

Gender disparity in 12-lead electrocardiogram acquisition by
Emergency Medical Service staff
for patients with cardiac-type chest pain

Bronwyn Henderson

MPhil

2016

Gender disparity in 12-lead electrocardiogram acquisition by
Emergency Medical Service staff
for patients with cardiac-type chest pain

Bronwyn Henderson

A thesis submitted to
Auckland University of Technology
in fulfilment of the requirements for the degree of
Master of Philosophy (MPhil)

2016

School of Clinical Sciences, Department of Paramedicine

Abstract

Background:

Female patients suffering from Acute Coronary Syndrome (ACS) receive fewer investigations and treatments than male patients, in both the pre-hospital and hospital environments. To accurately diagnose ACS a 12-Lead ECG is required and failure to acquire an early 12-lead ECG can impact on accessing timely treatment. This could be a barrier to women receiving appropriate medical care. Some authors suggest that, because female patients suffering ACS are more likely to present with atypical symptoms, their cardiac diagnosis is missed. Consequently, they receive inferior treatment to their male counterparts. Unlike previous studies exploring gender disparity in investigation of ACS, this study controlled for both the EMS staff members working diagnosis and the patient's presentation. The primary objective was to establish whether EMS staff exhibited gender disparity when assessing patients with cardiac-type chest pain, though 12-lead ECG acquisition rates when the attending EMS staff member's working diagnosis was that of ACS. Secondary objectives were to investigate procedural compliance, variables associated with reduced odds of 12-lead ECG acquisition and whether previously proposed explanations of gender disparity in ACS assessment were supported.

Methods and Results:

Intensive Care Paramedics, trained in data extraction, reviewed 26,273 patient report forms (PRFs) from four urban and rural centres across New Zealand. Study inclusion was limited to PRFs from patients who described cardiac-type chest pain and where the EMS staff member's working diagnosis was that of ACS. Partial verification double-entry was used to lower error rates whilst maintaining cost-effective data extraction for PRFs collected over a one year period (ending in November 2010).

A power calculation was undertaken based on data from a 2009 pilot study. This established that a minimum of 418 PRFs would be required to detect a difference in acquisition rates between male and female patients ($\alpha=0.05$, power=90%). A total of 1,675 PRFs met the study's inclusion criteria and were included in the study; 52% were from male patients. Overall rates of 12-lead ECG acquisition were low at 42% of cases. 50% of males ($n=431$) had a 12-lead ECG acquired compared with 34% of females ($n=275$) ($P<0.001$). After adjusting for potential confounders in a multiple logistic regression model, the odds ratio for female patients having a 12-lead ECG acquired was 0.50 (CI95%, 0.40 – 0.63) compared with male patients. The probability of having a 12-lead ECG acquired for both genders combined varied significantly between study centres, from 86% of the sample from the Rural B region to 33% of the sample from the Urban B region.

Conclusions

This study showed that the established gender disparity in ACS investigations cannot be fully explained by women's increased propensity for an atypical-ACS-presentation. Furthermore, a false negative ACS diagnosis on the basis of this atypical-presentation cannot fully explain the gender disparity either. We showed that when the patient's presentation and the EMS staff member's diagnosis were controlled for, female patients still had significantly fewer 12-lead

ECGs acquired than male patients. Secondary analysis identified substantial local variation in practice, suggesting the possibility of improving the frequency of this vital investigation in ACS through culture change.

Table of Contents	
Abstract	2
Attestation of Authorship	6
List of Figures.....	7
List of Tables	8
Co-Authored Contribution	9
Acknowledgements	10
Intellectual Property Rights:	11
Ethical Approval:	11
Confidential Material	11
Chapter 1: Introduction and overview	12
1.1 - Acute Coronary Syndrome Defined	12
1.2 - Epidemiology of IHD and AMI.....	14
1.3 - Diagnosis of ACS.....	14
1.4 - Management of ACS.....	16
1.5 – Recommendations for optimal AMI treatment	18
1.6 – Overview summary	24
1.7 - Aims of the study:	24
1.8 - Structure of the thesis:.....	25
Referencing Style	25
Chapter 2 – Literature Review	26
2.1 – Search strategy	26
2.2 – Article review	27
2.3 - Gender Disparity	36
2.4 – Reasons for gender disparity	42
Chapter 3 – Research Design.....	44
3.1 - Study design	44
3.2 – Setting	44
3.3 – Patients	47
3.4 – Variables and data sources	47
3.5 – Gender disparity.....	51
3.6 – Study size.....	53
3.7 – Quantitative variables.....	53

3.8 – Statistical methods	54
Chapter 4 – Results	58
4.1 – Participants	58
4.2 – Descriptive data	59
4.3 – Outcome data.....	60
4.4 – Main results	61
4.5 – Other analyses	65
Chapter 5 – Discussion	68
5.1 - Key Results	68
5.2 – Limitations	71
5.3 - Interpretation	71
5.4 - Generalisability	72
5.5 – Funding	73
5.6 - Conclusion	73
References	74
Appendix A	83
Appendix B	84
Appendix C	85
Appendix D	86
Appendix E	87
Appendix F	88
Appendix G	90
Appendix H.....	91
Appendix I	92
Appendix J.....	93
Appendix K	94

Attestation of Authorship

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning. The statistical analysis for this thesis' research project was a joint effort in consultation with a biostatistician, Mr Steven Taylor. His percentage of contribution to each of the chapters is outlined at the beginning of the thesis.

A handwritten signature in blue ink, appearing to read 'Bronwyn Henderson', is centered on the page. The signature is fluid and cursive, with a large initial 'B' and 'H'.

Bronwyn Henderson

List of Figures

Figure 1: Declining in-hospital mortality in Australia due to AMI over ten years.....	19
Figure 2: Symptom onset-to-door times for men and women with AMI.....	21
Figure 3: Flowchart of this study's literature review.	27
Figure 4: Standardised mortality ratios for the Carstairs social deprivation scores.....	34
Figure 5: More females than males in the New Zealand population aged ≥ 80 years.....	48
Figure 6: Flow chart for study inclusion	58
Figure 7 Graphical demonstration of 12-lead ECG acquisition with treatment.....	64
Figure 8: AOR of 12-Lead ECG acquisition	65

List of Tables

Table 1: Symptom onset-to-door times according to first health-professional contact	21
Table 2: Pre-hospital ECG acquisition rates and Door-to-balloon times	23
Table 3: All journal articles for this study's literature review	29
Table 4 Recruitment methods for the 21 articles in this study's literature review	31
Table 5: Comorbidities according to gender for this study's literature review	35
Table 6: Areas where researchers investigated for gender disparity in ACS	37
Table 7 Time differences when comparing men and women with STEMI at PCI centres.....	41
Table 8 AOR for in-hospital mortality for women compared to men.....	42
Table 9: Proposed explanations for gender disparity amongst articles in the literature review...	43
Table 10: Each variable recorded in the study and why it was included	50
Table 11: Pilot study data from 2009 used to derive a necessary sample size.....	53
Table 12: Grouped quantitative variables of this study and why they were grouped.	54
Table 13: Characteristics of the study sample according to patient's gender	60
Table 14: Sample that were attended by paramedic and rate of 12-lead ECG acquisition.....	61
Table 15: Rates of 12-lead ECG acquisition categorised by data centre location.....	61
Table 16: Number and proportion of male and female patients in each of the data centres.....	61
Table 17: UORs of 12-Lead ECGs	63
Table 18: Gender subgroup analysis with multivariable logistic regression model and AORs ...	66

Co-Authored Contribution

Name and percentage contribution

Signature

Chapter 1

Bronwyn Henderson 100%



Chapter 2

Bronwyn Henderson 100%



Chapter 3

Bronwyn Henderson 100%



Chapter 4

Bronwyn Henderson 55%



Steven Taylor 45%

Mr Taylor is the biostatistician responsible for the statistical analysis behind almost all of the tables and all of the figures within this chapter. He also compiled the bulk of the table presentations.

Chapter 5

Bronwyn Henderson 100%



Acknowledgements

This thesis was completed through the School of Clinical Sciences, Department of Paramedicine at Auckland University of Technology (AUT), New Zealand (NZ). The generosity, hard-work, support and guidance from many people have allowed this research project and thesis to come to fruition and completion:

I'll start by thanking my ever supportive husband, Michael Henderson, for his easy-going "we can do it honey" encouragement. My quest for further education has always been nourished both financially and emotionally by him.

To my darling daughter Genevieve, you have been my biggest reward and challenge to date. Know that your mind is your most powerful possession, nourish it with education and seek the truth in all of your endeavours.

Thanks go to some special people in the Department of Paramedicine:

My supervisor, Ms Bronwyn Tunnage, has provided exemplary guidance, countless hours and much-needed encouragement to allow me to stay on track and focus on the completion of both the research and the thesis. Her flexible but steady negotiating around my busy timetable has provided freedom to develop my research skills whilst still providing a clear framework for the thesis construction. Ms Tunnage also contributed a large portion of the data capture from the Rural B and Urban B regions.

Mr Steven Taylor has also been gracious with his availability as our biostatistician and very understanding and insightful with his translation of the statistics. Mr Taylor has also contributed to this thesis by providing the tables and figures for this study's statistical analysis.

Thanks go to Brenda Costa-Scorse whom initially awoke the research-bug in me, through the Special Interest paper of the Paramedic degree.

My gratitude goes to the scientific advisory group of the National Heart Foundation of New Zealand for providing the research with a Small Project Grant, which was by no means small in enabling this project to proceed.

Many volunteer hours were gratefully received from dedicated, passionate and enthusiastic Intensive Care Paramedics; Andrew Christie, Brent Williams and Cheryl DesLandes. Thank you for your dedication to improving paramedic practice and patient outcomes. Thanks also extend to Dr Tony Smith as the Clinical Director of St John in allowing us to access the data for the research.

Intellectual Property Rights:

There are no intellectual property rights to be mentioned here.

Ethical Approval:

Ethical approval was sought and approved through the following:

Multi-region Ethics Committee; Ministry of Health:

19th of July 2010: Under section 11.9 for observational studies – expedited review is appropriate.

Auckland University of Technology Ethics Committee:

11th of October 2010: Ethics application approved under section 5.3.2.3

St John:

1st of May 2012: Written medical director approval.

Confidential Material

There is no confidential material in this thesis.

Chapter 1: Introduction and overview

This thesis examines gender disparity and procedural compliance in the assessment of Acute Coronary Syndrome (ACS) in the pre-hospital EMS field. The included observational study investigated whether gender disparity existed in the assessment of ACS when the patient's presentation and the attending EMS staff member's working diagnosis were controlled for. The study's null-hypothesis stated that there would be no difference in acquisition rates of 12-Lead ECGs from EMS staff, between male and female patients presenting with 'typical cardiac-type chest pain' when the EMS staff member's working-diagnosis was that of ACS. As the included study is observational in nature, the STROBE (Strengthening The Reporting of OBservational studies in Epidemiology) criteria will be used to guide the structure of this thesis, with an aim of clear and transparent reporting of the study's strengths and weaknesses (1).

Previous research into gender disparity for in-hospital ACS investigations and management is quite extensive compared to that within the pre-hospital EMS field. However, we were unable to find any previous research has controlled for both the patient's presentation and the practitioner's working-diagnosis in the assessment of ACS. This thesis attempts to fill this gap in the literature and hopefully clarify the cause of this established gender disparity.

Early acquisition of the relatively simple and non-invasive 12-lead ECG is the standard procedure for suspected ACS in pre-hospital emergency care. By investigating rates of 12-lead ECG acquisition for patients attended by EMS staff whose working diagnosis was that of ACS, this thesis attempts to clarify:

1. Whether EMS staff exhibited gender disparity when assessing patients with cardiac-type chest pain. Specifically; whether the rates of 12-lead ECG acquisition were different for male and female patients when the attending EMS staff member's working diagnosis was that of ACS.
2. The level of procedural compliance when assessing patients with suspected ACS.
3. Any variables that were associated with a lower rate of 12-Lead ECG acquisition.
4. Whether any exhibited gender disparity could be explained by the most common conclusions from previous research:
 - The gender disparity was due to a false negative diagnosis of ACS in women and/or
 - The gender disparity was due to women presenting atypically, which led to their physician giving them a false negative diagnosis of ACS.

1.1 - Acute Coronary Syndrome Defined

There are several interrelated cardiovascular conditions that contribute to and help to define the topic of ACS in the following sections.

1.1.1 - Cardiovascular disease and myocardial ischaemia

Cardiovascular disease (CVD) is an overarching term which covers all diseases and conditions of the heart and blood vessels (2). The heart's muscle (myocardium) receives its blood supply through the coronary arteries, which run from the superficial myocardium (epicardium) to the

deeper myocardium (endocardium) (3). When the myocardium's demand for oxygenated blood is greater than its supply through the coronary arteries, myocardial ischaemia ensues. The decreased perfusion which characterises myocardial ischaemia not only results in the heart being starved of oxygen, but also comprises nutrient substrate depletion and inadequate removal of metabolites (4).

1.1.2 - Atherosclerosis and Coronary Artery Disease

The cause of the decreased coronary perfusion that gives rise to myocardial ischaemia is due to atherosclerotic obstruction of the coronary arteries in 90% of cases (4). Briefly, atherosclerosis is a slow, multi-factorial disease process which starts in childhood and involves injury to and dysfunction of the internal vascular lining (known as the endothelium). This endothelial dysfunction is due to the formation of atherosclerotic plaque and atheroma in the vasculature walls and is the main underlying cause of CVD (2), (5). In the coronary arteries, the progressive narrowing associated with atherosclerotic change is known as coronary artery disease (CAD) (5).

1.1.3 - Ischaemic Heart Disease

When CAD is severe enough to render the myocardium ischaemic, a group of closely related syndromes ensue which are termed Ischaemic Heart Disease (IHD). Two of these syndromes are angina pectoris and myocardial infarction:

1. Angina pectoris:

Comprises a symptom complex with a variable presentation (discussed later), that is characterised by transient episodes (15 seconds to 15 minutes) of reversible myocardial ischaemia. There is no grouped cell or localised tissue death (known as necrosis) with angina pectoris. (4), (6)

Angina pectoris can be further divided into three sub-types:

- Stable angina; with a predictable pattern of onset of ischaemia due to increased cardiac workload. This is usually relieved through rest or nitroglycerin,
- Prinzmetal angina; an uncommon pattern of episodic angina, which often occurs at rest and is due to coronary artery spasm and
- Unstable angina (UA); presenting with increasing frequency and is progressively precipitated with less effort, occurs with a prolonged duration and often occurs at rest. (4)

2. Myocardial Infarction (MI):

Occurs when the severity and duration of myocardial ischaemia causes necrosis.

- Myocardium is unable to survive severe, sustained ischaemia for longer than 20-40 minutes before it infarcts (6).
- MI is most commonly associated with a complete coronary artery occlusion (4).
- A complete coronary artery occlusion is not commonly associated with slow atherosclerotic plaque deposition but with abrupt plaque change (4).
- When the MI results in ECG changes that significantly elevate the ST-segment, the infarction is known as an ST-Elevation Myocardial Infarction (STEMI) (3).

- If the MI does not result in an elevated ST-segment on the ECG it is described as a non-STEMI (3).

1.1.4 - Acute Coronary Syndrome

Mechanical stress on an atherosclerotic coronary artery's wall may result in sudden plaque change, which disrupts the endothelium. This disruption exposes either the underlying plaque constituents or the subendothelial basement membrane which are both highly thrombogenic (4). Formation of a superimposed blood clot in the vessel's lumen (known as a thrombus) or haemorrhage into the atheroma are likely to result from this exposure. The sudden decrease in the vessel's lumen size leads to a sudden decrease in arterial perfusion through the coronary artery (4), (6).

Acute duration is commonly defined with a time period of minutes to hours and less than 24 hours (7). When acute myocardial ischaemia results from decreased coronary artery perfusion, the resultant syndromes of UA, acute MI (AMI) and sudden cardiac death are referred to as the Acute Coronary Syndromes (ACS) (4), (6). This mechanism of coronary plaque rupture is the common mechanism of all ACS (8).

1.2 - Epidemiology of IHD and AMI

The World Health Organisation presents mortality statistics relating to cause of death. These causes are grouped as general (such as 'cancer') or specific (such as 'lung cancer'). Ischaemic Heart Disease (IHD) is the leading specific cause of adult death in the world at 15% of all mortality for over 14 year olds (9). In New Zealand however, whilst IHD is still the leading specific cause of death, it is responsible for a greater portion of mortality at 19% of all deaths (10). AMI is a common manifestation of IHD, with approximately 25-35% of patients dying from AMI before receiving medical treatment; this is usually due to the AMI initiating lethal arrhythmias such as ventricular fibrillation (Vf) (11). Most importantly for pre-hospital EMS providers; more than 50% of deaths from AMI occur before arrival at hospital (12).

There are 865,000 predicted new and recurrent AMIs for the United States (US) annually, with 500,000 being STEMIs (13). Approximately 683,000 patients were discharged from US hospitals with a diagnosis of ACS in 2009 (14). There is currently no register of ACS in Australia, but national estimates are derived from two administrative data sets held by the Australian Institute of Health and Welfare (AIHW) - the National Mortality Database (NMD) and the National Hospital Morbidity Database (NHMD) (15). These show that in 2007-08, Australian hospitals recorded 94,751 admissions due to ACS (15). Of those admissions, 3,259 patients died (15). The total number of deaths in Australia with an underlying cause of AMI, Angina or other acute CAD was 11,678 in 2007 (15). New Zealanders living with IHD also amounts to a large number of adults at 161,000 (16). There are 118,500 New Zealand patients suffering from angina and 89,400 patients having had at least one hospital admission for AMI (16).

1.3 - Diagnosis of ACS

As this thesis examines the assessment, treatment and outcome for patients with suspected ACS, I will introduce 'best practice' for these here:

The diagnosis of ACS is based upon presenting signs and symptoms, ECG changes and serum cardiac biomarkers (6). A careful clinical history and examination is the corner-stone of ACS diagnosis (17) but the standard 12-lead ECG is the most sensitive early indicator of ACS and the single best test to identify AMI on emergency department (ED) presentation (7), (18).

1.3.1 - Presenting signs and symptoms of ACS diagnosis

The most typical presentation of ACS is described as:

- Precordial chest discomfort (including descriptions such as pain, tightness, heaviness, pressure and fullness). This discomfort can radiate to the shoulder, arm, jaw, neck, back or epigastrium;
- the symptoms are commonly associated with dyspnoea, nausea or vomiting, diaphoresis, feeling weak and light-headed;
- the symptoms are exacerbated by physical exertion or psychological stress;
- the symptoms are not alleviated by rest or use of glyceryl trinitrate (GTN) (7), (19).

1.3.2 - 12-Lead ECG for AMI diagnosis

As the endocardium receives blood before the epicardium, and even more so in the left ventricle (LV), as the wall is thicker, the damage observed after coronary artery occlusion is most commonly greatest in the inner wall of the LV (20). Thus, a standard 12-lead ECG is set-up to observe the electrical activity from the LV.

The 2013 American College of Cardiology Foundation/ American Heart Association (ACCF/AHA) guideline for the management of STEMI (14) list the ECG criteria required for AMI diagnosis as being either one of the following two points:

1. In the absence of left ventricular (LVH) hypertrophy or left bundle-branch block (LBBB):

- ST-segment elevation at the J-point in two or more contiguous leads. This elevation must be:
 - New or presumed new onset.
 - At least 2mm in leads V2-V3 for men and at least 1.5mm for females.
 - At least 1mm in all other contiguous chest or limb leads.

Note: ST-depression in two or more chest leads (V1-V4) may indicate transmural posterior injury.

2. New or presumed new LBBB with a history consistent with myocardial ischaemia.

An MI which is at least 24 hours old can result in the presence of pathological Q-waves. The definition of pathological Q-waves is:

- Q-waves: in leads V1-V3 or
- Q waves in leads I, II, aVL, aVF and V4-V6 which are at least 30ms
 - These Q-wave changes must be present in two or more contiguous leads and
 - Must be at least 0.1mV in depth
- A Q-wave equivalent in a posterior MI shows as a dominant R wave in leads V1 and V2 (21).

1.3.3 - Serum biomarkers for AMI diagnosis

Serum cardiac biomarkers rise when myocardial cells lyse, releasing their contents into the interstitium and eventually into the blood. These serum biomarkers can be detected at varying rates post infarction and include myoglobin, creatine kinase MB and the cardiac troponins I and T (6). Cardiac troponin is the preferred biomarker for diagnosis of MI and where available, high sensitivity troponin assays should be used in preference to conventional assays (14), (17). A positive finding identifies patients at increased risk, but does not provide definitive evidence of MI (17).

1.4 - Management of ACS

Which intervention is best for patients with ACS is governed by a complex set of variables including the availability of treatment, risk vs benefit for the patient, patient preference and treatment timings. As this study is focused on improving health professional practice for patients with ACS, we will list some of the considerations and the associated evidence for treatment choices here.

The aim of treatment for ACS is to reperfuse the myocardium in a timely and sustainable manner. This may be achieved through decreasing the cardiac workload with rest and nitroglycerin for patients with UA. But for patients with AMI, the aim of treatment is to reduce the enlarging infarct size and to salvage as much of the ischaemic myocardial penumbra as possible. This is achieved through clot lysis with a pharmacological agent, or through mechanical opening or bypass of the occluded coronary artery/s (7). These treatments are briefly discussed next.

1.4.1 - Pharmacologic reperfusion

Pharmacologic interventions include fibrinolytic and antiplatelet therapy, which are indicated for patients suffering symptomatic STEMI with a duration of ≤ 12 hours (7).

As life threatening bleeding, including cerebral haemorrhage can be a consequence of fibrinolysis administration, careful assessment of bleeding risk should be undertaken before using these agents (7). In comparison to medical treatment without reperfusion therapy, fibrinolytic therapy reduces mortality rates at 35 days post STEMI and left ventricular systolic function is improved (giving a lowered morbidity) (11). Fibrinolytic therapy restores angiographically normal blood flow in 50 to 60% of patients with AMI (11).

1.4.2 - Mechanical reperfusion

There are two ways of achieving reperfusion mechanically for the patient suffering AMI, this is with:

1. Percutaneous Coronary Intervention (PCI); where access to the patient's occluded coronary vessels is obtained via the femoral, radial or brachial artery and the stenosis is compressed with an inflatable balloon (balloon angioplasty) or by scraping away the atheroma (atherectomy) (7), (8).
 - If PCI is performed without preceding pharmacologic interventions, it is referred to as 'primary PCI'.

2. Coronary Artery Bypass Graft (CABG); where the stenosed coronary artery is bypassed by anastomosing an autologous vein or artery from the ascending aorta to the offending coronary artery, distal to the blockage (8). This procedure involves opening the thorax, so is extremely invasive.

1.4.3 - Comparing Fibrinolysis, primary PCI and CABG

Balloon angioplasty will restore angiographically normal blood flow in more than 90% of patients (22). In comparison to fibrinolysis alone, rates of non-fatal re-infarction and stroke are reduced, along with mortality rates for primary PCI (11). However, although primary PCI may have superior results over fibrinolysis when performed rapidly at high-volume centres, 60% to 70% of STEMI patients present initially to hospitals without ready access to primary PCI. So, fibrinolysis may be more suitable as an initial reperfusion strategy for most patients (13). Early routine angiography and revascularisation should be considered for patients receiving fibrinolysis for their AMI regardless of the success of that pharmacologic reperfusion (17).

PCI procedures have become increasingly popular due to better survivability statistics when performed in patients suffering AMI in comparison to CABG (8). PCI is also less-invasive and quicker than CABG, which can save valuable myocardium and hence improve mortality and morbidity rates.

1.4.4 - Treatment Timing

The type of reperfusion therapy used may not be the most important factor in managing AMI treatment when compared to timing. A clinical review by Kleinschmidt and Brady (23) concluded that the speed of reperfusion after infarct onset may be more important than whether pharmacologic or mechanical intervention is used. There is a direct correlation between how quickly an artery is re-opened and how quickly and completely a patient will recover (23).

The ACCF/AHA (14) recommends a medical contact to treatment time of ≤ 30 minutes for fibrinolysis in patients with STEMI and a Door-To-Balloon (DTB) time (arrival at hospital to PCI) of ≤ 90 minutes. Data from the National Registry of Myocardial Infarction (NRM1)-2, -3, -4 and -5 (14) showed that delays of more than two hours were experienced for patients being transferred for primary PCI and this negated the survival advantage of PCI over fibrinolysis. Fibrinolysis may be the preferred treatment if the patient presents within the first two hours of symptoms, particularly if PCI can't be performed within 60 minutes from medical presentation (24).

1.4.5 - Pre-hospital fibrinolysis and Facilitated-PCI:

Pre-hospital administration of fibrinolysis by EMS staff, compared to hospital administration, for STEMI can significantly decrease:

- the time it takes from onset of symptoms to receiving fibrinolysis (this time is known as 'symptom onset-to-needle time') (25),
- short and long-term and all-cause mortality (25), (26) and
- time to ST-segment resolution (26).

A study by Thiele et al. (27) revealed that pre-hospital fibrinolysis can be extremely effective at revascularisation for AMI. In 69% of patients, at the time of angiography, the infarcted vessel

had been re-opened completely with pre-hospital fibrinolysis (27). This supports the view that very early treatment of AMI has the highest success rates (27). The expedited pharmacologic reperfusion achieved with pre-hospital fibrinolysis administration can not only minimise the delay to treatment pre-hospitally, but also within the hospital. EMS personnel can minimise in-hospital delay by identifying candidates for further in-hospital reperfusion therapy (5).

If prehospital fibrinolysis is followed by urgent PCI, the combination is termed facilitated-PCI (27). This can have positive effects on both morbidity and mortality for patients suffering STEMI when compared to primary PCI (that is, PCI without any prehospital fibrinolysis). Denktas et al. (28) compared facilitated-PCI with primary PCI for just over 2,800 patients who suffered from STEMI. After controlling for the confounding effects of age, creatinine, hyperlipidaemia, prior MI, family history and diabetes mellitus with multivariate analysis, they found that:

Facilitated-PCI was associated with:

- greatly reduced 30-day mortality (RR 0.54, 95% CI, (0.33-0.89), $p=0.02$),
- no significant change in 30-day re-infarction,
- no significant increase in 30-day stroke rate (1.4% vs. 1.1%, $p = 0.42$) and
- decreased infarct size (RR 0.54, 95% CI, (0.32 – 0.91), $p = 0.02$) (28).

