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Title

Variation in cardiovascular disease care: An Australian cohort study on gender inequalities in receipt of coronary procedures

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ABSTRACT

Objectives: To quantify gender variation in diagnostic and revascularisation coronary procedures within one year of hospitalisation for acute myocardial infarction (AMI) or angina.

Design: Prospective cohort study. Baseline questionnaire (January 2006-April 2009) data from the Sax Institute's 45 and Up Study were linked to hospitalisation and mortality data (to 30 June 2016).

Setting: New South Wales, Australia.

Participants: Participants aged ≥45 years with no history of IHD who were admitted to hospital with a primary diagnosis of AMI (n=4,580), or a primary diagnosis of angina or chronic IHD with secondary diagnosis of angina (n=4,457).

Outcome Measures: Coronary angiography and coronary revascularisation with percutaneous coronary intervention or coronary artery bypass graft (PCI/CABG) within one year of index admission. Cox regression models compared male and female coronary procedure rates, adjusting sequentially for age, sociodemographic variables and health characteristics.

Results: Among patients admitted with AMI, 71.6% of men (crude rate: 3.45/person-year) and 64.7% of women (2.62/person-year) received angiography; 57.8% of men (1.73/person year) and 37.4% of women (0.77/person-year) received PCI/CABG. Fully adjusted hazard ratios (HRs) for men versus women were 1.00(0.92-1.08) for angiography and 1.51(1.38-1.67) for PCI/CABG; corresponding HRs among patients with angina were 1.27(1.17-1.37) and 2.46(2.19-2.77). In the angina group, rates were: angiography: males=2.43/person-year, females=1.34/person-year; PCI/CABG: males=0.94/person-year, females=0.28/person-year.

Conclusions: Men are more likely than women to receive coronary procedures, particularly revascularisation. This difference is most evident among people with angina, where care is more discretionary compared to AMI.

Keywords: Cardiovascular disease, Coronary procedure, Linked data, 45 and Up Study, Health inequality

ARTICLE SUMMARY

Strengths and limitations of this study

- This study uses population-based survey data linked to routinely collected health data.
- This study has a relatively large number of participants, with virtually complete capture of procedures.
- This study has adjusted for a large range of baseline sociodemographic and health factors, however clinical factors upon presentation to hospital were not included.
- While diagnosis of AMI is highly valid within hospital data, there is relatively low concordance for angina diagnoses, with possible over- or underrepresentation of rates.
- The Study cohort, while broadly representative of the general population, is likely to be healthier and have lower hospitalisation and mortality rates than their peers.

BACKGROUND

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide,[1] and a leading cause of death in Australia.[2] While incidence of CVD is higher among men,[3] in many parts of the world women experience worse outcomes.[4] Coronary interventions, including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), contribute to improved outcomes following an acute coronary event in both men and women.[4] Despite the significant disease burden and availability of effective interventions, CVD in women as a whole remains underdiagnosed and less aggressively treated.[5, 6] Women are underrepresented in clinical trials,[6] and there are important gaps in the evidence for recognition and treatment of adverse coronary events.

It is known that incident acute myocardial infarction (AMI) and angina pectoris present on average 7-10 years later in women compared to men.[6, 7] Women generally present to hospital older and with a greater number of risk factors than men,[6] experiencing higher mortality and re-infarction rates following a first AMI.[7] Disparities in care received by women compared to men have been documented in the United States (US), even when accounting for income, education and site of care.[8] Evidence from Europe and the US demonstrate that women with CVD are less likely to undergo diagnostic angiograms or intervention with PCI or CABG,[6, 7] procedures with documented clinical benefit.[4, 5]

There is limited information on gender inequalities in cardiovascular care in Australia, including diagnosis and management with coronary procedures. Age-standardised rates of procedures are lower among women compared to men,[9] however underlying CVD and other factors related to delivery of care are not taken into consideration in these figures. Hence, the extent to which these differences in rates reflect inequalities in care is uncertain. This study aimed to quantify gender inequalities in care delivery by comparing coronary procedure rates in men and women admitted with AMI or angina, adjusting for other sociodemographic and health-related factors.

METHODS

Data sources

Data were obtained from the Sax Institute's 45 and Up Study, a population-based cohort study involving 267,153 men and women aged 45 and over from New South Wales (NSW) Australia. 45 and Up Study participants were randomly selected from the Department of Human Services (formerly Medicare Australia) database, Australia's universal health insurance system, with oversampling of individuals living in rural areas and those over the age of 80 by a factor of 2. All individuals living in remote areas were invited to participate. Participants enrolled by completing a mailed self-administered questionnaire and provided signed consent for long-term follow-up and data-linkage with a range of health databases. Approximately 10% of the NSW population aged 45 and over were included in the sample, an overall response rate of 18%. The Study is described in detail elsewhere,[10] with questionnaires available online.[11]

Baseline data from 45 and Up Study participants were linked to hospital data from the NSW Admitted Patient Data Collection (APDC, 1 July 2000 to 30 June 2016) and death data from the NSW Registry of Births, Deaths and Marriages and the National Death Index (1 January 2006 to 30 June 2016). The latter was linked by the Australian Institute of Health and Welfare. Included in the APDC is a record of all hospitalisations in NSW, dates of admission and discharge, and reason for admission. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) and Australian Classification of Health Interventions codes are incorporated into the APDC, with each record containing up to 51 diagnosis and 50 procedure codes. Death data included date of death (used for censoring).

Data were linked probabilistically by the Centre for Health Record linkage using personal information (full name, date of birth, gender, and address). It is likely that during the follow-up period a small but unknown number of participants may have moved interstate. Though hospitalisations in neighbouring states are not included, these are estimated to make up fewer than 2% of admissions in NSW residents. Follow-up for hospitalisations is considered to be ~98% complete among those who continue to live in NSW. Quality assurance data on the data linkage show false positive and negative rates of <0.5% and <0.1% respectively.

Study Population

All 45 and Up Study participants admitted to hospital with a primary diagnosis of AMI or angina (stable or unstable) following entry into the 45 and Up Study were included in the sample. Those with a primary diagnosis of chronic ischaemic heart disease (IHD) and secondary diagnosis of angina were also included, due to the possibility of angina patients being admitted for elective revascularisation under these diagnostic codes. ICD-10-AM diagnosis codes (I21, I20, and I25 respectively) were used to ascertain admission. Participants with a prior history of IHD were excluded, defined as self-reported heart disease on the baseline questionnaire and/or admission to hospital for IHD (120-125), and/or a related interventional procedure (angiogram, PCI or CABG – defined below), as ascertained by diagnosis and procedure code fields of APDC in the six years prior to entering the 45 and Up Study.

Variables

The study outcomes were investigation with angiography, and coronary intervention with PCI or CABG, within 12 months of index admission to hospital.

Outcomes were ascertained using all 50 APDC procedure-code fields, coded using the Australian Classification of Health Interventions which is used in conjunction with ICD-10-AM,[12]: angiography (38215, 38218), PCI (35304-00, 35305-00, 35304-01, 35305-01, *38300-00, 38303-00* (block: 670), 35310-00, 35310-01, 35310-02, 35310-03, 35310-05, *38306-00, 38306-01, 38306-02, 38306-03, 38306-05* (block: 671)) and CABG (38497-00 to 38497-07, 38500-00 to 38500-04, 38503-00 to 38503-04, 90201-00 to 90201-03, *38500-05, 38503-05* (blocks 672-679)). Italicised codes have been included to reflect changes in procedure coding during the follow-up period.

The main exposure of interest was gender (male or female), self-reported on the baseline questionnaire. Sociodemographic and health characteristics that may confound/mediate the relationship between gender and receipt of coronary procedures were also measured on the baseline questionnaire. These included: country of birth (Australia/New Zealand or other), region of residence (major city, inner regional, or outer regional/remote/very remote), highest qualification (no school certificate, school/trade certificate or diploma, or tertiary degree), private health insurance (no private health insurance, or health care/Department of Veterans Affairs concession card), marital status (married/de facto, or not), obesity (body mass index (BMI)≥30kg/m^2, or not, based on self-reported height and weight), physical functioning (no/minor limitations, moderate limitations, or severe limitations, based on levels of functional limitation, as adapted from the Medical Outcomes Score Physical Functioning Subscale [13]), and psychological distress (low[10-<16], moderate[16-<22], or high[22-50], as per the Kessler 10).[14]

Analysis

Cox proportional hazard regression was used to model the association between gender and receipt of coronary procedures. For each analysis, participants contributed person-years from the date of index admission for AMI or angina until either the specified outcome of interest, death from any cause, or end of follow up 30 June 2016, whichever was the earliest, to a maximum of one calendar year. Proportional hazards assumption was tested, with the p-value set *a priori* to p<0.01. All analyses were conducted separately for patients whose index admission was for AMI, and for those whose index admission was for angina. Patients presenting concurrently with AMI and angina were included in the AMI sample.

For each outcome, we calculated crude incidence rates separately for men and women, then ran a series of Cox regression models to estimate hazard ratios (HRs) in relation to gender. Model 1 was adjusted for age (5-year age categories from 45-54years through to ≥85years). Model 2 was adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, private health insurance and marital status). Model 3 was further adjusted for additional baseline health characteristics (obesity, physical functioning and psychological distress). Participants with missing values for covariates were included in the models, with missing coded as a separate category.

Four sensitivity analyses were performed. First, we used a maximum follow-up period of 30 days after index admission rather than 12 months. Second, we used an alternative indicator of baseline health – self-rated health, measured with three categories (excellent/very good, good, fair/poor) – instead of functional limitation, obesity and psychological distress (Model 3). Third, we additionally controlled for comorbidity using the Charlson index,[15] using all diagnostic codes in the 12 months prior to the index admission, with scores categorised as 0, 1 or ≥2. Fourth, we restricted analysis of the angina patients to those admitted with a primary diagnosis of unstable angina (ICD-10: I20.0).

Analyses were performed using Stata 14.[16]

The conduct of the 45 and Up Study was approved by the University of New South Wales Human Research Ethics Committee. Ethics approval for this study was obtained from the Australian National University Human Ethics Committee (2015/513) and the NSW Population and Health Services Research Ethics Committee (HREC/10/CIPHS/33; CI NSW Study Reference 2010/05/234).

RESULTS

A total of 9,037 patients were included in the study, 4,580 admitted with AMI and 4,457 admitted with angina. There were no patients in the sample who had IHD as a primary diagnosis and angina as a secondary diagnosis. Sample characteristics are shown in Table 1. The profiles of patients within the AMI and angina groups were similar, with a few exceptions. Notably, those in the angina group were less likely to be aged 85 and over (8.56% vs 19.4%), and more likely to have private health insurance at baseline (64.6% vs 56.9%) than those in the AMI group. There was a greater percentage of men within both AMI and angina groups, 63.6% and 56.2% respectively.

