BMJ Open

Absolute cardiovascular disease risk score and pharmacotherapy at the time of admission in patients presenting with acute coronary syndrome due to coronary artery disease in a single Australian tertiary centre: a cross-sectional study

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To cite: Bailey A, Korda R, Agostino J, *et al*. Absolute cardiovascular disease risk score and pharmacotherapy at the time of admission in patients presenting with acute coronary syndrome due to coronary artery disease in a single Australian tertiary centre: a cross-sectional study. *BMJ Open* 2021;**11**:e038868. doi:10.1136/bmjopen-2020-038868

► Prepublication history and additional material for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-038868).

Received 27 March 2020
Revised 21 August 2020
Accepted 09 October 2020

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ABSTRACT

Objectives To describe (1) absolute cardiovascular disease risk (ACVDR) scores in patients presenting to hospital with acute coronary syndrome (ACS) and (2) proportions of these patients on guideline-recommended pharmacotherapy according to their ACVDR score.

Design Cross-sectional study.

Setting Single-site tertiary centre hospital, Queensland, Australia over a 12-month period.

Participants Patients >18 years of age presenting to hospital with ACS due to coronary artery disease (CAD) confirmed by angiography.

Primary and secondary outcome measures Proportion of patients without prior history of CVD with a high ACVDR score, and of patients with a prior history of CVD, who are on guideline-recommended pharmacotherapy.

Results 527 ACS patients were included of whom the mean age was 63 years and 75% were male. Overall, 66% (350) had no prior CVD and 34% (177) patients had prior CVD.

In patients with no prior CVD, the proportions of patients with low, intermediate and high CVD risk scores were 41%, 24% and 36%. In the no prior CVD, high-risk patient group, 48% were on no preventative pharmacotherapy, 32% on single pharmacotherapy and 20% patients on complete guideline-recommended pharmacotherapy. In the prior CVD group, 7% patients were on no pharmacotherapy, 40% on incomplete pharmacotherapy and 53% were on complete guideline-recommended pharmacotherapy.

Conclusion This study adds to the evidence on implementation gaps in guideline-recommended management of ACVDR, showing that a large proportion of patients presenting with ACS due to CAD were at high risk of developing CVD prior to the event and most were not on guideline-recommended treatment. A significant proportion of these events are likely to have been preventable, and therefore, increased assessment and appropriate treatment of ACVDR in primary care is needed to reduce the incidence of CVD events in the population.

Strengths and limitations of this study

- ► First survey to report the absolute cardiovascular disease risk (ACVDR) scores in patients presenting with acute coronary syndromes to hospital and the proportions of these patients on guideline-recommended pharmacotherapy in relation to their ACVDR score.
- ► Adds to evidence that many Australians at high CVD risk are not receiving recommended combination therapy.
- ► Limited to single centre in Queensland, Australia.

INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in Australia, and its prevention is a National Health Priority.[1 2] In Australia, CVD accounted for 27% of all deaths in 2017 and was the main cause of hospital admissions.[2 3] A large proportion of CVD is preventable by appropriate population-level interventions and individual management of risk .[3] The National Vascular Disease Prevention Alliance of Australia recommends calculating risk using the absolute cardiovascular disease risk (ACVDR) Score.[4–6] A 5-year risk for the development of CVD is calculated and categorised according whether a patient is low (<10%), moderate (10%–15%) or high risk (>15%). Preventative medication is recommended if the ACVDR is higher than 15%, or 10%–15% with other risk factors. Recommended primary preventative pharmacotherapy consists of prescription of both a cholesterol-lowering and an

antihypertensive agent.[4] For patients with prior CVD, the recommended secondary prevention consists of three agents: an antiplatelet agent such as aspirin (or anticoagulant if indicated), a statin and an antihypertensive triple therapy.[5]

Despite clear guidelines, most Australians at high CVD risk are not receiving recommended combination therapy. This treatment gap is likely multifactorial, including underutilisation of CVD risk calculators.[7–10] The undertreatment of patients at high CVD risk results in a significant missed opportunity in the prevention of cardiovascular events. To date, there are limited Australian data demonstrating gaps in implementation of guidelines and hence missed opportunities for prevention. In particular, there are no studies that have quantified CVD risk scores and appropriateness of pharmacological treatment at the time of patient presentation to hospital with acute coronary syndrome (ACS).

