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## ORIGINAL ARTICLE

# Maintenance of statin use over 3 years following acute coronary syndromes: a national data linkage study (ANZACS-QI-2)

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## ABSTRACT

**Objective** To describe patterns of statin use and predictors of poor maintenance over a 3-year period following an acute coronary syndrome (ACS).

**Methods** National hospitalisation, mortality and pharmaceutical dispensing data were linked for all subjects aged 35–84 years discharged from a public hospital with an ACS in New Zealand in 2007.

A Medication Possession Ratio (MPR; percentage of follow-up days patients were dispensed statins) was calculated for each patient. Adequate maintenance was defined by a MPR  $\geq 80\%$ .

**Results** In 2007, 11 348 patients aged 35–84 years were discharged from hospital with ACS. Within 90 days of discharge, 83% had received a statin. Over the follow-up period, 66% were adequately maintained on a statin (MPR  $\geq 80\%$ ): 69% in the first year, 67% in the second year and 66% in the third year. Patients taking statins prior to admission and those who underwent a coronary procedure were 20–50% more likely to have a MPR  $\geq 80\%$  over 3 years than others. In contrast, people aged 35–45 years and those of Maori or Pacific ethnicity were 13–25% less likely to have a MPR  $\geq 80\%$  than those aged 55–64 years and Europeans.

**Conclusions** One-third of patients were not adequately maintained on statins over the 3-year period following ACS, but 82% of those on a statin prior to admission had an MPR  $\geq 80\%$  over 3 years of follow-up. These findings define achievable treatment levels and identify groups who may benefit from efforts to improve statin use.

## INTRODUCTION

Despite the well-documented safety and effectiveness of statins for the secondary prevention of cardiovascular disease (CVD),<sup>1–2</sup> many studies report suboptimal statin use in people following an acute coronary syndrome (ACS). Among patients dispensed statins at least once after an ACS, studies suggest that one-half to three-quarters will have discontinued their medications by 2 years after discharge.<sup>3–5</sup>

In New Zealand there are few external barriers to long-term statin use. The universal healthcare system has a strong primary care focus, in-hospital medications are free of charge and statins are heavily subsidised by the government (at the time of the study, each 3-month prescription cost NZD\$3). The country also has comprehensive up-to-date data on public hospitalisations, mortality and government-subsidised

pharmaceutical dispensing. Using these linked datasets, we have previously investigated 1-year statin maintenance among patients hospitalised for acute coronary events.<sup>6</sup> In this study we assessed statin maintenance for up to 3 years and identified independent predictors of statin use among patients with ACS.

## METHODS

### Study population

We included all New Zealand residents aged 35–84 years discharged from a public hospital with a diagnosis of ACS (ST elevation myocardial infarction (STEMI), non-ST elevation MI (NSTEMI), MI unspecified and unstable angina (UA)) between 1 January and 31 December 2007. The ICD-10-AM codes used to define the four ACS types used in the analysis are listed in online supplementary appendix 1. We excluded people who died within 90 days of discharge or those who spent less than 90 days out of hospital over follow-up as statin use in this subset is likely to differ significantly from other patients. We also excluded patients aged <35 years due to diagnostic uncertainty and those aged  $\geq 85$  years as treatment decisions for this group are likely to be significantly influenced by factors such as quality of life and comorbidities. While comorbidities may also be common in patients aged 75–84 years, they represent about one-third of the total ACS population and are therefore an important group to investigate.

### Data sources

The study cohort was created by linking national datasets of public hospital diagnoses, mortality records and national pharmaceutical claims data. Linkage was carried out using an encrypted version of the National Health Index number, a unique identifier assigned to all New Zealand residents who have had contact with publicly-funded health services (about 98% of the population).<sup>7</sup> Private hospital admissions were excluded because data are unreliable and represent <5% of all coronary heart disease (CHD) hospitalisations, mostly chronic CHD and non-acute procedures.<sup>8</sup>

### Main outcome measure

Statin use over a 3-year follow-up period (starting at the discharge date of the person's index event and ending 1095 days later) was assessed by calculating a Medication Possession Ratio (MPR) for each person. The MPR was the number of days a



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statin was assumed to be in a patient's possession (based on dispensed drugs) divided by the number of days spent out of hospital from the date of hospital discharge through to the end of the follow-up period or the date of death, whichever came first. Days spent in hospital were excluded because medications supplied to inpatients are not included in the national drug dispensing database. For patients dispensed a statin in the 90 days before hospitalisation, the number of statin days remaining at the time of their hospitalisation was added to the numerator of the MPR; therefore, some patients had a MPR >1.0.

