Curtin Medical School

Equitable assessment of Acute Coronary Syndromes across Western Australia – 2007 to 2015

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

The research presented and reported in this thesis was conducted in accordance with the National Statement on Ethical Conduct in Human Research 2007 from the National Health and Medical Research Council's (NHMRC). The proposed research study received human research ethics approval from the Curtin University Human Research Ethics Committee (EC00262), Approval Number # HR 66/2013; the Department of Health WA Human Research Ethics Committee (EC00422), Approval # 2013/20; and the Sir Charles Gairdner and Osborne Park Health Care Group Human Research Ethics Committee (EC00271), Approval # 2013-067.

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Abstract

Acute Coronary Syndrome (ACS) represents a global morbidity and mortality burden with optimal outcomes often dependent on the total infarct time – that is the time from symptom onset to reperfusion of the culprit vessel or vessels. Treatment options involve pharmacotherapy to dissolve thrombus within the coronary vessels causing the blockage; or percutaneous coronary intervention (PCI) where a balloon and/or stent are introduced into the stenosed coronary vessels, or a coronary artery bypass graft (CABG) to bypass the stenosed vessel altogether. While recommendations for treatment are clear, previous literature reports variation in the rates of revascularisation citing comorbidities as a barrier to some treatment pathways in addition to the type of coronary disease, direct presentation to a PCI-capable hospital and country, region, age and ethnicity also playing key roles. In Western Australia (WA), the challenge for rural patients is receiving treatment, particularly PCI, in a timely manner despite the vast distances required to travel to advanced medical facilities, centred in the Perth metropolitan region; while for metropolitan patients the challenge is arriving at a facility capable of 24/7 PCI in the first instance avoiding unnecessary treatment delays involved with interhospital transfers. The aim of the study was to evaluate the rate of admissions across WA for incident presentations of ACS for metropolitan and rural patients, their associated outcomes, and the treatment delay burden of inter-hospital transfers for metropolitan patients.

Two data sets were employed for analysis. Nine years of Linked Administrative Health Data from the WA Data Linkage System were used to evaluate the rates of, and treatment pathways and outcomes for, incident admissions for ACS using the hospital morbidity data system, the emergency department data collection and mortality data. A single centre cardiac registry based at one of Perth's coronary

interventional hospitals were used to investigate door-to-balloon times and inter-hospital transfer delays; over a seven-month data collection period. Patients were included in the study if they were aged 18 years or over; with a WA residential postcode who were admitted with a confirmed diagnosis of ACS.

In 2015 there were 2332 incident admissions for ACS in WA of which 64% were male and 25% were from a rural residential postcode. The overall rate of ACS presentations, and ST-segment elevation myocardial infarction (STEMI), remained stable across the study period, however the rates of non-ST-segment elevation myocardial infarction (NSTEMI) showed an increase with each year with an associated decreased in unstable angina (UA), likely due to improvements in testing the sensitivity of troponin assays resulting in fewer diagnoses of UA, in favour of an increased incidence of myocardial infarction. Further, the rates of first-time admissions for ACS were more than double in the rural residential cohort, including higher rates of STEMI. All-cause in-hospital mortality was higher in direct presentations and almost double for STEMI presentations, compared to NSTEMI (7.3% compared to 2.3%). Comorbidities represented a significant burden on all presentations, with 78% and 88% of patients presenting with three or more comorbid conditions, diagnosed in the one and five years prior to their incident admission, respectively. Metropolitan inter-hospital transfers occurred in 42% of metropolitan STEMI admissions; adding to the overall system delay, statistically significantly increasing their time to treatment and therefore infarct times, measured from first hospital arrival time to balloon inflation.

Accurate presentations rates are essential to monitor the burden of ACS across WA and globally. With advances in health care combined with an aging population, comorbid conditions presenting in ACS patients will present an ongoing challenge for recommendations around reperfusion therapy and long-term prognosis. While metropolitan transfers may be reduced with initiatives including ambulance activated

STEMIs in the past five years, inter-hospital transfers for rural patients will remain a reality in an environment such as WA due to the sparse population density and the infeasible nature of equipping rural hospital with interventional capabilities, necessitating transfer for immediate PCI or rescue PCI after pharmacotherapy. However, ongoing strategies to reduce unnecessary inter-hospital transfers for metropolitan patients remains a challenge.

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Publications included as part of the Thesis

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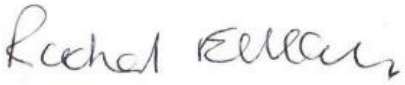
Statement of Contributions of Others

I contributed the original writing of all the chapters in this thesis. Chapters 1, 2 and 6 include re-drafting following suggestions and corrections from my supervisory team, Zhonghua Sun, Rachael Moorin and Christopher Reid. Chapters 3, 4 and 5 there were again suggestions, corrections, and collaborations with my supervisory team, Zhonghua Sun, Rachael Moorin and Christopher Reid; and specific contributions are detailed in the Section Publications presented in the Thesis (page 155 – 184). As is almost always the case in conducting research studies with assistance by collaborators, other researchers made contributions to the work that were significant enough to warrant co-authorship on the resulting journal articles.

René Forsyth

Zhonghua Sun



Rachael Moorin

Christopher Reid

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List of Abbreviations

ABS	Australian Bureau of Statistics
ACCF	American College of Cardiology Foundation
ACHI-10	Australian Classification of Health Interventions 10th Edition
ACS	Acute Coronary Syndrome
AHA	American Heart Association
AIHW	Australian Institute of Health and Welfare
CABG	Coronary Artery Bypass Graft
CAD	Coronary artery disease
CCL	Cardiac Catheterisation Laboratory
CHF	Congestive Heart Failure
COD	Cause of death
CSANZ	Cardiac Society of Australia and New Zealand
CTCA	Computed Tomography Coronary Angiography
CVD	Cardiovascular diseases
CXR	Chest X-ray
DAPT	Dual Antiplatelet Therapy
DTB	Door-to-balloon time
DTB(First)	First hospital arrival to first balloon inflation

DTB(PCI-H)	PCI-H arrival-to-first balloon inflation
DTE	Door-to-needle time
ECG	Electrocardiogram
EDDC	Emergency Department Data Collection
ESC	European Society of Cardiology
FMC	First medical contact
FMC-B	First medical contact-to-balloon time
GP	General Practitioner
GRACE	Global Registry of Acute Coronary Events
HMDS	Hospital Morbidity Data Set
ICD-10-AM	International Classification of Diseases 10th Edition Australian Modification
IHD	Ischemic heart diseases
IHT	Inter-Hospital Transfer
LOS	Length of stay
MACCE	Major Adverse Cardiovascular and Cerebrovascular Events
MACSS	Multipurpose Australian Comorbidity Scoring System
MPI	Myocardial Perfusion Imaging
MRI	Magnetic Resonance Imaging

MUGA	Multi-gated acquisition scan
NCDR	National Cardiovascular Data Registry
NHFA	National Heart Foundation Australia
NHPF	National Health Performance Framework
NSTEACS	Non-ST-segment elevation acute coronary syndrome
NSTEMI	Non-ST-segment elevation myocardial infarction
PACS	Picture Archiving and Communications System
PCI	Percutaneous coronary intervention
PCI-H	Percutaneous coronary intervention Hospital
PY	Person-years
RNA	Radionuclide Angiography
RNV	Radionuclide Ventriculography
SEIFA	Socio-Economic Indexes for Areas
STD(First)	Symptom-onset to first hospital arrival
STD(PCI-H)	Symptom-onset to PCI-H arrival
STEMI	ST-segment elevation myocardial infarction
UA	Unstable Angina
WA	Western Australia
WADLS	Western Australian Data Linkage System

Summary of Figures

Summary of Tables

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Thesis Structure

This thesis is presented in six chapters. The first chapter presents a review on literature regarding acute coronary syndromes, including the sub-diagnoses and causes; diagnosis and treatment options; and the worldwide burden of the disease. Chapter 2 summaries the data sources and their key variables and the types of analyses used. Chapters 3 to 5 are formatted as research papers, of which Chapters 3 and 4 have been published in peer review journals, as discussion in Section II. Chapter 3, “Rates and patterns of admissions for first time presentations of Acute Coronary Syndrome in Western Australia 2007 – 2015”, chronologically was published second and discusses the rates of presentations, including inter-hospital transfers, for incident admissions of Acute Coronary Syndrome. Chapter 4, titled “Inter-hospital transfers and door-to-balloon times for presentations of Acute Coronary Syndrome from a single-centre cardiac registry in Western Australia 2013”, published first, goes into further detail regarding inter-hospital transfers and the associated delay from symptom onset to treatment. Chapter 5 is “Treatment pathways, mortality and readmissions following admission for incident diagnoses of Acute Coronary Syndromes across Western Australia using Linked Administrative Health Data 2007 – 2015” and discusses outcomes following first time admissions for acute coronary syndrome, particularly focuses on those patients who experience an inter-hospital transfer and to compare metropolitan versus rural dwelling patients. Finally, a discussion, conclusion and summary of future directions is presented in Chapter 6.

Chapter 1 Literature Review

1.1 Introduction

> *"Equity is defined by WHO as the absence of avoidable differences between people, be it socially, economically, demographically or geographically – it is a primary goal of health systems around the world and is integral to the measurement of health performance as it cuts across all the domains of the National Health Performance Framework (NHPF) and is relevant to all levels of reporting analysis[1]".*

Cardiovascular diseases (CVD) represent a significant health care and mortality burden globally, annually killing more individuals than any other cause[2-3]. The Australian Institute of health and Welfare (AIHW) estimated 59 100 people in 2017 aged 25 years and older experienced an acute coronary syndrome (ACS) event, a subset of CVD, based on hospitalisation and mortality data[4]. While ACS is the focus of a great volume of research worldwide, it still contributes a significant burden on health care systems globally with varying degrees of uptake of clinical guidelines and recommendations including access to appropriate treatments in a timely fashion[5]. Primary percutaneous coronary intervention (PCI) is noted to be the gold standard treatment for the majority of patients; but cardiac catheterisation laboratories are often centralised to hospitals within large population centres. Rural and remote populations are at a particular disadvantage accessing invasive medical treatment in an emergency, due to the sheer distances required to travel in order to reach hospitals equipped with facilities and staff to invasively treat ST-segment elevation myocardial infarction (STEMI). Although this situation in not unique to Australia, it is a significant problem in our largest states for the small populations residing outside of large population centres.

This chapter will present a summary of the existing literature surrounding rates of ACS, current treatment recommendations in Australia and globally and the role of

comorbidities, which will highlight the gap and limitations in current data collection methods, namely cardiac registries, for tracking the global ACS burden.

1.2 Acute Coronary Syndromes

1.2.1 Definitions and Distinctions

Acute coronary syndromes (ACS) is the collective term used to account for clinical symptoms that are compatible with acute myocardial infarction (MI) and unstable angina (UA). Distinctions between the type of ACS can be subcategorised into ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndromes (NSTEACS)[6-7]. The latter is further subdivided into UA and non-ST-segment elevation myocardial infarction (NSTEMI). The diagnosis of, and distinction between, ACS subtypes requires clinical evaluation, electrocardiograms (ECG), biochemical testing, invasive and/or non-invasive imaging and clinical evaluation as baseline investigations, all of which are discussed later in this chapter. The most unfavourable manifestation of ACS, STEMI, is associated with higher mortality and morbidity rates compared to NSTEACS, with the prognosis correlated with the infarct size and the length of time from symptom onset to definitive medical intervention[8]. The term accounts for the manifestation of unstable atheromatous plaques or endothelial disruption, which causes permanent or transient thrombotic occlusion of coronary arteries leading to myocardial ischemia and infarction[9]. Acute myocardial infarction occurs when plaque within a coronary artery ruptures or erodes, forming a thrombus which goes on to completely occlude the vessel and therefore blood flow to the myocardium[10-11]. Approximately 50% of patients presenting with STEMI will present with multivessel disease, with one of more culprit vessels causing the ischemia[12]. Angina occurs when the plaque or thrombus causes narrowing of the vessel, without total occlusion, which may progressively worsen or remain stable for long periods[10].

1.3 Epidemiology

1.3.1 *Burden of Disease*

Acute coronary syndrome represents a significant worldwide burden. In Australia alone, there were approximately 59,100 confirmed ACS events in 2017[4] while there are an estimated 500,000 patients presenting each year with chest pain, of which only 20% investigated for ACS will have this diagnosis confirmed[9]. The National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016[9] summarised the prevalence of different diagnoses in the Australian setting as: 2-5% STEMI, 5-10% NSTEMI, 5-10% UA, 15-20% other cardiac conditions and 50-70% non-cardiac related disease.

Mortality due to CVD is attributed to 44.6% and 42.5% of all cause deaths in rural and urban Chinese populations in 2014, respectively and the rates are slowly climbing[13]. Across Europe there are an estimated 3.9 million CVD related deaths annually, 45% of all-cause mortality rates[14]. Despite absolute numbers of CVD presentations increasing across Europe, CVD mortality is starting to decrease across the continent[14].

1.3.2 *Financial Burden*

Inpatient expenditure attributable to ACS reached $886.7 million across Australia in 2012-13[15]. This figure has been trending upwards annually, peaking in 2011-12. Although a significant sum of money, the individual cost per hospital separation, irrespective of the number of total separations, must be considered. The inpatient expenditure related to STEMI, NSTEMI and UA have increased by 6.4%, 4.8% and 4.2% respectively between 2004-05 to 2012-13, according to a report prepared by the National Heart Foundation[15]. Calculations presented in the same report for the

unit costs of expenditure for combined in-patient and non-admitted components of the health care chain are an estimated average of $26,305, $19,853 and $12,718 per separation for STEMI, NSTEMI and UA respectively. While NSTEMI admitted costs are less compared to STEMI the high volume of NSTEMI presentations account for a significant financial burden on the government[15].

1.3.3 *Demographics*

Acute coronary syndromes typically affects more men than women, increasing in frequency with increasing age across many countries[16]. A study by Yilmaz et al. found STEMI patients were typically younger than NSTEMI patients; with more males than females in both diagnosis groups[17]. Angiographic findings in the STEMI and NSTEMI cohorts revealed STEMI patients were more likely to have a higher incident of single vessel disease with less extensive coronary artery disease (CAD); while NSTEMI patients were more likely to have multivessel disease[17]. A study by Viana et al. found patients presenting the NSTEACS were significantly older than those diagnosed with STEMI and high-risk NSTEACS patients were less often men, less educated and had a lower income[5]. Further cardiovascular risk factors were more prevalent among NSTEACS diagnoses, except for smoking which was more present in the STEMI cohort[5]. Although more men are diagnosed with CVD, heart disease is a leading cause of death in older women worldwide[18]. Fewer women experience typical chest pain and may not be aware of typical and atypical symptoms resulting in pre-hospital delays. A meta-analysis of 26 studies found women with AMI had both lower odds and a lower rate of chest pain than men. However, women had higher odds of presenting with fatigue, neck pain, nausea, syncope, right arm pain, dizziness, and jaw pain. It was also shown women were more likely to have palpitations, back pain, dyspnoea, vomiting, left arm pain than men, but they were less likely to present with sweating. It was also shown women were more likely to have a history of congestive heart failure. Overall summary of

the study showed that women suffering from AMI are typically older than men, more likely to have a history of congestive heart failure (CHF), significantly less likely to than men to suffer chest pain and more likely to present with fatigue, neck pain, syncope, right arm pain, dizziness and jaw pain[18].

The burden of CVD is more often felt in lower socio-economic demographics, Indigenous populations, people from diverse cultural backgrounds and those living in rural and remote areas[16]. Widening inequalities in health outcomes between the higher and lower socio-economic demographics can be partly attributed to improved public health prevention, including nutrition and smoking cessation in addition to medical management of comorbid conditions such as hypertension and dyslipidaemias and more invasive interventions for coronary revascularisation resulting in high-income countries showing more marked reductions in CVD mortality rates[16]. A 2016 research paper by Chetty et al.[19] found life expectancy to increase continuously with income with a life expectancy difference of 15 years for men and 10 years for women between top 1% and bottom 1% of income brackets. In addition to physical barriers to treatment, rural populations are often reported to have lower socio-economic profiles. Thompson et al.[16] reported rural and remote dwelling Australians have more CVD risk factors, higher rates of CVD-related hospitalisations and are also more likely they are to die from a CVD event compared to metropolitan counterparts[16]. In addition, CVD is recognised as a leading cause of Indigenous Australians' burden of disease, contributing 17% of the total burden which is reportedly 4.6 times higher in the Indigenous community compared to the non-Indigenous community[16]. Between 2000 and 2004 Indigenous West Australians comprised only 2.4% of the population aged between 25 and 75 years yet represented 7.4% of the 10 040 AMI incident cases identified using linked administrative health data[20]. An original report of the Australian Institute of Health and Welfare reported higher levels of health risk factors in those who live outside of

major cities, including smoking, hazardous levels of alcohol consumption, being overweight or obese and physical inactivity[21]. This is further compounded by lower levels of education, fewer employment opportunities, some physically risky occupations such as farming, forestry, fishing and mining and lastly travelling longer distances at high speeds with fatigue and potential animals or livestock on the roads[16,21].

1.4 Comorbid Conditions and Health Risk Factors

Comorbidities in patients presenting with ACS are not uncommon due to increased life expectancies and advancements in medical care which give rise to increased survival and therefore more people living with comorbid conditions[22]. Patients are rarely diagnosed with a single comorbid condition and many patients who experience an ACS event have several comorbidities[22]. Multiple studies have evaluated the impact on comorbidities on patient outcomes post-ACS and if the presence of comorbidities impacts the treatment decisions[22]. Zhang, et al. reported one in five patients presenting with ACS suffered from five or more comorbid conditions and demonstrated an association between the number and severity of comorbidities and ACS-related adverse events. The authors also noted a higher economic burden of healthcare for these patients caused by longer length of stay and higher hospitalisation charges. Identified risk factors for CVD are smoking, hypertension, hypercholesterolemia, poor nutrition, obesity and physical inactivity[16,23]. Rurality compounds risk factor management as members of a rural community might encounter problems accessing and following health advice relevant for prevention and/or management of disease[16,24]. Alston, et al. reported one-third of CVD deaths in rural residents were due to health risk factors and if rural Australians had the same level of health risk factors to their metropolitan counterparts, the rural-metropolitan mortality gap could be reduced by 38.2%[16,25]. The extent to which comorbidities are associated with ACS outcomes have been

limited to a few studies, predominately in single centre analyses with small sample sizes or limited to specific cohorts or geographical regions[22,26-28].

1.5 Non-Invasive Diagnostic Tests for ACS

The utility of any diagnostic test needs to be weighed against its sensitivity (probability of a positive test result in a person with the disease) and specificity (probability of a negative test result in a person without the disease) in addition to ease of access, cost and what is known to be the gold standard in a given disease[29]. As ACS is a time critical diagnosis, the sensitivity and negative predictive value for the Suspected ACS Assessment Protocol (Suspected ACS-AP) to exclude ACS is crucial in order to minimise delays in the decision to admit, treat or discharge avoiding in hospital delays[9]. In ACS, diagnostic tools are required that discriminate between ischemic changes, non-ischemic symptoms and non-cardiac related symptoms[29]. Patients with ACS can present with a variety of typical (chest, shoulder, arm, jaw or upper abdominal pain; shortness of breath; nausea; vomiting and diaphoresis) and atypical symptoms (fatigue)[9].

International Guidelines, including the National Heart Foundation (NHF) of Australia & Cardiac Society of Australia and New Zealand (CSANZ) Australian Clinical Guidelines for the Management of Acute Coronary Syndromes[9], American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) Guidelines for the Management of ST-Elevation Myocardial Infarction[30], American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) Focused Update Incorporated Into the ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina / Non-ST-Elevation Myocardial Infarction[6], and the European Society of Cardiology (ESC) Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation[7] aim to assist clinical decision pathways for patients with symptoms

suggestive of a coronary nature to ensure rapid diagnosis and risk stratification for patients suspected of ACS.

1.5.1 *Electrocardiogram (ECG)*

An ECG is non-invasive, widely available and inexpensive tool for the assessment of symptoms suggestive of ACS, including chest pain[31]. The ECG measures electrical activity of the heartbeat, recording the electrical impulse of each beat to show electrical behaviour of the heart, including alterations in the ECG waveform[32]. Changes to the ST-segments, T-wave and development of the Q-waves reflected in the ECG traces help differentiate between STEMI and NSTEACS[33]. Australian, American and European Guidelines call for a 12-Lead ECG to be performed within 10 minutes of first medical contact for patients presenting with acute chest pain, or other symptoms mentioned above, suspicious for ACS[7,9,30]. Repeated ECGs should be acquired at regular intervals and compared in sequence, until symptom resolution[7,9,30].

ECG changes are a key diagnostic tool for risk stratification of patients, identifying the most time critical type of heart attack - STEMI verses the less time critical but equally dangerous NSTEMI[34]. It is estimated that between four and 22% of patients with NSTEACS have a normal ECG which could be due to small infarct size, the location of the infarction or the early phase of the myocardial infarction[31]. As such, patients presenting with symptoms suggestive of ACS with normal ECG traces are at risk of being under-diagnosed and should have further investigations with cardiac troponin testing and serial ECGs[31]. In some parts of Australia and across many emergency services systems worldwide, ECG is now performed by a trained paramedic en route to medical centres, allowing faster triage of STEMI cases to expediate treatment, including direct presentation to the most appropriate hospital facility, bypassing the need for a subsequent inter-hospital transfer[9,34-35]. Presenting

to PCI-capable hospitals in the first instance significantly reduces infarction times[36-38].

According to the 2012 ACCF/AHA Focused Update Incorporated into the ACCF/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non–ST-Elevation Myocardial Infarction, UA and NSTEMI are defined on ECG as ST-segment depression or prominent T-wave inversion and/or positive biomarkers of necrosis, such as troponins, in the absence of ST-segment elevation with associated appropriate clinical indications, such as chest discomfort or anginal equivalent. With improvements with the sensitivity of troponin assays, the incidence of UA is decreasing with a proportional increase in the incidence of NSTEMI[6,9]. The definition of STEMI is the presence of both ST-segment changes on ECG, consistent with infarction and a positive cardiac troponin test[8].

1.5.2 *Cardiac Biomarkers*

Cardiac biomarker testing, also known as cardiac troponins, is a sensitive and specific blood test for myocardial injury and necrosis[9,30]. Troponin I and T subtypes are considered cardiac specific and become elevated from one to three hours after myocardial infarction[9]. In the last decade there have been improvements gained in the sensitivity of troponin assays, which has resulted in less patients receiving a final diagnosis of UA, in favour of an increased incidence of MI[9-10].

1.5.3 *Killip Classification*

The Killip Classification is a system to assess the severity of left ventricular failure during an episode of ACS. First published in 1967[39], it is one of the most widely used tools to predict the risk of mortality, taking into account physical examination and the development of left ventricular failure[33].

1.6 Diagnostic Imaging

Diagnostic imaging can be utilised to evaluate significant underlying CAD in the event of symptom resolution, non-ischemic ECG findings and normal serial troponin tests[9]. However, imaging tests are neither 100% sensitive or specific for diagnosing ACS and must be used in conjunction with clinical history and other available diagnostic data[29]. Results of imaging tests are unlikely to add significant clinical data for patients already considered to be at a high probability of experiencing ACS due to typical symptoms, known CAD, elevated cardiac troponins or ECG changes[29]; while imaging performed on patients with a low probability of ACS due to the absence of the aforementioned features may lead to more false-positive results, increasing unnecessary follow up tests[29]. Both scenarios lead to potentially unnecessary ionising radiation exposure and resource utilisation. Diagnostic imaging can be used to assess ventricular function or coronary anatomy and will be most effective for assessment of those patients who present with symptoms suggesting an intermediate probability for ACS[29].

1.6.1 *Chest X-ray (CXR)*

Chest X-ray (CXR) is a fast, non-invasive and low radiation exposure imaging test, to assess cardiac enlargement or rule out non-coronary causes to explain chest pain where the diagnosis is not yet confirmed[9,33].

It is crucial that the acquisition of a CXR does not delay reperfusion and as such they are often performed portably in the antero-posterior (AP) erect, semi-erect or supine projection in the emergency department or coronary care unit[33]. The AP projection is considered sub-optimal for the assessment of heart size due to increased magnification of the heart in this position. Optimal CXRs are performed in the radiology department with the patient standing in the postero-anterior (PA)

position. Despite the limitations of CXR, they should be performed to avoid missing significant changes to the heart, lungs and mediastinum parenchyma[33].

1.6.2 *Echocardiography (Echo)*

An echocardiogram is a non-invasive, fast and portable tool that produces real-time images of the heart using high frequency sound waves, or ultrasound[32]. It can identify wall-motion abnormalities in patients with non-diagnostic ECG changes and persistent chest pain[29] and can assist in the visualization of the hearts chambers, valves, walls and blood vessels[32]. The procedure can be used to evaluate cardiac pain and presence of myocardial infarction including site and extent of the infarction, haemodynamic assessment, diagnosis of possible acute complications, detection of silent changes to the ventricle and provide an overall prognostic assessment[33].

1.6.3 *Myocardial Perfusion Imaging (MPI)*

Myocardial perfusion imaging (MPI) is a radionuclide imaging technique for assessing suspected or confirmed ACS. It is a non-invasive test which highlights how well blood flows, or perfuses, through the myocardium[32-33]. This test is considered functional in nature, rather than simply anatomical image, as the radiotracer is only absorbed by functioning myocytes, assessing myocardial viability. The test is useful for patient experiencing chest pain as it can determine if the symptoms are likely arising from active ischemia – a lack of blood flow to the heart muscle due to narrowed or blocked coronary arteries[29,32].

1.6.4 *Radionuclide Ventriculography/Angiography (RNV/RNA)*

Radionuclide ventriculography (RNV) or radionuclide angiography (RNA), sometimes referred to a as a multi-gated acquisition (MUGA) scan, is a radionuclide imaging technique that measures how much blood they heart ejects from the left

ventricle with each heartbeat, known as the ejection fraction. Is it referred to a multi-gated as multiple images are acquired at specific times during each heartbeat[32].

1.6.5 *Computed Tomography Coronary Angiography (CTCA)*

Computed Tomography Coronary Angiography (CTCA) is a non-invasive test using multi-detector CT to acquire images of the heart, usually during a single heartbeat. It produces images of the coronary anatomy with excellent spatial resolution[29]. While CTCA can be used in an emergency setting for the assessment of chest pain and coronary physiology[33], its utility should not delay treatment in cases of suspected and confirmed STEMI. The non-invasive nature of CTCA has resulted in the emergence of this imaging technique in the CAD setting[40] specifically to exclude the presence of stenosis of the coronary vessels[41-42]. This modality has been shown to have a superior sensitivity and specificity compared to nuclear stress testing and stress echocardiography for occlusions of 50% or more. However, CTCA can pose a challenge compared to invasive coronary angiography due to the small size of coronary vessels and often rapid heartbeat cycles[43]. Further, CTCA is not without risks associated with exposure to ionizing radiation and its use should be carefully considered in conjunction with the risks and benefits of performing the test, in line with clinical indications and possible alternative imaging modalities, particularly in young women where exposure to the breast tissues is a significant factor[44]. While CTCA also has the added benefit of the ability to acquire a pre-contrast calcium score of the coronary arteries for the assessment of calcified and non-calcified plaques, this modality cannot adequately assess physiology as a standalone test and further increases the overall radiation dose burden[43].

1.6.6 *Cardiac Magnetic Resonance Imaging (MRI)*

Cardiac Magnetic Resonance Imaging (MRI) has emerged as a versatile technique in cardiovascular imaging due to the possibility of a wide range of imaging

sequences and imaging planes and the absence of harmful effects, including ionising radiation and potential iodine-based contrast agent reactions[33,45]. This technique is another example of functional imaging due to the continuous nature of cardiac and great vessel motion. The contrast agent gadolinium can be used to further enhance imaging and allows tissue characterization of the myocardium[45-46]. Advancements in cardiac MR angiography has led to significant improved accuracy with the main strength and its ability to provide additional physiological and functional assessment of CAD, although still limited by its inability to assess plaque due to inferior spatial resolution[43].

1.7 Reperfusion for Acute Coronary Syndrome

Patient's may present with full or partial occlusions of one or more coronary vessels. There are two primary treatment pathways in ACS – pharmacotherapy and invasive therapy. The most appropriate treatment method, or combination, for ACS varies depending on the type of ACS manifestation, patient comorbidities, available services at the presenting medical facility and time elapsed from symptom onset. The aim of any reperfusion strategy is to minimize the extent of the myocardial infarction and reduce mortality by restoring coronary flow and myocardial perfusion[9]. The differences between invasive therapy and pharmacotherapy are discussed in Sections 1.8 and 1.9.

1.8 Invasive Coronary Intervention

Invasive coronary angiography plays a pivotal role both in diagnosis and reperfusion in ACS. Percutaneous coronary intervention (PCI) involves cardiac catheterization, via a femoral or radial artery approach, introducing a flexible catheter, guidewire, balloon and/or stent into coronary vessels under the guidance of intravenous contrast and image intensification[47-49]. Coronary Artery Bypass Grafting (CABG) involves taking a donor vessel from elsewhere in the body and using it to bypass the

occluded vessel by inserting it above and below the narrowing[47-48]. The purpose of PCI and CABG are to relieve the underlying myocardial ischemia by restoration of blood flow[50]. In the case of multivessel disease, the treatment options vary from culprit artery only PCI; multivessel PCI of the culprit and non-culprit but diseased arteries; and PCI of the culprit artery followed by scheduled PCI of non-culprit arteries[12]. Primary PCI may involve balloon inflation of the obstructed area to re-establish blood flood with or without stent insertion. There are two types of stents widely available – bare metal stents and drug-eluding stents[51].

There are further surgical options for treatment including transmyocardial revascularisation and implantable medical devices[33,52], but these therapies are beyond the scope of this research.

1.9 Pharmacotherapy

Pharmacotherapy utilises medications with aim of short-term symptom relief. Such therapy should not be considered an alternative to early invasive management for patients where revascularisation is clinically appropriate, as they have not been shown to reduce the incidence of recurrent MI or death[9]. There are three primary pharmacotherapies – Acute Anti-Ischaemic Therapies, Antiplatelet Therapy and Anticoagulant Therapy.

Acute anti-ischaemic therapies employ nitrates, beta blockers and opioid analgesia. Nitrates control symptoms of ischaemia by ensuring vasodilation and lowering blood pressure. Beta Blockers decrease myocardial oxygen demands through the inhibition of catecholamine effects. Opioids such as morphine or fentanyl, can be considered in patients with ongoing chest pain despite administration of other anti-ischaemic therapies. However opioid agents can delay the absorption of other oral ACS therapies, including Antiplatelet therapies[9].

Oral and parenteral antiplatelet therapies have established efficacy in the treatment of ACS but the optimal timing, combination of agents and the interactions when used with anticoagulants are continues to evolve. Aspirin acts as an inhibitor of platelet formation to prevent thrombus forming and/or sticking together. Ticagrelor or prasugrel medications are considered P2Y12 inhibitors as they prevent platelet activation and aggregation by antagonising the platelets P2Y12 receptor and their use has been effective in reducing recurrent ischaemic events across the spectrum of ACS presentations[9]. Dual Antiplatelet Therapy (DAPT) often combines aspirin and P2Y12 inhibitors and will be used as part of the long-term care plan after stent insertions or CABG[9,52].

Anticoagulant therapy involves medications such as heparin and enoxaparin which reduce the risk of venous thrombosis formation and is recommended for patients experiencing ACS at intermediation to high risk of ischaemic events[9].

1.10 Risk Assessment

There are two widely used and validated tools for induvial risk assessment, the Thrombolysis in Myocardial Infarction (TIMI) score[53] and the Global Registry of Acute Coronary Events (GRACE) calculator [54].

The TIMI score is a prognostication score to evaluate the risk of death and further ischemic events for individual patients diagnosed with NSTEACS[53]. The score encompasses age, risk factors for coronary artery disease (CAD) (hypertension, hypercholesterolemia, diabetes, family history of CAD or current smoker), known CAD with stenosis greater than 50%, aspirin use in the previous seven days, severe angina, ST-segment changes on ECG and positive cardiac biomarkers.

The GRACE calculator uses age, pulse rate, systolic blood pressure, kidney function, presence of cardiac arrest on admission, ST-segment elevation on ECG,

abnormal cardiac enzymes and Killip classification to predict in-hospital 6-months, 1-year and 3-year mortality risk following an AMI[54].

1.11 Choice of Treatment Strategy

In STEMI presentations, the immediate priority is to commence an emergency reperfusion strategy to improve both short- and long-term outcomes including cardiac function[9]. The National Heart Foundation of Australia & Cardiac Society of Australia and New Zealand: Australian Clinical Guidelines for the Management of Acute Coronary Syndromes 2016 and International guidelines recommend primary PCI as the preferred reperfusion strategy for STEMI and NSTEACS presentations with intermediate to high-risk factors when the procedure can be performed within 90 minutes of first medical contact[7,9,30,55-56]. If this timeframe is not possible, fibrinolytic therapy is preferred, unless contraindicated[9]. More specifically, the reperfusion strategy choice needs to take into account time from symptom onset to FMC, the extent of ischaemic myocardium, any haemodynamic compromise in the presenting patient, their bleeding risk from fibrinolytic therapy and expected delays in commencing PCI, including inter-hospital transfer times to PCI capable hospitals[9].

Primary PCI has been shown to be superior to fibrinolytic therapy in mortality reductions, recurrent MI and stroke[9,57]. A recent study by Yilmaz et al. found PCI to be a common procedure for STEMI at 86.7%, compared to 4.4% patients receiving thrombolysis[17]. Coordinated management strategies have the potential to increase the proportion of patients treated within the recommendation, be it primary PCI, thrombolysis, or rescue PCI[8]. Not surprisingly rates of invasive treatment received by metropolitan and rural patients and low- versus high-risk groups vary. In Australia, Aboriginal and Torres Strait Islander people experience coronary events at a rate three times more than that of non-Indigenous Australians and are twice as likely to die during their hospital admission for CHD and fewer receive invasive

treatment[34]. Patients who present to a hospital equipped with a cardiac catheterisation laboratory (CCL) have been shown to be more likely to undergo invasive angiography, compared to those who do not[58]. A CCL is a specialized surgical theatre equipped with specialized angiographic imaging equipment, used for guidance during catherization and/or balloon insertion. A 2006 Government Report found Aboriginal Australians who present with ACS symptoms experienced a 40% lower rate of both angiography and coronary angioplasty and a 20% lower rate of CABG[59]. Further, Indigenous Australians experienced a higher overall case fatality rate across all age groups[59]. However, results have shown early versus late administration of thrombolytic treatment lead to reduction in mortality[60].

Some studies report underutilisation of invasive coronary angiography, however this could be in part due to patient suitability, or lack thereof, for the procedure given PCI is not without risks[55,61-64]. Underutilisation of evidence-based therapies is a complex problem in ACS care. For example, patients presenting with ACS and diabetes often experience a higher comorbidity burden and more diffuse coronary disease, combined with a typically older age at presentation[62]. A patient is rarely diagnosed with a single comorbid condition and the effects of any comorbidities need to be evaluated, including both cardiovascular and non-cardiovascular conditions[65]. An American 2020 study using data from the National Inpatient Sample found 740 patients with STEMI reported lower rates of coronary reperfusion (primary PCI or thrombolysis) for those patients with a higher chronic comorbidity score[22]. A New Zealand study noted revascularisation rates were higher in non-Maori non-Pacific New Zealanders; with maintenance on statin medications in the 12 months after ACS events higher in European patients compared to Maori. Variation in the rates of revascularisation can be due to a number of factors, namely the comorbidities influencing the revascularisation decision pathway, type of coronary disease, rates

of initial presentation to hospital during the acute event and adverse social determinants[66].

1.12 Major Adverse Cardiovascular and Cerebrovascular Events

Major adverse cardiovascular and cerebrovascular events (MACCE) are routinely reported in literature for procedural, short and long-term outcomes in cardiovascular research[67]. While there is no one standard definition of MACCE several studies report typical 30-day and 1-year all-cause mortality rates, recurrent MI and nonfatal stroke as clinical end points in ACS[68-71]. Death from all causes and non-fatal myocardial infarction have been described as common primary indicators of MACCE[67-68,72-73], while target vessel revascularization, stent thrombosis and bleeding have been described as secondary MACCE[74]. Morbidity and early and late mortality following an ACS event is a burden to the Australian and New Zealand health systems[58]. Outcomes following an acute cardiac event are largely determined by total ischemic times and other complications, such as cardiac arrest[75]. During the ACS Snapshot Study[58] the overall mortality during the 18 months after presentation for ACS was 10.5%; with STEMI and NSTEMI contributing the highest mortality rates at 16.2% and 16.3% respectively. The lower rates of mortality observed in the UA cohort (6.8%) reflects the lower risk status of the condition[58]. In-hospital management contributes only one aspect of a patients short and long term recovery and optimal outcomes rely on long term follow up to avoid readmissions for ACS or MACCE or premature death[76]. Prevention of future events requires the coordination of cardiologists/primary care physicians, nurses, pharmacists, pathology services and cardiac rehabilitation[77]. The continuum of care post-discharge following ACS including rehabilitation, remains a significant barrier to optimal care, particularly for rural demographics and low socio-economic communities[76].

As more people survive their initial heart attack, there is a shift in focus to prevent further events and the associated disability in order to reduce the health burden associated with CHD in Australia[34]. The NHF/ACSANZ Clinical Guidelines call for attendance to a cardiac rehabilitation service or participation in a structured secondary prevention service for all patients hospitalised with ACS[9]. Preventing recurrence needs to start at the first admission for an acute coronary syndrome. Estimates show that one third of patients admitted for CHD are readmitted within 24 months and readmissions account for up to a third of the total costs of atherothrombotic disease[34]. Some readmissions could be prevented and therefore show improved long-term outcomes for patients and reduce the burden of these readmissions on the health care system. A study by Mrdovic, et al. found older patients more frequently suffered from MACCE while there was also a higher incidence among diabetes patients, those with prior cardiovascular disease, including MI and stroke, prior revascularisations and multi-vessel coronary disease[68]. As such, those at a suspected higher risk of MACCE need to be identified during the original admission and appropriate outpatient care arranged to prevent further admissions for MACCE.

1.13 International Guidelines for Time to Therapy

Rapid identification of STEMI is essential to facilitate early reperfusion strategies via primary PCI, thrombolytic therapy, or rescue PCI, with earlier reperfusion considerably improving prognosis and mortality rates[5,8,78-80]. A previous study showed a correlation to an increased absolute risk of in-hospital mortality of 1% for every 30-minute delay to PCI[81]. As the benefit of coronary reperfusion with thrombolysis or angiography declines with treatment delays the major aim of STEMI care is to maximally shorten the delay from symptom onset to definitive care because we know there is a correlation between a longer delay to reperfusion and the subsequent increase in infarct size[8,50,82]. Additionally, NSTEACS diagnoses

require risk stratification to determine the most suitable course of treatment to minimise any infarct present and ensure best long-term outcomes[5,10,78]. Ongoing ischemia due to occluded coronary arteries compromises cardiac function and output while sudden cardiac death following myocardial infarction is attributable to ventricular fibrillation which can occur at any time[16]. During arrhythmia the heart rhythm becomes rapid and erratic and fails to pump blood around the body, resulting in rapid loss of consciousness and death[16].

As previously discussed, current Australian, American, and European guidelines recommend reperfusion therapy for all patients with confirmed STEMI presenting within 12 hours of symptom onset, with PCI the preferred therapy choice for patients able to undergo such a procedure within 90 minutes of first medical contact (FMC)[9,30,80]. If this timeframe is not achievable the recommendations advise fibrinolytic therapy[9,30,80]. If patients are in a non-PCI equipped hospital, immediate or early transfer to a PCI-capable hospital is recommended for angiography and PCI if indicated. Patients who received fibrinolytic therapy and demonstrate less than 50% ST-segment recovery between 60-90 minutes or show haemodynamic instability should also undergo immediate transfer to a PCI-capable hospital for angiography and rescue-PCI[9].