This study aimed to report: (1) the ACVD risk scores in patients presenting to hospital with ACS due to coronary artery disease (CAD) and (2) the proportions of these patients according to their risk, on guideline-recommended pharmacotherapy.

METHODS

Study design and population

This study was a cross-sectional study of patients presenting with ACS to a single tertiary hospital in Australia over a 12-month period from 1 November 2016 to 31 October 2017. All patients over 18 years of age presenting with ST-elevation myocardial infarction (STEMI) or non-ST elevation MI (NSTEMI) with type 1 MI (defined by the Fourth Universal definition of MI), and who underwent coronary angiography demonstrating significant CAD (defined as at least one lesion of ≥50% stenosis) were included.[11] Patients with unstable angina were also included and defined as ischaemic sounding chest pain with significant coronary disease. Patients were excluded if they presented with ACS but did not undergo coronary angiography or where the discharge diagnosis was not thought due to atherosclerotic coronary artery disease such as a type 2 MI (spontaneous coronary artery dissection, Takotsubo cardiomyopathy, MI with non-obstructive coronary artery disease on angiography or myocarditis).

Data collection and variables

Demographic and health data were collected from patient's non-anonymised medical records and included information on past medical history of ischaemic heart disease, peripheral vascular disease, cerebrovascular events, diabetes mellitus, hypercholesterolaemia and hypertension, as well as smoking status.

Blood collected during the first 24 hours of admission was used to identify renal function and document HbA1c and lipid profile for risk factor calculation. Patients without a noted history of diabetes mellitus but with an HbA1c>6.5% on admission were considered to have diabetes mellitus for risk calculation.[6] As per guidelines, patients were considered to be at automatic high risk if the total cholesterol ≥7.5 mmol/L, systolic blood pressure (BP) ≥180 mm Hg or diastolic BP ≥110 mm Hg, glomerular filtration rate was <45 mL/min/1.73 m^2 or a previous diagnosis of familial hypercholesterolemia was documented.[6] Data regarding diabetes with microalbuminuria were not available. Patients were recorded as having a family history of CVD if documented in the notes by the treating physician.

Medication use at admission was collected from the patient medical record, which includes self-reported medication use as well as, where available, pharmacist admission history which cross references self-reported medication use with general practitioner prescriptions and pharmacy dispensing history for increased accuracy.

Calculation of absolute cardiovascular disease risk scores

Patient were classified into two groups based on their history of cardiovascular disease. Prior CVD was based on a history of CVD defined as a reported history of ischaemic heart disease, ischaemic cerebrovascular disease or peripheral vascular disease. In patients with no prior CVD, the online Australian ACVDR calculator was used to determine the patient's risk of a CVD event in the next 5 years: low (<10%), intermediate (10%–15%) or high (>15%).[6] This calculator requires identifying clinically determined high CVD risk based on sex, age, systolic BP, smoking status, total cholesterol, high-density lipoprotein cholesterol, diagnosis of diabetes and evidence of left ventricular hypertrophy on ECG (online supplemental figure 1).[7] The systolic BP used for this calculation was a mean of two recordings taken as the first recordings in a ward setting when the patient was pain free and before to the initiation of new medical therapies (wherever possible). An ECG diagnosis of left ventricular hypertrophy was based on Sokolow-Lyon criteria.[12] The ACVD risk calculator was developed for patients not on preventative medical therapy and scores have not been validated in those on treatment. For the purposes of our study, it is valid to assume that those found to be at high risk despite being on preventative therapy, are still high risk. This approach has been used in previous studies.[13] 'Low' and 'moderate' risk scores were also calculated despite a proportion of these patients (see results) taking cholesterol-lowering and/or antihypertensive medication (see the Discussion, Limitations section).