Patients who receive pre-hospital fibrinolysis and don't receive urgent PCI for their STEMI have been shown to be at a disadvantage both in morbidity and mortality.

Thiele et al. (27) randomised STEMI patients to either pre-hospital fibrinolysis alone or to facilitated-PCI. Patients treated with facilitated PCI had:

- smaller infarct size on Magnetic Resonance Imaging (5.3% vs. 10.4% of the LV, $p = 0.001$),
- increased rates of complete ST-segment resolution (80.0% vs. 41.9%, $p < 0.001$),
- smaller infarct size with respect to creatine kinase release (517 vs. 599 $\mu\text{mol/L/h}$, $p = 0.04$) and
- there was a trend toward a lower event rate (of death, re-infarction, disabling stroke and major bleeding during the first 6 months after randomisation).

The implications of these findings are pertinent for the EMS industry as timing of treatment is so important. Also, in order to provide optimal treatment for patients suffering AMI, EMS need to prioritise early prehospital fibrinolysis followed by urgent transport to a facility with PCI capability in suitable patients.

1.5 – Recommendations for optimal AMI treatment

Advancements in treatment of AMI have resulted in improved survival. (Figure 1) shows that the percentage of people that died in-hospital in Australia from AMI declined steadily over the ten years from 1998 to 2008 from approximately 10.5% to 6.5% (15). This significant decrease of approximately 40% is mainly achieved through timely reperfusion of the myocardium via fibrinolysis and/or PCI (29), (30).

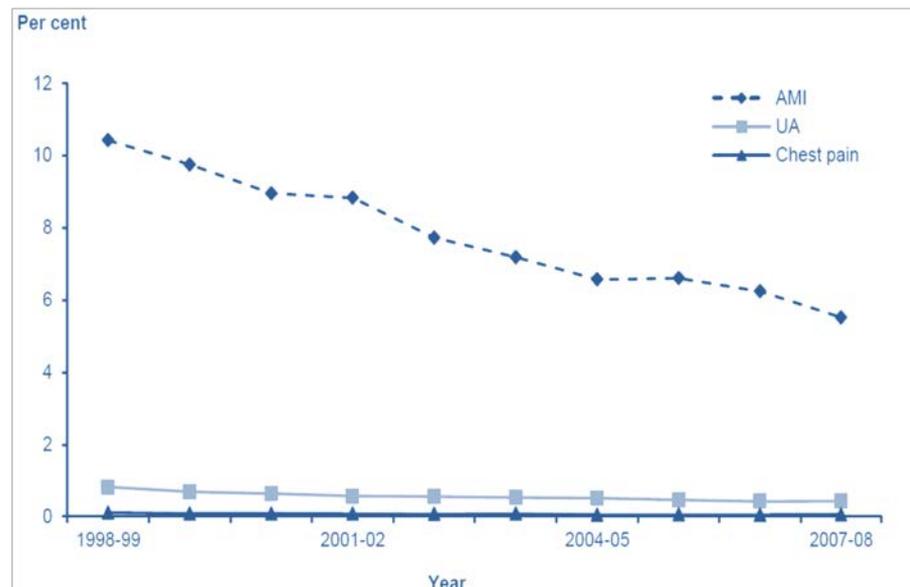


Figure 1: Declining in-hospital mortality in Australia due to AMI over ten years, from 1998 to 2008, NHMD Australia (15 p. 37)

Certain subpopulations have not benefited from the full decline in mortality from AMI however. Higher rates of mortality from ACS have been linked to non-adherence with procedures and lack of provision of care (29). Certain populations/groups may be more likely to be subject to barriers to optimal ACS treatment, so early recognition of these groups can help circumvent potential poor outcomes for them.

1.5.1 – Recognising the atypical presentation of ACS:

An atypical presentation of ACS can act as a barrier to optimal care, as patients with this presentation often have a delayed diagnosis, receive less aggressive treatment and have higher in-hospital mortality rates compared to patients with a typical ACS presentation (31). Patients with an atypical ACS presentation without chest-pain are frequently misdiagnosed, undertreated and have higher mortality (32). The patients most likely to present with atypical ACS without chest pain are female, older and have a history of hypertension, heart failure and diabetes (32), (33).

An atypical presentation of ACS can present with the signs and symptoms listed in the two categories below: The patient may have chest discomfort which differs in quality from that described in a typical presentation of ACS (listed in 1.3.1) or they may have no discomfort in the chest, but symptoms listed in category 2. below:

1. Chest discomfort
 - which is localised or positional,
 - or is described as a burning, tingling or numbness,
 - or is reproducible on palpation of the chest wall
 - or is pleuritic in nature (19), (31)
2. Symptoms without chest discomfort
 - which may be isolated or a combination of,
 - unexplained dyspnoea;

- localised pain or numbness and tingling in the arm(s), shoulder, jaw, between the shoulder blades or epigastrium;
- indigestion type symptoms,
- nausea and vomiting,
- diaphoresis,
- light-headedness,
- fatigue or generalised weakness,
- syncope,
- palpitations, cardiac arrhythmias, cardiac arrest,
- central nervous system manifestations such as focal neurology or unexplained confusion (19)· (31).

1.5.2 – Present to medical services early

The longer it takes for a patient with an AMI to initially present to medical services, the longer it takes for a patient to receive definitive treatment. As described above, it is imperative for AMI treatment to be delivered in a timely manner in order to decrease infarct size. In fact, the AMI may be aborted in up to 25% of patients that receive fibrinolysis within one hour of symptom onset (29). The trends and gender differences associated with a delayed presentation to medical services, along with the significant delays associated with presenting to the General Practitioner (GP) rather than calling an ambulance are briefly discussed below.

Decreasing the time it takes to contact medical services will obviously decrease the time it takes to receive treatment for AMI. Women who suffer an AMI, as a group, tend to present to hospital later compared to men (34). The time it takes from the initial onset of symptoms of the AMI to arrival at the hospital door is termed 'symptom onset-to-door time' (30).

The importance of getting to hospital quickly when suffering an AMI seems to be understood better now than previously, (Figure 2) shows that symptom onset-to-door times for patients suffering AMI in the United States improved significantly over 16 years. All patients suffering from AMI, on average, presented to hospital 25% faster (approximately 130 minutes in 1990 to approximately 100 minutes in 2006). Women suffering an AMI however, still haven't improved their symptom onset-to-door times to match that of their male counterparts. (Figure 2) shows that women were about 30% slower than men in 1990; with a 160 minute symptom onset-to-door time compared to 120 minutes for men. This improved in 2006 to 120 minutes, but was still 30% slower than the 90 minute symptom onset-to-door time for men with AMI (30).

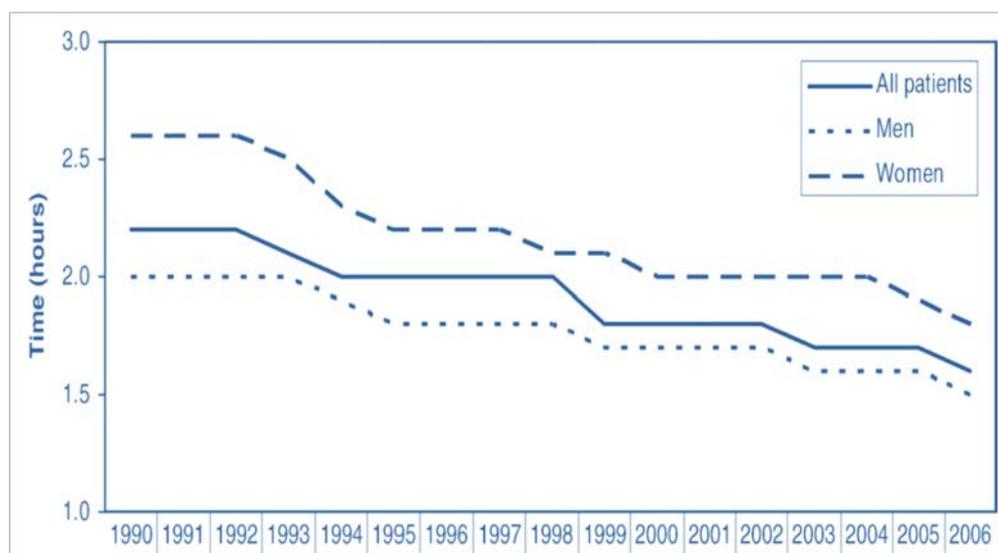


Figure 2: Showing symptom onset-to-door times (hours) for men and women with AMI from 1990 to 2006 (30 p. 1038)

The reasons for women presenting later are varied and complicated. One reason is the lack of understanding that women have about female heart disease. The Australian National Heart Foundation’s Heart Watch survey found that only 31% of women understood that heart disease is their number one killer (34). This survey concluded that women tend to dismiss their symptoms and seek help late (34).

1.5.3 - Call an ambulance rather than going to the GP

A New Zealand study of 1068 patients, admitted to a Coronary Care Unit (CCU), with a first admission for ACS, revealed that only 43% had called an ambulance directly (35). The symptom onset-to-door times for patients who sought ambulance help directly were markedly shorter than for all other first health professional contacts (35). This is shown in (Table 1) with a symptom onset-to-door time being at least 3 times less for ambulance help than any other initial contact and an initial contact with the GP resulted in times over seven times that of the ambulance (35).

Professional help sought	% (N)	Median time (IQR), min	P-Value	Mean time (SD) min
Ambulance	43 (348)	76 (34, 195)	<0.0001	269 (769)
Hospital by self-referral	14 (109)	220 (84, 536)		649 (1749)
GP	34 (275)	556 (162, 1716)		1590 (3201)
Private A&E	8 (65)	300 (110, 740)		791 (1391)
Other	1 (5)	2334 (764, 3810)		2241 (1845)
Unavailable/don’t know	<1 (3)			

Table 1: Symptom onset-to-door times according to first health-professional contact for patients diagnosed with ACS and admitted to Middlemore Hospital CCU from Jan 2009 to July 2010 (35).

These findings suggest that there is a need for patient education on the importance of rapid presentation to EMS when suffering symptoms of AMI. It is especially important to target females in this education programme, due to their currently extended symptom-to-door times.

1.5.4 – Acquire a pre-hospital 12-lead ECG and communicate the results with the hospital

Early acquisition and communication of a pre-hospital 12-lead ECG can facilitate speedy treatment for the patient suffering STEMI. Some of the benefits of pre-hospital 12-lead ECG acquisition are discussed below:

Facilitation of a pre-hospital diagnosis

12-lead ECGs performed by the EMS whilst enroute to hospital facilitates pre-hospital diagnosis, allowing patients to receive appropriate treatment and to be triaged and directed to PCI centres (17), (36), (37). Common causes for a false positive STEMI diagnosis from 12-lead ECG by paramedics are pericarditis, myocarditis, early repolarization changes, left ventricular hypertrophy, LBBB and non-STEMI (37). Interestingly though, Le May et al. (37) found that the false positive rate for paramedics diagnosing STEMI and activating the CCL was the same as it was for patients referred by ED physicians.

Communication with the receiving hospital

Hospitals that receive patients from an EMS that have performed and interpreted a pre-hospital 12-lead ECG, have the fastest median DTB times for patients suffering STEMI (38). Especially when the paramedic notifies the ED of the ECG result and emphasises that their patient has a suspected STEMI (38). The emergency physician's trust of the EMS staff member's ECG interpretation is necessary to expedite patient transfer of care from the EMS into the hospital. Feedback and communication between EMS staff and ED physicians helps to ensure this trust (38).

1.5.5 – Improve the education level of EMS staff

Improved training and qualification of EMS staff attending patients with cardiac-type chest pain can result in improved quality of care and better outcomes. Fischer et al. (39) studied four different EMS agencies to evaluate treatment outcomes for patients with cardiac-type chest pain, dyspnoea and out-of-hospital cardiac arrest. They identified 2446 patients meeting the criteria for cardiac-type chest pain and measured the quality of care delivered in association with the treating EMS staff member's qualification (39). Criteria for improved quality of care involved improved patient vital signs, improved pain scores and thorough recording of vital signs and pain scores for these potentially critical patients. There was a positive correlation between increased level of staff qualification and quality of care delivered to patients with cardiac-type chest pain with a positive health benefit until admission (39).

A study investigating the effect of a formalised feedback programme for improving 12-lead ECG acquisition rates for EMS staff was undertaken by Daudeline et al. (40). They first studied rates of acquisition and quality of interpretation of pre-hospital ECGs by paramedics for patients with suspected ACS from two EMS agencies in Massachusetts. Data from 1589 patients was collected for 6 months to determine baseline, prior to a feedback intervention period. The intervention entailed feedback for each individual paramedic, for 5405 patients over a 15-month intervention period, ending in May 2007. Feedback on acquisition rates was provided monthly via online graphs, comparing the individual's performance with blinded data from their

colleagues. A randomised 20% sample was also discussed face-to-face with the medical director for ECG interpretation, (including missed STEMI) (40).

Results are shown in (Table 2) showing a large and significant (48%) improvement in pre-hospital ECG acquisition rates for patients, who should have been evaluated for ACS, between the baseline and feedback periods. The proportion of patients with confirmed STEMI who received a pre-hospital ECG increased from 77% to 99%. Most significantly, the median DTB times for these patients almost halved. The proportion of patients receiving PCI in ≤ 90 minutes more than doubled with a rise from 27% to 67% (P = 0.0001).

Variable	Baseline	Feedback period	P Value
Patient number	1589	5405	
Pre-hospital ECG	57%	84%	0.0001***
Confirmed STEMI with pre-hospital ECG	77%	99%	0.0001***
DTB median (minutes)	158	80	0.04*
PCI in ≤ 90 minutes	27%	67%	0.0001***

Table 2: Results for patients with an ACS-type presentation, treated by paramedics from two Massachusetts EMSs, before (baseline) and after a feedback intervention. Outcomes measured were pre-hospital ECG acquisition rates for all included patients, pre-hospital ECG rates for patients with a confirmed diagnosis of STEMI at hospital, DTB times and proportion of PCI in ≤ 90 minutes for these patients with STEMI (40).

* p<0.05, **p<0.01, ***p<0.001

1.5.6 - Paramedic initiated PCI with direct transport to the CCL

Paramedic initiation of the CCL (as opposed to ED physician initiation) (41), (36), (37) speeds DTB times. Several studies reviewed DTB times for patients with STEMI according to their arrival mode. They found that patients who had their PCI initiated by the EMS transporting them to hospital, not only had significantly shorter DTB times, but that this translated to better outcomes with decreased mortality rates (41), (36), (37).

A study by Greenberg et al. (42) revealed that patients who were transported to a hospital's ED which had a Myocardial Infarction alert initiated by EMS, instead of a hospital-initiated alert, had a significantly reduced time to catheter lab arrival. They concluded that a prehospital activation of the MI Alert process decreased time to catheter lab by 19 minutes (95% CI = 13.2, 24.8, P < 0.001) (42).

1.5.7 – Recognise that women with ACS can be disadvantaged

This topic will be investigated in detail within the literature review. However, I have briefly listed the consensus of findings here:

Compared to men, women with the same high risk stratification for ACS/AMI receive less:

- stress tests (43), in-hospital (44) and pre-hospital ECGs (40),
- cardiac monitoring and pulse oxygenation (44),
- coronary angiography (33), (42), (43), (45), (46), cardiac catheterisations, coronary angioplasty revascularisation and CABG surgery (33), (43), (47), (48), (45), (49), (50), (46).

Women's outcome post AMI is also less favourable than that of their male counterparts with:

- Increased rates of refractory ischaemia (51) heart failure (33), (49), (52), (46) and rehospitalisation (53)
- lower quality-of-life (QoL) scores (53) and
- higher in-hospital mortality (54), (55), (56) and 12-month mortality rates (51), (53), (50).

In fact, females less than 50 years old who suffer an AMI are at a particularly high risk of death, with these women being twice as likely to die from their AMI than males are (51), (57).

Reasons given for the gender disparity:

Several studies postulate that the established gender disparity found in ACS care and outcome is due to atypical female ACS presentation which results in a false negative ACS diagnosis from the practitioner (33), (46), (58). Another conclusion may be that practitioners could potentially be affected by a gender norms hypothesis, where physicians believe women have a lower pre-test probability of infarction (59).

1.6 – Overview summary

Better outcomes for patients suffering STEMI are associated with:

- early recognition of symptoms and an early call to an EMS by the patient
- rapid dispatch of EMS staff that are well educated in Advanced Life Support (ALS)
- early pre-hospital 12-Lead ECG acquisition, interpretation and communication with the hospital
- early fibrinolysis by EMS and transport to a primary PCI facility,
- paramedic initiated PCI en route,

This shows that the pre-hospital 12-lead ECG is essential for best practice when treating patients with suspected ACS.

Gender disparity in the assessment and treatment of ACS has already been established and is to the detriment of ACS care in women. Previous researchers have attributed this disparity to the increased propensity of women to present atypically and practitioners false negatively diagnosing these women for ACS.

1.7 - Aims of the study:

The primary objective of the study sought to establish whether EMS staff exhibited gender disparity when assessing patients with suspected ACS. This was achieved through investigating the study's null-hypothesis:

- There would be no difference in acquisition rates of 12-Lead ECGs from EMS staff, between male and female patients presenting with 'typical cardiac-type chest pain' when the EMS staff member's working-diagnosis was that of ACS.

Secondary objectives were to investigate:

- The level of procedural compliance in the assessment of ACS in the pre-hospital EMS field.
- Any variables associated with a reduced odds of EMS staff acquiring prehospital 12-lead ECGs for all patients with suspected ACS.

- Whether previously proposed explanations for gender disparity in ACS assessment treatment were supported.

1.8 - Structure of the thesis:

Chapter 1 identifies the purpose of this study: to establish whether gender disparity exists, in pre-hospital 12-lead ECG acquisition rates, when patient presentation and practitioner diagnosis are controlled for. The position of the study within the current body of research and the gap in the literature that this study aims to fill has been stated.

Chapter 2 presents a critical review of the existing literature on pre-hospital gender disparity in ACS assessment, treatment and outcome differences. Review of previous author's explanations for any gender disparity will be noted.

Chapter 3 describes the research design and the methodological approach for this study. The multiple-logistic regression model used for statistical analysis of the data is described and the variables within it are explained.

Chapter 4 presents the key findings from an analysis of the research data using quantitative research methods.

Chapter 5 discusses the findings of the study with reference to each of the research questions and identifies the study's limitations, strengths and implications.

Referencing Style

Publications and other sources used in this work are referenced using ISO 690 – British Standard (numeric) system (2010) referencing style.

Chapter 2 – Literature Review

The primary focus of this study's literature review was to investigate gender disparity in relation to ACS. Original, current research from the last ten years (2005 to 2015) was reviewed in order to establish if there was a gap in the research with regards to prehospital assessment and treatment of ACS compared with hospital assessment and treatment of ACS.

2.1 – Search strategy

EBSCO host search engine was chosen to perform an 'Advanced Search' of the data bases titled 'Medline' and 'CINAHL Plus with full text'. These two data bases were chosen to provide a wide search coverage in order to include both biomedical focused journals (through MEDLINE) and allied health focused journals (through CINAHL Plus with full text).

2.1.1 – Choice of Databases

'MEDLINE' database has a broad coverage of biomedicine and health with citations from more than 5,600 worldwide journals (60). This database was deemed necessary to cover articles with a focus on hospital based medicine. 'CINAHL Plus with full text' provided full text of over 700 nursing and allied health journals (61). The additional coverage of allied health gave a wider search of prehospital research, as articles based in EMS may have been more likely to be published in an allied health journal.

2.1.2 – Expanders, limiters and search terms

The search mode used was 'Boolean/Phrase' and expanders and limiters were used to improve the search's sensitivity and specificity to the topic. These are listed here:

Expanders

- Also search within the full text of the articles

Limiters

- Published Date 2005-2015
- English language

Searching within the full text of the articles increased the sensitivity of the search as both Myocardial Infarction and Acute Coronary Syndrome are often shortened to their acronyms (MI and ACS) in article titles. Limiting the search to articles from the past 10 years resulted in current research results. Initially, a limiter of 'Human' was used, but this resulted in a loss of relevant human based research that had not had 'Human' specified in the data base. The results only returned one non-human based article, so this limiter was removed from the search criteria.

The search terms "Myocardial Infarction" OR "Acute Coronary Syndrome" were used as phrases. Choosing a phrase helped to increase the specificity of the search. This was particularly important for the terms "Acute" and "Syndrome" as they are very general terms that would return too many unrelated articles if they were not included in a phrase type search. This returned 120,445 articles which were then searched with the terms "gender bias" OR "gender

disparity” as phrases. Older articles tended to use the term “gender bias” but new articles were more likely to use the term “gender disparity”. So using both phrases with an ‘OR’ term, improved the searches’ sensitivity and resulted in a relevant return of 39 articles. The final results were decreased to 21 articles and the flowchart of the decision making process for their inclusion is shown in (Figure 3).

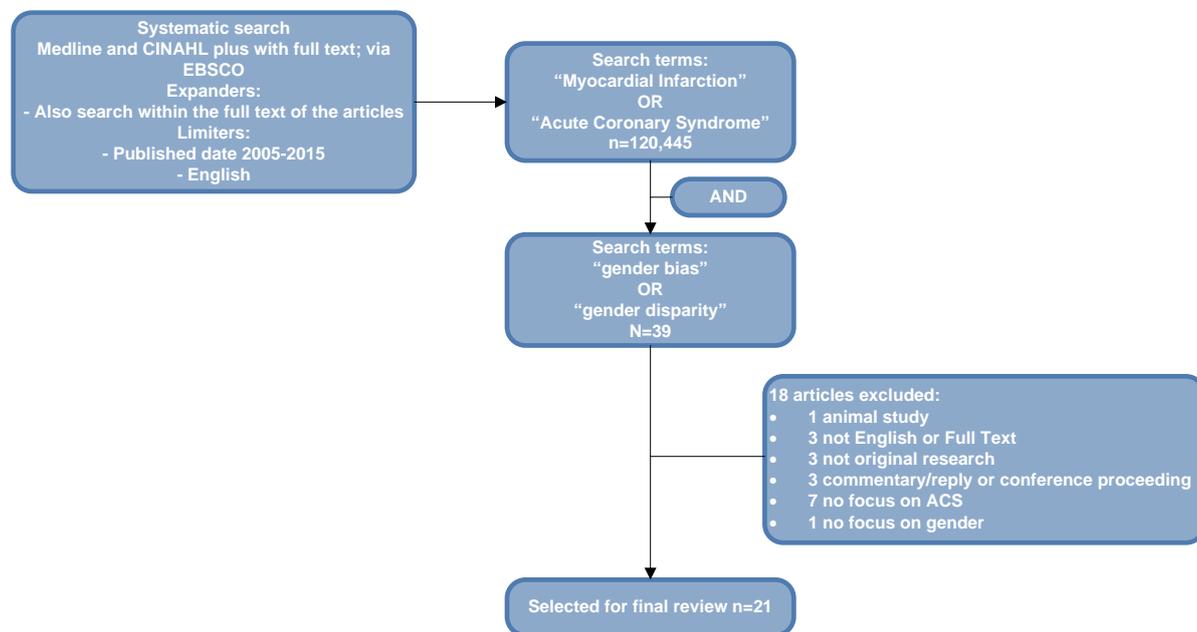


Figure 3: Shows a flowchart of this study’s literature review. The review included original peer reviewed research of gender disparity in Acute Coronary Syndrome. The databases used were ‘CINAHL plus with full text’ and ‘Medline’ for articles over the past 10 years. Using EBSCO host as the searching database, 21 articles met the search criteria for this study.

2.2 – Article review

Publications were assessed on several criteria listed below:

- sample size, setting and location (Table 3),
- study location (Table 3),
- recruitment methods used (Table 4),
- sample co-morbidities and medications by gender (Table 5),
- finding of gender disparity or not (Table 6),
- area of gender disparity, (for example; assessment, treatment or outcome) (Table 6),
and
- any explanations given for a gender disparity (Table 9).

Article's author/s Location	Sample size	Age (years) (mean/median)	Data centres Study time period
Zhang et al. (62) Shanghai, China	1,574 men 468 women	63.9 men 71.7 women	Data centres not specified. 2.5 years, ending 2008.
Fransoo et al. (63) Manitoba Canada	4,199 men 2,645 women	67.4 men 74.3 women	Manitoba population based 3 years ending 2002.
Greenberg et al. (42) Location not disclosed	862 men 369 women	59 men 68 women	1 hospital 8.5 years ending 2008
Griffith et al. (64) Dumfries, Scotland	966 men 597 women	66.9 men 73.2 women	1 hospital 7 years ending 2000
Dreyer et al. (58) Adelaide, Australia	562 men 173 women	60 men 67 women	4 hospitals 4 years ending 2010
Madrid Willingham and Kilpatrick (59) East Yorkshire and Hull, Britain	2,505 men 2,323 women	66 men 74 women	2 hospitals 1 year ending 2002
Chang et al. (43) Pennsylvania, United States	2,547 men 3,514 women	51.6 men 52.6 women	1 hospital Study time period: Not stated
Assiri (2011) (48) Southwest Saudi Arabia	397 men 148 women	60 men 62.9 women	1 hospital 2 years ending 2009
Aguilar et al. (65) San Diego, United States	11,622 men 10,218 women	59 men 65 women	All EMS transports meeting inclusion criteria for the state of San Diego 5 years ending 2008
Heer et al. (45) Germany	66,3807 men 35,1189 women	67 men 69 women	National population based, included 218 hospitals 6 years ending 2009
Fang and Alderman (49) New York, United States	52,947 men 41,031 women	66.1 men 73.6 women	4 boroughs of New York City population based. 7 years ending 2002.
Huang et al. (50) Taiwan	58,690 men 20,670 women	63.5 men 69.7 women	National population based. 10 years ending 2007
Roncalli et al. (54) France	<u>Non/Emergency</u> 5,668/1,343 men 1,668/410 women	<u>Non/Emergency</u> 65.6/62.3 men 71.7/71.1 women	Single PCI centre. 3.5 years ending 2008
Nguyen et al. (33) Minneapolis-St Paul area, United States	1,378 men 1,242 women	Women were 5.4 years older than men.	Minneapolis population based, included 21 hospitals 1 year ending 2002
Zhang et al. (55) Liaoning district China	<u>Non/Emergency</u> 439/602 men 236/152 women	<u>Non/Emergency</u> 63.3/58.2 men 71.6/67.5 women	Liaoning district population based, including 20 hospitals 1 year ending 2010
Greenberg et al. (66) Location not disclosed	305 men§ 304 women§	69 men 76 women	1 hospital 1 year ending 2006
Jibrán, Khan and Hoyer (2010) (67) United Kingdom	331 men 137 women	60.7 men 66.1 women	1 hospital 1 year ending 2008
Iyanoye (56) New Jersey, United States	27,346 men 12,869 women	60.7 men 68.3 women	New Jersey State population based. 8 years ending 2010

Ouhoumane et al. (52) Quebec, Canada	15,603 men 8,097 women	Used patient age brackets. More women ≥75	Quebec population based. 2 years ending 1997
Ben-Ami et al. (68) Beer Sheva, Israel	146 men 80 women	66 men 71 women	1 hospital 2 months ending 2000
Hvelplund et al. (46) Denmark	15,818 men 9,132 women	65.1 men 71.1 women	National population based. 3 years ending 2007

Table 3: All included journal articles for this study's literature review with their authors, sample location, study sample numbers, patient ages by gender, data centre location and study time periods listed.