The guidelines for the optimal treatment in NSTEACS are less clear with patients presenting on a spectrum from low risk who would benefit from conservative treatment, up to high-risk patients who are at heighten risks of further cardiovascular events and mortality, who require a more invasive approach. The recommendations for these high and very high-risk patients with a diagnosis of NSTEACS is to be investigated with invasive coronary angiography as soon as practical with coronary revascularisation where appropriate[9,30,80,83]. The 2016 Australian Clinical Guidelines for the management of ACS recommend an invasive strategy with coronary revascularisation (PCI or CABG) where appropriate for high- and very-high risk

NSTEACS presentations[9]. Patients with no recurrent symptoms and considered to be at a low risk for ischaemic events should be managed with a selective invasive guided strategy pending further tests[9]. Current European guidelines call for invasive management in under two hours for very high-risk patients; within 24 hours for high-risk patients and within 72 hours for those considered to be at an intermediate risk[5,64]. The 2014 AHA ACC guidelines call for an early invasive strategy (less than 24 hours since admission) for initially stable, but high-risk NSTEACS patients without serious comorbidities or contraindications[56]. For those patients deemed to be at a less high-risk level, a delayed invasive approach (24 to 72 hours) is considered reasonable[56].

While clear guidelines exist, adhering to the optimal pathway in a rural and remote setting may not be an option[16]. In these situations, the aim of evidence-based pathways is to assist physicians to differentiate between low- and high-risk patients who could be discharged for outpatient follow up, or require immediate or early transfer[34].

1.14 Service Provisions for Treatment

In Australia, more than half the population live in major cities and approximately 86.1% of the total land area is occupied by just 2.9% of the population[84-85]. In 2017 the estimated resident population of Western Australia was 2.58 million, with 92% living in the South West Land Division and 79% living in the greater Perth region, leaving a significant proportion of the state sparsely populated[86]. A key principle of the Australian public health system is equitable access to health services[87]. However, rural, or remote populations and the Indigenous community often experience inequalities in health outcomes, compared to metropolitan counterparts, due to spatial inaccessibility (physical distance, travels times and transport costs) and cultural barriers[16,75,87-89]. Further compounding the issue, a rural-urban divide is

recognised in Australia and internationally, reporting populations living outside of large population centres have reported poorer health status including higher rates of health risk factors[25,89-93]. Current WA cardiac service provisions are predominantly centred in the capital city region with three tertiary hospitals, several secondary and private hospitals with round-the-clock catheterisation laboratories and one regional centre in the South West offering coronary intervention for planned admissions[10]. Multiple clinical trials have redefined optimal care for ACS over the decades and evidence from such studies has guided the development of standardised clinical practice guidelines and recommendations. Despite the acknowledgement and dissemination of these guidelines, the adoption of all recommendations has varied worldwide due to barriers to services which hinder the widespread benefits of interventions and consequently long term outcomes[94]. While optimal health and the degree to which health interventions are required is dependent upon biological, environmental (physical and social) and behavioural interactions, so too is the ease of access to health services for early interventions[93]. In urban areas, suspected ACS patients may be triaged en-route to a hospital facility with STEMI patients diverted to a centre capable of PCI. Rural and remote presentations for suspected ACS do not have this same capability. Rural communities are often characterized by geographical isolation and small populations leading to smaller health services which lack experienced skilled staff, variances in treatment protocols and variable access to appropriate treatments such as thrombolytic therapy and varying degrees of performance indicators compound the impaired access to advance medical facilities[10,84,95]. Death rates increase as the degree of rurality/remoteness increases in Australia, with socioeconomic factors such as higher prevalence obesity and smoking and inequitable access to medical services thought to play a role[96]. Although treatment is available for ACS, positive patient outcomes are dependent on rapid response to symptoms, appropriate diagnostic measures and efficient medical interventions including administration of thrombolysis and PCI within a short

time-frame[23]. Consequently, rural, and remote WA ACS patients are considered to be at a disadvantage since their access to appropriate medical facilities in the Perth metropolitan area within a small this timeframe is often limited by sheer distance[93,96-97]. In addition, post-operative recovery and rehabilitation can take time and patients may be required to stay in the Perth metropolitan region, adding to the financial, psychological, and emotional burden. The Global Registry of Acute Coronary Events (GRACE) found PCI rates were markedly higher when patients presented to teaching hospitals or those with PCI-facilities. This is a reflection of the need for the specialist skills and availably of advanced equipment[98].

1.15 Inter-Hospital Transfer versus Direct Presentation to PCI-Hospitals

The influence of the delays associated with inter hospital transfers on STEMI outcomes have been the focus of attention worldwide, with multiple national initiatives monitoring inter-hospital transfer related delays and how to reduce the time to treatment pathway[7-9,30,99-101]. Even in efficient STEMI-activation networks, previous studies have shown at least one third of patients still present to local non-PCI hospital and require transfer [101-104] highlighting the need for ongoing emergency services training for ECG interpretation in addition to data transmission to accessibility cardiac centres[101]. However, pre-hospital triage cannot account for ST-segment elevations that present after admittance to a local, secondary hospital, or self-presentation of the patient to their local hospital[101]. In the case of rural and remote suspected ACS presentations where the first hospital of presentation can only be a non-PCI hospital, a program of rapid triage and pre-hospital activation for the incoming PCI-equipped hospital has been shown to reduce in-hospital mortality and gradual improvements of door-to-balloon times in this cohort[104].

1.16 System of Delay

Worldwide ACS guidelines encourage certain targets for reperfusion strategies and time-to-treatment, there is still a gap between knowledge and current practice, some of which is explained by time-to-treatment delays[5]. Delays to treatment can be due to patient response times, unclear symptoms evolving over time and service provisions. A five-year study by Blankership et al.[104] found improvements during each step of the transfer chain improved the over system of delay. Initial hospitals decreased time from arrival to ECG by half and activated helicopter transfer much earlier. Further, the PCI-capable hospitals significantly reduced the time between hospital arrival and cardiac catheterization laboratory arrival by bypassing ED; with door to balloon times halving[104]. A Chinese study conducted over two-years found significantly shorter reperfusion delays by aiming for direct presentation to a PCI-hospital and earlier activation of the CCL[105]. Due to STEMI's unfavourable risk of mortality and morbidity, the focus has long been centred on reducing time from symptom onset to definitive reperfusions[8].

Literature has recognised three phases in delay in ACS presentations, which are summarised in Figure 1.1.

Figure 1.1: System of Delays to Treatment for Acute Coronary Syndrome

Patients and pre-hospital delays can occur for a variety of reasons and the problems are universally recognized worldwide[97]. Patients and the people in their immediate area are responsible for triggering the initial call for care at symptom onset. Poor symptom recognition, especially in the presence of comorbidities; lack of the significance of the symptoms being of cardiac nature in the face of other demands and obligations; concerns associated with gender roles, socio-cultural priorities;

communication disjunction with health services; and the implications or fear of the symptom response[16]. Many education and mass media campaigns have promoted the symptoms of a myocardial infarction, of “heart attack” to raise awareness of symptoms and prompt quicker help-seeking responses[16]. However, while these have improved recognition of heart attached symptoms, they have not effectively shortened pre-hospital delays[16]. A study by Viana et al. found patient characteristics explained differences in help-seeking behaviour, namely women with increasing age and a higher prevalence of chronic health conditions, leading to atypical symptoms which was associated with longer patient delays[5]. However, patients who recognized their symptoms as being of cardiac in nature were less likely to delay. Ambulance use, rather than private transport, and correct interpretation of symptoms were found to be pivotal in reducing time-to-treatment[5].

1.16.1 *Pre-hospital Delays*

An original theoretical model by Andersen detailed the process a patient undergoes during the appraisal of their symptoms and inferring illness[106]. Although these models have primarily been applied to cancer research, delays are often experienced in ACS patients for the same reasons described by Anderson. The first delay phase, known as the pre-hospital phase, is the main component of delay and similar patterns in pre-hospital delays have been observed across Australia, the United Kingdom, and the United States. Cognitive and emotional processes play a part in patients seeking help for their symptoms. A patient’s lack of recognition and awareness of the symptoms of heart attacks are often the primary source of treatment delay. Furthermore, delays are caused when patients with a history of CHD fail to seek help despite a heart attack being likely. Atypical symptoms described previously, patients attributing the symptoms to something else and inappropriate consultation with their general practitioner (GP) regarding the symptoms prior to contacting emergency services can add to the delay. Research

has shown this delay phase has not improved over time, nor do patients with known cardiovascular disease respond any quicker. Residing in rural or remote locations are also considered primary factors associated with pre-hospital delays.

There are a number of reasons which contribute to patient delays. Socio-demographics (gender, age, socio-economic status, race, marital status and health insurance); contextual (onset while at home/being alone); cognitive (match/mismatch of symptoms expected and symptoms experienced, perceived control over symptoms, knowledge of AMI and perceived threat, including susceptibility and seriousness); affective/psychological (fear of consequences and denial, fear of troubling others and embarrassment of seeking care); behavioural (waiting for symptoms to go away/trying to relax, telling someone about the symptoms, calling the emergency medical services, calling or visiting the primary care provider) and clinical factors (past medical history/coexisting morbidities and nature of symptoms)[97,107]. Rural patients may experience fear of being transported to unfamiliar and distance environments without their family and peer support network[16]. Lambert, et al. designed a study to simultaneously assess a patient's knowledge of stroke and heart attack while simultaneously assessing their risk for these incidents to determine if a relationship exists between subject knowledge and risk factors. This study was potentially policy forming – allowing for more targeted public health campaigns[23]. Participants in the study were more likely to identify myocardial infarction as a leading cause of death and were more able to recognize myocardial infarction symptoms, compared to stroke. On the other hand, participants were more likely to recognize high blood pressure as a risk factor for strokes but did not associate smoking as a risk for MI. Across the board knowledge of MI was consistently higher than knowledge of stroke. The highest increase in knowledge occurred between those who had only received a high school education, compared to those who had received a college education[23].

1.16.2 *Transport Delays*

The use of ambulances over private transport have shown to decrease delays to treatment[5]. Ambulances, equipped with ECG equipment can assess patients en-route to a medical facility and divert, where appropriate, to a PCI-capable facility. Further, ambulances are equipped with defibrillators to assist treatment of cardiac arrest, in conjunction with cardiopulmonary resuscitation[16]. Pre-hospital activation of the CCL has also shown to reduce D2B times, particularly in large metropolitan areas[38]. As more focus is placed in the prehospital setting it is imperative health care facilities implement evidenced based strategies with tested quality improvement methodologies to improve prehospital care which can directly translate to short first medical contact to balloon or needle times and improved outcomes for patients[38]. Pre-hospital triage, ECG and interpretation of symptoms, en-route to medical facilities can ensure patients present to PCI-capable hospitals from the outset, thus avoiding the associated delay with an inter-hospital transfer[5]. Several studies have noted transfer from a non-PCI-capable hospital were among the strongest predictor of delays over 90 minutes or more[5,8,108]. In a rural setting, there is an additional time burden of the travel to a medical facility and a lack of readily available transport options. Reducing delays to treatment where sheer distance acts as a barrier further impacts time to treatment delays[16]. Conversely, for rural patients transport delays can be lengthy and unavoidable, often necessitating the need to investigate alternative initial therapies for STEMI; and appropriate risk stratification for NSTEACS[5]. These initial therapies were discussed in Section 1.7. Rezaee calculated the maximum allowable transport time based on time on scene and in hospital inductors, resulting in a maximum transports time of 43-46 minutes to achieve FMC to Balloon times under 90 minutes. While the in-hospital metrics of the emergency department to Cath lab time and table to device time will differ slightly for

each medical centre, it does highlight the enormous challenges faced for rural and remote patients where the lifesaving centres are based in metropolitan areas[38].

1.16.3 *In-Hospital Delays*

In-hospital delay, also known as system delay, is the time between arrival at a hospital to the commencement of reperfusion therapy. It is also known as door-to-treatment delay, which can be further categorised into door-to-needle and door-to-balloon times [107]. While in-hospital delays are more readily modifiable by organizational measures compared to patient and transport delays[7] and are often considered the least contributing factor, can cause delays in the event of a difficult or unclear diagnosis[109]. This is particularly a challenge in rural communities where clinicians may encounter difficulties seeking specialist advice and lack experience in cardiac diagnoses[16]. In any setting, atypical symptoms in patients presenting with complex comorbidities; cultural barriers to discussing pain and symptoms; and language barriers for culturally diverse communities may limit a clinician's early ability to rapidly triage patients[16]. Further, overseas trained doctors who also do not have English as a first language can further impact cultural and language barriers[16]. Prior research has developed in-hospital systems to address and minimize in-hospital delays, including pre-hospital or ED activation of the CCL[38,82,109-110], single call CCL activation[109-110], immediate patient transfer[109] and early feedback of the results[109].

1.17 Prior Research and International Data Registries

The Western Australian Data Linkage System (WADLS) is a valuable and validated research tool to investigate population-based health outcomes in Western Australia (WA). Data linkage can be utilised for clinical needs analysis, patterns of admissions and outcomes and disease aetiology[111-112]. Data linkage is the process where records derived from different sources but derived from the same individuals records

are combined in one database[112]. A study by Clark, et al. found WA to be highly representative of the whole Australian population in terms of socio-demographic and health economic indicators, establishing WADLS as a valuable tool not only for WA, but for all of Australia[88]. Further, with populations distributed across high accessible, moderately accessible and remote regions, the effect of geography on outcomes can be determined[87]. The linked databases allow whole populations to be evaluated and followed through multiple admissions over many facilities[88]. Further, linked data has the capacity to identify patients who were prevalent at the beginning of the study period in questions, compared to those with a first-time incident admission, by way of a look back period. The WADLS draws on administrative data and has the potential to provide a large and diverse population-based review of all major health events experienced by Western Australian individuals at a relatively low cost. However, linked administrative data employed by the WADLS can be deficient in detailed clinical end points, required for holistic evaluation of health services for an individual[111]. This has both strengths and weaknesses compared to prospective clinical data or data abstraction from individual medical records. Administrative data can lack detail on specific end points and times of diagnoses and interventions, and they can be plagued with coding errors. In addition, administrative data linkage requires a significant investment of resources before research possibilities are realised. However, once established, administrative data linkage can provide diverse longitudinal population-based studies over a given time frame despite which service is accessed[112].

The ACS Snapshot Study prospectively audited the care received by consecutive patients hospitalised with suspected or confirmed ACS between the 14th and 27th of May 2012 across multiple participating sites in Australia and New Zealand[113]. A total of 286 hospitals enrolled 4398 patients and were able to collect more in-depth data point compared to linked administrative data, including Killip Class (predicted risk of

mortality based on physical examination and development of heart failure during MI) at presentation and GRACE risk score (estimates of in-hospital six-month, one- and three-year mortality risk after a heart attack)[113]. Although this type of data collection contains a wealth of in-depth data and clinical end points, it is unable to follow patients beyond their admission for further subsequent admissions and is a selective subset of cardiac services across Australia and New Zealand, rather than whole of population.

The CONCORDANCE Registry is a prospective data collection, based in Australia, reporting clinical characteristics, management, and outcomes for ACS hospitalisations. The ongoing data collection from a series of representative hospitals enables spatial and temporal trends in practice and treatment to be analysed[114-116].

A study by Dondo, et al. utilised patient-level data of demographics, cardiovascular risk factors, medical and clinical characteristics at the time of admission were extracted from hospital registries from all National Health Service hospitals in England; and showed how such patient-level registries allowed for more robust interrogation of pathways of care in ACS[117].

The Global Registry of acute coronary event (GRACE) is a multinational observational study applying regression models to predict in-hospital and post-discharge mortality in patients presenting with ACS[118].

1.18 Justification of importance / significance

It has been recognized in Australia that rural and remote populations have poorer access to medical facilities and therefore they represent an important population in health research. This study will provide an analysis of the rates of presentations of first-time admissions for ACS across WA, stratified by health regions; the impact of

delays associated with inter-hospital transfers; the comorbidity burden and outcomes following an incident admission of ACS in WA, including in-hospital mortality, invasive intervention rates and short- and long-term survival and/or readmission. Assessment of the rates of, and outcomes, for rural and transferred patients will inform the debate about resource utilisation. In WA, most service provisions for primary cardiac care and rehabilitation are centred to the greater Perth region; with one rural service in the South West for elective admissions only.

As discussed in the previous section, linked administrative data is an extremely valuable research tool that has yet to be used for a comprehensive study regarding the rates and outcomes of ACS in WA. Linked data has two main strengths for the analysis of ACS, namely the ability to overcome over-counting admissions due to inter-hospital transfers and the ability to include a look-back period within the data, to identify a patient's first admission for ACS. Cardiac registries offer in depth and critical information, not otherwise possible in large scale linked databases; but are usually single- or limited-centre studies over a short period of time. While these datasets are usual for capturing specific information, they cannot be used for long-term, ongoing evaluation of the total burden of disease.

Chapter 3 presents the rates of admission across WA over nine years, with an additional five years of data analysed preceding the study time frame, to identify first-time admissions of ACS utilised linked data from the Hospital Morbidity Data System, Emergency Department Data Collection and Mortality data. Rates are calculated using population data from the Australian Bureau of Statistics (ABS) for accurate population estimates across WA, stratified by sex, 10-year age groups and health region of residence. Chapter 5 goes on to present the same incident ACS population and the outcomes associated with the admission, including the proportion of inter-hospital transfers, in-hospital mortality, time to readmission, or death, after discharge and the impact of comorbidities. Chapter 4 presents a subset of data from

a Perth-based single centre cardiac registry. Although this study is not whole of population for ACS presentations, it does record every adult patient who presented with a confirmed diagnosis of ACS to this PCI-equipped hospital and provided in-depth time variables, not otherwise available in linked administrative health data. This allowed for the time burden of inter-hospital transfers to be assessed and inform the debate about the need to pre-hospital triage of STEMI and high-risk NSTEMI patients.

The combination of this information will significantly contribute to what we know about ACS in WA, a state considered representative of other Australian states and territories; and highlight the need for further aligned cardiac registries within the Perth metropolitan region.

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Chapter 2 Data and Key Variables

This chapter provides an overview of the data sources, study populations, data variables and analytic approaches used in Chapters 3 to 5 and an outline of how the literature was selected for the comprehensive literature review (Chapter 2).

This thesis combines two different methods of data collection. The first method employed data from a single centre in the Perth Metropolitan region who had developed their own cardiac registry to monitor their internal performance and match this against recommended guidelines. The second method used data from the Western Australian Data Linkage System (WADLS) which links whole population administrative data from multiple sources. The first method was employed for paper 2 (Chapter 4) while the linked administrative data method was used for papers 1 and 3 (Chapters 3 and 5).

The WADLS draws together administrative data and has the potential to provide a large and diverse population-based cohort capturing all major health events experienced by Western Australian individuals at a relatively low cost. This has both strengths and weaknesses compared to prospectively collected clinical data or data abstracted from individual medical records. Administrative data can lack detail on specific end points and times of diagnoses and interventions. In addition, administrative data linkage requires a significant investment of infrastructure and resources before research possibilities are realised. However, once established, administrative data linkage can provide diverse longitudinal population-based studies over a given time frame despite which service is accessed. Further, data linkage involves stringent de-identification processes prior to the release of data to researchers, minimising the risks of beaching individual privacy. As such, systematic record linkage and prospective data collection or an audit of individual medical records are complimentary research strategies[1-4]. Both clinical registries and linked administrative data can suffer from data entry coding errors; however this limitation

is lessened in Australia by having a standardised training program for clinical coders and quality assurance programs in place[5-6].

2.1 Data Source - Single Centre Cardiac Register

Unlinked data from a single Perth Metropolitan Tertiary (Teaching) Hospital's (Hospital X) Cardiac Registry are routinely captured as part of an internal auditing system for evaluation of performance indices. Data from Hospital X included all adult patients who presented to Hospital X with a confirmed diagnosis of acute coronary syndrome between 01/06/2013 to 31/12/2013. Standard demographic and clinical details were recorded, including date of birth, sex, identification as being of Indigenous or Torres Strait Islander decent, postcode of residence, admission and discharge date, method of arrival, length of stay, in-hospital mortality, and principal procedure. Key time variables (first hospital arrival, first hospital departure, Hospital X arrival, time of first ECG and balloon inflation time) were coded based on recorded medical data; while time of symptom onset was based on patient recollection. Data were de-identified prior to release to the research team.

2.2 Data Source - Western Australian Data Linkage System

2.2.1 *Brief Description*

The WADLS utilises routinely collected, longitudinal, whole-population, administrative health data and medical data [7]. Data linkage occurs through rigorous, internationally accepted privacy persevering protocols and probabilistic matching to create a system of links between disparate data sets to follow an individual's healthcare pathway. Demographic information including names, date of birth and address can change or be recorded with errors. As such probabilistic statistical methods are used to ensure high quality matches and often involve a manual review of created links[8]. Linked data ensures a comprehensive survey of the Western

Australian population since it encompasses all individuals who utilise any of the services linked in this system including births, deaths, hospital admission and emergency department visits[1-2,8]. The methods employed by WADLS ensure a high quality of large-scale linkages; whilst maintaining an individual's privacy and confidentiality.

This study utilised data from the Hospital Morbidity Data System (HMDS); The Emergency Department Data Collection (EDDC); the Picture Archiving and Communications System (PACS); and the Western Australian (WA) Mortality register. The initial cohort selection occurred via the HMDS which consisted of all adult individuals with a HMDS record indicating a confirmed acute coronary syndrome (ACS) between 01/01/2007 and 31/12/2015 and all subsequent records. The definitions used to determine an ACS diagnosis are discussed in Section 2.2.2. An additional five years of HMDS data from 01/01/2002 was also included as a look-back period to enable identification of first-time ACS events and to identify any comorbidities in the years prior to admission, which will be explained in more detail in the following section. All records pertaining to the study cohort were linked with all EDDC, PACS and WA Mortality records from 01/01/2007 to 31/12/2015 inclusive.

2.2.2 *Classification of Acute Coronary Syndromes and Comorbid Conditions*

The International Classification of Diseases, Australian Modification 10th Edition (ICD10-AM)[9] is a system used to code and identify diseases and disorders in HMDS and EDDC records. These classifications are employed in linked data research to identify the cohort of interest and any comorbid conditions associated with their hospitalisation.

HMDS records contain a primary diagnosis field, a secondary diagnosis field and up to 20 additional diagnosis fields for patients with multiple comorbid conditions or diagnoses relevant to the episode of care. The EDDC has one diagnosis field.

Patients were identified as having ACS if they were diagnosed with either myocardial infarction (with or without ST-segment elevation on ECG) or unstable angina (UA) during the episode of care, including transfers. These codes are presented in Appendix 1. In the event a patient was diagnosed with more than one ACS type during the full episode of care, a previously validated diagnosis hierarchy was employed whereby the most severe diagnosis was carried through as the final diagnosis for the episode of care[10-11]. This hierarchy defines ST-segment elevation myocardial infarction (STEMI) as the most severe form of ACS, followed by non-ST-segment elevation myocardial infarction (NSTEMI) and lastly UA as the least severe[10-12]. The HMDS includes one primary intervention and up to 10 secondary interventions which are coded using the Australian Classification of Health Interventions, 10th Edition (ACHI)[13] to determine the treatment pathways utilised during a patients episode of care.

The Multipurpose Australian Comorbidity Scoring System (MACSS)[14-15] was employed to identify comorbid conditions which were grouped into no commodities, one, two or three or more comorbidities in the one- and five-years prior to the admission for ACS. This system was selected as it was specifically developed for use with linked administrative data and has been shown to be a better model fit compared to the Charlson and Elixhauser algorithms [14-15]. A summary of the ICD10-AM codes used for the identification of the ACS cohort and comorbidities; and the ACHI variables for treatment of ACS are included in Appendix 1 and Appendix 2.

2.2.3 *Summary of Study Period and Identification of Incident Events*

This study covers a nine-year period between 01 January 2007 to 31 December 2015. However, to identify the first-time (incident) admission for ACS and to remove prevalent cases, an additional five years of HMDS data, prior to the commencement of the study, were included, that is from 01/01/2002. Incident ACS admissions were

defined as individuals with no records in the HDMS indicating a primary or secondary diagnosis for ACS in the five-year lookback time frame. Individuals who had ACS events prior to the commencement of the study period were excluded from the cohort.

2.2.4 *Summary of the Data Variables*

The HMDS, EDDC, PACS and Mortality Register all feature common variables that the WADLS can use to link each data set and provide basic patient demographics for researchers (date of birth, sex, Indigenous status and residential postcode, as summarised in Table 2.1. Within the individual data sets are unique coding structures for specific information pertaining to each data set. A summary of the data items and their meaning is provided in Table 2.1 to Table 2.5.

Table 2.1: Summary of the common data items between the Hospital Morbidity Data System (HMDS), the Emergency Department Data Collection (EDDC), the Picture Archiving and Communications System (PACS) and the Western Australian Mortality register

Variable	Description
Root	WADLS De-identified Unique Patient ID
lpnum	Episode Number allocated for the period of treatment between admission and separation, irrelevant of formal or statistical separation
Month and year of birth	MM.YYYY. Date of birth is only provided to researchers as month and year unless a case is made for the need for full date of birth as it is classified as a sensitive variable.
Sex	Male; Female; Unspecified
Indigenous Status	Aboriginal; Torres Strait Islander; Aboriginal & Torres Strait Islander; None
Postcode	Postcode of Residence

Table 2.2: Summary of the variables provided in the Emergency Department Data Collection (EDDC)

Variable	Description
Presentation Date	Date on which a non-admitted patient presents for treatment in an emergency department (DDMMYY)
Presentation Time	Time at which a non-admitted patient presents for treatment in an emergency department (mm:hh)
Establishment Type	Tertiary or other emergency department
Triage Category on Arrival	The urgency of the patient's need for medical and nursing care
Mode of Disposal	The status of the patient at the end of the non-admitted patient emergency department service episode (i.e., Admitted to ward/other admitted patient unit; ED service event completed; departed under own care; transferred to another hospital for admission; did not wait to be attended by medical officer; left at own risk; died in ED; dead on arrival, not treated in ed; referred AHGP; unknown; admitted to ED observation ward; admitted to hospital in the home; admitted from HATH; nursing home; returned to HITH; returned to RITH; returned to HATH; transferred from HITH; transferred from RITH; discharged after admission)
Destination	The place to where the patient was discharged or transferred (i.e., Did not wait; left at own risk; nursing home/hostel; transferred; mortuary; admitted; other hospital; home; unknown; other; admitted to ed observation ward)
Reason for Visit	The reason the patient presents to an emergency department (i.e., Emergency Presentation; return visit – planned; unplanned return visit; outpatient/outpatient clinic; privately referred: non-admitted patient; prearranged admission: clerical only; pre-arranged admission: nursing & clerical; pre-arranged admission: full clinical; patient in transit; dead on arrival; health direct referral; GP referral; referral from another hospital; referral from another facility; transfer from other hospital; direct admission no access to GP; not stated/unknown; HITH; RITH; HATH; other inpatient; for AHGP referral; returned from AHGP)
Mode of Arrival	The mode of transport by which a patient arrives at the emergency department (i.e., Private transport; public transport; ambulance; hospital transport; police/correctional services; helicopter rescue; Royal Flying Doctor Service; other; not stated/unknown; taxi)
Diagnosis	Primary diagnosis of the non-admitted episode of care at discharge or admission to hospital, based on ICD-10-AM coding

Table 2.3: Summary of the variables provided in the Hospital Morbidity Data System (HMDS)

Variable	Description
Admission Date	Date on which an admitted patient commences an in-patient event (DDMMYY)
Admission Status	Elective; Emergency via ED Presentation; Emergency via direct Admission
Admission Time	Time at which an admitted patient commences an in-patient event (mm:hh)
Admitted From	Establishment or facility from which patient is admitted from (e.g. emergency department; another hospital)
Hospital Region	Region of WA where the admitting hospital is located (North metropolitan; South metropolitan; East metropolitan; South West; Great Southern; Goldfields; Wheatbelt; Midwest; Pilbara or Kimberley)
Length of Stay	Total days in hospital for that in-patient event
Mode of Separation	Establishment or facility to where the patient is discharged or transferred (i.e., Discharge/transfer to an (other) acute hospital; transfer to residential aged care service; transfer to psychiatric hospital; transfer to other health care accommodation; statistical discharge - type change; left against medical advice; statistical discharge from leave; deceased; other, including discharge to usual residence/own accommodation/welfare institutions)
Discharged to	The Establishment or Facility to which the patient was discharged or transferred to when they left hospital (i.e. Admitted to ward/other admitted patient unit; ed service event completed; departed under own care; transferred to another hospital for admission; did not wait to be attended by medical officer; left at own risk; died in ED; dead on arrival, not treated in ED; referred A/H GP; unknown; admitted to ED observation ward; admitted to Hospital in the Home (HITH); admitted from HITH; nursing home; returned to HITH; returned to RITH; returned to HATH; transferred from HITH; transferred from RITH; discharged after admission)
Source of Referral Location	Where the patient was prior to the in-patient event (i.e., Home; residential aged care service; other health care accommodation; acute hospital; psychiatric hospital; prison; other)

Table 2.3 Continued: Summary of the variables provided in the Hospital Morbidity Data System (HMDS)

Source of Referral Professional	Speciality of the clinician who referred the patient to admitted in-patient event (i.e., General practitioner; specialist clinician; outpatient department clinician; emergency department clinician; hospital clinician (re-admission); community health clinician; statistical admission; other)
Source of Referral Transport	Mode of transport to the admitted episode of care (i.e., Private/public transport; ambulance - patient transport; ambulance – emergency; Royal Flying Doctor Service; helicopter (evacuation); other)
Separation Date	Date on which an admitted patient completes an inpatient event (DDMMYY)
Separation Time	Time at which an admitted patient completes an inpatient event (mm:hh)
Diagnosis	Principal Diagnosis of the episode of care, based on ICD-10-AM Codes (See Appendix 1)
Additional Diagnoses	Up to 20 additional diagnoses of care that were deemed relevant to the in-patient event, based on ICD-10-AM Codes
Operation	Principal procedure of the episode of care (See Appendix 1)
Operation Date	Date of the principal procedure of the episode of care
Additional Procedures	Up to 10 additional procedure of the episode of care
Additional Procedure Date	Date of any additional procedure of the episode of care

Table 2.4: Summary of the variables provided in the Picture Archiving and Communications System (PACS)

Variable	Description
Status	Status of the patient for the given radiology examination (e.g. inpatient; outpatient; emergency)
Funding	Funding source of the patient for the given radiology examination (e.g. Medicare; Department Veteran Affairs)
Provider	Tertiary or Secondary Public Radiology Provider *Note: These are completely public Radiology providers run by WA Health; and not subcontracted to private Radiology providers*
Exam Name	The examination undertaken
Exam Code	The associated exam code for the exam name

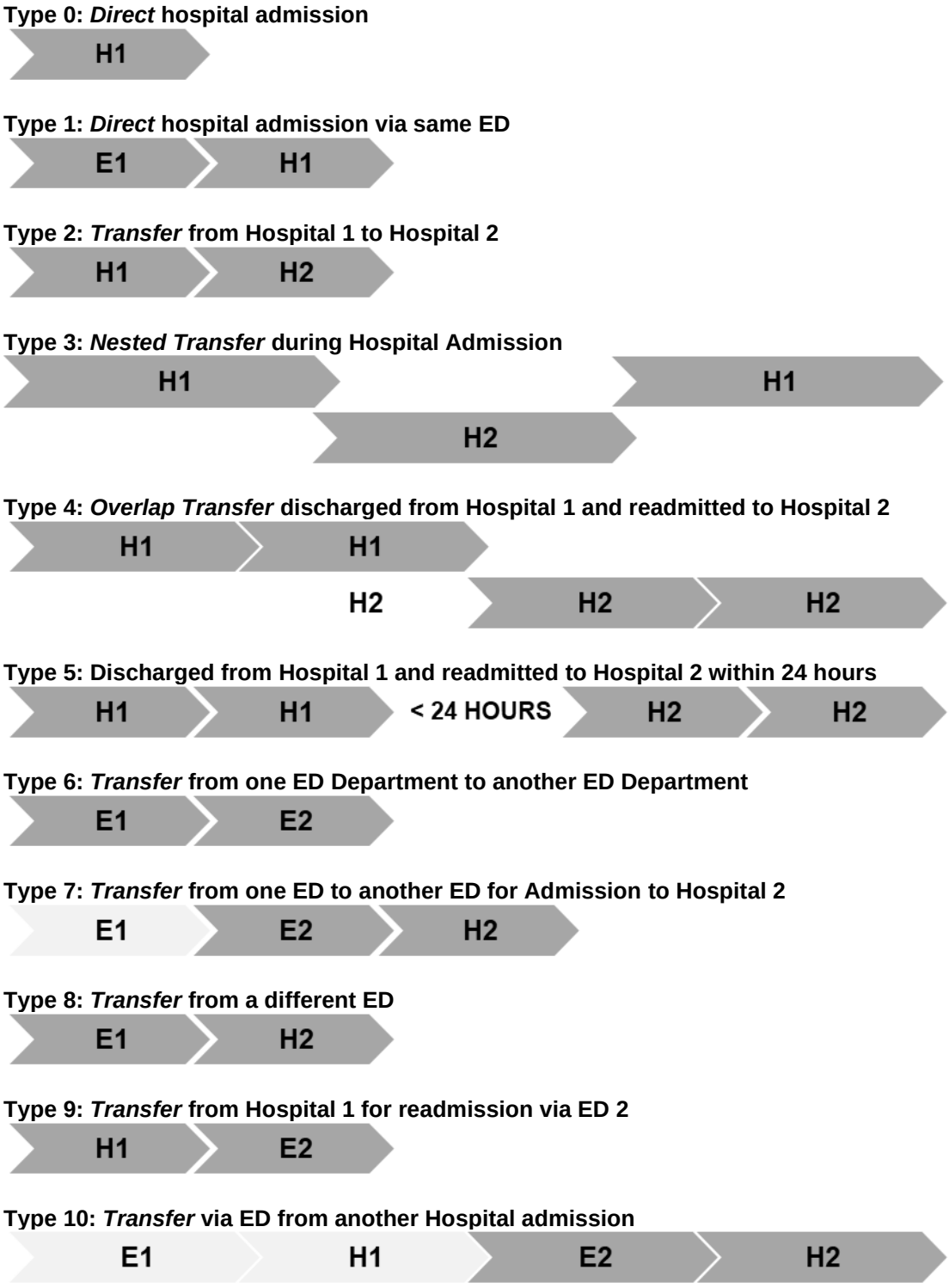
Table 2.5: Summary of the variables provided in the Western Australian Mortality Register

Variable	Description
Cause of Death	Cause of death, based on ICD-10-AM coding (See Appendix 1)
Date of Death	Recorded data of death (DDMMYY)
Death during hospital admission	Dichotomous yes/no for in-hospital mortality

2.2.5 *Methodology to account for multiple patient records during the same episode of care – inter-hospital and statistical transfers*

A significant challenge for many cardiac registries worldwide is over-counting due to inter-hospital transfers[16-17]. As discussed in Chapter 1, a proportion of patients presenting with ACS will require an inter-hospital transfer for PCI, as it is not feasible to have CCL facilities in every hospital. Linked administrative data has the ability to track inter-hospital transfers during the same episode of care and therefore it is possible to construct a complete episode of in-patient care that encompass several overlapping or contiguous hospitalisation events. As the records are linked at the patient level emergency department arrival, hospital admission and separation times are recorded for every emergency department and in-patient episode of care, patients can be tracked through standalone admissions or multiple transfers, both physical and statistical using the dates provided with these activities[18]. Patients presenting with ACS will often have more than one HMDS record. These records can represent the same contiguous episode of care; or can be standalone hospital admissions and separation. Using the time of hospital arrival and separation, in addition to certain variables such as referral source and method of separation, patient episodes can be tracked and assigned as the same episode of care versus a new standalone admission. Transfer types are summarised in Figure 2.1. In this thesis all analyses for a patient episode of care were conducted on the first record, be it the first of several records for the same episode of care; or a standalone admission.

Figure 2.1: Summary of Transfer Types based on the arrival and separation times from the Hospital Morbidity Data System and Emergency Department Data Collection



E1: First Emergency Department of presentation; E2: Secondary Emergency Department of Presentation; H1: First Hospital of presentation; H2: Secondary Hospital of presentation

2.3 Statistical Analysis

Detailed description of individual analyses are discussed in Chapters 3 to 5. All analyses were undertaken using IBM SPSS Statistics for Windows, Version 25.0[19] and Stata Statistical Software: Release 16[20]. The level of statistical significance was set at $p<0.05$ for all analyses.

Across Chapters 3 to 5 categorical data were reported as frequencies and percentages and continuous data were reported as the mean or median, with standard deviations and range. The Mann-Whitney U Test and the Pearson Chi Squared test were used for between-group analyses.

Unadjusted rates to estimate the person-time at risk, described in Chapter 3, were calculated using data from the Australian Bureau of Statistics[21] for the denominator, based on age and sex data from the 30th of June for each year. Separation numbers from the Australian Institute of Health and Welfare[18,22] were used as the denominator for the calculation of annual rate of separations for ACS presentations, compared to all-cause hospital separations. Categorical data from within the incident admission pool were used for calculation of rates within the admitted cohort as the denominator where applicable.

Evaluation of key time variables presented in Chapter 4 involved multivariable generalised linear modelling with a Gamma distribution and log link function, controlling for sex, age, socio-economic status, method of arrival to the treating hospital and presentation date/time, pre-hospital ECG, pre-hospital activation and transfer status using backwards stepwise selection.

2.4 Literature Review Search Methodology and Prisma Flow Chart

Literature was identified using a comprehensive search strategy at multiple time points throughout the project, starting in 2012 for the initial literature review in the Research proposal. There were several inclusion criteria set for literature eligibility:

1. Population: adult patients with a diagnosis of acute coronary syndrome (ACS) were considered, including unstable angina, ST-segment elevation, myocardial infarction, and non-ST-segment elevation myocardial infarction.