The possession of statins during 80% or more of follow-up time (ie, MPR  $\geq$ 0.8) was used to classify those adequately maintained on medications, as reported elsewhere.<sup>9</sup> We also considered MPR=0, indicating no dispensing at all. The MPR is a direct measure of medication dispensing and is assumed to be a reasonable proxy measure of medication use.

An overall MPR was calculated for the entire cohort and subgroups of it, regardless of death during follow-up, based on total days of medication supplied and total days of follow-up spent in the community. MPRs were also calculated separately for each year of follow-up. MPRs for the second and third years excluded deaths in previous years.

### Other variables

Socioeconomic deprivation was assessed by the NZDep01 score, a census-based small-area 10-point index of deprivation based on a person's domicile.<sup>10</sup> This score was aggregated into three groups: 1–3 the least deprived, 8–10 the most deprived and 4–7 intermediate. Ethnicity was determined from hospital records and, if more than one ethnicity was recorded, it was prioritised in the following order: Māori, Pacific, Indian and New Zealand European/other; so, for example, a person identified as both European and Māori is classified as Māori. A coronary procedure was considered to have occurred during a patient's index hospitalisation if it was performed within 30 days of the event.

Diabetes was determined from previous hospitalisations and/or pharmaceutical dispensing data.<sup>11</sup> A history of CVD was defined by hospitalisation between 2002 and the index event with any of the following conditions: CHD, a coronary procedure, heart failure, ischaemic stroke, atherosclerotic peripheral

vascular disease and/or a peripheral arterial procedure (see online supplementary appendix 1 for ICD-10-AM codes). Hospitalisation data prior to 2002 were not used as they are incomplete.

### Statistical analysis

Descriptive statistics were used to compare patient characteristics among ACS groups. Poisson regression modelling using a robust variance estimator was used to identify predictors of statin maintenance after 1 year and up to 3 years of follow-up and to estimate relative risks for adequate statin maintenance.<sup>12 13</sup> Variables considered in the modelling included: ACS type, age group, gender, ethnicity, socioeconomic deprivation, statin use in the 90 days prior to admission, coronary procedure, history of CVD, diabetes, time spent in hospital and interaction of ACS type with age, gender and ethnicity, respectively. Variables were considered significantly associated with statin use when  $p < 0.05$ . Analyses were conducted in Stata statistical software V.11.0.<sup>14</sup>

### RESULTS

Between 1 January and 31 December 2007, 16 591 people were discharged from a public hospital with ACS. Applying exclusion criteria, 631 were not New Zealand residents and 3097 were excluded because 55 were aged <35 years and 3042 were aged  $\geq$ 85 years. A further 1429 died within 90 days of discharge and another 86 spent less than 90 days out of hospital over the follow-up period. A total of 3371 people (26%) who met age and residency inclusion criteria died during the 3 years of follow-up with over 40% of these deaths occurring in the first 90 days.

Once exclusions were applied, 11 348 people remained in the study cohort. Baseline characteristics, stratified by ACS type, are shown in table 1. Approximately half the cohort was diagnosed with NSTEMI, 34% with UA, 14% with STEMI and 3% with unspecified MI. Compared with other ACS types, the group with STEMI was younger, had fewer women and fewer subjects with a history of CVD, diabetes and prior statin use, but more who had undergone a coronary procedure.