Table 1: Characteristics of patients admitted to hospital with acute myocardial infarction (AMI) or angina by gender

	AMI Sample (n=4,580)				**Angina Sample** (n=4,457)			
	Men		Women		Men		Women	
	n	%	n	%	n	%	n	%
Total	2911	63.6	1669	36.4	2503	56.2	1954	43.8
Age at admission								
45-54	190	6.5	80	4.8	152	6.1	151	7.7
55-64	685	23.5	277	16.6	628	25.1	499	25.5
65-74	807	27.7	414	24.8	897	35.8	622	31.8
75-84	757	26.0	481	28.8	634	25.3	493	25.2
85+	472	16.2	417	25.0	192	7.7	189	9.7
Region of residence								
Major city	1485	51.0	807	48.4	1321	52.8	972	49.7
Inner regional	1025	35.2	629	37.7	886	35.4	717	36.7
Regional/remote	354	12.2	200	12.0	259	10.4	237	12.1
Highest qualification								
No school certificate	417	14.3	357	21.4	305	12.2	326	16.7
School/ certificate/ diploma	1923	66.1	1085	65.0	1629	65.1	1310	67.0
Tertiary degree	497	17.1	175	10.5	502	20.1	276	14.1
Country of birth								
Australia/ NZ	2142	73.6	1323	79.3	1888	75.4	1576	80.7
Other	728	25.0	327	19.6	583	23.3	353	18.1
Marital status								
Single	647	22.2	750	44.9	465	18.6	638	32.7
Married/ de facto	2244	77.1	916	54.9	2011	80.3	1313	67.2
BMI								
Not obese (BMI<30kg/m^2)	2079	71.4	1100	65.9	1713	68.4	1260	64.5
Obese (BMI≥30kg/m^2)	625	21.5	394	23.6	619	24.7	479	24.5
Physical functioning								
No or minor limitation	1412	48.5	469	28.1	1221	48.8	691	35.4
Moderate limitations	646	22.2	386	23.1	647	25.9	517	26.5
Severe limitations	393	13.5	392	23.5	301	12.0	373	19.1
Psychological distress								
Low	1958	67.3	948	56.8	1,681	67.2	1,131	57.9
Moderate	339	11.7	205	12.3	337	13.5	273	14.0
High	188	6.5	111	6.7	178	7.1	172	8.8
Health Insurance								
No private health insurance	1164	40.0	807	48.4	845	33.8	731	37.4
Health care/DVA	1746	60.0	862	51.7	1658	66.2	1223	62.6

% of missing cases: AMI sample (men, women): region of residence (1.6, 2.0); highest qualification (2.5, 3.1); country of birth (1.4, 1.1); marital status (0.7, 0.2); BMI (7.1, 10.5); physical limitations (15.8, 25.3); psychological distress (14.6, 24.3); health insurance (<0.1, 0.0). Angina sample (men, women): region of residence (1.5, 1.4); highest qualification (2.7, 2.2); country of birth (1.3, 1.3); marital status (1.1, 0.1); BMI (6.8, 11.0); physical limitations (13.3, 19.1); psychological distress (12.3, 19.3); health insurance (0.0, 0.0).

Coronary procedures in AMI patients

Among those admitted to hospital with AMI, 69.1% received angiography, 71.6% of men vs 64.7% of women, and 50.4% PCI/CABG, 57.8% vs 37.4% respectively. The proportion of AMI patients who survived the follow-up period and who had a procedure was 75.6% for angiography (77.6% v 71.9%), and 55.4% for PCI/CABG (63.2% vs 41.0%).

Crude rates per person-year of angiography were 3.45 (3.31-3.60) and 2.62 (2.47-2.78) in men and women respectively, and crude rates of PCI/CABG were 1.73 (1.64-1.81) and 0.77 (0.71-0.83) respectively (Table 2).

Cox models showed angiography rates were similar in men and women, with no difference after adjustment for sociodemographic and health variables (HR=1.00, 0.92-1.08) (Table 2). In contrast, rates for PCI/CABG were around 50% higher in men than women (adjusted HR=1.51, 1.38-1.67).

Table 2: Rates of coronary procedures within one year of admission with AMI by gender and associated hazard ratios (n=4,580)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	2085/604.1	3.45 (3.31-3.60)	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.00 (0.92-1.08)
Women	1079/411.7	2.62 (2.47-2.78)	1.00	1.00	1.00
PCI/CABG					
Men	1682/975.0	1.73 (1.64-1.81)	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.51 (1.38-1.67)
Women	624/814.3	0.77 (0.71-0.83)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Coronary procedures in angina patients

Among those admitted to hospital with angina, 64.2% received angiography, 70.2% of men vs 56.4% of women, and 35.9% PCI/CABG, 47.7% vs 20.9% respectively. The proportion of angina patients who survived to the end of the follow-up period and who had a procedure was 64.6% for angiography (70.9% vs 56.6%), and 36.1% for PCI/CABG (48.2% vs 20.7%).

Crude rates for angiography were 2.43 (2.32-2.55) and 1.34 (1.27-1.42) for men and women respectively, and crude rates for PCI/CABG were 0.94 (0.89-1.00) and 0.28 (0.25-0.31) respectively (Table 3).

Cox models showed angiography rates were around 30% higher among men after adjusting for all factors (HR=1.27, 1.17-1.37). Rates for PCI/CABG in men were around 150% times those of women (adjusted HR=2.46, 2.19-2.77).

Table 3: Rates of coronary procedures within one year of admission with angina by gender and associated hazard ratios (n=4,457)

	Procedures/ pys	**Crude rate per py (95%CI)**	**Model 1 HR (95%CI)**	**Model 2 HR (95%CI)**	**Model 3 HR (95%CI)**
Angiography					
Men	1758/723.6	2.43 (2.32-2.55)	1.33 (1.24-1.44)	1.29 (1.19-1.39)	1.27 (1.17-1.37)
Women	1101/820.1	1.34 (1.27-1.42)	1.00	1.00	1.00
PCI/CABG					
Men	1193/1262.6	0.94 (0.89-1.00)	2.58 (2.31-2.89)	2.51 (2.24-2.82)	2.46 (2.19-2.77)
Women	408/1471.1	0.28 (0.25-0.31)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

There were no violations of the proportional hazards assumption for the gender variable in the models with 12 months of follow-up.

Sensitivity analyses using a 30-day follow-up period produced almost identical HRs (Supplementary Tables S1-S2). While violations of the proportional hazards assumption were found on testing in both the AMI and angina samples, there were no major violations detected in log-log plots. Hazard ratios were not materially different to those in the main analysis when adjusted for self-rated health as an alternative indicator of health (Tables S3-S4), when additionally adjusted for the Charlson index (Tables S5-S6), or when estimated on a sample restricted to patients admitted with a primary diagnosis of unstable angina (Table S7).

DISCUSSION

Our findings demonstrate clear gender differences in receipt of coronary procedures. Men were more likely to receive coronary revascularisation (PCI/CABG) for the management of AMI or angina. Differences in revascularisation rates were most pronounced among those admitted with angina, among whom men were also more likely to undergo diagnostic angiography.

This study uses Australian data, with findings generally consistent with published evidence internationally. There is evidence from the US and Sweden that men are more likely than women to receive revascularisation procedures such as PCI or CABG following hospital admission with AMI or angina.[7, 17] Our finding that rates of PCI/CABG among men were 1.5 and 2.5 times those for women for AMI and angina respectively, is consistent with the above studies. A cohort study from the United Kingdom demonstrated this relationship for CABG, with men having twice the odds of receiving CABG than women (OR=1.90,1.21-3.00), however no difference in overall revascularisation rates was found (p=0.14).[18] Evidence regarding angiography is less consistent. There is evidence from the US, including a review, that suggests gender differences exist,[19, 20] however these considered acute coronary syndrome as a whole, rather than AMI and angina separately. No significant difference was found in the United Kingdom for receipt of CVD investigations, including angiography.[18] This is consistent with our findings on angiography in AMI patients, but differ from our findings in angina patients where we found a 30% difference in rates between men and women.

Factors driving the observed gender differences in procedure rates are not known, however likely contributors include differences in clinical presentation. There are established gender differences in the pathophysiology, diagnosis and outcome of therapies related to AMI and angina.[7] For example, greater proportions of small vessel coronary disease among women, including Takotsubo cardiomyopathy and other forms of myocardial infarction with non-obstructive coronary arteries,[21] could contribute to lower rates of PCI/CABG following AMI. Following CABG, women experience higher complication rates and increased mortality compared to men, a finding that is more pronounced in younger age groups.[6] While this may contribute to the lower rate of procedures among women, the directionality of this relationship cannot be assumed. While we did adjust for physical functioning and comorbidity, clinical factors including symptom severity were not accounted for in our models. A US review, however, concluded that clinical factors do not fully explain the discrepancies in procedure rates between genders.[22] Thus, while we cannot exclude the possibility of the gender differences representing appropriate clinical care, this seems an unlikely explanation for the total observed variation in procedure rates, with multiple factors likely at play.[22]

Another possible explanation for our findings is unwarranted variation due to gender discrimination. This includes the possibility of unconscious gender bias, with one systematic review demonstrating implicit bias towards patients by healthcare professionals.[23] Australia's universal health system, providing free access to hospital care, should present few barriers to receiving equitable care. There are clear guidelines for the use of coronary procedures among patients presenting with AMI, however the use of procedures for those presenting with angina is more discretionary.[24] Gender differences found in receipt of coronary procedures, particularly for the more discretionary cases of angina, reinforce the suggestion that these differences reflect an inequality in care. This raises two distinct issues. First, the possible underuse of coronary procedures in women, which may indicate that the health care needs of a portion of Australians are not being adequately met, and second, the possible overuse of coronary procedures in men, which raises the question of waste within a health care system with limited resources.[24]

Strengths of this study include the use of population-based survey data linked to routinely collected data. The number of participants included was relatively large, with virtually complete capture of procedures. Questionnaire and other data permitting, there was adjustment for a large range of baseline sociodemographic and health factors (most of which are not included in administrative data). Additionally, the diagnosis of AMI is highly valid within hospital data, with high concordance between diagnostic codes and physician review.[25] This is not true for angina however, where concordance is relatively low.[25] This may have led to an over- or underestimation of procedure rates for angina. As only those admitted to hospital were included in this study, it is possible that some participants with angina, who could benefit from a coronary procedure, were not captured. While the 45 and Up Study cohort is broadly representative of the general population, participants are likely to be healthier and have lower hospitalisation and mortality rates than others in this age group, consistent with the healthy cohort effect.[26] However, while this may mean that the absolute rates of coronary procedures among those with coronary heart disease in this study differ from those of the general population, internal comparisons are unlikely to be influenced by this bias, hence relative rates in relation to gender are likely to remain valid.[27, 28]

CONCLUSION

Cardiovascular disease is a national health priority for Australia, with substantial morbidity and mortality. This study showed that men are more likely than women to receive coronary revascularisation procedures following admission to hospital with an AMI or angina. This relationship was particularly evident among the angina group, for whom care is more discretionary. While we cannot exclude that this discrepancy reflects appropriate care due to differences in clinical presentation, this is unlikely to fully explain the observed findings. Rather, clear gender differences, accounting for sociodemographic position and health-related factors, may indicate that the health care needs of a portion of the Australian population are not being adequately met. Morbidity and mortality among Australian women may be unnecessarily increased due to not receiving coronary intervention following AMI or angina. Alternatively, relative over-use in men cannot be ruled out. Either way, there is potential for health gain in elucidating and addressing this gender inequality in receipt of coronary intervention, increasing awareness and delivery of best practice care.

Abbreviations

CVD: Cardiovascular Disease; AMI: Acute Myocardial Infarction; NSW: New South Wales; APDC: NSW Admitted Patients Data Collection; ICD-10-AM: International statistical Classification of Diseases and related health problems, tenth revision, Australian Modification; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Grafting; IHD: Ischaemic Heart Disease; HR: Hazard Ratio; CI: Confidence Interval; BMI: Body Mass Index; PY: person years.

DECLARATIONS

Ethics approval

Ethics approvals for this project were obtained from the NSW Population and Health Services Research Ethics Committee, the University of NSW Human Research Ethics Committee and the Australian National University Human Research Ethics Committee. Participants in the 45 and Up Study provided signed consent for linkage of their information to a range of health-related databases.