Analysis

Data were described separately according to prior CVD (with/without), with continuous variables reported as means and SD and categorical variables as counts and proportions. Although non-anonymised data were used to collect patient information and variables, this was then deidentified for analysis and storage.

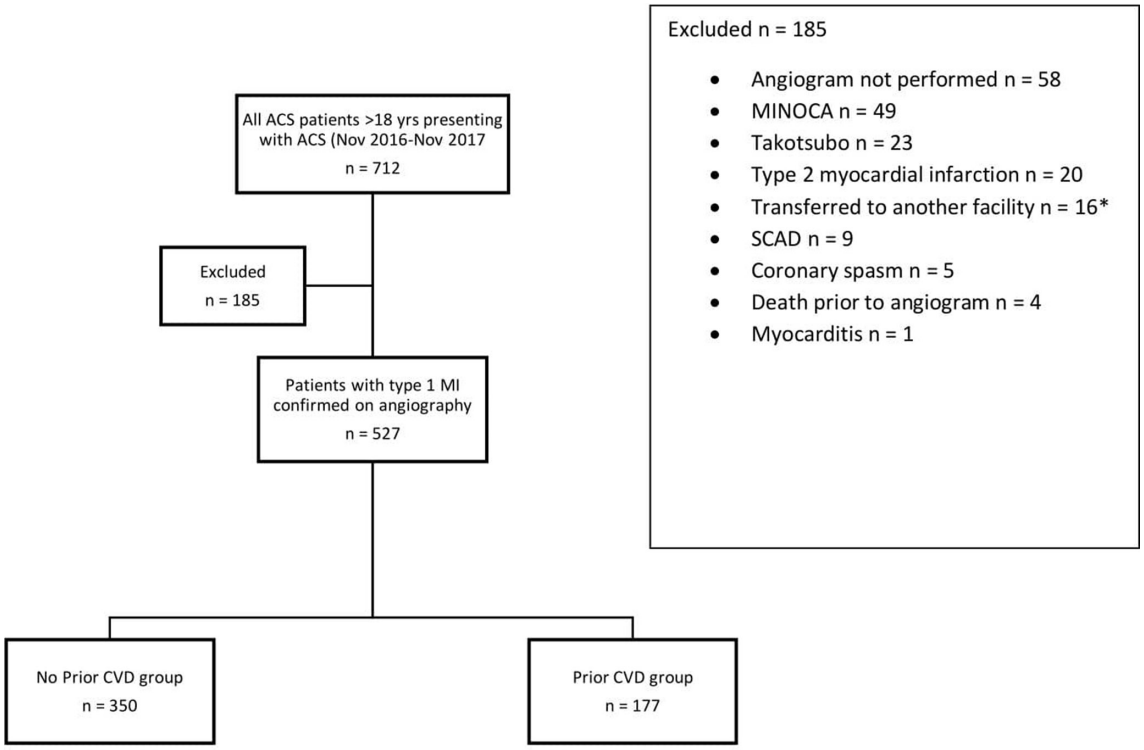

Figure 1 Study population. A history of cardivascular disease (CVD) defined as reported history of ischaemic heart disease, ischaemic cerebrovascular disease or peripheral vascular disease. *These patients had a private healthcare cover and chose to be transferred to private hospitals for their ongoing investigation and management. ACS, acute coronary syndrome; MI, myocardial infarction; MINOCA: myocardial infarction with nonobstructive coronary arteries; SCAD: spontaneous coronary artery dissection.

RESULTS

Patient characteristics

From November 2016 to October 2017, 712 patients presented with an ACS. Of these 185 (26%) were excluded from analysis, the key reasons being that the patient did not undergo angiography (n=58), no significant coronary artery disease was found on angiography (n=49) or the diagnosis was considered takotsubo cardiomyopathy (n=23) (figure 1). The remaining 527 patients included in the study were composed of 350 (66%) patients with no prior CVD, and 177 (34%) patients with prior CVD.