**Table 1** Characteristics of total study cohort and by ACS type

n (% of total)	Total cohort N=11 348	STEMI n=1555	NSTEMI n=5611	MI unspecified n=310	Unstable angina n=3872
Mean age (SD)	67.2 (11.7)	63.0 (12.2)	68.3 (11.7)	67.6 (11.5)	67.4 (11.1)
Women	4198 (37%)	423 (27%)	2135 (38%)	121 (39%)	1519 (39%)
European/other	9538 (84%)	1310 (84%)	4667 (83%)	253 (82%)	3308 (85%)
Māori	1168 (10%)	144 (9%)	604 (11%)	39 (13%)	381 (10%)
Pacific	391 (3%)	54 (4%)	231 (4%)	10 (3%)	96 (3%)
Indian	251 (2%)	47 (3%)	109 (2%)	8 (3%)	87 (2%)
Least deprived 3 deciles*	2269 (20%)	323 (21%)	1153 (21%)	54 (17%)	739 (19%)
Intermediate 4 deciles	4739 (42%)	657 (42%)	2330 (42%)	132 (43%)	1620 (42%)
Most deprived 3 deciles	4307 (38%)	568 (37%)	2111 (38%)	124 (40%)	1505 (39%)
Prior statin†	4964 (44%)	357 (23%)	2205 (39%)	103 (33%)	2299 (59%)
Diabetes	3263 (29%)	307 (20%)	1723 (31%)	87 (28%)	1146 (30%)
History of CVD	3876 (34%)	232 (15%)	1796 (32%)	87 (28%)	1761 (45%)
Coronary procedure‡	3724 (33%)	884 (57%)	1753 (31%)	93 (30%)	994 (26%)

\*NZDep01 data were missing in 33 people (<1% of cohort).

†Statin dispensed in the 90-day period prior to index admission.

‡Angioplasty or coronary bypass grafting within 30 days of index admission.

ACS, acute coronary syndrome; CVD, cardiovascular disease; STEMI, ST elevation myocardial infarction; NSTEMI, non-ST elevation myocardial infarction.

**Table 2** Proportion of people with a Medication Possession Ratio (MPR)  $\geq 0.8$  during follow-up

Time period	Number included in analysis*	Patients still alive at the end of follow-up (n=9490)	
		Total cohort % with MPR $\geq 0.8$ †	% with MPR $\geq 0.8$ †
Year 1	11 348	69	71
Year 2	10 645	67	68
Year 3	9988	66	66
Years 1–3	11 348	66	68

\*To account for deaths during follow-up, this analysis also excluded patients who did not spend any days out of hospital during that year.

†During the time period stated in the left-hand column of the table.

Overall, 59% of the cohort had a statin dispensed within 7 days of hospital discharge, 71% within 30 days and 83% within 90 days.

### Statin use over 3 years

Using a MPR threshold of 0.8, 66% of the cohort were adequately treated with a statin up to 3 years after hospital discharge (table 2). Overall, statin use remained relatively stable, with 69% of the cohort achieving a MPR  $\geq 0.8$  in the first year, 67% in the second year and 66% in the third year; 10% of patients received no statins during the 3-year follow-up period.

In patients still alive at the end of follow-up (n=9490), we examined changes in maintenance over the study period. Of those who received no statin in the first year (MPR=0), 82% received none in the third year. Similarly, 82% of those who were adequately maintained on a statin in the first year (MPR  $\geq 0.8$ ) were also adequately maintained in year 3. However, 4% of patients with optimal dispensing in the first year received no statin in the third year and 14% had inadequate statin maintenance.

Online supplementary figures S1–7 in appendix 2 show how the proportion of people with a MPR  $\geq 0.8$  varied between different levels of demographic and clinical subgroups.

**Table 3** Adjusted\* relative risk (95% CI) of maintaining a Medication Possession Ratio  $\geq 0.8$  over 1 year and up to 3 years following an ACS hospitalisation

	1 year	Up to 3 years
Age 35–44 years	0.84 (0.77 to 0.91)	0.75 (0.67 to 0.83)
Age 45–54 years	0.97 (0.93 to 1.01)	0.94 (0.90 to 0.99)
Age 55–64 years		
Age 65–74 years	1.00 (0.97 to 1.03)	1.02 (0.99 to 1.06)
Age 75–84 years	0.96 (0.93 to 1.00)	0.97 (0.94 to 1.01)
Female	0.95 (0.93 to 0.98)	0.94 (0.91 to 0.96)
European/other		
Maori	0.88 (0.84 to 0.92)	0.87 (0.83 to 0.92)
Pacific	0.82 (0.76 to 0.89)	0.82 (0.75 to 0.90)
Indian	1.01 (0.94 to 1.08)	0.98 (0.91 to 1.07)
STEMI	1.18 (1.14 to 1.22)	1.15 (1.10 to 1.19)
Coronary procedure	1.24 (1.21 to 1.27)	1.22 (1.19 to 1.25)
Previous CVD	0.94 (0.91 to 0.96)	0.96 (0.93 to 0.98)
Prior statin use	1.57 (1.53 to 1.62)	1.56 (1.52 to 1.61)

All figures in parenthesis are 95% CIs.

