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Gender Differences in Presentation, Coronary Intervention, and Outcomes of 28,985 Acute Coronary Syndrome Patients in Victoria, Australia

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A B S T R A C T

Background: Differences in demographics, presenting characteristics, and treatment of heart disease in women may contribute to adverse outcomes. The purpose of this paper was to describe gender differences in the epidemiology, treatment, and outcomes of all admissions for acute coronary syndrome (ACS) in Victoria that occurred between June 2007 and July 2009.

Methods: We undertook a retrospective cohort study of all patients admitted to Victorian hospitals with a first time diagnosis of ACS. Use of angiograms, percutaneous coronary intervention (PCI), coronary artery bypass graft (CABG), and adverse outcomes (death and/or unplanned readmission) were compared by gender and hierarchical logistic regression models were used to account for confounding variables.

Results: Of a total of 28,985 ACS patients, 10,455 (36%) were women. Compared with men, women were older (aged ≥75 years: 54% vs 31%; $p < .001$), more likely to present with multiple comorbidities (>1 comorbidity: 53% vs 46%; $p < .001$), and more likely to be diagnosed with non–ST-segment elevation ACS (86% vs 80%; $p < .001$). Women were less likely to receive coronary interventions (angiogram: adjusted odds ratio [aOR], 0.71; 95% CI, 0.66–0.75; PCI: aOR, 0.73; 95% CI, 0.66–0.80; CABG: aOR, 0.58; 95% CI, 0.53–0.64). Adverse outcomes were similar in women and men after accounting for confounding variables.

Conclusions: Our results show that women in Victoria were less likely to receive coronary interventions after an admission for ACS. Clinicians should be wary of inherent gender bias in decisions to refer patients for angiography.

Myocardial infarction and unstable angina, collectively described as acute coronary syndrome (ACS), are the major clinical forms of coronary heart disease (CHD), which is the largest single cause of death in Australia and around the world (Australian Institute of Health and Welfare, 2012; Sharma & Gulati, 2013). In 2009, CHD accounted for 15% of all female deaths in Australia, compared with 4% from breast cancer (Australian Institute of Health and Welfare, 2012). ACS occurs when an atherosclerotic plaque ruptures or erodes causing thrombosis and distal embolization resulting in a reduction in coronary blood flow (Hamm et al., 2011). The diagnosis of ACS is based on presenting symptoms such as changes detected by electrocardiogram and, depending on the site and severity of the ischemia, may involve the presence of cardiac biomarkers indicating myocardial necrosis (National Heart Foundation of Australia & Cardiac Society of Australian and New Zealand, 2006). Strategies for the treatment of ACS require the determination of presence or absence of persistent ST-segment elevation on electrocardiogram and classification into ST-segment elevation myocardial infarction (STEMI) or non–ST-segment elevation ACS (NSTEACS; National Heart Foundation of Australia & Cardiac

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Society of Australian and New Zealand, 2006). Contemporary data indicate that there are close to 100,000 hospitalizations for ACS in Australia per year, with just over one-third (35%) being women (Australian Institute of Health and Welfare, 2011, 2012). Although ACS is less common in women than in men, the relative risk of in-hospital death after an ACS admission is higher for women than for men (Australian Institute of Health and Welfare, 2011). Yet, despite these statistics, the impact of CHD on women is often overlooked (deGoma, Karlsberg, Judelson, & Budoff, 2010).