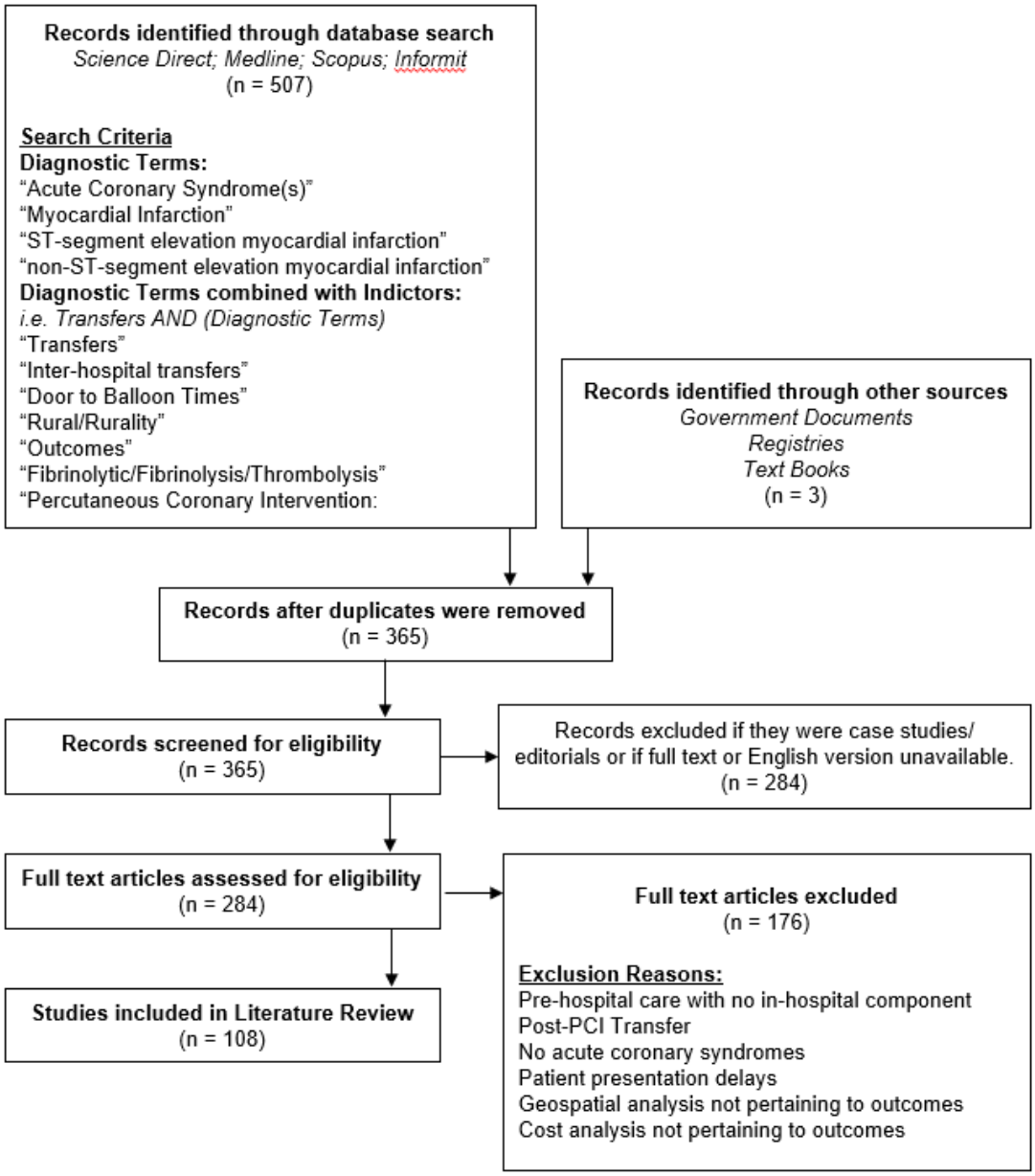
2. Intervention: studies outlining inter-hospital transfers to PCI-capable hospitals; percutaneous coronary intervention; administration of fibrinolytic therapy; and/or outcomes following a diagnosis of ACS

3. Outcome: primary outcome measures were in-hospital death, length of hospital stay, major adverse cardiovascular events and 30-day and 1-year mortality.

4. Setting: original research articles including randomised clinical trials, observational and interventional studies pertaining to inter-hospital transfers for primary percutaneous treatment for acute coronary syndromes (or acute myocardial infarction) published since 2002 (10-years prior to the start of literature search), excluding editorials or commentary where no new data is generated or syntheses performed.

An outline of the Prisma method of literature searching is outlined in Figure 2.2.

Figure 2.2: Prisma Flow Chart of Literature Review Search and Eligibility



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Chapter 3 Rates and Patterns of First-Time Admissions for Acute Coronary Syndromes across Western Australia Using Linked Administrative Health Data 2007–2015

3.1 Abstract

Acute coronary syndrome (ACS) is globally recognised as a significant health burden, for which the reduction in total ischemic times by way of the most suitable reperfusion strategy has been the focus of national and international initiatives. In a setting such as western Australia, characterised by 79% of the population dwelling in the greater capital region, transfers to hospitals capable of percutaneous coronary intervention (PCI) is often a necessary but time-consuming reality for outer-metropolitan and rural patients.

Hospital separations, emergency department admissions and death registration data between 1 January 2007 and 31 December 2015 were linked by the Western Australian Data Linkage Unit, identifying patients with a confirmed first-time diagnosis of ACS, who were either a direct admission or experienced an inter-hospital transfer.

Although the presentation rates of ACS remained stable over the nine years evaluated, the rates of first-time admissions for ACS were more than double in the rural residential cohort, including higher rates of ST-segment elevation myocardial infarction, the most time-critical manifestation of ACS. Consequently, rural patients were more likely to undergo an inter-hospital transfer. However, 42% of metropolitan admissions for a first-time ACS also experienced a transfer.

While the time burden of inter-hospital transfers for rural patients is a reality in health care systems where it is not feasible to have advanced facilities and workforce skills outside of large population centres, there is a concerning trend of inter-hospital transfers within the metropolitan region highlighting the need for further initiatives to streamline pre-hospital triage to ensure patients with symptoms indicative of ACS present to PCI-equipped hospitals.

3.2 Introduction

Cardiovascular disease (CVD) represents a significant global burden, annually killing more people than any other cause[1]. In Australia alone, it was estimated that 59,100 people aged 25 years and over experienced an acute coronary syndrome (ACS) event in 2017[2], with Australia's population for the same year estimated to be 24.6 million[3]; equating to approximately 2.4 ACS events per 1000 person–years. Worldwide data collection on ACS utilises a variety of methods. Cardiac registries such as the CONCORDANCE Registry in Australia[4]; the ACS Snapshot Study of Australia and New Zealand[5]; the All New Zealand Acute Coronary Syndrome-Quality Improvement (ANZACS-QI)[6] and the National Cardiovascular Data Registry (NCDR) of the American College of Cardiology[7] enrol representative hospitals or clinics to inform on clinical characteristics, management and outcomes for ACS hospitalisations. Similarly, government agencies gather data on the numbers of ACS hospitalisations for a given time period using admission statistics. Both methods offer advantages and disadvantages. Cardiac registries provide in depth data on clinical characteristics and outcomes that cannot be derived from hospital admission data alone. However, these are often based on the voluntary participation of hospitals or clinics in the registries and often are for a short snapshot of time rather than an ongoing, whole population cohort[5,8]. Conversely, hospital admission data can capture more accurate rates of ACS hospitalisations but can lack in depth clinical data necessary to inform policy and can be prone to double-counting, secondary to inter-hospital transfers[9].

The Western Australian Data Linkage System (WADLS)[10] provides anonymised population-based records using hospital admission data (for both public and private hospitals), public emergency department data and mortality records all linked via probabilistic matching allowing patients to be followed throughout multiple

hospitalisations for related conditions based on the International Classification of Diseases (Australian Modification) coding.

The diagnosis of the type of ACS requires interpretation of an electrocardiogram (ECG) for the critical distinction between the ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndromes (NSTEACS) which is further categorised into non-ST-segment elevation myocardial infarction (NSTEMI) or unstable angina (UA), based on patient history, examination and cardiac enzyme biomarkers[11]. Early diagnosis of STEMI as well as the appropriate assessment and risk stratification of NSTEACS, are essential to facilitate early reperfusion by primary percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), pharmacotherapy or fibrinolytic therapy for improved morbidity and mortality[11-14].

The challenge for some parts of the world such as western Australia (WA), is the remoteness of a large section of the community outside capital cities. The estimated resident population of WA was 2.58 million people in 2017 of which 92% live in the South West Land Division and more specifically 79% living in the greater capital city region, leaving the rest of the state sparsely populated[15]. In addition, current service provisions for ACS are predominantly centred in the capital city area with three tertiary hospitals, several secondary and private hospitals with round-the-clock catheterisation laboratories and one regional centre in the South West offering coronary intervention for planned admissions[16]. It is not feasible to expect advanced cardiac catheterisation laboratory (CCL) facilities in every hospital across the world, necessitating inter-hospital transfers to facilities capable of PCI, where indicated. Furthermore, in the rural setting, the lack of advanced medical facilities is further compounded by staff shortages and variable workforce experience and skills[16]. However, these centres have provisions for the administration of fibrinolytic therapy prior to emergent or elective transfer for PCI, known as facilitated or rescue PCI. In

more metropolitan settings, strategies to ensure ambulance ECG with transmission to a cardiac facility for the evaluation of STEMI is essential to ensure that ambulances can bypass secondary hospitals in favour of PCI-capable facilities wherever possible in the metropolitan region and prevent the inherent delays associated with triage and inter-hospital transfer (IHT)[17-18].

The aim of this study was to evaluate the whole-of-population rates of admission for first-time presentations of ACS in Western Australia (WA), accounting for the number of inter-hospital transfers, over a period of nine years using Linked Administrative Data from the WA Data Linkage System (WADLS)[10] and Population Census Data from the Australian Bureau of Statistics (ABS)[19].

3.3 Methods

This paper follows the Reporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) Statement[20].

3.3.1 *Data Sources*

Data from the WA Hospital Morbidity Data System (HMDS), WA Emergency Department Data Collection (EDDC) and WA Death Registrations from 1 December 2007 to 31 December 2015, with further data to establish a look-back period from the HMDS available from 01 January 2002 were linked by the WADLS. The WADLS uses routinely collected, longitudinal, whole-population, administrative health and medical data with linkages obtained through key demographic information including name, date of birth, home address and hospital medical record numbers. Privacy is ensured by linking records from different datasets using pre-established linkage keys, removing identifiable demographic data and providing only non-identifiable demographic data such as month and year of birth, sex and postcode; in addition content data describing what happened to the person during each record, such as

diagnosis and treatment codes[10]. The WADLS provides data under a waiver of consent due to the de-identified nature of the data and the research team is required to work under strict conditions to ensure the security of the data.

Routinely collected data include socio-economic data (date of birth; sex; postcode of residence; Socio-Economic Indexes for Areas (SEIFA)[21]) and clinical service utilisation data for each hospital admission, namely the admission date and time; separation (discharge) date and time; primary, secondary and co-diagnoses (up to 20 fields); primary and up to ten secondary interventions including procedural dates; hospital region; admission status (emergency presentation or elective) and insurance status (private or public).

Population data were sourced from the Australian Bureau of Statistics (ABS)[19] and reported age groups were determined so as to align with the available ABS age groups. All-cause hospital separations were sourced from the Australian Institute of Health and Welfare[22-23] to evaluate the rate of hospitals for ACS compared to all separations for the same time period.

3.3.2 *Population and Ascertainment of ACS Events*

The cohort consisted of all individuals admitted into a WA hospital having a first-time record indicating a primary diagnosis of ACS between 01 January 2007 and 31 December 2015, identified using the International Classification of Diseases, Australian Modification (ICD-10-AM) codes[24] (Appendix 1). First-time ACS admissions were defined as individuals with no records indicating a primary or secondary diagnosis of ACS prior to 01 January 2007, using HMDS and EDDC data from 01 January 2002 as a look-back period. Individuals who had ACS events prior to the commencement of the study period (i.e. 01 January 2007) were excluded from the cohort. Subsequent admissions for patients after their incident event were

included as readmission events if they were in relation to a primary or secondary diagnosis of ACS.

3.3.3 *Patient Characteristics*

Sex, identification of being of Aboriginal or Torres Strait decent and date of birth were coded directly within the data. Reported ages were then categorised based on the age of the patient at the time of their incident ACS admission to match available population data. Residential postcodes were used to determine the health region of residence and SEIFA. The primary and secondary diagnosis fields were used to identify those patients admitted for ACS with the remaining 20 co-diagnosis fields used to identify specific comorbid conditions during the same episode of care. These data were also used to ascertain total comorbidity using the Multipurpose Australian Comorbidity Scoring System (MACSS)[25] at one year and five years prior to the incident event. A summary of the diagnosis codes used to define comorbidity is shown in Appendix 2. In the event a patient was diagnosed with two or more types of ACS within the same episode of care, the method of diagnosis hierarchy previously validated by Sanfilippo et al and Lopez et al was applied where the final diagnosis was the most severe diagnosis; with STEMI being the most severe, followed by NSTEMI and lastly UA[26-27]. The determination of the interventions performed was based on The Australian Classification of Health Interventions, Tenth Revision from the National Centre for Classification in Health[28] (Appendix 1).

The EDDC was combined with the HDMS to identify those patients who presented to an emergency department and were admitted at the same hospital, versus those patients who were transferred to another hospital. Distinction between IHT during the same episode of care, as opposed to a readmission, were identified by a secondary HMDS record within 24 hours of the time of separation, where the method of patient discharge and discharge destination from the first hospital

indicated a transfer. A new admission beyond 24 hours post discharge and in the absence of the aforementioned discharge indicators within 24 hours, the record was assigned as a readmission.

Emergency versus elective admissions are coded directly in the HMDS. In-hospital mortality, including the date of death, is coded within the HMDS; while post-discharge mortality, including data of death and cause of death (COD) based on ICD-10-AM coding, was determined using the linked mortality dataset. Reported time frames calculated between the date of separation for the first admission and the date of death. The ICD-10-AM was used to categorise the COD into acute myocardial infarction (AMI), other ischemic heart diseases (IHD) excluding AMI and non-IHD causes for 0 to 30-day, 30-day to 1-year and beyond 1-year mortality.

3.3.4 *Statistical Analysis*

Unadjusted estimates of the person's time at risk were calculated using the number of persons residing in WA in each age bracket (18–39, 40–49, 50–59, 60–69, 70–79 and 80+ years) on 30th June for each year from the ABS as the denominator. The Australian Institute of Health and Welfare data on annual separation rates were used as the denominator to calculate the rate of first-time ACS separations versus all-cause hospital separations. Categorical data were reported as frequencies and percentages and continuous data were reported as the means, standard deviations and ranges. Where appropriate, categorical data were also presented as rates, using the admitted cohort as the denominator unless otherwise specified. Confidence intervals were calculated using a confidence interval calculator for single incidence rates with the two-sided confidence level assigned at 95%[29]. The Mann–Whitney U test and the Pearson chi-squared tests were used for between group analyses. Statistical significance was assigned at the level of $p < 0.05$. All analyses

were performed using IBM SPSS Statistics for Windows, Version 25.0[30] and Stata Statistical Software: Release 16[31].

3.4 Results

Rates of admissions for the first-time diagnoses of ACS remained steady throughout the nine-year study timeframe averaging ten per 10,000 person years with an average of 2405 admissions per calendar year (

) and 21,648 total admissions between 01 December 2007 and 31 December 2015 (Appendix 1). However, rates of UA and STEMI decreased from 2010 to 2015 as NSTEMI rates showed an increase. Annual rates of UA showed a statistically significant difference from 2010, decreasing with each subsequent year. Rates of STEMI presentations were statistically significantly lower between 2009 and 2011 and between 2014 and 2015. Rates of NSTEMI steadily increased with each year from 2010 and although not always a statistically significant change per year within NSTEMI, this condition does contribute statistically significantly higher rates of the ACS burden from 2009 compared to UA and STEMI (Figure 3.2). In-hospital mortality rates were stable for UA and NSTEMI with a slow decline noted for STEMI patients (

Figure 3.3) and the overall all-cause mortality rate at 30 days also remained stable at an average of 459 per 10,000 person–years (PY), increasing to an average of 583 per PY for 30-day to 1-year mortality (Figure 3.4). The rates of first-time admissions were higher in males and increased with each 10-year incremental rise in age (Figure 3.5 and Figure 3.6). Rates of PCI including one or more stent insertion increased from 56 procedures per 100 PY in 2007 to 68 per 100 PY for every confirmed diagnosis of ACS, with rates of CABG contributing approximately five procedures per 100 PY per annum over the nine years (Figure 3.7). The data for Figures 3.1 to 3.7 are tabulated in more depth in Appendices 3-5.

Figure 3.1: Number and rates of all first-time admissions for acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015.

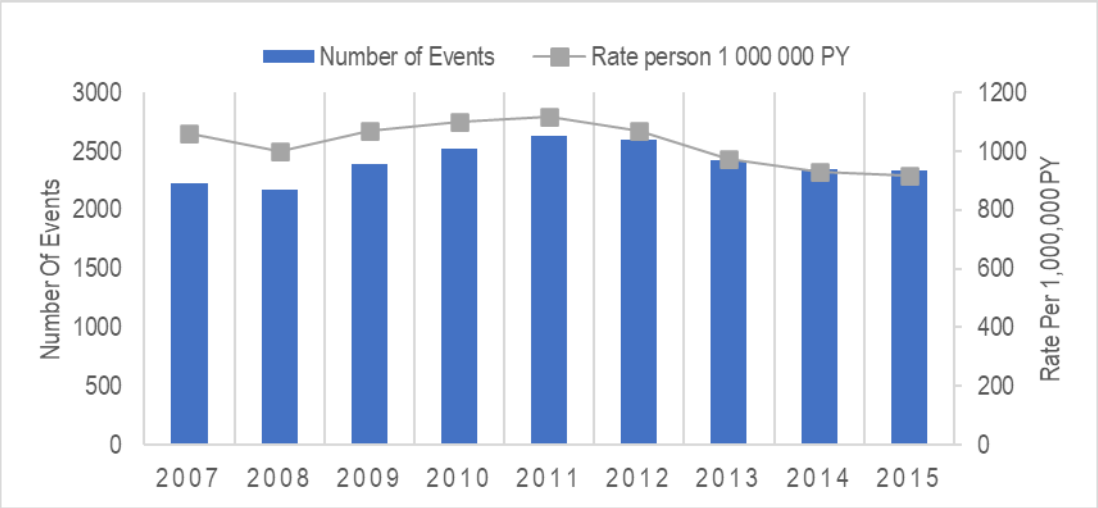


Figure 3.2: Rates of all first-time admissions by acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

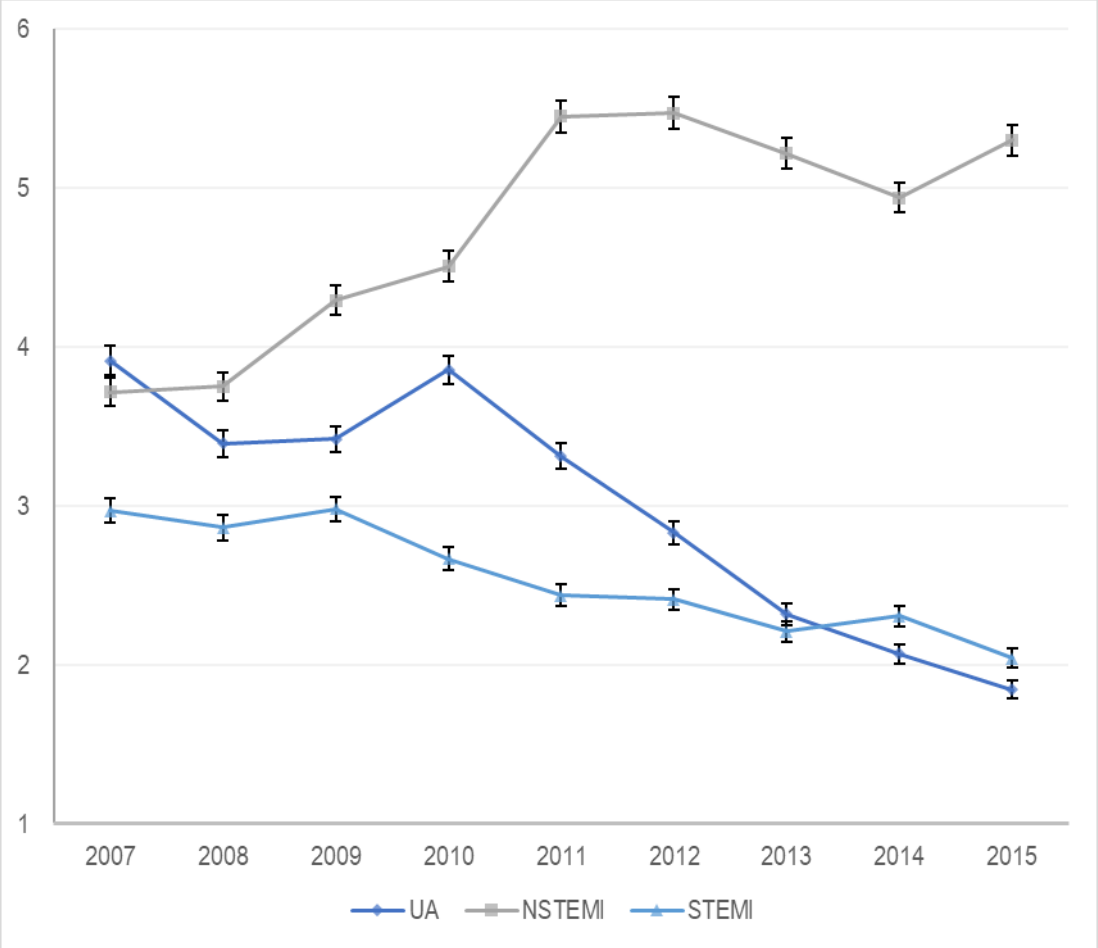


Figure 3.3: In-hospital mortality rates of first-time admissions by acute coronary syndromes per 10,000 person–years for all first-time admissions for acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

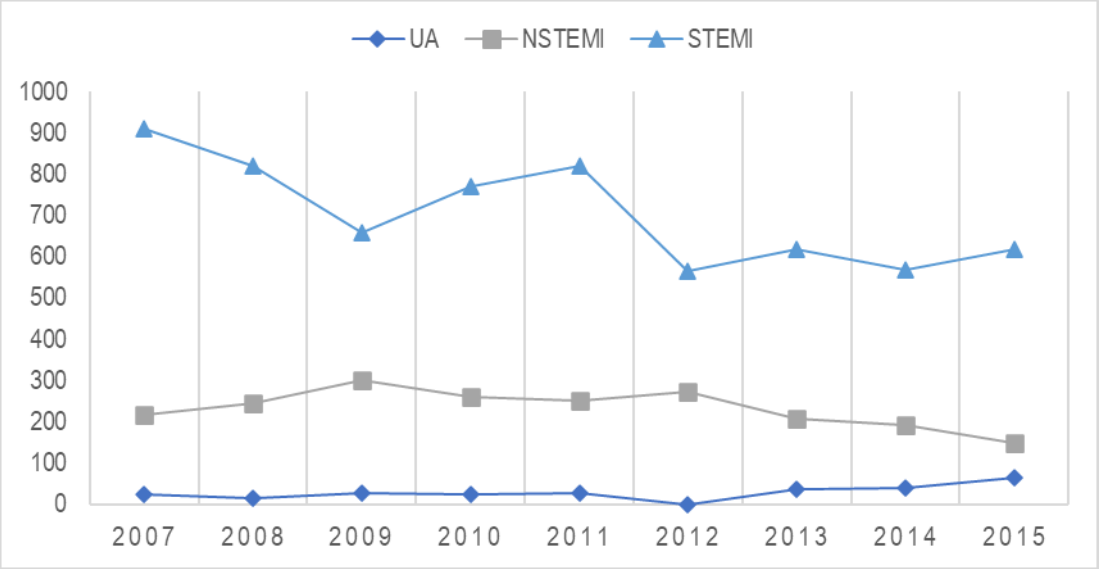


Figure 3.4: Mortality rates for first-time admissions by acute coronary syndrome per 1000 person–years for all first-time admissions for acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015.

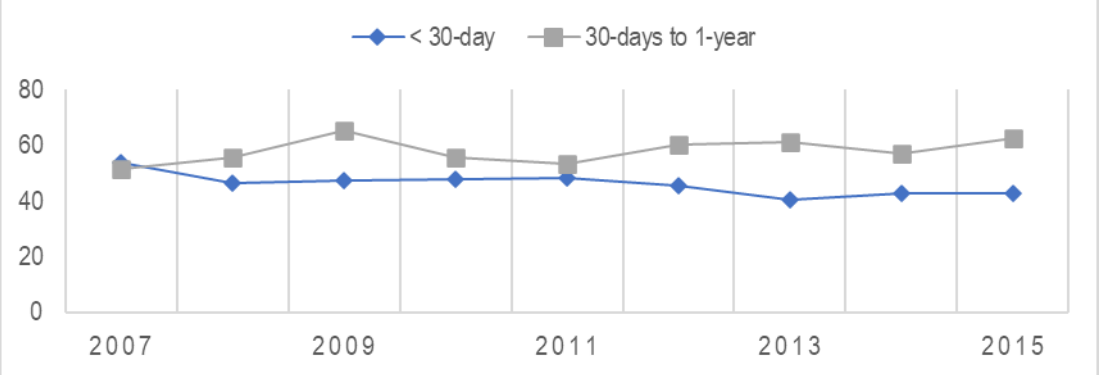


Figure 3.5: Rates of first-time admissions per 10,000 person–years by sex for all first-time admissions for acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015.

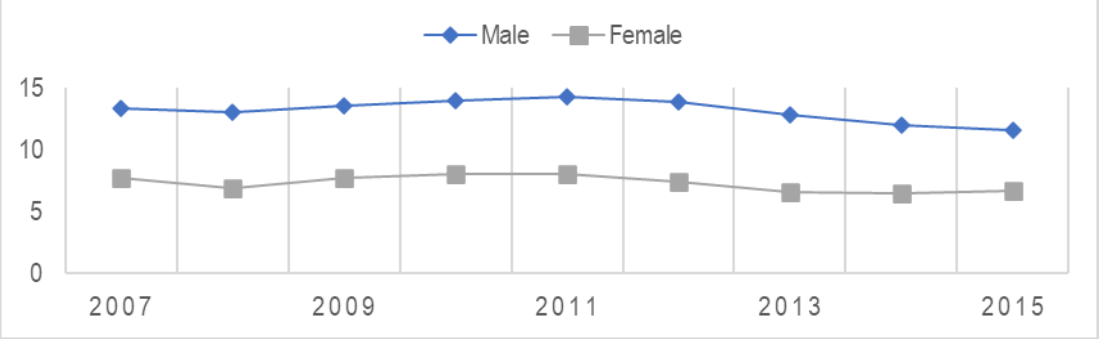


Figure 3.6: Rates of first-time admissions per 10,000 person–years by age for all first-time admissions for acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015.

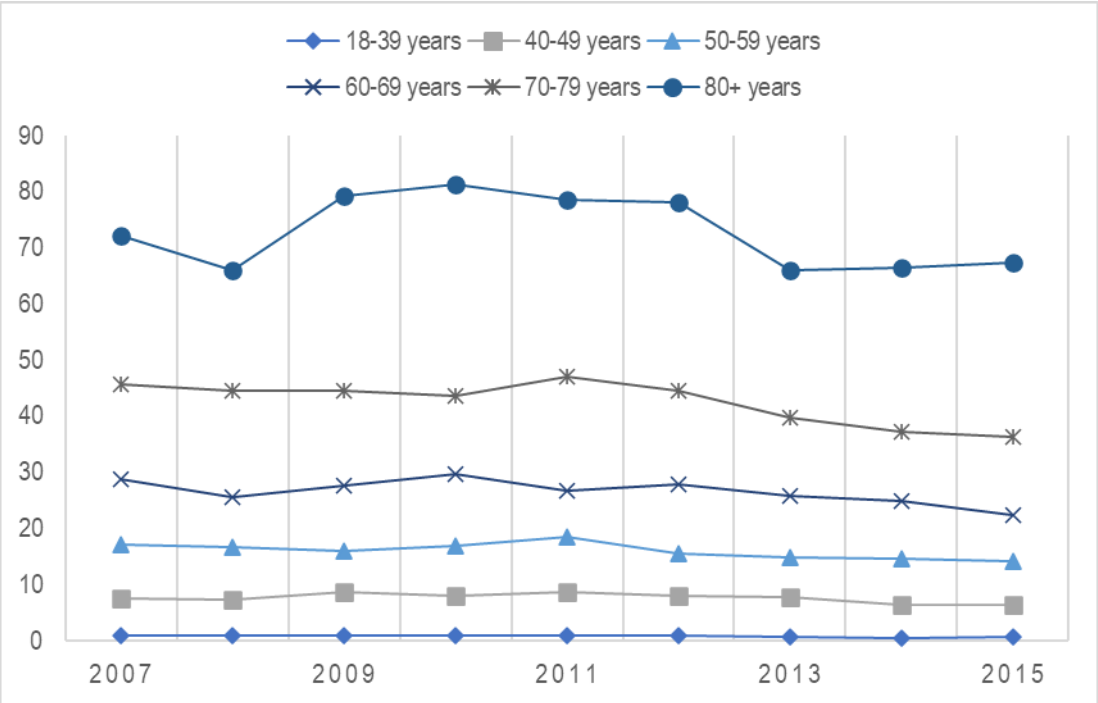
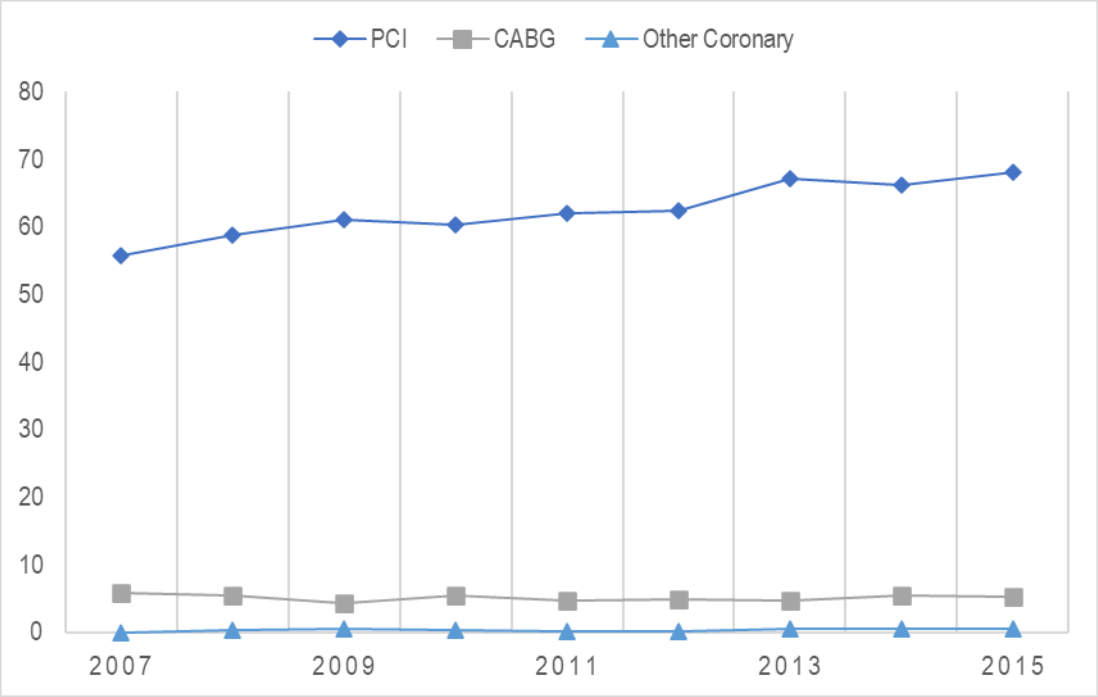


Figure 3.7: Rates of PCI including one or more stent insertions; CABG and other coronary procedures for all first-time admissions for acute coronary syndrome in Western Australia between 01/01/2007 to 31/12/2015. PCI: percutaneous coronary intervention including one or more stent insertions; CABG: coronary artery bypass grafting; Other Coronary: other procedures of the coronary artery including angiography and excision.



Rates of incident (first-time) ACS separations remained stable as all-cause hospital separations increased, resulting in an average rate of 25 admissions per 10,000 PY, or 0.25% of all admission attributable to first-time ACS events annually (Figure 3.8). A higher number of metropolitan patients were admitted directly for care compared to rural patients in the NSTEMI and STEMI cohorts with similar numbers of direct admission and inter-hospital transfer in the UA cohort (Figure 3.9).

Figure 3.8: Rates of incident acute coronary syndrome (ACS) separations versus all-cause separations in western Australian between 01/01/2007 to 31/12/2015 financial years.

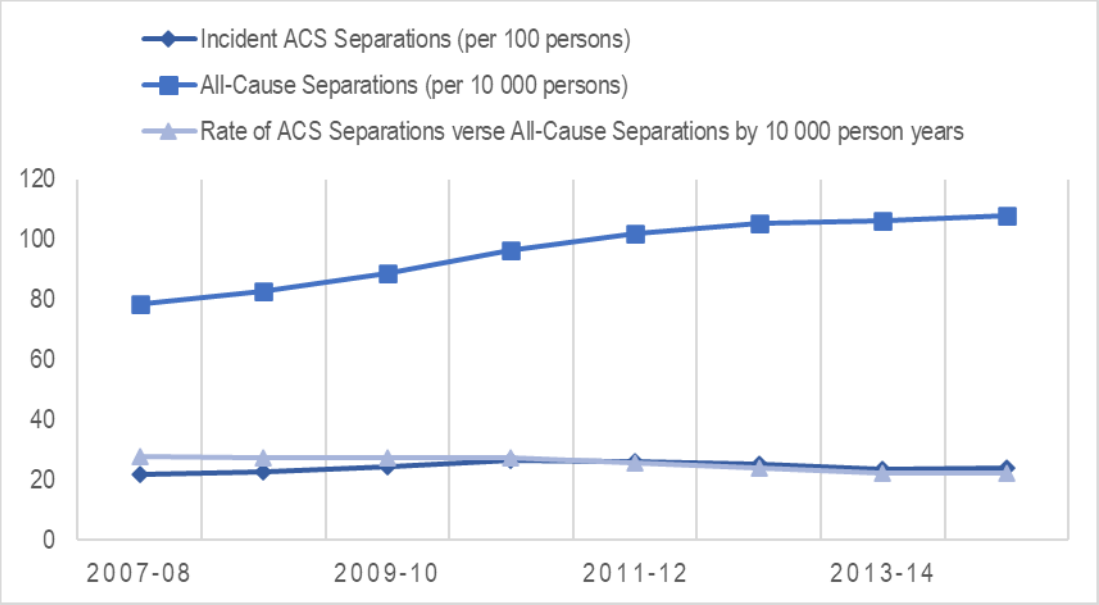
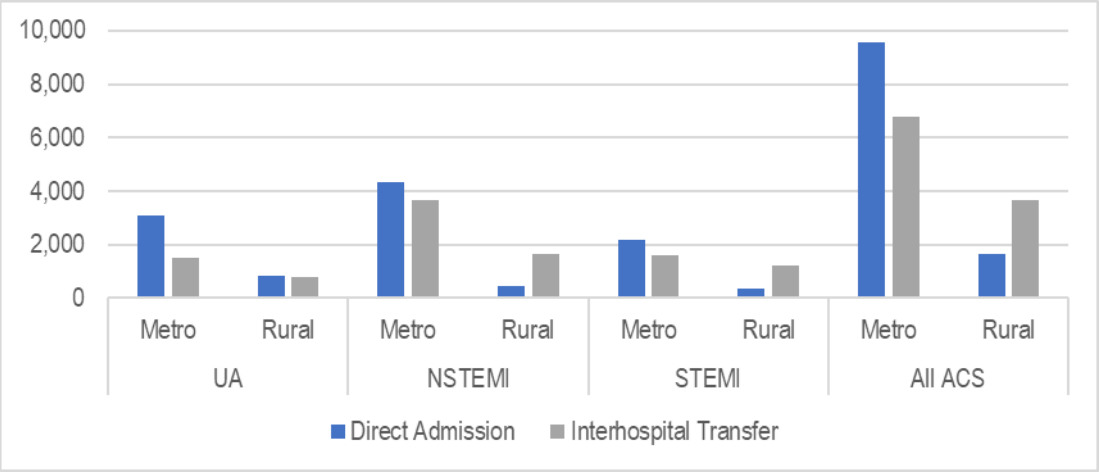


Figure 3.9: Number of direct admissions versus inter-hospital transfers for acute coronary syndromes in western Australia between 01/01/2007 to 31/12/2015 by metropolitan and rural residence. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.



As demonstrated in Table 3.1, two-thirds of ACS admissions were male with a mean age of 65 years and 63 years for metropolitan and rural patients, respectively. The mean age for rural female patients was 66 years which is statically significantly younger than metropolitan female admissions with a mean age of 72 years ($p< 0.001$). More rural admissions were identified as being of Aboriginal and/or Torres Strait Islander descent at 14% compared to 2% of metropolitan admissions and two-thirds of rural patients were from the high- and highest-disadvantaged SEIFA compared to nearly 50% of metropolitan admissions, which pertained to individuals living in the least or less disadvantaged areas. Metropolitan patients used emergency services more frequently than rural patients (50% and 35%, respectively). NSTEMI accounted for the highest proportion of primary diagnoses with STEMIs at 23% and 29% for metropolitan and rural admissions, respectively. More than half of all metropolitan admissions presented directly to the treating hospital (58%) whereas 69% of rural patients experienced a transfer.

Table 3.2 presents the rates of primary diagnosis, principal procedure, inter-hospital transfers and in-hospital and post-discharge mortality between the metropolitan and rural cohorts. The rate of admissions for STEMI was higher in rural patients at 29.3 admissions per 100 PY of all ACS admissions, while NSTEMI presentations were higher in the metropolitan cohort. Metropolitan admissions also had a higher rate of PCI and lower rates of inter-hospital transfer. All-cause in-hospital mortality was statistically significantly higher in the metropolitan cohort at 3.1 deaths per 100 PY. The highest rate of 30-day mortality was due to AMI causes at 46 deaths per 100 PY, which was particularly high in the rural cohort at 51 deaths per 100 PY compared to 45 deaths in the metropolitan group, although these figures showed no statistically significant difference.

A higher proportion of transferred patients was diagnosed with NSTEMI and only 1% more STEMI cases compared to direct presentations, as shown in Table 3.3. The

rate of patients to have a PCI including one or more stent insertion was 57 per 100 PY for non-transferred patients and 72 per 100 PY for admissions that incorporated an inter-hospital transfer. Transferred patients had slightly lower rates of comorbidities diagnosed during the same episode of care, with all but obesity statistically significantly different between the two groups.

The rate of in hospital mortality was significantly higher in non-transferred patients as was the rate of post-discharge mortality at both 30 days and 30 days to 1 year. However, the rate of mortality occurring more than 1 year post discharge was higher in the transferred group. Post-discharge mortality rates for non-ischemic heart disease and AMI were higher in transferred patients.

Table 3.1 Characteristics and outcomes of first-time admissions for acute coronary syndrome among metropolitan and rural western Australians, based on residential postcode at the time of admission between 1 January 2007 and 31 December 2015.

	Metro	Rural	Total	Sig *
	n (% *)	n (% *)	n (% *)	p < 0.05
	n = 16,357	n = 5290	n = 21,647	
Demographics				
Male Age, Mean (std dev) (range)	65.05 (13.698) (18–101)	62.54 (14.065) (18–99)	64.43 (13.832) (18–101)	0.056
Female Age, Mean (std dev) (range)	72.37 (14.149) (18–103)	65.58 (15.137) (22–101)	70.77 (14.673) (18–103)	<0.001
Male	10,519 (64.3)	3484 (65.9)	14,003 (64.7)	0.040
Indigenous Australian	310 (1.9)	713 (13.5)	1023 (4.7)	<0.001
Socio-Economic Indexes for Areas (SEIFA)				
Highest Disadvantage	1737 (10.6)	1476 (27.9)	3213 (14.8)	<0.001
High Disadvantage	3951 (24.2)	2169 (41.0)	6120 (28.3)	
Moderate Disadvantage	2841 (17.4)	940 (17.8)	3781 (17.5)	
Less Disadvantage	2679 (16.4)	549 (10.4)	3228 (14.9)	
Least Disadvantage	5149 (31.5)	156 (2.9)	5305 (24.5)	
Comorbidities during the Same Admission				
Diabetes	3043 (18.6)	1064 (20.1)	4107 (9.0)	0.015
Cardiac Arrest	238 (1.5)	65 (1.2)	303 (1.4)	0.223
Heart Failure	1832 (11.2)	445 (8.4)	2277 (10.5)	<0.001
Chronic Pulmonary Disease	112 (0.7)	37 (0.7)	149 (0.7)	0.910
Renal Insufficiency < 29 mL/min	412 (2.5)	127 (2.4)	539 (2.5)	0.632
Mode of Arrival to 1st Hospital or ED				
Ambulance/Royal Flying Doctor Service	8133 (49.7)	1848 (34.9)	9981 (46.1)	<0.001
Private/Public Transport	7575 (46.3)	3242 (61.3)	10,817 (50.0)	
Other	448 (2.7)	79 (1.5)	527 (2.4)	
Unknown	201 (1.2)	121 (2.3)	322 (1.5)	
Region of 1st Hospital of Admission				
North Metro	6012 (36.8)	496 (9.4)	6508 (30.1)	<0.001
East Metro	5248 (32.1)	738 (14.0)	5986 (27.7)	
South Metro	4880 (29.8)	270 (5.1)	5150 (23.8)	
South West	48 (0.3)	1321 (25.0)	1369 (6.3)	
Great Southern	16 (0.1)	540 (10.2)	556 (2.6)	
Wheatbelt	7 (0.0)	239 (4.5)	246 (1.1)	
Goldfields	17 (0.1)	485 (9.2)	502 (2.3)	
Midwest	27 (0.2)	532 (10.1)	559 (2.6)	
Pilbara	78 (0.5)	328 (6.2)	406 (1.9)	
Kimberley	24 (0.1)	341 (6.4)	365 (1.7)	
Transfer Status by Primary Diagnosis				
Transfer for UA	1532 (33.3)	780 (47.7)	2312 (37.1)	<0.001
Transfer for NSTEMI	3645 (45.7)	1670 (79.3)	5315 (52.7)	
Transfer for STEMI	1610 (42.6)	1212 (78.1)	2822 (53.0)	

% *: the total percent for each cohort (e.g., Metro); Sig *: statistical significance. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

Table 3.2: Rates of primary diagnosis, principal procedure, inter-hospital transfers and mortality per 100 person–years for first-time admissions for acute coronary syndrome for metropolitan and rural western Australians, based on residential postcode at the time of admission between 01/01/2007 to 31/12/2015.