\*Adjusted for the variables shown in this table: age, gender, ethnicity, STEMI diagnosis, coronary procedure within 30 days of admission, previous CVD and statin use in the 90 days before admission.

ACS, acute coronary syndrome; CVD, cardiovascular disease; STEMI, ST elevation myocardial infarction.

### Multivariate analysis

The relative risks of being adequately maintained on a statin over 1 and 3 years, adjusted for clinical and demographic factors, are shown in table 3. A relative risk of  $>1$  is associated with better statin maintenance.

Socioeconomic deprivation and time spent in hospital were not statistically significant and were not used as adjustment variables. STEMI was included in the models as an adjustment variable rather than the four classes of ACS type, as statin maintenance in this group of patients differed markedly from other groups. There was no evidence for an interaction between STEMI and ethnicity, age and gender ( $p>0.3$  for each).

After adjusting for all other variables, being young ( $<45$  years) and of Maori or Pacific ethnicity were the strongest predictors of poor statin maintenance. The strongest predictors of good statin maintenance were previous statin use, having a coronary procedure and a diagnosis of STEMI. Women and those with a history of CVD were slightly less likely to be maintained on a statin than men and those without a history of CVD, respectively. Similar patterns were also observed for statin maintenance over 1 year of follow-up.

Models were also constructed to include only survivors of the entire 3-year follow-up period. These yielded similar results to those presented, indicating that the factors associated with statin maintenance and their magnitude of effect were the same regardless of death during follow-up (data not shown).

### DISCUSSION

In this national cohort of people discharged from hospital following an ACS in 2007, 83% were dispensed statins within 90 days of discharge and 66% maintained an adequate supply of medication overall with minimal change in the second and third years. Younger people and those of Maori and Pacific ethnicity had poorer statin maintenance. Over the 3 years of follow-up, only 46% of people aged 35–44 years, 54% of Pacific peoples and 55% of Maori were adequately maintained on a statin compared with 71% of people aged 65–74 years, 68% of European/others and 71% of Indians. Of those on a statin prior to admission, 82% were adequately maintained on a statin over the follow-up period.

Rates of statin maintenance in our study are higher than reported in previous studies from New Zealand (59% over 1 year),<sup>6</sup> Canada (40% over 2 years)<sup>15</sup> and the USA (43% over 3 years).<sup>16</sup> However, a higher rate was reported in France (76% over 30 months) using data from the general health insurance scheme, which covered 70% of the population and included only those with STEMI or NSTEMI.<sup>17</sup> The lower statin dispensing reported in the other studies may be due in part to their inclusion of patients with angina<sup>6</sup> and data that are now more than 10 years old.<sup>15</sup>

One of the strengths of our study is that almost all patients with ACS aged 35–84 years in New Zealand during the study period were included. Also, as all statins are heavily publicly subsidised, it is likely that nearly all statin dispensing in the community is captured in the national pharmaceutical database. Another strength is the length of follow-up. Internationally, few studies have examined statin use past 1 year post-ACS.<sup>18</sup> Moreover, studies with longer follow-up tend to be small,<sup>16</sup> use data more than 10 years old<sup>19</sup> or samples that may not be representative of the entire population.<sup>4 20</sup>

Individual patterns of statin maintenance in our cohort changed a little between the first and third years after discharge. We found that 82% of patients who maintained an optimal statin MPR in the first year continued to do so in the third year. Of the remaining 18% of patients, 4% stopped statins completely. This suggests that, if adequate statin maintenance can be achieved in the first year following an ACS, patients are likely to continue it subsequently.