2.2.1 – Study locations:

A good international spread of locations from both the Eastern and Western Worlds were covered by the articles in the literature review. The majority of the studies came from Countries with a Developed Economy, but the Developing Economy Regions (69) were represented with studies from China (62), (55), Taiwan (50), Israel (68) and Saudi Arabia (48). North and Sub-Saharan Africa were not represented by any of the retrieved articles. Data availability in the form of hospital or population based health databases may have influenced the study's locations as these may be more readily available in Countries with a Developed Economy. North America had the largest representation with five studies coming from different States within the United States (33), (43), (49), (56), (65) and two studies coming from Canada (52), (63). The next most represented region was the United Kingdom with three studies, (59), (64), (67). Three more studies from other European Countries were from Germany (45), Denmark (46) and France (54). Finally, one study from Australia (58) represented the Oceania region. There were no studies from New Zealand, highlighting a regional gap in the literature which is covered by this study.

2.2.2 – Study sample size and recruitment methods:

Patient numbers varied widely between the studies (Table 3), ranging from 226 in a small unicentred Israeli study (68) to 1,014,996 in a National German based study (45). With the exception of the five studies (listed below), all of the studies found that there were significantly more males than females in their sample of ACS patients. Zhang et al. (62) had the largest difference with just under four times as many male to female patients (Table 3). Their recruitment method may have contributed to this as their inclusion criteria was patients with an acute STEMI diagnosed with 'ischaemic chest pain' and they also had to undergo primary PCI with stenting of the coronary artery. As women are more likely to have an atypical presentation of ACS than men, having 'ischaemic chest pain' listed in the inclusion criteria could result in less women in the study. Also, women may be less likely to undergo invasive cardiac procedures (discussed below in 2.3), so having an invasive procedure in the inclusion criteria could also diminish the number of women included.

In the five studies with no significant difference in patient numbers with regards to gender, recruitment methods differed in comparison to all the other studies. They either did not involve a hospital diagnosis of ACS or their sampling method was altered to specifically include more female patients. These are described here:

1. Madrid Willingham and Kilpatrick (59) used a recruitment method which included all patients who had a cTnT acquired for an acute admission of non-traumatic chest pain.
2. Chang et al. (43) used a recruitment method which included all patients who presented to the ED with a complaint of chest pain and who had an ECG acquired.
3. Aguilar et al. (65) was the only study based in the prehospital field. Its recruitment method included all patients that were attended by EMS and had 'chest pain of suspected cardiac origin' selected as part of a working diagnosis.
4. Nguyen et al. (33) used a differential random sampling method which over-sampled female and elderly subjects. This method included 50% of males and 100% of females for ages 30–74, 50% males and 50% females for ages 75–84, and 100% for both genders aged 85 and older.
5. Greenberg et al. (66) recruited all patients that presented to an ED and had a troponin level $\geq 4\text{ng/mL}$ and no ST-segment elevation on an ECG.

All of the other study's recruitment methods required either a hospital diagnosis of ACS or an invasive procedure such as PCI (45), (54) (Table 4). As women may be less likely to receive a diagnosis of ACS, even with positive serum biomarkers (59), it is not surprising that there are more male patients in the studies which require a diagnosis of ACS in their inclusion criteria.

Authors	Recruitment method
Zhang et al. (62)	Patients diagnosed with acute STEMI who underwent primary PCI with implantation of sirolimus-eluting stent. Had to have ischaemic chest pain with new ST-segment elevation and elevated cardiac enzymes to at least 3 x more than normal.
Fransoo et al. (63)	Hospital diagnosis of AMI for pts aged ≥ 40 and had at least a 3 day stay in hospital.
Greenberg et al. (42)	ED patients that had the 'MI Alert' activated. Inclusion criteria were chest pain within 12 hours of arrival to ED, ST-segment elevation or new LBBB in the setting of angina
Griffith et al. (64)	Hospital admission with diagnosis of first AMI
Dreyer et al. (58)	STEMI registry from 4 primary PCI capable hospitals, pts admitted for primary PCI
Madrid Willingham and Kilpatrick (59)	Retrospective review of troponin levels compared with the discharge diagnosis of ACS with cTnT of $>0.05\mu\text{g/l}$ indicating significant myocardial damage. Troponin was only measured in acute admissions with non-traumatic chest pain.
Chang et al. (43)	Patients presenting to the ED with chest pain which prompted an ECG by the treating physician.
Assiri (48)	Diagnosis of ACS in hospital
Aguilar et al. (65)	Patients given a 'chest pain of suspected cardiac origin' diagnosis by treating EMS staff.
Heer et al. (45)	Patients enrolled in the Coronary Angiography and PCI Registry of the German Society of Cardiology who underwent coronary angiography.
Fang and Alderman (49)	Patients admitted with a principal diagnosis of AMI.
Huang et al. (50)	All patients admitted with primary diagnosis of AMI (first event)
Roncalli et al. (54)	Patients who received PCI from a single centre.
Nguyen et al. (33)	Minnesota Heart Survey Acute Myocardial Infarction project. Survey of patients discharged with a diagnosis of AMI. Diagnosis validated using combination of symptoms, ST-elevation on early ECG or positive serologic biomarkers.
Zhang et al. (55)	Hospital diagnosis of STEMI and underwent PCI
Greenberg et al. (66)	Patients who presented to ED with NSTEMI (troponin I $\geq 4\text{ng/mL}$, excluded if they had a STEMI)
Jibrán, Khan and Hoyer (67)	Patients admitted for PCI for ACS.
Iyanoye (56)	Hospital discharge data for patients with stent implantation within 30 days of first presentation of AMI
Ouhoumane et al. (52)	Patients admitted to hospital for a first AMI in any hospital in Quebec
Ben-Ami et al. (68)	Patients discharged after hospitalisation in the cardiology department or wards with diagnosis of UA. Also, data from Acute Coronary Syndromes Israel 2000 (ACSIS 2000) study - all patients with a discharge diagnosis of ACS during Feb and March 2000 in different hospitals in Israel.
Hvelplund et al. (46)	Patients to hospital for first MI or UA diagnosis.

Table 4 showing the recruitment methods for the 21 articles in this study's literature review

Key: APO – Acute Pulmonary Oedema, BP – Blood Pressure, CABG – Coronary Artery Bypass Graft, CAD – Coronary Artery Disease, CHF – Congestive Heart Failure, COPD – Chronic Obstructive Pulmonary Disease, cTnT – Cardiac Troponin T, ECG – Electrocardiogram, HR – Heart Rate, HT – Hypertension, IHD – Ischaemic Heart Disease, LMCA – Left Main Coronary Artery, MI – Myocardial Infarction, NSTEMI – Non ST-Elevation Myocardial Infarction, PCI – Percutaneous Coronary Intervention, PVD – Peripheral Vascular Disease, SES – Socio Economic Status, STEMI – ST-Elevation Myocardial Infarction, UA – Unstable Angina, VF – Ventricular Fibrillation.

2.2.3 – Patient demographics:

Most of the studies reported on some aspect of their sample's demographics. However three studies reported no demographic information apart from patient age.

1. Fransoo et al. (63) – used a large population based study sample in Manitoba, with 4,199 men and 2,645 women. Inclusion criteria was a hospital diagnosis of AMI and they investigated rates of invasive cardiac procedures in this group (controlling for age only). It seems that both the large sample number and the access to hospital data could have provided useful demographic information.
2. Madrid Willingham and Kilpatrick (59) – used data from 2 Yorkshire hospitals to obtain a large sample of 2,505 men 2,323 women. This study evaluated rates of AMI diagnosis in patients with cTnT levels that were indicative of AMI and compared genders. The authors mentioned that they used a multivariable logistic regression model in their result analysis, however, the potentially confounding variables that they used in the model were not stipulated. They do discuss that independently from cTnT, female gender was a predictor of decreased likelihood of AMI diagnosis but that age wasn't. So, age and gender are the only variables that we know were in their multivariable logistic regression model. This study was published as a 'Scientific Letter' and perhaps the low word limit of this style of publication contributed to the brevity of information for this study.
3. Aguilar et al. (65) – as discussed above, this prehospital based study in San Diego included 11,622 men, 10,218 women. Age was the only demographic listed. As a prehospital based study, using the EMS staff member's 'run sheet' as the data source could be problematic in providing accurate and complete patient demographic information as it relies entirely on patient recall and disclosure. This may be why the authors chose not to include any other demographic information.

The studies that did include demographic information found the following:

Age:

All of the 21 articles found that the women included in their study of patients with ACS were significantly older than the male patients. This ranged in a difference of median age from one year older, for patients presenting to one hospital's ED with chest pain in Pennsylvania (52), to nine years older, for patients receiving PCI in public and private hospitals throughout France (54). This makes age a very important variable to control for when analysing differences between the genders.

Ethnicity:

Only two studies reported on patient ethnicity and they were both based in the United States (43), (49). It is unclear which ethnicities were included in these studies, but both studies reported that women were 'more likely to be black'. With regards to the generalisability of these studies data:

- Chang et al. (43) based their study in Pennsylvania and although they had an adequate sample size in which to draw a conclusion with 2,547 men and 3,514 women, their

population from which they sampled was only from one hospital. Their ethnicity data may be skewed from their narrow selection area. They also don't stipulate the time period for their study, so they may have obtained their data over a very long time period from a very narrow range of the population.

- Fang and Alderman (49) had a wider population in which to select their study sample, in that data was included from 4 different boroughs of New York City, so their data may be more generalisable. However, the data is still only from one city's population and may be more specific to New York.

With regards to including ethnicity data at all, both of these studies used multivariable regression analysis and were able to include race as a potentially confounding variable. This was particularly important in studies comparing gender, as women were more likely to be black in these studies. It is unclear why so few studies included ethnicity in their data, especially the hospital based studies where this type of information is commonly readily available.

Socioeconomic status:

Three articles referenced the SES of their study samples. Two studies found that compared to the men in their samples, women were either more likely to live in 'areas of lower income' (49) or to have a 'lower SES' (52).

- Fang and Alderman (49) had a large sample size of 52,947 men and 41,031 women. Patient income was divided into 'low, middle and high' based on the patient's zip code from the '2000 census data'. They found that women were more likely to live in areas of lower income.
- Ouhoumane et al. (52) used a large population based recruitment method in Quebec and included 15,603 men and 8,097 women. SES was assigned to each patient by using the patient's post code and correlating it with 'The Quebec Index of Material and Social Deprivation' (70). This measure of SES is a contextual measure in that it includes indicators for education, employment, income, marital status, living arrangement and single-parent status for a geographical area and assigns the average category for that area to each individual in the study sample (71). The authors reported that compared to the men in their sample, women of all ages were more likely to have a lower SES (52).

One other study made reference to SES and found no difference in SES with regards to gender.

- Griffith et al. (64) included 966 men and 597 women from one hospital in Scotland. A social deprivation category was assigned to each patient using the 'Carstairs deprivation' index (Figure 4). The Carstairs deprivation index is also a contextual measure of SES and it includes indicators for overcrowding, male unemployment, low social class and no-car. A patient was regarded as socially deprived if their postcode correlated with a Carstairs deprivation category of ≥ 4 . The percentages of patients that were classified in this way were then compared between the genders, but was not found to be significantly different.

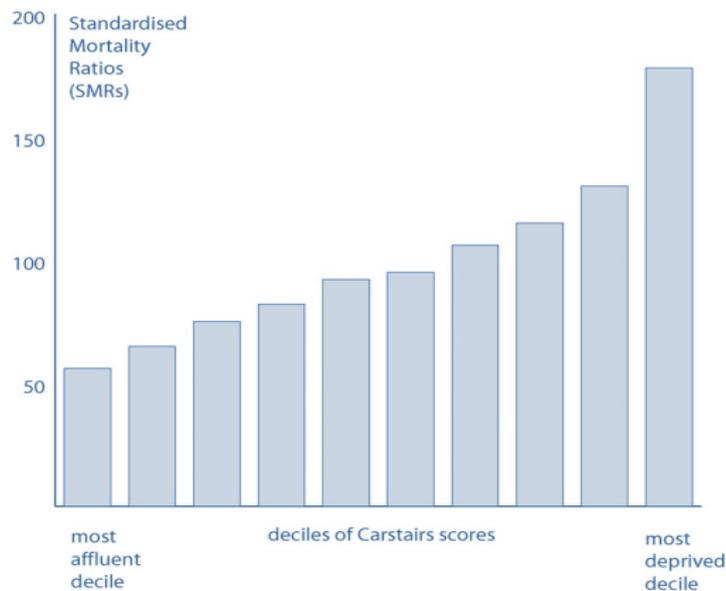


Figure 4: Standardised mortality ratios (age and sex standardised) for the Carstairs social deprivation scores (grouped into deciles) in Scotland (ages 0-64, for 2000-2002). The graph shows that the most deprived decile has the highest mortality ratio (72 p. 20).

An evaluation of SES when assessing healthcare quality and outcomes is quite valid, especially when referring to ACS. Social deprivation has been associated with increased mortality ratios (Figure 4). Also, several studies have found that lower SES can lead to a more adverse pattern of CVD risk factor levels (73) and is associated with a detriment in ACS care and outcomes (72), (74) - (76). When evaluating gender in the context of SES, women with a low SES can have even poorer treatment and outcomes for ACS when compared to men with a low SES (77). Access to timely reperfusion seems to be a main contributor to poorer outcomes for patients with lower SES (75), (76).

Each of the studies that assessed the SES of their samples, used a contextual method. This method is used commonly when evaluating a population's SES with the argument that each individual within that population is influenced by their surrounding environment (71). A slightly different method was used to obtain the data in each of the studies however. Fang and Alderman (49) and Ouhoummane et al. (52) used methods which evaluated the overall SES of each gender and compared the two groups to find any difference. This is a different method to that used by Griffith et al. (64) which consisted of assigning a cut off Carstairs deprivation index value of ≥ 4 and assessing whether there were differing numbers of each gender with that index value. The difference in method changes the question that the studies are asking, that is, Fang and Alderman (49) ask "do men and women have the same SES?" Ouhoummane et al. (52) ask "do men and women live in areas of differing income?" and Griffith et al. (64) ask "are more women classified as 'socially deprived' than men?".

The two studies that found that women were more likely to have a lower SES, or live in areas of lower income, selected their large sample sizes from large population bases; New York (49) and

Quebec (52). This makes their results less likely to be specific to a small area and therefore more generalisable to the whole population. In contrast to this, Griffith et al. (64) selected their relatively smaller sample size, from a more isolated population of one hospital's patients. They were able to obtain sample numbers that were large enough for statistical significance by sampling for a seven year period. However, with such an isolated population in which to sample from, it would be difficult to extrapolate their findings to a wider population. Such an extended sampling period also allows for changes in conditions.

Presentation, comorbidities and medications:

Many of the studies in this review found differing patterns of comorbidities and medication use between the genders in their sample (Table 5).

Presentation and Comorbidities	Women had more	Men had more	No Difference
Atypical ACS symptoms	(33), (48), (55), (68)		
Transport via ambulance	(42)		(58), (55), (66)
Hypertension	(33), (62), (64), (58), (49), (55), (56)		(43), (48), (67)
Diabetes	(62), (45), (49), (55), (52), (46)		(64), (48), (67)
Hyperlipidaemia	(62)	(33), (43), (48)	(67)
Smoking		(33), (43), (62), (64), (58), (48), (55), (68)	(67)
Aspirin and β -Blocker use prior to admission	(58)		(42), (66)
Rates of comorbidity (stroke, arrhythmia, COPD, cancer, anaemia)	(50), (56), (46)	(68) PVD	(64), (66), (67)
Renal Failure	(54)	(33), (68)	
CAD Hx/ \uparrow severe CAD		(33) (43), (48), (54), (68), (46)	(67)
CHF	(33), (49), (52), (46)		
Emergency admissions	(49)		
Normal ECGs	(43)		
NSTEMIs	(56)		(67)
STEMIs		(48), (56)	(67)
Previous MI		(43), (54), (68)	(67)
Family Hx of CAD		(48), (55)	(67)
Admitted to PCI hospital		(49), (46)	
Previous Coronary angiography/PCI/CABG)		(43), (64), (45), (54), (56), (68)	(67)

Table 5: Sample comorbidities according to gender, including previous medical history and medications for this study's literature review.

Women have more atypical presentations of ACS

As a consensus, although chest pain was the most common symptom of ACS in both genders, women were more likely than men to have an atypical presentation of ACS (33), (48), (55), (68). Chang et al. (43) evaluated the quality of chest pain in their sample and found that both men and women had the same quality of chest pain but women had more associated symptoms of nausea/vomiting and men had more diaphoresis. An atypical presentation of ACS can be a hindrance to ACS diagnosis and can impact negatively on ACS care (31), (32).

Women have more HT, Diabetes, CHF and higher rates of comorbidities

On the whole, the women in these studies presented with more HT, Diabetes, CHF and higher rates of comorbidities, but they were older and these diseases are more common in the elderly. As discussed in the introduction (1.5.1) the patients most likely to present with atypical ACS without chest pain are female, older and have a history of hypertension, heart failure and diabetes (32), (33).

Men smoke more and have more previous CAD and STEMIs

Men had more smoking, hyperlipidaemia, STEMIs, previous CAD and more severe CAD, more previous MIs and more previous invasive procedures to their coronary arteries. Smoking in particular is a very strong risk factor not only for development of CAD but also for greater mortality of IHD. The NHF of Australia's Policy Paper on Tobacco and cardiovascular disease (2007-2010) (78) states that smokers have a 70% greater mortality from IHD compared to non-smokers. However, even with such strongly related comorbidities and previous medical conditions to increase mortality, women still had greater mortality than men from ACS. Assiri (48) used a sample of admitted patients who received a diagnosis of ACS from one hospital in the southwest of Saudi Arabia, over a two year period. The men in the sample were more than twice as likely to present with a STEMI (40.8%) than the women (18.9%), $p < 0.001$. One study by Jibrán, Khan and Hoye (67) found no difference between the genders in all of the dimensions that they assessed, including more smoking in men, which contradicts all the other studies that studied smoking rates and found it to be higher in men (Table 5). This study however, had relatively small patient numbers (331 men and 137 women) (67) sampled from a narrow population of one United Kingdom hospital. It is not surprising then that when the sample size was diminished even further, by evaluating the numbers of smoking patients within their sample, that they didn't have the statistical power to detect a difference between their genders.

2.3 - Gender Disparity

Of the 21 articles in this study's literature review, 19 found some form of gender disparity in their investigation of men and women with ACS. The gender disparity found in either the assessment, referral, treatment or outcome of ACS was most commonly to the detriment of women. (Table 6) shows each of the areas where researchers found gender disparity and these are discussed in detail below.

	Higher in women	Higher in men	No difference
Assessment and Referral			
On scene time delay	(65)		
ECG time delay	(58), (66)		(42)
Admission to a PCI capable hospital		(43), (49)	
Rates of stress tests	(33)§	(43)	
Diagnostic coronary angiography		(33),(42), (43),(45), (46)	(48), (68)
Diagnosis and activation of treatment protocol			
Diagnosis of MI		(59)	
ED physician diagnostic impression of cardiac disease		(43)	
Door to CODE, Lab to balloon, code to balloon, door to balloon time delay	(58)		
Door to catheter lab arrival time delay			(42)
Treatment			
Door to β -Blocker time delay	(66)		
Stent placed prior to discharge		(56)	
Acute medication treatment for ACS (includes Heparin, aspirin, Glycoprotein IIb/IIIa inhibitor)		(67)	(68)
Rates of cardiac procedures (includes revascularisation, cardiac catheterisation, coronary angiography, angioplasty, stent insertion & CABG)		(33),(43), (48),(45), (49),(50), (46)	(63), (45)
Outcome			
Longer hospital stays	(62), (56)		
In-hospital mortality	(54), (55), (56)		
In-hospital & 30 day major adverse cardiac event			(62)
30 day mortality	(52)		(64), (56)
One year mortality	(50)		(56)

Table 6: Areas where researchers investigated for gender disparity in ACS.

§ Stress tests prior to angiography.

Key: ACE-I – Angiotensin Converting Enzyme – Inhibitor.

2.3.1 – Assessment and referral for ACS

Gender disparity was apparent in both the timing and rates of assessment procedures and in referral of patients with ACS.

Timing

A delay on scene prior to transporting women with ‘chest pain of suspected cardiac origin’ was found by Aguilar et al. (65). The mean on scene time was 3.02 ($p=0.001$) minutes longer for women than for men. As discussed in the introduction (1.5.2) it is imperative for AMI treatment to be delivered in a timely manner in order to decrease infarct size. So, any identified time delays for either gender can affect optimal delivery of ACS care and potentially affect patient outcome.

Delay in Door to ECG

Two studies found that it took longer to acquire an ECG from women with ACS than it did for men in the ED from the time of their arrival (58), (66). This is different to the findings of one study which found that there was no difference in door-to-ECG time for men and women.

Dreyer et al. (58) reviewed a STEMI registry from four primary PCI capable hospitals in Adelaide Australia. Patients were included in the study if they were admitted for primary PCI over a four year period ending in 2010. There were significantly more men (562) compared to women (173) in their sample, which is consistent with other studies showing that women were less likely to be admitted to hospitals with PCI capability (discussed below) or to be diagnosed with STEMI (48), (56). Student's independent t-tests and non-parametric Mann-Whitney U-tests were used where appropriate to compare median values for times of assessments or treatments between genders. A multiple linear regression model was then constructed to examine the effect of gender on DTB times only (discussed below in Door to Balloon time). Women had a longer time from onset of pain to arrival at hospital (147 min, IQR 62,349) of almost an hour compared to men (97 min IQR 55,255), $p = 0.011$. This is consistent with the findings from the National Heart Foundation, discussed in the introduction (1.5.2).

Once women did present to the hospital, it then took 2 minutes longer for them to have an ECG (8 min, IQR 5,13) than it did for men (6 min, IQR 3,11), $p=0.001$. There was no adjustment for any clinical covariates between the genders for these times as the authors' primary outcome was to investigate DTB time. It would have been interesting to see results controlled for symptoms such as 'cardiac-type chest pain' so that a conclusion as to whether atypical symptoms were a contributing factor to the delay to hospital arrival and delay for door-to-ECG was appropriate or not.

Greenberg et al. (66) included patients who presented to the ED with NSTEMI (troponin I $\geq 4\text{ng/mL}$, excluded if they had a STEMI). Unfortunately the authors omitted to disclose the study's location, but state that their data was from one hospital with 24 hour catheter laboratory access. The sample number is also unclear as they provide a percentage of the overall study number for each gender, but do not explicitly state the numbers for each gender. This is poor practice as it is difficult to interpret the relevance of the results with regards to our own region. The aim of the study was to evaluate time to ECG, time to beta blocker and time to heparin over 6 months and then implement a training programme to improve these times. In the initial 6 month period, results showed that women had an ECG acquired on average 4 minutes later than men (19 min for women, 23 min for men, $p = 0.013$). After the training programme, time-to-ECG improved significantly for women, down to (12 min), $p = 0.011$, but not for males (16 min), $p = 0.80$.

The authors used chi-squared and fisher exact tests and Kruskal-Wallis procedure. Although a multivariable regression analysis wasn't used, they note that there was no difference between genders in time of symptom onset, current medications, allergies, episodes of bradycardia or hypotension, triage assignment, method of arrival to ED, comorbidities or DNR orders. We can conclude that there was a difference in time to ECG between genders with this type of analysis, but we are less able to say that either gender was a significant variable associated with an increased time to ECG unless a multivariable regression model was used.

Rates

None of the studies investigated the rates of ECGs in their samples. This makes sense as the bulk of the study's inclusion criteria was a diagnosis of AMI, which requires a 12-Lead ECG. Several researchers found that women were less intensively examined than their male counterparts (33), (42), (43), (45), (46).

Rates of diagnostic coronary angiography

Chang et al. (43) conducted an observational cohort study of 2,547 men and 3,514 women, ≥ 30 years old, who presented to one hospital's ED with a complaint of chest pain which prompted an ECG. Their objective was to evaluate whether there were diagnostic evaluation differences and whether any differences could be explained by presenting characteristics, cardiac risk, or hospital course. The authors used chi-square tests, Fisher's exact tests and t-tests to evaluate the presenting characteristics between men and women. Multivariate regression analysis was used to investigate rates of cardiac catheterisation with adjustments for age, race, total number of cardiac risk factors, Thrombolysis in Myocardial Infarction (TIMI) risk score, initial ECG, whether serum biomarkers were significant for AMI and outcome at 30 days (which included death or recurrent AMI). Results revealed that men were significantly more likely to undergo cardiac catheterisation than women (OR 1.60, 95% CI = 1.29, 1.98).

The study's (43) inclusion criteria did not involve an ACS diagnosis, thus it controlled for potentially including more men in their sample, as women may be less likely to receive a diagnosis of ACS (59) and this is demonstrated by their sample including more women than men. It did however rely on the ED physician's decision to acquire an ECG and there is no report on the number of patients that presented to the ED with chest pain, who did not have an ECG acquired. This would have allowed for analysis of rates of ECGs for each gender.