	Metro	Rural	Total	Sig *
	n (R *)	n (R *)	n (R *)	p < 0.05
Primary Diagnosis (Total Events)	(n = 16,357)	(n = 5290)	(n = 21647)	
UA	4603 (28.1)	1634 (30.9)	6237 (28.8)	<0.001
NSTEMI	7978 (48.8)	2105 (39.8)	10,083 (46.6)	
STEMI	3776 (23.1)	1551 (29.3)	5327 (24.6)	
Percutaneous Coronary Interventions (PCI) (Total Events)	(n = 16357)	(n = 5290)	(n = 21647)	
Other Coronary Procedures	48 (0.3)	11 (0.2)	59 (0.3)	<0.001
PCI +/- Stent	10,394 (63.5)	3150 (59.5)	13,544 (62.6)	
Coronary Artery Bypass Grafting	819 (5.0)	292 (5.5)	1111 (5.1)	
Inter-Hospital Transfer Status (Total Events)	(n = 16357)	(n = 5290)	(n = 21647)	
Direct/No IHT	9570 (58.5)	1628 (30.8)	11,198 (51.7)	<0.001
Yes, IHT	6787 (41.5)	3662 (69.2)	10,449 (48.3)	
In-Hospital Mortality—All Cause (Total Events)	(n = 16357)	(n = 5290)	(n = 21647)	
Yes, Died in Hospital	509 (3.1)	117 (0.7)	626 (3.8)	0.001
Mortality—Non-IHD COD (Total Events)	(n = 2848)	(n = 806)	(n = 3654)	
30-Day Mortality	326 (11.4)	97 (12.0)	423 (11.6)	0.804
30-Day to 1-Year Mortality	650 (22.8)	189 (23.4)	839 (23.0)	
More than 1-Year Mortality	1872 (65.7)	520 (64.5)	2392 (65.5)	
Mortality—AMI COD (Total Events)	(n = 854)	(n = 240)	(n = 1094)	
30-Day Mortality	387 (45.3)	122 (50.8)	509 (46.5)	0.301
30-Day to 1-Year Mortality	194 (22.7)	47 (19.6)	241 (22.0)	
More than 1-Year Mortality	273 (32.0)	71 (29.6)	344 (31.4)	
Mortality—IHD COD, Excluding AMI (Total Events)	(n = 408)	(n = 122)	(n = 530	
30-day mortality	51 (12.5)	15 (12.3)	66 (12.5)	0.624
30-Day to 1-Year Mortality	142 (34.8)	37 (30.3)	179 (33.8)	
More than 1-Year Mortality	215 (52.7)	70 (57.4)	285 (53.8)	

R*: rate per 100 person–years; Sig*: statistical significance; UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; IHD: ischemic heart disease; COD: cause of death; IHT: inter-hospital transfer; PCI +/- Stent: percutaneous coronary intervention, with or without stent insertion.

Table 3.3: Rates of primary diagnosis, principal procedure, comorbidities, and mortality per 100 person–years for first-time admissions for acute coronary syndrome for Perth metropolitan admissions based on transfer status between 01/01/2007 to 31/12/2015.

	Direct/No IHT	IHT	Total	Sig *
	n (R *)	n (R *)	n (R *)	p < 0.05
Primary Diagnosis (Total Events)	(n = 9570)	(n = 6787)	(n = 16357)	
UA	3071 (32.1)	1532 (22.6)	4603 (28.1)	<0.001
NSTEMI	4333 (45.3)	3645 (53.7)	7978 (48.8)	
STEMI	2166 (22.6)	1610 (23.7)	3776 (23.1)	
Percutaneous Coronary Interventions (PCI) (Total Events)	(n = 9570)	(n = 6787)	(n = 16357)	
Other Coronary Procedures	28 (0.3)	20 (0.3)	48 (0.3)	<0.001
PCI +/- Stent	5479 (57.3)	4916 (72.4)	10395 (63.6)	
Coronary Artery Bypass Grafting	347 (3.6)	473 (7.0)	820 (5.0)	
Comorbidities during the Same Admission (Total Events)	(n = 9570)	(n = 6787)	(n = 16357)	
Diabetes	1880 (19.6)	1163 (17.1)	3043 (18.6)	<0.001
Cardiac Arrest	163 (1.7)	75 (1.1)	238 (1.5)	0.002
Heart Failure	1180 (12.3)	652 (9.6)	1832 (11.2)	<0.001
Chronic Pulmonary Disease	79 (0.8)	33 (0.5)	112 (0.7)	0.010
Renal Insufficiency < 29 ml/min	275 (2.9)	137 (2.0)	412 (2.5)	0.001
Obese	211 (2.2)	133 (2.0)	344 (2.1)	0.282
In-Hospital Mortality (Total Events)	(n = 9570)	(n = 6787)	(n = 16357)	
Yes, Died in Hospital	418 (4.4)	91 (1.3)	509 (3.1)	<0.001
Post-Discharge Mortality by COD (Total Events)	(n = 2718)	(n = 1392)	(n = 4110)	
Non-IHD COD	1843 (67.8)	1005 (72.2)	2848 (69.3)	<0.001
AMI COD	608 (22.4)	246 (17.7)	854 (20.8)	
IHD COD, Excluding AMI	267 (9.8)	141 (10.1)	408 (9.9)	
Post-Discharge Mortality by Time Points (Total Events)	(n = 2718)	(n = 1392)	(n = 4110)	
30-Day Mortality	545 (20.1)	219 (15.7)	764 (18.6)	<0.001
30-Day to 1-Year Mortality	665 (24.5)	321 (23.1)	986 (24.0)	
More than 1-Year Mortality	1508 (55.5)	852 (61.2)	2360 (57.4)	

R*: rate per 100 person–years; Sig *: statistical significance; IHT: inter-hospital transfer; UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; IHD: ischemic heart disease; COD: cause of death; PCI +/- Stent: percutaneous coronary intervention, with or without stent insertion.

3.5 Discussion

The construct of the right patient–right treatment–right time is not new in ACS reporting. Rates of first-time admission for ACS were more than double in the rural residential cohort compared to metropolitan patients with disparities in health conditions and outcomes for rural patients recognised globally and within Australia [9,32-33]. One of the largest challenges facing a rural patient in the event of ACS is access to care in a timely manner from symptom onset, with clear guidelines for the treatment of STEMI, depending on access to a PCI-capable hospital, inter-hospital transfer travel times, and a patient's suitability for PCI, CABG or fibrinolytic therapy [34]. In our study, nearly 80% of rural admissions for STEMI and NSTEMI were transferred, which is not a surprising finding given the unavailability of PCI-capable hospitals in rural WA. However, of greater concern is the proportion of metropolitan patients also being transferred during the episode of care. With 54% and 24% of NSTEMI and STEMI patients being transferred, respectively, of which 80% go on to have PCI including one or more stent insertion or CABG. The era of ambulance ECG, rapid assessment of chest pain or less common symptoms of AMI enroute to the hospital means that STEMI patients can be triaged and bypass non-PCI-capable hospitals. This should result in fewer inter-hospital transfers, particularly for in metropolitan STEMI patients, consequently reducing time to definitive treatment [34-35]. Previous research [18,34,36] has also indicated that inter-hospital transfers in a metropolitan cohort is an ongoing reality and suggests that more focus needs to be put into a coordinated pre-hospital framework to ensure STEMI patients are rapidly identified, allowing for ambulance diversion to an appropriate PCI-capable facility [37]. In comparison, NSTEMI diagnoses, often made more complicated by the requirement of serial troponins in addition to ECG and detailed clinical history, require risk stratification to determine the need for invasive or conservative treatment at an appropriate time interval from symptom onset [11,38]. Consequently,

inter-hospital transfers in the presentation of NSTEMI may remain a necessity after risk stratification with previous literature indicting little long-term benefits of early invasive strategies for NSTEACS patients without recurrent symptoms and a low risk of further ischemic events[11,38-39].

Although the overall rate of ACS presentations in our study remained stable over the nine-year time frame, rates of NSTEMI increased with each year with decreasing rates of UA while STEMI presentations remained steady. This trend has previously been reported in the Department of Health's Model of Care for Acute Coronary Syndromes in WA [16] which attributed an apparent decline in angina presentations with a correlating increase in NSTEMI presentations between 1999 and 2008 based on sensitive and specific biomarkers of myocardial injury, primarily troponins, resulted in a decline in angina diagnoses in favour of NSTEMI. The same trend is noted in our study from 2010 onwards, which could be partially explained by the uptake time of the new definitions in the WA health system.

We found that in-hospital all-cause mortality was higher for direct presentations compared with transferred patients. Although counterintuitive given what is known about longer infarct times due to the postponement of reperfusion to facilitate an inter-hospital transfer to a PCI-capable hospital, this finding concurs with previously published randomised controlled trials citing similar results [34,40-42]. Kawecki et al [34] theorised that this may be due to the longer delay associated with an inter-hospital transfer resulting in more patients dying prior to arrival at a PCI-capable hospital compared to their direct counterparts, thereby positively pre-selecting the cohort eligible for analysis (a form of immortal time bias) [43]. The same pattern can be noted for death within 30 days post discharge, however, the rate of death between 30 day and 1 year are almost identical between transferred and non-transferred patients. After the first year post discharge, transferred patients experience a higher mortality rate at 5 more deaths per 100 PY compared to the non-transferred cohort, indicating

a poorer outcome. While differences in comorbidity between transferred and non-transferred patients could explain this, we found that patients with important comorbid conditions such as diabetes, heart failure, congestive pulmonary disease, renal insufficiency, obesity and cardiac arrest were less likely to undergo an inter-hospital transfer. Thus, in our study, confounding due to comorbidity is likely to lead to worse outcomes for direct admissions, hence our estimation of the difference in post 1-year death rates resulting from inter-hospital transfer is likely conservative. Due to the anonymisation of the data, it is unknown if these direct admissions were at a PCI-capable hospital as the first port of call. However, given what is known about the comorbid conditions and rates of invasive treatments, there are two likely explanations for the differences of observed comorbidity between direct and transferred patients. The first is the patient is too unwell to undergo invasive angiography and therefore there is no need for a transfer to a PCI-capable facility. The alternative option is due to the nature of the patient's comorbidities they may likely be deemed at higher risk and are therefore taken directly to a tertiary facility with PCI-capable faculties, as a matter of triage.

3.6 Strengths and Limitations

A key strength of this study is the identification of first-time events. This study assigned incident events of ACS if the patient was admitted for ACS during the 9-year period if the same individual had no prior admission for ACS from 01 January 2002. This ensured prevalent individuals could be removed from the analysis and allowed for accurate follow-up time periods for post-discharge mortality.

A further strength of linked administrative data is the ability to overcome the challenges associated with over-counting due to inter-hospital transfers which can plague other cardiac registries, which gives WA a unique position to track and monitor trends in ACS admissions.

Although this study has the strength of a large sample size using whole-of-population data during the study time frame, it is not without limitations. The analysis of linked administrative health data is an important tool for the longitudinal tracking of patients over time due to a lack of loss to follow up a complete capture of the population using health services. However, long-term (i.e., greater than one year) outcomes can only be evaluated if sufficient data are available beyond each year or composite end point. Furthermore, the WADLS has no current capacity to track patients who are admitted for the same condition in another Australian State or Territory. However, the data can lack some clinical detail which would create a more holistic approach which cardiac registries could overcome. This includes, but is not limited to, the time of symptom onset, time of first medical contact, whether an ECG was performed en route to the hospital, records of serial troponin levels over time, details of any administered pharmaceuticals, including fibrinolytic medications, accurate arrival times and times of balloon inflation in the cardiac catheterisation laboratory. The addition of these variables to a study such as this would allow for the adherence to the evidence-based guidelines developed by the NHFA/CSANZ to be assessed [11]. While the overall rates of admission for ACS can be reported via linked data, smaller internal registries can inform where the overall delays patients experienced, be it direct presentations or inter-hospital transfers. To overcome the limitations of the data, an aligned previous study by Forsyth et al [18] used data from a single Perth metropolitan tertiary (teaching) hospital with round-the-clock PCI facilities which recorded key time points as part of their internal auditing process. This study highlighted the significantly longer infarct times for patients who required an inter-hospital transfer for treatment, despite the pre-hospital activation of the CCL at the treating hospital and shorter door-to-balloon times at the treating hospital, compared to direct presentations. Given 43% of Perth metropolitan admissions for first-time presentations of STEMI require an inter-hospital transfer, this is a large

volume of patients experiencing a longer time-to-treatment burden and having poorer long-term outcomes.

Finally, this descriptive study is limited as the association between transfer status and patient outcomes was not evaluated. Rather, it sought to determine, at the population level, the rate of all first-time admissions for ACS in WA including the numbers of inter-hospital transfers according to geographic location and patient characteristics. Therefore, results reporting mortality rates should be regarded as exploratory in nature and will be the subject to further evaluation using appropriate modelling and/or quasi-experimental methods.

3.7 Conclusion

This paper provides information about the rates of ACS presentations in WA hospitals between 2007 and 2015, according to health, region, age and type of ACS. Accurate presentation numbers are essential to monitor the burden of ACS across the world informing researchers and governments alike on disparities between health regions and service utilisation. Of particular concern in our study is the percentage of metropolitan patients still requiring inter-hospital transfers for PCI, despite efforts to ensure STEMI presentations present directly to PCI-capable hospitals. With 48% of all patient admissions during the study period undergoing an inter-hospital transfer during their first admission for ACS, previously reported ACS presentation figures should be interpreted with care as they may be reporting total admission figures, not taking into account inter-hospital transfers during the same episode of care.

3.8 Publication Declarations

R.F. collected and analysed the data and wrote the manuscript; R.M. supervised data collection and analysis and was a contributor to the writing of the manuscript;

Z.S. supervised analysis and was involved with manuscript editing. C.R. supervised the analysis and was involved with manuscript editing. All authors read and approved the final manuscript.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Department of Health WA Human Research Ethics Committee (protocol code #2013/20 and date of approval 19/05/2013)

Informed Consent Statement: Patient consent was waived due to the nature of Linked Administrative Data which provides whole-of-population under stringent de-identification of datasets prior to distribution to research teams.

Data Availability Statement: The datasets generated and/or analysed during the current study are not publicly available due to strict requirements set out by the Human Ethics Research Committees regarding the storage and use of the data by authorised investigators. Due to the small cell size of the study we can only produce results in aggregate form to preserve anonymity and confidentially.

Conflicts of Interest: The authors declare no conflict of interest.

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Chapter 4 Inter-hospital transfers and door-to-balloon times for STEMI: a single centre cohort study

4.1 Abstract

Key performance indices such as door-to-balloon times have long been recognised as quality metrics in reducing time to care for patients with acute coronary syndromes (ACS). In the situation where patients do not present to a facility capable of 24/7 percutaneous coronary interventions (PCI) delays in time to therapy can exceed the recommendation of 90 minutes or less. This study evaluated the impact of transfers on performance indices for patients diagnosed with ST-elevation myocardial infarction (STEMI).

Over a seven-month collection period, all patients presenting with symptoms suggestive of ACS and admitted for PCI were studied. Patients were divided into dichotomous groups of direct presentations or transfers from a secondary non-PCI capable hospital with key times recorded, including symptom-onset, first hospital and PCI-capable hospital arrival and balloon inflation times to evaluate time to therapy for STEMI patients.

Of the 87 patients diagnosed with STEMI, transferred patients experienced statistically significant delays in symptom-onset to the PCI-capable hospital (PCI-H) arrival (215 v 95 mins; $p<0.001$), symptom-onset to balloon inflation (224 v 160 mins; $p=0.009$) and first hospital arrival to balloon inflation times (106 v 56 mins; $p<0.001$). Only 28% (n=9) of transferred patients underwent balloon inflation within 90 minutes from first hospital arrival, while 60% (n=19) did within 120 minutes, although all received balloon inflation within 90 minutes from arrival at the PCI-H. After controlling for confounding factors of socio-economic status, presentation date/time and diagnostic category, transferred patients experienced an average 162% longer delays from symptom-onset to PCI-H door arrival, and 98% longer delays in symptom-onset to balloon inflation; compared to patients who present

directly to the PCI-H. No statistically significant differences were noted between transferred and direct patients when measured from PCI-H door-to-balloon times.

This study shows that transferred patients experience a greater overall system delay, compared to patients who present directly for PCI, significantly increasing their time to treatment and therefore infarct times. Despite the majority of transfers experiencing pre-hospital activation, their treatment hospital arrival to balloon times are no less than direct presenters after controlling for confounding factors, further compounding the overall delay to therapy.

4.2 Introduction

Cardiovascular disease is recognised as a leading cause of death and disability across the globe with troubling disparities noted between metropolitan and rural communities [1-3]. Australia has identified this as an area of priority under the National Health Priority Area initiative [4]. Specifically, acute coronary syndrome (ACS) which collectively spans presentations of acute myocardial infarction (AMI), including ST-segment elevation AMI (STEMI), non-ST-segment-elevation (nSTEMI) and unstable angina [5-6] was the cause of death for 6.1% Western Australians in 2015 [7]. Presentations of STEMI are considered medical emergencies and positive outcomes including lower mortality rates are highly correlated with timely reperfusion of the culprit vessel [8-11]. Given this time crucial nature there has been considerable focus surrounding the reduction of measurable performance indices for time to therapy, namely door-to-electrocardiogram (ECG) (DTE), door-to-needle (DTN) and door-to-balloon (DTB) times for ACS patients; and more recently time from first medical contact to balloon times (FMC-B). Reduction in time to therapy is associated with improved outcomes and as such several international professional organisations have reached a consensus, calling for DTE times within 10 minutes for all presentations and DTB times of 90 minutes or less for patients who present

direct to a hospital equipped with a cardiac catheterisation laboratory (CCL) for percutaneous coronary interventions (PCI) [8-9,12-13]. Those patients who require transfers for PCI should have early activation of the CCL to reduce avoidable delays [13]. The 2016 Australian Clinical Guidelines for the Management of Acute Coronary Syndromes recommends primary PCI as the preferred reperfusion strategy for those patients diagnosed with STEMI, if it can be performed within 90 minutes of first medical contact (FMC); otherwise proceed to thrombolysis in the absence of contraindications [14]. Prior to the 2016 update, door-to-balloon times within 90 minutes were the key performance objective in Australia [13].

Timely transfer to PCI capable hospitals has been shown to reduce rates of death, re-infarction and stroke compared to on-site fibrinolysis [14-15] and strategies have been introduced to reduce avoidable delays namely emergency department activation [16-17]; pre-hospital activation [17]; 30 minute mobilisation of on call staff [16-17]; and ambulance based ECG results transmission [18-19].

The aim of this study was to analyse the impact of inter-hospital transfers within the Perth Metropolitan region on overall time-to-treatment when a patient needs to be transferred from a non-PCI capable metropolitan hospital to a facility that can offer round-the-clock PCI.

4.3 Methods

4.3.1 *Study population*

Data of all WA resident patients aged 18 years or older who presented to a single Perth metropolitan teaching hospital, PCI-H, with round-the-clock CCL facilities with a diagnosis of ST-segment elevation myocardial infarction (STEMI) between 1st June 2013 and 31st December 2013 were de-identified for analysis. Data for every admission to the PCI-H Cardiovascular Medicine Department are routinely collected

as part of the department's standard clinical management program, as a single-centre cardiac registry. Human Research Ethical approval was obtained prior to data collection from the Human Research Ethics Committees of the Western Australian Department of Health; Curtin University; and the PCI-H.

4.3.2 *Characteristics of participants*

Socio-demographic data included a unique de-identified patient number, birth year, sex and postcode of residence; in addition to the clinical variables of admission date, discharge date, time of symptom-onset, PCI-H arrival time, time of ECG, time of CCL activation, procedure start time, time of first balloon inflation, procedure end time, principal diagnosis, principal procedure (PCI, stent insertions, CABG), mode of arrival, length of stay in hospital and mode of discharge from the PCI-H. Additionally for those patients who were transferred from another hospital, first hospital arrival time and first hospital departure time were also available. Time-to-event variables were calculated from the difference in the time recorded between the two key events of interest and span symptom-onset to first hospital arrival (STD(First)), symptom-onset to PCI-H arrival (STD(PCI-H)), symptom-onset to first balloon inflation (STB), first hospital arrival to first balloon inflation (DTB(first)), PCI-H arrival-to-first balloon inflation (DTB(PCI-H)), first hospital length of stay (referral LOS) and inter-hospital transfers (IHTs), all measured in minutes. Pharmacological treatments are not coded in the data and as such door to needle (DTN) times could not be assessed; and it is unknown if transferred patients received thrombolytic therapy prior to transfer. Times of ambulance arrival were not recorded within the dataset and as such FMC to balloon times could not be evaluated.

4.3.3 *Statistical analysis*

All analyses were performed using SPSS Statistics Version 22 (IBM Corporation, Armonk, NY, USA) [20]. Statistical significance was assigned at the level of $p<0.05$. Categorical data were reported as frequencies and percentages, while continuous variables were reported as mean or medians, with standard deviations and range. 'Between-group' analyses were completed using Mann-Whitney U Test and the Pearson Chi Squared test, respectively. Multivariable generalised linear modelling applying a Gamma distribution with a log link function were performed to evaluate key times and identify predictors impacting length of stay for STEMI patients: candidate variables were chosen as those likely to contribute to confounding given the observational nature of the study (sex, age, socio-economic status, method of arrival to the PCI-H, presentation date/time, pre-hospital ECG, pre-hospital activation and transfer status) and were included in final models after backwards stepwise selection using $p>0.05$ as the level of significance for variable inclusion.

4.4 Results

Table 4.1 presents 107 subjects who met inclusion criteria with a mean age of 60 years, of which 85% were males predominantly from the North Metropolitan Health Service catchment area (90%). Medical transport was attributed to 86% of those who presented directly to the PCI-H; while it is unknown how patients presented to the first non-PCI-H. All transfers were via ambulance. Pre-hospital activation occurred in 30% of direct presentations and 92% of transfers; conversely pre-hospital ECGs were obtained in 43% of direct presentations but only in 11% of transfers prior to arriving at the first non-PCI capable hospital. Primary PCI was attempted in 97% of patients, of which 75% went on to have at least one stent inserted in the target vessel. Median length of stay was three days with an in-hospital mortality rate of 6% (n=6).

Analysis was limited to only those patients diagnosed as STEMI, as this categorises those in immediate need of PCI. As shown in Table 4.2: Crude key times (minutes) to treatment for all patients diagnosed with STEMI at PCI-H between 01/06/2013 to 31/12/2013, by transfer status. Table 4.2, in the crude (unadjusted for potential confounders) analysis no statistically significant differences were noted in time between symptom-onset and first hospital arrival between direct and transfers.

Table 4.1: Socio-demographic, clinical characteristics and outcomes for all patient diagnosed with STEMI at PCI-H between 01/06/2013 to 31/12/2013, by transfer status.

		All (n=107)	Direct (n=66)	Transfers (n=41)
		n (%)	n (%)	n (%)
Age, years	Mean (std dev) [range]	60 (11.7) [35-87]	60 (11.3) [37-87]	59 (12.3) [35-83]
Sex	Male	87 (81.3)	56 (84.8)	31 (75.6)
	Female	20 (18.7)	10 (15.2)	10 (24.4)
SEIFA	Highest Disadvantage	7 (6.6)	5 (7.6)	2 (5)
	High Disadvantage	8 (7.5)	3 (4.5)	5 (12.5)
	Moderate Disadvantage	15 (14.2)	11 (16.7)	4 (10)
	Less Disadvantage	16 (15.1)	11 (16.7)	5 (12.5)
	Least Disadvantage	60 (56.6)	36 (54.5)	24 (60)
Health Service Area	North Metropolitan	95 (89.6)	57 (86.4)	38 (95)
	South Metropolitan	8 (7.5)	6 (9.1)	2 (5)
	WA Country	3 (2.8)	3 (4.5)	0 (0)
Arrival Mode	Medical Transport (SJA/RFD)	90 (86.5)	52 (78.8)	38 (100)
	Private Transport	14 (13.5)	14 (21.2)	- (-)
Presentation date/time^	Weekday, 8am - 5pm	40 (40)	26 (44.1)	14 (34.1)
	Weekday, after hours	33 (33)	19 (32.2)	14 (34.1)
	Weekend, 8am-5pm	16 (16)	8 (13.6)	8 (19.5)
	Weekend, after hours	11 (11)	6 (10.2)	5 (12.2)
Pre-hospital Activation	Yes	27 (42.9)	15 (30)	12 (92.3)
	No	36 (57.1)	35 (70)	1 (7.7)
Pre-hospital ECG	Yes	27 (30)	23 (42.6)	4 (11.1)
	No	63 (70)	31 (57.4)	32 (88.9)
Primary Diagnosis	STEMI	87 (81.3)	51 (77.3)	36 (87.8)
	NSTEMI	6 (5.6)	5 (7.6)	1 (2.4)
	Unstable Angina	1 (0.9)	0 (0)	1 (2.4)
	Subsequent AMI‡	10 (9.3)	8 (12.1)	2 (4.9)
	Other	3 (2.8)	2 (3)	1 (2.4)
Principal Procedure	PCI	24 (22.4)	16 (24.2)	8 (19.5)
	PCI + Stent Insertion	80 (74.8)	49 (74.2)	31 (75.6)
	CABG	1 (0.9)	0 (0)	1 (2.4)
	Other§	2 (1.9)	1 (1.5)	1 (2.4)
Length of stay, days	Median (std dev) [range]	3 (4.0) [0-32]	3 (3.0) [0-16]	3 (5.2) [1-32]
In-hospital mortality	Discharged	101 (94.4)	62 (93.9)	39 (95.1)
	Deceased	6 (5.6)	4 (6.1)	2 (4.9)

^ First hospital of presentation. § Other intervention, non-coronary. ‡ Within 28 days of original AMI; n*: Due to missing data, 'n' may not sum to the total sample size of 107; %**: Percentage of total reported cases for each characteristic within each group.

Transferred patients experienced statistically significant delays in STD(PCI-H) times (215 v 95 mins; p<0.001), STB times (224 v 160 mins; p=0.009) and DTB(first) times (106 v 58 mins; p<0.001). However, transferred patients DTB(PCI-H) times were statistically significantly shorter than direct presenters (34 v 58 mins; p=0.012). This trend continues in

Table 4.3 with 28% of transfers having experienced balloon inflation within 90 minutes of first hospital arrival; and 59% within 120 minutes, and yet all transfers met target when measured from DTB(PCI-H) times.

Table 4.2: Crude key times (minutes) to treatment for all patients diagnosed with STEMI at PCI-H between 01/06/2013 to 31/12/2013, by transfer status.

	All (n=51) Median [IQR]	Direct (n=42) Median [IQR]	Transfers (n=9) Median (Std. Dev) [IQR]	Sig. p>0.05
[1]STD(first)	90 [56 -165]	95 [59 -148]	76 [41 -277]	0.711
[2]STD(PCI-H)	110 [72 -215]	95 [59 -148]	215 [146 -695]	<0.001
[3]STB	181 [135 -289]	160 [125 -250]	224.5 [166 -405]	0.009
[4]DTB(first)	80 [53 -109]	57.5 [44 -81]	106.5 [89 -145]	<0.001
[5]DTB(PCI-H)	54 [41 -77]	57.5 [44 -81]	34 [30 -56]	0.012
[6]LOS (referral hospital)	43 [36 -72]	-	43 [36 -72]	-
[7]IHT travel time	25 [17 -35]	-	25 [17 -35]	-

Data are presented as median [interquartile range]. [1]Symptom onset to first hospital door arrival. [2]Symptom onset to PCI-H door arrival. [3]Symptom onset to balloon inflation. [4]First hospital door arrival to balloon inflation. [5]PCI-H door arrival to balloon inflation. [6]Referral hospital length of stay. [7]Inter-hospital transfer travel time. *p value: tested between direct and inter-hospital transfer patients using Mann Whitney U.

Table 4.3: Crude numbers and percentages of patient door-to-balloon times for all STEMI patients at PCI-H between 01/06/2013 to 31/12/2013, by transfer status.

		All (n=87) n (%)	Direct (n=51) n (%)	Transfers (n=36) n (%)	Sig. p>0.05
[1]DTB(first)	90 minutes or less	49 (62.8)	40 (87)	9 (28.1)	<0.001
	Greater than 90 minutes	29 (37.2)	6 (13)	23 (71.9)	
[2]DTB(first)	120 minutes or less	61 (78.2)	42 (91.3)	19 (59.4)	0.001
	Greater than 120 minutes	17 (21.8)	4 (8.7)	13 (40.6)	
[3]DTB(PCI-H)	90 minutes or less	51 (89.5)	40 (87)	11 (100)	0.205
	Greater than 90 minutes	6 (10.5)	6 (13)	0 (0)	

[1]First hospital door arrival to balloon inflation (90 minutes or less). [2]First hospital door arrival to balloon inflation (120 minutes or less). [3]PCI-H door arrival to balloon inflation. *p value: tested between direct and inter-hospital transfer patients using Chi Squared.

Table 4.4 shows that after accounting for confounding by socio-economic status, presentation date/time, transfer status, pre-hospital activation, pre-hospital ECG, mode of transport to the PCI-H, age and sex, statistically significant differences were observed with transfers having on average 118% longer delays from symptom-onset to first hospital arrival. This difference was further exacerbated when comparisons were made between STD (PCI-H) times, with transferred patients facing delays on average 162% greater than their direct counterparts, with model predicted average delays of 555 minutes (340-906 minutes) compared to 110 minutes (85-143 minutes) respectively. Transferred patients also experienced statistically significantly longer delays in STB times of 98% with model based predicted delays for direct patients at 167 minutes (141-198 minutes) rising to 447 minutes (307-652 minutes) for transfers. First hospital DTB times are 1.26 times longer for transferred patients, with the model predicting average times of 195 minutes (143-267 minutes) compared to just 55 minutes (48-64 minutes) for direct presentations. However, when measured from PCI-H arrival, no significant differences were observed.

Failure to have a pre-hospital activation notably increased DTB (first) by 81% and DTB (PCI-H) by 74%, increasing the overall time to treatment burden with predicted average first hospital DTB times of 69 minutes for those with pre-hospital activation jumping to 156 minutes for those without. Pre-hospital ECG statistically significantly reduced DTB (PCI-H) by 27% with an estimated marginal means of 49 (41-59 minutes) minutes; increasing to 64 (55-75) minutes for those who did not have a pre-hospital ECG. Experiencing DTB times of 90 minutes or less measured from both the first hospital and the PCI-H were found to significantly reduce the estimated mean length of stay by 51% and 59%, from four days to seven (5-9 days) and eight (5-13 days) respectively.

Table 4.4: Adjusted mean times‡ to treatment and length of stay by transfer status, cardiac catheterisation laboratory activation and pre-hospital ECG for all STEMI patients presenting to PCI-H between 01/06/2013 to 31/12/2013.

	Generalised Linear Model				Estimated Marginal Means					
		95% CI				95% CI			95% CI	
	Coef*	Lower	Upper	p>z	Mean	Lower	Upper	Mean	Lower	Upper
Transfer Status										
	(Inter-hospital transfer is baseline)				Direct Presentation			Inter-hospital Transfer		
[1]STD(first)	1.18	0.49	1.87	0.001	113	83	154	369	205	665
[2]STD(tertiary)	1.62	1.05	2.19	0.000	110	85	143	555	340	906
[3]STB	0.98	0.58	1.39	0.000	167	141	198	447	307	652
[4]DTB(first)	1.26	0.91	1.61	0.000	55	48	64	195	143	267
[5]DTB(PCI-H)	0.19	-0.17	0.55	0.308	55	48	63	67	49	91
CCL Activation										
	(No activation is baseline)				Pre-hospital Activation			No Pre-hospital Activation		
[3]STB	0.34	0.01	0.68	0.045	230	184	289	324	239	441
[4]DTB(first)	0.81	0.52	1.10	0.000	69	58	83	156	120	202
[5]DTB(PCI-H)	0.74	0.49	1.00	0.000	39	32	46	81	69	95
ECG										
	(No ECG is baseline)				Pre-hospital ECG			No Pre-Hospital ECG		
[3]STB	-0.51	-0.85	-0.17	0.004	353	256	487	212	171	262
[4]DTB(first)	0.15	-0.13	0.42	0.286	97	75	125	112	95	133
[5]DTB(PCI-H)	0.27	0.02	0.52	0.033	49	41	59	64	55	75
Length of Stay (Days) [for those with DTBs 90 mins or less]										
	(DTB > 90 mins is baseline)				DTB 90 mins or less			DTB Greater than 90 mins		
[4]DTB(first)	0.510	0.204	0.816	0.001	4	3	5	7	5	9
[5]DTB(PCI-H)	0.593	0.137	1.048	0.011	4	4	5	8	5	13

‡Models were adjusted for sex, age, socio-economic status, method of arrival to PCI-H, presentation date/time, pre-hospital ECG, pre-hospital activation and transfer status. *Coef: Coefficient B (relative proportional change in the mean value of the outcome variable in those transferred compared with the mean value in the baseline group). **p value: tested between groups within transfer status, cardiac catheterisation laboratory activation and pre-hospital ECG; using Wald Chi Square. ***Estimated Marginal Means: Estimated Marginal Means adjust for the covariate by reporting the means of Y for each level of the factor at the mean value of the covariate. [1]Symptom onset to first hospital door arrival. [2]Symptom onset to PCI-H door arrival. [3]Symptom onset to balloon inflation. [4]First hospital door arrival to balloon inflation. [5]PCI-H door arrival to balloon inflation.

4.5 Discussion

Despite DTB times from first hospital of presentation resulting in significantly longer delays to treatment for transferred patients, the majority of these patients experience pre-hospital activation and therefore fortunately have similar, if not improved, DTB(PCI-H) times compared to direct presentations. However, the inherent delay associated with initial presentation to a secondary hospital without CCL capabilities, requiring triage and diagnosis prior to transfer by road to a CCL hospital has important implications in the WA setting with travel notably hindering time to treatment[21]. An Italian study[22] showed similar results with the overall time to treatment metric longer for inter hospital transfers but those same patients showed a significantly shorter door to balloon delay when measured from the single centre, due to early mobilisation of the CLL team. Rezaee et al broke down the different components of delay after emergency medical services arrival and after accounting for 15 minutes as the median time-on-scene, a further 29-32 minutes for ED transfer to a CCL facility and consequent balloon inflation, found the maximum allowable transport time was 43-46 minutes [18]. In the Greater Perth region this figure may be challenging to achieve for outer metro patients, let alone their rural and remote counterparts due to the distances involved. Average travel times by road, from the most northern, southern and eastern tips of the Greater Perth region (Greater Capital City Statistical Areas) to Perth City central are 75 minutes [23]. Inter hospital transfers are a topic of debate worldwide with numerus initiatives addressing the need to reduce transfer related delays in the primary treatment of ACS[24]. A 2012 study from Brazil[25] showed direct presentations were associated with decreased total ischemia time, improve myocardial reperfusion markers and a non-significant decrease in hospital mortality; despite an integrated system which allows for a 60 minute time interval for inter-hospital transfer.

Pre-hospital ECGs have previously shown to reduce DTB times[26]; although this was not the case in our study when measured from first hospital DTB times, after controlling for the effects of transfers status and pre-hospital activation. However, PCI-H DTB times were impacted with 27% shorter DTB times for patients who had a pre-hospital ECG (49 v 64 mins; p=0.033). Similarly to this study, it has previously been shown any in-hospital time saving benefits from the acquisition of pre-hospital ECGs were only fully realised with the addition of pre-hospital CCL activation[18].

No statistically significant differences were noted in sociodemographic factors between direct and transfers for patient diagnosed as STEMI as per the International Classification of Disease[27]. Further, there were no statistically significant differences in the type of interventions performed. In lieu of more detailed data on severity of disease these figures indicate transferred patients were no more or less critical than direct presentations. Taking into consideration the overall longer delay to PCI therapy due to triage at the first hospital and time to transfer, in conjunction with pre-hospital activation, it would be reasonable to expect rapid DTB times once arriving at PCI-H to reduce overall delay burden. Unfortunately, this was not the case. Although the transfers occurred within recommended guidelines for a single hospital, the overall system delay needs to be taken into consideration.

The data does not include information on how patients arrived at secondary hospitals. Ambulance ECG was introduced to Western Australia in during 2012/2013[28]. Assuming all patients with ECG changes consistent with STEMI were taken directly to an available CCL, the patients who required transfer from a secondary hospital would have either self-presented to their nearest emergency department or were current inpatients. Given the transfer cohort would have known diagnoses of STEMI at the time of transfer, with 78% having pre-PCI-H CCL activation, it would be reasonable to expect rapid PCI-H DTB times. Although within

the guidelines for a single centre, overall, the burden of delay for these patients is well outside recommendations.

The single most effective measure to reduce the time burden from first medical contact to definitive treatment has been shown to utilise ambulance-initiated ECG. Early identification of STEMI changes en route means patients can be rerouted directly to a PCI-equipped hospital, avoiding transfers after ED triage[5,11,29-30]. A secondary option is the development of a coordinated system to record the time of ED arrival or ambulance retrieval which can then be accessed at the final receiving hospital to contribute to the time metrics analysis. Data including ECG changes, biomarkers and any initial treatments are recorded. There is compelling evidence Cardiac Registries across the world drive continuous improvements in patient care and inform a medical centres ability to adhere to guideline recommendations. Such registries can be utilised in conjunction with linked administrative health data, to complete the long-term picture of the burden of ACS and the short- and long-term outcomes[29,31-33].

If primary PCI cannot be performed within 90 minutes of first medical contact, thrombolysis should be considered as a primary reperfusion method. Every patient in this study was transferred for primary PCI as part of the inclusion criteria. However, as this is a single centre study, treatments and therapies initiated at the first hospital of treatment were not coded within the data to identify those patients being transferred for rescue PCI.

It is beyond the scope of this study to analyse patient outcomes post-therapy. Clinical recommendations have been established for the known improvements in outcomes with reduced time to therapy and as such the focus of the paper is on the impact of transfers on time to therapy, rather than short- and long-term outcomes. However, it has previously been shown that for every 30-minute delay in PCI there

is a 1% increase in absolute risk of dying in hospital[16,34] while another study showed an increase of 7.5% in risk of one-year mortality for every 30 minute delay to treatment[35]. In accordance with these findings, the median referral hospital length of stay of 52 minutes and mean transfer time of 25 minutes infers the addition of over an hour to the overall patient journey, ultimately increasing the absolute risk of in-hospital mortality by 2.0% with the one-year mortality risk at least 15% greater for transferred patients.