Our finding that previous statin use was a predictor of subsequent use is consistent with previous studies.<sup>6 21</sup> It is likely that many of those on statins prior to admission are long-term statin users. As most statin intolerance occurs early, these long-term users are less likely than newly prescribed patients to discontinue due to intolerance; they have also demonstrated adherence through previous dispensings. In contrast, patients with a prior indication but no recent statin dispensing are more likely to have had a real or perceived statin intolerance or other reasons for non-adherence. One strategy to address these issues is discharge counselling,<sup>5</sup> where any patient with CVD not already taking statins receives specific therapeutic advice. This would need to be delivered within a multimodal approach.<sup>22</sup> In particular, those with previous side effects should be carefully evaluated as the label of 'statin intolerant' is difficult to change after discharge. Our experience is that it is often possible to successfully establish such patients on an alternative statin or a reduced dose.

As mentioned above, young people and those of Māori or Pacific ethnicity have poor statin maintenance. The finding concerning age is consistent with some studies,<sup>20 23 24</sup> but not others.<sup>5 15 25</sup> The effect of ethnicity has not been well-described, with one meta-analysis identifying only three out of 22 eligible papers that examined ethnicity as a predictor of statin maintenance.<sup>21</sup> All three studies found that non-white ethnic groups were less likely to be maintained on statins than white patients.<sup>23 25 26</sup> The reasons for these ethnic differences are likely to be multifactorial and may be related to differences in prescribing patterns for people of different ethnic groups, language and/or cultural barriers that may lead to differential access to healthcare or health behaviours.<sup>27</sup>

Our results suggest that targeted interventions to increase the use of statin therapy after ACS will be necessary, particularly for young people and some ethnic groups. Younger patients with ACS are at the highest lifetime risk of CHD, but may be less likely to perceive themselves as being at risk.<sup>21</sup> They stand to gain most from secondary prevention therapy: life expectancy is approximately halved in patients with a history of MI at all ages, but absolute differences are much greater in younger than in older individuals.<sup>28</sup> There are marked ethnic inequalities in cardiovascular health in New Zealand,<sup>29</sup> so it is vital that every effort is made to increase the use of effective preventive treatments in Māori and Pacific peoples.

An important limitation of studies like ours, based on routine datasets, is the lack of clinical information on comorbidities other than prior CVD and diabetes or on common risk factors. There were no data on medication prescribing (only dispensing)

or whether patients had a history of statin intolerance. Therefore, we cannot be certain what proportion of the calculated statin underuse was due to underprescribing, patients' decisions not to take medications, the occurrence of side effects or other contraindications. Second, we used dispensing of statins as a marker of statin use, but some patients may not have taken their medications. However, this method is considered to have high specificity (identify those not taking medication) and is more likely than clinical trials to reflect a 'real world' situation.<sup>9</sup> Third, the proportion of people with a history of CVD is likely to be underestimated as hospitalisation data prior to 2002 were not included.

In conclusion, this national study has demonstrated that one-third of patients with ACS are not adequately maintained on a statin 3 years after discharge, and that previous statin use, age and ethnicity are important predictors of future statin use. The significant differences we observed indicate that long-term maintenance levels of >80% are achievable but are only 50% in some groups. Knowing which patients may be at increased risk of discontinuation of this cheap and effective therapy could help healthcare organisations to develop better support and follow-up systems for these high-risk patient groups.

### Key messages

#### What is already known on this subject

- ▶ Long-term statin use is well-established as a safe and effective component of secondary prevention following an acute coronary syndrome (ACS). Studies suggest that statin use is suboptimal even over the short term, and that increasing age and previous statin use may be important predictors of statin maintenance following an ACS.

#### What this study adds

- ▶ We examined statin use over a longer time period than most previous studies and found that 66% of patients with ACS were adequately maintained on a statin up to 3 years after their original coronary event. Of patients dispensed optimal amounts of statin in the first year, 82% were still taking a statin in the third year. People of younger age and/or of Māori or Pacific ethnicity were less likely, whereas those who had a coronary procedure were more likely, to be maintained on statin treatment over the long term.

#### How this might impact on clinical practice

- ▶ Our findings suggest that, if adequate statin maintenance can be achieved in the first year following an ACS, a patient is likely to continue it in subsequent years. Efforts to increase statin use need to consider the particular needs of the young and those of Māori or Pacific ethnicity.

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**Competing interests** None.