Historically, CHD has been considered a man's disease and it has been shown that this stereotypical belief can influence the diagnostic and clinical decision making process (Bonte et al., 2008; Wenger, 2012). Over the last few years, it has been recognized that underestimation of CHD risk among women may have resulted in more conservative treatment and contributed to poorer outcomes (Poon et al., 2012; Shehab et al., 2013). Consequently, the issue of gender disparities in the diagnosis, treatment, and outcomes of ACS has started to be examined more closely (Wenger, 2012) with a view to understanding how differences in the demographics, presenting characteristics, pathophysiology, and treatment of heart disease in women may have contributed to adverse outcomes (Sharma & Gulati, 2013; Worrall-Carter, Ski, Scruth, Campbell, & Page, 2011). A number of differences in terms of the presentation and treatment of ACS in women have been well-described, whereas others are the subject of ongoing research. For example, women tend to experience ACS at an older age than men and are more likely to have hypertension, diabetes, and/or hypercholesterolemia but less likely to have a history of smoking (Claassen, Sybrandy, Appelman, & Asselbergs, 2012; Worrall-Carter et al., 2011). Women also tend to have lower rates of obstructive coronary artery disease (CAD), but a greater prevalence of microvascular dysfunction that, if not detected and well-managed with appropriate pharmacotherapy, results in adverse outcomes in terms of symptoms, hospitalizations, and mortality (Gulati, Shaw, & Bairey Merz, 2012). Nevertheless, a substantial number of women with ACS present with "male-pattern" CAD, for which cardiac catheterization and reperfusion with percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) are highly effective strategies in both men and women (Anderson et al., 2013). In response to calls to better track the impact of ACS on women (Australian Institute of Health and Welfare, 2011), the aim of this study was to examine gender differences in the epidemiology, treatment, and outcomes of patients admitted to hospitals in Victoria, Australia, with a primary diagnosis of ACS.

Material and Methods

This retrospective cohort study analyzed a database maintained by the Victorian State government. The Victorian Admitted Episodes Data Set comprises demographic, clinical, and administrative details for every admitted episode of care occurring in Victorian hospitals, rehabilitation centers, extended care facilities, and day procedure centers (Department of Health, 2014). Clinical information is coded in the format of International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian modification (ICD-10-AM; Roberts, Innes, & Walker, 1998). Data for all patients admitted to hospital with a first time primary diagnosis of ACS between June 2007 and July 2009 were extracted, including any subsequent ACS admissions during the same 2-year period. ICD codes I210 through I213 were classified as STEMI; I214 as non-STEMI (NSTEMI); and I200 as unstable angina. I214 and I200 were grouped together as NSTEACS. With reference to national guidelines for the stratification of risk in NSTEACS (National Heart Foundation of Australia & Cardiac Society of Australian and New Zealand, 2006), the following comorbidities were classified as high-risk: congestive heart failure, cardiac arrhythmias, renal failure, and diabetes (uncomplicated and complicated). Consequently, high-risk NSTEACS were defined as all NSTEMI plus any unstable angina with high-risk comorbidities.

Variables were created for coronary interventions and outcomes that occurred for the patient during any admission across the 2-year period (e.g., angiogram any admission). Coronary interventions analyzed were angiogram, PCI, and CABG. Outcomes were in-hospital death (defined using the variable 'sepMode' coded as death for that patient during the 2-year study period) and unplanned second ACS admission (no intention to readmit recorded on first admission, but patient had a second ACS admission). Socioeconomic status (SES) was based on the Australian Bureau of Statistics Socio-Economic Indexes for Areas Index of Relative Socio-Economic Advantage and Disadvantage (ABS, 2011). For analysis purposes the deciles were regrouped into low SES (1–2), middle SES (3–8), or high SES (9–10).

Data were analyzed using SPSS V21 with comparisons between demographic or diagnostic subgroups (e.g., aged 15–59 vs aged $\geq$60; STEMI vs NSTEACS) calculated using χ^2 tests, odds ratios (OR), and 95% CI. Multivariate logistic regressions were performed to assess predictors for using coronary interventions and for adverse outcomes in females versus males. Dependent variables associated with the independent variable (e.g., angiogram any admission) with at least 80% significance (i.e., $p < .2$) were included in the multivariate model and these varied for different interventions and outcomes.

The research has been approved by the Human Research Ethics Committee at St Vincent's Hospital Melbourne, Australia.

Results

Data for 28,985 patients admitted to hospital for the first time with a primary diagnosis of ACS during the specified period were included, of whom 10,455 (36%) were female, 178 (1%) were Indigenous Australians, and 7,855 (27%) preferred to speak a language other than English. In total, there were 3,8126 ACS admissions during the 2-year period; close to one in four patients (23%) were admitted to hospital with ACS on more than one occasion. Approximately one-half (46%) of those second admissions were unplanned. Further analyses were conducted either at the patient level or first admission diagnosis level (i.e., $n = 28{,}985$).

