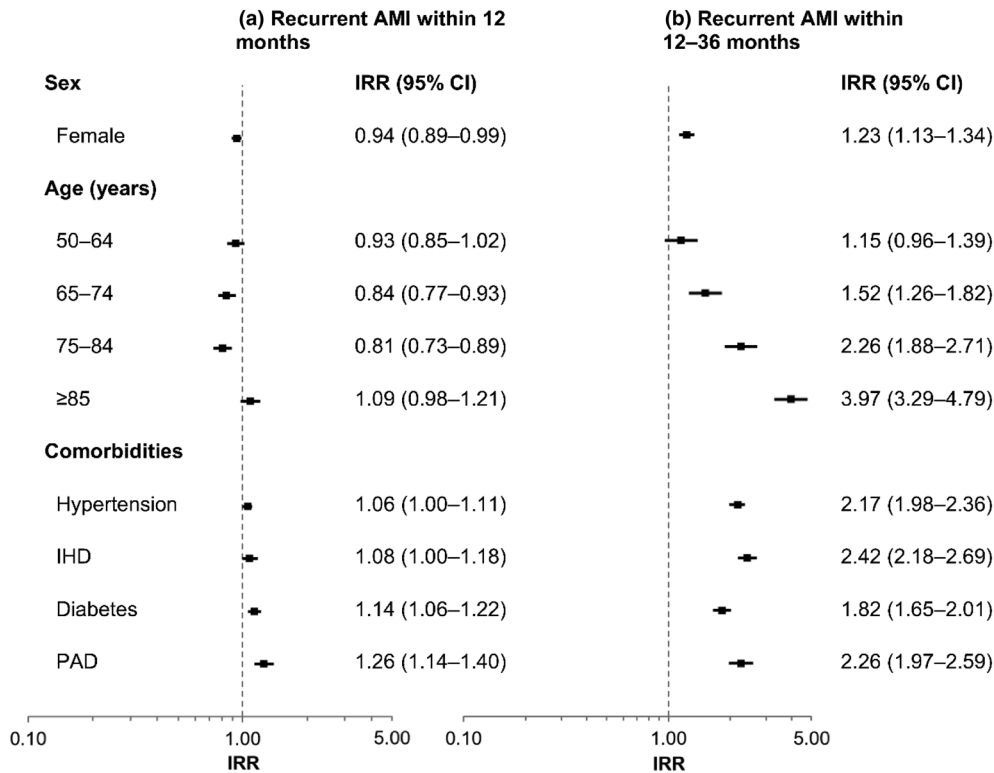
The incidence of a first recurrent MI was notably higher during the first 12 months' follow-up than at 12–36 months. At 12 months, incidence rates were 156.8 per 1000 person-years (95% CI: 152.0–161.7) in men

and 147.5 (95% CI: 140.8–154.5) in women. At 12–36 months, incidence rates were 31.9 per 1000 person-years (95% CI: 30.3–33.6) in men and 39.2 per 1000 person-years (95% CI: 36.6–42.0) in women. Rates by age group and comorbidities analysed can be found in Table S2. Crude IRRs for the risk of first recurrent MI among patient subgroups at 12 months and 12–36 months are presented in Figure 2 and Table S2. Risks of recurrent MI were broadly similar between patient subgroups during the first 12 months of follow-up, although reduced risks were seen for females (IRR 0.94, 95% CI: 0.89–0.99) and for patients aged 65–74 years (IRR 0.84, 95% CI: 0.77–0.93) or 75–84 years (IRR 0.81, 95% CI: 0.73–0.89) when compared with those aged 18–49 years. Higher risks were seen for patients with diabetes (IRR 1.14, 95% CI: 1.06–1.22) or PAD (IRR 1.26, 95% CI: 1.14–1.40). Differences in the risk of recurrent MI were seen between patient subgroups at 12–36 months' follow-up. A clear increase in risk was seen with increasing age; compared with patients aged 18–49 years at the index date, IRRs were 1.52 (95% CI: 1.26–1.82) for 65–74 years, 2.26 (95% CI: 1.88–2.71) for 75–84 years, and 3.97 (95% CI: 3.29–4.79) for ≥85 years. Increased risks during this later follow-up period were also seen among females (IRR 1.23, 95% CI: 1.13–1.34) and among patients with hypertension (IRR 2.17, 95% CI: 1.98–2.36), IHD

**TABLE 2** Medication use at baseline, during the first 3 months after a first incident AMI, and for all individuals who did not experience a recurrent AMI 12 months after their first incident AMI