In the no prior CVD group, the mean age was 63 years, 75% were male, 54% presented with an STEMI, 39% with NSTEMI, and 7% with unstable angina (table 1). In regard to risk factors, 29% were current smokers, 39% had a family history of premature cardiovascular disease, 21% had diabetes, 34% hypercholesterolaemia and 50% a history of hypertension.

The prior CVD group most commonly had a history of ischaemic heart disease (82%) rather than peripheral vascular disease (11%) or cerebrovascular disease (18%). In regard to risk factors, there were lower rates of current smokers (18%), however, there were high rates of other comorbidities including hypertension (78%), chronic kidney disease (11%), diabetes (24%) and hypercholesterolaemia (70%).

Patients with no prior CVD (primary prevention)

Figure 2 shows the proportions of patients in the different ACVD risk score categories including those with and without prior CVD. Out of 350 patients with no prior CVD, 26 (7%) patients had missing data and CVD risk could not be calculated. Of the remaining 324 (93%), 41% were low risk, 24% intermediate risk and 35% at high risk of a CVD event.

In those at high risk, 48% were not on any preventative therapy, 32% were on single preventative therapy and 20% were on both lipid-lowering and antihypertensive therapy. Of the latter group, four patients not previously known to be diabetic were found to have diabetes based on elevated admission HbA1c values and were not on antiglycaemic therapy. Therefore overall, one in five patients at high primary CVD risk (20%) were on complete guideline-recommended primary preventative therapy (figure 3).

In both the low and moderate risk groups, 57% were not on any preventative therapy, 29% and 32% were on single preventative therapy, and 14% and 11% were on both lipid-lowering and anti-hypertensive therapy, respectively (online supplemental figure 2).

Patients with prior CVD (secondary prevention)

Among the 177 patients with prior CVD (figure 2), 7% were not on any treatment at the time of admission, 8%

Table 1 Sample characteristics: acute coronary syndrome patients with and without prior CVD

	No prior CVD group n=350	Prior CVD group n=177
Age—years	63.1±12.0	70.5±10.1
Male sex—no (%)	263 (75.1)	135 (76.3)
BMI	28.4±5.1	28.4±5.1
Total cholesterol—mmol/L	5.3±1.4	4.3±1.4
HDL—mmol/L	1.1±0.3	1.1±0.3
LDL—mmol/L	3.3±1.2	2.5±1.2
Systolic BP—mm Hg	129.8±18.4	132.3±18.0
Diastolic BP—mm Hg	76.8±11.1	73.6±9.7
Left ventricular hypertrophy on ECG	24 (6.6%)	–
Smoking status		
Never smoker	121 (34.6%)	66 (37.3%)
Ex-smoker	123 (35.1%)	76 (42.9%)
Current smoker	103 (29.4%)	31 (17.5%)
History of		
Family history of CVD	136 (38.9%)	57 (32.3%)
Rheumatoid arthritis	3 (0.9%)	0
Chronic kidney disease	11 (3.1%)	20 (11.3%)
Diabetes	72 (20.6%)	43 (24.3%)
Hypercholesterolaemia	120 (34.3%)	124 (70.1%)
Hypertension	174 (49.7%)	138 (78.0%)
Prior CVD		
IHD		145 (81.9%)
PVD		20 (11.3%)
CVA		32 (18.1%)
Type of acute coronary syndrome		
STEMI	188 (53.7%)	48 (27.1%)
NSTEMI	138 (39.4%)	94 (53.1%)
UA	24 (6.9%)	35 (19.8%)
Management after angiography		
Medical treatment	21 (6.0%)	44 (24.9%)
PCI	286 (81.7%)	109 (61.6%)
CABG	43 (12.3%)	23 (13.0%)

SD given. STEMI.
BMI, body mass index; BP, blood pressure; CABG, coronary artery bypass graft; CVA, cardiovascular accident; CVD, cardiovascular disease; IHD, ischemic heart disease; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; STEMI, ST-elevation myocardial infarction; UA, unstable angina.

were on a single agent (statin, antihypertensive or antiplatelet/anticoagulant), 32% on dual therapy and 53% on guideline-recommended triple therapy. Of these, six were diabetic and not on antiglycaemic medication. Therefore, among patients with prior CVD, approximately half were on optimal guideline-recommended pharmacotherapy (figure 3).