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**Appendix 1: ICD-10-AM codes used to define ACS, diabetes mellitus, coronary procedures and previous cardiovascular disease**

<b>Condition</b>	<b>Subtypes</b>	<b>ICD-10-AM codes</b>
Acute coronary syndrome	STEMI	[I210-I213,I220,I221,I228,I229
	NSTEMI	I214 and I222
	MI unspecified	I219
	Unstable angina	I200
Diabetes Mellitus		E10-E14, O24.0-O24.3
Previous cardiovascular disease	Coronary heart disease	ACS plus: I20x,I21x,I23x, I24x, I252, I255, I256, I258, I259, I46x
	Coronary procedure	3530306, 3530400, 3530401, 3530500, 3530501, 3530906-3530909, 353100x, 3863700, 3865308, 3845619, 384970x, 385000x, 385030x, 3850500, 902010x
	Heart failure	I500, I501, I509
	Ischaemic stroke	I63x, I64x, I66x, I678, I693
	Atherosclerotic peripheral vascular disease	I65x, I74x, I702, I71x, I739, I74x, E1052, E1152, E1452
	Peripheral arterial procedure	3270x-3276x, 3305000, 3305500, 3307000, 3307500, 3308000, 3310000-3318100, 335x, 3380000, 3380302, 33806x, 353120x, 353150x, 9023000, 9022900

**Appendix 2: Figures showing the percentages of people with  $MPR \geq 0.8$  in different demographic and clinical subgroups**