4.6 Limitations

Despite this study focusing on a single centre in the Perth Metropolitan area, all presentations of STEMI within the study time period were included, avoiding selection bias. Although the single centre nature may limit generalisability, reputable peer-reviewed publications[36-37] and leading epidemiological theorists[38] acknowledge cohort studies rely on validity or international comparisons to avoid systematic error. As such they do not need to be random sample of a large population to provide generalisable knowledge. Internationally renowned cohort studies, such as the British Doctors Study and US Nurses' Health Study are regarded as generalizable knowledge despite their highly selected study samples, as external validity of generalisation depends on considerations regarding effect modification rather than bias/confounding. The study sample included individuals from all five tiers of socio-economic status from north metropolitan, south metropolitan and WA country health catchment areas. The strength of this study is the routine and systematic nature of the collection of data on all patents presenting to the centre which reduced both selection and recall bias and the comprehensive inclusion of both clinical and administrative data points, allowing for the analysis of time to therapy, not typically possible with administrative datasets. This study was limited by the lack of available data pertaining to why patients presented to a secondary hospital in the first

instance and as such determinants of why patients did not present directly to the PCI-H are unknown.

Further times of ambulance arrival are not recorded within the data; and as such FMC-B cannot be measured. However, some patients would have self-presented to the first non-PCI hospital via private transport. In these instances, the secondary hospital arrival time would in fact be their FMC. A brief analysis of linked administrative health data using Emergency Department records in Western Australia (WA) shows 58% of ACS patients arriving at secondary hospitals were via private transport. Although this data is derived from a different source, it is from the same pool of ACS patients in WA and therefore these percentages are likely to be generalisable to our sample. Thus, if the secondary hospital arrival time is used as proxy for FMC, this would be the actual FMC for approximately 58% of our patients. The remaining 42% would therefore have time-to-treatments that are an under-estimation of the true burden of delay. In addition, there are no variables within the dataset that outline if the hospital received an ambulance ECG transmission; or if the PCI-H was notified of the incoming transfer. In lieu of this information, time of ECG, CCL activation and PCI-H arrival times were used to calculate pre-hospital ECGs for all patients; and pre-PCI-H activation of the CCL for transfers. Further limitations included the small number of cases in the dataset and some incomplete/empty data variables, particularly in time variables. The study was unable to follow patients after discharge and therefore unable to further assess 30-day and one year mortality. However, these outcomes were beyond the scope of this study which was concerned with determining the magnitude of delay associated with transfer from hospital type rather than its impact on patient outcomes.

4.7 Conclusions

Transferred patients' overall delay times from symptom-onset to balloon inflation is 98% longer than that of direct presentations, resulting in significantly longer infarct times and potentially poorer outcomes in the long term. This study highlights the extent to which the transfer process adds to the time to treatment burden and system delay. Despite pre-CCL capable hospital activation, PCI-H DTB times are not statistically significantly shorter than their direct cohort counterparts, representing a missed opportunity in the system to reduce the time delay burden for patients who required transfer for PCI. Inter-hospital transfers will remain an ongoing and unavoidable reality in WA's emergent treatment of ACS due to geographic and service provision challenges. The need for efficient triage to streamline transfer processes, avoidance of any unnecessary transfers by presenting directly to CCL facilities where possible, continuing education for the general public about using ambulance services and continued performance of pre-hospital activations are crucial to reduce system delay in the treatment of ACS.

4.8 Publication Declarations

Ethics approval and consent to participate.

Human Research Ethics Committee approval was obtained from Curtin University (HR 66/2013) and Sir Charles Gardiner Hospital (2013-067).

Availability of data and material

The datasets generated and/or analysed during the current study are not publicly available due to strict requirements set out by the Human Ethics Research Committees regarding the storage and use of the data by authorised investigators. Due to the small cell size of the study we can only produce results in aggregate form to preserve anonymity and confidentially.

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Chapter 5 Treatment pathways, mortality and readmissions following admission for incident diagnoses of Acute Coronary Syndromes across Western Australia using Linked Administrative Health Data 2007 – 2015

5.1 Abstract

Acute coronary syndromes (ACS) are responsible for morbidity, premature mortality, and rising healthcare costs across the world. In 2015 there were 2332 incident admissions for ACS in Western Australia (WA), 25% of which were rural patients. While primary percutaneous coronary intervention (PCI) is the recommended treatment pathway for presentations of ST-segment elevation myocardial infarction (STEMI), the most critical ACS manifestation, it is not feasible to have the necessary interventional facilities in every hospital. As a result, this leaves those STEMI presentations outside major population centres without timely access to such care, presenting a challenge for service utilisation across WA. The aim of this paper is to evaluate the in-hospital and post-discharge mortality, readmissions for ACS and treatment pathways for all incident admissions of ACS, including STEMI, across WA.

Linked Administrative Data between 01/01/2007 and 31/12/2015 from the WA Data Linkage System (WADLS) was used to identify whole-population admissions of adults presenting with an incident diagnosis of ACS. Socio-demographic and clinical characteristics were used to identify the comorbidity burden for each patient and their short- and long-term outcomes. Binary logistic regression, ordinal logistic regression and cox proportional hazards regression were used to model the association of rurality and transfers on the number of readmissions, the effect of comorbidities, rurality and primary diagnosis on the interventional treatment method used and the time to death or readmission, respectively.

65% of all admissions were males with a median presentation age of 64 years, compared to females at 73 years. Almost 25% of incident admissions were attributable to STEMI with an associated in-hospital mortality of 7% in this cohort. However, non-ST-segment elevation myocardial infarction (NSTEMI) accounted for the highest ACS burden at 47% of admissions. Approximately 78% of patients were

diagnosed with three or more comorbidities in the year prior to their incident admission. Rural patients had a 23% likelihood of undergoing PCI, compared to 66% of metropolitan admissions and all STEMI diagnoses had a 76% likelihood of undergoing PCI. Transferred patients experienced a 73% decrease in the risk of in-hospital mortality while rural patients who stay at the initial presenting hospital experienced a 21% higher risk of death from date of admission to all-cause mortality.

NSTEMI accounted for the highest number of presentations but can be one of the hardest manifestations to determine a treatment pathway. While in-hospital mortality was higher for STEMI presentations (7% compared to 2% for NSTEMI), in the subsequent year mortality in the NSTEMI cohort almost doubled that of STEMI patients, at 8% and 4% respectively. This highlights NSTEMI admissions represent a vulnerable group in ACS presentations. Appropriate risk-stratification for NSTEMI is important to inform the decision to treat in addition to appropriate post-discharge care and rehabilitation. This study showed the number of comorbidities is not a barrier to invasive treatment in WA even though 78% of the population had three of more comorbid conditions. Transferred patients also experienced lower rates of in-hospital mortality, which contrasts with what is known about longer infarct times and likely represents a number of patients who should have been transferred died prior to transfer, thereby positively pre-selecting this cohort.

Linked administrative data is an invaluable tool to evaluate the impact of rurality and transfers on short- and long-term outcomes encompassing the whole population of incident ACS presentations in Western Australia. However, the in-depth nature of cardiac registries should be used to compliment this data to further drive research in ACS, particularly in terms of the use of pre-hospital ECG, fibrinolysis and any risk-tools used to stratify NSTEMI presentations.

5.2 Introduction

Acute coronary syndromes (ACS) are a global health problem, contributing to significant morbidity and mortality. In 2015 there were 2332 admissions for an incident (first-time) diagnosis of ACS in Western Australia (WA) alone, an average of six admissions every day, of which 25% were attributable to rural dwelling patients[1]. Presentations of ACS are time-critical with earlier definitive treatment associated with more favourable outcomes, both short- and long-term[2-3]. This is particularly true for the most severe form of ACS, ST-segment elevation myocardial infarction (STEMI). Non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA), the two less serious manifestations require appropriate diagnosis and risk stratification to ensure treatment, preventative measures or rehabilitation are appropriated to minimise future morbidity or mortality[4-6]. A significant challenge in the WA landscape, and indeed for many similar landscapes across the world, is the vast land mass populated by a small proportion of the total state population[7-8]. The estimated resident population of WA in 2015 was 2.59 million; of which 79% live in greater Perth capital city region[9], resulting in sparsely populated rural and remote regions. In addition to physical barriers to treatment, rural and remote Australians are often characterised by poorer health, including comorbidities associated with ACS such as diabetes, smoking, alcohol consumption, poor diet, and irregular exercise[10-13].

Treatment of ACS may involve pharmacotherapy, invasive intervention, or a combination of both[4,14-15]. While pharmacotherapy can be administered by trained personnel in rural and remote areas, it is not always considered the gold standard of treatment in STEMI and high-risk NSTEMI. According to the 2016 National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand Clinical Guidelines for the Management of ACS patients presenting with STEMI within 12 hours of symptom onset should go on to have reperfusion therapy, either with

fibrinolytic therapy or primary percutaneous coronary intervention (PCI), unless contraindicated by advanced age, frailty or comorbidities which may impact overall survival [4]. The recommendations are to proceed with primary PCI as the preferred strategy in STEMI if it can be performed within 90 minutes of first medical contact (FMC). While this target may still be achievable for metropolitan presentations to non-PCI hospitals, although hindered by inter-hospital transfer delays, rural and remote presentations will experience significant unavoidable travel delays outside the recommended 90 minutes from FMC. Such presentations may be treated with fibrinolytic therapy and if there is less than 50% recovery of the ST-segment within 60-90 minutes or the presence of haemodynamic instability it is recommended the patient undergoes immediate transfer to a PCI-equipped hospital for angiography and rescue PCI, or transfer within 24 hours if PCI is still indicated[4].

Additional barriers to treatment are the number of comorbidities ACS patients may present with due to increased life expectancies[16]. Comorbid conditions are rarely diagnosed in isolation and there is anecdotal evidence that STEMI patients with higher comorbidity scores receive lower rates of reperfusion therapy[17] and experience a higher burden of ACS-related adverse events, including mortality, reinfarction and stoke[16]. With more people surviving their incident admission for ACS, the focus is turning to preventing further readmissions for ACS or other major adverse cardiovascular and cerebrovascular events (MACCE)[18]. Primary and secondary clinical endpoints are often described using MACCE including re-hospitalisation for reinfarction, heart failure, cardiac arrest, stroke and all-cause mortality[13,19].

With the previously aligned study[1] identifying 25% of admissions attributable to patients with a rural residential postcode, of which a quarter were diagnosed as STEMI; and 39% of all metropolitan presentations experiencing a transfer during the incident admission; and the high rate of incident admission being associated with

three or more comorbid conditions, the aim of this study was to evaluate the impact of rurality, inter-hospital transfers and comorbidity on the immediate, short- and long-term outcomes for incident presentations of ACS in Western Australia, namely in-hospital mortality, predicted survival following an admission for ACS and readmissions due to ACS or MACCE.

5.3 Methods

This paper has followed the Reporting of Studies Conducted Using Observational Routinely Collected Health Data (RECORD) Statement[20]. Detailed methodology including data sources, population selection, ascertainment of incident ACS events and patient characteristic have been previously published in an aligned study[1].

5.3.1 *Data Sources*

Linked Administrative Data from the WA Data Linkage System (WADLS) utilised the databases of the WA Hospital Morbidity Data System (HMDS), WA Emergency Department Data Collection (EDDC) and WA Death Registrations between 1 January 2007 to 31 December 2015, with a further five-year look-back period included for the HMDS collection, previously described in Forsyth et al.[1]

5.3.2 *Population*

Patients were identified and included in the cohort if they were 18 years of age or older with a WA residential postcode, admitted into a WA hospital between 1 January 2007 and 31 December 2015 for a first-time primary diagnosis of ACS. The International Classification of Diseases, Australian Modification (ICD-10-AM) codes were used to determine ACS events and comorbid conditions; while the Australian Classification of Health Interventions (ACHI), Tenth Revision from the National Centre for Classification in Health were used to determine ACS-related interventions.

5.3.3 *Patient Demographic and Clinical Data*

The socio-demographic variables of age, sex, Aboriginal or Torres Strait islander decent, postcode of residence and the Socio-Economic Indexes for Areas (SEIFA)[21] were coded directly within the data; as were clinical factors such as emergency department presentation date and time; hospital admission and discharge date and time; primary and secondary diagnoses of the admission and up to 20 additional diagnosis fields for identification of comorbid conditions using the Multipurpose Australian Comorbidity Scoring System (MACSS) [22]; principal procedure and up to 10 secondary procedures, including dates; and date of death.

In the event a patient was diagnosed with multiple types of ACS within the same episode of care, due to physical and statistical transfers within the data, the previous validated diagnosis hierarchy was applied, where the final diagnosis was the most severe, starting with STEMI, followed by NSTEMI and lastly UA as the least severe [1,23-24]. The first readmission after discharge from the incident event were reported if the diagnosis codes indicated the admission was due to ACS or MACCE. Subsequent readmissions were not included in the analysis. A summary of the ICD-10-AM and ACHI codes used for diagnosis, MACCE and interventions are included in Appendix 1.

5.3.4 *Statistical Analysis*

Categorical data were reported as frequency and percentages while continuous data were reported as the mean, standard deviation, and range. The Mann–Whitney U test and the Pearson chi-squared tests were used for between group analyses. The association between the number of readmission events and dichotomous variables for direct admissions versus transferred and metropolitan versus rural patients were estimated using binary logistic regression and presented as odds ratios with 95% confidence intervals and 5% level of significance. Ordinal logistic regression and

multinomial logistic regression was used to analyse the influence of comorbidities, metropolitan versus rural cohorts and primary diagnosis on the interventional treatment used. Cox proportional hazards regression was used to model the time at risk from admission to death or readmission, compared to survival to end of the study (census). The data sets were stratified by direct and transferred patients in order to meet the proportional hazards assumption. Candidate variables for both binary and multivariate logistic regression and Cox proportional hazards regression were selected as those likely to contribute to confounding given the observational nature of the data. These variables were age, sex, indigenous status, primary diagnosis, SEIFA, inter-hospital transfers (when not used to stratify the test) and one- and five-year cumulative MACSS, using a backward stepwise selection method, with $p>0.05$ set as the level of significance for variable inclusion. The number of incident admissions; and the number of patients who survived the incident admission, were used as the denominator to calculate the rates of mortality, readmission and comorbidities between metropolitan and rural patients.

5.4 Results

Unadjusted presentation numbers, stratified by primary diagnosis and metropolitan and rural transfers, are presented in Table 5.1, and demonstrate approximately 65% of admissions for incident ACS events were male, with the median presentation age of 64. Conversely female patients had a median presentation age of 73 years; with rural female patients presenting at a younger age, compared to metropolitan patients. NSTEMI accounted for the highest number of presentations over the nine-year study period (n = 10083), with males accounting for 60%, 64% and 72% of UA, NSTEMI and STEMI presentations, respectively. Almost half of all patients did not undergo any inter-hospital transfers; with 63% of UA presentations staying at the admitting hospital, compared to 53% of both NSTEMI and STEMI presentations being transferred during the incident admission. Of all STEMI presentations, 54%

underwent PCI (including balloon inflation and/or one or more stent insertions) and 24% under some other coronary procedure (catheterisation, angiography without balloon inflation or excision). Most admissions were categorised as emergent and diabetes was diagnosed in 19% of all admissions, while 2% of admissions experienced cardiac arrest a during the episode of care. There was a significant comorbidity burden with 78% and 88% of patients diagnosed with three or more comorbidities in the one and five years prior to the incident admission, respectively. In-hospital mortality was higher in the direct presentation groups for both metropolitan and rural admissions (4.4% and 5.3%). In-hospital mortality was highest in the STEMI group at 7%, followed by NSTEMI at 2% while in the 30 days after discharge mortality was similar for both NSTEMI and STEMI (2.8% and 2.5%). In the subsequent year after discharge, mortality was almost double for NSTEMI patients, compared to STEMI.

The adjusted prediction of receiving interventional treatment for ACS are presented in Table 5.2, after controlling for the effects of age, sex, primary diagnosis, inter-hospital transfers and one- and five-year MACSS scores. Rural patients had an average estimated probability of 53% ($p<0.001$) of receiving PCI therapy compared to 66% ($p<0.001$) of metropolitan patients. Rural patients were less likely to undergo any procedure of the coronary arteries (estimated probability = 0.426) than the metropolitan cohort (estimated probability = 0.291). STEMI diagnoses had an average estimated probability 76% ($p<0.001$) of receiving PCI therapy, and 3.3% ($p<0.001$) probability of CABG. Patients diagnosed with UA had the highest probability of undergoing CABG compared to NSTEMI AND STEMI at 6% ($p<0.001$); with 48% ($p<0.001$) of UA patients are treated with PCI. NSTEMI patients had the highest probability of being treated by PCI at 66% ($p<0.001$) and 5.3% ($p<0.001$) for CABG.

Table 5.1: Characteristics and outcomes of incident admissions for acute coronary syndromes by primary diagnosis and metropolitan and rural presentations in Western Australian between 01/01/2007 and 31/12/2015.

	All Incident Admissions			
	Total	**UA**	**NSTEMI**	**STEMI**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Total	n = 21648	6238 (28.8)	10083 (46.6)	5327 (24.6)
Male	14003 (64.7)	3753 (60.2)	6412 (63.6)	3838 (72.0)
Female	7645 (35.3)	2485 (39.8)	3671 (36.4)	1489 (28.0)
Age in years, males, median [std dev]	64 [13.8]	64 [12.7]	67 [14.1]	61 [13.9]
Age in years, females, median [std dev]	73 [14.7]	68 [13.7]	76 [14.6]	73 [15.3]
Nil procedures of the Coronary Arteries	6934 (32.0)	2864 (45.9)	3102 (30.8)	968 (18.2)
Percutaneous Coronary Intervention (PCI)*	13603 (62.8)	3014 (48.3)	6410 (63.6)	4179 (78.4)
Coronary Artery Bypass Graft	1111 (5.1)	360 (5.8)	571 (5.7)	180 (3.4)
Cardiac Arrest	366 (1.7)	21 (0.3)	112 (1.1)	233 (4.4)
Heart Failure	2639 (12.2)	236 (3.8)	1658 (16.4)	745 (14.0)
Diabetes	4107 (19.0)	1066 (17.1)	2143 (21.3)	898 (16.9)
No Comorbidities in 1 year prior	310 (1.4)	201 (3.2)	77 (0.8)	32 (0.6)
1 Comorbidity in 1 year prior	1767 (8.2)	587 (9.4)	677 (6.7)	503 (9.4)
2 Comorbidities in 1 year prior	2802 (12.9)	774 (12.4)	1184 (11.7)	844 (15.8)
3 or more Comorbidities in 1 year prior	16769 (77.5)	4676 (75.0)	8145 (80.8)	3948 (74.1)
No Comorbidities in 5 years prior	126 (0.6)	76 (1.2)	35 (0.3)	15 (0.3)
1 Comorbidity in 5 years prior	832 (3.8)	255 (4.1)	313 (3.1)	264 (5.0)
2 Comorbidities in 5 years prior	1529 (7.1)	389 (6.2)	643 (6.4)	497 (9.3)
3 or more Comorbidities in 5 years prior	19161 (88.5)	5518 (88.5)	9092 (90.2)	4551 (85.4)
Died during incident ACS admission	640 (3.0)	17 (0.3)	236 (2.3)	387 (7.3)
Died 0-30 Days after discharge	440 (2.0)	28 (0.4)	280 (2.8)	132 (2.5)
Died 31-365 Days after discharge	1194 (5.5)	192 (3.1)	787 (7.8)	215 (4.0)
Died 366+ Days after discharge	3004 (13.9)	794 (12.7)	1621 (16.1)	589 (11.1)
Readmission for UA	1016 (4.7)	496 (8.0)	351 (3.5)	169 (3.2)
Readmission for NSTEMI	1614 (7.5)	150 (2.4)	1290 (12.8)	174 (3.3)
Readmission for STEMI	661 (3.1)	49 (0.8)	157 (1.6)	455 (8.5)

PCI* including cardiac catheterisation, angiography, atherectomy, balloon angioplasty and one or more stent insertion. UA: Unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI ST-segment elevation myocardial infarction. n = total observed number in each category. %: percentage of total reported cases for each characteristic within each group. IHT: inter-hospital transfer.

Table 5.1 continued: Characteristics and outcomes of incident admissions for acute coronary syndromes by primary diagnosis and metropolitan and rural presentations in Western Australian between 01/01/2007 and 31/12/2015.

	Metropolitan		Rural	
	Direct	Yes, IHT	Direct	Yes, IHT
	n (%)	n (%)	n (%)	n (%)
Total	9590 (58.5)	6790 (41.5)	1609 (30.5)	3659 (69.5)
Male	6063 (63.2)	4476 (65.9)	963 (59.9)	2501 (68.4)
Female	3527 (36.8)	2314 (34.1)	646 (40.1)	1158 (31.6)
Age in years, males, median [std dev]	65 [13.90]	64 [13.41]	66 [14.97]	61 [13.48]
Age in years, females, median [std dev]	77 [14.02]	71 [13.96]	70.5 [16.04]	64 [14.18]
Nil procedures of the Coronary Arteries	3724 (38.8)	1377 (20.3)	1140 (70.9)	693 (18.9)
Percutaneous Coronary Intervention (PCI)*	5519 (57.5)	4941 (72.8)	409 (25.4)	2734 (74.7)
Coronary Artery Bypass Graft	347 (3.6)	472 (7.0)	60 (3.7)	232 (6.3)
Cardiac Arrest	164 (1.7)	108 (1.6)	15 (0.9)	79 (2.2)
Heart Failure	1186 (12.4)	827 (12.2)	181 (11.2)	445 (12.2)
Diabetes	1888 (19.7)	1343 (19.8)	336 (20.9)	896 (24.5)
No Comorbidities in 1 year prior	176 (1.8)	33 (0.5)	89 (5.5)	12 (0.3)
1 Comorbidity in 1 year prior	935 (9.7)	441 (6.5)	178 (11.1)	213 (5.8)
2 Comorbidities in 1 year prior	1302 (13.6)	860 (12.7)	198 (12.3)	442 (12.1)
3 or more Comorbidities in 1 year prior	7177 (74.8)	5456 (80.4)	1144 (71.1)	2992 (81.8)
No Comorbidities in 5 years prior	69 (0.7)	15 (0.2)	39 (2.4)	3 (0.1)
1 Comorbidity in 5 years prior	435 (4.5)	201 (3.0)	90 (5.6)	106 (2.9)
2 Comorbidities in 5 years prior	704 (7.3)	485 (7.1)	85 (5.3)	255 (7.0)
3 or more Comorbidities in 5 years prior	8382 (87.4)	6089 (89.7)	1395 (86.7)	3295 (90.1)
Died during incident ACS admission	422 (4.4)	97 (1.4)	85 (5.3)	36 (1.0)
Died 0-30 Days after discharge	179 (7.8)	135 (10.4)	37 (9.1)	89 (14.0)
Died 31-365 Days after discharge	616 (26.8)	316 (24.4)	104 (25.5)	158 (24.8)
Died 366+ Days after discharge	1502 (65.4)	845 (65.2)	267 (65.4)	390 (61.2)
Readmission for UA	474 (4.9)	313 (4.6)	86 (5.3)	143 (3.9)
Readmission for NSTEMI	804 (8.4)	523 (7.7)	92 (5.7)	195 (5.3)
Readmission for STEMI	287 (3.0)	182 (2.7)	66 (4.1)	126 (3.4)

PCI* including cardiac catheterisation, angiography, atherectomy, balloon angioplasty and one or more stent insertion. UA: Unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI ST-segment elevation myocardial infarction. n = total observed number in each category. %: percentage of total reported cases for each characteristic within each group. IHT: inter-hospital transfer.

Table 5.2: Estimated probability of receiving a treatment pathway, stratified by rural versus metropolitan patients and primary diagnosis for incident admissions of acute coronary syndromes between 01/01/2007 and 31/12/2015 in Western Australia (Multivariable Logistic Regression)

		Risk	95% CI		Sig.	Estimated	95% CI		Sig.
		Ratio	Lower	Upper	p<0.05	Probability	Lower	Upper	p<0.05
Residential Cohort									
Metro	**NIL**	-	-	-	-	0.291	0.285	0.297	<0.001
	PCI	-	-	-	-	0.657	0.651	0.664	<0.001
	CABG	-	-	-	-	0.052	0.048	0.055	<0.001
Rural	**NIL**	-	-	-	-	0.426	0.414	0.438	<0.001
	PCI	0.432	0.398	0.470	<0.001	0.526	0.514	0.538	<0.001
	CABG	0.519	0.443	0.608	<0.001	0.048	0.042	0.053	<0.001
Primary Diagnosis									
UA	**NIL**	-	-	-	-	0.445	0.434	0.455	<0.001
	PCI	-	-	-	-	0.488	0.477	0.499	<0.001
	CABG	-	-	-	-	0.067	0.061	0.074	<0.001
NSTEMI	**NIL**	-	-	-	-	0.290	0.282	0.297	<0.001
	PCI	2.577	2.380	2.790	<0.001	0.657	0.649	0.665	<0.001
	CABG	1.466	1.258	1.707	<0.001	0.053	0.049	0.058	<0.001
STEMI	**NIL**	-	-	-	-	0.212	0.201	0.222	<0.001
	PCI	4.574	4.139	5.054	<0.001	0.756	0.744	0.767	<0.001
	CABG	1.337	1.092	1.637	0.005	0.033	0.028	0.037	<0.001

UA: Unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI ST-segment elevation myocardial infarction. NIL: nil procedures of the coronary arteries; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft. Estimated Probability: the estimated average probability of the outcome based on the model (average predicted probability of selecting each alternative). 95% CI: 95% Confidence Intervals; Sig: statistical significance set to p<0.05. Variables in the model: cohort, age, sex, inter-hospital transfer, primary diagnosis, total comorbidities in the one year prior (1 Year MACSS) and total comorbidities in the five years prior (5 Year MACSS).

In the one-year prior to the incident admission, patients with no identified comorbidities had an average estimated probability of 72% ($p<0.001$) for not undergoing any procedure of the coronary arteries (Table 5.3). The average estimated probability of receiving PCI was 60% ($p<0.001$), 61% ($p<0.001$) and 64% ($p<0.001$) respectively for one, two and three or more comorbid conditions identified in the one year prior to the incident admission.

The adjusted odds (adjusted for age, sex, primary diagnosis, and one- and five-year MACSS scores) of dying in hospital were a fraction lower for rural patients, although not statistically significantly different to metropolitan patients. However, inter-hospital transfers had a 72% decrease in the odds of in-hospital mortality (OR=0.281 $p<0.001$). Rural presentations experience lower odds of readmission for UA and NSTEMI (OR=0.838, p=0.027 and OR=0.785, p=0.001) but 23% higher odds in readmission for STEMI (OR=1.233, p=0.034) compared to metropolitan patients. Patients who underwent an inter-hospital transfer have statistically significantly lower odds of being readmitted for NSTEMI, STEMI and heart failure (OR=0.8.24, p=0.003; OR=0.738, p=0.001; OR=0.807, p=0.001). The odds of readmissions for cardiac arrest and stroke were no different between metropolitan and rural patients, or between direct presentations and inter-hospital transfers. These results are summarised in Table 5.4.

Table 5.3: Estimated probability of receiving a treatment pathway, stratified by the number of comorbidities in the one- and five-years prior to an incident admission for acute coronary syndromes between 01/01/2007 and 31/12/2015 in Western Australia (Ordinal Logistic Regression)

		Odds	95% CI		Sig.	Estimated	95% CI		Sig.
		Ratio	Lower	Upper	p<0.05	Probability	Lower	Upper	p<0.05
MACSS in 1-Year Prior to Incident Admission									
0 Comorbidities	**NIL**	-	-	-	-	0.721	0.673	0.769	<0.001
	PCI	-	-	-	-	0.272	0.226	0.318	<0.001
	CABG	-	-	-	-	0.007	0.005	0.010	<0.001
1 Comorbidity	**NIL**	6.406	4.761	8.620	<0.001	0.352	0.332	0.371	<0.001
	PCI	-	-	-	-	0.604	0.588	0.620	<0.001
	CABG	-	-	-	-	0.044	0.039	0.049	<0.001
2 Comorbidities	**NIL**	6.486	4.849	8.675	<0.001	0.349	0.334	0.365	<0.001
	PCI	-	-	-	-	0.606	0.593	0.619	<0.001
	CABG	-	-	-	-	0.044	0.041	0.048	<0.001
3+ Comorbidities	**NIL**	7.915	5.968	10.497	<0.001	0.312	0.306	0.318	<0.001
	PCI	-	-	-	-	0.635	0.628	0.641	<0.001
	CABG	-	-	-	-	0.053	0.050	0.056	<0.001
MACSS in 5-Years Prior to Incident Admission									
0 Comorbidities	**NIL**	-	-	-	-	0.760	0.694	0.827	<0.001
	PCI	-	-	-	-	0.234	0.169	0.298	<0.001
	CABG	-	-	-	-	0.006	0.003	0.008	<0.001
1 Comorbidity	**NIL**	7.306	4.662	11.447	<0.001	0.373	0.344	0.402	<0.001
	PCI	-	-	-	-	0.587	0.563	0.610	<0.001
	CABG	-	-	-	-	0.040	0.034	0.046	<0.001
2 Comorbidities	**NIL**	8.337	5.377	12.925	<0.001	0.348	0.326	0.369	<0.001
	PCI	-	-	-	-	0.607	0.590	0.625	<0.001
	CABG	-	-	-	-	0.045	0.040	0.050	<0.001
3+ Comorbidities	**NIL**	9.689	6.323	14.846	<0.001	0.319	0.313	0.325	<0.001
	PCI	-	-	-	-	0.629	0.623	0.635	<0.001
	CABG	-	-	-	-	0.052	0.049	0.055	<0.001

MACSS: Multipurpose Australian Comorbidity Scoring System. NIL: nil procedures of the coronary arteries; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft. 95% CI: 95% Confidence Intervals; Sig: statistical significance set to p<0.05. Variables in the model: cohort, age, sex, primary diagnosis.

Table 5.4: Estimated probability of in-hospital mortality and readmission for rural patients and inter-hospital transfers after an incident admission for acute coronary syndrome between 01/01/2007 and 31/12/2015 in Western Australia (Binary Logistic Regression)

		Odds	95% CI		Sig.	Estimated	95% CI		Sig.
		Ratio	Lower	Upper	p<0.05	Probability	Lower	Upper	p<0.05
Outcome by Residential Postcode									
	Metro	-	-	-	-	0.024	0.022	0.026	<0.001
Died In-Hospital	Rural	0.920	0.714	1.185	0.519	0.022	0.018	0.027	<0.001
	Metro	-	-	-	-	0.050	0.047	0.054	<0.001
Readmission for UA	Rural	0.838	0.716	0.980	0.027	0.043	0.037	0.048	<0.001
	Metro	-	-	-	-	0.077	0.073	0.081	<0.001
Readmission for NSTEMI	Rural	0.785	0.679	0.909	0.001	0.062	0.055	0.069	<0.001
	Metro	-	-	-	-	0.029	0.026	0.031	<0.001
Readmission for STEMI	Rural	1.233	1.016	1.497	0.034	0.035	0.030	0.040	<0.001
	Metro	-	-	-	-	0.003	0.002	0.004	<0.001
Readmission for Cardiac Arrest	Rural	0.865	0.456	1.641	0.657	0.002	0.001	0.004	0.001
	Metro	-	-	-	-	0.058	0.054	0.061	<0.001
Readmission for Heart Failure	Rural	1.059	0.907	1.237	0.468	0.060	0.053	0.068	<0.001
	Metro	-	-	-	-	0.007	0.006	0.009	<0.001
Readmission for Stroke	Rural	0.926	0.625	1.374	0.704	0.007	0.004	0.009	<0.001
Outcome stratified by Inter-Hospital Transfers									
	Direct	-	-	-	-	0.035	0.032	0.038	<0.001
Died In-Hospital	IHT	0.281	0.224	0.352	<0.001	0.011	0.009	0.013	<0.001
	Direct	-	-	-	-	0.048	0.044	0.052	<0.001
Readmission for UA	IHT	1.000	0.876	1.143	0.997	0.048	0.044	0.053	<0.001
	Direct	-	-	-	-	0.079	0.074	0.084	<0.001
Readmission for NSTEMI	IHT	0.842	0.753	0.942	0.003	0.068	0.063	0.073	<0.001
	Direct	-	-	-	-	0.035	0.031	0.039	<0.001
Readmission for STEMI	IHT	0.738	0.621	0.876	0.001	0.026	0.023	0.029	<0.001
	Direct	-	-	-	-	0.003	0.002	0.004	<0.001
Readmission for Cardiac Arrest	IHT	0.884	0.527	1.482	0.640	0.003	0.002	0.004	<0.001
	Direct	-	-	-	-	0.063	0.059	0.068	<0.001
Readmission for Heart Failure	IHT	0.807	0.710	0.916	0.001	0.053	0.048	0.057	<0.001
	Direct	-	-	-	-	0.007	0.006	0.009	<0.001
Readmission for Stroke	IHT	1.067	0.773	1.474	0.692	0.008	0.006	0.009	<0.001

UA: Unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI ST-segment elevation myocardial infarction. IHT: inter-hospital transfer. 95% CI: 95% Confidence Intervals; Sig: statistical significance set to p<0.05. Variables in the model: cohort, age, sex, Indigenous status, inter-hospital transfer, primary diagnosis, total comorbidities in the one year prior (1 Year MACSS) and total comorbidities in the five years prior (5 Year MACSS).

As described in Table 5.5, direct presentations in the rural cohort had a 21% (p=0.007) higher risk of death from the date of incident admission to all-cause mortality, 11% (p=0.038) higher risk of dying in-hospital and 22% (p<0.001) higher risk of death after discharge, for those who survived the hospital admission after adjusting for confounders (rural versus metropolitan cohort, age, sex, Indigenous status, primary diagnosis and total comorbidities in the one- and five-years prior to admission). Comparatively, the inter-hospital transfers group also experienced higher risks of death in the rural population from admission to death, in-hospital mortality, and post-discharge mortality (HR=1.318, p<0.001; HR=1.637, p<0.001; HR=1.260, p<0.001). Rural patients who did not undergo inter-hospital transfer had a non-statistically significant higher risk of readmission compared to metropolitan patients; and inter-hospital transfers had a slightly lower risk of readmission, although non-statistically different to metropolitan patients.

Table 5.5: Hazard Ratio for rural versus metropolitan patients, stratified by inter-hospital transfers, from incident admission for acute coronary syndrome to all-cause mortality or readmission after an incident admission for acute coronary syndrome between 01/01/2007 and 31/12/2015 in Western Australia (Multivariable Cox-Proportional Hazards Regression)

	Direct Presentations				Inter-Hospital Transfers			
Outcome	**Hazard**	**95% CI**		**Sig.**	**Hazard**	**95% CI**		**Sig.**
Time at Risk	**Ratio**	**Lower**	**Upper**	**p<0.05**	**Ratio**	**Lower**	**Upper**	**p<0.05**
Admission to Post-Discharge Death	1.210	1.054	1.389	0.007	1.318	1.152	1.508	<0.001
Admission to In-Hospital Death	1.113	1.006	1.232	0.038	1.637	1.418	1.890	<0.001
Discharge to Death	1.224	1.100	1.361	<0.001	1.260	1.137	1.398	<0.001
Discharge to Readmission	1.060	0.912	1.232	0.448	0.908	0.803	1.026	0.122

95% CI: 95% Confidence Intervals; Sig: statistical significance set to p<0.05. Variables in the model: cohort, age, sex, inter-hospital transfer, primary diagnosis, total comorbidities in the one year prior (1 Year MACSS) and total comorbidities in the five years prior (5 Year MACSS).

5.5 Discussion

Comorbidities rarely occur in isolation, as was found in this study, with over 77% of admitted patients experiencing three or more comorbid conditions diagnosed in the year prior to admission and 88% in the five years prior. Comorbidities represent a unique challenge in ACS treatment with the number and severity of comorbidities contributing to increased adverse outcomes, including mortality, reinfarction, ischemic stroke and major bleeding. Previous literature has sighted a higher economic burden associated with increasing comorbidities, due to longer length of hospital stays and higher hospitalisation charges[16]. Further, there is anecdotal evidence from outside of Australia to suggest rates of fibrinolysis and PCI are lower in the higher comorbidity score demographic group[16-17]. After controlling for the effects of age, sex, SEIFA, inter-hospital transfers and one- and five-year MACSS this study found that the number of comorbid conditions was not a barrier to patients receiving invasive therapy, with 68% of all presentations undergoing PCI or CABG, with almost 80% of STEMI diagnoses being treated by PCI while patients diagnosed with UA were more likely to undergo CABG. The distinction between the two treatment pathways (PCI versus CABG) has been the debate of several randomised control trials which showed CABG was more effective in the treatment in UA, resulting in fewer repeat revascularisation procedures, despite the more invasive approach with a higher risk of procedural stroke and sternotomy wound infection[25]. Further, randomised control trials have shown CABG to be associated with lower mortality rates in diabetic patients with multi vessel coronary disease[26]. Admitted patients with no identified comorbidities were 72% less likely to undergo any invasive intervention procedure. Although this trend is in contrast to international literature[16] these patients could be considered “less sick” and therefore after risk stratification can be appropriately managed with medications and/or lifestyle modifications; or be discharged and be followed up in the outpatient setting.

Unadjusted data showed in-hospital mortality was three times higher for STEMI presentations compared to NSTEMI. However, in the first 30 days after discharge crude mortality was similar in both cohorts and between 31-days and 1-year, NSTEMI mortality almost doubled that of STEMI. While NSTEMI also contributes the highest number of incident ACS presentations, it can be the most challenging to diagnose and determine the most appropriate treatment pathway[4], particularly with the NSTEMI demographic having a higher median age compared to STEMI and UA counterparts. These patients require risk stratification for the most appropriate intervention, if any, to prevent further infarction or mortality[4-5,27-28]. While the recommendations for treatment of STEMI and high-risk NSTEMI are definitive, low-risk NSTEMI is less clear with an estimation of the risk of infarct used for evaluation for the appropriateness of the site of care, including if inter-hospital transfer is indicated and the selection of reperfusion therapy[5]. Routine early use of an invasive strategy in all patients presenting within NSTEMI and UA, in the absence of individual risk identification, has been shown to be unlikely to reduce mortality, recurrent myocardial infarction or bleeding and as such the benefit associated with an invasive approach within 24 hours of first medical contact, in those who do not exhibit high or very-high risk criteria, are not yet proven[4]. Yet, this group in the 12 months after discharge for an incident presentation of ACS have the highest mortality and therefore represent a particularly vulnerable group in ACS. It has been recognised that individuals who have survived an acute cardiac event are at an increased risk of further cardiac events, including readmission for ACS or MACCE and death[29]. Therefore, with NSTEMI patients showing worse long-term outcomes, these patients require particular attention post-discharge including cardiac rehabilitation and lifestyle modifications becoming a priority[18].

Although unadjusted numbers of in-hospital mortality were lower in both the rural and transferred cohorts, this appears to be counterintuitive given that rurality and inter-hospital transfers can be associated with longer infarct times prior to invasive

treatment, often compounded by reportedly higher life-style risk factors and comorbidities, this trend has been cited in previous literature surrounding inter-hospital transfers[1,3,30-32]. The explanation for this finding could be that this cohort is positively pre-selected for analysis, as some will have died prior to transfer or arrival to a medical facility, a form of immortal time bias[32]. In our study rural patients had increased odds of being readmitted for STEMI, but decreased odds for UA and NSTEMI; while transferred patients had lower odds of readmission for NSTEMI, STEMI and heart failure. This trend could be explained by several factors, namely the aforementioned positive pre-selection of these patients surviving their initial hospitalisation combined with appropriate risk stratification and treatment pathways meaning they are less likely to be readmitted in the future. Comparatively, these figures could be explained by fewer patients surviving their second ACS event, dying prior to readmission.