Women were more likely than men to be aged 75 or older across all ACS types. Women were also more likely to present with multiple comorbidities (>1 comorbidity: STEMI, 53% vs 40% [$p < .001$]; NSTEACS, 53% vs 48% [$p < .001$]) and had greater prevalence of all commonly occurring (i.e., $\geq$7% of patients) comorbid conditions. They were less likely than men to have a history of smoking (Table 1). Women were more likely than men to be diagnosed with NSTEACS (86% vs 80%; $p < .001$); within NSTEACS, there was no gender difference in the proportion classified as high risk.

On univariate analysis, women were less likely than men to undergo invasive coronary intervention (angiogram, PCI, CABG) across all types of ACS (Table 2). Other variables significantly associated with use of coronary interventions in univariate

Table 1
Gender Differences in Demographics, Interventions, and Outcomes by Type of ACS

	Total, *n* (%)	Diagnosis on First Admission									
		All ACS		STEMI		NSTEACS		High-Risk NSTEACS		Lower-Risk NSTEACS	
		Female, *n* (%)	Male, *n* (%)	Female, *n* (%)	Male, *n* (%)	Female, *n* (%)	Male, *n* (%)	Female, *n* (%)	Male, *n* (%)	Female, *n* (%)	Male, *n* (%)
Total	28,985	10,455	18,530	1,460	3,662	8,995	14,868	6,338	10,433	2,657	4,435
Age (y)											
15–59	7,555 (26)	1,700 (16)	5,855 (32)*	314 (22)	1,602 (44)*	1,386 (15)	4,253 (29)*	768 (12)	2,687 (26)*	618 (23)	1,566 (35)*
60–74	9,962 (34)	3,103 (30)	6,859 (37)*	447 (31)	1,303 (36)**	2,656 (30)	5,556 (37)*	1,648 (26)	3,679 (35)*	1,008 (38)	1,877 (42)*
≥75	11,468 (40)	5,652 (54)	5,816 (31)*	699 (48)	757 (21)*	4,953 (55)	5,059 (34)*	3,922 (62)	4,067 (39)*	1,031 (39)	992 (22)*
Indigenous	178 (1)	82 (1)	96 (1)**	13 (1)	26 (1)	69 (1)	70 (0)**	40 (1)	44 (0)	29 (1)	26 (1)***
Socioeconomic status											
Low	4,221 (15)	1,536 (15)	2,685 (14)	224 (15)	555 (15)	1,312 (15)	2,130 (14)	926 (15)	1,482 (14)	386 (15)	648 (15)
Middle	20,625 (71)	7,412 (71)	13,213 (71)	1,041 (71)	2,621 (72)	6,371 (71)	10,592 (71)	4,460 (70)	7,385 (71)	1,911 (72)	3,207 (72)
High	4,139 (14)	1,507 (14)	2,632 (14)	195 (13)	486 (13)	1,312 (15)	2,146 (14)	952 (15)	1,566 (15)	360 (14)	580 (13)
Language other than English	7,885 (27)	2,857 (27)	5,028 (27)	341 (23)	750 (20)***	2,516 (28)	4,278 (29)	1,707 (27)	2,799 (27)	809 (30)	1,479 (33)***