Figure 1: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by age group

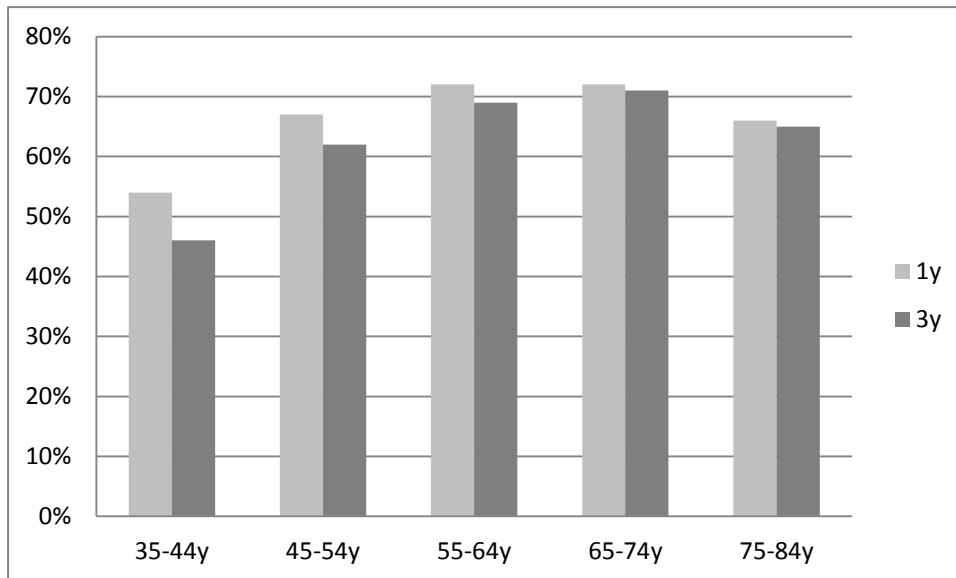


Figure 2: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by gender

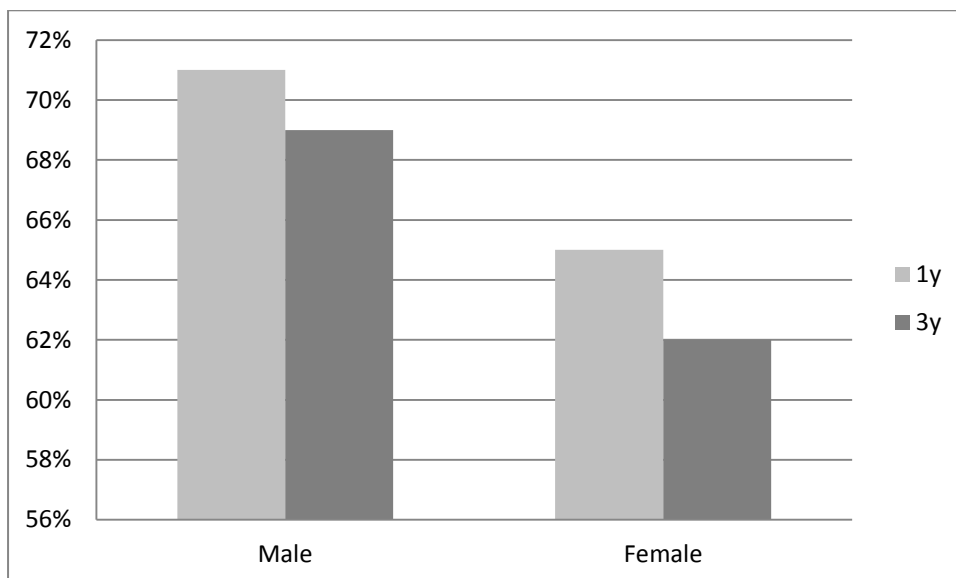


Figure 3: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by ethnic group

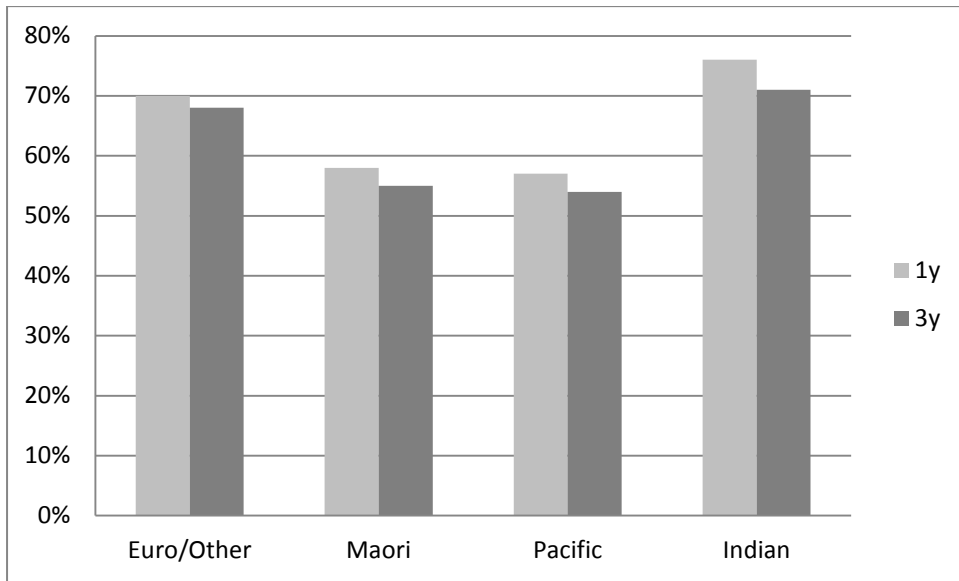


Figure 4: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by ACS type

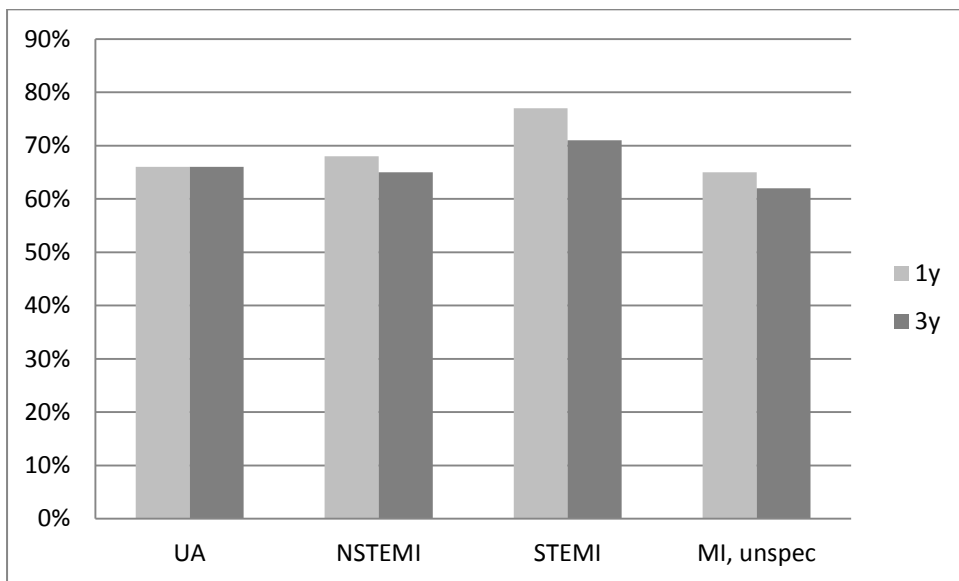




Figure 5: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by receipt of coronary procedure within 30 days of admission