Chang et al. (43) used a robust method of multivariate statistical analysis with relevant adjustment for potential confounders in investigation of rates of cardiac catheterisation. In conclusion, this yields a rigorous study with results that are consistent with the consensus from the other articles in the literature review and suggests that a real gender disparity may explain the results.

Consensus for diagnostic coronary angiography

The consensus with regards to diagnostic coronary angiography was that women were less likely to undergo the procedure than men (Table 6). However, some authors found that when angiography was performed, women tended to have less severe CAD than men (33), (43), (45), (48). Also, women tended to have more bleeding complications (67) and smaller coronary artery vessel sizes (62). These factors change the risk vs benefit ratio of this invasive procedure for women and may contribute to the physician's relative reluctance with regards to referring women for diagnostic angiography.

Two authors found no difference between genders with regards to coronary angiography (48). Interestingly, both studies were based in the Middle East. Assiri (48) found that exactly 62.2% of both genders had coronary angiography performed (92/147 for women and 247/397 for men).

The author states that the diagnosis of ACS for >18 year olds was the only inclusion criteria and that the different types of ACS were based on the American College of Cardiology clinical data standards. However, the inclusion criteria were not explicitly stated, so it is difficult to interpret why the results of coronary angiography rates between the genders differs from the general consensus. For example, if typical chest pain was a criteria for ACS diagnosis than coronary angiography for those patients may be more likely. It may also help explain the large difference in the numbers between genders in the sample with women being more likely than men to have an atypical ACS presentation.

Rates of admission to PCI capable hospitals

Two studies found that women were less likely to be admitted to hospitals that had PCI revascularisation capability compared to men (43), (49). Chang et al. (43) state that more men were admitted than women to their PCI capable hospital, but don't include any data on that point. Fang et al. (49) used a univariate analysis to describe patient characteristics between genders for patients with a diagnosis of AMI, who were admitted to New York hospitals over a seven year period (ending 2002). Women were found to be more likely than men to live in a neighbourhood with revascularisation resources, that is, a local hospital with PCI capability. Logistical regression analyses were conducted to determine factors associated with an admission to PCI capable hospitals and adjusted for age, race, gender, co-morbidity status, complication, income, insurance status, neighbourhood with/without revascularisation resource and admission status. Men were 22% more likely to be admitted to a PCI capable hospital than women (OR 1.22, 95% CI = 1.18, 1.26, $p < 0.05$), even though women were more likely to live in a neighbourhood with revascularisation resources.

2.3.2 – Diagnosis and activation of treatment protocol

Only two of the studies reviewed rates of diagnosis for ACS, with both finding that physicians were more likely to form a diagnosis/impression of ACS for men than for women (43), (59).

Rates

The study by Madrid Willingham and Kilpatrick (59), described above in (2.2.3), reviewed patient records from patients with acute admissions with non-traumatic chest pain, with a cTnT level that was positive for significant myocardial damage. Their finding was that women were less likely to have received a discharge diagnosis of AMI compared to men. Of those patients with a significant Troponin level, 46% of males had an AMI diagnosis compared with 33% of females, which after a multivariate regression analysis gave females an OR of 0.61 ($p < 0.0001$) for receiving an AMI diagnosis.

Chang et al. (43) found that men were more likely than women to receive an 'initial ED impression' of cardiac aetiology (67.8% vs 60.5%, $P < 0.001$) by their ED physician. It's unclear when this impression was formed in the timeline of the patient's ED stay, that is, whether the impression was formed before or after ECG acquisition. Women were more likely than men to have an ECG interpretation of 'normal' (51.6% vs 40.9%, $P < 0.001$). So, if 'initial ED impression' was formed after ECG interpretation, the results of the ECG could have influenced the ED physician's impression for women.

Timing

Further to their finding of a delay in door to ECG time for women (discussed above in Delay in Door to ECG); Dreyer et al. (58) found that time delays continued for women with ACS. (Table 7) sets out the areas where time delays continued for women throughout their stay in the ED.

	Men median (minutes)	Women median (minutes)	p-value
Pain to Door	97	147	0.011*
Door to ECG	6	8	0.001**
Door to CODE	17	23	0.012*
Lab to Balloon	19	23	0.008*
Code to Balloon	57	63	0.001**

Table 7 shows the time differences that Dreyer et al (58) found when comparing men and women with STEMI at PCI centres in Adelaide, Australia.

*p<0.05, **p<0.01, ***p<0.001

The initial delay in door to ECG time of 2 minutes for women cannot account for the 6 minute delay in Door to CODE and suggests that the time delays for assessment in ACS continue through the ED stay.

The study by Greenberg et al. (42) did not find a gender difference in door to ECG time or time to CCL arrival for patients with STEMI. The main focus of the study was to evaluate time to CCL in relation to an 'MI alert' being activated by the ED physician or by the EMS transporting the patient to the hospital (discussed in the 'Introduction 1.5.6'). Gender analysis was evaluated with a chi-squared test and door to ECG is not discussed in the results. Instead, there is a table with median times for Door to ECG of exactly 6.4 minutes for both genders. Time to CCL is listed as 'Time to intervention' in the same table, so it is unclear whether this represents time to CCL arrival or Time to Balloon. 'Time to Intervention' was 79 minutes for men and 81 minutes for women (p=0.38). The statistical methods did not control for any potential confounders for this study and the presentation of the results is confusing and lacking in clarity. Interestingly, Greenberg et al. (42) they found that 88.9% of the men and 80.8% of the women who had an MI alert were referred to the CLL but did not evaluate this data further.

2.3.3 – Treatment

Treatment of ACS is where most of the articles in this literature review focused their research.

Rates

By far, the majority of articles found that men had higher rates of cardiac procedures, revascularisation, cardiac catheterisation, coronary angiography, angioplasty, stent insertion and CABG (33), (43), (45), (46), (48) - (50). Nguyen et al. (33) used a multivariate logistic regression model to evaluate data from patients who were discharged with a diagnosis of MI and included 1,378 men and 1242 women, as previously discussed in (2.2.2). After controlling for age, race, hypertension, diabetes, hyperlipidaemia, smoking status, family history of CAD, previous diagnosis of MI or heart failure, prior PCI or CABG, symptoms of chest pain, dyspnoea, neck pain, diaphoresis, nausea, weakness, abdominal pain, back pain, bradycardia, hypotension, renal insufficiency, anaemia, elevated cardiac biomarkers, and ST-elevation on

ECG they found that men were more likely to receive coronary angiography, giving women an AOR of 0.73, 95% CI (0.57, 0.94), $p < 0.01$.

Fransoo et al. (63) disagreed with this finding however and concluded that once they controlled for patient age, there was no longer a gender disparity in rates of cardiac procedures.

Timing

Iyanoye et al. (56) didn't find any gender disparity in their primary outcome, which was to investigate rates of use for drug eluting stents versus bare metal stents between male and female patients within 30 days of their first AMI. They did however find that stents were more likely to be placed prior to discharge for men and after discharge for women. There was also an associated increase in mortality for women and this is discussed further below.

Door to Balloon time

Dreyer et al. (58) adjusted for several potential confounders in a multiple logistic regression model to investigate any gender disparity and variables associated with increased DTB times. After controlling for age, hypercholesterolaemia, HT, diabetes, family history of heart disease, history of smoking, previous CAD, peak ST-elevation on ECG, initial heart rate, initial Systolic Blood Pressure (SBP), APO, VF arrest, office hours presentation, arrival status (self vs non self-arrival) and triage category, they found that gender was still a significant variable and women had a 13% increase in DTB median (1.13, 95% CI 1.02-1.26 $p = 0.022$).

2.3.4 - Outcome

There were no conflicting findings for two of the outcomes investigated by the articles in the review. These were:

1. Women who suffered an AMI had longer hospital stays than men (56), (62), and
2. Women had higher rates of in-hospital mortality post AMI (54) - (56).

Further to that discussed above, Iyanoye et al. (56) found that women had higher in-hospital mortality rates for both types of stent and for both types of infarct suffered (STEMI or NSTEMI). They recruited a very large sample number (12,869 women and 27,346 men) over an eight year period. A multivariate logistic regression model was used to explore associations among gender, type of stent used, in-hospital and 30 day all-cause mortality and were determined with adjusted odds ratios. The models adjustments are listed in (Table 8).

	Bare metal stent	Drug eluting stent
NSTEMI	1.89, 95% CI(1.25-2.87), $p = 0.003$	1.38 (0.92, 2.06), $p = 0.10$
STEMI	1.41, 95% CI (1.1-1.81), $p = 0.006$	1.73, 95% CI (1.34-2.24), $p < 0.0001$

Table 8 AOR for in-hospital mortality for women, compared to men who received a coronary artery stent within 30 days of their first presentation for AMI in New Jersey. Adjustments were made for age, race, medical insurance, site of AMI, pre or post discharge stent implantation, comorbidities and vascular complications. The data is presented with regards to the type of infarct and the type of stent used (56).

2.4 – Reasons for gender disparity

The final area of investigation of the literature review is to examine the proposed explanations that the researchers postulated for any gender bias demonstrated. (Table 9) lists the proposed

explanations, some of which are concerning, but the most common listed is that women have atypical symptoms of ACS (33), (46), (58). Another explanation postulated is that women take longer to seek help and by the time they do, the sense of urgency in triage them as an acute patient is lost (58), (65). Women are older is an explanation from two of the studies, but the bulk of the other studies controlled for age and still found a significant gender bias. Only two authors mentioned that a true gender disparity may be responsible for the results.

Reasons for gender disparity	
Age difference only	(63), (65)
Women have atypical symptoms of ACS so false negative diagnosis.	(33), (46), (58)
Women have a longer symptom onset to seeking help time (no sense of urgency).	(58), (65)
Presence of breasts in women makes ECG electrode placement difficult.	(58)
Physicians believe women have a lower pre-test probability of infarction	(59)
Women may have different insurance status	(43)
Women may be refusing	(43)
True gender disparity	(43), (48)
Women have smaller coronary arteries	(48)
Women have less severe arteriosclerosis of the coronary arteries	(48), (49)
Women are less likely to be admitted to PCI capable hospital so don't receive as much revascularisation	(49), (50)
Physician misperception of women's preferences	(50)
Women have poor adherence to medical advice	(50)
Physician concerns over increased bleeding risk in women (older and lower weight compared to men)	(67)

Table 9: Shows the proposed explanations for gender disparity amongst the articles in the literature review.

In summary

There were many different study objectives, methods and findings. The main consensus is described here with a brief summary of findings.

Women with ACS are more likely to experience a scene delay when attended by EMS and less likely to be admitted to a PCI capable hospital. Once in the ED women are more likely to experience a delay in acquisition of an ECG compared to men. Women are also less likely to receive a diagnosis of ACS and less likely to be referred to the CCL, to undergo diagnostic angiography or other revascularisation. If women do receive a coronary artery stent, it is most likely after discharge, whereas men are more likely to receive a stent prior to discharge. There is no difference in the type of stent received between men and women. After an AMI, compared to men, women are more likely to die in hospital and to have longer hospital stays and resultant CHF. There are many different explanations postulated for these gender biases but the most common is that women receive a false negative ACS diagnosis due to their atypical ACS presentation.

Chapter 3 – Research Design

This chapter describes the study design, methods for data acquisition and analysis, as well as the ethical and cultural considerations.

3.1 - Study design

This was a retrospective observational cross-sectional study of rates of 12-lead ECG acquisition, for patients with cardiac-type chest pain, who were attended by St John New Zealand (NZ) Emergency Medical Service (EMS) staff. At the time that this study was undertaken, St John ambulance was the largest emergency ambulance service provider in NZ. St John ambulance was also the only front-line emergency ambulance provider to service the whole of New Zealand, apart from the Taranaki and the greater Wellington regions.

Data were acquired from Patient Report Forms (PRFs) that were recorded by the EMS staff at the time of attending each patient. The aim of this research involved investigation of the 'routine' practice of EMS staff. It was therefore important that the research itself would not interfere with the practice that it was attempting to investigate. A retrospective observational study design could avoid the 'Hawthorne effect' of improved performance with knowledge of being observed (79). The design then could potentially improve the likelihood that the results could be more generalisable to 'routine' practice. An advantage of a cross-sectional study design is in its ability to estimate prevalence of an outcome of interest (80). As this study was investigating prevalence of 12-lead ECG acquisition, the cross-sectional study design was most appropriate.

12-lead ECG acquisition was chosen as the outcome investigation as:

1. Prehospital 12-lead ECG acquisition has been shown to improve outcomes in ACS patients (discussed in the introduction).
2. 12-lead ECG acquisition was standard practice for all EMS staff qualified to the level of paramedic and above.
3. The clinical procedures that the EMS staff were working from included 12-lead ECG acquisition for all patients with suspected myocardial ischaemia, as long as the acquisition didn't significantly delay transport.

3.2 – Setting

A stratified sample of PRFs recorded over a 12-month period (ending in November 2010) supplied the data for this study. A mix of urban and rural regions were selected from each of the North and South Islands to account for possible regional or cultural variations in practice throughout New Zealand. The aim was to obtain enough data, so that a separate test for gender disparity could be performed for each location.

3.2.1 – Locations

In order to obtain a representative sample for NZ, it was important to sample from multiple regions throughout the country. Originally, sampling was planned for 6 centres, (three from each of the North and South Islands). However, two were retrospectively removed from the study, due to inadequate PRF numbers or due to logistical issues associated with PRF storage. The final four centre locations were an urban and rural centre from both the North and South Islands. In order to not create stigma towards a particular region, these will be anonymised here as Urban A and Rural A for the North Island regions and Urban B and Rural B for the South Island.

3.2.2 - Dates

Data were sampled from PRFs recorded from patients during a specific 48 hours for each month. The time period was 12-months, ending in November 2010, from all locations. Urban A was the largest city in NZ, having 1,333,300 (31%) of the 4,315,800 total NZ population at the 30th of June 2009 (81). This corresponded with Urban A having the busiest EMS as well. Due to a lower number of EMS call-outs in all other data centres, an increased time period was needed for all areas outside of the Urban A region in order to capture enough data. This was devised by sampling from the same 48 hour period for all regions, but then adding an additional sample from an additional 48 hour period for each regional area (Appendix D).

3.2.3 – Permission to access the data

Verbal permission to access every PRF through St John ambulance, for data collection purposes, was provided from the St John Clinical Director and Regional Operations Manager (ROM) Northern Region in December 2010. Due to an absence of ethical review processes at the time, formal written confirmation of this approval was received on the 7th of May 2011 from the ROM and on the 1st of May 2012 from the Clinical Director.

To ensure that the sample was representative of the population, it was necessary to have access to PRFs from a broad sample of patients and also recorded by a broad sample of EMS staff. Access to every PRF from every ambulance attendance over the study period was also a necessity. Finally, the PRFs would need to reliably contain sufficient detail to meet the requirements of the study.

3.2.4 – Ethical Approval

An expedited ethical review from the Health and Disability Ethics Committees for this study was undertaken on the 19th of July 2010 (Appendix E). This confirmed that ethical approval was not required (under section 11.9 of the Ethical Guidelines for Observational Studies) as this project is an observational study performed by people who already had access to the data and did not involve children. Auckland University of Technology Ethics Committee (AUTECH) then approved an Ethics Application for the study on the 3rd of November 2010 (Appendix F) in accordance with section 5.3.2.3 of AUTECH's *Applying for Ethics Approval: Guidelines and Procedures*.

3.2.5 – Data Collection

All St John patient data was stored as a hard copy of a hand-written PRF that the attending EMS staff wrote (Appendix G) for a fictitious example). Each PRF consisted of a top-copy and two carbon-copies. The top-copy was submitted into the patient's hospital notes, if they are transported to hospital by ambulance, or was left with the patient, if they were not transported. The carbon copies, as well as a copy of any recorded ECGs, were sent to St John administration for audit, billing and secure storage purposes. It was these carbon copies that were used for this research.

Each PRF contained the following information:

- Dates and times (ambulance dispatch from base, ambulance located at scene, ambulance departed scene, ambulance at destination, treatments and observations)
- Logistical identifiers (job number, ambulance vehicle number)
- Patient status (level of severity of condition)
- National case code (a code assigned to each patient by the treating EMS staff member, which represents their working diagnosis (Appendix H))
- Patient Identifiers (name, date of birth, gender and residential address)
- Incident location and patient destination
- Ethnicity (Maori, Pacific Island, Other and Not Stated)
- Patient's chief complaint and relevant history
- Current medications and allergies
- A chronological list of all treatments and observations whilst with the EMS staff.
- Attending EMS staff identifiers (names, qualifications, unique staff number and signature of the main person treating).

This level of detail provided all the information needed for the study.

These aspects made St John ambulance NZ the logical provider for this study's data acquisition: with:

- Complete access to the greatest number of EMS staff in NZ,
- The widest coverage of the NZ ambulance patient population and
- Reliable and relatively complete data detail.

3.2.6 – Division of labour

As the data collection involved the laborious task of reading through thousands of hand-written carbon copies of PRFs, it was divided between five chart abstractors. Chart abstractors were qualified as an Intensive Care Paramedic (ICP) and PRF audit was part of their regular work duties. The ICP qualification was the highest qualification obtainable within St John and reflected a higher practice and experience level.

3.3 – Patients

Inclusion criteria were constructed with the aim of identifying PRFs from patients that were at least 16 years of age and who were attended by an EMS staff member on the dates specified in the study. These PRFs were included if they reported symptoms that were consistent with a typical presentation of ACS whilst in the presence of the EMS staff member (described below in 3.3.1). Specific parameters were listed in the study manual and were applied as inclusion and exclusion criteria. The exclusion criteria were designed to exclude PRFs from patients that described precordial discomfort that was more likely caused from conditions other than ACS (described below in 3.3.2). These were identified as somatic chest wall and pleuritic or respiratory derived precordial discomfort (7).

3.3.1 – Specific inclusion criteria

To be included in the study, the patient's PRF was required to contain:

- Information from a patient that was at least 16 years old and was attended by an EMS staff member in a front-line ambulance on the dates specified in Appendix D only.
- A description of a patient that experienced acute precordial discomfort (as defined above in (1.3.1)). The precordium was defined as the anterior thorax, from the suprasternal notch to the xiphoid process and between the left and right midaxillary lines (7).
- Information that enabled the reader to determine that the paramedic's working diagnosis was that of ACS. This variable is described further in (3.7.2).

3.3.2 – Specific exclusion criteria

Patient Report Forms were excluded from the study if they:

- Contained information from a patient that described their precordial discomfort as increasing with deep inspiration or movement
- Contained information from a patient that experienced a traumatic injury prior to the onset of their chest discomfort.

3.4 – Variables and data sources

A pre-formatted electronic spreadsheet was distributed to each chart abstractor. The spreadsheet format involved columns with designated headings and a "yes" and "no" category beneath each heading. Information from each individual PRF was displayed as a single row within the spreadsheet. Data was recorded by placing a "1" in the appropriate "yes" or "no" column (Appendix I).

3.4.1 – Included variables

It was important to record a wide selection of variables so that potential confounders of the gender disparity odds ratio (OR) of acquiring a 12-Lead ECG could be identified. It was especially important if these variables were particularly associated with either patient gender. For example; if being older affected the odds of having a 12-lead ECG acquired and there were more older females in our sample than older males, the results could be potentially confounded

if age was not recorded as a variable. It was not unreasonable to expect that our female patient sample would have a higher age median than the male patient sample as the median age for females in NZ is 2.5 years older than for males (82). The older NZ population also has a significantly larger percentage of females than males (Figure 5).

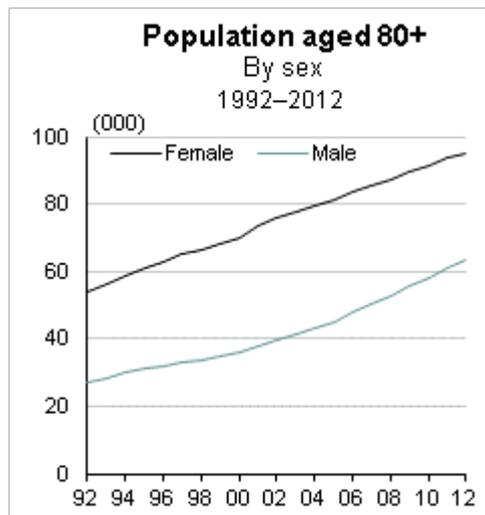


Figure 5: Showing significantly more females than males in the New Zealand population aged ≥ 80 years, from 1992 to 2012. There are approximately 46% more females (95,000) aged ≥ 80 years than males (65,000) (82 p. 2)

As patient age was recorded, this could then be included in a multivariable logistic regression model to see the effect on the outcome. (Table 10) shows the variables that data were collected for and a brief description of why each was included.

Variable	Reason for inclusion
Was the main treating EMS staff member's working diagnosis that of ACS?	This was listed as inclusion criteria. This enabled a selective investigation of PRFs from patients where the EMS staff had diagnosed the chest pain as cardiac in origin. The importance of this was that a false negative diagnosis for ACS as a cause for gender disparity in 12-Lead ECG acquisition could be ruled out. Determination of the EMS staff member's working diagnosis is discussed below in (3.4.3).
12-Lead ECG capable cardiac monitor available at the time	Also listed as inclusion criteria. Only PRFs from patients that were in an ambulance equipped with a 12-Lead ECG capable cardiac monitor were included.
Patient's gender	Main focus of the study
Data Centre Location	Although all regions operated under the same clinical procedures, auditing and education was conducted at a local level. This meant that the local culture within the organization had the potential to effect practice.
Patient's age	Possible confounder associated with increased numbers of elderly women in the population. Also, perhaps EMS staff would be less likely to perform a 12-lead ECG on certain age brackets.
Primary treating EMS staff gender	Possible confounder if any of the data centres had a different ratio of male to female EMS staff and if EMS staff were less likely to acquire a 12-lead ECG on a patient of the opposite sex.
The gender of all other EMS staff present – as a group	This allows us to review whether the presence of EMS staff of the opposite gender will affect any gender disparity present
Whether a 3-lead ECG and 12-lead ECG had been acquired	Main focus of the study
≥ 2 EMS staff present	If the EMS staff member was alone and had to drive, perhaps they would not choose to acquire a 12-Lead ECG due to the time-delay or being busy with other tasks. Also, rural data centres may have been more likely to have ambulances that were staffed with a sole EMS staff member.
Patient retrieved from a medical centre	If the patient already had a 12-Lead ECG acquired, would this decrease the likelihood of EMS staff choosing to continue monitoring the patient's 12-Lead ECG? Also, even if no 12-lead ECG was acquired, EMS staff may be more likely to treat a patient retrieved from a medical as a 'transfer' (no treatment required), even though it was still a 'front-line ambulance' retrieval.
The time taken on-scene and time spent travelling	Time constraints for shorter transports may decrease the likelihood of 12-Lead ECG acquisition
Type of monitor	If a model of cardiac monitor was more complicated or had less training available, perhaps EMS staff would be less likely to acquire a 12-Lead ECG with it.
Was the patient transported?	Could provide interesting data on the types of patients that refuse ambulance transport. Patients that had a recommendation of non-transport from the EMS staff would also be investigated through this variable.
Highest EMS staff qualification present	If all of the EMS staff present were not trained to the level of a paramedic, they may not have received training on how to acquire a 12-Lead ECG.
Treatments received – Morphine, oxygen, nitrates, aspirin, intravenous access attempted.	These treatments are listed within the St John clinical procedures (2007-2009) as the treatment options for cardiac chest pain. Reviewing the number and rates of treatments could provide information on how well the treatment protocol for ACS was followed. Also, a potential confounder if an increased number of treatments for a very unwell patient may take precedence of a 12-Lead ECG acquisition.

Patient refused assessment or treatment or treatment was medically contraindicated	Are either gender more likely to refuse treatments, especially when there is a gender difference between patient and EMS staff? If so, this would result in a difference in treatments/assessments received.
Coded unique identifier for each EMS staff.	If a particular EMS staff member was more or less likely to acquire 12-Lead ECGs and they were over represented in the data, the results may be skewed.
Date, run number and data centre	Each PRF could be uniquely identified for inter-and intra-rater reliability testing.
Total number of PRFs reviewed for each 24 hour period	Could provide extra information such as rates of ACS presentations to the ambulance service.

Table 10: Showing each variable recorded in the study and why it was included

3.4.2 – Partial double data entry

The use of locally based chart abstractors to gather data helped to reduce travel costs and allowed for partial double data entry. A visiting chart abstractor travelled to each data centre in order to allow for this double data entry of a portion of the data. A total of 10% of the collected data was double entered which allowed for evaluation of error rates, for both data entry and PRF inclusion and exclusion throughout the data collection. This method was shown to lower error rates whilst maintaining cost-effective data extraction (83), (84).

Prior to starting the data collection, processes were implemented that were consistent with recommendations by To, Estrabillo, Wang, Chengning, Cicutt and Lisaon on improving intra-rater and inter-rater reliability for medical chart extraction studies (85). In particular:

- A chart abstraction guide was designed with:
 - a quick reference flowchart of inclusion and exclusion criteria (Appendix J),
 - abstraction procedures,
 - coding instructions,
 - several scenarios for discussion that would enable chart abstractors to handle potentially challenging medical charts in a consistent manner,
 - explicitly defined inclusion criteria and exclusion criteria.
 - Chart abstractors took part in training workshop sessions, led by the author, that introduced the study and research methodology and focused on:
 - how to identify PRFs that met the study's inclusion or exclusion criteria
 - and how to reliably enter the de-identified data into the spreadsheet.
- Additional site visits were conducted to review data collection processes and to ensure that research protocols were being followed.
- Other ongoing communication methods included phone calls, email and teleconferencing.