Smoking (current/past)	11,941 (41)	2,823 (27)	9,118 (49)*	379 (26)	1,525 (42)*	2,444 (27)	7,593 (51)*	1,714 (27)	5,397 (52)*	730 (27)	2,196 (50)*
Comorbidities											
0	5,120 (18)	1,541 (15)	3,579 (19)*	213 (15)	850 (23)*	1,328 (15)	2,729 (18)*	604 (10)	1,420 (14)*	724 (27)	1,309 (30)***
1	9,825 (34)	3,399 (33)	6,426 (35)*	480 (33)	1,352 (37)**	2,919 (32)	5,074 (34)**	1,574 (25)	2,869 (27)*	1,345 (51)	2,205 (50)
2	6,170 (21)	2,411 (23)	3,759 (20)*	344 (24)	741 (20)**	2,067 (23)	3,018 (20)*	1,651 (26)	2,406 (23)*	416 (16)	612 (14)*
≤3	7,870 (27)	3,104 (30)	4,766 (26)*	423 (29)	719 (20)*	2,681 (30)	4,047 (27)*	2,509 (40)	3,738 (36)*	172 (6)	309 (7)
Hypertension	19,148 (66)	7,228 (69)	11,920 (64)*	944 (65)	2,060 (56)*	6,284 (70)	9,860 (66)*	4,536 (72)	7,050 (68)*	1,748 (66)	2,810 (63)***
Cardiac arrhythmias	7,678 (26)	2,915 (28)	4,763 (26)*	430 (29)	896 (24)*	2,485 (28)	3,867 (26)**	2,485 (39)	3,867 (37)**	0 (0)	0 (0)
Fluid and electrolyte disorders	6,107 (21)	2,630 (25)	3,477 (19)*	402 (28)	715 (20)*	2,228 (25)	2,762 (19)*	1,956 (31)	2,410 (23)*	272 (10)	352 (8)
Renal failure	3,982 (14)	1,574 (15)	2,408 (13)*	162 (11)	273 (7)*	1,412 (16)	2,135 (14)**	1,412 (22)	2,135 (20)**	0 (0)	0 (0)
Peripheral vascular disorders	1,936 (7)	625 (6)	1,311 (7)*	81 (6)	195 (5)	544 (6)	1,116 (8)*	439 (7)	887 (9)	105 (4)	229 (5)***
Chronic pulmonary disease	1,895 (7)	697 (7)	11,98 (6)	98 (7)	146 (4)*	599 (7)	1,052 (7)	515 (8)	913 (9)	84 (3)	139 (3)
Coronary intervention (any admission)											
Angiogram	16,566 (57)	4,771 (46)	11,795 (64)*	989 (68)	3,036 (83)*	3,782 (42)	8,759 (59)*	2,706 (43)	6,419 (62)*	1,076 (40)	2,340 (53)*
PCI	3,400 (12)	862 (8)	2,538 (14)*	266 (18)	900 (25)*	596 (7)	1,638 (11)*	402 (6)	1,164 (11)*	194 (7)	474 (11)*
CABG	2,657 (9)	628 (6)	2,029 (11)*	75 (5)	302 (8)*	553 (6)	1,727 (12)*	441 (7)	1,373 (13)*	112 (4)	354 (8)*
No intervention	11,456 (40)	5,429 (52)	6,027 (33)*	453 (31)	553 (15)*	4,976 (55)	5,474 (37)*	3,479 (55)	3,594 (34)*	1,497 (56)	1,880 (42)*
Outcomes in-hospital death	938 (3)	449 (4)	489 (3)*	155 (11)	161 (4)*	294 (3)	328 (2)*	279 (4)	316 (3)*	15 (1)	12 (0)
Unplanned readmission	3,109 (11)	1,046 (10)	2,063 (11)**	111 (8)	312 (9)	935 (10)	1,751 (12)**	713 (11)	1,303 (12)***	222 (8)	448 (10)***