Although patients with a rural residential postcode made up a quarter of total admissions over the study timeframe, actual presentation rates are slightly higher in the rural cohort compared to metropolitan patients, using the estimated residential population from the Australian Bureau of Statistics[1,33]. Rural patients are often characterised by poorer health status and have poorer access to recommended treatment pathways in the setting of ACS[4,10-13,34]. After controlling for the effects of age, sex, inter-hospital transfer, primary diagnosis and comorbidities, rural patients are less likely to undergo PCI which could be attributed to less readily available access to interventions, including PCI and CABG, plus longer infarct times from first medical contract, when the time of inter-hospital transfer is considered, putting these patients outside the recommended guidelines for primary PCI. Rural patients have a worse survival prognosis with higher hazard ratios in both direct and transferred cohorts after controlling for cohort, age, sex, inter-hospital transfer, primary diagnosis, total comorbidities in the one year prior (1 Year MACSS) and total comorbidities in the five years prior (5 Year MACSS). Of most concern is the risk of

in-hospital death for transferred patients (HR=1.637). While inter-hospital transfers are an unavoidable reality for rural patients when invasive therapy is indicated, these patients experience poorer survival in-hospital and slightly poor survival post-discharge compared to transferred metropolitan patients. Although likely due to the compounding nature of longer infarct times with poorer health status, initiatives to improve morbidity and mortality in rural populations must continue to be a focus to reduce the metropolitan-rural health differential. While it is unrealistic to expect PCI-equipped facilities in every rural centre, primary health care can play a role to identify patients at risk prior to an ACS event and encourage life-style modifications or appropriate risk stratification and outpatient diagnostic tests, to treat patients before an acute event. In addition, patient recognition of symptoms and the willingness to seek help need to be improved; followed up adherence to current Australian guidelines for treatment in ACS.

5.6 Strengths and Limitations

This study has several key strengths and limitations. The first strength is the ability of linked administration data to overcome the challenges of over-counting due to multiple inter-hospital and statistical data transfers which can plague cardiac registries[35] . In addition, as this method is whole-of-population, there is no sampling bias since every adult having a hospitalisation for ACS is included within the cohort. This allows for a large sample size, generalisable results and enables researchers to capture absolute values, such an incidence, prevalence and risk within the specified population. In addition, there is no loss to follow up within the included time frame and as the WADLS uses linkage keys for anonymised data, there is high accuracy in identifying the same patient across multiple episodes of care. However, the WADLS has no current way to track patients who may be admitted to hospital for ACS or MACCE, or die, in another state or territory.

As fibrinolytic therapy and prescribed medications were unavailable data sources within the WADLS at the time of data collection, nor the times of symptom onset, first medical contact, hospital arrival time and balloon or needle time, it is beyond the scope of this study to assess adherence to current Australian guidelines. Further, the lack of further finite clinical detail, including height, weight, and other lifestyle factors. In these areas cardiac registries have the ability to out-perform linked administrative data; although are often not whole of population or may capture data for only a short time period.

5.7 Conclusion

This paper provides information on the impact of rurality, comorbidities, and inter-hospital transfers on treatment pathways, mortality, and readmissions for ACS. This study presents conflicting data with that of previous publications regarding an inverse relationship between increased numbers of comorbidities and invasive treatment approaches. Our population had a high comorbidity burden with 78% of all presentations presenting with three or more comorbidities identified in the 12 months prior to admission yet 68% went on to receive some sort of invasive treatment pathway, be it PCI with balloon inflation or one or more stent insertions; or CABG. Further, this study has highlighted the inherent problems of emergent service utilisation for rural patients, with lower numbers of in-hospital mortality likely reflecting a positive pre-selection for the cohort, with more patients dying prior to admission. In-hospital mortality for all patients stood at 3% with 7% of STEMI presentations dying in hospital. A system of integrated cardiac monitoring, utilising both linked administrative data and on site cardiac registries have the potential to further inform resource utilisation, in-hospital and post-discharge outcomes for patients presenting with ACS[4].

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Chapter 6 Discussion, Conclusion and Future Directions

This study has highlighted the significant burden of acute coronary syndromes (ACS) in Western Australia (WA) and the potential economic impact this condition represents to the government. Chapter 3 presents whole-of-population rates of admission between 2007 and 2015 in WA, stratified by health region, age and type of ACS diagnosis. Accurate presentation numbers are essential to evaluate the true burden of ACS across WA, future health service utilisation planning, and assessing the economic burden to the state government. Although ST-segment elevation myocardial infarction (STEMI) accounts for the most significant in-hospital and 30-day mortality, the substantial number of non-ST-segment elevation myocardial infarction (NSTEMI) presentations, almost double that of STEMI, combined with the higher rates of 1-year mortality and readmissions for NSTEMI show these patients are a vulnerable population. Appropriate risk assessment for NSTEMI and unstable angina (UA) is essential for improving both short- and long-term outcomes including future admissions. In addition, due to the geography of WA, inter-hospital transfers are likely to cause unavoidable delay for many presentations of ACS.

With clear guidelines for treatment, particularly in STEMI presentations, treatment options for those patients outside the window of treatment with primary percutaneous coronary intervention (PCI) can rely on fibrinolytic therapy and rescue PCI if required. An integrated and coordinated health care system is essential for both diagnosing, triaging, and deciding on the most appropriate therapy given the time elapsed since symptom onset and the realistic time to transfer to a PCI-equipped facility. For metropolitan patients, the analysis of and symptom-onset to balloon inflation times showed the overall delay for patients requiring an inter-hospital transfer is 98% longer compared to direct presentations to a PCI-equipped hospital. As this component of the study focused on a metropolitan cohort only, it highlights the missed opportunity to assess and triage ambulance patients enroute and bypass non-PCI equipped hospitals. Conversely, pre-hospital triage is not

possible for patients who present to hospitals in private transport, emphasizing the need for further education campaigns to raise awareness of the symptoms of ACS and the importance of calling an ambulance when experiencing symptoms.

As discussed in Chapter 1, the two validated tools for individual risk assessment (TIMI Score[1] and GRACE Calculator[2]) require finite details of pulse rates, systolic blood pressure, renal function, presence of cardiac arrest, coronary artery disease risk factors and known coronary artery disease, diabetes, ST-segment changes on ECG and abnormal cardiac biomarkers. Although potentially a routine part of all cardiac care assessment in Australian hospitals, as these variables are not coded within the HMDS there is no way for linked administrative data to evaluate long-term outcomes such as survival and readmissions based on TIMI or GRACE. However, the data is poised to evaluate the long-term survival of patients presenting with ACS. If hospital-led cardiac registries were to record this information, larger research studies in the future may incorporate HMDS data with clinical cardiac registries which would put WA in the unique position to evaluate short- and long-term outcomes for patients, not just based on their diagnosis and type of invasive therapy received but also on their individual risk assessments at the time of presentation.

While the opportunity for pre-hospital care is an administrative challenge, it is an essential component to reduce the time-to-treatment burden by allowing pre-hospital triage. Strategies including ambulance acquisition of 12-lead ECG enroute ensure direct presentation to a hospital equipped and staffed for PCI for those patients presenting within a suitable time from symptom onset to first medical contact; while in more rural and remote settings pre-hospital triage could ensure earlier activation of emergency transfer, by road or air; and administration of fibrinolytic therapy unless contraindicated. Rural and remote populations are recognised as being more at risk for in-hospital and post-discharge mortality and present at a younger age compared to metropolitan counterparts. Although rural and remote patients

represent a more vulnerable community, it is unrealistic to expect cardiac catheterisation facilities outside of densely populated regions, nor to have sufficient and continually developing staff skill levels available in remote areas. As such, for rural and remote West Australians and many isolated populations across the world, equitable health care will mean the burden of inter-hospital transfer will remain an ongoing reality.

This thesis presents both the advantages and limitations of both linked administrative data available through the Western Australian Data Linkage System (WADLS) and standalone cardiology department data registries. The integration of these data collection systems would result in fewer gaps in the health care chain of triage, diagnosis, treatment, and future prevention. Future models of care for improved patient outcomes require a coordinated system-wide approach from patient recognition and initiation of calling for help, rapid stabilisation of patients suspected of ACS and expediated reperfusion options for STEMI and high risk NSTEACS, including presentations of cardiac arrest. For both metropolitan and rural outcomes to be effectively assessed and improvements tracked overtime, assessment of the full chain of care through reliable systemic record keeping and analysis of the long-term trends and patterns for ACS admissions and outcomes will drive public policy and continue to be a benchmark for decision makers. Clinician led clinical registries are considered to be at the forefront of evaluation of health care delivery[3] providing assessment of the performance of therapeutic and rehabilitative interventions globally and more locally ensuring performance of individual health services meet minimum benchmarks. However, the “bigger picture”, that is whole-of-population longitudinal data, should be considered just as essential for evaluation of service delivery and patient outcomes.

As such, future research directions should focus on the integration of the two types of clinical data sets presented in this thesis. This will involve further research and infrastructure to allow individual cardiac registries to be linked into the WADLS to enhance the already extensive datasets available. The single cardiac registry presented in this thesis already has the potential to be linked into the WADLS chain as key demographics are routinely collected (name, date of birth, address) although this was de-identified prior to the provision of this data. However, that process is both outside the scope and ethical approval of this study. Further, as the cardiac registry was non-compulsory, some data points for certain admissions were missed. For this to be successful long term, there would need to be a rigorous system of data entry, similar to the standards outlined for HMDS and EDDC data collections.

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Publications presented in the Thesis

Statement of Contributions of Others – Paper 1 (Chapter 4)

Journal: Journal of Geriatric Cardiology

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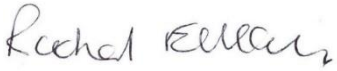
	Conception and Design	Acquisition of Data and Method	Data Conditioning and Manipulation	Analysis and Statistical Method	Interpretation and Discussion	Final Approval	Total % Contribution
Co-Author 1: R. Forsyth	40	40	40	40	25	25	35
Co-Author 1 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
Co-Author 2: Z. Sun	10	10	10	15	25	25	16
Co-Author 2 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
Co-Author 3: C. Reid	10	10	10	15	25	25	16
Co-Author 3 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
Co-Author 4: R. Moorin	40	40	40	30	25	25	33
Co-Author 4 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
Total %	100	100	100	100	100	100	100

Copy of the original publication (Paper 1 – Chapter 4)

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Research Article · Open Access ·

Inter-hospital transfers and door-to-balloon times for STEMI: a single centre cohort study

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Abstract

Background Key performance indices such as door-to-balloon times have long been recognized as quality metrics in reducing time to care for patients with acute coronary syndromes (ACS). In the situation where patients do not present to a facility capable of 24/7 percutaneous coronary interventions (PCI) delays in time to therapy can exceed the recommendation of 90 minutes or less. This study aimed to evaluate the impact of transfers on performance indices for patients diagnosed with ST-segment elevation myocardial infarction (STEMI). **Methods** Over a seven month collection period, all patients presenting with symptoms suggestive of ACS and admitted for PCI were studied. Patients were divided into dichotomous groups of direct presentations or transfers from a secondary non-PCI capable hospital with key times recorded, including symptom-onset, first hospital and PCI-capable hospital arrival and balloon inflation times to evaluate time of treatment for STEMI patients. **Results** Of the 87 patients diagnosed with STEMI, transferred patients experienced statistically significant delays in symptom-onset to the PCI-capable hospital (PCI-H) arrival (215 *vs.* 95 min, $P < 0.001$), symptom-onset to balloon inflation (225 *vs.* 160 min, $P = 0.009$) and first hospital arrival to balloon inflation times (106 *vs.* 56 min, $P < 0.001$). Only 28% ($n = 9$) of transferred patients underwent balloon inflation within 90 minutes from first hospital arrival, while 60% ($n = 19$) did within 120 minutes, although all received balloon inflation within 90 minutes from arrival at the PCI-H. After controlling for confounding factors of socio-economic status, presentation date/ time and diagnostic category, transferred patients experienced an average 162% longer delays from symptom-onset to PCI-H door arrival, and 98% longer delays in symptom-onset to balloon inflation; compared to patients who present directly to the PCI-H. No statistically significant differences were noted between transferred and direct patients when measured from PCI-H door-to-balloon times. **Conclusions** This study shows that transferred patients experience a greater overall system delay, compared to patients who present directly for PCI, significantly increasing their time to treatment and therefore infarct times. Despite the majority of transfers experiencing pre-hospital activation, their treatment hospital arrival to balloon times are no less than direct presenters after controlling for confounding factors, further compounding the overall delay to therapy.

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Keywords: Acute coronary syndrome; Door-to-balloon times; Inter-hospital transfers; ST-segment elevation myocardial infarction

1 Introduction

Cardiovascular disease is recognised as a leading cause of death and disability across the globe with troubling disparities noted between metropolitan and rural communities.[1–3] Australia has identified this as an area of priority under the National Health Priority Area initiative.[4] Specifically, acute coronary syndrome (ACS) which collectively spans presentations of acute myocardial infarction, including ST-segment elevation myocardial infarction (STEMI), non-STEMI and unstable angina[5,6], was the cause of death for 6.1% Western Australians in 2015.[7] Presentations of STEMI are considered medical emergencies and positive outcomes including lower mortality rates are highly correlated with timely reperfusion of the culprit vessel.[8–11] Given this time crucial nature, there has been considerable focus surrounding the reduction of measurable performance indices for time to therapy, namely door-to-

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electrocardiogram (DTE), door-to-needle (DTN) and door-to-balloon (DTB) times for ACS patients; and more recently time from first medical contact to balloon times (FMC-B). Reduction in time to therapy is associated with improved outcomes and as such several international professional organisations have reached a consensus, calling for DTE times within 10 minutes for all presentations and DTB times of 90 minutes or less for patients who present direct to a hospital equipped with a cardiac catheterisation laboratory (CCL) for percutaneous coronary interventions (PCI).[8,9,12,13] Those patients who require transfers for PCI should have early activation of the CCL to reduce avoidable delays.[13] The 2016 Australian Clinical Guidelines for the Management of Acute Coronary Syndromes recommends primary PCI as the preferred reperfusion strategy for those patients diagnosed with STEMI, if it can be performed within 90 minutes of first medical contact (FMC); otherwise proceed to thrombolysis in the absence of contraindications.[14] Prior to the 2016 update, DTB times within 90 minutes were the key performance objective in Australia.[13]

Timely transfer to PCI capable hospitals has been shown to reduce rates of death, re-infarction and stroke compared to on-site fibrinolysis[14,15] and strategies have been introduced to reduce avoidable delays namely emergency department activation[16,17]; pre-hospital activation;[17] 30 minutes mobilisation of on call staff;[16,17] and ambulance based electrocardiogram (ECG) results transmission.[18,19]

The aim of this study was to analyse the impact of inter-hospital transfers within the Perth Metropolitan region on overall time-to-treatment when a patient needs to be transferred from a non-PCI capable metropolitan hospital to a facility that can offer round-the-clock PCI.

2 Methods

2.1 Study population

Data of all Western Australians resident patients aged 18 years or older who presented to a single Perth metropolitan teaching hospital, PCI-capable hospital (PCI-H), with round-the-clock CCL facilities with a diagnosis of STEMI between June 2013 and December 2013 were de-identified for analysis. Data for every admission to the PCI-H Cardiovascular Medicine Department are routinely collected as part of the department's standard clinical management program, as a single-centre cardiac registry. Human Research Ethical approval was obtained prior to data collection from the Human Research Ethics Committees of the Western Australian Department of Health, Curtin University, and the PCI-H.

2.2 Characteristics of participants

Socio-demographic data included a unique de-identified patient number, birth year, sex and postcode of residence; in addition to the clinical variables of admission date, discharge date, time of symptom-onset, PCI-H arrival time, time of ECG, time of CCL activation, procedure start time, time of first balloon inflation, procedure end time, principal diagnosis, principal procedure (PCI, stent insertions, coronary artery bypass graft), mode of arrival, length of stay in hospital and mode of discharge from the PCI-H. Additionally for those patients who were transferred from another hospital, first hospital arrival time and first hospital departure time were also available. Time-to-event variables were calculated from the difference in the time recorded between the two key events of interest and span symptom-onset to first hospital arrival [STD (First)], symptom-onset to PCI-H arrival [STD (PCI-H)], symptom-onset to first balloon inflation (STB), first hospital arrival to first balloon inflation [DTB (First)], PCI-H arrival-to-first balloon inflation [DTB (PCI-H)], first hospital length of stay (referral LOS) and inter-hospital transfers (IHTs), all measured in minutes. Pharmacological treatments are not coded in the data and as such DTN times could not be assessed, and it is unknown if transferred patients received thrombolytic therapy prior to transfer. Times of ambulance arrival were not recorded within the dataset and as such FMC to balloon times could not be evaluated.

2.3 Statistical analysis

All analyses were performed using SPSS Statistics Version 22 (IBM Corporation, Armonk, NY, USA). Statistical significance was assigned at the level of $P < 0.05$. Categorical data were reported as frequencies and percentages, while continuous variables were reported as mean or medians, with standard deviations and range. 'Between-group' analyses were completed using Mann-Whitney *U* Test and the Pearson Chi Squared test, respectively. Multivariable generalised linear modelling applying a Gamma distribution with a log link function were performed to evaluate key times and identify predictors impacting length of stay for STEMI patients: candidate variables were chosen as those likely to contribute to confounding given the observational nature of the study (sex, age, socio-economic status, method of arrival to the PCI-H, presentation date/time, pre-hospital ECG, pre-hospital activation and transfer status) and were included in final models after backwards stepwise selection using $P > 0.05$ as the level of significance for variable inclusion.

3 Results

Table 1 presents 107 subjects who met inclusion criteria

Table 1. Socio-demographic, clinical characteristics and outcomes for all patient diagnosed with STEMI by transfer status.

	All (n = 107)		Direct (n = 66)		Transfers (n = 41)	
	n*	%**	n*	%**	n*	%**
Age, yrs	60 ± 11.7		60 ± 11.3		59 ± 12.3	
Sex						
Male	87	81.3	56	84.8	31	75.6
Female	20	18.7	10	15.2	10	24.4
SEIFA						
Highest disadvantage	7	6.6	5	7.6	2	5.0
High disadvantage	8	7.5	3	4.5	5	12.5
Moderate disadvantage	15	14.2	11	16.7	4	10.0
Less disadvantage	16	15.1	11	16.7	5	12.5
Least disadvantage	60	56.6	36	54.5	24	60.0
Health service area						
North metropolitan	95	89.6	57	86.4	38	95.0
South metropolitan	8	7.5	6	9.1	2	5.0
Western Australia country	3	2.8	3	4.5	0	0.0
Arrival mode						
Medical transport	90	86.5	52	78.8	38	100.0
Private transport	14	13.5	14	21.2	-	-
Presentation date/time^						
Weekday, 8 am–5 pm	40	40.0	26	44.1	14	34.1
Weekday, after hours	33	33.0	19	32.2	14	34.1
Weekend, 8 am–5 pm	16	16.0	8	13.6	8	19.5
Weekend, after hours	11	11.0	6	10.2	5	12.2
Pre-hospital activation						
Yes	27	42.9	15	30.0	12	92.3
No	36	57.1	35	70.0	1	7.7
Pre-hospital ECG (without electronic transmission)						
Yes	27	30.0	23	42.6	4	11.1
No	63	70.0	31	57.4	32	88.9
Primary diagnosis						
STEMI	87	81.3	51	77.3	36	87.8
NSTEMI	6	5.6	5	7.6	1	2.4
Unstable angina	1	0.9	0	0.0	1	2.4
Subsequent AMI'	10	9.3	8	12.1	2	4.9
Other	3	2.8	2	3.0	1	2.4
Principal procedure						
PCI	24	22.4	16	24.2	8	19.5
PCI + Stent insertion	80	74.8	49	74.2	31	75.6
Coronary artery bypass graft	1	0.9	0	0.0	1	2.4
Other intervention, non-coronary	2	1.9	1	1.5	1	2.4
Length of stay, days	3 (0–32)		3 (0–16)		3 (1–32)	
In-hospital mortality						
Discharged	101	94.4	62	93.9	39	95.1
Deceased	6	5.6	4	6.1	2	4.9

Data are presented as means ± SD or median (interquartile range). *Refer to due to missing data, 'n' may not sum to the total sample size of 107. **Refer to percentage of total reported cases for each characteristic within each group. ^Refer to first hospital of presentation. 'Refer to within 28 days of original AMI. AMI: acute myocardial infarction; ECG: electrocardiogram; NSTEMI: non-ST-segment elevation myocardial infarction; PCI: percutaneous coronary interventions; SEIFA: socio-economic indexes for areas; STEMI: ST-segment elevation myocardial infarction.

with a mean age of 60 years, of which 85% were males predominantly from the North Metropolitan Health Service catchment area (90%). Medical transport was attributed to 86% of those who presented directly to the PCI-H, while it is unknown how patients presented to the first non-PCI-H. All transfers were via ambulance. Pre-hospital activation occurred in 30% of direct presentations and 92% of transfers, conversely pre-hospital ECGs were obtained in 43% of direct presentations but only in 11% of transfers prior to arriving at the first non-PCI capable hospital. Primary PCI was attempted in 97% of patients, of which 75% went on to have at least one stent inserted in the target vessel. Median length of stay was three days with an in-hospital mortality rate of 6% ($n = 6$).

Analysis was limited to only those patients diagnosed as STEMI, as this categorises those in immediate need of PCI. As shown in Table 2, in the crude (unadjusted for potential confounders) analysis no statistically significant differences were noted in time between symptom-onset and first hospital arrival between direct and transfers. Transferred patients experienced statistically significant delays in STD (PCI-H) times (215 *vs.* 95 min, $P < 0.001$), STB times (224 *vs.* 160 min, $P = 0.009$) and DTB (First) times (106 *vs.* 58 min, $P < 0.001$). However, transferred patients DTB (PCI-H) times were statistically significantly shorter than direct presenters (34 *vs.* 58 min, $P = 0.012$). This trend continues in Table 3 with 28% of transfers having experienced balloon inflation within 90 minutes of first hospital arrival; and 59% within 120 minutes, and yet all transfers met target when measured from DTB (PCI-H) times.

Table 4 shows that after accounting for confounding by socio-economic status, presentation date/time, transfer status, pre-hospital activation, pre-hospital ECG, mode of transport to the PCI-H, age and sex, statistically significant differences were observed with transfers having on average 118% longer delays from symptom-onset to first hospital arrival. This difference was further exacerbated when comparisons were made between STD (PCI-H) times, with transferred

Table 2. Crude key times to treatment for all patients diagnosed with STEMI by transfer status.

	All ($n = 51$)	Direct ($n = 42$)	Transfers ($n = 9$)	$P > Z^*$
[a]STD (First)	90 (56–165)	95 (59–148)	76 (41–277)	0.711
[b]STD (PCI-H)	110 (72–215)	95 (59–148)	215 (146–695)	< 0.001
[c]STB	181 (135–289)	160 (125–250)	224.5 (166–405)	0.009
[d]DTB (First)	80 (53–109)	57.5 (44–81)	106.5 (89–145)	< 0.001
[e]DTB (PCI-H)	54 (41–77)	57.5 (44–81)	34 (30–56)	0.012
[f]LOS (Referral hospital)	43 (36–72)	-	43 (36–72)	-
[g]IHT travel time	25 (17–35)	-	25 (17–35)	-

Data are presented as median (interquartile range). [a]Refer to symptom onset to first hospital door arrival. [b]Refer to symptom onset to PCI-H door arrival. [c]Refer to symptom onset to balloon inflation. [d]Refer to first hospital door arrival to balloon inflation. [e]Refer to PCI-H door arrival to balloon inflation. [f]Refer to referral hospital length of stay. [g]Refer to inter-hospital transfer travel time. *Refer to test between direct and inter-hospital transfer patients using Mann Whitney *U*. DTB: door-to-balloon; IHT: inter-hospital transfer; LOS: length of stay; PCI-H: percutaneous coronary interventions-capable hospital; STB: symptom onset to balloon inflation; STD: symptom onset to first hospital door arrival; STEMI: ST-segment elevation myocardial infarction.

Table 3. Crude numbers and percentages of patient door-to-balloon times for all STEMI* patients by transfer status.

	All ($n = 87$)	Direct ($n = 51$)	Transfers ($n = 36$)	$P > Z^{**}$
[a]DTB (First)				
90 minutes or less	49 (62.8%)	40 (87.0%)	9 (28.1%)	< 0.001
Greater than 90 minutes	29 (37.2%)	6 (13.0%)	23 (71.9%)	
[b]DTB (First)				
120 minutes or less	61 (78.2%)	42 (91.3%)	19 (59.4%)	0.001
Greater than 120 minutes	17 (21.8%)	4 (8.7%)	13 (40.6%)	
[c]DTB (PCI-H)				
90 minutes or less	51 (89.5%)	40 (87.0%)	11 (100.0%)	0.205
Greater than 90 minutes	6 (10.5%)	6 (13.0%)	0	

[a]Refer to first hospital door arrival to balloon inflation (90 minutes or less). [b]Refer to first hospital door arrival to balloon inflation (120 minutes or less). [c]Refer to PCI-H door arrival to balloon inflation. *Refer to patients with confirmed ST-elevation myocardial infarction on electrocardiogram. **Refer to test between direct and inter-hospital transfer patients using Chi Squared. DTB: door-to-balloon; PCI-H: percutaneous coronary interventions-capable hospital; STEMI: ST-segment elevation myocardial infarction.

Table 4. Adjusted mean times to treatment and length of stay by transfers, pre-hospital ECG activation.

	Generalised linear model[a]				Estimated marginal means[***]					
	Coef[c]	95% CI		P > Z[**]	Mean	95% CI		Mean	95% CI	
		Lower	Upper			Lower	Upper		Lower	Upper
Transfer status										
	Inter-hospital transfer is baseline				Direct presentation			Inter-hospital transfer		
[b]STD (First)	1.18	0.49	1.87	0.001	113	83	154	369	205	665
[b]STD (Tertiary)	1.62	1.05	2.19	0.000	110	85	143	555	340	906
[c]STB	0.98	0.58	1.39	0.000	167	141	198	447	307	652
[d]DTB (First)	1.26	0.91	1.61	0.000	55	48	64	195	143	267
[e]DTB (PCI-H)	0.19	–0.17	0.55	0.308	55	48	63	67	49	91
CCL activation										
	No activation is baseline				Pre-hospital activation			No pre-hospital activation		
[c]STB	0.34	0.01	0.68	0.045	230	184	289	324	239	441
[d]DTB (First)	0.81	0.52	1.10	0.000	69	58	83	156	120	202
[e]DTB (PCI-H)	0.74	0.49	1.00	0.000	39	32	46	81	69	95
ECG										
	No ECG is baseline				Pre-hospital ECG			No pre-hospital ECG		
[c]STB	–0.51	–0.85	–0.17	0.004	353	256	487	212	171	262
[d]DTB (First)	0.15	–0.13	0.42	0.286	97	75	125	112	95	133
[e]DTB (PCI-H)	0.27	0.02	0.52	0.033	49	41	59	64	55	75
Length of stay, days (For those with DTBs 90 min or less)										
	DTB > 90 min is baseline				DTB 90 min or less			DTB greater than 90 min		
[d]DTB (First)	0.510	0.204	0.816	0.001	4	3	5	7	5	9
[e]DTB (PCI-H)	0.593	0.137	1.048	0.011	4	4	5	8	5	13

[a]Refer to symptom onset to first hospital door arrival. [b]Refer to symptom onset to PCI-H door arrival. [c]Refer to symptom onset to balloon inflation. [d]Refer to first hospital door arrival to balloon inflation. [e]Refer to PCI-H door arrival to balloon inflation. [f]Refer to models were adjusted for sex, age, socio-economic status, method of arrival to PCI-H, presentation date/time, pre-hospital ECG, pre-hospital activation and transfer status. [g]Refer to coefficient B (relative proportional change in the mean value of the outcome variable in those transferred compared with the mean value in the baseline group). [**]Refer to test between groups within transfer status, cardiac catheterisation laboratory activation and pre-hospital ECG; using Wald Chi Square. [***]Refer to estimated marginal means adjust for the covariate by reporting the means of year for each level of the factor at the mean value of the covariate. DTB: door-to-balloon; ECG: electrocardiogram; PCI-H: percutaneous coronary interventions-capable hospital; STB: symptom onset to balloon inflation; STD: symptom onset to first hospital door arrival.

patients facing delays on average 162% greater than their direct counterparts, with model predicted average delays of 555 minutes (340–906 minutes) compared to 110 minutes (85–143 minutes) respectively. Transferred patient's also experienced statistically significantly longer delays in STB times of 98% with model based predicted delays for direct patients at 167 minutes (141–198 minutes) rising to 447 minutes (307–652 minutes) for transfers. First hospital DTB times are 1.26 times longer for transferred patients, with the model predicting average times of 195 minutes (143–267 minutes) compared to just 55 minutes (48–64 minutes) for direct presentations. However, when measured from PCI-H arrival, no significant differences were observed.

Failure to have a pre-hospital activation notably increased DTB (First) by 81% and DTB (PCI-H) by 74%, increasing the overall time to treatment burden with predicted average first hospital DTB times of 69 minutes for those with pre-hospital activation jumping to 156 minutes for those without. Pre-hospital ECG statistically significantly reduced DTB (PCI-H) by 27% with an estimated marginal means of 49 minutes (41–59 minutes); increasing to 64 minutes (55–75 minutes) for those who did not have a pre-hospital ECG. Experiencing DTB times of 90 minutes or less measured from both the first hospital and the PCI-H were found to significantly reduce the estimated mean length of stay by 51% and 59%, from four days to seven days (5–9 days) and eight days (5–13 days), respectively.

4 Discussion

Despite DTB times from first hospital of presentation resulting in significantly longer delays to treatment for

transferred patients, the majority of these patients experience pre-hospital activation and therefore fortunately have similar, if not improved, DTB (PCI-H) times compared to direct presentations. However, the inherent delay associated with initial presentation to a secondary hospital without CCL capabilities, requiring triage and diagnosis prior to transfer by road to a CCL hospital has important implications in the Western Australians setting with travel notably hindering time to treatment.[20] An Italian study[21] showed similar results with the overall time to treatment metric longer for inter hospital transfers; but those same patients showed a significantly shorter door to balloon delay when measured from the single centre, due to early mobilisation of the CLL team. Rezaee, *et al*.[18] broke down the different components of delay after emergency medical services arrival and after accounting for 15 minutes as the median time-on-scene, a further 29–32 minutes for in-hospital assessment and transfer from the ED to the CCL and consequent balloon inflation, found the maximum allowable transport time was 43–46 minutes. In the Greater Perth region, this figure may be challenging to achieve for outer metro patients, let alone their rural and remote counterparts due to the distances involved. Average travel times by road, from the most northern, southern and eastern tips of the Greater Perth region (Greater Capital City Statistical Areas) to Perth City central are 75 minutes.[22] Inter hospital transfers are a topic of debate worldwide with numerus initiatives addressing the need to reduce transfer related delays in the primary treatment of ACS.[23] A 2012 study from Brazil, *et al*.[24] showed direct presentations were associated with decreased total ischemia time, improve myocardial reperfusion markers and a non-significant decrease in hospital mortality; despite an integrated system which allows for a 60 minute-time interval for inter-hospital transfer.

Pre-hospital ECGs have previously shown to reduce DTB times,[25] although this was not the case in our study when measured from first hospital DTB times, after controlling for the effects of transfers status and pre-hospital activation. However, PCI-H DTB times were impacted with 27% shorter DTB times for patients who had a pre-hospital ECG (49 *vs*. 64 min, $P = 0.033$). Similarly to this study, it has previously been shown any in-hospital time saving benefits from the acquisition of pre-hospital ECGs were only fully realised with the addition of pre-hospital CCL activation.[18]

No statistically significant differences were noted in sociodemographic factors between direct and transfers for patient diagnosed as STEMI as per the International Classification of Disease.[26] Further, there were no statistically significant differences in the type of interventions performed. In lieu of more detailed data on severity of disease, these figures indicate transferred patients were no more or less critical than direct presentations. Taking into consideration the overall longer delay to PCI therapy due to triage at the first hospital and time to transfer, in conjunction with pre-hospital activation, it would be reasonable to expect rapid DTB times once arriving at PCI-H to reduce overall delay burden. Unfortunately, this was not the case. Although the transfers occurred within recommended guidelines for a single hospital, the overall system delay needs to be taken into consideration.

The data does not include information on how patients arrived at secondary hospitals. Ambulance ECG was introduced to Western Australia in during 2012/2013.[27] Assuming all patients with ECG changes consistent with STEMI were taken directly to an available CCL, the patients who required transfer from a secondary hospital would have either self-presented to their nearest emergency department or were current inpatients. Given the transfer cohort would have known diagnoses of STEMI at the time of transfer, with 78% having pre PCI-H CCL activation, it would be reasonable to expect rapid PCI-H DTB times. Although within the guidelines for a single-centre, overall the burden of delay for these patients is well outside recommendations.

The single most effective measure to reduce the time burden from first medical contact to definitive treatment has been shown to utilise ambulance-initiated ECG. Early identification of STEMI changes en route means patients can be rerouted directly to a PCI-equipped hospital, avoiding transfers after ED triage.[5,11,28,29] A secondary option is the development of a coordinated system to record the time of ED arrival or ambulance retrieval, which can then be accessed at the final receiving hospital to contribute to the time metrics analysis. Data including ECG changes, biomarkers and any initial treatments are recorded. There is compelling evidence Cardiac Registries across the world drive continuous improvements in patient care and inform a medical centres ability to adhere to guideline recommendations. Such registries can be utilised in conjunction with linked administrative health data, to complete the long term picture of the burden of ACS and the short- and long-term outcomes.[28,30–32]

If primary PCI cannot be performed within 90 minutes of first medical contact, thrombolysis should be considered as a primary reperfusion method. Every patient in this study was transferred for primary PCI as part of the inclusion criteria. However, as this is a single centre study, treatments and therapies initiated at the first hospital of treatment were not coded within the data to identify those patients being

transferred for rescue PCI.

It is beyond the scope of this study to analyze patient outcomes post-therapy. Clinical recommendations have been established for the known improvements in outcomes with reduced time to therapy and as such the focus of the paper is on the impact of transfers on time to therapy, rather than short- and long-term outcomes. However, it has previously been shown that for every 30-minute delay in PCI, there is a 1% increase in absolute risk of dying in hospital;[16,33] while another study showed an increase of 7.5% in risk of one-year mortality for every 30 minutes delay to treatment.[34] In accordance with these findings, the median referral hospital length of stay of 52 minutes and mean transfer time of 25 minutes infers the addition of over an hour to the overall patient journey, ultimately increasing the absolute risk of in-hospital mortality by 2.0% with the one-year mortality risk at least 15% greater for transferred patients.

4.1 Limitations

Some limitations in our study should be acknowledged. Despite this study focusing on a single centre in the Perth Metropolitan area, all presentations of STEMI within the study time period were included, avoiding selection bias. Although the single centre nature may limit generalisability, reputable peer-reviewed publications[35,36] and leading epidemiological theorists[37] acknowledge cohort studies rely on validity or international comparisons to avoid systematic error. As such, they do not need to be random sample of a large population to provide generalisable knowledge. Internationally renowned cohort studies, such as the British Doctors Study and US Nurses' Health Study are regarded as generalizable knowledge despite their highly selected study samples, as external validity of generalisation depends on considerations regarding effect modification rather than bias/confounding. The study sample included individuals from all five tiers of socio-economic status from north metropolitan, south metropolitan and Western Australians country health catchment areas. The strength of this study is the routine and systematic nature of the collection of data on all patents presenting to the centre which reduced both selection and recall bias and the comprehensive inclusion of both clinical and administrative data points, allowing for the analysis of time to therapy, not typically possible with administrative datasets. This study was limited by the lack of available data pertaining to why patients presented to a secondary hospital in the first instance and as such determinants of why patients did not present directly to the PCI-H are unknown.

Further times of ambulance arrival are not recorded within the data; and as such FMC-B cannot be measured. However, some patients would have self-presented to the first non-PCI hospital via private transport. In these instances, the secondary hospital arrival time would in fact be their FMC. A brief analysis of linked administrative health data using Emergency Department records in Western Australia shows 58% of ACS patients arriving at secondary hospitals were via private transport. Although this data is derived from a different source, it is from the same pool of ACS patients in Western Australia and therefore these percentages are likely to be generalisable to our sample. Thus, if the secondary hospital arrival time is used as proxy for FMC, this would be the actual FMC for approximately 58% of our patients. The remaining 42% would therefore have time-to-treatments that are an under-estimation of the true burden of delay. In addition, there are no variables within the dataset that outline if the hospital received an ambulance ECG transmission; or if the PCI-H was notified of the incoming transfer. In lieu of this information, time of ECG, CCL activation and PCI-H arrival times were used to calculate pre-hospital ECGs for all patients; and pre-PCI-H activation of the CCL for transfers. Further limitations included the small number of cases in the dataset and some incomplete/empty data variables, particularly in time variables. The study was unable to follow patients after discharge and therefore unable to further assess 30-day and one-year mortality. However, these outcomes were beyond the scope of this study, which was concerned with determining the magnitude of delay associated with transfer from hospital type rather than its impact on patient outcomes.

4.2 Conclusions

Transferred patients' overall delay times from symptom-onset to balloon inflation is 98% longer than that of direct presentations, resulting in significantly longer infarct times and potentially poorer outcomes in the long term. This study highlights the extent to which the transfer process adds to the time to treatment burden and system delay. Despite pre-CCL capable hospital activation, PCI-H DTB times are not statistically significantly shorter than their direct cohort counterparts, representing a missed opportunity in the system to reduce the time delay burden for patients who required transfer for PCI. Inter-hospital transfers will remain an ongoing and unavoidable reality in Western Australia's emergent treatment of ACS due to geographic and service provision challenges. The need for efficient triage to streamline transfer processes, avoidance of any unnecessary transfers by presenting directly to CCL facilities where possible, continuing education for the general public about using ambulance services and continued per-

formance of pre-hospital activations are crucial to reduce system delay in the treatment of ACS.

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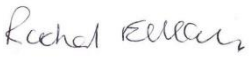
Co-Author 2: Z. Sun	20	10	10	20	25	25	18.3
Co-Author 2 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
Co-Author 3: C. Reid	20	10	10	20	25	25	18.3
Co-Author 3 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
Co-Author 4: R. Moorin	25	40	40	30	25	25	30.8
Co-Author 4 Acknowledgment: I acknowledge that these represent my contribution to the above research output. Signed: 							
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Article

Rates and Patterns of First-Time Admissions for Acute Coronary Syndromes across Western Australia Using Linked Administrative Health Data 2007–2015

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Abstract: Acute coronary syndrome (ACS) is globally recognised as a significant health burden, for which the reduction in total ischemic times by way of the most suitable reperfusion strategy has been the focus of national and international initiatives. In a setting such as Western Australia, characterised by 79% of the population dwelling in the greater capital region, transfers to hospitals capable of percutaneous coronary intervention (PCI) is often a necessary but time-consuming reality for outer-metropolitan and rural patients. Methods: Hospital separations, emergency department admissions and death registration data between 1 January 2007 and 31 December 2015 were linked by the Western Australian Data Linkage Unit, identifying patients with a confirmed first-time diagnosis of ACS, who were either a direct admission or experienced an inter-hospital transfer. Results: Although the presentation rates of ACS remained stable over the nine years evaluated, the rates of first-time admissions for ACS were more than double in the rural residential cohort, including higher rates of ST-segment elevation myocardial infarction, the most time-critical manifestation of ACS. Consequently, rural patients were more likely to undergo an inter-hospital transfer. However, 42% of metropolitan admissions for a first-time ACS also experienced a transfer. Conclusion: While the time burden of inter-hospital transfers for rural patients is a reality in health care systems where it is not feasible to have advanced facilities and workforce skills outside of large population centres, there is a concerning trend of inter-hospital transfers within the metropolitan region highlighting the need for further initiatives to streamline pre-hospital triage to ensure patients with symptoms indicative of ACS present to PCI-equipped hospitals.