DISCUSSION

In this study, one-third of the patients with no prior CVD presenting with ACS were found to have a high ACVD risk score, and of these, only one in five were on appropriate guideline-recommended pharmacotherapy. Among those patients with prior CVD and ACS, only half were receiving guideline recommended pharmacotherapy. Importantly, the majority of patients (two-thirds) presenting with ACS due to CAD, had no prior history of CVD.

All major CVD prevention guidelines use some method of risk factor assessment to calculate estimated risk for developing cardiovascular events with subsequent prescription of lifestyle and medication to reduce this risk.[14–16] Previous studies have shown both the under-recognition of these patients and the undertreatment, with the majority of research in this areas focused on the primary care setting.[10 13 17] In contrast, this study describes the risk profiles and associated preventative therapies among patients presenting with ACS, which has not previously been reported on in an Australian population.

An estimated 80% of CVD events are preventable by intervening to reduce risk.[18 19] Absolute CVD risk assessment and management is current best practice and recommended for ages 45–74 years in Australia.[4] Reductions in BP and lipids using standard treatments are able to halve risk but previous research suggests that 76% of Australians at high primary CVD risk are not receiving these basic best practice preventive therapies.[13 20] This evidence is supported by our study which showed that one-third of patients presenting with ACS and no prior history of CVD, were at previously at high risk of developing CVD, and of these 80% were not on correct preventative pharmacotherapy. In those patients with prior CVD presenting with ACS, approximately half are not on correct pharmacotherapy.

There are likely multiple reasons for the underutilisation of preventative medication recommended by evidence-based guidelines on primary and secondary prevention.[9 21] These include the underutilisation of risk calculators, reluctance to prescribe medication and reliance on lifestyle measures and poor medication compliance.[10 17 22] Heeley showed that only 60% of general practitioners reported utilising cardiovascular risk calculators.[10] Additionally, when general practitioners (GPs) were asked to estimate patients' risk of CVD events, the perceived risk was often underestimated—even patients with established CVD, 60% were thought to be low or intermediate risk.[10] A further difficulty is that for those patients who are appropriately assessed and prescribed CVD preventative medications, the adherence to medications is poor at 50% compliance for patients where the