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; NSTEACS, non–ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

Note. High-risk NSTEACS defined as unstable angina with comorbid arrhythmias, congestive heart failure, diabetes or renal failure plus all non-STEMI. Chi-square tests performed for female vs male within each subgroup.
*$p < .001$. **$p < .01$. ***$p < .05$.

Table 2
Use of Coronary Interventions and Prevalence of Outcomes—All ACS

	Total, *n*	Angiogram, *n* (%)	Intervention (Any Admission)		No Intervention, *n* (%)	Outcome	
			PCI, *n* (%)	CABG, *n* (%)		In-Hospital Death (Any Admission), *n* (%)	Unplanned Readmission, *n* (%)
Gender							
Female	10,455	4,771 (46)*	862 (8)*	628 (6)*	5,429 (52)*	449 (4)*	1,046 (10)**
Male	18,530	11,795 (64)*	2,538 (14)*	2,029 (11)*	6,027 (33)*	489 (3)*	2,063 (11)**
Age (y)							
15–59	7,555	5,424 (72)*	1,279 (17)*	640 (8)***	1,914 (25)*	45 (1)*	663 (9)*
60–74	9,962	6,577 (66)*	1,307 (13)*	1,306 (13)*	2,908 (29)*	181 (2)*	1,073 (11)
≥75	11,468	4,565 (40)*	814 (7)*	711 (6)*	6,634 (58)*	712 (6)*	1,373 (12)*
Indigenous	178	97 (54)	16 (9)	11 (6)	77 (43)	1 (1)***	12 (7)
Socioeconomic status							
Low	4,221	2,263 (54)*	452 (11)***	399 (9)	1,809 (43)*	158 (4)***	481 (11)
Middle	20,625	11,696 (57)***	2,372 (12)	1,865 (9)	8,237 (40)***	653 (3)	2,218 (11)
High	4,139	2,607 (63)*	576 (14)*	393 (9)	1,410 (34)*	127 (3)	410 (10)
Language other than English	7,885	5,273 (67)*	983 (12)***	872 (11)*	2,280 (29)*	207 (3)*	907 (12)**
Smoking (current/past)	11,941	7,260 (61)*	1,338 (11)***	1,361 (11)*	4,203 (35)*	254 (2)*	1,631 (14)*
Comorbidities							
0	5,120	3,192 (62)*	835 (16)*	159 (3)*	1,851 (36)*	76 (1)*	217 (4)*
1	9,825	6,136 (62)*	1,529 (16)*	594 (6)*	3,427 (35)*	186 (2)*	795 (8)*
2	6,170	3,467 (56)	576 (9)*	752 (12)*	2,440 (40)	230 (4)***	720 (12)**
≥3	7,870	3,771 (48)*	460 (6)*	1,152 (15)*	3,738 (47)*	446 (6)*	1,377 (17)*
Diagnosis on first admission							
STEMI	5,122	4,025 (79)*	1,166 (23)*	377 (7)*	1,006 (20)*	316 (6)*	423 (8)*
High-risk NSTEACS	16,771	9,125 (54)*	1,566 (9)*	1,814 (11)*	7,073 (42)*	595 (4)*	2,016 (12)*
Lower-risk NSTEACS	7,092	3,416 (48)*	668 (9)*	466 (7)*	3,377 (48)*	27 (0)*	670 (9)*

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; NSTEACS, non–ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
Note. High-risk NSTEACS defined as unstable angina with comorbid arrhythmias, congestive heart failure, diabetes or renal failure plus all non-STEMI. Chi-squared tests performed for each subgroup vs. others (e.g., 15–39 vs. ≥40).
*$p < .001$. **$p < .01$. ***$p < .05$.

analysis were younger age and fewer comorbid conditions. In terms of ACS type, there was greater use of angiography and PCI for patients diagnosed with STEMI compared with NSTEACS. There was greater use of CABG for patients with high-risk NSTEACS than other types of ACS. Higher socioeconomic status was associated with increased use of angiography and PCI but not CABG (Table 2). Lower rates of coronary intervention in women persisted across STEMI and NSTEACS after adjusting for potential confounders (Table 3).

In terms of adverse outcomes, the overall rate of in-hospital death was 4% and varied according to ACS type (STEMI vs. high-risk NSTEACS: 6.2% vs, 3.5% [$p < .001$]; high-risk vs lower risk NSTEACS: 3.5% vs 0.4% [$p < .001$]). In-hospital death was higher amongst patients who did not receive coronary intervention than those who did (5.7% vs. 1.6%; $p < .001$). Interestingly, unplanned second admission was higher for those initially diagnosed with high-risk NSTEACS than for those diagnosed with STEMI (12.0% vs. 8.3%; $p < .001$), with this pattern being consistent for both genders. After adjusting for potential confounding factors, the odds of death for those with STEMI was similar in men and women whereas for those with NSTEACS women had lower adjusted odds of death and unplanned readmission than men (Table 3).