	Baseline n (%)	First 3 months n (%)	13–15 months n (%)
<b>Antiplatelets</b>	11 923 (27.3)	43 548 (99.5)	27 445 (78.0)
DAPT	206 (0.5)	34 190 (78.1)	3862 (11.0)
Low-dose aspirin	11 213 (25.6)	40 829 (93.3)	26 422 (75.1)
P2Y-12 inhibitors	426 (1)	36 907 (84.4)	4800 (13.6)
Clopidogrel	404 (0.9)	23 770 (54.3)	2453 (7.0)
Ticagrelor	18 (0)	10 992 (25.1)	1773 (5.0)
Prasugrel	4 (0)	2968 (6.8)	593 (1.7)
<b>Antihypertensives</b>	21 518 (49.2)	40 060 (91.6)	27 707 (78.7)
Diuretics	5393 (12.3)	10 612 (24.3)	5578 (15.8)
Beta-blockers	10 207 (23.3)	35 118 (80.3)	22 317 (63.4)
Peripheral vasodilators	34 (0.1)	17 (0)	10 (0)
Calcium antagonists	6665 (15.2)	5387 (12.3)	4416 (12.5)
Renin-angiotensin system drugs	13 785 (31.5)	24 280 (55.5)	16 758 (47.6)
Other	618 (1.4)	468 (1.1)	336 (1.0)
Lipid-modifying drugs	11 101 (25.4)	38 516 (88.0)	24 900 (70.7)
Nitrates	3395 (7.8)	11 857 (27.1)	3323 (9.4)
Antidiabetic drugs	5042 (11.5)	5251 (12.0)	4133 (11.7)
Insulin	1748 (4.0)	1918 (4.4)	1407 (4.0)
NSAIDs	6022 (13.8)	2179 (5.0)	2223 (6.3)
Acid secretory drugs	7024 (16.1)	12 242 (28.0)	8104 (23)

Abbreviations: ASA, acetylsalicylic acid; NSAID, nonsteroidal anti-inflammatory drug.



**FIGURE 2** IRRs for first recurrent AMI at (a) 12 months, and (b) 12–36 months according to sex, age and comorbidities. Note: Reference groups were male, age 18–49 years and having the respective comorbidity. AMI, acute myocardial infarction; CI, confidence interval; IHD, ischemic heart disease; IRR, incidence rate ratio; PAD, peripheral artery disease

(IRR 2.42, 95% CI: 2.18–2.69), diabetes (IRR 1.82, 95% CI: 1.65–2.01), and PAD (IRR 2.26, 95% CI: 1.97–2.59).

