New Zealand Paramedic-Based Systems of Care for ST-Elevation Myocardial Infarction Patients:

Autonomous Provision of Fibrinolysis and Cardiac Catheterisation Laboratory Referral

Paul Davis

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

2017

Discipline of Paramedicine, School of Clinical Sciences,
Faculty of Health and Environmental Science

Abstract

The pathology of ST-elevation myocardial infarction (STEMI) represents a serious and potentially life-threatening medical emergency that affects thousands of unsuspecting New Zealanders each year. To optimise patient outcomes, efficient and contemporary systems of care are required with a primary goal of achieving timely diagnosis and access to definitive reperfusion therapy. Internationally, paramedics have played a crucial role in helping meet this objective through a variety of processes and given their strategic position within the community. They are often the first health practitioners to attend STEMI patients, and thus are well-positioned to expedite the process of diagnosis, treatment, management and referral. However, within this capacity, the New Zealand paramedic workforce has been under-utilised. Although some regions have adopted ambulance-based programmes for pre-hospital fibrinolysis and early hospital notification, the antiquated physician-assisted telemetry-based models employed are often costly, time-consuming and prone to technological failings.

This doctoral thesis details three investigations undertaken with the St John Ambulance Service, the country's main emergency ambulance provider. It includes a preliminary simulation-based study followed by two multi-regional clinical trials, with an overarching focus on a new autonomous paramedic-based STEMI management system. The efficiency, safety and feasibility of an independent paramedic decision making model for the provision of out-of-hospital fibrinolysis and cardiac catheterisation laboratory (CCL) activation is examined in a real-world setting. Comparisons are then made to that of previous processes requiring physician-oversight and authorisation. Internationally, this research is the first to undertake such an analysis.

The results of this research have shown significant improvements among all treatment timeline metrics for both fibrinolysis and primary percutaneous coronary intervention (PPCI) in favour of an autonomous paramedic model. In some cases, this expedited care has subsequently yielded both morbidity and mortality benefit and in all cases, a reduced hospital length of stay. Moreover, our New Zealand paramedics have demonstrated highly accurate clinical decision making abilities, reflective of recent professional advancements in both education and training. These findings have served to address several failings within our current healthcare system towards the treatment and management of STEMI patients, while making a significant contribution to the knowledge and understanding of paramedicine, both nationally and abroad. This research

has the capacity to inform multidisciplinary policies and bring about meaningful clinical practice change in New Zealand.

Table of Contents

List of Figures

List of Tables

List of Abbreviations and Acronyms

ACH	=	Auckland City Hospital
ACH-CIU	=	Auckland City Hospital Cardiac Intervention Unit
ACS	=	acute coronary syndrome
AEC	=	Ambulance Education Council
AHA	=	American Heart Association
ALS	=	advanced life support
AMI	=	acute myocardial infarction
ANOVA	=	analysis of variance
BBB	=	bundle branch block
BER	=	benign early repolarisation
BLS	=	basic life support
BMI	=	body mass index
CABG	=	coronary artery bypass grafting
CCC	=	clinical communications centre
CCL	=	cardiac catheterisation laboratory
CCU	=	coronary care unit
CPGs	=	clinical practice guidelines
CSANZ	=	Cardiac Society of Australia and New Zealand
CTB	=	call-to-balloon
CTN	=	call-to-needle
CVD	=	cardiovascular disease
DPI	=	deprivation index
DTB	=	door-to-balloon
EAS	=	emergency ambulance service
ECG	=	electrocardiogram
ECP	=	extended care paramedic
ED	=	emergency department
EMS	=	emergency medical services
ETB	=	emergency medical services contact-to-balloon
ETN	=	emergency medical services contact-to-needle
EMT	=	emergency medical technician
ePRF	=	electronic patient report form
ETITO	=	Electro Technology Industry Training Organisation

FMCTB	=	first medical contact-to-balloon
FMCTD	=	first medical contact-to-door
GIS	=	geographic information system
GPs	=	general practitioners
GRACE	=	Global Registry of Acute Coronary Events
IABP	=	intra-aortic balloon pump
ICH	=	intracranial haemorrhage
ICP	=	intensive care paramedic
IHD	=	ischaemic heart disease
ILS	=	intermediate life support
IRA	=	infarct related artery
IV	=	intravenous
KPI	=	key performance indicator
LBBB	=	left bundle branch block
LMWH	=	low molecular weight heparin
LOS	=	length of stay
LVH	=	left ventricular hypertrophy
MI	=	myocardial infarction
NAOTS	=	National Ambulance Officer Training School
NASO	=	National Ambulance Sector Office
NDAP	=	National Diploma in Ambulance Practice
NRH	=	Northland Rescue Helicopter
NSTEMI	=	Non-ST-elevation myocardial infarction
NZDep	=	New Zealand socioeconomic deprivation index
PTN	=	pain-to-needle
PCI	=	percutaneous coronary intervention
PHT	=	pre-hospital thrombolysis
PPCI	=	primary percutaneous coronary intervention
PTE	=	private training establishment
RBBB	=	right bundle branch block
rPA	=	reteplase
rtPA	=	recombinant tissue plasminogen activator
SHO	=	senior house officer
SK	=	streptokinase
SMI	=	silent myocardial ischaemia

SPSS	=	statistical package for social sciences
SOP	=	standard operating procedure
STEMI	=	ST-elevation myocardial infarction
TIMI	=	time in myocardial infarction
TNK	=	tenecteplase
UAP	=	unstable angina pectoris
UFH	=	unfractionated heparin
VF	=	ventricular fibrillation
VT	=	ventricular tachycardia

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.