Discussion

The main findings from this study included that women (who comprised just greater than one-third of all ACS patients) were more likely than men to have an initial diagnosis of NSTEACS. In line with well-documented epidemiology, we also found that women were older than men, more likely to have multiple comorbidities, and had a greater prevalence of most comorbid conditions, but were less likely to have smoked. The study further found that, for all ACS types, women were around one-half as likely to be treated with an invasive strategy. This disparity in the use of coronary interventions, although being somewhat attenuated by differences in female and male patient characteristics, remained significant after adjusting for potential confounders. However, the higher rate of in-hospital death among women than men was explained fully when data were analyzed to adjust for confounding factors such as ACS type, age, and number of comorbidities. In the multivariate model, female patients with NSTEACS were less likely to suffer adverse outcomes than their male counterparts, despite being less likely to receive a coronary intervention.

These findings were consistent with those of many other recent international studies where the investigators similarly found that women comprised around a third of the ACS population (Andre et al., 2014; Chew et al., 2013), were more likely to be diagnosed with NSTEACS (Chew et al., 2013; Shehab et al., 2013; Yu et al., 2011), and had more comorbidity than men at presentation (Poon et al., 2012; Yu et al., 2011). The proportion of NSTEACS classified as high risk was similar to another Australian study that used the National Health Data Dictionary classification of high risk (Chew et al., 2007). The identification of patients with high-risk NSTEACS is important in light of evidence-based guidelines that indicate the need for an evaluation of the coronary anatomy using angiography for all patients classified high risk, regardless of gender (Anderson et al., 2013; Hamm et al., 2011; National Heart Foundation of Australia & Cardiac Society of Australian and New Zealand, 2006). On the other hand, strategies employed in the treatment of lower-risk NSTEACS can be either early invasive or conservative, where the latter involves medical therapy and patients are referred for angiography only if

Table 3
Gender Differences for Coronary Interventions and Outcomes by ACS Type

	Female *n* (%)	Male *n* (%)	*p*	Unadjusted		Adjusted	
				OR	95% CI	OR	95% CI
All ACS	10,455	18,530					
Angiogram any admission	4,771 (46)	11,795 (64)	.000	**0.48**	**0.46–0.50**	**0.71**	**0.66–0.75**
PCI any admission	862 (8)	2,538 (14)	.000	**0.57**	**0.52–0.61**	**0.73**	**0.66–0.80**
CABG any admission	628 (6)	2,029 (11)	.000	**0.52**	**0.47–0.57**	**0.58**	**0.53–0.64**
No intervention any admission	5,429 (52)	6,027 (33)	.000	**2.24**	**2.13–2.35**	**1.51**	**1.42–1.61**
In-hospital death any admission	449 (4)	489 (3)	.000	**1.66**	**1.45–1.89**	0.94	0.81–1.08
Unplanned readmission	1,046 (10)	2,063 (11)	.003	**0.89**	**0.82–0.96**	**0.90**	**0.83–0.98**
STEMI	1,460	3,662					
Angiogram any admission	989 (68)	3,036 (83)	.000	**0.43**	**0.38–0.50**	**0.73**	**0.62–0.86**
PCI any admission	266 (18)	900 (25)	.000	**0.68**	**0.59–0.80**	**0.85**	**0.72–1.00**
CABG any admission	75 (5)	302 (8)	.000	**0.60**	**0.46–0.78**	**0.59**	**0.44–0.77**
No intervention any admission	453 (31)	553 (15)	.000	**2.53**	**2.19–2.92**	**1.47**	**1.24–1.73**
In-hospital death any admission	155 (11)	161 (4)	.000	**2.58**	**2.05–3.25**	1.23	0.95–1.58
Unplanned readmission	111 (8)	312 (9)	.282	0.88	0.71–1.12	0.98	0.77–1.25
NSTEACS	8,995	14,868					
Angiogram any admission	3,782 (42)	8,759 (59)	.000	**0.51**	**0.48–0.53**	**0.68**	**0.64–0.72**
PCI any admission	596 (7)	1,638 (11)	.000	**0.57**	**0.52–0.63**	**0.68**	**0.62–0.76**
CABG any admission	553 (6)	1,727 (12)	.000	**0.50**	**0.45–0.55**	**0.58**	**0.52–0.64**
No intervention any admission	4,976 (55)	5,474 (37)	.000	**2.13**	**2.02–2.24**	**1.57**	**1.48–1.67**
In-hospital death any admission	294 (3)	328 (2)	.000	**1.50**	**1.28–1.76**	**0.83**	**0.70–0.99**
Unplanned readmission	935 (10)	1,751 (12)	.001	**0.87**	**0.80–0.95**	**0.90**	**0.82–0.98**