Patient and Public Involvement

Not applicable. Patients were not involved in the development of this study.

Availability of data and material

The datasets used during the current study are available upon application to the Sax Institute (www.saxinstitute.org.au/our-work/45-up-study). To do so, one must have a scientifically sound and feasible research proposal, ethics approval for the proposal, data custodian approval for access to linked data, and be able to meet 45 and Up Study license and SURE user charges.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

AF provided input into the study design, performed statistical analysis, interpreted the data and drafted the manuscript. JW provided input into the study design, performed statistical analysis and reviewed the manuscript. EB provided input into the study design and reviewed the manuscript. WA reviewed the manuscript. RK conceived and designed the study and assisted in writing the manuscript. All authors read and approved the final manuscript.

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Supplementary Material

Variation in cardiovascular disease care: A cohort study on gender inequalities in receipt of coronary procedures

Table S1: Rates of coronary procedures within 30 days of admission with AMI by gender and associated hazard ratios (n=4,580)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	2049/73.7	27.8 (26.6-29.0)	1.08 (1.00-1.16)	1.02 (0.95-1.10)	0.99 (0.92-1.07)
Women	1060/48.9	21.7 (20.4-23.0)	1.00	1.00	1.00
PCI/CABG					
Men	1624/108.9	14.9 (14.2-15.67)	1.60(1.46-1.76)*	1.54(1.40-1.69)*	1.49(1.36-1.65)*
Women	600/83.8	7.15 (6.60-7.75)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status) Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning and psychological distress). * indicates that the proportional hazard assumption is violated.

Table S2: Rates of coronary procedures within 30 days of admission with angina by gender and associated hazard ratios (n=4,457)

	Procedures /pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1685/74.9	22.5 (21.5-23.6)	1.32 (1.22-1.42)	1.27 (1.17-1.37)	1.25 (1.15-1.35)
Women	1054/79.4	13.3 (12.5-14.1)	1.00	1.00	1.00
PCI/CABG					
Men	1083/127.4	8.50 (8.01-9.02)	2.50(2.23-2.82)*	2.43(2.15-2.74)*	2.37(2.10-2.67)*
Women	371/132.7	2.79 (2.52-3.09)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status) Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning and psychological distress). * indicates that the proportional hazard assumption is violated.

Table S3: Associated hazard ratios for coronary procedures within one year of admission with AMI by gender (n=4,580)

	Model 1 HR (95% CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.02 (0.94-1.10)
Women	1.00	1.00	1.00
PCI/CABG			
Men	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.55 (1.41-1.71)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and socio-variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (self-rated health only).

Table S4: Associated hazard ratios for coronary procedures within one year of admission with angina by gender (n=4,457)

	Model 1 HR (95% CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.33 (1.24-1.44)	1.29 (1.19-1.39)	1.28 (1.19-1.39)
Women	1.00	1.00	1.00
PCI/CABG			
Men	2.58 (2.31-2.89)	2.51 (2.24-2.82)	2.52 (2.25-2.83)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (self-rated health only).

Table S5: Associated hazard ratios for coronary procedures within one year of admission with AMI by gender (n=4,580)

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.00 (0.92-1.08)
Women	1.00	1.00	1.00
PCI/CABG			
Men	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.53 (1.39-1.68)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress and the Charlson index).

Table S6: Associated hazard ratios for coronary procedures within one year of admission with angina by gender (n=4,457)

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.33 (1.24-1.44)	1.29 (1.19-1.39)	1.27 (1.18-1.37)
Women	1.00	1.00	1.00
PCI/CABG			
Men	2.58 (2.31-2.89)	2.51 (2.24-2.82)	2.49 (2.21-2.79)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress and the Charlson index).

Table S7: Rates for coronary procedures within one year of admission with unstable angina (I20.0) gender and associated hazard ratios (n=2,131)

	Procedures /pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	735/429.5	1.71 (1.59-1.84)	1.32 (1.18-1.48)	1.31 (1.17-1.47)	1.30 (1.15-1.46)
Women	491/448.5	1.09 (1.00-1.20)	1.00	1.00	1.00
PCI/CABG					
Men	481/665.5	0.72 (0.66-0.79)	2.55 (2.14-3.04)	2.54 (2.13-3.03)	2.53 (2.11-3.02)
Women	173/746.5	0.23 (0.20-0.27)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is further adjusted for country of birth, region of residence, highest qualification, marital status and health insurance. Model 3 is further adjusted for obesity, physical functioning and psychological distress.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Variation in cardiovascular disease care: An Australian cohort study on sex differences in receipt of coronary procedures.

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Title

Variation in cardiovascular disease care: An Australian cohort study on sex differences in receipt of coronary procedures

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ABSTRACT

Objectives: To quantify sex differences in diagnostic and revascularisation coronary procedures within one year of hospitalisation for acute myocardial infarction (AMI) or angina.

Design: Prospective cohort study. Baseline questionnaire (January 2006-April 2009) data from the Sax Institute's 45 and Up Study were linked to hospitalisation and mortality data (to 30 June 2016) in a time-to-event analysis, treating death as a censoring event.

Setting: New South Wales, Australia.

Participants: Participants aged ≥45 years with no history of IHD who were admitted to hospital with a primary diagnosis of AMI (n=4,580), or a primary diagnosis of angina or chronic IHD with secondary diagnosis of angina (n=4,457).

Outcome Measures: Coronary angiography and coronary revascularisation with percutaneous coronary intervention or coronary artery bypass graft (PCI/CABG) within one year of index admission. Cox regression models compared coronary procedure rates in men and women, adjusting sequentially for age, sociodemographic variables and health characteristics.

Results: Among AMI patients, 71.6% of men (crude rate: 3.45/person-year) and 64.7% of women (2.62/person-year) received angiography; 57.8% of men (1.73/person year) and 37.4% of women (0.77/person-year) received PCI/CABG. Adjusted hazard ratios (HRs) for men versus women were 1.00(0.92-1.08) for angiography and 1.51(1.38-1.67) for PCI/CABG. In the angina group, 71.6% of men (crude rate: 2.36/person-year) and 64.7% of women (1.32/person-year) received angiography; 57.8% of men (0.90/person-year) and 37.4% of women (0.26/person-year) received PCI/CABG. Adjusted HRs were 1.24(1.14-1.34) and 2.44(2.16-2.75) respectively.

Conclusions: Men are more likely than women to receive coronary procedures, particularly revascularisation. This difference is most evident among people with angina, where care is more discretionary compared to AMI.

Keywords: Cardiovascular disease, Coronary procedure, Linked data, 45 and Up Study, Health inequality

ARTICLE SUMMARY

Strengths and limitations of this study

- This study uses population-based survey data linked to routinely collected health data.
- This study has a relatively large number of participants, with virtually complete capture of procedures.
- This study has adjusted for a large range of baseline sociodemographic and health factors, however clinical factors upon presentation were not included.
- While diagnosis of AMI is highly valid within hospital data, there is relatively low concordance for angina diagnoses, with possible over- or underrepresentation of rates.
- The study cohort, while broadly representative of the general population, is likely to be healthier and have lower hospitalisation and mortality rates than their peers.

BACKGROUND

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide,[1] and a leading cause of death in Australia.[2] While incidence of CVD is higher among men,[3] in many parts of the world women experience worse outcomes.[4] Coronary interventions, including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), contribute to improved outcomes following an acute coronary event in both men and women.[4] Despite the significant disease burden and availability of effective interventions, CVD in women as a whole remains underdiagnosed and less aggressively treated.[5, 6] Women are underrepresented in clinical trials,[6] and there are important gaps in the evidence for recognition and treatment of adverse coronary events.

It is known that incident acute myocardial infarction (AMI) and angina pectoris present on average 7-10 years later in women compared to men.[6, 7] Women generally present to hospital older and with a greater number of risk factors than men,[6] experiencing higher mortality and re-infarction rates following a first AMI.[7] Disparities in care received by women compared to men have been documented in the United States (US), even when accounting for income, education and site of care.[8] Evidence from Europe and the US demonstrate that women with CVD are less likely to undergo diagnostic angiograms or intervention with PCI or CABG,[6, 7] procedures with documented clinical benefit.[4, 5]

There is limited information on sex differences in cardiovascular care in Australia, including diagnosis and management with coronary procedures. Age-standardised rates of procedures are lower among women compared to men,[9] however underlying CVD and other factors related to delivery of care are not taken into consideration in these figures. Hence, the extent to which these differences in rates reflect inequalities in care is uncertain. This study aimed to quantify sex differences in care delivery by comparing coronary procedure rates in men and women admitted with AMI or angina, adjusting for other sociodemographic and health-related factors.

METHODS

Data sources

Data were obtained from the Sax Institute's 45 and Up Study, a population-based cohort study involving 267,153 men and women aged 45 and over from New South Wales (NSW) Australia. 45 and Up Study participants were randomly selected from the Department of Human Services (formerly Medicare Australia) database, Australia's universal health insurance system, with oversampling of individuals living in rural areas and those over the age of 80 by a factor of 2. All individuals living in remote areas were invited to participate. Participants enrolled by completing a mailed self-administered questionnaire and provided signed consent for long-term follow-up and data-linkage with a range of health databases. Approximately 10% of the NSW population aged 45 and over were included in the sample, an overall response rate of 18%. The Study is described in detail elsewhere,[10] with questionnaires available online.[11]

Baseline data from 45 and Up Study participants were linked to hospital data from the NSW Admitted Patient Data Collection (APDC, 1 July 2000 to 30 June 2016) and death data from the NSW Registry of Births, Deaths and Marriages and the National Death Index (1 January 2006 to 30 June 2016). The latter was linked by the Australian Institute of Health and Welfare. Included in the APDC is a record of all hospitalisations in NSW, dates of admission and discharge, and reason for admission. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) and Australian Classification of Health Interventions codes are incorporated into the APDC, with each record containing up to 51 diagnosis and 50 procedure codes. Death data included date of death (used for censoring as per time-to-event analysis), based on death from any cause.

Data were linked probabilistically by the Centre for Health Record linkage using personal information (full name, date of birth, sex, and address). It is likely that during the follow-up period a small but unknown number of participants may have moved interstate. Though hospitalisations in neighbouring states are not included, these are estimated to make up fewer than 2% of admissions in NSW residents. Follow-up for hospitalisations is considered to be ~98% complete among those who continue to live in NSW. Quality assurance data on the data linkage show false positive and negative rates of <0.5% and <0.1% respectively.

Study Population

All 45 and Up Study participants admitted to hospital with a primary diagnosis of AMI or angina (stable or unstable) following entry into the 45 and Up Study were included in the sample. Those with a primary diagnosis of chronic ischaemic heart disease (IHD) and secondary diagnosis of angina were also included, due to the possibility of angina patients being admitted for elective revascularisation under these diagnostic codes. ICD-10-AM diagnosis codes I21 (acute myocardial infarction), I20 (angina pectoris), and I25 (chronic ischaemic heart disease), were used to ascertain admission. Note that these are clinicopathological diagnoses, with angina specifically referring to chest pain from insufficient myocardial oxygenation and coronary artery disease. I21 coding for AMI includes both ST-elevation and non-ST elevation myocardial infarcts, with current ICD-10 coding unable to reliably distinguish between these.[12]

Participants with a prior history of IHD were excluded, defined as self-reported heart disease on the baseline questionnaire and/or admission to hospital for IHD (120-125), and/or a related interventional procedure (angiogram, PCI or CABG – defined below), as ascertained by diagnosis and procedure code fields of APDC in the six years prior to entering the 45 and Up Study.