### 3.3.2 | Cumulative incidences of recurrent MI, stroke, MACE and all-cause death

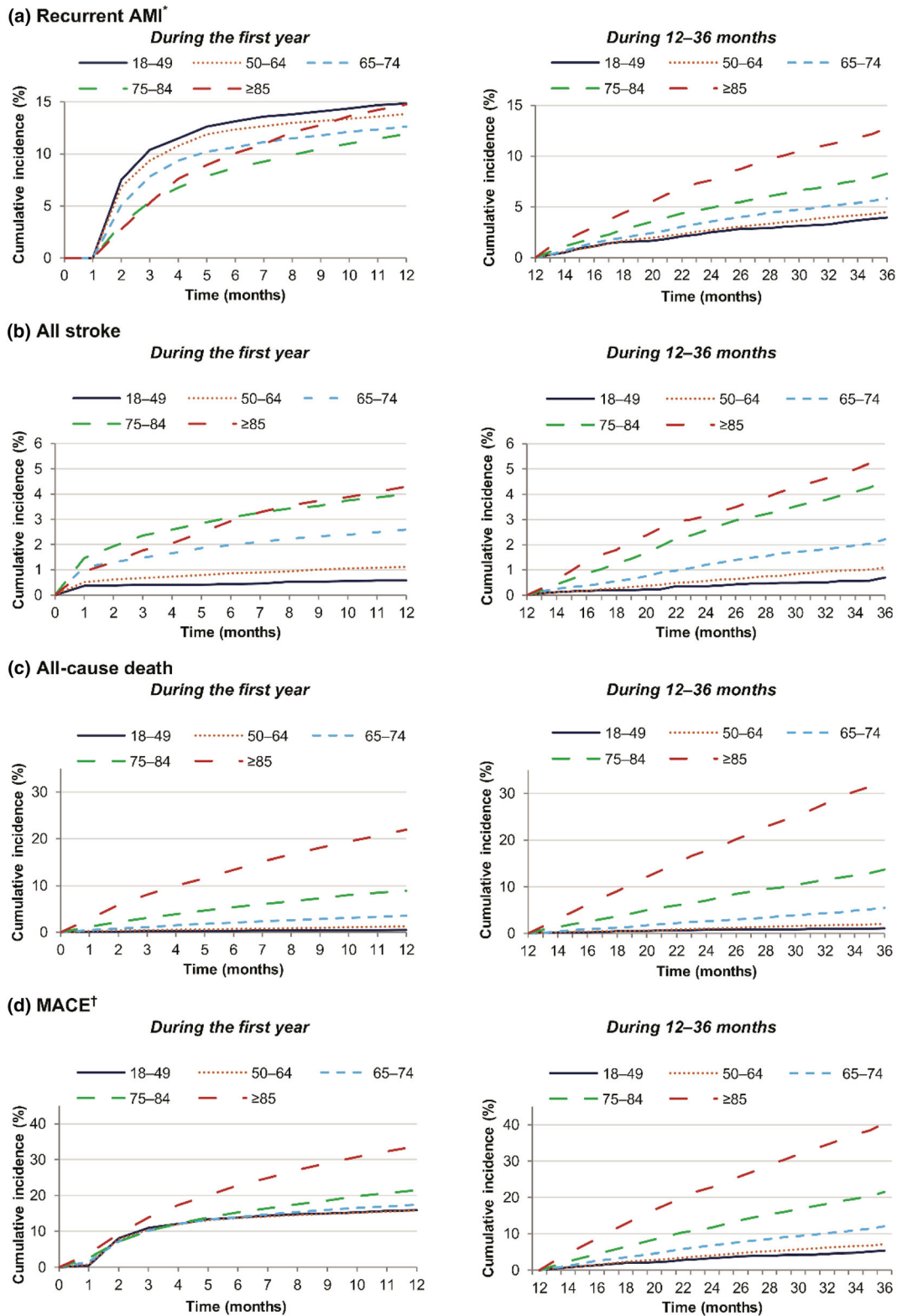
Cumulative incidences of the study outcomes are shown in Figure 3 and Tables S3–S6. Cumulative incidences at 12 months' follow-up were 13.3% (recurrent MI), 2.4% (stroke), 5.8% (all-cause death), and 19.5% (MACE), each being higher among the oldest age group (≥85 years) throughout this first year except, notably, for recurrent MI, where incidences were highest in the youngest age group (18–49 years). Cumulative incidence at 36 months' follow-up were 18.6% (recurrent MI), 4.7% (stroke), 13.6% (all-cause death) and 31.1% (MACE). For recurrent MI, cumulative incidence was 13.3% at 12 months and 18.6% at 3 years and was highest among the youngest age group (18–49 years) throughout the first 12 months' follow-up, and thereafter highest among the oldest age group (≥85 years); incidences ranged from 11.9% (75–84 years) to 14.8% (18–49 years and ≥85 years). This age pattern, however, was not seen for stroke, MACE or all-cause death, where cumulative incidences were highest in the oldest age group—a pattern that was also clearly evident for all outcomes at 12–36 months. Among patients who survived their first MI without experiencing a recurrent MI in the first 12 months,

cumulative incidences increased throughout the subsequent 2 years (i.e., 12–36 from the index MI) in all age groups for each study outcome. These were highest and increased most rapidly in the older age groups.

## 4 | DISCUSSION

In this large population-based nationwide study of over 40 000 patients with a first MI in Norway, use of secondary cardiovascular prevention medications was high in the acute treatment phase (3-months post-event) with close to 80% receiving DAPT, 93.3% low-dose aspirin, 91.6% antihypertensives, 88.0% lipid-lowering drugs and 80.3% beta-blockers. However, low-dose aspirin use, which is indicated as life-long therapy, was reduced to 75.1% at 13–15 months. Approximately one in five experienced a recurrent MI, a stroke or died within a year of their index MI, increasing to nearly a third of patients by 3 years.

Close to 80% of patients in our study received DAPT in the 3 months post-event, dropping to 11.0% at 13–15 months, consistent with the recommended 1-year duration. However, other secondary prevention medication use decreased when moving from the acute to chronic treatment phase. Reductions in cardiovascular pharmacotherapy between acute and longer-term treatment phases following MI has been reported by others [13] and is expected considering the multifactorial issues relating to long-term adherence of preventative medications. Our estimates of secondary prevention drug use



**FIGURE 3** Residual risk of (a) recurrent AMI, (b) stroke, (c) all-cause death, and (d) MACE during the first year, and during the period from 12 to 36 months (landmark analysis) after a first incident AMI. \*AMI events occurring in the first 40 days of follow-up were not included as recurrent events to avoid potential misclassification. †Composite of MI, ischaemic stroke, all-cause mortality. AMI, acute myocardial infarction; MACE, major adverse cardiovascular events; MI, myocardial infarction