Abbreviations: ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; NSTEACS, non–ST-segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.
Note. Bold text represents a statistically significant relationship.
ALL ACS: Variables with $p < .2$ were included in the model: Angiogram, PCI and No intervention: sex, age, socioeconomic status, preferred language, smoking history, number of comorbidities, ACS type; CABG: sex, age, indigenous status, smoking history, number of comorbidities, ACS type; Died: sex, age, preferred language, smoking history, number of comorbidities, ACS type; Unplanned readmission: sex, age, preferred language, smoking history, number of comorbidities, ACS type.
STEMI: Variables with $p < .2$ were included in the model: Angiogram and No intervention: sex, age, socioeconomic status, smoking history, number of comorbidities; PCI and CABG: sex, age, socioeconomic status, preferred language, smoking history, number of comorbidities; Died and unplanned readmission: sex, age, smoking history, number of comorbidities.
NSTEACS: Variables with $p < .2$ were included in the model: Angiogram, No intervention, Died and unplanned readmission: sex, age, indigenous, socioeconomic status, preferred language, smoking history, number of comorbidities; PCI: sex, age, indigenous, socioeconomic status, preferred language, number of comorbidities; CABG: sex, age, preferred language, smoking history, number of comorbidities.

their symptoms fail to abate with medical therapy or if they are reassessed as high risk. The underestimation of risk in women is thought to be one of the major factors leading to the underuse of guideline medications and coronary interventions amongst this population group (Poon et al., 2012). Our recent systematic review and meta-analysis concluded that women had a 23% greater odds of being classified as high risk than men when stratified using guideline endorsed risk scoring methods (e.g., GRACE, TIMI, PURSUIT risk scores; Worrall-Carter et al., in press). We acknowledge that results of that meta-analysis are contrary to the present findings, which found no gender difference in the proportion of NSTEACS patients who were high risk. We suggest that the inconsistency is owing to differences in the method of risk stratification. Specifically, risk scoring tools typically include age as a variable which increases risk, whereas the paradigm for risk stratification in the national guidelines does not include age as a high-risk feature (National Heart Foundation of Australia & Cardiac Society of Australian and New Zealand, 2006).

Our finding of lower rates of coronary angiography in women is consistent with the findings of several other recent studies (Bugiardini, Estrada, Nikus, Hall, & Manfrini, 2010; Dey et al., 2009; Poon et al., 2012; Shehab et al., 2013). Importantly, we were able to show that lower rates of coronary intervention could not be explained by confounding factors such as ACS type or age. The current study also found that women were less likely to receive revascularization with PCI or CABG. The decision to revascularize is driven by angiographically assessed coronary anatomy and, as foreshadowed, it is well-known that women presenting with symptoms of ACS are less likely to have obstructive CAD, which is suitable for PCI or CABG; therefore, lower rates of revascularization in women are not surprising (Gulati et al., 2012). However, while appreciating the risk of microvascular CAD in women, it is also important to remember that a substantial proportion of women with ACS symptoms do have male-pattern obstructive CAD (Gulati et al., 2012), so it can be argued that the frequent decision not to refer women for angiography means that their underlying coronary anatomy is not assessed and that opportunities to revascularize eligible women may be missed (Banks, 2008). Recent systematic reviews have confirmed the benefit of an early invasive therapy in women with ACS, while noting the under-representation of women in many trials and the problem of limited reporting of results by gender (Dolor et al., 2012; Lundberg & King, 2012).

In-hospital mortality after ACS has been shown to vary across different countries and to depend on patients' baseline characteristics and clinical management (Andre et al., 2014). However, the rate of in-hospital mortality in Victorian hospitals from our study was similar to that reported in other ACS registries (Assiri, 2011; Chew et al., 2013; Mohanan et al., 2013). In univariate analysis, in-hospital mortality in our study was associated with female gender, advanced aged ($\geq$75 years), low SES, more comorbidity, and having STEMI or high-risk NSTEACS. When these confounding factors were accounted for, women were no longer more likely to have adverse outcomes than men. In this regard, our results differ to several studies where female gender remained an independent predictor of in-hospital death (Kuhn, Page, Rahman, & Worrall-Carter, 2015; Poon et al., 2012), although there have also been studies that have found no

gender difference in mortality after ACS (Assiri, 2011; Yu et al., 2011).