3.4.3 - Determining a working diagnosis of ACS

This variable was difficult to define as there were multiple ways of revealing the EMS staff member's working diagnosis. Each of the items listed below were ways of determining this variable:

- Any patient treated with aspirin from the EMS staff.
 - The only indications listed in the St John Clinical Procedures 2009-2011 (86) for aspirin administration were "Cardiac Chest Pain" or "objective evidence of myocardial ischemia on 12 lead ECG".
 - EMS staff wrote that they intended to administer aspirin but that it was contraindicated due to the patient's aspirin allergy or the patient already receiving aspirin prior to EMS staff arrival.
 - 'Chief Complaint' listed as:
 - "Cardiac Chest Pain" or "CCP"
 - "Myocardial Ischaemia" or "angina" or "unstable angina"
 - "Acute Myocardial Infarction" or "AMI" or "MI"
 - "Acute Coronary Syndrome" or "ACS"
- Patient has been assigned a status code of "2" by the EMS staff and this was in the absence of any other reason for this level of severity. A status code is a numerical means of describing an estimate of the severity of the patient's condition (86). The St John Clinical Procedures (2009-2011) (86) describe the status codes from '1' (the most critical) to '4' (the least critical). These procedures directed EMS staff to assign patients with unrelieved 'cardiac chest pain' to a status code of "2" (86).
- Patient was treated with GTN in the absence of signs of cardiogenic pulmonary oedema. GTN was only indicated as a treatment for two conditions in the St John Clinical Procedures (2009-2011) (86) :
 1. Cardiac Chest Pain and
 2. Cardiogenic Pulmonary Oedema

3.4.3 – Privacy and confidentiality

No data was ever recorded in a form that contained identifiable information from either the patient or the EMS staff. Each EMS staff member was assigned a unique numerical identifier by applying a confidential code to their unique staff number. The numerical identifier was recorded for every inclusion for the off-chance that a particular EMS staff member was over represented in the data and therefore had the potential to bias the results. Data was entered into a specifically designed spreadsheet and emailed to the biostatistician at regular intervals.

3.5 – Gender disparity

Several potential sources of gender disparity were identified prior to data abstraction and efforts were made to address these in the study's design. Aspects of the population to be studied for example, could potentially skew the data, such as cultural and ethnic influences in one particular geographical location compared to another (this and other potential sources of gender disparity are discussed below).

3.5.1 – Cultural and ethnic influences on capture rates

It was considered that various regions may have concentrations of ethnic or cultural groups that could influence the results. Particularly with regard to cultures that have a higher threshold around modesty and nudity and especially where there is a gender difference between the patient and the health care provider. As this study reviewed the rates of a procedure that involved exposing patient's chests in order to acquire a 12-lead ECG, a cultural focus within a region had potential to bias the results.

People of Maori ethnicity have higher rates of IHD than the general population. A recent report from the Ministry of Health reviewed the data from the 'New Zealand Health Survey' and determined that diagnosed IHD was 1.8 times higher in the Maori population versus the non-Maori population (87). Identifying the ethnicity of the patient was very desirable in this study but unfortunately this data was unavailable as the relevant field of the PRF was routinely incomplete.

3.5.2 - Regional variation in practice norms due to local auditing

The training for each qualification level of EMS staff in St John NZ was standardised and centralised. The audit process to review each EMS staff member's practice and performance with each patient was however undertaken locally by fellow EMS staff. Ideally the auditor is of equal or higher qualification compared to the auditee. It was postulated that this local audit process had the potential to curb local practice from a non-standardised emphasis of a particular practice point. For example; not acquiring a 12-Lead ECG in a patient with cardiac-type chest pain may be consistently emphasised as an area for practice improvement in one local region, but not in another. As this regional variation in practice had the potential to bias our results, we attempted to address this by sampling from multiple locations and including location as a variable in the statistical models.

3.5.3 – Temperature and seasonal variation

There was a possibility that cooler temperatures in the various regions within this study and also varying throughout the calendar year, could contribute to different rates of 12- Lead ECG acquisition. It was postulated that patients may have been more likely to refuse to disrobe for a 12-Lead ECG in a cooler climate. For example; Urban B has a historical temperature average of -5°C to 20°C (88) for the month of June, whereas Urban A's is 3°C to 19°C (89). This potential source of bias was addressed by obtaining a stratified sample covering each month equally through a 12 month period. Also, the study incorporated data from the exact same dates and times for all centres.

3.5.4 – Staff variation

A single watch calendar system operated throughout all St John regions. So, a stratified sample was chosen that would equally cover watch calendars, shift times and designated annual leave periods. The selection of a 48 hour period from each month meant that a full day and night shift for each EMS staff watch grouping was selected to ensure an even coverage of EMS staff selection. This was to account for possible training, managerial and audit variations amongst the different watches. It also ensured that a wider number of staff were included in the study

thus reducing introduction of bias due to individual operator practice. This was especially important in areas with smaller staff numbers.

3.6 – Study size

A pilot study of 7,454 PRFs recorded from the Urban A region was undertaken in June 2009 in order to determine the required PRF numbers for this study. The pilot study found 255 patients who met the inclusion criteria, 53% were male. A 12-lead was acquired for 35 (25.9%) of males and 15 (12.5%) of females. A sample size calculation is shown in (Table 11).

	12-Lead ECG	Mean rate	SD	Derivations	P-Value
Male patient group (135)	35	0.259	0.438		0.011
Female patient group (120)	15	0.125	0.331		
Magnitude of difference to detect				-0.134	
SD of difference				0.549	
Required group size				209	
Number of PRFs (male and female patients)				418	

Table 11: Showing pilot study data from 2009 used to derive a necessary sample size of 418 PRFs for this study. The parameters of the test were a Desired Power (sensitivity) of 90% and Alpha (level of significance) of 5%.

Key: SD (Standard Deviation, assuming binomial distribution)

Based on the 255 patients in the pilot study, a power calculation determined that 418 PRFs would be needed to meet the inclusion criteria. This was in order to detect a significant difference (alpha=0.05, power=90%) between rates of 12-Lead ECG acquisition for male and female patients. If the study was able to obtain data from 418 patients, this would allow detection of an effect at least equal to the size seen in the pilot study undertaken in the Urban A area. If the study was able to obtain data from 418 patients in each centre, this would also allow for independent detection of an effect for each centre.

3.7 – Quantitative variables

The quantitative variables included in the study were mostly quite simple and dichotomous in that the variable was either present or not. For example; patient was retrieved from a medical centre, or not. There were only a few quantitative variables that were grouped together in this study. These are listed in (Table 12).

Grouped variable	Reason for grouping
Age of the patient (years): Age brackets of: ➤ <50 ➤ 50-69 ➤ ≥70	Potential confounder if EMS staff were more or less likely to acquire a 12-lead ECG from a certain age bracket.
Total time with the patient (mins): ➤ ≤ 19 ➤ 20 to 29 ➤ ≥ 30	Grouping these variables allowed for evaluation of shorter vs longer time with the patients in order to assess for time as a confounder of the outcome. If time with the patient was longer, perhaps EMS staff would be more likely to acquire a 12-lead ECG. Longer times may also have been associated with either patient gender. For example: it may take longer to take a history from a male patient and therefore they may have extended on scene times. Shorter transport times could be associated with a patient gender if EMS staff perceived a patient's condition to be more critical they may travel more quickly to the hospital. A cut-off of 20 minutes was selected as this was when EMS staff would receive a message from the EMS dispatcher to prompt their departure from a scene.
Officer gender: ➤ Male EMS staff member present ➤ Female EMS staff member present	Perhaps the gender of the EMS staff could influence the likelihood of acquiring a 12-lead ECG.
Highest qualification of EMS staff	EMS staff of Primary Care and Ambulance Officer qualification were not formally trained to acquire a 12-lead ECG (Appendix K), so would be less likely to acquire one. If either gender were more likely to have a higher or lower qualification of EMS staff dispatched to them, then this could confound the outcome findings.
MONAI Score Treatments grouped together for Morphine, Oxygen, Nitrates, Aspirin and Intravenous Cannula.	This variable was evaluated as it was speculated that the more treatments a patient received, the less likely it was that a 12-lead ECG would be acquired as the EMS staff may be too busy to prioritise this assessment. Each treatment was assigned a score of '1' and was added with each treatment received, that is, a score of 3 meant that three treatments had been received by the patient.

Table 12: Showing the grouped quantitative variables of this study and why they were grouped.

3.8 – Statistical methods

This study used descriptive statistics to describe the study's patients. Inferential statistics were used to test its null-hypothesis and to generate a measure of effect size (as an odds ratio) to estimate the over-all gender disparity effect. The null-hypothesis to be tested was that there would be no difference in acquisition rates of 12-Lead ECGs from EMS staff, between male and female patients presenting with 'typical cardiac-type chest pain' when the EMS staff member's working-diagnosis was that of ACS.

3.8.1 – Descriptive statistics of the study patients

Numbers of male and female patients were evaluated as a whole number and as a percentage/proportion of the total patients. Proportions of males and females in the study sample were compared using a binomial test. Medians were calculated for the male and female patient's ages and contact times as well as a binomial test of the three broad categories according to gender described in (Table 12). Rates of 12-lead ECG acquisition were evaluated as a percentage of all patients and for the male and female patients separately. Analysis of the null-hypothesis was undertaken with a regression method (discussed in detail below).

3.9.2 Missing data

Several variables were regarded as compulsory for inclusion in the study. These were:

- Date
- Patient gender
- Age of the patient
- EMS staff member's working diagnosis of ACS
- 12-Lead ECG acquisition
- 12-Lead ECG capable monitor available to EMS staff members.

If these variables were missing, then the patient's data would be excluded from the study. If other variables were missing, evaluation would be made as to the inclusion of the patient for dichotomous variables or calculation of a continuous variable. For continuous variables, the median value would be established for that variable across all patients and then substitute for the missing variable.

3.8.3 – 12-Lead ECG acquisition rate

Evaluation of the rates of 12-lead ECG acquisition between male and female patients was undertaken using a logistic multivariable regression method. Associations with 12-lead ECG acquisition were analysed with this method and included the following explanatory variables:

- patient gender
- age band of patient
- geographical location
- medical centre retrieval
- gender mix of EMS staff
- highest qualification of EMS staff
- contact time
- MONAI score.

Interaction terms by patient gender were included for age band, geographical location, gender mix of attending EMS staff and highest qualification of attending EMS staff to test for variations of gender disparity by those variables. The other variables (medical centre, contact time and MONAI score) were included as adjustments for potential confounding effects.

3.8.4 – Choice of statistical model

Percentages, proportions and medians:

It is standard to present binary and categorical variables as a percentage (90). This study chose to evaluate the central tendency of the continuous data sets (such as patient age) with calculation of their medians, rather than their means, as the median is less influenced by outliers (90). Measures of dispersion were included for continuous data medians as an interquartile range (IQR) in order to give a clearer description of the data set.

Proportions of male and female patients were compared using a binomial test as the outcome is binary. Random errors were accounted for by using a P-value that exceeded an alpha level of 0.05 with a confidence interval of 95% (91). Using a P-value of 0.05 as a measure of statistical significance meant that (if there was no difference between the male and female patient groups) the probability of getting a study result with at least as much difference between the groups was 5% (90).

Multivariable logistic regression model:

Regression methods allow for assessment of an outcome variable and can model the odds of a binary outcome occurring when describing two comparative variables. They also allow for assessment of the relationship between an outcome variable (such as 12-lead ECG acquisition) and several predictor variables (such as patient age, sex or medical centre transport) in a single analysis. Adjustment for potential confounding variables (such as contact time) is also possible with this method (90).

The outcome measure for this study was the 12-lead ECG acquisition rate between genders and this was derived firstly from a bivariable logistic model (i.e. one explanatory variable being gender vs one dependent variable being outcome). Secondly, to assess for potential confounders that may be associated with 12-lead ECG acquisition and gender, a multivariable regression model was utilised. As the outcome measure for this study was dichotomous (i.e. 12-Lead ECG acquired or not), a logistic regression model was used to obtain an adjusted odds ratio. This is an appropriate model to use as opposed to a linear regression model, which would be used for evaluation of a continuous outcome (90), (91).

The use of logistic regression coefficients also allowed for the secondary objective of this study, which was to evaluate variables associated with a lower probability of having a pre-hospital 12-Lead ECG acquired for the sample as a whole. Alexopoulos (91) describes that odds ratios can be estimated for each of the independent variables in a model through the use of logistic regression coefficients. Adjusted odds ratios (AOR) were then determined for each group of variables that were identified as being associated with a lower probability of having a prehospital 12-Lead ECG acquired. All analyses were performed using R Software, version 3.1.1 (92).

3.8.5 Regional variation

An evaluation of rates of prehospital 12-Lead ECG acquisition in each of the four data centres was planned. This was designed to explore whether localised EMS staff practice and regional organisational culture could influence the odds of 12-lead ECG acquisition.

Chapter 4 – Results

This chapter presents the findings that answer the following research questions:

- Do EMS staff exhibit gender disparity when assessing patients with suspected ACS? Specifically; are the rates of 12-lead ECG acquisition different for male and female patients with cardiac-type chest pain when the attending EMS staff member's working diagnosis is that of ACS?
- What is the level of procedural compliance in the assessment of ACS in the pre-hospital EMS field?
- What variables are associated with a reduced odds of EMS staff acquiring prehospital 12-lead ECGs in all patients with suspected ACS?

4.1 – Participants

A total of 26,273 PRFs from patients attended by front-line EMS staff were reviewed by the four chart abstractors. The PRF were stratified for a selection of dates, over a 12-month period, from Dec 2009 to November 2010. Of those PRFs, 6.4% (1,675) met the inclusion criteria. (Figure 6) shows the process used to derive the final sample number included in the study.

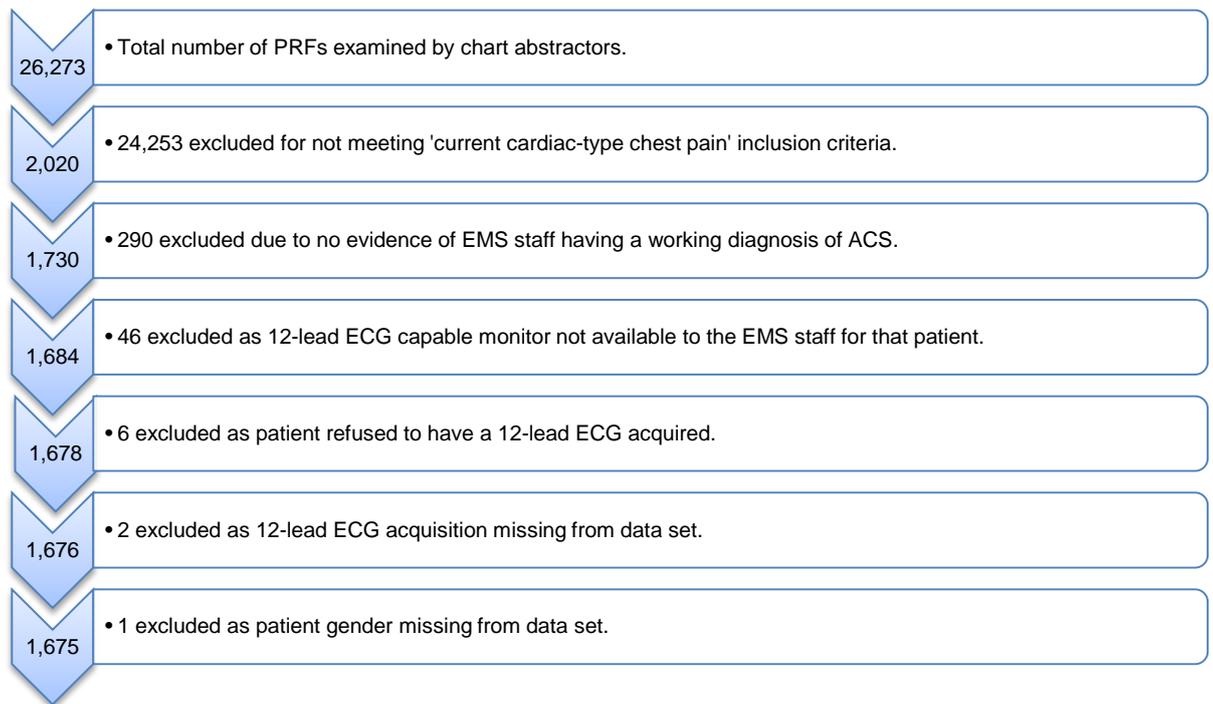


Figure 6: Flow chart starting with total number of patient PRFs examined and ending with the sample number included in this study, with the reasons for exclusion throughout.

4.2 – Descriptive data

With respect to the sample as a whole the median age in years was 68, quartiles 55 to 79 (IQR 24). Representation increased by age as 16% of the sample were aged less than 50 years whilst 38% were aged between 50 to 60 years and 46% were aged 70 years or older. 90% (1,502) of the sample were attended by an EMS staff member of at least paramedic qualification. The most common qualification of EMS staff to attend the patients a Paramedic (49% of the sample) followed by an Advanced Paramedic (40% of the sample).

Contact time with EMS staff was more often at least 30 minutes (57% of the sample) with 86% of the sample having at least 20 minutes and only 12% of the sample having less than 20 minutes with EMS staff. Only 16 patients were attended by EMS staff and not transported in the ambulance. Almost all of the sample were attended to by two or more EMS staff, with only three patients attended by a single EMS staff member. 23% (385) of the patients were retrieved from a medical centre by EMS staff. The main treating EMS staff member was male for 69% (1,155) of the sample.

4.2.1 – Data centre characteristics

The target number of cases (418) was reached in each of the two urban centres, with Urban A and Urban B centres having 483 and 767 patients respectively. The two regional centres failed to reach the target number of cases however, with 292 and 133 patients in the Rural A and Rural B centres respectively (Table 13). Cases from the two urban centres contributed 75% of the data.

4.2.2 – Specific gender characteristics

Males and females were in similar proportion in the study sample, although there were slightly more males included, with 52% (869) of the included PRFs coming from male patients (Table 13). Women were slightly, but significantly older than men, with a 2 year median age difference between the genders. The median age of the males in the sample was 67 years and 69 years for the females. There was also a statistically significant difference in numbers of male and female patients in the various age bands with a larger proportion of males in the <50 age band and a larger proportion of women in the ≥70 age band. No other significant gender variations were seen in the sample (Table 13). Both males and females typically received the same contact time with EMS staff as well as the same EMS staff gender mix and highest qualification of EMS staff.

Variable	Total % (number)	Male patients	Female patients	P-value
Study sample	(1,675)	52 (869)	48 (806)	0.11
Age band (years)				0.007**
➤ <50	16 (268)	58 (156)	42 (112)	
➤ 50-69	38 (635)	54 (342)	46 (293)	
➤ ≥70	46 (772)	48 (371)	52 (401)	
Location				0.59
➤ Urban A	29 (483)	54 (259)	46 (224)	
➤ Urban B	46 (767)	50 (384)	50 (383)	
➤ Rural A	17 (292)	53 (156)	47 (136)	
➤ Rural B	8 (133)	53 (70)	47 (63)	
Gender mix of EMS staff				0.5
➤ Mixed crew	45 (753)	53 (400)	47 (112)	
➤ Male only	46 (769)	54 (342)	46 (293)	
➤ Female only	9 (153)	48 (371)	52 (401)	
Highest EMS staff qualification				0.12
➤ Advanced Paramedic	40 (675)	54 (364)	46 (311)	
➤ Paramedic	49 (827)	51 (419)	49 (408)	
➤ Ambulance Officer	10 (166)	48 (80)	52 (86)	
➤ Primary Care	<1 (7)	86 (6)	14 (1)	
Contact time (minutes)*				0.68
➤ ≤ 19	12 (203)	53 (108)	47 (95)	
➤ 20-29	29 (491)	53 (261)	47 (230)	
➤ ≥ 30	57 (957)	51 (488)	49 (469)	

Table 13: Shows the characteristics of the study sample according to patient's gender. Patient numbers and proportions within each age band and location, as well as the EMS staff characteristics and contact time for each gender are listed. A binomial test provides the unadjusted level of significance (p-value, 95% CI) for the difference in proportions for each gender.

Notes: **p<0.01

4.2.3 – Missing data

Two patients were excluded from the sample as the value for the '12-lead ECG acquired' subgroup was missing from the data set and this variable was compulsory. The only included variable with missing values was contact time, which was missing for 24 patients. Contact time was only of interest for confounder adjustment. The missing values of contact time were replaced by the median contact time of 32 minutes. No other imputation was performed and all eligible cases were included in the analyses.

4.3 – Outcome data

From the sample of 1,675 patients, 42.1% (706) had a 12-lead ECG acquired. With regards to the primary objective, significantly more male patients 49.6% (431) had a 12-Lead ECG acquired compared to female patients 34.1% (275). In regards to the secondary objective of procedural compliance, of the 1,502 patients that were attended by an EMS staff member who was qualified to at least the level of paramedic, 45% (673) had a 12-lead ECG acquired (Table 14). Evaluation of the 12-lead ECG acquisition rate for those 673 patients, according to contact time, revealed an increasing acquisition rate to a maximum of 54% for ≥ 30 minutes.

	Attended by EMS staff with at least paramedic qualification % (N)	12-lead ECG acquisition % (N)
Study sample	90 (1,502)	45 (673)
Contact time (minutes)		
➤ < 20 minutes	13 (191)	20 (39)
➤ 20 to 29 minutes	30 (453)	38 (172)
➤ ≥ 30 minutes	56 (836)	54 (454)

Table 14: The number and percentage of the sample that were attended by EMS staff who were qualified to the level of paramedic or above and the rate of 12-lead ECG acquisition for those patients. The contact time that those patients had with their attending EMS staff member is listed with reference to the grouped time bands that were discussed in the methods section. The 12-lead ECG acquisition rate and number is then listed for each time band.

4.3.1 – Outcome data with reference to location

Rates of 12-Lead ECG acquisition varied widely and significantly for both genders combined, between the study centres (Table 15). Urban B region had the lowest acquisition rate at 32.6% and the Rural B region had the highest acquisition rate at 85.7% (2.7 times that of Urban B).

Data Centre	Had 12-Lead ECG % (number)	UOR of 12-Lead ECG (CI95)	P-Value
Urban A	41.2 (199)	1	
Urban B	32.6 (250)	0.69 (0.55, 0.87)	0.0021 **
Rural A	49.0 (143)	1.37 (1.02, 1.83)	0.035 *
Rural B	85.7 (114)	8.56 (5.10, 14.38)	<0.001 ***

Table 15: Rates of 12-lead ECG acquisition for patients with acute cardiac-type chest pain by EMS staff member's whose working diagnosis was that of ACS. Rates are categorised by data centre location and the UORs are given for each centre in relation to Urban A. 95% CI and p-values are listed for level of significance.

Notes: *p<0.05, **p<0.01, ***p<0.001.

There was no statistically significant difference in patient gender proportion between the data centres (Table 16).

Location	Male % (number)	Female % (number)	P-value
Urban A	54 (259)	46 (224)	0.59
Urban B	50 (384)	50 (383)	
Rural A	53 (156)	47 (136)	
Rural B	53 (70)	47 (63)	

Table 16: Shows the number and proportion of male and female patients in each of the data centres, with no significant difference between them.

4.4 – Main results

Subgroup analysis allowed for a determination of the odds of 12-lead ECG acquisition. An UOR was determined for each subgroup, in relation to the subgroup listed first for each variable (Table 17). In regards to the primary outcome, patient gender was a significant variable with regards to odds of a 12-lead ECG with an UOR of 0.53 for female patients having a 12-Lead ECG acquired (95% CI, (0.41 to 0.64), p-value <0.001) compared to male patients (Table 17).

Variable	Subgroup	12-Lead acquired % (N)	UOR	CI95	P value
Patient gender					
	Male	49.6 (431)			
	Female	34.1 (275)	0.53	(0.43, 0.64)	<0.001***
Location					
	Urban A	41.2 (199)			
	Urban B	32.6 (250)	0.69	(0.55, 0.87)	0.0021**
	Rural A	49.0 (143)	1.37	(1.02, 1.83)	0.035*
	Rural B	85.7 (114)	8.56	(5.10, 14.38)	<0.001***
Patient's age (years)					
	Under 50	42.9 (115)			
	50 to 69	41.9 (266)	0.96	(0.72, 1.28)	0.78
	70 and over	42.1 (325)	0.97	(0.73, 1.28)	0.82
Gender of the main treating EMS staff member					
	Male	41.2 (476)			
	Female	44.1 (230)	1.13	(0.91, 1.39)	0.27
Male staff member present					
	Yes	41.1 (625)			
	No	52.9 (81)	1.61	(1.16, 2.25)	0.0049**
Female staff member present					
	Yes	43.6 (395)			
	No	40.4 (311)	0.88	(0.72, 1.07)	0.19
≥2 EMS staff present					
	No	43.5 (10)			
	Yes	42.1 (696)	0.95	(0.41, 2.17)	0.9
Patient retrieved from a medical centre					
	No	47.3 (610)			
	Yes	24.9 (96)	0.37	(0.29, 0.48)	<0.001***
Time spent on scene (mins)					
	0 to 9	23.7 (81)			
	10 to 19	42.9 (344)	2.43	(1.82, 3.23)	<0.001***
	20+	53.1 (279)	3.65	(2.70, 4.95)	<0.001***
Time spent travelling (mins)					
	0 to 9	33.9 (104)			
	10 to 19	41.2 (342)	1.37	(1.04, 1.80)	0.025*
	20+	48.8 (251)	1.86	(1.39, 2.50)	<0.001***
Monitor model					
	LP12	41.5 (466)			
	Other	43.5 (240)	1.08	(0.88, 1.33)	0.44
Not transported from the scene					
	No	42.1 (699)			
	Yes	43.8 (7)	1.07	(0.40, 2.88)	0.9
Highest EMS staff qualification					
	Advanced Paramedic	49.6 (335)			
	Paramedic	40.9 (338)	0.70	(0.57, 0.86)	<0.001***
	Ambulance Officer	19.1 (33)	0.24	(0.16, 0.36)	<0.001***
Treated with oxygen					
	No	36.0 (187)			
	Yes	44.9 (519)	1.45	(1.17, 1.79)	<0.001***
Treated with oral aspirin					
	No	32.8 (170)			
	Yes	46.3 (536)	1.77	(1.42, 2.19)	<0.001***

Treated with sublingual nitroglycerin					
	No	33.8 (188)			
	Yes	46.3 (518)	1.69	(1.37, 2.09)	<0.001***
Treated with intravenous morphine					
	No	37.7 (519)			
	Yes	63.0 (187)	2.81	(2.17, 3.65)	<0.001***
Intravenous catheter inserted/attempted					
	No	24.6 (186)			
	Yes	56.6 (520)	3.99	(3.23, 4.93)	<0.001***
Aspirin contraindicated					
	No	43.3 (586)			
	Yes	37.3 (120)	0.78	(0.61, 1.00)	0.049*

Table 17: A binomial test is applied to each of the variables listed to evaluate the odds of 12-Lead ECG. An UOR is related to the first subgroup of each variable. The 12-Lead ECGs were acquired by EMS staff for front-line ambulance patients with acute cardiac-type chest pain when the EMS staff member's working-diagnosis was that of ACS. Acquisition rates are given as a percentage and (total number) for each variable, followed by the UOR.