are highly consistent with those from Halvorsen et al, [14] which also used a nationwide Norwegian register but over a slightly earlier time period (2009–2013), and not necessarily restricted to those with a first MI. In their study, 72% received DAPT, 19% single antiplatelet therapy, 90% statin therapy, 82% beta-blockers, and 60% angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs) during the 30 days post-discharge for their MI. In addition, our estimates of drug use are greater than findings from Jorgensen et al [9] among patients with a first MI in Denmark during 2003–2006, especially for low-dose aspirin (69.7%) and statin (77.3%) therapy in the 3 months post-discharge for their MI. Among the smaller studies from other countries on this topic, Huber et al [15] evaluated 4349 patients from Switzerland hospitalised for MI during 2012–2015 and reported that 63% received DAPT and 86% received antiplatelet therapy within the 30 days after discharge. And, in a study from France, of 461 patients with MI during 2004–2007, Bezin et al [16] found drug use in the 2 months post-MI to be 86.6% for beta-blockers, 94.1% for antiplatelet therapy, 93.5% for lipid-lowering drugs, and 77.2% for ACE inhibitors or ARBs.

Another aspect of our findings pertains to the clear residual cardiovascular risks seen following a first MI [17]. In a study of 108 315 patients discharged with MI in Sweden between 2006 and 2011, Jernberg et al [18] reported an 18.3% cumulative incidence of their composite of MI, stroke and cardiovascular death during the first-year post discharge. This is higher than our estimate but, unlike in our study, they included patients with previous MI. Cumulative incidence at 3 years in Jernberg et al was, however, 18.6%, which is very similar to our estimate (19.5%). In our present study, we saw that at 12–36 months post index MI, the incidence of recurrent MI was significantly higher among older patients, those with IHD, PAD, diabetes or hypertension, and among females, yet this was not as evident during the first-year post index MI. Thus, these patient groups might benefit the most from long-term close monitoring and maintenance of pharmacological prophylaxis [19]. This, combined with other preventative measures, such as changes to modifiable lifestyle factors, is key to minimising residual cardiovascular risks. The high risk of MI recurrence during the first year following MI seen in younger patients (<50 years) in our study is an interesting yet unexplained finding, which warrants further exploration—this observation was not seen for the other study outcomes of stroke, MACE or all-cause death.

Our study aimed to describe the broad incident MI population of Norway and describe residual cardiovascular risks by means of crude quantification, and thereby provide a snapshot of the current clinical landscape of MI patients in terms of their characteristics, treatments received and outcomes. It did not aim to evaluate independent epidemiological associations between particular

patient characteristics or drug treatments and clinical outcomes by way of statistical analyses with control for confounders, and this should be kept in mind when interpreting our findings. Notwithstanding this, our study provides a benchmark from which others can potentially derive hypotheses for further investigation. A strength of the study is the use of data from mandatory nationwide registries in a public healthcare system covering all residents of Norway, giving our findings good external validity. Other strengths are the higher completeness and quality of the registries used [10], and the large cohort, which enabled precise estimates of longitudinal drug use and residual risks. As low-dose aspirin (75–100 mg tablets) are not available OTC in Norway, misclassification of low-dose aspirin exposure from unrecorded OTC use was not a matter of concern. The main limitation relates to the rapid evolution of recommendations on this topic during recent years, therefore our findings may not necessarily reflect the most-up-to-date clinical practice patterns [20]. Furthermore, data collected in health registries were originally collected for administrative use and information on some key risk factors such as smoking and BMI were not available. Another limitation is that a small proportion of patients may not have collected their prescribed medication (i.e., not dispensed); therefore, our estimates of drug use may be slight underestimations.

In conclusion, our findings suggest that secondary prevention medication is reduced after a year following a first MI among patients in Norway. Twenty per cent of patients experience a recurrent MI, stroke or die within a year of their event, rising to around 30% by 3 years. Patients with a first MI should continue to be closely monitored and treated with optimal pharmacotherapy beyond the first year, especially the elderly and those with high-risk comorbidities such as IHD, PAD, diabetes, and hypertension. Additionally, younger patients (those aged <50 years) experiencing a first MI should be observed with diligence in the year following their event due to their high risk of MI recurrence during this time period.

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## CONFLICT OF INTEREST

DA reports personal fees from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol Meier Squibb, MSD, Novartis, Pfizer, Roche-Diagnostics, Amgen and Sanofi, and grants to my institution from Bayer, Medtronic, and BMS. NGO is an employee of Bayer AS. GB and BF were employees of Bayer AB, and JC was an employee of Bayer AS, at the time the study



was carried out. CJ declares personal fees from Bayer for work related to study protocol writing and IEC/registry holder approvals. From October 2019, CJ was a member of the author group without receiving financial compensation for work related to the study.

## ETHICAL APPROVAL

This study was approved on 02.07.2018 by the Regional Ethics Committee of South-Eastern Norway, approval number 2018/977. The study was also approved by the Norwegian Patient Registry under the National Health Directorate on 22.11.2018 for data interrogation and extraction, approval number 18/28195-11.

## DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author. Restrictions by the national privacy act legislation will have to be taken into account.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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