Variables

The study outcomes were investigation with angiography, and coronary intervention with PCI or CABG, within 12 months of index admission to hospital.

Outcomes were ascertained using all 50 APDC procedure-code fields, coded using the Australian Classification of Health Interventions which is used in conjunction with ICD-10-AM,[13]: angiography (38215, 38218), PCI (35304-00, 35305-00, 35304-01, 35305-01, *38300-00, 38303-00* (block: 670), 35310-00, 35310-01, 35310-02, 35310-03, 35310-05, *38306-00, 38306-01, 38306-02, 38306-03, 38306-05* (block: 671)) and CABG (38497-00 to 38497-07, 38500-00 to 38500-04, 38503-

00 to 38503-04, 90201-00 to 90201-03, *38500-05, 38503-05* (blocks 672-679)). Italicised codes have been included to reflect changes in procedure coding during the follow-up period.

The main exposure of interest was sex (male or female), self-reported on the baseline questionnaire. Sociodemographic and health characteristics that may confound/mediate the relationship between sex and receipt of coronary procedures were also measured on the baseline questionnaire. These included: country of birth (Australia/New Zealand or other), region of residence (major city, inner regional, or outer regional/remote/very remote), highest qualification (no school certificate, school/trade certificate or diploma, or tertiary degree), private health insurance (no private health insurance, or health care/Department of Veterans Affairs concession card), marital status (married/de facto, or not), obesity (body mass index (BMI)≥30kg/m^2, or not, based on self-reported height and weight), physical functioning (no/minor limitations, moderate limitations, or severe limitations, based on levels of functional limitation, as adapted from the Medical Outcomes Score Physical Functioning Subscale [14]), and psychological distress (low[10-<16], moderate[16-<22], or high[22-50], as per the Kessler 10).[15]

Analysis

Cox proportional hazard regression was used to model the association between sex and receipt of coronary procedures. For each analysis, participants contributed person-years from the date of index admission for AMI or angina until either the specified outcome of interest, death from any cause, or end of follow up 30 June 2016, whichever was the earliest, to a maximum of one calendar year. Data from patients in the angina sample were also censored if they were subsequently admitted with AMI. Proportional hazards assumption was tested, with the p-value set *a priori* to p<0.01. All analyses were conducted separately for patients whose index admission was for AMI, and for those whose index admission was for angina. Patients presenting concurrently with AMI and angina were included in the AMI sample.

For each outcome, we calculated crude incidence rates separately for men and women, then ran a series of Cox regression models to estimate hazard ratios (HRs) in relation to sex. Model 1 was adjusted for age (5-year age categories from 45-54years through to ≥85years). Model 2 was adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, private health insurance and marital status). Model 3 was further adjusted for additional baseline health characteristics (obesity, physical functioning and psychological distress). Participants with missing values for covariates were included in the models, with missing coded as a separate category.

Multiple sensitivity analyses were performed. First, we used a maximum follow-up period of 30 days after index admission rather than 12 months. Second, we used an alternative indicator of baseline health – self-rated health, measured with three categories (excellent/very good, good, fair/poor) – instead of functional limitation, obesity and psychological distress (Model 3). Third, we additionally controlled for comorbidity using the Charlson index,[16] using all diagnostic codes in the 12 months prior to the index admission, with scores categorised as 0, 1 or ≥2. Fourth, we restricted analysis of the angina patients to those admitted with a primary diagnosis of unstable angina (ICD-10: I20.0). Further sensitivity analyses were performed, excluding patients who were aged 85 and older, and then controlling for additional patient factors of smoking, self-rated diabetes, treatment for high blood pressure, treatment for high cholesterol, and family history of heart disease.

Analyses were performed using Stata 14.[17]

The conduct of the 45 and Up Study was approved by the University of New South Wales Human Research Ethics Committee. Ethics approval for this study was obtained from the Australian National University Human Ethics Committee (2015/513) and the NSW Population and Health Services Research Ethics Committee (HREC/10/CIPHS/33; CI NSW Study Reference 2010/05/234).

RESULTS

A total of 9,037 patients were included in the study, 4,580 admitted with AMI and 4,457 admitted with angina. There were no patients in the sample who had IHD as a primary diagnosis and angina as a secondary diagnosis. Sample characteristics are shown in Table 1. The profiles of patients within the AMI and angina groups were similar, with a few exceptions. Notably, those in the angina group were less likely to be aged 85 and over (8.56% vs 19.4%), and more likely to have private health insurance at baseline (64.6% vs 56.9%) than those in the AMI group. There was a greater percentage of men within both AMI and angina groups, 63.6% and 56.2% respectively.

Table 1: Characteristics of patients admitted to hospital with acute myocardial infarction (AMI) or angina by sex

	AMI Sample (n=4,580)				**Angina Sample** (n=4,457)			
	Men		Women		Men		Women	
	n	%	n	%	n	%	n	%
Total	2911	63.6	1669	36.4	2503	56.2	1954	43.8
Age at admission								
45-54	190	6.5	80	4.8	152	6.1	151	7.7
55-64	685	23.5	277	16.6	628	25.1	499	25.5
65-74	807	27.7	414	24.8	897	35.8	622	31.8
75-84	757	26.0	481	28.8	634	25.3	493	25.2
85+	472	16.2	417	25.0	192	7.7	189	9.7
Region of residence								
Major city	1485	51.0	807	48.4	1321	52.8	972	49.7
Inner regional	1025	35.2	629	37.7	886	35.4	717	36.7
Regional/remote	354	12.2	200	12.0	259	10.4	237	12.1
Highest qualification								
No school certificate	417	14.3	357	21.4	305	12.2	326	16.7
School/ certificate/ diploma	1923	66.1	1085	65.0	1629	65.1	1310	67.0
Tertiary degree	497	17.1	175	10.5	502	20.1	276	14.1
Country of birth								
Australia/ NZ	2142	73.6	1323	79.3	1888	75.4	1576	80.7
Other	728	25.0	327	19.6	583	23.3	353	18.1
Marital status								
Single	647	22.2	750	44.9	465	18.6	638	32.7
Married/ de facto	2244	77.1	916	54.9	2011	80.3	1313	67.2
BMI								
Not obese (BMI<30kg/m^2)	2079	71.4	1100	65.9	1713	68.4	1260	64.5
Obese (BMI≥30kg/m^2)	625	21.5	394	23.6	619	24.7	479	24.5
Physical functioning								
No or minor limitation	1412	48.5	469	28.1	1221	48.8	691	35.4
Moderate limitations	646	22.2	386	23.1	647	25.9	517	26.5
Severe limitations	393	13.5	392	23.5	301	12.0	373	19.1
Psychological distress								
Low	1958	67.3	948	56.8	1681	67.2	1131	57.9
Moderate	339	11.7	205	12.3	337	13.5	273	14.0
High	188	6.5	111	6.7	178	7.1	172	8.8
Health Insurance								
No private health insurance	1164	40.0	807	48.4	845	33.8	731	37.4
Health care/DVA	1746	60.0	862	51.7	1658	66.2	1223	62.6

% of missing cases: AMI sample (men, women): region of residence (1.6, 2.0); highest qualification (2.5, 3.1); country of birth (1.4, 1.1); marital status (0.7, 0.2); BMI (7.1, 10.5); physical limitations (15.8, 25.3); psychological distress (14.6, 24.3); health insurance (<0.1, 0.0). Angina sample (men, women): region of residence (1.5, 1.4); highest qualification (2.7, 2.2); country of birth (1.3, 1.3); marital status (1.1, 0.1); BMI (6.8, 11.0); physical limitations (13.3, 19.1); psychological distress (12.3, 19.3); health insurance (0.0, 0.0).

Coronary procedures in AMI patients

Among those admitted to hospital with AMI, 69.1% received angiography, 71.6% of men vs 64.7% of women; and 50.4% underwent PCI/CABG, 57.8% vs 37.4% respectively. The proportion of AMI patients who survived the follow-up period and who had a procedure was 75.6% for angiography (77.6% v 71.9%), and 55.4% for PCI/CABG (63.2% vs 41.0%).

Crude rates per person-year of angiography were 3.45 (3.31-3.60) and 2.62 (2.47-2.78) in men and women respectively; and crude rates of PCI/CABG were 1.73 (1.64-1.81) and 0.77 (0.71-0.83) respectively (Table 2).

Cox models showed angiography rates were similar in men and women, with no difference after adjustment for sociodemographic and health variables (HR=1.00, 0.92-1.08) (Table 2). In contrast, rates for PCI/CABG were around 50% higher in men than women (adjusted HR=1.51, 1.38-1.67).

Table 2: Rates of coronary procedures within one year of admission with AMI by sex and associated hazard ratios (n=4,580)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	2085/604.1	3.45 (3.31-3.60)	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.00 (0.92-1.08)
Women	1079/411.7	2.62 (2.47-2.78)	1.00	1.00	1.00
PCI/CABG					
Men	1682/975.0	1.73 (1.64-1.81)	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.51 (1.38-1.67)
Women	624/814.3	0.77 (0.71-0.83)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Coronary procedures in angina patients

Among those admitted to hospital with angina, 61.9% received angiography, 67.3% of men vs 54.9% of women; and 33.6% underwent PCI/CABG, 44.6% vs 19.5% respectively. The proportion of angina patients who survived to the end of the follow-up period and who had a procedure was 62.4% for angiography (68.1% vs 55.1%), and 33.9% for PCI/CABG (45.3% vs 19.4%).

Crude rates for angiography were 2.36 (2.25-2.47) and 1.32 (1.24-1.40) for men and women respectively; and crude rates for PCI/CABG were 0.90 (0.85-0.95) and 0.26 (0.24-0.29) respectively (Table 3).

Cox models showed angiography rates were around 25% higher among men after adjusting for all factors (HR=1.24, 1.14-1.34). Rates for PCI/CABG in men were around 150% times those of women (adjusted HR=2.44, 2.16-2.75).

Table 3: Rates of coronary procedures within one year of admission with angina by sex and associated hazard ratios (n=4,457)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1685/715.0	2.36 (2.25-2.47)	1.31 (1.21-1.41)	1.26 (1.16-1.36)	1.24 (1.14-1.34)
Women	1072/814.3	1.32 (1.24-1.40)	1.00	1.00	1.00
PCI/CABG					
Men	1117/1242.2	0.90 (0.85-0.95)	2.57 (2.28-2.88)	2.49 (2.21-2.80)	2.44 (2.16-2.75)
Women	381/1450.8	0.26 (0.24-0.29)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

There were no violations of the proportional hazards assumption for the sex variable in the models with 12 months of follow-up.

Sensitivity analyses using a 30-day follow-up period produced almost identical HRs (Supplementary Tables S1-S2). While violations of the proportional hazards assumption were found on testing in both the AMI and angina samples, there were no major violations detected in log-log plots. Hazard ratios were not materially different to those in the main analysis when adjusted for self-rated health as an alternative indicator of health (Tables S3-S4), when additionally adjusted for the Charlson index (Tables S5-S6), or when estimated on a sample restricted to patients admitted with a primary diagnosis of unstable angina (Table S7). Similarly, hazard ratios were not materially different to those in the main analysis when participants 85 and over were excluded from the sample (Tables S8 (AMI patients) and S9 (angina patients)), and when additionally adjusting for smoking, self-rated diabetes, treatment for high blood pressure, treatment for high cholesterol, and family history of heart disease (Table S10).