95% CI and p-value for level of significance.

Notes: *p<0.05, **p<0.01, ***p<0.001.

There were several variables that did not show a statistically significant difference in acquisition rate between subgroups and their variables and subgroupings are translated from (Table 17) here for clarity:

- Patient's age: Acquisition rates of 12-lead ECGs was very similar between the various age brackets.
- The gender of the main treating EMS staff member: Acquisition rates of 12-lead ECGs varied only slightly and insignificantly for patients that were mainly treated by either a male or female EMS staff member.
- Female EMS staff member present: There was very little difference in acquisition rates of 12-lead ECGs for patients who were attended by either:
 - An EMS crew that consisted of male and female or an all-female crew, or
 - An all-male crew.
- ≥ 2 EMS staff present: There was no real difference between rates of 12-lead ECG acquisition for patients attended by a solo EMS staff member compared with those who were attended by ≥ 2 EMS staff.
- Monitor model: The type of ECG monitor used to acquire the 12-lead ECG made no difference to acquisition rates.
- Not transported from the scene: No difference could be detected in rates of 12-lead ECGs for patients that were assessed but not transported to hospital by the EMS staff members, compared to those that were transported.

4.4.1 – Unadjusted estimates

Apart from female patient gender compared to male patient gender, many of the other subgroups showed a statistically significant difference in the UOR of a 12-lead ECG being acquired, and allowed for further determination of the secondary objective – what variables were associated with a decreased odds of a 12-lead ECG being acquired? The following points are the subgroups (listed in Table 17) where there was a statistically significant difference between the UORs for each variable:

- Location – In comparison to Urban A, patients were less likely to have a 12-lead ECG acquired in Urban B and more likely in the Rural A and Rural B.
- Male EMS staff member present – If a male EMS staff member was present on the ambulance, patients were less likely to have a 12-Lead ECG acquired.
- Patient retrieved from medical centre – If the patient was retrieved from a medical centre they were less likely to have a 12-lead ECG acquired.
- Scene time and transport time to hospital – the longer these combined times were, the more likely a patient was to have a 12-lead ECG acquired.
- Highest EMS staff qualification – The higher the qualification of the EMS staff member, the more likely a patient was to have a 12-lead ECG acquired.
- Treatment – Each treatment was associated with a higher UOR of having a 12-lead ECG acquired, with intravenous catheter insertion associated with the highest increase in UOR.

For each additional treatment recorded by the MONAI score, the odds of acquisition increased by AOR=1.38 ($p<0.001$) and this effect was very close to linear across the whole range from zero to five treatments. (Figure 7) provides a graphical demonstration of the association of increased treatment number with increased rates of 12-lead ECGs. The largest number of patients received 3 treatments, whilst the least number of patients received no treatment.

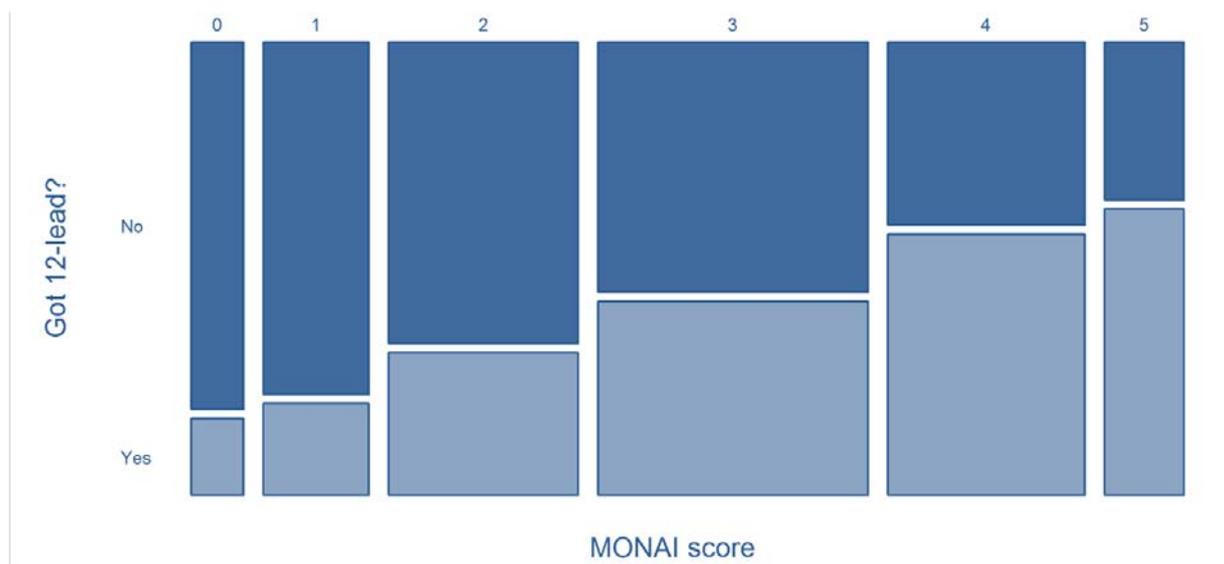


Figure 7 provides a graphical demonstration of the increased rates of 12-lead ECG acquisition with each added treatment (Morphine, Oxygen, Nitrates, Aspirin and IV catheter insertion). The width of each column provides a visual cue to the number of patients within each group.

4.4.2 – Confounder adjusted estimates of 12-lead ECG acquisition

Variables were further tested with a multivariable logistic regression model to control for potential confounders. The explanatory variables are listed in Section 3.8.3 – 12-Lead ECG acquisition rate', of this thesis. Patient gender still remained as a significant variable with an AOR 0.50, 95% CI (0.40 – 0.63), p -value <0.001 for a female patient having a 12-lead ECG acquired compared to a male patient (Figure 8). Statistical assumptions of the regression model (regarding residuals, dispersion and multicollinearity) were assessed and found to be acceptable, thus ensuring a good model fit.

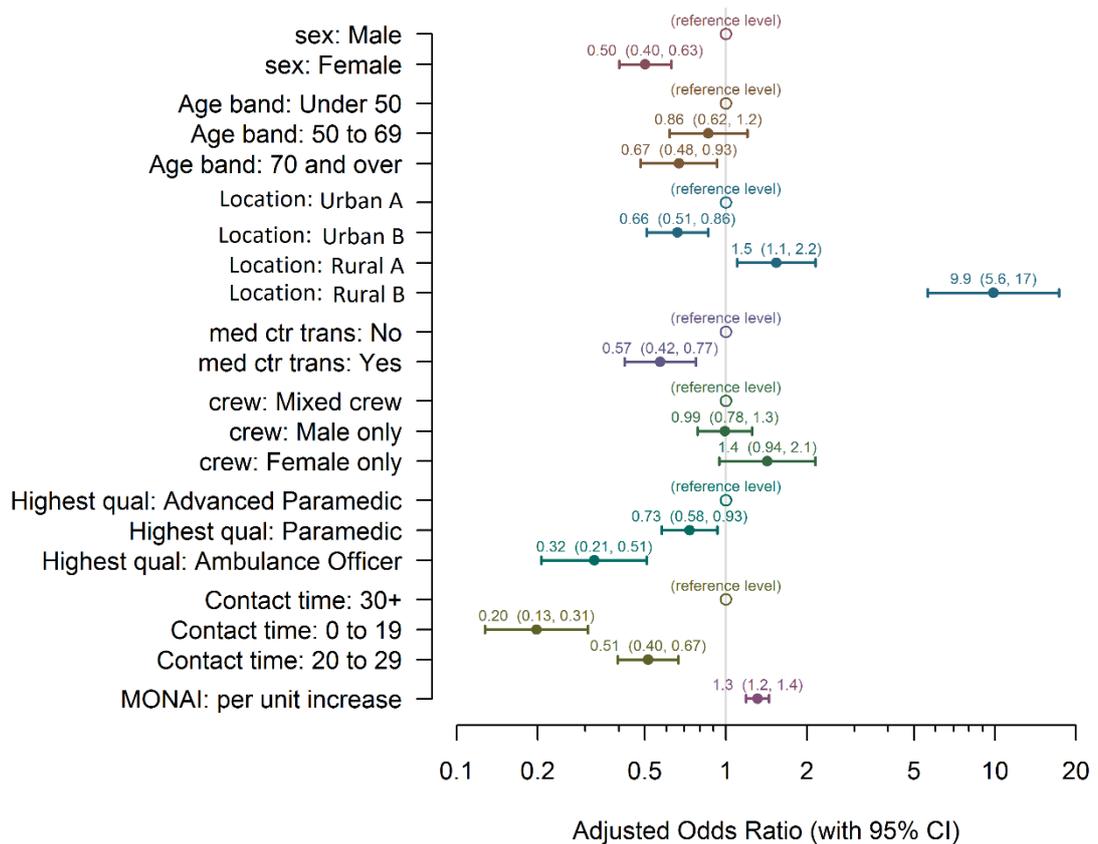


Figure 8: AOR of 12-Lead ECG acquisition by EMS staff for patients with cardiac-type chest pain when the EMS staff member's working-diagnosis was that of ACS. A reference level is listed first and then followed by a comparative variable, with its AOR and confidence intervals listed. All variables which resulted in a statistically significant AOR compared to their reference level are listed here. Each CI is illustrated graphically with a coloured line parallel to the x-axis. Subgroups which are significantly different from their reference value are represented with a coloured line that doesn't cross the reference level line. 95% CI

Apart from patient gender the other significant variables after potential confounder adjustment were:

- Patient age ≥ 70 years was associated with a reduced odds of 12-lead ECG acquisition.
- Location – In comparison to Urban A, patients were less likely to have a 12-lead ECG acquired in Urban B and more likely in the Rural A and Rural B.
- Medical centre transport: If a patient was retrieved from a medical centre they were less likely to have a 12-lead ECG acquired by their attending EMS staff.
- Highest EMS staff qualification – The lower the qualification of the EMS staff member, the less likely a patient was to have a 12-lead ECG acquired.
- Contact time – the longer the scene and travel times were, the more likely a patient was to have a 12-lead ECG acquired.

4.5 – Other analyses

To investigate which subgroups were significantly associated with gender disparity in 12-lead ECG acquisition, further subgroup analyses were undertaken with a multiple logistic regression model. Interaction terms by patient gender were included for age band, geographical location, gender mix of attending EMS staff and highest qualification of attending EMS staff to test for

variations of gender disparity by those variables. The other variables (medical centre, contact time and MONAI score) were included as adjustments for potential confounding effects. (Table 18) shows the results of this analysis.

	Empirical odds of 12-lead				Multivariable model results		
	Patients	Male	Female	UOR	AOR	(95% CI)	P-value
Study sample	1675	0.98	0.52	0.53	0.50	(0.43, 0.64)	<0.001***
Age band							
Under 50	268	0.90	0.58	0.64	0.57	(0.32, 0.99)	0.048*
50 to 69	635	0.99	0.49	0.49	0.47	(0.33, 0.68)	<0.001***
70 and over	772	1.02	0.52	0.52	0.52	(0.38, 0.72)	<0.001***
Location							
Urban A	483	1.04	0.43	0.41	0.44	(0.29, 0.65)	<0.001***
Urban B	767	0.68	0.33	0.49	0.48	(0.34, 0.66)	<0.001***
Rural A	292	1.14	0.79	0.69	0.70	(0.42, 1.17)	0.172
Rural B	133	6.78	5.30	0.78	0.78	(0.28, 2.15)	0.632
Gender mix of EMS staff							
Mixed crew	753	0.95	0.51	0.53	0.53	(0.38, 0.74)	<0.001***
Male only	769	0.98	0.45	0.46	0.44	(0.32, 0.61)	<0.001***
Female only	153	1.16	1.09	0.94	0.94	(0.45, 1.97)	0.874
Highest qualification							
Advanced Paramedic	675	1.30	0.71	0.54	0.55	(0.39, 0.78)	<0.001***
Paramedic	827	0.95	0.49	0.52	0.49	(0.35, 0.66)	<0.001***
Ambulance Officer	173	0.32	0.16	0.50	0.47	(0.21, 1.05)	0.066

Table 18: Gender subgroup analysis showing the number of patients within each subgroup and the empirical odds of having a 12-Lead ECG acquired by an EMS staff member for male and female patients presenting with cardiac-type chest pain, when the EMS staff member's working diagnosis was that of ACS. An UOR for 12-Lead ECG acquisition for female patients compared to male patients is presented for the study sample as a whole and is then categorised into the subgroups of age band, location, gender mix of EMS staff and the highest qualification of the EMS staff attending the patient. After analysis with a multivariable logistic regression model, AORs are given with 95% CI levels of significance listed as a p-value.

Notes: *p<0.05, **p<0.01, ***p<0.001.

4.5.1 – Subgroups with gender disparity

The subgroups with the largest significant gender disparity, where women were less than or equal to half as likely to have a 12-lead ECG acquired compared to men (in descending order of magnitude were):

1. Location – Urban A and EMS gender – all male: both of these subgroups had an AOR of 0.44 (p<0.001) for women compared to men.
2. Patient age – 50 to 69: AOR of 0.47 (p<0.001) compared to men.
3. Location – Urban B: AOR of 0.48 (p<0.001).
4. Qualification level – Paramedic: All qualification levels exhibited a gender disparity in 12-lead ECG acquisition, but paramedics AOR of 0.49 (p<0.001) was larger than the Advanced Paramedics and the Ambulance Officers AOR was not significant (p>0.05).
5. Patient gender – female: AOR 0.50 (p<0.001).

Gender disparity was prevalent in every age group of the sample, but the largest gender disparity was for patients age 50 to 69 with women AOR of 0.47 (p<0.001) (Table 18). Both urban centres demonstrated a large and statistically significant gender disparity. Urban A had

the largest gender disparity, not only in comparison with the other locations, but in comparison with all subgroups, with female patients having an AOR of 0.44 ($p < 0.001$). Women in Urban B were also less than half as likely to have a 12-lead ECG acquired compared to men with an AOR of 0.48 ($p < 0.001$). The two regional locations did not show a statistically significant gender disparity (both $p > 0.05$). However, it's worth noting that sample size numbers were below target in the two regional locations.

If there was a male EMS staff member present, a gender disparity was also present, with female patients less likely to have a 12-lead ECG acquired. This was most notable for an all-male crew where female patients had an AOR of 0.44 ($p < 0.001$). An AOR of 0.44 is the greatest gender disparity found in the study. The two variables with this AOR are 'double male crew' and 'location Urban A'. A crew that consisted of at least one male and one female EMS staff member resulted in an AOR of 0.53 ($p < 0.001$) for female patients. There was no gender disparity demonstrated with an all-female crew, AOR 0.94 ($p = 0.874$).

Gender disparity was demonstrated by both paramedic and advanced paramedic EMS staff members, with a greater disparity demonstrated by the paramedic qualified staff. Female patients had an AOR of 0.49 ($p < 0.001$), if the highest qualification of the EMS staff members that attended a patient was paramedic level. The AOR was slightly improved for female patients that were attended by an Advanced paramedic, but was still significant with an AOR of 0.55 ($p < 0.001$).

Insignificant values

There were only four subgroups where an AOR for 12-lead ECG acquisition was insignificant. All four of these groups had relatively low numbers of patients in comparison to the other subgroups (Table 18). For three of those subgroups, there was still an associated AOR for women that was well below parity with men. Patients from the two rural regions, had AORs of 0.70 and 0.78 but insignificant ($p > 0.05$). The third subgroup with an insignificant p-value was patients attended by EMS staff where the highest qualified staff member held an Ambulance Officer qualification. In this case, women had a very low AOR of 0.47 and a p-value=0.066.

The fourth and final subgroup with an insignificant p-value were all-female crews with an AOR for 12-lead ECG acquisition that was the closest to parity out of all of the subgroups analyzed at 0.94 ($p = 0.874$).

Chapter 5 – Discussion

This chapter summarises and discusses the findings of this research study on gender disparity and procedural compliance in the assessment of ACS in the pre-hospital EMS field. Gender disparity in the assessment and treatment of ACS patients has been well documented in hospital patients. Several studies have also examined this in the pre-hospital setting, but no studies have investigated EMS staff's decision making process with regards to the assessment of patients who were suspected to have ACS. In limiting the inclusion criteria to patients with cardiac-type chest pain, that were attended by front-line EMS staff and the attending EMS staff's working diagnosis was that of ACS, this study controlled both for the patient's presentation and the practitioner's diagnosis. Using this study design helped to determine four key points:

1. Whether EMS staff exhibited gender disparity when assessing patients with cardiac-type chest pain. Specifically; whether the rates of 12-lead ECG acquisition were different for male and female patients when the attending EMS staff member's working diagnosis was that of ACS.
2. The level of procedural compliance when assessing patients with suspected ACS.
3. Any variables that were associated with a lower rate of 12-Lead ECG acquisition.
4. Whether any exhibited gender disparity could be explained by the most common conclusions from previous research:
 - The gender disparity was due to a false negative diagnosis of ACS in women and/or
 - The gender disparity was due to women presenting atypically, which led to their physician giving them a false negative diagnosis of ACS.

5.1 - Key Results

The primary objective was to investigate the null-hypothesis that there would be no difference in acquisition rates of 12-lead ECGs by EMS staff for male and female patients presenting with acute cardiac-type chest pain when the EMS staff member's working-diagnosis was that of ACS.

5.1.1 - Primary objective

The null-hypothesis was rejected here as, after controlling for potential confounders, women were half as likely to have a 12-lead ECG acquired than their male counterparts. A statistically significant decrease in the rate of 12-lead ECG acquisition was exhibited for women in almost all of the subgroups, except for those women at regional locations or attended by an all-female EMS crew. The largest gender disparity was demonstrated in female patients in Urban A or Urban B, aged 50 to 69 and attended by an EMS staff member of paramedic qualification.

5.1.2 - Secondary objectives

Secondary objectives were to investigate procedural compliance for these acute patients and to identify which variables were associated with a decreased rate of 12-lead ECG acquisition. Finally, investigation was undertaken to identify whether previously proposed explanations of

gender disparity in ACS assessment were supported. In particular, if the gender disparity in ACS could be explained by:

1. Women having an atypical ACS presentation and
2. Women receiving a false negative ACS diagnosis due to their atypical presentation

Procedural compliance

With regards to procedural compliance, overall acquisition rates of 12-lead ECGs were low at 42.1% of the sample, especially as all patients in the sample were potentially eligible for 12-lead ECG acquisition due to their presentation (cardiac-type chest pain) and their EMS staff member's working diagnosis (ACS). However, there are three aspects to take into consideration when reviewing procedural compliance.

1. 12-lead ECG acquisition was only standard practice for EMS staff qualified to the level of paramedic. If we review only those patients that were attended by an EMS staff member qualified to paramedic level or above, procedural compliance should be close to 90% of the sample. As the acquisition rate was 85.6% in The Rural B region, it appears that procedural compliance was good there. But this still leaves the other three centres with poor procedural compliance with acquisition rates of 41.2%, 32.6% and 49% for Urban A, Urban B and Rural A respectively. However, there are two more aspects to take into account when reviewing procedural compliance and these are listed below:
 2. The clinical procedures, that all EMS staff operated under, stipulated that a 12-lead ECG should be acquired for all patients where myocardial ischaemia was suspected provided that it did not 'significantly delay treatment or transport' (86). We suspected that patients who received more treatment would be less likely to have a 12-lead ECG acquired as the attending EMS staff may have been too busy with life-saving treatment to perform the assessment. However, results revealed that patients who were attended by an EMS staff member who provided more treatment (higher MONAI score), were also more likely to have a 12-lead ECG acquired. This may suggest that patients that were attended by a proactive practitioner were more likely to be thoroughly assessed and treated for their suspected ACS.
 3. Thirdly, with regards to timing, 12-lead ECG acquisition rates were understandably lower for decreased contact time with EMS staff. However, 86% of the sample had at least 20 minutes of contact time with EMS staff. When the sample was evaluated for patients that were attended by an EMS staff member of at least paramedic qualification and a contact time of ≥ 20 minutes, the result was still a large proportion at 77% ($n = 1,289$) of the sample. This leaves the 12-lead ECG acquisition rates for Urban A (41.2%), Urban B (32.6%) and Rural A (49%) still far from par with procedural compliance.
- For further clarification on the effect of contact time with 12-lead ECG acquisition rate, the highest rate exhibited for patients attended by an EMS staff member of at least paramedic qualification and a contact time of ≥ 30 minutes was only 54%.

Variables associated with decreased rates of 12-lead ECG acquisition

The variables associated with a decreased odds of 12-lead ECG acquisition were female patients aged ≥ 70 years, located in Urban B, retrieved from a medical centre and a shorter contact time. To discuss these points individually;

- EMS staff may have been less likely to acquire a 12-lead ECG in patients that were more elderly if they believed that the patient would not receive any further management for their ACS. We grouped patients aged ≥ 70 years into one group which may have included extremely elderly palliative patients and EMS staff may have been less likely to aggressively investigate these patients for comfort sake.
- The low rates of 12-lead acquisition for patients located in Urban B, at 32.6% of the sample, is concerning for that region. A cultural difference in that region within the EMS service may have resulted in a lack of procedural compliance with regards to:
 - Failing to complete the PRF fully and not documenting 12-lead ECG acquisition and interpretation.
 - Failing to staple a copy of the 12-lead ECG to the EMS carbon copy.
 - Failing to acquire a 12-lead ECG in a patient with cardiac-type chest pain that the EMS staff member suspects is ACS.
- A decreased rate of 12-lead ECG acquisition for patients retrieved from medical centres is also concerning. These patients were assessed by a Doctor and an ambulance was requested for their admission to hospital for ACS. The patients still had cardiac-type chest pain whilst in the presence of the EMS staff and a 12-lead ECG was not acquired by those staff enroute to the hospital. As discussed in the introduction, patients who sought assessment from a GP were at a disadvantage in receiving timely care for their ACS compared to those patients that called an ambulance or those that attended the hospital directly. A lack of complete assessment by EMS staff for these patients may further impede care.
- Contact time has already been discussed in point 3. above.

Can these results be explained by an atypical presentation or false negative ACS diagnosis?

This study shows, for the first time, that when the patient's presentation and the EMS staff member's working diagnosis were controlled for by the study design, female patients still had significantly fewer 12-lead ECGs acquired than male patients. Even women with acute typical cardiac-type chest pain that were given a working diagnosis of ACS by the attending front-line EMS personnel, received less investigations than their male counterparts. This finding is significant because it refutes conclusions from previous studies that the gender bias demonstrated in ACS assessment was due to women's propensity to have an atypical ACS presentation. Furthermore, a false negative ACS diagnosis on the basis of this atypical-presentation cannot fully explain the gender disparity either.

5.2 – Limitations

This study was unable to investigate some important aspects associated with gender disparity, that is; ethnicity, comorbidities and SES. These have been shown to be associated with different levels of ACS care and may be associated more with women. As a case was only included in the study if the EMS staff member's working diagnosis was ACS, a false negative ACS diagnosis associated with these variables was controlled for. However, the decision of whether or not to acquire a 12-lead ECG due to other factors such as the patient's ethnicity, comorbidities or SES patient cannot be identified.

Follow up data with patient outcome was also not investigated in this study so the real effect of a decreased rate of prehospital 12-lead ECG for women could not be assessed. However, other studies have concluded that both morbidity and mortality is improved for patients with STEMI and a prehospital 12-lead ECG compared to no prehospital ECG (17), (36), (37) (as discussed in the introduction). Feedback was not sought from the EMS staff members for an explanation of their decision to acquire a 12-lead ECG or not. Therefore, our conclusions as to the reasons for the gender disparity are limited to ruling out atypical presentation and false negative ACS diagnosis.

Data acquisition was laborious and sometimes difficult to extract from hand-written patient report forms and accuracy of the data may have been affected due to this. 12-lead ECG acquisition rates for the sample as a whole may have been under reported if EMS staff did acquire a 12-lead ECG but failed to mention this on the PRF, or failed to staple a copy to the EMS carbon copy. There is no reason to suspect that women would be less likely to have their ECG kept compared to men however. Electronic PRFs will make data extraction much faster and more likely; this may help to fill the gap in the literature for prehospital based studies.

5.3 - Interpretation

In this study, female patients were slightly but significantly older than the male patients. This is consistent with all of the studies included in the literature review. Prior investigators have shown that women with ACS are more likely to have an atypical presentation (43), (59) and they are less likely to receive a cardiac diagnosis (33), (48), (55), (68). These barriers to optimal ACS care may well account for some of the gender disparity that has been established in women with ACS being less intensively examined (33), (42), (43), (45), (46), receiving less revascularisation for AMI (33), (43), (45), (46), (48) - (50) and having higher in hospital mortality rates post AMI (54) - (56).

This study supports the finding that women are less intensively examined for ACS than men as they were less likely to have a 12-lead ECG acquired even though it was part of standard practice. This study refutes the assumption that an atypical presentation of ACS in women and a false negative ACS diagnosis for women is the only explanation for this disparity, as this study controlled for those and there was still a large and significant decrease in rates of assessment for women. Some investigators have proposed that patient preference may explain why women with ACS are less intensively examined. We disagree with this as well as we controlled for it by excluding the six patients which refused a 12-lead ECG.

With regards to our finding of no statistically significant gender disparity in the regional locations and the patients attended by Ambulance Officer qualified staff, it is difficult to say with certainty that the absence of evidence was evidence of absence. Especially as these subgroups still had AORs that were well below the reference level (one) for women. The regional centres did not meet their target number of patients, which is likely to explain a large role in the insignificance of the results from those areas.

The still significant, but decreasing gender disparity with increasing EMS staff qualification level, may suggest a better understanding of how vital the 12-lead ECG is for these acute time dependant patients. In addition, the more experienced officers may feel less uncomfortable with exposing women's chests. With regards to patients attended with an all-female crew, it is more likely that this subgroup really was not associated with lower rates of 12-lead ECG acquisition for women as the AOR was very close to the reference level. We did not find any other studies that evaluated gender disparity in the assessment of patients with ACS based on practitioner gender. This is an interesting finding that could provide some insight into an explanation for the gender disparity if explored further in future research.