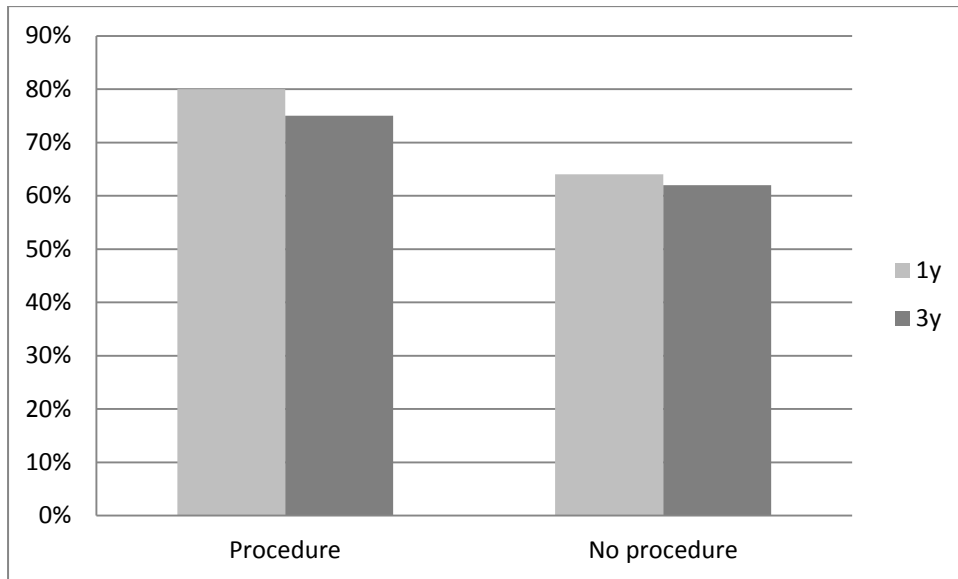


Figure 6: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by history of cardiovascular disease

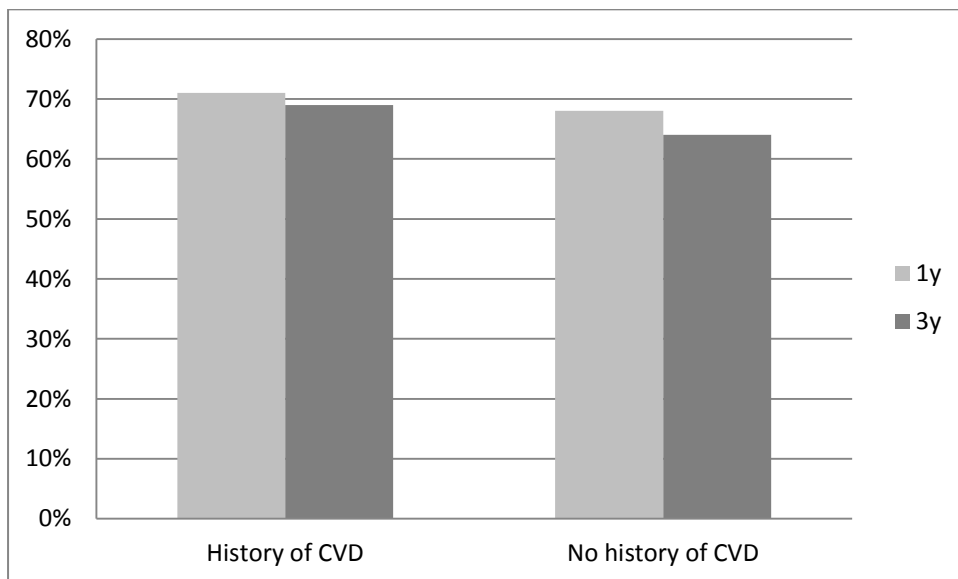


Figure 7: Percentages of people with  $MPR \geq 0.8$  after one year and up to three years post ACS by statin use in the 90 days prior to admission