DISCUSSION

Our findings demonstrate clear sex differences in receipt of coronary procedures. Men were more likely to receive coronary revascularisation (PCI/CABG) for the management of AMI or angina. Differences in revascularisation rates were most pronounced among those admitted with angina, among whom men were also more likely to undergo diagnostic angiography.

This study uses Australian data, with findings generally consistent with published evidence internationally. There is evidence from the US and Sweden that men are more likely than women to receive revascularisation procedures such as PCI or CABG following hospital admission with AMI or angina.[7, 18] Our finding that rates of PCI/CABG among men were 1.5 and 2.4 times those for women for AMI and angina respectively, is consistent with the above studies. A cohort study from the United Kingdom demonstrated this relationship for CABG, with men having twice the odds of receiving CABG than women (OR=1.90,1.21-3.00), however no difference in overall revascularisation rates was found (p=0.14).[19] Evidence regarding angiography is less consistent. There is evidence from the US, including a review, that suggests sex differences exist,[20, 21] however these considered acute coronary syndrome as a whole, rather than AMI and angina separately. No significant difference was found in the United Kingdom for receipt of CVD investigations, including angiography.[19] This is consistent with our findings on angiography in AMI patients, but differ from our findings in angina patients where we found a 25% difference in rates between men and women.

Factors driving the observed sex differences in procedure rates are not known, however likely contributors include differences in clinical presentation. There are established sex differences in the pathophysiology, diagnosis and outcome of therapies related to AMI and angina.[7] For example, greater proportions of small vessel coronary disease among women, including Takotsubo cardiomyopathy and other forms of myocardial infarction with non-obstructive coronary arteries,[22] could contribute to lower rates of PCI/CABG following AMI. Previous studies have shown that women who present with AMI or stable angina are more likely to have non-obstructive coronary artery disease compared to men, i.e. <50% stenosis of coronary arteries.[23,24]

Following CABG, women experience higher complication rates and increased mortality compared to men, a finding that is more pronounced in younger age groups.[6] While this may contribute to the lower rate of procedures among women, the directionality of this relationship cannot be assumed.

The use of questionnaire data linked to large-scale routine data enabled a wide range of personal characteristics and other factors to be included in models, such as socio-economic position and physical functioning, however clinical factors relating to patient presentation and symptom severity were not available in the dataset. A US review, however, concluded that clinical factors do not fully explain the discrepancies in procedure rates between sexes.[25] Thus, while we cannot exclude the possibility of the sex differences representing appropriate clinical care, this seems an unlikely explanation for the total observed variation in procedure rates, with multiple factors likely at play.[25]

Another possible explanation for our findings is unwarranted variation due to discrimination. This includes the possibility of unconscious gender bias, with one systematic review demonstrating implicit bias towards patients by healthcare professionals.[26] Australia's universal health system, providing free access to hospital care, should present few barriers to receiving equitable care. There are clear guidelines for the use of coronary procedures among patients presenting with AMI, however the use of procedures for those presenting with angina is more discretionary.[27] Sex differences found in receipt of coronary procedures, particularly for the more discretionary cases of angina, reinforce the suggestion that these differences reflect an inequality in care. This raises two distinct issues. First, the possible underuse of coronary procedures in women, which may indicate that the health care needs of a portion of Australians are not being adequately met, and second, the possible overuse of coronary procedures in men, which raises the question of waste within a health care system with limited resources.[27]

Strengths of this study include the use of population-based survey data linked to routinely collected data. The number of participants included was relatively large, with virtually complete capture of procedures. Questionnaire and other data permitting, there was adjustment for a large range of baseline sociodemographic and health factors (most of which are not included in administrative data). Additionally, the diagnosis of AMI is highly valid within hospital data, with sensitivity and specificity of ≥86% and a positive predictive value of ≥93%,[28] and high concordance between diagnostic codes and physician review.[29] This is not true for angina however, where concordance is relatively low.[29] This may have led to an over- or underestimation of procedure rates for angina. As only those admitted to hospital were included in this study, it is possible that some participants with angina, who could benefit from a coronary procedure, were not captured. While the 45 and Up Study cohort is broadly representative of the general population, participants are likely to be healthier and have lower hospitalisation and mortality rates than others in this age group, consistent with the healthy cohort effect.[30] However, while this may mean that the absolute rates of coronary procedures among those with coronary heart disease in this study differ from those of the general population, internal comparisons are unlikely to be influenced by this bias, hence relative rates in relation to sex are likely to remain valid.[31,32]

CONCLUSION

Cardiovascular disease is a national health priority for Australia, with substantial morbidity and mortality. This study showed that men are more likely than women to receive coronary revascularisation procedures following admission to hospital with an AMI or angina. This relationship was particularly evident among the angina group, for whom care is more discretionary. While we cannot exclude that this discrepancy reflects appropriate care due to differences in clinical presentation, we must consider the possibility that sex differences, accounting for sociodemographic position and health-related factors, may indicate that the health care needs of a portion of the Australian population are not being adequately met. Morbidity and mortality among Australian women may be unnecessarily increased due to not receiving coronary intervention following AMI or angina. Alternatively, relative over-use in men cannot be ruled out. Either way, there is potential for health gain in elucidating and addressing this sex difference in receipt of coronary intervention, increasing awareness and delivery of best practice care.

Abbreviations

CVD: Cardiovascular Disease; AMI: Acute Myocardial Infarction; NSW: New South Wales; APDC: NSW Admitted Patients Data Collection; ICD-10-AM: International statistical Classification of Diseases and related health problems, tenth revision, Australian Modification; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Grafting; IHD: Ischaemic Heart Disease; HR: Hazard Ratio; CI: Confidence Interval; BMI: Body Mass Index; PY: person years.

DECLARATIONS

Ethics approval

Ethics approvals for this project were obtained from the NSW Population and Health Services Research Ethics Committee, the University of NSW Human Research Ethics Committee and the Australian National University Human Research Ethics Committee. Participants in the 45 and Up Study provided signed consent for linkage of their information to a range of health-related databases.

Patient and Public Involvement

Not applicable. Patients were not involved in the development of this study.

Availability of data and material

The datasets used during the current study are available upon application to the Sax Institute (www.saxinstitute.org.au/our-work/45-up-study). To do so, one must have a scientifically sound and feasible research proposal, ethics approval for the proposal, data custodian approval for access to linked data, and be able to meet 45 and Up Study license and SURE user charges.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

AF provided input into the study design, performed statistical analysis, interpreted the data and drafted the manuscript. JW provided input into the study design, performed statistical analysis and reviewed the manuscript. EB provided input into the study design and reviewed the manuscript. WA reviewed the manuscript. RK conceived and designed the study and assisted in writing the manuscript. All authors read and approved the final manuscript.

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Supplementary Material

Variation in cardiovascular disease care: A cohort study on gender inequalities in receipt of coronary procedures

Table S1: Rates of coronary procedures within 30 days of admission with AMI by gender and associated hazard ratios (n=4,580)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	2049/73.7	27.8 (26.6-29.0)	1.08 (1.00-1.16)	1.02 (0.95-1.10)	0.99 (0.92-1.07)
Women	1060/48.9	21.7 (20.4-23.0)	1.00	1.00	1.00
PCI/CABG					
Men	1624/108.9	14.9 (14.2-15.7)	1.60(1.46-1.76)*	1.54(1.40-1.69)*	1.49(1.36-1.65)*
Women	600/83.8	7.15 (6.60-7.75)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status) Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning and psychological distress). * indicates that the proportional hazard assumption is violated.

Table S2: Rates of coronary procedures within 30 days of admission with angina by gender and associated hazard ratios (n=4,457)

	Procedures /pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1624/74.3	21.9 (20.8-23.0)	1.30 (1.20-1.40)	1.25 (1.15-1.35)	1.23 (1.13-1.33)
Women	1026/79.0	13.3 (12.5-14.1)	1.00	1.00	1.00
PCI/CABG					
Men	1023/125.9	8.13 (7.64-8.64)	2.51(2.22-2.84)*	2.42(2.14-2.74)*	2.36(2.08-2.68)*
Women	347/131.3	2.64 (2.38-2.94)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status) Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning and psychological distress). * indicates that the proportional hazard assumption is violated.

Table S3: Associated hazard ratios for coronary procedures within one year of admission with AMI by gender (n=4,580)

	Model 1 HR (95% CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.02 (0.94-1.10)
Women	1.00	1.00	1.00
PCI/CABG			
Men	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.55 (1.41-1.71)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and socio-variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (self-rated health only).

Table S4: Associated hazard ratios for coronary procedures within one year of admission with angina by gender (n=4,457)

	Model 1 HR (95% CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.31 (1.21-1.41)	1.26 (1.16-1.36)	1.25 (1.16-1.36)
Women	1.00	1.00	1.00
PCI/CABG			
Men	2.57 (2.28-2.88)	2.49 (2.21-2.80)	2.50 (2.22-2.81)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (self-rated health only).

Table S5: Associated hazard ratios for coronary procedures within one year of admission with AMI by gender (n=4,580)

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.00 (0.93-1.08)
Women	1.00	1.00	1.00
PCI/CABG			
Men	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.53 (1.39-1.68)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress and the Charlson index).

Table S6: Associated hazard ratios for coronary procedures within one year of admission with angina by gender (n=4,457)

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.31 (1.21-1.41)	1.26 (1.16-1.36)	1.24 (1.14-1.34)
Women	1.00	1.00	1.00
PCI/CABG			
Men	2.57 (2.28-2.88)	2.49 (2.21-2.80)	2.46 (2.18-2.77)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress and the Charlson index).

Table S7: Rates for coronary procedures within one year of admission with unstable angina (I20.0) gender and associated hazard ratios (n=2,131)

	Procedures /pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	672/423.5	1.59 (1.47-1.71)	1.26 (1.12-1.42)	1.25 (1.11-1.41)	1.24 (1.10-1.40)
Women	468/444.2	1.05 (0.96-1.15)	1.00	1.00	1.00
PCI/CABG					
Men	420/650.1	0.64 (0.59-0.71)	2.52 (2.09-3.04)	2.50 (2.07-3.03)	2.50 (2.06-3.02)
Women	151/729.8	0.21 (0.18-0.24)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is further adjusted for country of birth, region of residence, highest qualification, marital status and health insurance. Model 3 is further adjusted for obesity, physical functioning and psychological distress.

Table S8: Rates of coronary procedures within one year of admission with AMI by sex and associated hazard ratios, excluding those aged 85 years and over (n=3691)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1891/438.3	4.31 (4.12-4.51)	1.08 (0.99-1.16)	1.03 (0.95-1.12)	1.02 (0.94-1.1)
Women	912/258.9	3.52 (3.3-3.76)	1.00	1.00	1.00
PCI/CABG					
Men	1543/767.2	2.01 (1.91-2.11)	1.69 (1.53-1.87)	1.65 (1.49-1.82)	1.61 (1.46-1.79)
Women	517/608.8	0.85 (0.78-0.93)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Table S9: Rates of coronary procedures within one year of admission with angina by sex and associated hazard ratios, excluding those aged 85 years and over (n=4076)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1603/629.1	2.55 (2.43-2.68)	1.29 (1.19-1.4)	1.25 (1.16-1.36)	1.24 (1.14-1.34)
Women	1010/707.2	1.43 (1.34-1.52)	1.00	1.00	1.00
PCI/CABG					
Men	1066/1131.6	0.94 (0.89-1.00)	2.65 (2.35-2.99)	2.57 (2.28-2.91)	2.53 (2.23-2.86)
Women	347/1322.5	0.26 (0.24-0.29)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Table S10: Hazard ratios for coronary procedures within one year of admission with AMI (n=4,580) or angina (n=4,457) (in relation to sex, adjusted for age, sociodemographic variables and health-related variables including cardiovascular risk factors

	AMI HR (95%CI)	Angina HR (95%CI)
Angiography		
Men	1.01 (0.93-1.09)	1.24 (1.14-1.34)
Women	1.00	1.00
PCI/CABG		
Men	1.52 (1.38-1.67)	2.45 (2.17-2.76)
Women	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and socio-variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables health-related variables (obesity, physical functioning, psychological distress), and CVD risk factors (smoking, self-rated diabetes, treated for high blood pressure, treated for high cholesterol and family history of heart disease).