Some of our findings were surprising, such as the increased propensity to acquire a 12-lead ECG with an increased number of treatments. This may suggest that among EMS staff some individuals have higher procedural compliance than others and would be another interesting topic for future research. The very low overall 12-lead ECG acquisition rate for Urban B region is concerning. It may be that this represents the true practice of the EMS staff in that region or that those staff are less likely to record when they have acquired a 12-lead ECG as a regional culture. Either way, both show poor procedural compliance and improvement could only be to the benefit of their patients.

5.4 - Generalisability

This study provides a clearer picture of gender disparity in the prehospital assessment of patients with ACS and unfortunately agrees with other studies in finding that women are disadvantaged. As a 12-lead ECG is a necessity for diagnosis of a STEMI, the ramifications of missing this could lead to increased mortality and morbidity for women. Further study into explanations for this gender disparity could focus on EMS staff gender and education. As well as a review of the logistics surrounding privacy barriers in the back of ambulances. EMS regional culture may lead to clinical practices that differ greatly from that prescribed by clinical management and may be a good focus for future review and further education. With improved procedural compliance, may come improved data acquisition, for example, completing / recording the ethnicity box on the PRF. This could provide great data for future research, especially in the context of higher rates of cardiac disease in Maori and Pacific populations in NZ.

This study reviewed both urban and regional areas throughout NZ and included a relatively large number of patients. This increases the likelihood that the study will be generalisable to the NZ population as a whole. Many of the other studies in ACS gender disparity have been conducted in the hospital setting. This study was conducted in the prehospital setting and

although it helps to fill a gap in the research, it may not be as generalisable to the bulk of the hospital based research. For example, the decision to acquire a 12-lead ECG for women in the less private environment of the back of an ambulance may not apply to the hospital setting.

5.5 – Funding

The scientific advisory group of the National Heart Foundation of New Zealand provided a Small Project Grant to the research study for this thesis.

5.6 - Conclusion

For the first time, this study established that gender disparity in the assessment of patients with suspected ACS persists, even when the patient's presentation is controlled for in the study design. Women with cardiac-type chest pain were half as likely to have a 12-lead ECG acquired by EMS staff than men, even when the EMS staff member's working diagnosis was that of ACS. We refute previous study conclusions that gender disparity in ACS assessment can be accounted for by women's propensity for an atypical ACS presentation or with a false negative ACS diagnosis from the practitioner. We suggest that an acknowledgment of the practitioner's decision making process with regards to assessing women with ACS would be helpful in reducing the gender bias. Also, education programmes which acknowledge this gender disparity may help to reduce its prevalence.

This study further established that overall rates of 12-lead ECG acquisition for both male and female patients with suspected ACS was low, suggesting poor procedural compliance. Apart from patient gender, the other variables that were associated with a decreased rate of 12-lead ECG acquisition were increased patient age, located in Urban B, medical centre retrieval and a decreased contact time with EMS staff. These variables could help to guide future targeted training programmes to improve procedural compliance and hopefully improve patient outcomes.

References

1. von Elm, Erik; Egger, Matthias; Altman, Douglas G; Pocock, Stuart J; Gotzsche, Peter C; Vandembroucke, Jan P. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies, *British Medical Journal*, October 2007, **335**, pp.806-808.
2. Australian Institute of Health and Welfare. Cardiovascular disease: Australian facts 2011. *Cardiovascular disease series. Cat. no. CVD 53*. Canberra : AIHW, 2011c.
3. Garcia, Tomas B and Holtz, Meil E. *12-lead ECG, the art of interpretation*. Sudbury : Jones and Bartlett Publishers, 2001.
4. Kumar, Vinay, Abbas, Abul K and Fausto, Nelson. *Robbins and Cotran pathologic basis of disease*. 7th ed. Philadelphia : Elsevier Saunders, 2005.
5. Libby, P and Theroux, P. Pathophysiology of Coronary Artery Disease. *Circulation*, 2005, **111**, pp. 3481-8.
6. Porth, Carol Mattson. *Essentials of pathophysiology, concepts of altered health states*. 2nd ed. Philadelphia : Lippincott Williams & Wilkins, 2007.
7. Tintinalli, Judith E, Kelen, Gabor D and Stapczynski, J Stephan. *Emergency medicine, a comprehensive study guide*. 6th ed. McGraw-Hill Professional, 2004.
8. Kumar, Parveen and Clark, Michael. *Kumar and Clark's clinical medicine*. 7th ed. Saunders Elsevier Limited, 2009.
9. World Health Organization, Department of Measurement and Health Information. Mortality and burden of disease estimates for WHO member states in 2008. *Global Health Observatory Data Repository* [online] April 2011. [Accessed 10 April 2012] Available from : <http://apps.who.int/ghodata/?vid=10011>
10. Ministry of Health. *Mortality and Demographic Data 2009*. Wellington : Ministry of Health, 2012.
11. Keeley, Ellen C and Hillis, L David. Primary PCI for Myocardial Infarction with ST-Segment Elevation. *New England Journal of Medicine*, 2007. **356**, pp. 47-54.
12. National Heart Foundation of Australia. *Heart Attack Facts* [online] n.d. [Accessed 15 October 2012] Available from: <http://www.heartattackfacts.org.au/heart-attack-facts/>
13. Boden, William E., Eagle, Kim and Granger, Christopher B. Reperfusion Strategies in Acute ST-Segment Elevation Myocardial Infarction. *Journal of the American College of Cardiology*, October 2007, **50**, pp. 917-929.
14. O'Gara, Patrick T; Kushner, Frederick G; Ascheim, Deborah D; Casey, Donald E; Chung, Mina K; de Lemos, James A; Ettinger, Steven M; Fang, James C; Fesmire, Francis M; Franklin, Barry A; Granger, Christopher B; Krumholz, Harlan M; Linderbaum, Jane A; Morrow, David A;

Newby, Kristin; Ornato, Joseph P; Ou, Narith; Radford, Martha J; Tamis-Holland, Jacqueline E; Tommaso, Carl L; Tracy, Cynthia M; Woo, Joseph; Zhao, David X. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. A report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. *Journal of the American College of Cardiology*, January 2013, **61**, pp. e78-140.

15. Australian Institute of Health and Welfare. *Monitoring acute coronary syndrome using national hospital data: an information paper on trends and issues. Cat. no. CVD 57.* Canberra : AIHW, 2011.

16. Ministry of Health. *A portrait of health. Key results of the 2006/2007 New Zealand Health Survey.* Wellington : s.n., 2008.

17. Chew, Derek P; Aroney, Constantine` N; Aylward, Philip E; Kelly, Anne-Maree; White, Harvey D; Tideman, Philip A; Wadell, Jill; Azadi, Leva; Wilson, Alison j; Ruta, Leah-anne M. 2011 Addendum to the National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand Guidelines for the management of Acute Coronary Syndromes (ACS) 2006, *Heart, Lung and Circulation* February 2011, **20**, pp. 487-502.

18. Davis, Daniel P; Graydon, Cheryl; Stein, Robert; Wilson, Siobhan; Buesch, Barbara; Berthiaume, Shelley; Lee, David M; Rivas, Jaime; Vilke, Gary M; Leahy, Dennis R. The Positive Predictive Value of Paramedic Versus Emergency Physician Interpretation of the Prehospital 12-Lead Electrocardiogram. *Prehospital Emergency Care*, 2007, **11**, pp. 399-402.

19. Canto, John G; Goldberg, Robert J; Hand, Mary H; Bonow, Robert O; Sopko, George; Pepine, Carl J; Long, Terry. Symptom presentation of women with Acute Coronary Syndromes: Myth vs Reality, *Archives of Internal Medicine*, December 2007, **167**, pp. 2405-2413.

20. Berne, Robert M and Levy, Matthew N. *Physiology.* 4th ed. St. Louis: Mosby, Inc, 1998.

21. ST-elevation myocardial infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand. ST-elevation myocardial infarction: New Zealand management guidelines, *The New Zealand Medical Journal*, 2005, **118**, pp. 1-21.

22. Stone, G W; Brodie, Bruce R; Griffin, John J; Morice, Marie Claude; Costantini, Costantino; Goar, Frederick G; Overlie, Paul A; Popma, Jeffrey J; McDonnell, Joann; Jones, Denise; O'Neill, William W; Grines, Cindy L. Prospective, multicenter study of the safety and feasibility of primary stenting in acute myocardial infarction: in-hospital and 30-day results of the PAMI stent pilot trial, *Journal of the American College of Cardiology*, January 1998, **31**, pp. 23-30.

23. Kleinschmidt, K and Brady, W J. Acute coronary syndromes: An evidence-based review and outcome optimizing guidelines for patients with and without procedural coronary intervention (PCI), *American Health Consultant*, 2000, **25**, pp. 286-295.

24. Persse, David E; McCarthy, James J; Vooletich, Mary; Richter, Bonnie K; Anderson, H Vernon; Denktas, Ali E; Sdringola, Stefano M; Smalling, Richard W. Prehospital fibrinolysis in

concert with rapid PCI: Clinical trial shows promising results for use of clot-dissolving agents in the field, *JEMS* March 2008, pp. 74-88.

25. Schofield, Peter M. Acute myocardial infarction: the case for pre-hospital thrombolysis with or without percutaneous coronary intervention, *Heart*, 2005, **91**, Suppl III, pp. iii7-iii11.

26. Sayah, A J and Roe, M T. The role of fibrinolytics in the prehospital treatment of ST-elevation myocardial infarction (STEMI), *Journal of Emergency Medicine*, December 2007

27. Thiele, H, Engelmann, L and Elsner, K. Comparison of pre-hospital combination-fibrinolysis plus conventional care with pre-hospital combination-fibrinolysis plus facilitated percutaneous coronary intervention in acute myocardial infarction, *European Heart Journal*, 2005, **19**, pp. 1956-1963.

28. Denktas, Ali E; Athar, Haris; Henry, Timothy D; Larson, David M; Simons, Michael; Chan, Roger S; Niles, Nathaniel W; Thiele, Holger; Schuler, Gerhard; Ahn, Chul; Sdringola, Stefano; Anderson, Vernon; McKay, Raymond G; Smalling, Richard W. Reduced-dose fibrinolytic acceleration of ST-segment elevation myocardial infarction treatment coupled with urgent percutaneous coronary intervention compared to primary percutaneous coronary intervention alone. Results of the AMICO Registry, *Journal of the American College of Cardiology: Cardiovascular Interventions*, October 2008, **5**, pp. 504-510.

29. White, Harvey D and Chew, Derek P. Acute myocardial infarction, *Lancet*, August 2008, **372**, pp. 570-584.

30. Gibson, C Michael; Pride, Yuri B; Frederick, Paul D; Pollack, Charles V; Canto, John G; Tiefenbrunn, Alan J; Weaver, W Douglas; Lambrew, Costas T; French, William J; Peterson, Eric D; Rogers, William J. Trends in reperfusion strategies, door-to-needle and door-to-balloon times, and in-hospital mortality among patients with ST-segment elevation myocardial infarction enrolled in the National Registry of Myocardial Infarction from 1990 to 2006, *American Heart Journal*, December 2008, **156**, pp. 1035-1044.

31. Ryan, Catherine J, DeVon, Holli A and Johnson Zerwic, Julie. Typical and atypical symptoms: Diagnosing acute coronary syndromes accurately, *The American Journal of Nursing*, February 2005, **105**, pp. 34-36.

32. Brieger, David; Eagle, Kim A; Goodman, Shaun G; Steg, P Gabriel; Budaj, Andrzej; White, Kami; Montalescot, Gilles. Acute coronary syndromes without chest pain, an underdiagnosed and undertreated high-risk group: Insights from the Global Registry of Acute Coronary Events, *Chest*, August 2004, **126**(2), pp. 461-469.

33. Nguyen, John T; Berger, Alan K; Duval, Sue; Luepker, Russell V. Gender disparity in cardiac procedures and medication use for acute myocardial infarction, *American Heart Journal*, May 2008, **155**, pp. 862-868.

34. National Heart Foundation of Australia. *Women and heart disease forum report*. 2011.

35. Garofalo, Danniell; Grey, Corina; Lee, Mildred; Exeter, Daniel; Kerr, Andrew J. Pre-hospital delay in acute coronary syndromes: PREDICT CVD-18, *Journal of the New Zealand Medical Association*, 2012, **125**, pp. 12-22.
36. Gross, Brian W; Dauterman, Kent W; Moran, Mark G; Kotler, Todd S; Schnugg, Stephen J; Rostykus, Paul S; Ross, Amy M; Weaver, W Douglas. An approach to shorten time to infarct artery patency in patients with ST-segment elevation myocardial infarction, *American Journal of Cardiology*, 2007, **99**, pp. 1360-1363.
37. Le May, Michel R; Dionne, Richard; Maloney, Justin; Poirier, Pierre. The role of paramedics in primary PCI program for ST-elevation myocardial infarction, *Progress in Cardiovascular Diseases* 2010, **53**, pp. 183-187.
38. Bradley, Elizabeth H; Roumanis, Sarah A; Radford, Martha J; Webster, Tashonna R; McNamara, Robert L; Mattera, Jennifer A; Barton, Barbara A; Holmboe, Eric S; Blaney, Martha; Krumholz, Harlan M. Achieving door-to-balloon times that meet quality guidelines, *Journal of the American College of Cardiology*, 2005, **46**, pp. 1236-1241.
39. Fischer, Matthias; Kamp, Johannes; Riesgo, Luis Garcia-Castrillo; Robertson-Steel, Iain; Overton, Jerry; Ziemann, Alexandra; Krafft, Thomas. Comparing emergency medical service systems - A project of the European Emergency Data (EED) Project, *Resuscitation*, 2010, **82**, pp. 285-293.
40. Daudelin, Denise H; Sayah, Assaad J; Kwong, Manlik; Restuccia, Marc C; Porcaro, William A; Ruthazer, Robin; Goetz, Jessica D; Lane, William M; Beshansky, Joni R; Selker, Harry P. Improving use of prehospital 12-lead ECG for early identification and treatment of acute coronary syndrome and ST-elevation myocardial infarction, *Circulation: Cardiovascular Quality and Outcomes, Journal of the American Heart Association*, 2010, **3**, pp. 316-323.
41. Le May, Michel R; Davies, Richard F; Dionne, Richard; Maloney, Justin; Trickett, John; So, Derek; Ha, Andrew; Sherrard, Heather; Glover, Chris; Marquis, Jean-Francois; O'Brien, Edward R; Stiell, Ian G; Poirier, Pierre; Labinaz, Marino. Comparison of early mortality of paramedic-diagnosed ST-segment elevation myocardial infarction with immediate transport to a designated primary percutaneous coronary intervention center to that of similar patients transported to the nearest hospital, *American Journal of Cardiology*, 2006, **98**, pp. 1329-1333.
42. Greenberg, Marna Rayl; Miller, Andrew C; MacKenzie, Richard S; Richardson, David M; Ahnert, Amy M; Sclafani, Mia J; Jozefick, Jennifer L; Goyke, Terrence E; Rupp, Valerie A; Burmeister, David B. Analysis of sex differences in preadmission management of ST-Segment Elevation (STEMI) Myocardial Infarction, *Gender Medicine*, 2012, **9**, pp. 329-334.
43. Chang, Anna Marie; Mumma, Bryn; Lease, Keara L; Robey, Jennifer L. Gender bias in cardiovascular testing persists after adjustment for presenting characteristics and cardiac risk. *Academic Emergency Medicine*, July 2007, **14**(7), p. 599.

44. Pezzin, Liliana E, Keyl, Penelope M and Green, Gary B. Disparities in the Emergency Department evaluation of chest pain patients, *Academic Emergency Medicine*, 2007, **14**, pp. 149-156.
45. Heer, Tobias; Hochadel, Matthias; Schmidt, Karin; Mehilli, Julinda; Zahn, Ralf; Kuck, Karl-Heinz; Hamm, Christian; Bohm, Michael; Ertl, Georg; Andresen, Dietrich; Massberg, Steffen; Senges, Jochen; Pilz, Gunter; Gitt, Anselm K; Zeymer, Uwe. Gender differences in therapeutic recommendation after diagnostic coronary angiography: insights from the Coronary Angiography and PCI Registry of the German Society of Cardiology, *Clinical Research in Cardiology*, 2015, **104**, pp. 507-517.
46. Hvelplund, Anders; Glatius, Soren; Madsen, Mette; Rasmussen, Jeppe N; Rasmussen, Soren; Madsen, Jan Kyst; Sand, Niels P.R; Tilsted, Hans-Henrik; Thayssen, Per; Sindby, Eske; Hojbjerg, Soren; Abildstrom, Steen Z. Women with Acute Coronary Syndrome are less invasively examined and subsequently less treated than men, *European Heart Journal*, 2010, **31**, pp. 684-690.
47. Anand, Sonia S; Xie, Chang Chun; Mehta, Shamir; Franzosi, Maria Grazia; Joyner, Campbell; Chrolavicius, Susan; Fox, Keith A.A; Yusuf, Salim. Differences in the management and prognosis of women and men who suffer from acute coronary syndromes, *Journal of the American College of Cardiology*, November 2005, **46**, pp. 1845-51.
48. Assiri, Abdullah S. Gender differences in clinical presentation and management of patients with acute coronary syndrome in Southwest of Saudi Arabia, *Journal of the Saudi Heart Association*, January 2011, **23**, pp. 135-141.
49. Fang, Jing and Alderman, Michael H. Gender differences in revascularization in patients with Acute Myocardial Infarction, *American Journal of Cardiology*, 2006, **97**, pp. 1722-1726.
50. Huang, Nicole; Chou, Yinng-Jenq; Hu, Hsiao-Yun; Lee, Chang-Hua. Gender disparities in AMI management and outcomes among health professionals, their relatives, and non-health professionals in Taiwan from 1997-2007, *Social Science & Medicine*, 2013, **77**, pp. 70-74.
51. Pilote, Louise; Dasgupta, Kaberi; Guru, Veena; Humphries, Karin H; McGrath, Jennifer; Norris, Colleen; Rabi, Doreen; Tremblay, Johanne; Alamian, Arsham; Barnett, Tracie; Cox, Jafna; Ghali, William Amin; Grace, Sherry; Hamet, Pavel; Ho, TeresA; Kirkland, Susan; Lambert, Marie; Libersan, Danielle; O'Loughlin, Jennifer; Paradis, Gilles; Petrovich, Milan; Tagalakis, Vicky. A comprehensive view of sex-specific issues related to cardiovascular disease, *Canadian Medical Association Journal* March 2007, **176**, pp. S1-44.
52. Ouhoumane, N; Abdous, B; Emond, V; Poiriert, P. Impact of diabetes and gender on survival after acute myocardial infarction in the Province of Quebec, Canada - a population-based study, *Diabetic Medicine*, 2009, **26**, pp. 609-616.
53. Merz, C Noel Bairey; Shaw, Leslee J; Reis, Steven E; Bittner, Vera; Kelsey, Sheryl F; Olson, Marian; Johnson, Delia; Pepine, Carl J; Mankad, Sunil; Sharaf, Barry L; Rogers, William J;

Pohost, Gerald M; Lerman, Amir; Quyyumi, Arshed A; Sopko, George. Insights from the NHLBI-sponsored Women's Ischemia Syndrome Evaluation (WISE) study. Part II: Gender differences in presentation, diagnosis, and outcome with regard to gender-based pathophysiology of atherosclerosis and macrovascular and microvascular cor., *Journal of the American College of Cardiology*, February 2006, **47**(3 Supplement S), pp. 21S-29S.

54. Roncalli, Jerome; Elbaz, Meyer; Dumonteil, Nicolas; Boudou, Nicolas; Lairez, Olivier; Lhermusier, Thibault; Chilon, Talia; Baixas, Cecile; Galinier, Michel; Puel, Jacques; Fauvel, Jean-Marie; Carrie, Didier; Ruidavets, Jean-Bernard. Gender disparity in 48-hour mortality is limited to emergency percutaneous coronary intervention for ST-elevation myocardial infarction, *Archives of Cardiovascular Disease*, 2010, **103**, pp. 293-301.

55. Zhang, Bo; Zhang, Wei; Huang, Rong-chong; Zhang, Yan; Liu, Jun; Zheng, Zheng-guo; Jiang, Da-ming; Sun, Yu-jiao; Ren, Li-na; Zhou, Xu-chen; Qi, Guo-xian. Gender disparity in early death after ST-elevation myocardial infarction, *Chinese Medical Journal*, 2013, **126**, pp. 3481-3485.

56. Iyanoye, Adeyemi; Moreyra, Abel E; Swerdel, Joel N; Gandhi, Sampada K; Cabrera, Javier; Cosgrove, Nora M; Kostis, John B. Gender disparity in the use of Drug-Eluting Stents during Percutaneous Coronary Intervention for Acute Myocardial Infarction, *Catheterization and Cardiovascular Interventions*, 2015, **86**, pp. 221-228.

57. National Heart Foundation New Zealand. *Know the Facts: Statistics: General heart statistics for New Zealand: Women's Heart Disease* [online] 2012 [Accessed: 18 November 2012] Available from: <http://www.heartfoundation.co.nz/>

58. Dreyer, Rachel P; Beltrame, John F; Tavella, Rosanna; Air, Tracy; Hoffmann, Bernadette; Pati, Purendra K; Di Fiore, David; Arstall, Margaret; Zeitz, Christopher. Evaluation of gender differences in Door-To-Balloon time and ST-Elevation Myocardial Infarction, *Heart, Lung and Circulation*, April 2013, **22**, pp. 861-869.

59. Madrid Willingham, S A and Kilpatrick, E S. Evidence of gender bias when applying the new diagnostic criteria for myocardial infarction, *Heart*, 2005, **91**, pp. 237-238.

60. U.S. National Library of Medicine. *Fact Sheet, MEDLINE. National Institutes of Health U.S. National Library of Medicine* [online] 11th May 2015 [Accessed: 3rd September 2015] Available from: <http://www.nlm.nih.gov/pubs/factsheets/medline.html>

61. EBSCO Industries Inc. CINAHL Plus with Full Text. *EBSCO Nursing Resources* [online] 2015 [Accessed: 3rd September 2015] Available from: <https://www.ebscohost.com/nursing/products/cinahl-plus-with-full-text>

62. Zhang, Qi; Qiu, Jian-ping; Zhang, Rui-yan; Li, Yi-gang; He, Ben; Jin, Hui-gen; Zhang, Jun-feng; Wang, Xiao-long; Jiang, Li; Liao, Min-lei; Hu, Jian; Shen, Wei-feng. Absence of gender disparity in short-term clinical outcomes in patients with acute ST-segment elevation myocardial infarction undergoing sirolimus-eluting stent based primary coronary intervention: a report from

Shanghai Acute Coronary Event (SACE) Regist, *Chinese Medical Journal*, 2010, **123**, pp. 782-788.

63. Fransoo, Randall R; Martens, Patricia J; Prior, Heather J; Burland, Elaine; Chateau, Dan; Katz, Alan. Age difference explains gender difference in cardiac intervention rates after Acute Myocardial Infarction, *Healthcare policy*, January 2010, **6**, pp. 88-103.

64. Griffith, D; Hamilton, K; Norrie, J; Isles, C. Early and late mortality after myocardial infarction in men and women: prospective observational study, *Heart Journal*, 2005, **91**, pp. 305-307.

65. Aguilar, Steve A; Patel, Mitul; Castillo, Edward; Patel, Ekta; Fisher, Roger; Ochs, Ginger; Pringle, John; Mahmud, Ehtisham; Dunford, James V. Gender differences in scene time, transport time, and total scene to hospital arrival time determined by the use of prehospital electrocardiogram in patients with complaint of chest pain, *The Journal of Emergency Medicine*, 2012, **43**, pp. 291-297.

66. Greenberg, Marna Rayl; Bond, William F; MacKenzie, Richard S; Lloyd, Rezarta; Bindra, Monisha; Rupp, Valerie A; Crown, Anne-Marie; Reed, James F. Gender disparity in emergency department Non-ST Elevation Myocardial Infarction management, *The Journal of Emergency Medicine*, 2012, **42**, pp. 588-597.

67. Jibrán, Rushd, Khan, Junaid Alam and Hoye, Angela. Gender disparity in patients undergoing Percutaneous Coronary Intervention for Acute Coronary Syndromes - Does it still exist in contemporary practice, *Annals Academy of Medicine Singapore*, March 2010, **39**, pp. 173-178.

68. Ben-Ami, Tal; Gilutz, Harel; Porath, Avi; Sosna, Gilat; Liel-Cohen, Noah. No gender difference in the clinical management and outcome of unstable angina, *The Israel Medical Association Journal* April 2005, **7**, pp. 228-232.

69. United Nations. *Statistical annex; World Economic Situation and Prospects 2012* [online] 2012 [Accessed: 16th September 2015] Available from: http://www.un.org/en/development/desa/policy/wesp/wesp_current/2012country_class.pdf

70. Pampalon, Robert; Hamel, D; Gamache, P; Philibert, M D. Validation of the deprivation index for public health: a complex exercise illustrated by the Quebec index, *Chronic Diseases and Injuries in Canada*, February 2014, **34**, pp. 12-22.

71. Shavers, Vickie L. Measurement of Socioeconomic Status in health disparities research, *Journal of the National Medical Association*, September 2007, **99**, pp. 1013-1020.