Reasons for older age at the onset of ACS in women compared with men are thought to relate to the protective features of female sex hormones, which act as potent modulators of cardiac risk (Worrall-Carter et al., 2011). Thus, ACS is relatively rare in women of reproductive age, but increases after menopause (Choi et al., 2014). Advanced age and postmenopausal status are also associated with a higher rate of comorbidity and greater risk factor load. Women are susceptible to traditional, non-traditional, and gender-specific risk factors for heart disease, including high cholesterol, obesity, lack of physical activity, diabetes, depression, psychosocial risks associated with gender role, the metabolic syndrome, menopause, ovulation dysfunction, polycystic ovarian syndrome, issues that arise during pregnancy, and therapies used to treat breast cancer (Gulati et al., 2012; Worrall-Carter et al., 2011). Although women tend to be older than men at presentation, the risk of CHD in younger women should not be underestimated (deGoma et al., 2010). A recent study found that young women had a greater traditional and non-traditional risk factor burden than men (Choi et al., 2014). An analysis of trends in the annual incidence of ACS in Western Australia found that incidence had increased by 2.3% in 35- to 54-year-old women between 1996 and 2007, whereas it declined in all other groups (Nedkoff et al., 2011). Mortality rates also tend to be higher among young women with ACS, which means that women's health physicians need to remain vigilant regarding risks in this group (Claassen et al., 2012).

This study has a number of strengths. The population-based data that inform the study findings came from all Victorian hospitals, including public and private and, therefore, represent the whole state of Victoria in Australia. The large sample size facilitated extensive subgroup analyses and adjustment for confounding variables. The limitations of this study are similar to the restrictions encountered in any research using a secondary database. The data were retrospective, and as such were collected at the study hospitals as part of routine procedure and it was not possible to collect further information. Therefore, we were unable to generate risk scores for each case, which may have resulted in different risk stratification profiles for men and women with NSTEACS. Variables regarding the use of noninvasive imaging techniques were not available nor were we able to include patients' angiographically assessed disease severity (which guides decisions around revascularization) in our analyses. The quality of diagnostic coding in the Victorian Admitted Episodes Data Set is maintained through routine, external audit every 3 years. We tried to limit inclusions to patients experiencing a first ACS; however, there is the possibility that misclassification could occur if a patient experienced a first event in another state or country. Restricting the time period to 2 years eliminated any unplanned readmission beyond the study period from our analyses. The classification of comorbidity was based on a coded diagnosis in the hospital record and there may be a potential for under-reporting. However, risk of missed classification applies equally to men and women and is unlikely to introduce bias into the results of the present study.

Implications for Practice and/or Policy

Clinicians should be aware that female gender could bias decisions regarding referral for diagnostic angiography and that this may contribute to subsequent adverse outcomes in women. The literature suggests that possible reasons of reluctance to catheterize women are older age, more comorbidities, and increased risk of procedural complications (Dolor et al., 2012; Wenger, 2012). Although a number of noninvasive testing techniques exist that may be more appropriate in the detection of microvascular CAD in stable cases (Mieres, Shaw, & Wenger, 2014), catheterization remains the gold standard for acute cases involving STEMI or high-risk NSTEACS (Hamm et al., 2011). That notwithstanding, owing to the prevalence of microvascular CAD in women, disease management approaches that fail to look beyond the detection of critical stenosis may fail to identify those women critically at risk (Leuzzi & Modena, 2010). Therefore, an angiogram that shows clear coronary arteries should not lead to an assumption that the patient is disease free, but rather that she should be referred for further testing and appropriate medical therapy (Sharma & Gulati, 2013).

Conclusion

Our results show that women in Victoria were less likely than men to receive coronary interventions after an admission for ACS. Clinicians should be wary of inherent gender bias in decisions to refer patients for angiography.

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