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Manuscript page no.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	n/a
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	8
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	n/a
		(<u>*e*</u>) Describe any sensitivity analyses	8

Continued on next page

Results			Manuscript page no.
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	11
Outcome data	15	*Cohort study*—Report numbers of outcome events or summary measures over time	Tables 2 and 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Tables 2 and 3
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12 and Supplementary Tables
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17

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Variation in cardiovascular disease care: An Australian cohort study on sex differences in receipt of coronary procedures.

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Title

Variation in cardiovascular disease care: An Australian cohort study on sex differences in receipt of coronary procedures

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ABSTRACT

Objectives: To quantify sex differences in diagnostic and revascularisation coronary procedures within one year of hospitalisation for acute myocardial infarction (AMI) or angina.

Design: Prospective cohort study. Baseline questionnaire (January 2006-April 2009) data from the Sax Institute's 45 and Up Study were linked to hospitalisation and mortality data (to 30 June 2016) in a time-to-event analysis, treating death as a censoring event.

Setting: New South Wales, Australia.

Participants: Participants aged ≥45 years with no history of IHD who were admitted to hospital with a primary diagnosis of AMI (n=4,580), or a primary diagnosis of angina or chronic IHD with secondary diagnosis of angina (n=4,457).

Outcome Measures: Coronary angiography and coronary revascularisation with percutaneous coronary intervention or coronary artery bypass graft (PCI/CABG) within one year of index admission. Cox regression models compared coronary procedure rates in men and women, adjusting sequentially for age, sociodemographic variables and health characteristics.

Results: Among AMI patients, 71.6% of men (crude rate: 3.45/person-year) and 64.7% of women (2.62/person-year) received angiography; 57.8% of men (1.73/person year) and 37.4% of women (0.77/person-year) received PCI/CABG. Adjusted hazard ratios (HRs) for men versus women were 1.00(0.92-1.08) for angiography and 1.51(1.38-1.67) for PCI/CABG. In the angina group, 71.6% of men (crude rate: 2.36/person-year) and 64.7% of women (1.32/person-year) received angiography; 57.8% of men (0.90/person-year) and 37.4% of women (0.26/person-year) received PCI/CABG. Adjusted HRs were 1.24(1.14-1.34) and 2.44(2.16-2.75) respectively.

Conclusions: Men are more likely than women to receive coronary procedures, particularly revascularisation. This difference is most evident among people with angina, where clinical guidelines are less prescriptive than for AMI.

Keywords: Cardiovascular disease, Coronary procedure, Linked data, 45 and Up Study, Health inequality

ARTICLE SUMMARY

Strengths and limitations of this study

- This study uses population-based survey data linked to routinely collected health data.
- This study has a relatively large number of participants, with virtually complete capture of procedures.
- This study has adjusted for a large range of baseline sociodemographic and health factors, however clinical factors upon presentation were not included.
- While diagnosis of AMI is highly valid within hospital data, there is relatively low concordance for angina diagnoses, with possible over- or underrepresentation of rates.
- The study cohort, while broadly representative of the general population, is likely to be healthier and have lower hospitalisation and mortality rates than their peers.

BACKGROUND

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality worldwide,[1] and a leading cause of death in Australia.[2] While incidence of CVD is higher among men,[3] in many parts of the world women experience worse outcomes.[4] Coronary interventions, including percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG), contribute to improved outcomes following an acute coronary event in both men and women.[4] Despite the significant disease burden and availability of effective interventions, CVD in women as a whole remains underdiagnosed and less aggressively treated.[5, 6] Women are underrepresented in clinical trials,[6] and there are important gaps in the evidence for recognition and treatment of adverse coronary events.

It is known that incident acute myocardial infarction (AMI) and angina pectoris present on average 7-10 years later in women compared to men.[6, 7] Women generally present to hospital older and with a greater number of risk factors than men,[6] experiencing higher mortality and re-infarction rates following a first AMI.[7] Disparities in care received by women compared to men have been documented in the United States (US), even when accounting for income, education and site of care.[8] Evidence from Europe and the US demonstrate that women with CVD are less likely to undergo diagnostic angiograms or intervention with PCI or CABG,[6, 7] procedures with documented clinical benefit.[4, 5]

There is limited information on sex differences in cardiovascular care in Australia, including diagnosis and management with coronary procedures. Age-standardised rates of procedures are lower among women compared to men,[9] however underlying CVD and other factors related to delivery of care are not taken into consideration in these figures. Hence, the extent to which these differences in rates reflect inequalities in care is uncertain. This study aimed to quantify sex differences in care delivery by comparing coronary procedure rates in men and women admitted with AMI or angina, adjusting for other sociodemographic and health-related factors.

METHODS

Data sources

Data were obtained from the Sax Institute's 45 and Up Study, a population-based cohort study involving 267,153 men and women aged 45 and over from New South Wales (NSW) Australia. 45 and Up Study participants were randomly selected from the Department of Human Services (formerly Medicare Australia) database, Australia's universal health insurance system, with oversampling of individuals living in rural areas and those over the age of 80 by a factor of 2. All individuals living in remote areas were invited to participate. Participants enrolled by completing a mailed self-administered questionnaire and provided signed consent for long-term follow-up and data-linkage with a range of health databases. Approximately 10% of the NSW population aged 45 and over were included in the sample, an overall response rate of 18%. The Study is described in detail elsewhere,[10] with questionnaires available online.[11]

Baseline data from 45 and Up Study participants were linked to hospital data from the NSW Admitted Patient Data Collection (APDC, 1 July 2000 to 30 June 2016) and death data from the NSW Registry of Births, Deaths and Marriages and the National Death Index (1 January 2006 to 30 June 2016). The latter was linked by the Australian Institute of Health and Welfare. Included in the APDC is a record of all hospitalisations in NSW, dates of admission and discharge, and reason for admission. International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) and Australian Classification of Health Interventions codes are incorporated into the APDC, with each record containing up to 51 diagnosis and 50 procedure codes. Death data included date of death (used for censoring as per time-to-event analysis), based on death from any cause.

Data were linked probabilistically by the Centre for Health Record linkage using personal information (full name, date of birth, sex, and address). It is likely that during the follow-up period a small but unknown number of participants may have moved interstate. Though hospitalisations in neighbouring states are not included, these are estimated to make up fewer than 2% of admissions in NSW residents. Follow-up for hospitalisations is considered to be ~98% complete among those who continue to live in NSW. Quality assurance data on the data linkage show false positive and negative rates of <0.5% and <0.1% respectively.

Study Population

All 45 and Up Study participants admitted to hospital with a primary diagnosis of AMI or angina (stable or unstable) following entry into the 45 and Up Study were included in the sample. Those with a primary diagnosis of chronic ischaemic heart disease (IHD) and secondary diagnosis of angina were also included, due to the possibility of angina patients being admitted for elective revascularisation under these diagnostic codes. ICD-10-AM diagnosis codes I21 (acute myocardial infarction), I20 (angina pectoris), and I25 (chronic ischaemic heart disease), were used to ascertain admission. Note that these are clinicopathological diagnoses, with angina specifically referring to chest pain from insufficient myocardial oxygenation and coronary artery disease. I21 coding for AMI includes both ST-elevation and non-ST elevation myocardial infarcts, with current ICD-10 coding unable to reliably distinguish between these.[12]

Participants with a prior history of IHD were excluded, defined as self-reported heart disease on the baseline questionnaire and/or admission to hospital for IHD (120-125), and/or a related interventional procedure (angiogram, PCI or CABG – defined below), as ascertained by diagnosis and procedure code fields of APDC in the six years prior to entering the 45 and Up Study.

Variables

The study outcomes were investigation with angiography, and coronary intervention with PCI or CABG, within 12 months of index admission to hospital.

Outcomes were ascertained using all 50 APDC procedure-code fields, coded using the Australian Classification of Health Interventions which is used in conjunction with ICD-10-AM,[13]: angiography (38215, 38218), PCI (35304-00, 35305-00, 35304-01, 35305-01, *38300-00, 38303-00* (block: 670), 35310-00, 35310-01, 35310-02, 35310-03, 35310-05, *38306-00, 38306-01, 38306-02, 38306-03, 38306-05* (block: 671)) and CABG (38497-00 to 38497-07, 38500-00 to 38500-04, 38503-

00 to 38503-04, 90201-00 to 90201-03, *38500-05, 38503-05* (blocks 672-679)). Italicised codes have been included to reflect changes in procedure coding during the follow-up period.

The main exposure of interest was sex (male or female), self-reported on the baseline questionnaire. Sociodemographic and health characteristics that may confound/mediate the relationship between sex and receipt of coronary procedures were also measured on the baseline questionnaire. These included: country of birth (Australia/New Zealand or other), region of residence (major city, inner regional, or outer regional/remote/very remote), highest qualification (no school certificate, school/trade certificate or diploma, or tertiary degree), private health insurance (no private health insurance, or health care/Department of Veterans Affairs concession card), marital status (married/de facto, or not), obesity (body mass index (BMI)≥30kg/m^2, or not, based on self-reported height and weight), physical functioning (no/minor limitations, moderate limitations, or severe limitations, based on levels of functional limitation, as adapted from the Medical Outcomes Score Physical Functioning Subscale [14]), and psychological distress (low[10-<16], moderate[16-<22], or high[22-50], as per the Kessler 10).[15]

Analysis

Cox proportional hazard regression was used to model the association between sex and receipt of coronary procedures. For each analysis, participants contributed person-years from the date of index admission for AMI or angina until either the specified outcome of interest, death from any cause, or end of follow up 30 June 2016, whichever was the earliest, to a maximum of one calendar year. Data from patients in the angina sample were also censored if they were subsequently admitted with AMI. Proportional hazards assumption was tested, with the p-value set *a priori* to p<0.01. All analyses were conducted separately for patients whose index admission was for AMI, and for those whose index admission was for angina. Patients presenting concurrently with AMI and angina were included in the AMI sample.

For each outcome, we calculated crude incidence rates separately for men and women, then ran a series of Cox regression models to estimate hazard ratios (HRs) in relation to sex. Model 1 was adjusted for age (5-year age categories from 45-54years through to ≥85years). Model 2 was adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, private health insurance and marital status). Model 3 was further adjusted for additional baseline health characteristics (obesity, physical functioning and psychological distress). Participants with missing values for covariates were included in the models, with missing coded as a separate category.

Multiple sensitivity analyses were performed. First, we used a maximum follow-up period of 30 days after index admission rather than 12 months. Second, we used an alternative indicator of baseline health – self-rated health, measured with three categories (excellent/very good, good, fair/poor) – instead of functional limitation, obesity and psychological distress (Model 3). Third, we additionally controlled for comorbidity using the Charlson index,[16] using all diagnostic codes in the 12 months prior to the index admission, with scores categorised as 0, 1 or ≥2. Fourth, we restricted analysis of the angina patients to those admitted with a primary diagnosis of unstable angina (ICD-10: I20.0). Further sensitivity analyses were performed, excluding patients who were aged 85 and older, and then controlling for additional patient factors of smoking, self-rated diabetes, treatment for high blood pressure, treatment for high cholesterol, and family history of heart disease.