72. McLoone, Philip. *Carstairs scores for Scottish postcode sectors from the 2001 Census*. *Social and Public Health Sciences Unit* [online] March 2004 [Accessed: 25th September 2015] Available from: <http://www.sphsu.mrc.ac.uk/publications/carstairs-scores.html>

73. Metcalf, Patricia, Scragg, Robert and Davis, Peter. Relationship of different measures of socioeconomic status and cardiovascular disease risk factors and lifestyle in a New Zealand workforce survey, *The New Zealand Medical Journal*, January 2007, **120**, pp. 1-10.
74. De Leon, Antonio Ponce; Abbasi, Seyed Hesameddin; Kassaian, Sayed Ebrahim; Karimi, Abbasali; Sundin, Orjan; Jalali, Arash; Soares, Joaquim; Macassa, Gloria. Socioeconomic status and in-hospital mortality of Acute Coronary Syndrome: Can education and occupation serve as preventive measures?, *International Journal of Preventive Medicine*, May 2015, **6**, p. PMC4427988.
75. Koren, Avshalom; Steinberg, David M; Drory, Yaacov; Gerber, Yariv. Socioeconomic environment and recurrent coronary events after initial myocardial infarction, *Annals of Epidemiology*, 2012, **22**, pp. 541-546.
76. Yong, Celina M; Abnoui, Freddy; Asch, Steven M; Heidenreich, Paul A. Socioeconomic inequalities in quality of care and outcomes among patients with Acute Coronary Syndrome in the modern era of Drug Eluting Stents, *Journal of the American Heart Association*, 2014, **3**, p. e001029.
77. Fabreau, Gabriel E; Leung, Alexander A; Southern, Danielle A; Knudtson, Merrill L; McWilliams, Michael; Ayanian, John Z; Ghali, William A. Sex, socioeconomic status, access to cardiac catheterization and outcomes for Acute Coronary Syndromes in the context of universal healthcare coverage, *Circulation: Cardiovascular Quality and Outcomes*, July 2014, **7**, pp. 540-549.
78. National Heart Foundation of Australia. *Policy paper Tobacco and cardiovascular disease*, 2007.
79. McCarney, Rob; Warner, James; Iliffe, Steve; van Haselen, Robbert; Griffin, Mark; Fisher, Peter. The Hawthorne Effect: an randomised, controlled trial, *Biomed Central Medical Research Methodology*, July 2007, **7**.
80. Levin, Kate Ann. Study design III: Cross-sectional studies, *Evidence-Based Dentistry*, 2006, **7**, pp. 24-25.
81. Statistics New Zealand Tauranga Aotearoa. New Zealand in Profile: 2010 *Statistics New Zealand* [online] 30 June 2010 [Accessed: 12 December 2013] Available from: http://www.stats.govt.nz/browse_for_stats/snapshots-of-nz/nz-in-profile-2010/population.aspx
82. Bascand, Geoff. National Population Estimates: March 2012 quarter. *Statistics New Zealand Tauranga Aotearoa* [online] 14 May 2012 [Accessed: 12 December 2013] Available from: http://www.stats.govt.nz/browse_for_stats/population/estimates_and_projections/NationalPopulationEstimates_HOTPMar12qtr/Commentary.aspx
83. Day, Simon, Fayers, Peter and Harvey, Derek. Double data entry: What value, what price?, *Controlled Clinical Trials*, 1998, **19**, pp. 15-24.

84. Mullooly, John P. The Effects of Data Entry Error: An Analysis of Partial Verification, *Computers and Biomedical Research*, 1990, **23**, pp. 259-267.
85. To, Teresa; Estrabillo, Eileen; Wang, Chengning; Cicutto, Lisa. Examining intra-rater and inter-rater response agreement: A medical chart abstraction study of community-based asthma care program, *BMC Medical Research Methodology*, May 2008, **8**.
86. St John Clinical Management Group. *Clinical Procedures 2009-2011*, 2009.
87. Ministry of Health, New Zealand Government. The Health of Maori Adults and Children. *Ministry of Health* [online] 2013 [Accessed: 13th January 2014] Available from: <http://www.health.govt.nz/system/files/documents/publications/health-maori-adults-children-summary.pdf>
88. Meteorological Service of New Zealand Ltd. Rural Christchurch Past weather Historical Data. *MetService* [online] n.d. [Accessed: 2 July 2015] Available from: <http://www.metservice.com/rural/christchurch>
89. Meteorological Service of New Zealand Ltd. Towns and Cities Auckland Past weather Historical data. *MetService* [online] n.d. [Accessed: 2 July 2015] Available from: <http://www.metservice.com/towns-cities/auckland/auckland-central>
90. Donath, Susan, Davidson, Andrew and Babl, Franz E. A primer for clinical researchers in the emergency department: Part V: How to describe data and basic medical statistics, *Emergency Medicine Australasia*, February 2013, Vol. 25, pp. 13-21.
91. Alexopoulos, Evangelos C. Introduction to Multivariate Regression Analysis, *Hippokratia*, 2010, **14** (Suppl 1), pp. 23-28.
92. R Development Core Team. *R: A language and environment for statistical computing*. R Foundation ofr Statistical Computing. 2012.

Appendix D

Urban B, Rural A, Rural B

December	20-27
January	9-16
February	4-11
March	18-25
April	21-28
May	1-8
June	12-19
July	24-31
August	3-10
September	6-13
October	10-17
November	21-28

Urban A

December	20-21
January	9-10
February	4-5
March	18-19
April	21-22
May	1-2
June	12-13
July	24-25
August	3-4
September	6-7
October	10-11
November	21-22



Multi-region Ethics Committee

Ministry of Health
133 Malesworth Street
PO Box 5013
Wellington 6145
Phone (04) 470 0655
(04) 470 0646
Fax (04) 496 2340
Email: multiregion_ethicscommittee@moh.govt.nz

19 July 2010

Bronwyn Henderson
7 Outlook Road
Greenhithe,
Auckland 0632

Dear Bronwyn

Study Title: Gender inequity in acquisition of 12-lead ECGs from ambulance patients with non-traumatic chest pain

Thank you for submitting an application for expedited review which was received by our office on 15 July 2010. Upon review of your application, I can confirm that ethical approval for your study is not required under section 11.9 of the Ethical guidelines for observation studies. Your proposed study meets the exception of this clause, where ethical approval is not required for secondary use of data for the purpose of outcome analysis when undertaken by those employed or contracted by the health service provider holding the information.

Please do not hesitate to contact me should you have any queries.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Annisha Vasutavan'.

Annisha Vasutavan
Administrator
Multi-region Ethics Committee



MEMORANDUM

Auckland University of Technology Ethics Committee (AUTEC)

To: Bronwyn Tunnage
From: **Madeline Banda** Executive Secretary, AUTEC
Date: 3 November 2010
Subject: Ethics Application Number 10/223 **Gender inequity in acquisition of 12-lead ECG from ambulance patients with non-traumatic chest pain.**

Dear Bronwyn

Thank you for providing written evidence as requested. I am pleased to advise that it satisfies the point raised by the Auckland University of Technology Ethics Committee (AUTEC) at their meeting on 11 October 2010 and that I have approved your ethics application. This delegated approval is made in accordance with section 5.3.2.3 of AUTEC's *Applying for Ethics Approval: Guidelines and Procedures* and is subject to endorsement at AUTEC's meeting on 13 December 2010.

Your ethics application is approved for a period of three years until 3 November 2013.

Note: The Multi-Region Ethics Committee has stated that this application does not require ethics approval. While ethics approval has been waived by a Health and Disability Ethics Committee, AUTEC is responsible for ensuring that research undertaken by AUT staff or students meets its institutional standards. We are not seeking to undertake a further full review of the application.

Acting under delegated authority and subject to endorsement by AUTEC at its meeting on 13 December 2010, the Executive Secretary approved the satisfactory resolution of AUTEC's conditions.

I advise that as part of the ethics approval process, you are required to submit the following to AUTEC:

- A brief annual progress report using form EA2, which is available online through <http://www.aut.ac.nz/research/research-ethics/ethics>. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 3 November 2013;
- A brief report on the status of the project using form EA3, which is available online through <http://www.aut.ac.nz/research/research-ethics/ethics>. This report is to be submitted either when the approval expires on 3 November 2013 or on completion of the project, whichever comes sooner;

It is a condition of approval that AUTEC is notified of any adverse events or if the research does not commence. AUTEC approval needs to be sought for any alteration to the research, including any alteration of or addition to any documents that are provided to patients. You are reminded that, as applicant, you are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

Please note that AUTEK grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to make the arrangements necessary to obtain this.

When communicating with us about this application, we ask that you use the application number and study title to enable us to provide you with prompt service. Should you have any further enquiries regarding this matter, you are welcome to contact Charles Grinter, Ethics Coordinator, by email at ethics@aut.ac.nz or by telephone on 921 9999 at extension 8860.

On behalf of the AUTEK and myself, I wish you success with your research and look forward to reading about it in your reports.

Yours sincerely



Madeline Banda
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Bronwyn Henderson bronhendy@gmail.com, Steve Taylor

Patient report form



PART A DATA

DAY 10/11/10	MONTH 10/11	YEAR 10	JOB No. 732	CASE CODE 25	PATIENT STATUS 0 1 2 3 4 2
DEPARTCH 17.59	LOCATED 16.05	DEPART STATION 1610	DESTINATION 1627	NIH No. (IF KNOWN)	0 1 2 3 4 2

Is injury > 24 hours old? YES / NO

St. John Supporters Scheme? YES / NO

PART B PERSONAL DETAILS

Mr Mrs Ms Miss Child Mr Shudna F 2,2,60 50
 Family Name First Names M/F DOB Age

Address 209 conclusion Way Heperinthill Coronary Beach SuperSmooth Whitecross
 Phone No. (028) 7596211 Pts GP pt

Incident location SuperSmooth Whitecross
 Destination CHCH hospital Ethnicity Māori Pacific Island Other Not Stated

PART C PATIENT INFORMATION

Chief Complaint Chest Pain Date and time of onset 1750, 10/11/10

History pt driving home from work when felt sudden onset of crushing chest pain radiating down L arm & hand tingling, SOB, nil nausea, nil dizziness drove into A&E, GP gave 300mg aspirin, IV hand 29 TN (3x0.8mg), morphine 5mg IV, O₂ 6l/min acute mask, 12-lead ECG, showing inverted T waves in II, III & aVF, ambulance called for arranged admission to CHCH hospital. O/A - at supine on bed, O/E - cons & alert, @ patient/c tear, B) reg/clear/- bilat resp feels SOB nil obvious ↑ in WOB, speaking full sentences, C) reg/weak brady rad/pulses*

MEDICATIONS Enalapril, lipex, losac ALLERGIES Sulphur drugs → hives

PART D TREATMENT AND OBSERVATION DETAILS

Time	Drugs/Interventions	Dose	Route	Resp	Pulse	BP	GC5 (E V M)	O ₂ Sat	Old Gluc	Pain
1610	Ondansetron	8mg	PO	22	50	80/50	15		90% O/A	3/10
1615	pt vomiting			28	42	N/T	15		95% on O ₂	
E/R	0.9% NaCl	500ml	IV							
1620				22	48	90/60	15		95% on O ₂	
1627				22	50	110/90	15		96% on O ₂ 6l/10	

* skin warm cool/diaphoresis dripping from chin/pate, pt C/O dizziness & severe nausea, mild chest heaviness above L breast, nil arm pain now, pt look mask off at GPs as said the smell was making her sick, put nasa' prongs on at 4l/min after vomiting stopped.

E/R ↑ nausea, ↓ SOB, heaviness in chest ↑ at 1625

R40 to resus

Signature of main treating Officer(s) [Signature]

S. peedy 11004 DOVF O. verthehill 700662AP

HOSPITAL / PATIENT COPY

DATA COPY

ST JOHN PATIENT REPORT FORM (PRF) INSTRUCTIONS

- A full **PRF** (including the back of the hospital/patient copy) must be completed for each patient whenever:
 - The job involves assessing a single patient only or
 - The patient has a set of vital signs taken or
 - Treatment is provided to the patient or
 - The patient is transported or
 - The patient is dead
 Note, a PRF is **NOT** required for each patient if:
 - The patient is being transported between DHB hospitals or departments and **NO** treatment is provided enroute by St John members or
 - The scene involves more than one uninjured patient. Here however, a full PRF is required for any patient that has a set of vital signs taken
- Ambulance Trip Log (ATL)** – record **ALL** details including mileage for all vehicle responses
- Rhythm Strips – Attach to Hospital/Patient & Audit copies

NON TRANSPORT CODES

1	Deceased	5	Patient not found
2	Patient gone by other transport	6	Minor illness / injury, non injury
3	Patient declines transport	7	Patient recovered
4	Patient to see GP	8	Patient treatment only

PATIENT DECLINES TRANSPORT

If a patient/caregiver/guardian declines transport the following statement must be read and their signature obtained on the patient report form.

STATEMENT:

You (the patient/caregiver/guardian) acknowledge that you have been offered transport to a medical facility but have declined the assistance offered.

By signing this patient report form you are releasing the St John members present and St John from any responsibility for your future wellbeing as a result of this incident.

PATIENT STATUS CODES / TRIAGE TAGS

0	DEAD	WHITE/BLACK
1	CRITICAL	RED
2	SERIOUS	YELLOW
3	MODERATE	GREEN
4	MINOR	GREEN

QUALIFICATION ABBREVIATIONS

AP	Advanced Paramedic
P	Paramedic
AO	Ambulance Officer
PC	Primary Care 1 & 2
FA	First Aid
D	Doctor
N	Nurse

ADULT/CHILD GLASGOW COMA SCORE

Best Eye (E) Opening	Best Verbal (V) Response	Best Motor (M) Response
4 Spontaneously	5 Orientated	6 Obeys commands
3 To voice	4 Mildly confused	5 Localises pain
2 To Pain	3 Very confused	4 Withdraws from pain
1 None	2 Moans or groans	3 Flexion
	1 None	2 Extension
		1 None

INFANT GLASGOW COMA SCORE

Best Eye (E) Opening	Best Verbal (V) Response	Best Motor (M) Response
4 Spontaneously	5 Appropriate words	6 Spontaneous intentional movement
3 To voice	4 Cries but consolable	5 Localises pain
2 To Pain	3 Irritable, cries to pain	4 Withdraws from pain
1 None	2 Moans groans or grunts	3 Flexion
	1 None	2 Extension
		1 None

NATIONAL CASE CODES

CHARGE TO CUSTOMER

- 200 Attendances
- 210 Private Hire / Transfer / Discharge
- 270 Helipad to Hospital - ACC
- 275 Helipad to Hospital - Medical
- 290 Long Distance Private Hire

ROAD ACCIDENTS

- 400 Motor Car
- 410 Motor Bike
- 420 Truck
- 430 Bicycle
- 440 Bus
- 450 Pedestrian Vs Vehicle
- 460 Other Road Accident

NON-ROAD ACCIDENTS

- 500 Home
- 510 Workplace
- 520 School
- 530 Sports
- 540 Pedestrian / Walking
- 550 Drowning / Near Drowning
- 530 Intentional Injury by Another / Assault
- 565 Stings/Bites / Animal Attacks
- 570 Other Accident
- 580 Suicide Attempt / Overdose / Self Poisoning
- 590 ACC Secondary Transport

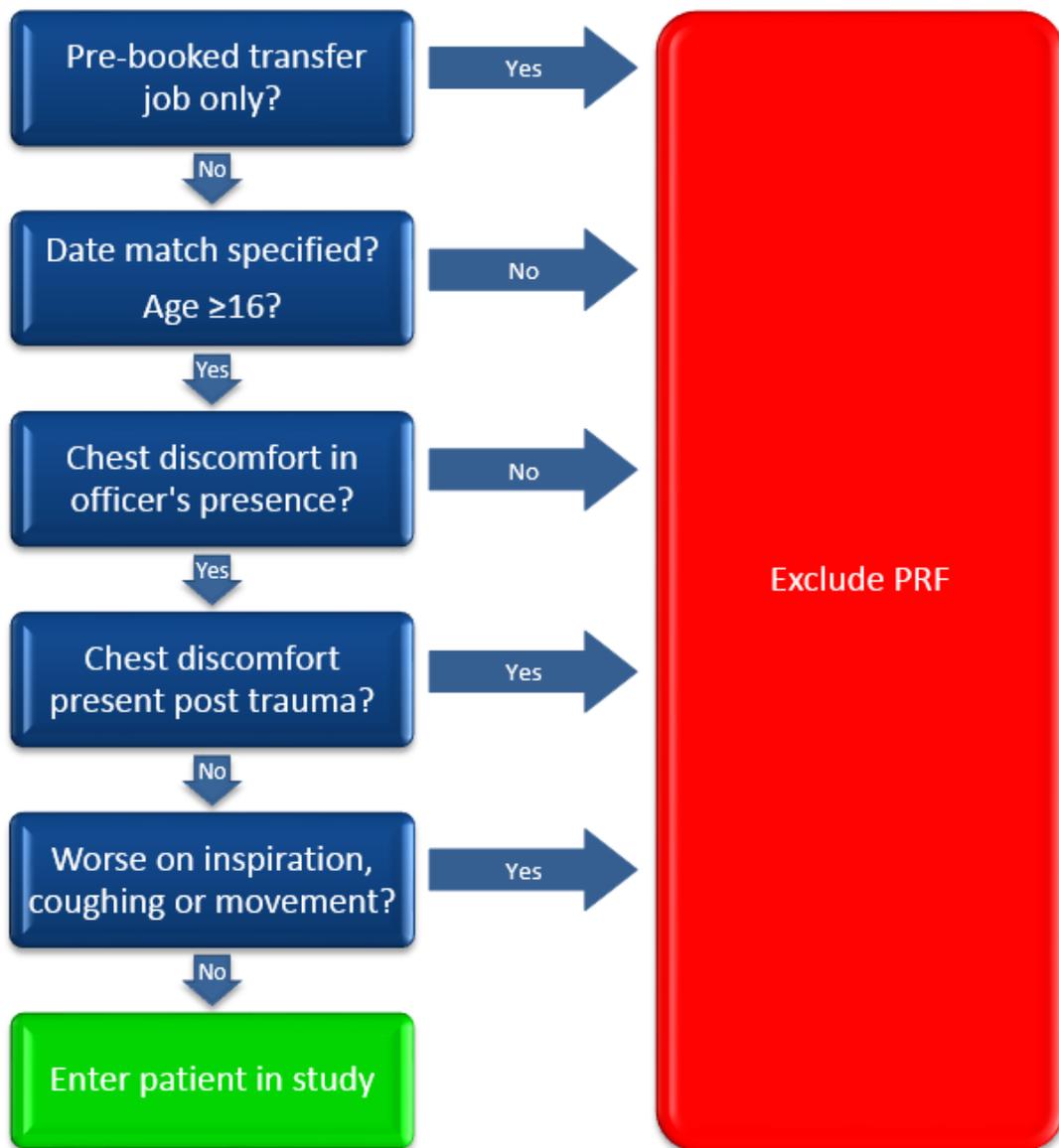
MEDICAL CASES

- 700 Asthma
- 701 COAD
- 702 Chest Infection / Pneumonia
- 703 Paediatric Croup / Bronchiolitis
- 704 Hyperventilation
- 705 Shortness of Breath (SOB)
- 706 SIDS / Near Miss
- 709 Other Respiratory
- 710 Fits / Convulsions
- 730 Cardiac Arrest
- 731 LVF / CHF
- 732 Cardiac Chest Pain
- 739 Other Cardiac
- 740 Hypoglycaemic Diabetic
- 741 Hyperglycaemic Diabetic
- 750 Anaphylaxis / Allergy
- 760 CVA / TIA / Hypertension
- 761 Possible Drug / Alcohol Impairment
- 762 Abdominal Pain
- 763 GI Bleed
- 764 Diarrhoea / Vomiting
- 765 Catheter / Colostomy
- 766 Oncological
- 767 Renal
- 770 Gynaecological / PV Bleed
- 771 Obstetric / Childbirth
- 780 Psychiatric
- 790 Syncope / Hypotension
- 792 Viruses & Infections
- 794 Medical Alarm - NOT Transported
- 795 Collapse Unknown
- 796 Pain - unknown cause
- 799 Other Medical

OTHER

- 800 Police / Fire Standby
- 810 Airport Standby
- 820 Standby at Home
- 830 Assist
- 840 Hoax
- 850 Area Standby
- 860 Other
- 870 Special Event Notification & Road Closure
- 900 Vehicle Transfer / Staff Transfer
- 901 Health Shuttle

REGIONAL CASE CODES & ACC READ CODES ISSUED SEPARATELY



<p>INTRODUCTION 5</p> <p>PRACTICE LEVELS AND DELEGATED SCOPES OF PRACTICE</p> <p>St John personnel do not legally have the independent ability to supply or administer prescription medicines to patients, or to use certain pieces of clinical equipment. This legal ability is individually granted to personnel by a St John Medical Advisor, by a process of granting authority to practice (ATP). Personnel must not provide clinical care (beyond first aid) to patients without using these procedures and must not use these procedures, or wear practice level patches, without individual ATP. Off duty personnel who come across an incident are, for the purposes of using these procedures, immediately deemed to be on duty.</p> <p>ATP is granted at a particular practice level (listed below as headings). Under each practice level is listed a delegated scope of practice. A delegated scope of practice is the medicines and interventions that personnel may administer or use when providing patient care. These procedures contain some new additions to scopes of practice; personnel must not use these new additions until they have received official training and sign off in writing. Ordinary interventions not formally described within any scope of practice (for example automated defibrillation) can be performed by all personnel.</p> <hr/> <p>Primary Care Entonox, methoxyflurane, aspirin, paracetamol.</p> <p>Ambulance Officer (BLS) All of the above plus nasopharyngeal airways, nebulised salbutamol, GTN spray, IM glucagon, laryngeal mask airway, oral ondansetron, PEEP valves, toumiquets.</p> <p>Paramedic (BLS) All of the above plus manual defibrillation, synchronised cardioversion, IV cannulation, IV fluid administration, IV glucose, SC lignocaine for IV cannulation, 12 lead ECG acquisition.</p> <p>Upskilled Paramedic (ILS) All of the above plus morphine, IV ondansetron, naloxone, nebulised adrenaline, IM adrenaline, IV adrenaline for cardiac arrest only.</p> <p>Advanced Paramedic (ALS) All of the above plus laryngoscopy, endotracheal intubation, capnography, cricothyroidotomy, chest decompression, intra-osseous needle access, adrenaline, atropine, frusemide, amiodarone, midazolam, ketamine, pacing, rapid sequence intubation* (*selected officers only).</p>	<p>RESPIRATORY AND CARDIAC 49</p> <p>2.8 CARDIAC CHEST PAIN</p> <p>This procedure is for adults, if you have a child consult with a medical specialist.</p> <ul style="list-style-type: none"> • Give oxygen via nasal prongs. • Determine and record cardiac rhythm. • Give 0.4-0.8 mg GTN provided systolic BP >100 mmHg. Use with caution and reduce dose if patient elderly, small or hypotensive. Use extreme caution if drug for erectile dysfunction taken within last 24 hrs. • Give 300 mg aspirin orally unless: <ol style="list-style-type: none"> 1. They have had 300 mg within the last hour or 2. They are known to be allergic to it or 3. They are an asthmatic with previous worsening of asthma after aspirin or non-steroidal anti-inflammatory drugs. • Gain IV access. • Acquire 12 lead ECG provided this does not significantly delay treatment or transport. Transmit if appropriate. • If taking part in a thrombolysis program, use separate thrombolysis procedure if appropriate. • If in a rural area where thrombolysis is provided by GPs, consult them early. • Repeat GTN every 2-5 minutes if it relieves pain, but do not continue to use it if not. Repeated GTN is usually inappropriate if the chest pain is secondary to a tachydysrhythmia. • If pain is significant, give morphine. Reduce dose if patient elderly, small or hypotensive. <hr/> <p>Commentary</p> <ul style="list-style-type: none"> • Some patients have atypical pain or discomfort, including face, jaw, neck or arm pain. Use this procedure if you strongly suspect such pain is due to myocardial ischemia. • Some patients have 'silent' myocardial ischemia without pain or discomfort - particularly diabetics and the elderly. They may present with any combination of - dysrhythmia, shortness of breath, fatigue, or light headedness. Use this procedure if you strongly suspect myocardial ischemia is the cause, provided there is objective evidence of myocardial ischemia on 12 lead ECG and there is no other obvious cause for their symptoms. In this circumstance only give repeated GTN if it is clearly associated with improvement. • GTN may interact with drugs used for erectile dysfunction. Prolonged hypotension may occur if GTN is used in patients who have taken these drugs in the previous 24 hours. If in doubt, seek medical advice.
<p>INTRODUCTION 6</p>	<p>RESPIRATORY AND CARDIAC 50</p>

Appendix K: Showing four pages from the Clinical Procedures for all St John EMS staff. Pages five and six describe the practice levels and clinical scope, showing that 12-Lead ECG acquisition is first listed in the Paramedic (BLS) scope of practice. Pages 49 and 50 describes the clinical procedure for assessment and management of patients with 'cardiac chest pain' or those where the EMS staff strongly suspects myocardial ischemia (86 pp. 5-6, 49-50).

EMan.



FORM PGR16 APPLICATION FOR RESTRICTED ACCESS TO A THESIS/DISSERTATION/EXEGESIS

- PLEASE NOTE**
- This form must be typed. Handwritten forms will not be accepted.
 - Double clicking on the check boxes enables you to change them from not-checked to checked.
 - The completed form, signed by the student and the primary supervisor, should be submitted to the appropriate Faculty Postgraduate Office when the thesis/exegesis is lodged for examination. If the application is approved by the Faculty Postgraduate Committee, the form will be signed by the Dean and sent to the University Postgraduate Centre for insertion into the print copies deposited. For more information consult the Postgraduate Handbook.

Student ID No	0174528	Name	Bronwyn Henderson
Faculty	Health & Environmental Sciences	School/Dept	Paramedicine
Programme	MPhil – AK 3720	Date of submission for examination	November 2015
Research Output	Thesis <input checked="" type="checkbox"/> Dissertation <input type="checkbox"/> Exegesis <input type="checkbox"/>	Points Value	120
Thesis Title	Gender disparity in 12-lead electrocardiogram acquisition by Emergency Medical Service staff for patients with cardiac-type chest pain		

EMBARGO TIMEFRAME

An embargo is requested on the public availability of the print and digital copies of the above thesis/exegesis from the date of submission for examination (maximum normally 36).

36 months

EMBARGO CATEGORIES

The thesis/dissertation/exegesis contains confidential or sensitive information which if publicly available may (Tick all that apply)

- Jeopardise the future intellectual property rights of the author (e.g. a patent application or publication)
- Breach a prior contractual arrangement with an external organisation (Please attach a copy of the relevant agreement(s))
- Infringe or endanger the right to privacy or cultural respect of an individual or group

The embargo would apply to

- The complete thesis/dissertation/exegesis
- A portion of the work (specify) : _____

SIGNATURES

Student		Date	13/11/2015
Primary Supervisor		Date	13/11/2015
Secondary Supervisor	_____	Date	_____
Supervisory Mentor	_____	Date	_____

RESTRICTED ACCESS APPROVED BY FACULTY DEAN (or delegate)

Signature		Date	16/11/15
-----------	--	------	----------

OFFICE USE **RELEASE DATE** *30 Nov 2018*