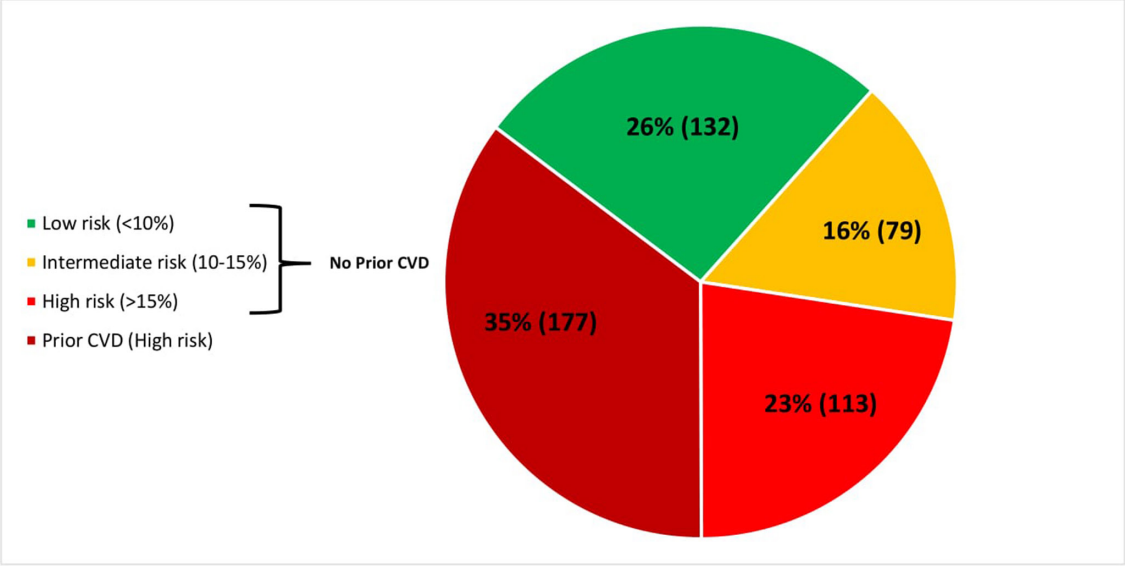

Figure 2 Australian cardiovascular disease risk (ACVDR) scores categories in patients presenting to hospital with acute coronary syndrome due to coronary artery disease. ACVDR Score: a 5-year risk for the development of CVD which is categorised according whether a patient is low (<10%), moderate (10%–15%) or high risk as shown by pattern red. Prior CVD: a history of CVD or peripheral vascular disease. Note that in 26 patients ACVDR score could not be calculated and these have been excluded from analysis. CVD, cardivascular disease.

indication is primary prevention and 66% for those with a history of cardiovascular disease.[23]

This study is important because it shows that the majority of high CVD risk patients who suffered an ACS due to coronary artery disease were not on the preventative therapy. According to guidelines, appropriate treatment of patients with high CVD risk will reduce future adverse cardiovascular events.[14 15] This suggests that in our study, for those patients who were found at presentation to be at high CVD risk and not on appropriate pharmacotherapy, a significant proportion of these adverse events could potentially have been avoided if preventative therapy had been previously instigated. This data from this study presents a highly persuasive argument to

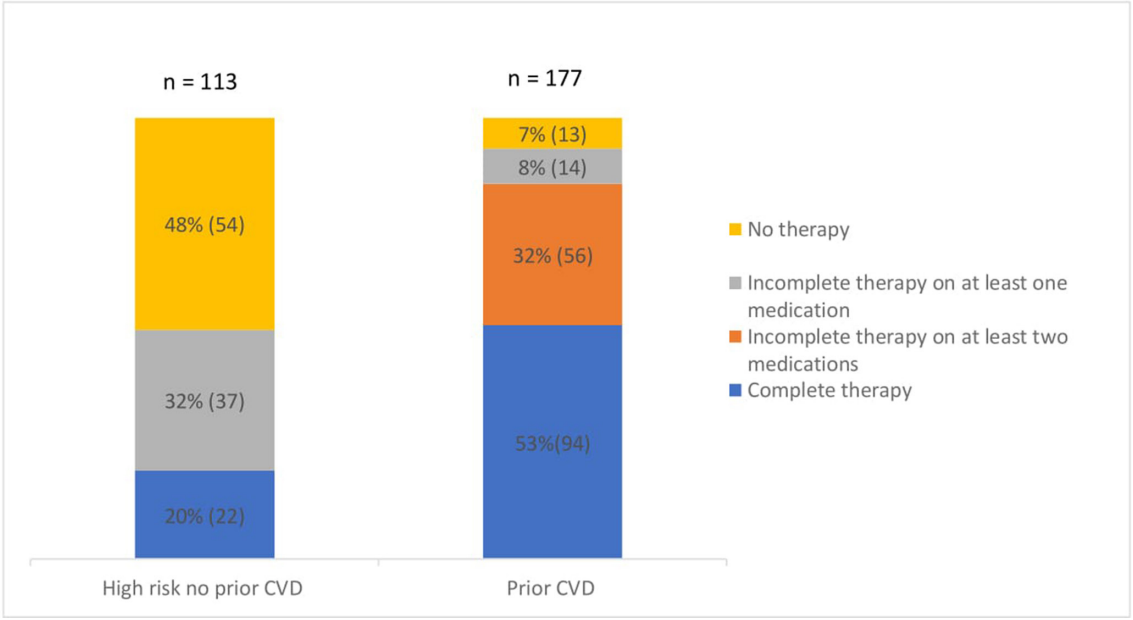

Figure 3 Proportions (%) and numbers of patients presenting with acute coronary syndrome due to coronary artery disease in the high risk no prior cardiovascular disease and prior cardiovascular disease groups or guideline-recommended pharmacotherapy. ACVDR Score: a 5-year risk for the development of CVD which is categorised according whether a patient is low (<10%) or high risk (>15%). Prior CVD: a history of CVD defined as reported history of ischaemic heart disease, ischaemic cerebrovascular disease or peripheral vascular disease. Note that in 26 patients AVCDR score could not be calculated and these have been excluded from analysis. ACVDR, absolute cardiovascular disease risk; CVD, cardiovascular disease.

both patients and GPs alike that ACVD risk assessment and appropriate early treatment is essential if the development of CVD is to be prevented.