Analyses were performed using Stata 14.[17]

The conduct of the 45 and Up Study was approved by the University of New South Wales Human Research Ethics Committee. Ethics approval for this study was obtained from the Australian National University Human Ethics Committee (2015/513) and the NSW Population and Health Services Research Ethics Committee (HREC/10/CIPHS/33; CI NSW Study Reference 2010/05/234).

Patient and Public Involvement

The 45 and Up Study has involved community and consumer representation from its inception, through its early-phase Community and Ethical Oversight Committee, and through engagement with its participants, who constitute 10% of the New South Wales general population in the target age range. Participants are regularly informed of study projects through newsletters and the Study website. The specific analyses in this project are part of a general initiative from the Heart Foundation of Australia on women and heart disease and have received consumer input through this organisation. Preliminary results were presented at a Heart Foundation event involving the general public, and further dissemination of results to the public are expected.

RESULTS

A total of 9,037 patients were included in the study, 4,580 admitted with AMI and 4,457 admitted with angina. There were no patients in the sample who had IHD as a primary diagnosis and angina as a secondary diagnosis. Sample characteristics are shown in Table 1. The profiles of patients within the AMI and angina groups were similar, with a few exceptions. Notably, those in the angina group were less likely to be aged 85 and over (8.56% vs 19.4%), and more likely to have private health insurance at baseline (64.6% vs 56.9%) than those in the AMI group. There was a greater percentage of men within both AMI and angina groups, 63.6% and 56.2% respectively.

Table 1: Characteristics of patients admitted to hospital with acute myocardial infarction (AMI) or angina by sex

	AMI Sample (n=4,580)				**Angina Sample** (n=4,457)			
	Men		Women		Men		Women	
	n	%	n	%	n	%	n	%
Total	2911	63.6	1669	36.4	2503	56.2	1954	43.8
Age at admission								
45-54	190	6.5	80	4.8	152	6.1	151	7.7
55-64	685	23.5	277	16.6	628	25.1	499	25.5
65-74	807	27.7	414	24.8	897	35.8	622	31.8
75-84	757	26.0	481	28.8	634	25.3	493	25.2
85+	472	16.2	417	25.0	192	7.7	189	9.7
Region of residence								
Major city	1485	51.0	807	48.4	1321	52.8	972	49.7
Inner regional	1025	35.2	629	37.7	886	35.4	717	36.7
Regional/remote	354	12.2	200	12.0	259	10.4	237	12.1
Highest qualification								
No school certificate	417	14.3	357	21.4	305	12.2	326	16.7
School/ certificate/ diploma	1923	66.1	1085	65.0	1629	65.1	1310	67.0
Tertiary degree	497	17.1	175	10.5	502	20.1	276	14.1
Country of birth								
Australia/ NZ	2142	73.6	1323	79.3	1888	75.4	1576	80.7
Other	728	25.0	327	19.6	583	23.3	353	18.1
Marital status								
Single	647	22.2	750	44.9	465	18.6	638	32.7
Married/ de facto	2244	77.1	916	54.9	2011	80.3	1313	67.2
BMI								
Not obese (BMI<30kg/m^2)	2079	71.4	1100	65.9	1713	68.4	1260	64.5
Obese (BMI≥30kg/m^2)	625	21.5	394	23.6	619	24.7	479	24.5
Physical functioning								
No or minor limitation	1412	48.5	469	28.1	1221	48.8	691	35.4
Moderate limitations	646	22.2	386	23.1	647	25.9	517	26.5
Severe limitations	393	13.5	392	23.5	301	12.0	373	19.1
Psychological distress								
Low	1958	67.3	948	56.8	1681	67.2	1131	57.9
Moderate	339	11.7	205	12.3	337	13.5	273	14.0
High	188	6.5	111	6.7	178	7.1	172	8.8
Health Insurance								
No private health insurance	1164	40.0	807	48.4	845	33.8	731	37.4
Health care/DVA	1746	60.0	862	51.7	1658	66.2	1223	62.6

% of missing cases: AMI sample (men, women): region of residence (1.6, 2.0); highest qualification (2.5, 3.1); country of birth (1.4, 1.1); marital status (0.7, 0.2); BMI (7.1, 10.5); physical limitations (15.8, 25.3); psychological distress (14.6, 24.3); health insurance (<0.1, 0.0). Angina sample (men, women): region of residence (1.5, 1.4); highest qualification (2.7, 2.2); country of birth (1.3, 1.3); marital status (1.1, 0.1); BMI (6.8, 11.0); physical limitations (13.3, 19.1); psychological distress (12.3, 19.3); health insurance (0.0, 0.0).

Coronary procedures in AMI patients

Among those admitted to hospital with AMI, 69.1% received angiography, 71.6% of men vs 64.7% of women; and 50.4% underwent PCI/CABG, 57.8% vs 37.4% respectively. The proportion of AMI patients who survived the one year follow-up period was 86.9% (88.6% men vs 84.0% women). Among these people, 75.6% received angiography (77.6% v 71.9%), and 55.4% PCI/CABG (63.2% vs 41.0%).

Crude rates per person-year of angiography were 3.45 (3.31-3.60) and 2.62 (2.47-2.78) in men and women respectively; and crude rates of PCI/CABG were 1.73 (1.64-1.81) and 0.77 (0.71-0.83) respectively (Table 2).

Cox models showed angiography rates were similar in men and women, with no difference after adjustment for sociodemographic and health variables (HR=1.00, 0.92-1.08) (Table 2). In contrast, rates for PCI/CABG were around 50% higher in men than women (adjusted HR=1.51, 1.38-1.67).

Table 2: Rates of coronary procedures within one year of admission with AMI by sex and associated hazard ratios (n=4,580)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	2085/604.1	3.45 (3.31-3.60)	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.00 (0.92-1.08)
Women	1079/411.7	2.62 (2.47-2.78)	1.00	1.00	1.00
PCI/CABG					
Men	1682/975.0	1.73 (1.64-1.81)	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.51 (1.38-1.67)
Women	624/814.3	0.77 (0.71-0.83)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Coronary procedures in angina patients

Among those admitted to hospital with angina, 61.9% received angiography, 67.3% of men vs 54.9% of women; and 33.6% underwent PCI/CABG, 44.6% vs 19.5% respectively. The proportion of angina patients who survived to the end of the one year follow-up period was 97.4% (96.9% men vs 98.0% women). Among these people, 62.4% received angiography (68.1% vs 55.1%), and 33.9% PCI/CABG (45.3% vs 19.4%).

Crude rates for angiography were 2.36 (2.25-2.47) and 1.32 (1.24-1.40) for men and women respectively; and crude rates for PCI/CABG were 0.90 (0.85-0.95) and 0.26 (0.24-0.29) respectively (Table 3).

Cox models showed angiography rates were around 25% higher among men after adjusting for all factors (HR=1.24, 1.14-1.34). Rates for PCI/CABG in men were around 150% times those of women (adjusted HR=2.44, 2.16-2.75).

Table 3: Rates of coronary procedures within one year of admission with angina by sex and associated hazard ratios (n=4,457)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1685/715.0	2.36 (2.25-2.47)	1.31 (1.21-1.41)	1.26 (1.16-1.36)	1.24 (1.14-1.34)
Women	1072/814.3	1.32 (1.24-1.40)	1.00	1.00	1.00
PCI/CABG					
Men	1117/1242.2	0.90 (0.85-0.95)	2.57 (2.28-2.88)	2.49 (2.21-2.80)	2.44 (2.16-2.75)
Women	381/1450.8	0.26 (0.24-0.29)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

There were no violations of the proportional hazards assumption for the sex variable in the models with 12 months of follow-up.

Sensitivity analyses using a 30-day follow-up period produced almost identical HRs (Supplementary Tables S1-S2). While violations of the proportional hazards assumption were found on testing in both the AMI and angina samples, there were no major violations detected in log-log plots. Hazard ratios were not materially different to those in the main analysis when adjusted for self-rated health as an alternative indicator of health (Tables S3-S4), when additionally adjusted for the Charlson index (Tables S5-S6), or when estimated on a sample restricted to patients admitted with a primary diagnosis of unstable angina (Table S7). Similarly, hazard ratios were not materially different to those in the main analysis when participants 85 and over were excluded from the sample (Tables S8 (AMI patients) and S9 (angina patients)), and when additionally adjusting for smoking, self-rated diabetes, treatment for high blood pressure, treatment for high cholesterol, and family history of heart disease (Table S10).

DISCUSSION

Our findings demonstrate clear sex differences in receipt of coronary procedures. Men were more likely to receive coronary revascularisation (PCI/CABG) for the management of AMI or angina. Differences in revascularisation rates were most pronounced among those admitted with angina, among whom men were also more likely to undergo diagnostic angiography.

This study uses Australian data, with findings generally consistent with published evidence internationally. There is evidence from the US and Sweden that men are more likely than women to receive revascularisation procedures such as PCI or CABG following hospital admission with AMI or angina.[7, 18] Our finding that rates of PCI/CABG among men were 1.5 and 2.4 times those for women for AMI and angina respectively, is consistent with the above studies. A cohort study from the United Kingdom demonstrated this relationship for CABG, with men having twice the odds of receiving CABG than women (OR=1.90,1.21-3.00), however no difference in overall revascularisation rates was found (p=0.14).[19] Evidence regarding angiography is less consistent. There is evidence from the US, including a review, that suggests sex differences exist,[20, 21] however these considered acute coronary syndrome as a whole, rather than AMI and angina separately. No significant difference was found in the United Kingdom for receipt of CVD investigations, including angiography.[19] This is consistent with our findings on angiography in AMI patients, but differ from our findings in angina patients where we found a 25% difference in rates between men and women.

Factors driving the observed sex differences in procedure rates are not known, however likely contributors include differences in clinical presentation. There are established sex differences in the pathophysiology, diagnosis and outcome of therapies related to AMI and angina.[7] For example, greater proportions of small vessel coronary disease among women, including Takotsubo cardiomyopathy and other forms of myocardial infarction with non-obstructive coronary arteries,[22] could contribute to lower rates of PCI/CABG following AMI. Previous studies have shown that women who present with AMI or stable angina are more likely to have non-obstructive coronary artery disease compared to men, i.e. <50% stenosis of coronary arteries.[23,24]

Following CABG, women experience higher complication rates and increased mortality compared to men, a finding that is more pronounced in younger age groups.[6] While this may contribute to the lower rate of procedures among women, the directionality of this relationship cannot be assumed.