Keywords: acute coronary syndrome; Western Australia; rates of admission; inter-hospital transfers; linked data; percutaneous coronary intervention

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1. Introduction

Cardiovascular disease (CVD) represents a significant global burden, annually killing more people than any other cause [1]. In Australia alone, it was estimated that 59,100 people aged 25 years and over experienced an acute coronary syndrome (ACS) event in 2017 [2], with Australia's population for the same year estimated to be 24.6 million [3]; equating to approximately 2.4 ACS events per 1000 person–years. Worldwide data collection on ACS utilises a variety of methods. Cardiac registries such as the CONCORDANCE Registry in Australia [4]; the ACS Snapshot Study of Australia and New Zealand [5]; the All New Zealand Acute Coronary Syndrome-Quality Improvement (ANZACS-QI) [6] and the National Cardiovascular Data Registry (NCDR) of the American College of Cardiology [7] enrol representative hospitals or clinics to inform on clinical characteristics, management

and outcomes for ACS hospitalisations. Similarly, government agencies gather data on the numbers of ACS hospitalisations for a given time period using admission statistics. Both methods offer advantages and disadvantages. Cardiac registries provide in depth data on clinical characteristics and outcomes that cannot be derived from hospital admission data alone. However, these are often based on the voluntary participation of hospitals or clinics in the registries and often are for a short snapshot of time rather than an ongoing, whole population cohort [5,8]. Conversely, hospital admission data can capture more accurate rates of ACS hospitalisations, but can lack in depth clinical data necessary to inform policy and can be prone to double-counting, secondary to inter-hospital transfers [9].

The Western Australian Data Linkage System (WADLS) [10] provides anonymised population-based records using hospital admission data (for both public and private hospitals), public emergency department data and mortality records all linked via probabilistic matching allowing patients to be followed throughout multiple hospitalisations for related conditions based on the International Classification of Diseases (Australian Modification) coding.

The diagnosis of the type of ACS requires interpretation of an electrocardiogram (ECG) for the critical distinction between the ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndromes (NSTEACS) which is further categorised into non-ST-segment elevation myocardial infarction (NSTEMI) or unstable angina (UA), based on patient history, examination and cardiac enzyme biomarkers [11]. Early diagnosis of STEMI as well as the appropriate assessment and risk stratification of NSTEACS, are essential to facilitate early reperfusion by primary percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), pharmacotherapy or fibrinolytic therapy for improved morbidity and mortality [11–14].

The challenge for some parts of the world such as Western Australia (WA), is the remoteness of a large section of the community outside capital cities. The estimated resident population of WA was 2.58 million people in 2017 of which 92% live in the South West Land Division and more specifically 79% living in the greater capital city region, leaving the rest of the state sparsely populated [15]. In addition, current service provisions for ACS are predominantly centred in the capital city area with three tertiary hospitals, several secondary and private hospitals with round-the-clock catheterisation laboratories and one regional centre in the South West offering coronary intervention for planned admissions [16]. It is not feasible to expect advanced cardiac catheterisation laboratory (CCL) facilities in every hospital across the world, necessitating inter-hospital transfers to facilities capable of PCI, where indicated. Furthermore, in the rural setting, the lack of advanced medical facilities is further compounded by staff shortages and variable workforce experience and skills [16]. However, these centres have provisions for the administration of fibrinolytic therapy prior to emergent or elective transfer for PCI, known as facilitated or rescue PCI. In more metropolitan settings, strategies to ensure ambulance ECG with transmission to a cardiac facility for the evaluation of STEMI is essential to ensure that ambulances can bypass secondary hospitals in favour of PCI-capable facilities wherever possible in the metropolitan region and prevent the inherent delays associated with triage and inter-hospital transfer (IHT) [17,18].

The aim of this study was to evaluate the whole-of-population rates of admission for first-time presentations of ACS in Western Australia (WA), accounting for the number of inter-hospital transfers, over a period of nine years using Linked Administrative Data from the WA Data Linkage System (WADLS) [10] and Population Census Data from the Australian Bureau of Statistics (ABS) [19].

2. Methods

This paper follows the Reporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) Statement [20].

2.1. Data Sources

Data from the WA Hospital Morbidity Data System (HMDS), WA Emergency Department Data Collection (EDDC) and WA Death Registrations from 1 December 2007 to 31 December 2015, with further data to establish a look-back period from the HMDS available from 01 January 2002 were linked by the WADLS. The WADLS uses routinely collected, longitudinal, whole-population, administrative health and medical data with linkages obtained through key demographic information including name, date of birth, home address and hospital medical record numbers. Privacy is ensured by linking records from different datasets using pre-established linkage keys, removing identifiable demographic data and providing only non-identifiable demographic data such as month and year of birth, sex and postcode; in addition content data describing what happened to the person during each record, such as diagnosis and treatment codes [10]. The WADLS provides data under a waiver of consent due to the de-identified nature of the data and the research team is required to work under strict conditions to ensure the security of the data.

Routinely collected data include socio-economic data (date of birth; sex; postcode of residence; Socio-Economic Indexes for Areas (SEIFA) [21]) and clinical service utilisation data for each hospital admission, namely the admission date and time; separation (discharge) date and time; primary, secondary and co-diagnoses (up to 20 fields); primary and up to ten secondary interventions including procedural dates; hospital region; admission status (emergency presentation or elective) and insurance status (private or public).

Population data were sourced from the Australian Bureau of Statistics (ABS) [19] and reported age groups were determined so as to align with the available ABS age groups. All-cause hospital separations were sourced from the Australian Institute of Health and Welfare [22,23] to evaluate the rate of hospitals for ACS compared to all separations for the same time period.

2.2. Population and Ascertainment of ACS Events

The cohort consisted of all individuals admitted into a WA hospital having a first-time record indicating a primary diagnosis of ACS between 1 January 2007 and 31 December 2015, identified using the International Classification of Diseases, Australian Modification (ICD-10-AM) codes [24] (Appendix A). First-time ACS admissions were defined as individuals with no records indicating a primary or secondary diagnosis of ACS prior to 1 January 2007, using HMDS and EDDC data from 1 January 2002 as a look-back period. Individuals who had ACS events prior to the commencement of the study period (i.e., 1 January 2007) were excluded from the cohort. Subsequent admissions for patients after their incident event were included as readmission events if they were in relation to a primary or secondary diagnosis of ACS.

2.3. Patient Characteristics

Sex, identification of being of Aboriginal or Torres Strait decent and date of birth were coded directly within the data. Reported ages were then categorised based on the age of the patient at the time of their incident ACS admission to match available population data. Residential postcodes were used to determine the health region of residence and SEIFA. The primary and secondary diagnosis fields were used to identify those patients admitted for ACS with the remaining 20 co-diagnosis fields used to identify specific comorbid conditions during the same episode of care. These data were also used to ascertain total comorbidity using the Multipurpose Australian Comorbidity Scoring System (MACSS) [25] at one year and five years prior to the incident event. A summary of the diagnosis codes used to define comorbidity is shown in Appendix B. In the event a patient was diagnosed with two or more types of ACS within the same episode of care, the method of diagnosis hierarchy previously validated by Sanfilippo et al. [26] and Lopez et al. [27] was applied where the final diagnosis was the most severe diagnosis; with STEMI being the most severe, followed by NSTEMI and lastly UA. The determination of the interventions performed

was based on The Australian Classification of Health Interventions, Tenth Revision from the National Centre for Classification in Health [28] (Appendix A).

The EDDC was combined with the HDMS to identify those patients who presented to an emergency department and were admitted at the same hospital, versus those patients who were transferred to another hospital. Distinction between IHT during the same episode of care, as opposed to a readmission, were identified by a secondary HMDS record within 24 h of the time of separation, where the method of patient discharge and discharge destination from the first hospital indicated a transfer. A new admission beyond 24 h post discharge and in the absence of the aforementioned discharge indicators within 24 h, the record was assigned as a readmission.

Emergency versus elective admissions are coded directly in the HMDS. In-hospital mortality, including the date of death, is coded within the HMDS; while post-discharge mortality, including data of death and cause of death (COD) based on ICD-10-AM coding, was determined using the linked mortality dataset. Reported time frames calculated between the date of separation for the first admission and the date of death. The ICD-10-AM was used to categorise the COD into acute myocardial infarction (AMI), other ischemic heart diseases (IHD) excluding AMI and non-IHD causes for 0 to 30-day, 30-day to 1-year and beyond 1-year mortality.

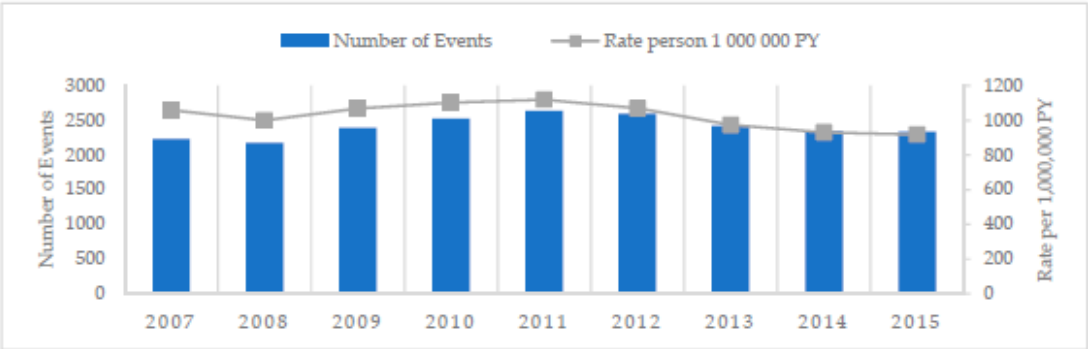
2.4. Statistical Analysis

Unadjusted estimates of the person's time at risk were calculated using the number of persons residing in WA in each age bracket (18–39, 40–49, 50–59, 60–69, 70–79 and 80+ years) on 30th June for each year from the ABS as the denominator. The Australian Institute of Health and Welfare data on annual separation rates were used as the denominator to calculate the rate of first-time ACS separations versus all-cause hospital separations. Categorical data were reported as frequencies and percentages and continuous data were reported as the means, standard deviations and ranges. Where appropriate, categorical data were also presented as rates, using the admitted cohort as the denominator unless otherwise specified. Confidence intervals were calculated using a confidence interval calculator for single incidence rates with the two-sided confidence level assigned at 95% [29]. The Mann–Whitney *U* test and the Pearson chi-squared tests were used for between group analyses. Statistical significance was assigned at the level of $p < 0.05$. All analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 [30] and Stata Statistical Software: Release 16 [31].

3. Results

Rates of admissions for the first-time diagnoses of ACS remained steady throughout the nine-year study timeframe averaging ten per 10,000 person years with an average of 2405 admissions per calendar year (Figure 1a) and 21,648 total admissions between 1 December 2007 and 31 December 2015 (Appendix C). However, rates of UA and STEMI decreased from 2010 to 2015 as NSTEMI rates showed an increase. Annual rates of UA showed a statistically significant difference from 2010, decreasing with each subsequent year. Rates of STEMI presentations were statistically significantly lower between 2009 and 2011 and between 2014 and 2015. Rates of NSTEMI steadily increased with each year from 2010 and although not always a statistically significant change per year within NSTEMI, this condition does contribute statistically significantly higher rates of the ACS burden from 2009 compared to UA and STEMI. (Figure 1b). In-hospital mortality rates were stable for UA and NSTEMI with a slow decline noted for STEMI patients (Figure 2a) and the overall all-cause mortality rate at 30 days also remained stable at an average of 459 per 10,000 person–years (PY), increasing to an average of 583 per PY for 30-day to 1-year mortality (Figure 2b). The rates of first-time admissions were higher in males and increased with each 10-year incremental rise in age (Figure 2c,d). Rates of PCI including one or more stent insertion increased from 56 procedures per 100 PY in 2007 to 68 per 100 PY for every confirmed diagnosis of ACS, with rates of CABG contributing approximately five procedures per 100 PY per annum over the nine years (Figure 2e). The data for Figure 1 are tabulated in more depth in Appendix A.

(a)



(b)

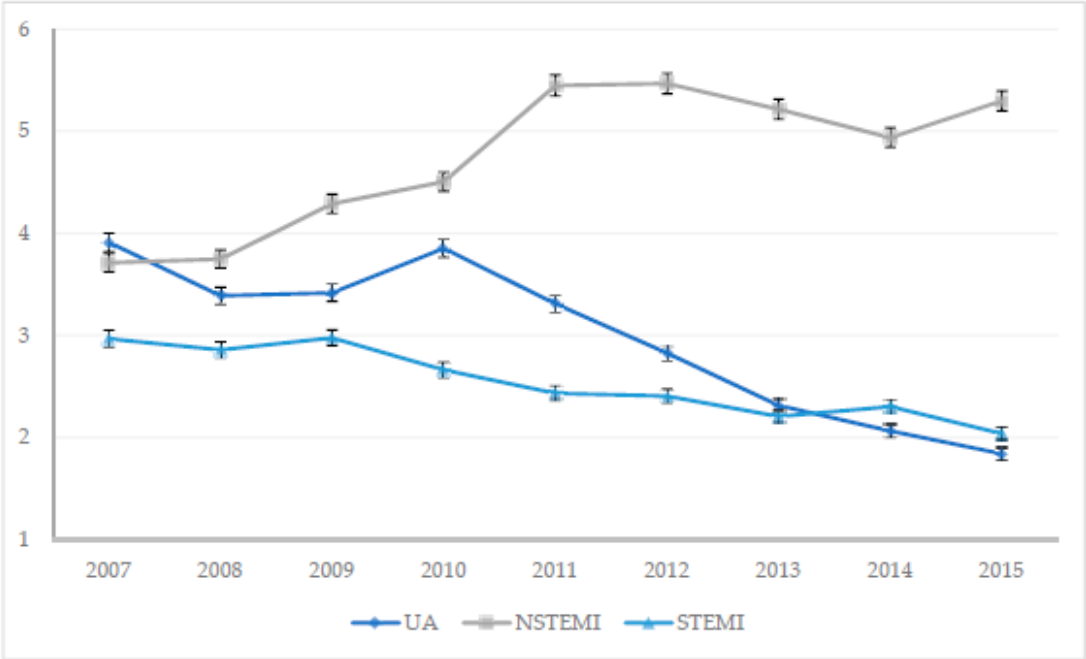


Figure 1. Rates of all first-time admissions for acute coronary syndrome in Western Australia between 1 January 2007 and 31 December 2015. (**a**): Number and rates of first-time admission for acute coronary syndrome per 1,000,000 person–years. (**b**): Rates of first-time admissions by acute coronary syndromes per 10,000 person–years (PY) with confidence intervals. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

Figure 2. Rates of all first-time admissions for acute coronary syndrome in Western Australia between 1 January 2007 and 31 December 2015. (**a**): In-hospital mortality rates of first-time admissions by acute coronary syndromes per 10,000 person–years. (**b**): Mortality rates for first-time admissions by acute coronary syndrome per 1000 person–years. (**c**): Rates of first-time admissions per 10,000 person–years by sex. (**d**): Rates of first-time admissions per 10,000 person–years by age. (**e**): Rates of PCI including one or more stent insertions; CABG and other coronary procedures. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; PCI: percutaneous coronary intervention including one or more stent insertions; CABG: coronary artery bypass grafting; Other Coronary: other procedures of the coronary artery not otherwise specified; MACSS: Multipurpose Australian Comorbidity Scoring System.

Rates of incident (first-time) ACS separations remained stable as all-cause hospital separations increased, resulting in an average rate of 25 admissions per 10,000 PY, or 0.25% of all admission attributable to first-time ACS events annually (Figure 3). A higher number of metropolitan patients were admitted directly for care compared to rural patients in the NSTEMI and STEMI cohorts with similar numbers of direct admission and inter-hospital transfer in the UA cohort (Figure 4).

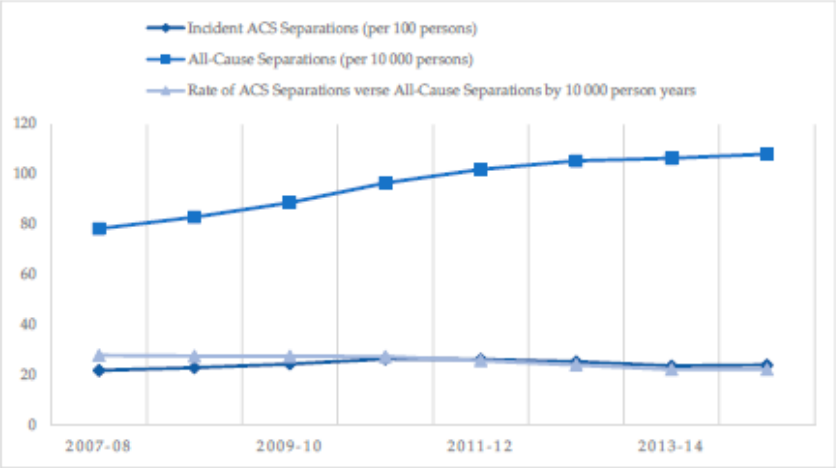


Figure 3. Rates of incident acute coronary syndrome (ACS) separations versus all-cause separations in Western Australian between 1 January 2007 and 31 December 2015 financial years.

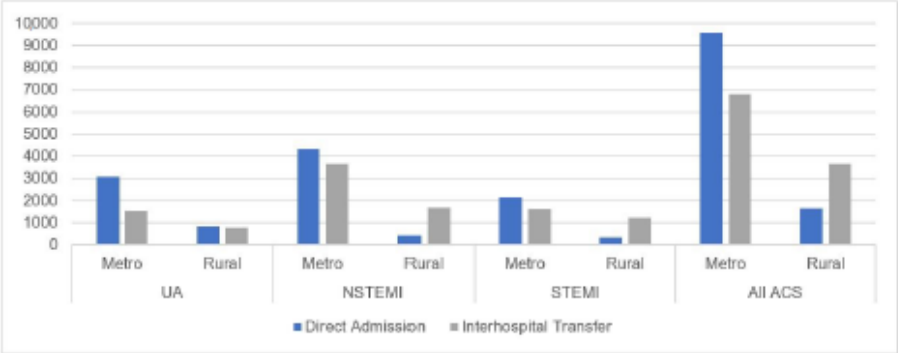


Figure 4. Number of direct admissions versus inter-hospital transfers for acute coronary syndromes in Western Australia between 1 January 2007 and 31 December 2015 by metropolitan and rural residence. UA: unstable angina; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction.

As demonstrated in Table 1, two-thirds of ACS admissions were male with a mean age of 65 years and 63 years for metropolitan and rural patients, respectively. The mean age for rural female patients was 66 years which is statically significantly younger than metropolitan female admissions with a mean age of 72 years ($p < 0.001$). More rural admissions were identified as being of Aboriginal and/or Torres Strait Islander descent at 14% compared to 2% of metropolitan admissions and two-thirds of rural patients were from the high- and highest-disadvantaged SEIFA compared to nearly 50% of metropolitan admissions, which pertained to individuals living in the least or less disadvantaged areas. Metropolitan patients used emergency services more frequently than rural patients (50%

and 35%, respectively). NSTEMI accounted for the highest proportion of primary diagnoses with STEMIs at 23% and 29% for metropolitan and rural admissions, respectively. More than half of all metropolitan admissions presented directly to the treating hospital (58%) whereas 69% of rural patients experienced a transfer.

Table 1. Characteristics and outcomes of first-time admissions for acute coronary syndrome among metropolitan and rural Western Australians, based on residential postcode at the time of admission between 1 January 2007 and 31 December 2015.

Variables	Metro	Rural	Total	Sig *
	n (% *)	*n* (% *)	*n* (% *)	$p < 0.05$
	16,357 (75.6)	5290 (24.4)	21,647	
Demographics				
Male Age, Mean (std dev) (range)	65.05 (13.698) (18–101)	62.54 (14.065) (18–99)	64.43 (13.832) (18–101)	0.056
Female Age, Mean (std dev) (range)	72.37 (14.149) (18–103)	65.58 (15.137) (22–101)	70.77 (14.673) (18–103)	<0.001
Male	10,519 (64.3)	3484 (65.9)	14,003 (64.7)	0.040
Indigenous Australian	310 (1.9)	713 (13.5)	1023 (4.7)	<0.001
Socio-Economic Indexes for Areas (SEIFA)				
Highest Disadvantage	1737 (10.6)	1476 (27.9)	3213 (14.8)	<0.001
High Disadvantage	3951 (24.2)	2169 (41.0)	6120 (28.3)	
Moderate Disadvantage	2841 (17.4)	940 (17.8)	3781 (17.5)	
Less Disadvantage	2679 (16.4)	549 (10.4)	3228 (14.9)	
Least Disadvantage	5149 (31.5)	156 (2.9)	5305 (24.5)	
Comorbidities during the Same Admission				
Diabetes	3043 (18.6)	1064 (20.1)	4107 (9.0)	0.015
Cardiac Arrest	238 (1.5)	65 (1.2)	303 (1.4)	0.223
Heart Failure	1832 (11.2)	445 (8.4)	2277 (10.5)	<0.001
Chronic Pulmonary Disease	112 (0.7)	37 (0.7)	149 (0.7)	0.910
Renal Insufficiency < 29 mL/min	412 (2.5)	127 (2.4)	539 (2.5)	0.632
Obese	344 (2.1)	132 (2.5)	476 (2.2)	0.091
Mode of Arrival to 1st Hospital or ED				
Ambulance/Royal Flying Doctor Service	8133 (49.7)	1848 (34.9)	9981 (46.1)	<0.001
Private/Public Transport	7575 (46.3)	3242 (61.3)	10,817 (50.0)	
Other	448 (2.7)	79 (1.5)	527 (2.4)	
Unknown	201 (1.2)	121 (2.3)	322 (1.5)	
Region of 1st Hospital of Admission				
North Metro	6012 (36.8)	496 (9.4)	6508 (30.1)	<0.001
East Metro	5248 (32.1)	738 (14.0)	5986 (27.7)	
South Metro	4880 (29.8)	270 (5.1)	5150 (23.8)	
South West	48 (0.3)	1321 (25.0)	1369 (6.3)	
Great Southern	16 (0.1)	540 (10.2)	556 (2.6)	
Wheatbelt	7 (0.0)	239 (4.5)	246 (1.1)	
Goldfields	17 (0.1)	485 (9.2)	502 (2.3)	
Midwest	27 (0.2)	532 (10.1)	559 (2.6)	
Pilbara	78 (0.5)	328 (6.2)	406 (1.9)	
Kimberley	24 (0.1)	341 (6.4)	365 (1.7)	
Transfer Status by Primary Diagnosis				
Transfer for UA	1532 (33.3)	780 (47.7)	2312 (37.1)	<0.001
Transfer for NSTEMI	3645 (45.7)	1670 (79.3)	5315 (52.7)	
Transfer for STEMI	1610 (42.6)	1212 (78.1)	2822 (53.0)	

% *: the total percent for each cohort (e.g., Metro); Sig *: statistical significance.

Table 2 presents the rates of primary diagnosis, principal procedure, inter-hospital transfers and in-hospital and post-discharge mortality between the metropolitan and rural cohorts. The rate of admissions for STEMI was higher in rural patients at 29.3 admissions per 100 PY of all ACS admissions, while NSTEMI presentations were higher in the metropolitan cohort. Metropolitan admissions also had a higher rate of PCI and lower rates of inter-hospital transfer.

All-cause in-hospital mortality was statistically significantly higher in the metropolitan cohort at 3.1 deaths per 100 PY. The highest rate of 30-day mortality was due to AMI causes at 46 deaths per 100 PY, which was particularly high in the rural cohort at 51 deaths per 100 PY compared to 45 deaths in the metropolitan group, although these figures showed no statistically significant difference.

Table 2. Rates of primary diagnosis, principal procedure, inter-hospital transfers and mortality per 100 person–years for first-time admissions for acute coronary syndrome for metropolitan and rural Western Australians, based on residential postcode at the time of admission between 1 January 2007 and 31 December 2015.

Variables	Metro	Rural	Total	Sig *
	n (R *)	*n* (R *)	*n* (R *)	$p < 0.05$
Primary Diagnosis (Total Events)	(*n* = 16,357)	(*n* = 5290)	(*n* = 21,647)	
UA	4603 (28.1)	1634 (30.9)	6237 (28.8)	<0.001
NSTEMI	7978 (48.8)	2105 (39.8)	10,083 (46.6)	
STEMI	3776 (23.1)	1551 (29.3)	5327 (24.6)	
Percutaneous Coronary Interventions (PCI) (Total Events)	(*n* = 16,357)	(*n* = 5290)	(*n* = 21,647)	
Other Coronary Procedures	48 (0.3)	11 (0.2)	59 (0.3)	<0.001
PCI +/− Stent	10,394 (63.5)	3150 (59.5)	13,544 (62.6)	
Coronary Artery Bypass Grafting	819 (5.0)	292 (5.5)	1111 (5.1)	
Inter-Hospital Transfer Status (Total Events)	(*n* = 16,357)	(*n* = 5290)	(*n* = 21,647)	
Direct/No IHT	9570 (58.5)	1628 (30.8)	11,198 (51.7)	<0.001
Yes, IHT	6787 (41.5)	3662 (69.2)	10,449 (48.3)	
In-Hospital Mortality—All Cause (Total Events)	(*n* = 16,357)	(*n* = 5290)	(*n* = 21,647)	
Yes, Died in Hospital	509 (3.1)	117 (0.7)	626 (3.8)	0.001
Mortality—Non-IHD COD (Total Events)	(*n* = 2848)	(*n* = 806)	(*n* = 3654)	
30-Day Mortality	326 (11.4)	97 (12.0)	423 (11.6)	0.804
30-Day to 1-Year Mortality	650 (22.8)	189 (23.4)	839 (23.0)	
More than 1-Year Mortality	1872 (65.7)	520 (64.5)	2392 (65.5)	
Mortality—AMI COD (Total Events)	(*n* = 854)	(*n* = 240)	(*n* = 1094)	
30-Day Mortality	387 (45.3)	122 (50.8)	509 (46.5)	0.301
30-Day to 1-Year Mortality	194 (22.7)	47 (19.6)	241 (22.0)	
More than 1-Year Mortality	273 (32.0)	71 (29.6)	344 (31.4)	
Mortality—IHD COD, Excluding AMI (Total Events)	(*n* = 408)	(*n* = 122)	(*n* = 530)	
30-day mortality	51 (12.5)	15 (12.3)	66 (12.5)	0.624
30-Day to 1-Year Mortality	142 (34.8)	37 (30.3)	179 (33.8)	
More than 1-Year Mortality	215 (52.7)	70 (57.4)	285 (53.8)	

R *: rate per 100 person–years; Sig *: statistical significance; UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; IHD: ischemic heart disease; COD: cause of death; IHT: inter-hospital transfer; PCI +/− Stent: percutaneous coronary intervention, with or without stent insertion.

A higher proportion of transferred patients was diagnosed with NSTEMI and only 1% more STEMI cases compared to direct presentations, as shown in Table 3. The rate of patients to have a PCI including one or more stent insertion was 57 per 100 PY for non-transferred patients and 72 per 100 PY for admissions that incorporated an inter-hospital transfer. Transferred patients had slightly lower rates of comorbidities diagnosed during the same episode of care, with all but obesity statistically significantly different between the two groups. The rate of in hospital mortality was significantly higher in non-transferred patients as was the rate of post-discharge mortality at both 30 days and 30 days to 1 year. However, the rate of mortality occurring more than 1 year post discharge was higher in the transferred group. Post-discharge mortality rates for non-ischemic heart disease and AMI were higher in transferred patients.

Table 3. Rates of primary diagnosis, principal procedure, comorbidities and mortality per 100 person–years for first-time admissions for acute coronary syndrome for Perth metropolitan admissions based on transfer status between 1 January 2007 and 31 December 2015.

Variables	Direct/No IHT	IHT	Total	Sig *
	n (R *)	*n* (R *)	*n* (R *)	$p < 0.05$
Primary Diagnosis (Total Events)	(*n* = 9570)	(*n* = 6787)	(*n* = 16357)	
UA	3071 (32.1)	1532 (22.6)	4603 (28.1)	<0.001
NSTEMI	4333 (45.3)	3645 (53.7)	7978 (48.8)	
STEMI	2166 (22.6)	1610 (23.7)	3776 (23.1)	
Percutaneous Coronary Interventions (PCI) (Total Events)	(*n* = 9570)	(*n* = 6787)	(*n* = 16357)	
Other Coronary Procedures	28 (0.3)	20 (0.3)	48 (0.3)	<0.001
PCI +/− Stent	5479 (57.3)	4916 (72.4)	10395 (63.6)	
Coronary Artery Bypass Grafting	347 (3.6)	473 (7.0)	820 (5.0)	
Comorbidities during the Same Admission (Total Events)	(*n* = 9570)	(*n* = 6787)	(*n* = 16357)	
Diabetes	1880 (19.6)	1163 (17.1)	3043 (18.6)	<0.001
Cardiac Arrest	163 (1.7)	75 (1.1)	238 (1.5)	0.002
Heart Failure	1180 (12.3)	652 (9.6)	1832 (11.2)	<0.001
Chronic Pulmonary Disease	79 (0.8)	33 (0.5)	112 (0.7)	0.010
Renal Insufficiency < 29 mL/min	275 (2.9)	137 (2.0)	412 (2.5)	0.001
Obese	211 (2.2)	133 (2.0)	344 (2.1)	0.282
In-Hospital Mortality (Total Events)	(*n* = 9570)	(*n* = 6787)	(*n* = 16357)	
Yes, Died in Hospital	418 (4.4)	91 (1.3)	509 (3.1)	<0.001
Post-Discharge Mortality by COD (Total Events)	(*n* = 2718)	(*n* = 1392)	(*n* = 4110)	
Non-IHD COD	1843 (67.8)	1005 (72.2)	2848 (69.3)	<0.001
AMI COD	608 (22.4)	246 (17.7)	854 (20.8)	
IHD COD, Excluding AMI	267 (9.8)	141 (10.1)	408 (9.9)	
Post-Discharge Mortality by Time Points (Total Events)	(*n* = 2718)	(*n* = 1392)	(*n* = 4110)	
30-Day Mortality	545 (20.1)	219 (15.7)	764 (18.6)	<0.001
30-Day to 1-Year Mortality	665 (24.5)	321 (23.1)	986 (24.0)	
More than 1-Year Mortality	1508 (55.5)	852 (61.2)	2360 (57.4)	

R*: rate per 100 person–years; Sig *: statistical significance; IHT: inter-hospital transfer; UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; IHD: ischemic heart disease; COD: cause of death; PCI +/− Stent: percutaneous coronary intervention, with or without stent insertion.

4. Discussion

The construct of the right patient–right treatment–right time is not new in ACS reporting. Rates of first-time admission for ACS were more than double in the rural residential cohort compared to metropolitan patients with disparities in health conditions and outcomes for rural patients recognised globally and within Australia [9,32,33]. One of the largest challenges facing a rural patient in the event of ACS is access to care in a timely manner from symptom onset, with clear guidelines for the treatment of STEMI, depending on access to a PCI-capable hospital, inter-hospital transfer travel times, and a patient's suitability for PCI, CABG or fibrinolytic therapy [34]. In our study, nearly 80% of rural admissions for STEMI and NSTEMI were transferred, which is not a surprising finding given the unavailability of PCI-capable hospitals in rural WA. However, of greater concern is the proportion of metropolitan patients also being transferred during the episode of care. With 54% and 24% of NSTEMI and STEMI patients being transferred, respectively, of which 80% go on to have PCI including one or more stent insertion or CABG. The era of ambulance ECG, rapid assessment of chest pain or less common symptoms of AMI en route to the hospital means that STEMI patients can be triaged and bypass non-PCI-capable hospitals. This should result in fewer inter-hospital transfers, particularly for in metropolitan STEMI patients, consequently reducing time to definitive treatment [34,35]. Previous research [18,34,36] has also indicated that inter-hospital transfers in a metropolitan cohort is an ongoing reality and suggests that more focus needs to be put into a coordinated pre-hospital framework to ensure STEMI patients are rapidly identified,

allowing for ambulance diversion to an appropriate PCI-capable facility [37]. In comparison, NSTEMI diagnoses, often made more complicated by the requirement of serial troponins in addition to ECG and detailed clinical history, require risk stratification to determine the need for invasive or conservative treatment at an appropriate time interval from symptom onset [11,38]. Consequently, inter-hospital transfers in the presentation of NSTEMI may remain a necessity after risk stratification with previous literature indicting little long-term benefits of early invasive strategies for NSTEACS patients without recurrent symptoms and a low risk of further ischemic events [11,38,39].

Although the overall rate of ACS presentations in our study remained stable over the nine-year time frame, rates of NSTEMI increased with each year with decreasing rates of UA while STEMI presentations remained steady. This trend has previously been reported in the Department of Health's Model of Care for Acute Coronary Syndromes in WA [16] which attributed an apparent decline in angina presentations with a correlating increase in NSTEMI presentations between 1999 and 2008 based on sensitive and specific biomarkers of myocardial injury, primarily troponins, resulted in a decline in angina diagnoses in favour of NSTEMI. The same trend is noted in our study from 2010 onwards, which could be partially explained by the uptake time of the new definitions in the WA health system.

We found that in-hospital all-cause mortality was higher for direct presentations compared with transferred patients. Although counterintuitive given what is known about longer infarct times due to the postponement of reperfusion to facilitate an inter-hospital transfer to a PCI-capable hospital, this finding concurs with previously published randomised controlled trials citing similar results [34,40–42]. Kawecki et al. [34] theorised that this may be due to the longer delay associated with an inter-hospital transfer resulting in more patients dying prior to arrival at a PCI-capable hospital compared to their direct counterparts, thereby positively pre-selecting the cohort eligible for analysis (a form of immortal time bias) [42]. The same pattern can be noted for death within 30 days post discharge, however, the rate of death between 30 day and 1 year are almost identical between transferred and non-transferred patients. After the first year post discharge, transferred patients experience a higher mortality rate at 5 more deaths per 100 PY compared to the non-transferred cohort, indicating a poorer outcome. While differences in comorbidity between transferred and non-transferred patients could explain this, we found that patients with important comorbid conditions such as diabetes, heart failure, congestive pulmonary disease, renal insufficiency, obesity and cardiac arrest were less likely to undergo an inter-hospital transfer. Thus, in our study, confounding due to comorbidity is likely to lead to worse outcomes for direct admissions, hence our estimation of the difference in post 1-year death rates resulting from inter-hospital transfer is likely conservative. Due to the anonymisation of the data, it is unknown if these direct admissions were at a PCI-capable hospital as the first port of call. However, given what is known about the comorbid conditions and rates of invasive treatments, there are two likely explanations for the differences of observed comorbidity between direct and transferred patients. The first is the patient is too unwell to undergo invasive angiography and therefore there is no need for a transfer to a PCI-capable facility. The alternative option is due to the nature of the patient's comorbidities they may likely be deemed at higher risk and are therefore taken directly to a tertiary facility with PCI-capable faculties, as a matter of triage.

A key strength of this study is the identification of first-time events. This study assigned incident events of ACS if the patient was admitted for ACS during the 9-year period if the same individual had no prior admission for ACS from 1 January 2002. This ensured prevalent individuals could be removed from the analysis and allowed for accurate follow-up time periods for post-discharge mortality.

A further strength of linked administrative data is the ability to overcome the challenges associated with over-counting due to inter-hospital transfers which can plague other cardiac registries, which gives WA a unique position to track and monitor trends in ACS admissions.

Although this study has the strength of a large sample size using whole-of-population data during the study time frame, it is not without limitations. The analysis of linked administrative health data is an important tool for the longitudinal tracking of patients over

time due to a lack of loss to follow up a complete capture of the population using health services. However, long-term (i.e., greater than one year) outcomes can only be evaluated if sufficient data are available beyond each year or composite end point. Furthermore, the WADLS has no current capacity to track patients who are admitted for the same condition in another Australian State or Territory. However, the data can lack some clinical detail which would create a more holistic approach which cardiac registries could overcome. This includes, but is not limited to, the time of symptom onset, time of first medical contact, whether an ECG was performed en route to the hospital, records of serial troponin levels over time, details of any administered pharmaceuticals, including fibrinolytic medications, accurate arrival times and times of balloon inflation in the cardiac catheterisation laboratory. The addition of these variables to a study such as this would allow for the adherence to the evidence-based guidelines developed by the NHFA/CSANZ to be assessed [11]. While the overall rates of admission for ACS can be reported via linked data, smaller internal registries can inform where the overall delays patients experienced, be it direct presentations or inter-hospital transfers. To overcome the limitations of the data, an aligned previous study by Forsyth et al. [18] used data from a single Perth metropolitan tertiary (teaching) hospital with round-the-clock PCI facilities which recorded key time points as part of their internal auditing process. This study highlighted the significantly longer infarct times for patients who required an inter-hospital transfer for treatment, despite the pre-hospital activation of the CCL at the treating hospital and shorter door-to-balloon times at the treating hospital, compared to direct presentations. Given 43% of Perth metropolitan admissions for first-time presentations of STEMI require an inter-hospital transfer, this is a large volume of patients experiencing a longer time-to-treatment burden and having poorer long-term outcomes.

Finally, this descriptive study is limited as the association between transfer status and patient outcomes was not evaluated. Rather, it sought to determine, at the population level, the rate of all first-time admissions for ACS in WA including the numbers of inter-hospital transfers according to geographic location and patient characteristics. Therefore, results reporting mortality rates should be regarded as exploratory in nature and will be the subject to further evaluation using appropriate modelling and/or quasi-experimental methods.

5. Conclusions

This paper provides information about the rates of ACS presentations in WA hospitals between 2007 and 2015, according to health, region, age and type of ACS. Accurate presentation numbers are essential to monitor the burden of ACS across the world informing researchers and governments alike on disparities between health regions and service utilisation. Of particular concern in our study is the percentage of metropolitan patients still requiring inter-hospital transfers for PCI, despite efforts to ensure STEMI presentations present directly to PCI-capable hospitals. With 48% of all patient admissions during the study period undergoing an inter-hospital transfer during their first admission for ACS, previously reported ACS presentation figures should be interpreted with care as they may be reporting total admission figures, not taking into account inter-hospital transfers during the same episode of care.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of Department of Health WA Human Research Ethics Committee (protocol code #2013/20 and date of approval 19/05/2013).

Informed Consent Statement: Patient consent was waived due to the nature of Linked Administrative Data which provides whole-of-population under stringent de-identification of datasets prior to distribution to research teams.

Data Availability Statement: The datasets generated and/or analysed during the current study are not publicly available due to strict requirements set out by the Human Ethics Research Committees regarding the storage and use of the data by authorised investigators. Due to the small cell size of the study we can only produce results in aggregate form to preserve anonymity and confidentially.

Conflicts of Interest: The authors declare no conflict of interest

Appendix A

Diagnosis codes for acute coronary syndromes from the International Classification of Diseases, Australian Modification 10th (ICD-10-AM) Edition and Procedural Codes for Primary Percutaneous Coronary Interventions from the Australian Classification of Health Interventions 10th Edition (ACHI-10) [24,28].

International Classification of Diseases, Australian Modification 10th Edition	
Acute MI [1]	I21, I22
Unstable Angina	I20.0
Australian Classification of Health Interventions, 10th Edition	
CABG [2]	38497-00, 38497-01, 38497-02, 38497-03, 38497-04, 38497-05, 38497-06, 38497-07, 38500-00, 38503-00, 38500-01, 38503-01, 38500-02, 38503-03, 38500-04, 38503-04, 38500-05, 38503-05, 90201-00, 90201-01, 90201-02, 90201-03
PCI [3] without stenting	38300-00, 38303-00, 38300-01, 38303-01
PCI [3] with stenting	38306-00, 38306-01, 38306-02, 38306-03, 38306-04, 38306-05
Cardiac Catheterisation	38200-00, 38203-00, 38206-00
Cardiac Angiography	38215-00, 38218-00, 38218-01, 38218-02
Other Coronary Procedures	38241-00, 38309-00, 38312-00, 38312-01, 38315-00, 38318-00 38318-01, 90218-00, 90218-01, 90218-02, 90218-03, 38505-00 38637-00, 38456-19, 38653-08

[1] myocardial infarction; [2] coronary artery bypass graft; [3] percutaneous coronary intervention.

Appendix B

Identification of Comorbid Conditions by International Classification of Diseases, 10th Edition, Australian Modification [24].