Strengths and limitations of this study

The strength of this study is that it only included consecutive patients who had ACS due to coronary artery disease. Participants (STEMI and NSTEMI) had to have a type 1 MI defined by acute myocardial injury and significant CAD on coronary angiography. Those patients who had unstable angina had to have ischaemic chest pain and evidence of significant CAD on coronary angiography.

There are several limitations in this study that should be considered. First, this was a small volume single centre study which may reflect a unique demographic or prescribing practice. In terms of representativeness, however, the Sunshine Coast appears to be ranked roughly mid-way in terms of heart-related hospital admissions and coronary heart disease mortality rates compared with the rest of the country.[24] Second, data were derived from written medical records, self-reported medical history and discharge summaries which may not always reflect accurately what happened during the admission. Third, calculation of CVD risk using the ACVDR score requires systolic BP for calculation. Ideally BP should be recorded as a mean of two readings taken after sitting for 5 min in a quiet room before antihypertensive medication is given and avoids the problem of recording overly high BP readings.[4] This is not always possible in an acute hospital environment, and the compromise in this study was to take the mean of two BP recordings in a ward setting. To our advantage all patients admitted to our hospital are given their own single room meaning their environment is quiet. The BP was also recorded where possible before the initiation of antihypertensive medication. For those patients where an antihypertensive medications had been given which was rare, the systolic BP may have been lower and CVD risk underestimated.

In addition, a proportion of patients in the low and moderate risk groups were receiving primary preventative therapies which may have reduced risk as calculated by the ACVDR calculator which is intended to be used in treatment naïve patients.[4 6] Therefore, interpretation of these results should be undertaken with caution.

However, the focus of this study was on those known to be at high risk. Those patients who experienced out-of-hospital cardiac arrest due to CAD and did not survive to hospital—this group along with their risk scores, are not represented in this study. This study did not ascertain why patients were not on the correct medications. It would be useful to know the reasons why and what proportions of patients were unbale to (eg, unable to tolerate) or actively decided not to take their prescribed medications. This information would be helpful for benchmarking targets in the surveillance of ACVDR score and appropriateness of treatment across populations. The proportions of patients presenting with ACS within the low and intermediate risk groups may appear at first glance, disproportionately high with respect to their overall risk. However, this assumption is incorrect. In order to estimate the true proportions of patients presenting with ACS from the low and moderate risk groups one would need to know the denominator for each risk category that is, the number of patients in each at-risk population from which the ACS patients presented and is not available. Furthermore, a proportion of the patients in these low and moderate risk groups were on anti-hypertensive and cholesterol-lowering medication. Therefore, in these patients the calculated risk scores are likely to be lower than their true risk. For these reasons, this study has predominantly focused on the high risk group only.

Conclusion

A large proportion of patients presenting with ACS were previously at high risk of developing CVD and the vast majority were not on guideline-recommended treatment. A significant proportion of these adverse events could have been potentially avoided if preventative therapy had been previously instigated. Increased assessment and appropriate treatment of ACVDR by GPs needs to increase if CVD events are to be reduced.

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intellectual content and gave final approval of the version to be published; JA agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. KG: made substantial contributions to the conception or design of the work; the acquisition, analysis and interpretation of data for the work; he revised it critically for important intellectual content and gave final approval of the version to be published; KG agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethics approval for this study was granted by The Prince Charles Hospital Human Research Ethics Committee (HREC/18/QPCH/43).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available. Release of data was not covered by ethics approval and therefore is not able to be provided.

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