The use of questionnaire data linked to large-scale routine data enabled a wide range of personal characteristics and other factors to be included in models, such as socio-economic position and physical functioning, however clinical factors relating to patient presentation and symptom severity were not available in the dataset. A US review, however, concluded that clinical factors do not fully explain the discrepancies in procedure rates between sexes.[25] Thus, while we cannot exclude the possibility of the sex differences representing appropriate clinical care, this seems an unlikely explanation for the total observed variation in procedure rates, with multiple factors likely at play.[25]

Another possible explanation for our findings is unwarranted variation due to discrimination. This includes the possibility of unconscious gender bias, with one systematic review demonstrating implicit bias towards patients by healthcare professionals.[26] Australia's universal health system, providing free access to hospital care, should present few barriers to receiving equitable care. There are clear guidelines for the use of coronary procedures among patients presenting with AMI, however the use of procedures for those presenting with angina is not as clear.[27] Sex differences found in receipt of coronary procedures, particularly in cases of angina, reinforce the suggestion that these differences reflect an inequality in care. This raises two distinct issues. First, the possible underuse of coronary procedures in women, which may indicate that the health care needs of a portion of Australians are not being adequately met, and second, the possible overuse of coronary procedures in men, which raises the question of waste within a health care system with limited resources.[27]

Strengths of this study include the use of population-based survey data linked to routinely collected data. The number of participants included was relatively large, with virtually complete capture of procedures. Questionnaire and other data permitting, there was adjustment for a large range of baseline sociodemographic and health factors (most of which are not included in administrative data).

Additionally, the diagnosis of AMI is highly valid within hospital data, with sensitivity and specificity of ≥86% and a positive predictive value of ≥93%,[28] and high concordance between diagnostic codes and physician review.[29] This is not true for angina however, where concordance is relatively low.[29] This may have led to an over- or underestimation of procedure rates for angina. As only those admitted to hospital were included in this study, it is possible that some participants with angina, who could benefit from a coronary procedure, were not captured. While the 45 and Up Study cohort is broadly representative of the general population, participants are likely to be healthier and have lower hospitalisation and mortality rates than others in this age group, consistent with the healthy cohort effect.[30] However, while this may mean that the absolute rates of coronary procedures among those with coronary heart disease in this study differ from those of the general population, internal comparisons are unlikely to be influenced by this bias, hence relative rates in relation to sex are likely to remain valid.[31,32]

CONCLUSION

Cardiovascular disease is a national health priority for Australia, with substantial morbidity and mortality. This study showed that men are more likely than women to receive coronary revascularisation procedures following admission to hospital with an AMI or angina. This relationship was particularly evident among the angina group, for whom clinical guidelines are less clear. While we cannot exclude that this discrepancy reflects appropriate care due to differences in clinical presentation, we must consider the possibility that sex differences, accounting for sociodemographic position and health-related factors, may indicate that the health care needs of a portion of the Australian population are not being adequately met. Morbidity and mortality among Australian women may be unnecessarily increased due to not receiving coronary intervention following AMI or angina. Alternatively, relative over-use in men cannot be ruled out. Either way, there is potential for health gain in elucidating and addressing this sex difference in receipt of coronary intervention, increasing awareness and delivery of best practice care.

Abbreviations

CVD: Cardiovascular Disease; AMI: Acute Myocardial Infarction; NSW: New South Wales; APDC: NSW Admitted Patients Data Collection; ICD-10-AM: International statistical Classification of Diseases and related health problems, tenth revision, Australian Modification; PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Grafting; IHD: Ischaemic Heart Disease; HR: Hazard Ratio; CI: Confidence Interval; BMI: Body Mass Index; PY: person years.

DECLARATIONS

Ethics approval

Ethics approvals for this project were obtained from the NSW Population and Health Services Research Ethics Committee, the University of NSW Human Research Ethics Committee and the Australian National University Human Research Ethics Committee. Participants in the 45 and Up Study provided signed consent for linkage of their information to a range of health-related databases.

Patient and Public Involvement

Not applicable. Patients were not involved in the development of this study.

Availability of data and material

The datasets used during the current study are available upon application to the Sax Institute (www.saxinstitute.org.au/our-work/45-up-study). To do so, one must have a scientifically sound and feasible research proposal, ethics approval for the proposal, data custodian approval for access to linked data, and be able to meet 45 and Up Study license and SURE user charges.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

AF provided input into the study design, performed statistical analysis, interpreted the data and drafted the manuscript. JW provided input into the study design, performed statistical analysis and reviewed the manuscript. EB provided input into the study design and reviewed the manuscript. WA reviewed the manuscript. RK conceived and designed the study and assisted in writing the manuscript. All authors read and approved the final manuscript.

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Supplementary Material

Variation in cardiovascular disease care: An Australian cohort study on sex differences in receipt of coronary procedures

Table S1: Rates of coronary procedures within 30 days of admission with AMI by sex and associated hazard ratios (n=4,580)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	2049/73.7	27.8 (26.6-29.0)	1.08 (1.00-1.16)	1.02 (0.95-1.10)	0.99 (0.92-1.07)
Women	1060/48.9	21.7 (20.4-23.0)	1.00	1.00	1.00
PCI/CABG					
Men	1624/108.9	14.9 (14.2-15.7)	1.60(1.46-1.76)*	1.54(1.40-1.69)*	1.49(1.36-1.65)*
Women	600/83.8	7.15 (6.60-7.75)	1.00	1.00	1.00

Notes: The proportion of AMI patients who survived the 30 day follow-up period was 93.3% (94.4% men vs 91.4% women). py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status) Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning and psychological distress). * indicates that the proportional hazard assumption is violated.

Table S2: Rates of coronary procedures within 30 days of admission with angina by sex and associated hazard ratios (n=4,457)

	Procedures /pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1624/74.3	21.9 (20.8-23.0)	1.30 (1.20-1.40)	1.25 (1.15-1.35)	1.23 (1.13-1.33)
Women	1026/79.0	13.3 (12.5-14.1)	1.00	1.00	1.00
PCI/CABG					
Men	1023/125.9	8.13 (7.64-8.64)	2.51(2.22-2.84)*	2.42(2.14-2.74)*	2.36(2.08-2.68)*
Women	347/131.3	2.64 (2.38-2.94)	1.00	1.00	1.00

Notes: The proportion of angina patients who survived the 30 day follow-up period was 99.6% (99.5% men vs 99.6% women). py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status) Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning and psychological distress). * indicates that the proportional hazard assumption is violated.

Table S3: Associated hazard ratios for coronary procedures within one year of admission with AMI by sex using self-rated health only as a health-related variable (n=4,580)

	Model 1 **HR (95% CI)**	**Model 2** **HR (95%CI)**	**Model 3** **HR (95%CI)**
Angiography			
Men	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.02 (0.94-1.10)
Women	1.00	1.00	1.00
PCI/CABG			
Men	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.55 (1.41-1.71)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and socio-variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (self-rated health only).

Table S4: Associated hazard ratios for coronary procedures within one year of admission with angina by sex using self-rated health only as a health-related variable (n=4,457)

	Model 1 **HR (95% CI)**	**Model 2** **HR (95%CI)**	**Model 3** **HR (95%CI)**
Angiography			
Men	1.31 (1.21-1.41)	1.26 (1.16-1.36)	1.25 (1.16-1.36)
Women	1.00	1.00	1.00
PCI/CABG			
Men	2.57 (2.28-2.88)	2.49 (2.21-2.80)	2.50 (2.22-2.81)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (self-rated health only).

Table S5: Associated hazard ratios for coronary procedures within one year of admission with AMI by sex using the Charlson index in addition to health-related variables used in the main analysis (n=4,580)

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.08 (1.01-1.17)	1.02 (0.95-1.10)	1.00 (0.93-1.08)
Women	1.00	1.00	1.00
PCI/CABG			
Men	1.62 (1.48-1.78)	1.56 (1.42-1.71)	1.53 (1.39-1.68)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress and the Charlson index).

Table S6: Associated hazard ratios for coronary procedures within one year of admission with angina by sex using the Charlson index in addition to health-related variables used in the main analysis (n=4,457)

	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography			
Men	1.31 (1.21-1.41)	1.26 (1.16-1.36)	1.24 (1.14-1.34)
Women	1.00	1.00	1.00
PCI/CABG			
Men	2.57 (2.28-2.88)	2.49 (2.21-2.80)	2.46 (2.18-2.77)
Women	1.00	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress and the Charlson index).

Table S7: Rates of coronary procedures within one year of admission with unstable angina only (I20.0) by sex, and associated hazard ratios (n=2,131)

	Procedures /pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	672/423.5	1.59 (1.47-1.71)	1.26 (1.12-1.42)	1.25 (1.11-1.41)	1.24 (1.10-1.40)
Women	468/444.2	1.05 (0.96-1.15)	1.00	1.00	1.00
PCI/CABG					
Men	420/650.1	0.64 (0.59-0.71)	2.52 (2.09-3.04)	2.50 (2.07-3.03)	2.50 (2.06-3.02)
Women	151/729.8	0.21 (0.18-0.24)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is further adjusted for country of birth, region of residence, highest qualification, marital status and health insurance. Model 3 is further adjusted for obesity, physical functioning and psychological distress.

Table S8: Rates of coronary procedures within one year of admission with AMI by sex and associated hazard ratios, excluding those aged 85 years and over (n=3691)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1891/438.3	4.31 (4.12-4.51)	1.08 (0.99-1.16)	1.03 (0.95-1.12)	1.02 (0.94-1.1)
Women	912/258.9	3.52 (3.3-3.76)	1.00	1.00	1.00
PCI/CABG					
Men	1543/767.2	2.01 (1.91-2.11)	1.69 (1.53-1.87)	1.65 (1.49-1.82)	1.61 (1.46-1.79)
Women	517/608.8	0.85 (0.78-0.93)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Table S9: Rates of coronary procedures within one year of admission with angina by sex and associated hazard ratios, excluding those aged 85 years and over (n=4076)

	Procedures/ pys	Crude rate per py (95%CI)	Model 1 HR (95%CI)	Model 2 HR (95%CI)	Model 3 HR (95%CI)
Angiography					
Men	1603/629.1	2.55 (2.43-2.68)	1.29 (1.19-1.4)	1.25 (1.16-1.36)	1.24 (1.14-1.34)
Women	1010/707.2	1.43 (1.34-1.52)	1.00	1.00	1.00
PCI/CABG					
Men	1066/1131.6	0.94 (0.89-1.00)	2.65 (2.35-2.99)	2.57 (2.28-2.91)	2.53 (2.23-2.86)
Women	347/1322.5	0.26 (0.24-0.29)	1.00	1.00	1.00

Notes: py: person-year. Model 1 is adjusted for age at first admission. Model 2 is adjusted for age and sociodemographic variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables and health-related variables (obesity, physical functioning, psychological distress).

Table S10: Associated hazard ratios for coronary procedures within one year of admission with AMI (n=4,580) or angina (n=4,457) by sex, adjusted for age, sociodemographic variables and health-related variables including cardiovascular risk factors

	AMI HR (95%CI)	Angina HR (95%CI)
Angiography		
Men	1.01 (0.93-1.09)	1.24 (1.14-1.34)
Women	1.00	1.00
PCI/CABG		
Men	1.52 (1.38-1.67)	2.45 (2.17-2.76)
Women	1.00	1.00

Notes: Model 1 is adjusted for age at admission (in 5-year age categories). Model 2 is adjusted for age and socio-variables (country of birth, region of residence, highest qualification, health insurance, marital status). Model 3 is adjusted for age, sociodemographic variables health-related variables (obesity, physical functioning, psychological distress), and CVD risk factors (smoking, self-rated diabetes, treated for high blood pressure, treated for high cholesterol and family history of heart disease).

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Manuscript page no.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	n/a
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	n/a
		(*c*) Explain how missing data were addressed	8
		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	8

Continued on next page

Results			Manuscript page no.
Participants	13	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	10 (Table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	-
Outcome data	15	*Cohort study*—Report numbers of outcome events or summary measures over time	11-12 (Tables 2 and 3)
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	n/a
		Cross-sectional study—Report numbers of outcome events or summary measures	n/a
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12 (Tables 2 and 3)
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12 and Supplementary Tables
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	17