Comorbid Conditions	ICD-10-AM Codes
Any Infectious or Parasitic Disease	A00.X-B99.X Z86.1
Any Neoplasms	C00.X-D29.0; D29.2-D48. Z85.X, Z86.0, Z51.0, Z51.1, Z51.2
Any Endocrine, Metabolic or Immune Disease	E00.X-E90.X, Z86.3
Any Blood Disease	D50.X-D99.X, R23.3, Z86.2
Any Mental Disorder	F00.X-F99.X, R44.X, R15.X, R32.X, Z86.5
Any Disease of the Nervous System or Sense Organs	B91, B94.X, E14.3X, E14.4X, G00.X-G80.X, G83.X-G99.X, H00.X-H95.X, R56.X, T85.0, T85.1, Z86.12, Z86.6, Z94.7, Z96.1, Z97.0, Z97.4, Z46.1
Any Diseases of the Circulatory System	I39.8, G81.X, I00.X-I84.9, I86.X-I99.X, K55.1, K55.9, Q22.X-Q23.X, R60.X, R47.X, R02, R45.7, R57.X, T82.X, T85.0, T85.1, G97.8, G97.9, Z86.7, Z94.1, Z94.3, Z95.X, Z45.0.
Any Diseases of the Respiratory System	J00.X-J99.X, Z87.0, Z94.2, Z94.3.
Any Diseases of the Digestive System	K00.X-K55.0, K55.2-K55.8, K56.0-K93.X, R17.X, R13, Z87.1X, Z94.4.
Any Diseases of the Genitourinary System	D29.1, E11.2X, I12.0, I13.1, I13.2, I13.9, I15.0, I15.1, N00.X-N99.X, R33, T83.X, Z87.4, Z94.0, Z96.0, Z99.2, Z46.6, Z49.X.
All Pregnancy, Childbirth and the Puerperium	O00.X-O99.X, Z87.5, Z32.X, Z33.X, Z34.X, Z35.X
Any Diseases of Skin or Subcutaneous Tissue	L00.X-L99.X, R21, Z87.2.
Any Diseases of the Musculoskeletal System and Connective Tissue	M00.X-M99.X, T84.X, Z87.3, Z96.XX.
Congenital Anomalies	Q00.X-Q99.X, Z87.7,
Any Symptoms, Signs and Ill-Defined Conditions	H03.5, G43.X, G44.X, G47.X, G93.3, L57.9, L85.8, L85.9, O28.X, R00.X, R01.X, R03.X-R07.X, R09.X-R12.X, R14, R16.X, R18.X-R20.X, R22.X-R23.X, R25.X-R27.X, R29.X-R30.X, R34-R36, R39.X, R40.X-R43.X, R45.X, R48.X-R55.X, R59.X, R61.X-R63.X, R68.X, R70.X-R99.X, Z87.8.
Any Injury or Poisoning	S00.X-T98.X, Z91.6, Z91.5.
Any Factor Influencing Health Status and Contact with Health Services	Z00.X-Z01.X, Z03.X-Z13.X, Z20.X-Z29.X, Z39.X, Z40.X-Z76.X, Z80.X-Z99.X

Appendix C

Rates of all first-time admissions for Acute Coronary Syndrome in Western Australian between 1 January 2007 and 31 December 2015.

			2007	2008	2009	2010	2011	2012	2013	2014	2015
		Person–Years	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)	* n († Pop*) (‡ Rate)
All First-Time Admissions for ACS		10,000 PY	2231 (2,106,139) (10.59)	2171 (2,171,700) (10.00)	2394 (2,240,250) (10.69)	2525 (2,290,845) (11.02)	2634 (2,353,409) (11.19)	2596 (2,425,507) (10.70)	2422 (2,486,944) (9.74)	2343 (2,517,608) (9.31)	2332 (2,540,672) (9.18)
Sex	Male	10,000 PY	1424 (1,061,703) (13.41)	1425 (1,094,894) (13.01)	1533 (1,129,438) (13.57)	1611 (1,154,064) (13.96)	1689 (1,185,050) (14.25)	1704 (1,223,614) (13.93)	1605 (1,254,322) (12.80)	1526 (1,266,894) (12.05)	1486 (1,276,698) (11.64)
	Female	10,000 PY	807 (1,044,436) (7.73)	746 (1,076,806) (6.93)	861 (1,110,812) (7.75)	914 (1,136,781) (8.04)	945 (1,168,359) (8.09)	892 (1,201,893) (7.42)	817 (1,232,622) (6.63)	817 (1,250,714) (6.53)	846 (1,263,974) (6.69)
Age Categories	18–39 years	10,000 PY	56 (664,579.8) (0.84)	65 (692,108) (0.94)	63 (721,124.2) (0.87)	69 (737,877.8) (0.94)	61 (759,428.8) (0.80)	67 (788,406.8) (0.85)	60 (812,349) (0.74)	39 (818,460.2) (0.48)	57 (820,681.6) (0.69)
	40–49 years	10,000 PY	238 (312,936) (7.61)	233 (319,462) (7.29)	280 (326,291) (8.58)	268 (331,769) (8.08)	297 (339,664) (8.74)	279 (348,097) (8.02)	275 (352,279) (7.81)	223 (352,549) (6.33)	222 (352,321) (6.30)
	50–59 years	10,000 PY	463 (271,099) (17.08)	459 (276,577) (16.60)	454 (283,168) (16.03)	487 (290,113) (16.79)	550 (298,183) (18.45)	475 (304,940) (15.58)	459 (311,027) (14.76)	460 (314,838) (14.61)	450 (317,069) (14.19)
	60–69 years	10,000 PY	518 (179,683) (28.83)	482 (188,757) (25.54)	545 (197,668) (27.57)	613 (206,391) (29.70)	577 (215,720) (26.75)	624 (223,304) (27.94)	600 (231,497) (25.92)	591 (237,551) (24.88)	545 (244,020) (22.33)
	70–79 years	10,000 PY	494 (108,340) (45.60)	494 (110,836) (44.57)	508 (113,943) (44.58)	510 (116,996) (43.59)	567 (120,746) (46.96)	558 (125,149) (44.59)	514 (129,259) (39.77)	501 (134,777) (37.17)	506 (139,722) (36.21)
	80+ years	10,000 PY	462 (63,991) (72.20)	438 (66,373) (65.99)	544 (68,650) (79.24)	578 (71,126) (81.26)	582 (73,962) (78.69)	593 (75,999) (78.03)	514 (77,914) (65.97)	529 (79,686) (66.39)	552 (81,786) (67.49)
Residential Region	North Metro	10,000 PY	529 (521,904) (10.14)	527 (538,186) (9.79)	583 (555,044) (10.50)	602 (566,661) (10.62)	657 (581,869) (11.29)	674 (598,095) (11.27)	547 (611,518) (8.94)	528 (618,424) (8.54)	545 (624,063) (8.73)
	East Metro	10,000 PY	331 (646,837) (5.12)	272 (668,176) (4.07)	338 (690,254) (4.90)	411 (708,164) (5.80)	387 (728,104) (5.32)	400 (751,439) (5.32)	354 (771,803) (4.59)	328 (783,807) (4.18)	349 (793,760) (4.40)
	South Metro	10,000 PY	814 (459,726) (17.71)	830 (476,498) (17.42)	888 (494,044) (17.97)	913 (506,307) (18.03)	980 (523,594) (18.72)	918 (543,328) (16.90)	897 (560,534) (16.00)	904 (571,692) (15.81)	851 (581,114) (14.64)
	South West	10,000 PY	195 (147,093) (13.26)	175 (151,495) (11.55)	172 (156,220) (11.01)	175 (159,873) (10.95)	188 (163,450) (11.50)	200 (168,774) (11.85)	194 (173,435) (11.19)	195 (176,511) (11.05)	197 (178,703) (11.02)

	Great Southern	10,000 PY	70 (55,271) (12.66)	78 (55,748) (13.99)	68 (56,411) (12.05)	68 (56,711) (11.99)	88 (57,237) (15.37)	81 (58,444) (13.86)	85 (59,445) (14.30)	78 (60,060) (12.99)	92 (60,290) (15.26)
	Wheatbelt	10,000 PY	96 (73,347) (13.09)	94 (73,935) (12.71)	98 (74,899) (13.08)	91 (75,540) (12.05)	86 (76,177) (11.29)	88 (77,469) (11.36)	80 (78,477) (10.19)	73 (78,506) (9.30)	84 (78,134) (10.75)
	Goldfields	10,000 PY	63 (55,407) (11.37)	55 (56,576) (9.72)	69 (57,636) (11.97)	92 (58,470) (15.73)	77 (59,425) (12.96)	62 (60,481) (10.25)	73 (61,096) (11.95)	58 (59,878) (9.69)	50 (58,521) (8.54)
	Midwest	10,000 PY	52 (60,885) (8.54)	60 (62,159) (9.65)	85 (63,361) (13.42)	90 (63,980) (14.07)	77 (64,985) (11.85)	90 (66,068) (13.62)	98 (66,929) (14.64)	84 (66,715) (12.59)	83 (66,000) (12.58)
	Pilbara	10,000 PY	49 (51,165) (9.58)	41 (53,670) (7.64)	49 (56,578) (8.66)	44 (58,912) (7.47)	46 (61,777) (7.45)	33 (63,606) (5.19)	44 (64,978) (6.77)	39 (64,297) (6.07)	35 (63,021) (5.55)
	Kimberley	10,000 PY	32 (34,504) (9.27)	38 (35,257) (10.78)	44 (35,803) (12.29)	38 (36,227) (10.49)	46 (36,791) (12.50)	48 (37,803) (12.70)	49 (38,729) (12.65)	53 (37,718) (14.05)	46 (37,066) (12.41)
	* Unplaced		0 (-) (-)	1 (-) (-)	0 (-) (-)	1 (-) (-)	2 (-) (-)	1 (-) (-)	1 (-) (-)	3 (-) (-)	0 (-) (-)
Primary Diagnosis	UA	10,000 PY	824 (2,106,139) (3.91)	736 (2,171,700) (3.39)	766 (2,240,250) (3.42)	883 (2,290,845) (3.85)	779 (2,353,409) (3.31)	686 (2,425,507) (2.83)	576 (2,486,944) (2.32)	520 (2,517,608) (2.07)	468 (2,540,672) (1.84)
	NSTEMI	10,000 PY	782 (2,106,139) (3.71)	814 (2,171,700) (3.75)	961 (2,240,250) (4.29)	1032 (2,290,845) (4.50)	1282 (2,353,409) (5.45)	1326 (2,425,507) (5.47)	1297 (2,486,944) (5.22)	1243 (2,517,608) (4.94)	1346 (2,540,672) (5.30)
	STEMI	10,000 PY	625 (2,106,139) (2.97)	621 (2,171,700) (2.86)	667 (2,240,250) (2.98)	610 (2,290,845) (2.66)	573 (2,353,409) (2.43)	584 (2,425,507) (2.41)	549 (2,486,944) (2.21)	580 (2,517,608) (2.30)	518 (2,540,672) (2.04)
In Hospital Mortality	UA	10,000 PY	2 (824) (24.27)	1 (736) (13.59)	2 (766) (26.11)	2 (883) (22.65)	2 (779) (25.67)	0 (686) (0.00)	2 (576) (34.72)	2 (520) (38.46)	3 (468) (64.10)
	NSTEMI	10,000 PY	17 (782) (217.39)	20 (814) (245.70)	29 (961) (301.77)	27 (1032) (261.63)	32 (1282) (249.61)	36 (1326) (271.49)	27 (1297) (208.17)	24 (1243) (193.08)	20 (1346) (148.59)
	STEMI	10,000 PY	57 (625) (912.00)	51 (621) (821.26)	44 (667) (659.67)	47 (610) (770.49)	47 (573) (820.24)	33 (584) (565.07)	34 (549) (619.31)	33 (580) (568.97)	32 (518) (617.76)
Mortality	30-day	1000 PY	120 (2231) (53.79)	101 (2171) (46.52)	113 (2394) (47.20)	121 (2525) (47.92)	127 (2634) (48.22)	118 (2596) (45.45)	98 (2422) (40.46)	100 (2343) (42.68)	100 (2332) (42.88)
	30-days to 1-year	1000 PY	115 (2231) (51.55)	121 (2171) (55.73)	156 (2394) (65.16)	141 (2525) (55.84)	141 (2634) (53.53)	157 (2596) (60.48)	148 (2422) (61.11)	134 (2343) (57.19)	146 (2332) (62.61)
	More than 1-year	1000 PY	555 (2231) (248.77)	489 (2171) (225.24)	481 (2394) (200.92)	442 (2525) (175.05)	368 (2634) (139.71)	316 (2596) (121.73)	208 (2422) (85.88)	130 (2343) (55.48)	32 (2332) (13.72)

Primary Treatment	PCI ± Stent	100 PY	1244 (2231) (55.76)	1275 (2171) (58.73)	1463 (2394) (61.11)	1525 (2525) (60.40)	1632 (2634) (61.96)	1622 (2596) (62.48)	1628 (2422) (67.22)	1553 (2343) (66.28)	1588 (2332) (68.10)
	CABG	100 PY	132 (2231) (5.92)	118 (2171) (5.44)	104 (2394) (4.34)	137 (2525) (5.43)	124 (2634) (4.71)	129 (2596) (4.97)	116 (2422) (4.79)	130 (2343) (5.55)	121 (2332) (5.19)
	Other Coronary	100 PY	1 (2231) (0.04)	8 (2171) (0.37)	11 (2394) (0.46)	8 (2525) (0.32)	4 (2634) (0.15)	2 (2596) (0.08)	11 (2422) (0.45)	14 (2343) (0.60)	14 (2332) (0.60)
Transfer Status	Direct Admission	100 PY	1266 (2231) (56.75)	1167 (2171) (53.75)	1313 (2394) (54.85)	1359 (2525) (53.82)	1286 (2634) (48.82)	1186 (2596) (45.69)	1147 (2422) (47.36)	1228 (2343) (52.41)	1247 (2332) (53.47)
	Interhospital Transfer	100 PY	965 (2231) (43.25)	1004 (2171) (46.25)	1081 (2394) (45.15)	1166 (2525) (46.18)	1348 (2634) (51.18)	1410 (2596) (54.31)	1275 (2422) (52.64)	1115 (2343) (47.59)	1085 (2332) (46.53)
Admission Status	Emergency Admission	100 PY	1944 (2231) (87.14)	1901 (2171) (87.56)	2148 (2394) (89.72)	2239 (2525) (88.67)	2448 (2634) (92.94)	2402 (2596) (92.53)	2244 (2422) (92.65)	2130 (2343) (90.91)	2063 (2332) (88.46)
	Elective Admission	100 PY	287 (2231) (12.86)	270 (2171) (12.44)	246 (2394) (10.28)	286 (2525) (11.33)	186 (2634) (7.06)	194 (2596) (7.47)	178 (2422) (7.35)	213 (2343) (9.09)	269 (2332) (11.54)
MACSS 1 Year	0 MACSS	100 PY	33 (2231) (1.48)	29 (2171) (1.34)	45 (2394) (1.88)	47 (2525) (1.86)	61 (2634) (2.32)	30 (2596) (1.16)	26 (2422) (1.07)	20 (2343) (0.85)	19 (2332) (0.81)
	1 MACSS	100 PY	140 (2231) (6.28)	197 (2171) (9.07)	216 (2394) (9.02)	248 (2525) (9.82)	274 (2634) (10.40)	224 (2596) (8.63)	165 (2422) (6.81)	157 (2343) (6.70)	146 (2332) (6.26)
	2 MACSS	100 PY	269 (2231) (12.06)	327 (2171) (15.06)	320 (2394) (13.37)	347 (2525) (13.74)	389 (2634) (14.77)	352 (2596) (13.56)	280 (2422) (11.56)	263 (2343) (11.22)	255 (2332) (10.93)
	3+ MACSS	100 PY	1789 (2231) (80.19)	1618 (2171) (74.53)	1813 (2394) (75.73)	1883 (2525) (74.57)	1910 (2634) (72.51)	1990 (2596) (76.66)	1951 (2422) (80.55)	1903 (2343) (81.22)	1912 (2332) (81.99)
MACSS 5 Year	0 MACSS	100 PY	14 (2231) (0.63)	9 (2171) (0.41)	21 (2394) (0.88)	21 (2525) (0.83)	25 (2634) (0.95)	11 (2596) (0.42)	11 (2422) (0.45)	6 (2343) (0.26)	8 (2332) (0.34)
	1 MACSS	100 PY	70 (2231) (3.14)	86 (2171) (3.96)	115 (2394) (4.80)	108 (2525) (4.28)	128 (2634) (4.86)	100 (2596) (3.85)	87 (2422) (3.59)	72 (2343) (3.07)	66 (2332) (2.83)
	2 MACSS	100 PY	141 (2231) (6.32)	177 (2171) (8.15)	172 (2394) (7.18)	196 (2525) (7.76)	212 (2634) (8.05)	188 (2596) (7.24)	146 (2422) (6.03)	154 (2343) (6.57)	143 (2332) (6.13)
	3+ MACSS	100 PY	2006 (2231) (89.91)	1899 (2171) (87.47)	2086 (2394) (87.13)	2200 (2525) (87.13)	2269 (2634) (86.14)	2297 (2596) (88.48)	2178 (2422) (89.93)	2111 (2343) (90.10)	2115 (2332) (90.69)

* *n*: number of patients; †Pop*: population for that year and demographic factor; ‡Rate: rate per X person-years, as per the person-years column UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; PCI +/− Stent: percutaneous coronary intervention, with or without stent insertion, ; CABG: coronary artery bypass graft; MACSS: multipurpose Australian comorbidity scoring system.

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Appendices

Appendix 1: Diagnosis codes for acute coronary syndromes from the International Classification of Diseases, Australian Modification 10th (ICD-10-AM) Edition and Procedural Codes for Primary Percutaneous Coronary Interventions from the Australian Classification of Health Interventions 10th Edition (ACHI-10) 1-2.

International Classification of Diseases, Australian Modification 10th Edition	
Acute MI[1]	I21, I22
Unstable Angina	I20.0
Australian Classification of Health Interventions, 10th Edition	
CABG2	38497-00, 38497-01, 38497-02, 38497-03, 38497-04, 38497-05, 38497-06, 38497-07, 38500-00, 38503-00, 38500-01, 38503-01, 38500-02, 38503-03, 38500-04, 38503-04, 38500-05, 38503-05, 90201-00, 90201-01, 90201-02, 90201-03
PCI3 without stenting	38300-00, 38303-00, 38300-01, 38303-01
PCI3 with stenting	38306-00, 38306-01, 38306-02, 38306-03, 38306-04, 38306-05
Cardiac Catheterisation	38200-00, 38203-00, 38206-00
Cardiac Angiography	38215-00, 38218-00, 38218-01, 38218-02
Other Coronary Procedures	38241-00, 38309-00, 38312-00, 38312-01, 38315-00, 38318-00 38318-01, 90218-00, 90218-01, 90218-02, 90218-03, 38505-00 38637-00, 38456-19, 38653-08

[1]Myocardial Infarction; [2]Coronary Artery Bypass Graft; [3]Percutaneous Coronary Intervention.

Appendix 2: Identification of Comorbid Conditions by International Classification of Diseases, 10th Edition, Australian Modification [1].

Comorbid Conditions.	ICD-10-AM Codes
Any Infectious or Parasitic Disease	A00.X – B99.X Z86.1
Any Neoplasms	C00.X-D29.0; D29.2-D48. Z85.X, Z86.0, Z51.0, Z51.1, Z51.2
Any Endocrine, Metabolic or Immune Disease	E00.X-E90.X, Z86.3
Any Blood Disease	D50.X-D99.X, R23.3, Z86.2
Any Mental Disorder	F00.X-F99.X, R44.X, R15.X, R32.X, Z86.5
Any Disease of the Nervous System or Sense Organs	B91, B94.X, E14.3X, E14.4X,G00.X- G80.X, G83.X-G99.X, H00.X-H95.X, R56.X, T85.0, T85.1, Z86.12, Z86.6, Z94.7, Z96.1, Z97.0, Z97.4, Z46.1
Any Diseases of the Circulatory System	I39.8, G81.X, I00.X- I84.9, I86.X-I99.X, K55.1, K55.9, Q22.X-Q23.X, R60.X, R47.X, R02, R45.7, R57.X, T82.X, T85.0, T85.1, G97.8, G97.9, Z86.7, Z94.1, Z94.3, Z95.X, Z45.0.
Any Diseases of the Respiratory System	J00.X-J99.X, Z87.0, Z94.2, Z94.3.
Any Diseases of the Digestive System	K00.X-K55.0, K55.2-K55.8, K56.0-K93.X, R17.X, R13, Z87.1X, Z94.4.
Any Diseases of the Genitourinary System	D29.1, E11.2X, I12.0, I13.1, I13.2, I13.9, I15.0, I15.1, N00.X-N99.X, R33, T83.X, Z87.4, Z94.0, Z96.0, Z99.2, Z46.6, Z49.X.
All Pregnancy, Childbirth and the Puerperium	O00.X-O99.X, Z87.5, Z32.X, Z33.X, Z34.X, Z35.X
Any Diseases of Skin or Subcutaneous Tissue	L00.X-L99.X, R21, Z87.2.
Any Diseases of the Musculoskeletal System and Connective Tissue	M00.X-M99.X, T84.X, Z87.3, Z96.XX.
Congenital Anomalies	Q00.X-Q99.X, Z87.7,
Any Symptoms, Signs, and Ill-Defined Conditions	E03.5, G43.X, G44.X, G47.X, G93.3, L57.9, L85.8, L85.9, O28.X, R00.X, R01.X, R03.X- R07.X, R09.X- R12.X, R14, R16.X, R18.X-R20.X, R22.X-R23.X, R25.X- R27.X, R29.X-R30.X, R34-R36, R39.X, R40.X- R43.X, R45.X, R48.X- R55.X, R59.X, R61.X-R63.X, R68.X, R70.X-R99.X, Z87.8.
Any Injury or Poisoning	S00.X-T98.X, Z91.6, Z91.5.
Any Factor Influencing Health Status and Contact with Health Services	Z00.X-Z01.X, Z03.X-Z13.X, Z20.X-Z29.X, Z39.X, Z40.X- Z76.X, Z80.X-Z99.X

Appendix 3: Rates of all first-time admissions for Acute Coronary Syndrome in western Australian between 01/01/2007 to 31/12/2009

		Person Years	2007 * *n* (†Pop^n) (‡Rate)	2008 * *n* (†Pop^n) (‡Rate)	2009 * *n* (†Pop^n) (‡Rate)
All First-Time Admissions for ACS		10,000	2231 (2,106,139) (10.59)	2171 (2,171,700) (10.00)	2394 (2,240,250) (10.69)
Sex	**Male**	10,000	1424 (1,061,703) (13.41)	1425 (1,094,894) (13.01)	1533 (1,129,438) (13.57)
	Female	10,000	807 (1,044,436) (7.73)	746 (1,076,806) (6.93)	861 (1,110,812) (7.75)
Age Categories	**18–39 years**	10,000	56 (664,579.8) (0.84)	65 (692,108) (0.94)	63 (721,124.2) (0.87)
	40–49 years	10,000	238 (312,936) (7.61)	233 (319,462) (7.29)	280 (326,291) (8.58)
	50–59 years	10,000	463 (271,099) (17.08)	459 (276,577) (16.60)	454 (283,168) (16.03)
	60–69 years	10,000	518 (179,683) (28.83)	482 (188,757) (25.54)	545 (197,668) (27.57)
	70–79 years	10,000	494 (108,340) (45.60)	494 (110,836) (44.57)	508 (113,943) (44.58)
	80+ years	10,000	462 (63,991) (72.20)	438 (66,373) (65.99)	544 (68,650) (79.24)
Residential Region	**North Metro**	10,000	529 (521,904) (10.14)	527 (538,186) (9.79)	583 (555,044) (10.50)
	East Metro	10,000	331 (646,837) (5.12)	272 (668,176) (4.07)	338 (690,254) (4.90)
	South Metro	10,000	814 (459,726) (17.71)	830 (476,498) (17.42)	888 (494,044) (17.97)
	South West	10,000	195 (147,093) (13.26)	175 (151,495) (11.55)	172 (156,220) (11.01)
	Great Southern	10,000	70 (55,271) (12.66)	78 (55,748) (13.99)	68 (56,411) (12.05)
	Wheatbelt	10,000	96 (73,347) (13.09)	94 (73,935) (12.71)	98 (74,899) (13.08)
	Goldfields	10,000	63 (55,407) (11.37)	55 (56,576) (9.72)	69 (57,636) (11.97)
	Midwest	10,000	52 (60,885) (8.54)	60 (62,159) (9.65)	85 (63,361) (13.42)
	Pilbara	10,000	49 (51,165) (9.58)	41 (53,670) (7.64)	49 (56,578) (8.66)
	Kimberley	10,000	32 (34,504) (9.27)	38 (35,257) (10.78)	44 (35,803) (12.29)
	***Unplaced**	10,000	0 (-) (-)	1 (-) (-)	0 (-) (-)
Primary Diagnosis	**UA**	10,000	824 (2,106,139) (3.91)	736 (2,171,700) (3.39)	766 (2,240,250) (3.42)
	NSTEMI	10,000	782 (2,106,139) (3.71)	814 (2,171,700) (3.75)	961 (2,240,250) (4.29)
	STEMI	10,000	625 (2,106,139) (2.97)	621 (2,171,700) (2.86)	667 (2,240,250) (2.98)
In Hospital Mortality	**UA**	10,000	2 (824) (24.27)	1 (736) (13.59)	2 (766) (26.11)
	NSTEMI	10,000	17 (782) (217.39)	20 (814) (245.70)	29 (961) (301.77)
	STEMI	10,000	57 (625) (912.00)	51 (621) (821.26)	44 (667) (659.67)
Mortality	**30-day**	1,000	120 (2231) (53.79)	101 (2171) (46.52)	113 (2394) (47.20)
	30-days to 1-year	1,000	115 (2231) (51.55)	121 (2171) (55.73)	156 (2394) (65.16)
	More than 1-year	1,000	555 (2231) (248.77)	489 (2171) (225.24)	481 (2394) (200.92)
Primary Treatment	**PCI ± Stent**	100	1244 (2231) (55.76)	1275 (2171) (58.73)	1463 (2394) (61.11)
	CABG	100	132 (2231) (5.92)	118 (2171) (5.44)	104 (2394) (4.34)
	Other Coronary	100	1 (2231) (0.04)	8 (2171) (0.37)	11 (2394) (0.46)
Transfer Status	**Direct Admission**	100	1266 (2231) (56.75)	1167 (2171) (53.75)	1313 (2394) (54.85)
	Interhospital Transfer	100	965 (2231) (43.25)	1004 (2171) (46.25)	1081 (2394) (45.15)
Admission Status	**Emergency Admission**	100	1944 (2231) (87.14)	1901 (2171) (87.56)	2148 (2394) (89.72)
	Elective Admission	100	287 (2231) (12.86)	270 (2171) (12.44)	246 (2394) (10.28)
MACSS 1 Year	**0 MACSS**	100	33 (2231) (1.48)	29 (2171) (1.34)	45 (2394) (1.88)
	1 MACSS	100	140 (2231) (6.28)	197 (2171) (9.07)	216 (2394) (9.02)
	2 MACSS	100	269 (2231) (12.06)	327 (2171) (15.06)	320 (2394) (13.37)
	3+ MACSS	100	1789 (2231) (80.19)	1618 (2171) (74.53)	1813 (2394) (75.73)
MACSS 5 Year	**0 MACSS**	100	14 (2231) (0.63)	9 (2171) (0.41)	21 (2394) (0.88)
	1 MACSS	100	70 (2231) (3.14)	86 (2171) (3.96)	115 (2394) (4.80)
	2 MACSS	100	141 (2231) (6.32)	177 (2171) (8.15)	172 (2394) (7.18)
	3+ MACSS	100	2006 (2231) (89.91)	1899 (2171) (87.47)	2086 (2394) (87.13)

*n: number of patients; †Popn: population for that year and demographic factor; ‡Rate: rate per X person–years, as per the person–years column UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; PCI +/- Stent: percutaneous coronary intervention, with or without stent insertion.; CABG: coronary artery bypass graft; MACSS: multipurpose Australian comorbidity scoring system.

Appendix 4: Rates of all first-time admissions for Acute Coronary Syndrome in western Australian between 01/01/2010 to 31/12/2012

		Person Years	2010 * *n* (†Pop^n) (‡Rate)	2011 * *n* (†Pop^n) (‡Rate)	2012 * *n* (†Pop^n) (‡Rate)
All First-Time Admissions for ACS		10,000	2525 (2,290,845) (11.02)	2634 (2,353,409) (11.19)	2596 (2,425,507) (10.70)
Sex	**Male**	10,000	1611 (1,154,064) (13.96)	1689 (1,185,050) (14.25)	1704 (1,223,614) (13.93)
	Female	10,000	914 (1,136,781) (8.04)	945 (1,168,359) (8.09)	892 (1,201,893) (7.42)
Age Categories	**18–39 years**	10,000	69 (737,877.8) (0.94)	61 (759,428.8) (0.80)	67 (788,406.8) (0.85)
	40–49 years	10,000	268 (331,769) (8.08)	297 (339,664) (8.74)	279 (348,097) (8.02)
	50–59 years	10,000	487 (290,113) (16.79)	550 (298,183) (18.45)	475 (304,940) (15.58)
	60–69 years	10,000	613 (206,391) (29.70)	577 (215,720) (26.75)	624 (223,304) (27.94)
	70–79 years	10,000	510 (116,996) (43.59)	567 (120,746) (46.96)	558 (125,149) (44.59)
	80+ years	10,000	578 (71,126) (81.26)	582 (73,962) (78.69)	593 (75,999) (78.03)
Residential Region	**North Metro**	10,000	602 (566,661) (10.62)	657 (581,869) (11.29)	674 (598,095) (11.27)
	East Metro	10,000	411 (708,164) (5.80)	387 (728,104) (5.32)	400 (751,439) (5.32)
	South Metro	10,000	913 (506,307) (18.03)	980 (523,594) (18.72)	918 (543,328) (16.90)
	South West	10,000	175 (159,873) (10.95)	188 (163,450) (11.50)	200 (168,774) (11.85)
	Great Southern	10,000	68 (56,711) (11.99)	88 (57,237) (15.37)	81 (58,444) (13.86)
	Wheatbelt	10,000	91 (75,540) (12.05)	86 (76,177) (11.29)	88 (77,469) (11.36)
	Goldfields	10,000	92 (58,470) (15.73)	77 (59,425) (12.96)	62 (60,481) (10.25)
	Midwest	10,000	90 (63,980) (14.07)	77 (64,985) (11.85)	90 (66,068) (13.62)
	Pilbara	10,000	44 (58,912) (7.47)	46 (61,777) (7.45)	33 (63,606) (5.19)
	Kimberley	10,000	38 (36,227) (10.49)	46 (36,791) (12.50)	48 (37,803) (12.70)
	***Unplaced**	10,000	1 (-) (-)	2 (-) (-)	1 (-) (-)
Primary Diagnosis	**UA**	10,000	883 (2,290,845) (3.85)	779 (2,353,409) (3.31)	686 (2,425,507) (2.83)
	NSTEMI	10,000	1032 (2,290,845) (4.50)	1282 (2,353,409) (5.45)	1326 (2,425,507) (5.47)
	STEMI	10,000	610 (2,290,845) (2.66)	573 (2,353,409) (2.43)	584 (2,425,507) (2.41)
In Hospital Mortality	**UA**	10,000	2 (883) (22.65)	2 (779) (25.67)	0 (686) (0.00)
	NSTEMI	10,000	27 (1032) (261.63)	32 (1282) (249.61)	36 (1326) (271.49)
	STEMI	10,000	47 (610) (770.49)	47 (573) (820.24)	33 (584) (565.07)
Mortality	**30-day**	1,000	121 (2525) (47.92)	127 (2634) (48.22)	118 (2596) (45.45)
	30-days to 1-year	1,000	141 (2525) (55.84)	141 (2634) (53.53)	157 (2596) (60.48)
	More than 1-year	1,000	442 (2525) (175.05)	368 (2634) (139.71)	316 (2596) (121.73)
Primary Treatment	**PCI ± Stent**	100	1525 (2525) (60.40)	1632 (2634) (61.96)	1622 (2596) (62.48)
	CABG	100	137 (2525) (5.43)	124 (2634) (4.71)	129 (2596) (4.97)
	Other Coronary	100	8 (2525) (0.32)	4 (2634) (0.15)	2 (2596) (0.08)
Transfer Status	**Direct Admission**	100	1359 (2525) (53.82)	1286 (2634) (48.82)	1186 (2596) (45.69)
	Interhospital Transfer	100	1166 (2525) (46.18)	1348 (2634) (51.18)	1410 (2596) (54.31)
Admission Status	**Emergency Admission**	100	2239 (2525) (88.67)	2448 (2634) (92.94)	2402 (2596) (92.53)
	Elective Admission	100	286 (2525) (11.33)	186 (2634) (7.06)	194 (2596) (7.47)
MACSS 1 Year	**0 MACSS**	100	47 (2525) (1.86)	61 (2634) (2.32)	30 (2596) (1.16)
	1 MACSS	100	248 (2525) (9.82)	274 (2634) (10.40)	224 (2596) (8.63)
	2 MACSS	100	347 (2525) (13.74)	389 (2634) (14.77)	352 (2596) (13.56)
	3+ MACSS	100	1883 (2525) (74.57)	1910 (2634) (72.51)	1990 (2596) (76.66)
MACSS 5 Year	**0 MACSS**	100	21 (2525) (0.83)	25 (2634) (0.95)	11 (2596) (0.42)
	1 MACSS	100	108 (2525) (4.28)	128 (2634) (4.86)	100 (2596) (3.85)
	2 MACSS	100	196 (2525) (7.76)	212 (2634) (8.05)	188 (2596) (7.24)
	3+ MACSS	100	2200 (2525) (87.13)	2269 (2634) (86.14)	2297 (2596) (88.48)

*n: number of patients; †Popn: population for that year and demographic factor; ‡Rate: rate per X person–years, as per the person–years column UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; PCI +/- Stent: percutaneous coronary intervention, with or without stent insertion.; CABG: coronary artery bypass graft; MACSS: multipurpose Australian comorbidity scoring system.

Appendix 5: Rates of all first-time admissions for Acute Coronary Syndrome in western Australian between 01/01/2013 to 31/12/2015

		Person Years	2013 * *n* (†Pop^n) (‡Rate)	2014 * *n* (†Pop^n) (‡Rate)	2015 * *n* (†Pop^n) (‡Rate)
All First-Time Admissions for ACS		10,000 PY	2422 (2,486,944) (9.74)	2343 (2,517,608) (9.31)	2332 (2,540,672) (9.18)
Sex	**Male**	10,000	1605 (1,254,322) (12.80)	1526 (1,266,894) (12.05)	1486 (1,276,698) (11.64)
	Female	10,000	817 (1,232,622) (6.63)	817 (1,250,714) (6.53)	846 (1,263,974) (6.69)
Age Categories	**18–39 years**	10,000	60 (812,349) (0.74)	39 (818,460.2) (0.48)	57 (820,681.6) (0.69)
	40–49 years	10,000	275 (352,279) (7.81)	223 (352,549) (6.33)	222 (352,321) (6.30)
	50–59 years	10,000	459 (311,027) (14.76)	460 (314,838) (14.61)	450 (317,069) (14.19)
	60–69 years	10,000	600 (231,497) (25.92)	591 (237,551) (24.88)	545 (244,020) (22.33)
	70–79 years	10,000	514 (129,259) (39.77)	501 (134,777) (37.17)	506 (139,722) (36.21)
	80+ years	10,000	514 (77,914) (65.97)	529 (79,686) (66.39)	552 (81,786) (67.49)
Residential Region	**North Metro**	10,000	547 (611,518) (8.94)	528 (618,424) (8.54)	545 (624,063) (8.73)
	East Metro	10,000	354 (771,803) (4.59)	328 (783,807) (4.18)	349 (793,760) (4.40)
	South Metro	10,000	897 (560,534) (16.00)	904 (571,692) (15.81)	851 (581,114) (14.64)
	South West	10,000	194 (173,435) (11.19)	195 (176,511) (11.05)	197 (178,703) (11.02)
	Great Southern	10,000	85 (59,445) (14.30)	78 (60,060) (12.99)	92 (60,290) (15.26)
	Wheatbelt	10,000	80 (78,477) (10.19)	73 (78,506) (9.30)	84 (78,134) (10.75)
	Goldfields	10,000	73 (61,096) (11.95)	58 (59,878) (9.69)	50 (58,521) (8.54)
	Midwest	10,000	98 (66,929) (14.64)	84 (66,715) (12.59)	83 (66,000) (12.58)
	Pilbara	10,000	44 (64,978) (6.77)	39 (64,297) (6.07)	35 (63,021) (5.55)
	Kimberley	10,000	49 (38,729) (12.65)	53 (37,718) (14.05)	46 (37,066) (12.41)
	***Unplaced**	10,000	1 (-) (-)	3 (-) (-)	0 (-) (-)
Primary Diagnosis	**UA**	10,000	576 (2,486,944) (2.32)	520 (2,517,608) (2.07)	468 (2,540,672) (1.84)
	NSTEMI	10,000	1297 (2,486,944) (5.22)	1243 (2,517,608) (4.94)	1346 (2,540,672) (5.30)
	STEMI	10,000	549 (2,486,944) (2.21)	580 (2,517,608) (2.30)	518 (2,540,672) (2.04)
In Hospital Mortality	**UA**	10,000	2 (576) (34.72)	2 (520) (38.46)	3 (468) (64.10)
	NSTEMI	10,000	27 (1297) (208.17)	24 (1243) (193.08)	20 (1346) (148.59)
	STEMI	10,000	34 (549) (619.31)	33 (580) (568.97)	32 (518) (617.76)
Mortality	**30-day**	1,000	98 (2422) (40.46)	100 (2343) (42.68)	100 (2332) (42.88)
	30-days to 1-year	1,000	148 (2422) (61.11)	134 (2343) (57.19)	146 (2332) (62.61)
	More than 1-year	1,000	208 (2422) (85.88)	130 (2343) (55.48)	32 (2332) (13.72)
Primary Treatment	**PCI ± Stent**	100	1628 (2422) (67.22)	1553 (2343) (66.28)	1588 (2332) (68.10)
	CABG	100	116 (2422) (4.79)	130 (2343) (5.55)	121 (2332) (5.19)
	Other Coronary	100	11 (2422) (0.45)	14 (2343) (0.60)	14 (2332) (0.60)
Transfer Status	**Direct Admission**	100	1147 (2422) (47.36)	1228 (2343) (52.41)	1247 (2332) (53.47)
	Interhospital Transfer	100	1275 (2422) (52.64)	1115 (2343) (47.59)	1085 (2332) (46.53)
Admission Status	**Emergency Admission**	100	2244 (2422) (92.65)	2130 (2343) (90.91)	2063 (2332) (88.46)
	Elective Admission	100	178 (2422) (7.35)	213 (2343) (9.09)	269 (2332) (11.54)
MACSS 1 Year	**0 MACSS**	100	26 (2422) (1.07)	20 (2343) (0.85)	19 (2332) (0.81)
	1 MACSS	100	165 (2422) (6.81)	157 (2343) (6.70)	146 (2332) (6.26)
	2 MACSS	100	280 (2422) (11.56)	263 (2343) (11.22)	255 (2332) (10.93)
	3+ MACSS	100	1951 (2422) (80.55)	1903 (2343) (81.22)	1912 (2332) (81.99)
MACSS 5 Year	**0 MACSS**	100	11 (2422) (0.45)	6 (2343) (0.26)	8 (2332) (0.34)
	1 MACSS	100	87 (2422) (3.59)	72 (2343) (3.07)	66 (2332) (2.83)
	2 MACSS	100	146 (2422) (6.03)	154 (2343) (6.57)	143 (2332) (6.13)
	3+ MACSS	100	2178 (2422) (89.93)	2111 (2343) (90.10)	2115 (2332) (90.69)

*n: number of patients; †Popn: population for that year and demographic factor; ‡Rate: rate per X person–years, as per the person–years column UA: unstable angina; NSTEMI: non-ST-segment elevation AMI; STEMI: ST-segment elevation AMI; AMI: acute myocardial infarction; PCI +/- Stent: percutaneous coronary intervention, with or without stent insertion.; CABG: coronary artery bypass graft; MACSS: multipurpose Australian comorbidity scoring system.

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