Paul Davis, 1st of December 2017

Co-Authored Works

Chapter	Publication Reference	Author %
Three	**Davis, P.R.,** Howie, G. J., Dicker, B., & Garrett, N. K. (2017). New Zealand Paramedics are ready for an autonomous pre-hospital thrombolysis protocol. *The Australasian Journal of Paramedicine*, *14*(3), 1-8. Retrieved from https://ajp.paramedics.org/index.php/ajp/article/view/244	PD: 80% GH:10% NG: 8% BD: 2%
Four	**Davis, P.R.,** Howie, G. J., Dicker, B., & Garrett, N. K., (2017). Paramedic-delivered fibrinolysis in the treatment of STEMI: Comparison of a physician-assisted versus autonomous paramedic approach. Manuscript submitted for publication.	PD: 80% GH:10% NG: 8% BD: 2%
Five	**Davis, P.R.,** Howie, G. J., Dicker, B., Garrett, N. K., Ruygrok, P. N., & Howard, R. (2017). Paramedic-initiated helivac to tertiary hospital for primary PCI: A strategy for improving treatment delivery times. Manuscript submitted for publication.	PD: 80% GH:10% NG: 4% BD: 2% PR: 2% RH: 2%

Paul Davis was responsible for the planning and design of all three studies listed, as well as statistical analysis of data and writing the final article. Graham Howie reviewed and provided feedback on each article, as did Bridget Dicker. Peter Ruygrok and Ryan Howard provided feedback for Study Three (Chapter Five) only. Nick Garrett provided statistical advice and general feedback for all three studies.

Conference abstract presentations

The following presentations were fully designed and written by Paul Davis, with general review and feedback provided by the other authors.

Davis, P.R., Howie, G. J., Dicker, B., & Garrett, N. K. (2017, September*). Paramedic-delivered fibrinolysis in the treatment of STEMI: Comparison of a physician-assisted versus autonomous paramedic approach*. Oral presentation at the AUT Paramedic Research Forum, Auckland.

Davis, P.R., Howie, G. J., Dicker, B., Garrett, N. K., Ruygrok, P. N., & Howard, R. (2016, June*). Paramedics initiated helivac to tertiary hospital for primary PCI: Final results.* Oral presentation at the Cardiac Society of Australia and New Zealand International Conference, Rotorua, New Zealand.

Davis, P.R., & Howie, G.J. (2014, July). *Are New Zealand paramedics ready for an autonomous pre-hospital thrombolysis protocol?* Oral presentation at the New Zealand Health Research Council Hui Whakapiripiri, Auckland, New Zealand.

Davis, P.R., Howie, G. J., Dicker, B., Garrett, N. K., Ruygrok, P. N., & Howard, R. (2014, June). *Paramedics initiated helivac to tertiary hospital for primary PCI: Initial experiences and outcomes.* Oral presentation at the Cardiac Society of Australia and New Zealand International Conference, Dunedin, New Zealand.

Davis, P.R., Howie, G. J., Dicker, B., & Garrett, N. K. (2013, October). *Are New Zealand Paramedics ready for an autonomous pre-hospital thrombolysis protocol?* Oral presentation at the Paramedics Australasia International Conference, Canberra, Australia. (This presentation won best postgraduate research award)

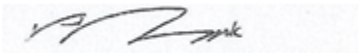
Davis, P.R., Howie, G. J., Dicker, B., & Garrett, N. K. (2013, September). *Are New Zealand Paramedics ready for an autonomous pre-hospital thrombolysis protocol?* Oral presentation at the AUT Paramedic Research Forum, Auckland.

Paul Davis

Dr Graham Howie

Dr Bridget Dicker

Dr Nick Garrett



Dr Peter Ruygrok

Dr Ryan Howard

Acknowledgements

Supervisory Team

A special thank you to my supervisory team who guided me throughout this PhD journey. Thank you to Brenda Costa-Scorse and Bronwyn Tunnage for their advice and support at the beginning of this process, and to my main supervisors Dr Graham Howie, Dr Bridget Dicker and Dr Nick Garrett. This was a long and arduous journey with many ups and downs, but one in which I was always grateful to have the experience and support of these amazing people. Thank you.

Funders and Support Groups

The St John Clinical Audit and Research Team and the St John Whangarei Area Committee provided extensive funding as well as administrative and logistical support for all three investigations detailed in this thesis. Key persons requiring acknowledgement include Tony Devanney, Dr Tony Smith, Dr Craig Ellis, Dr Colin Tan and Dan Ohs. Further funding for this research was provided by the Māori Committee of the New Zealand Health Research Council. In addition, the Department of Paramedicine led by Paul Davey in AUT's School of Clinical Sciences aided in developing the paramedic education package for Studies Two and Three. The overall support of these three groups was greatly appreciated.

Paramedic Participants

Thank you to all the paramedics from throughout the country who participated in this research. Your efforts and enthusiasm were awesome!

Technical Advisement

A special thank you to Dr Peter Ruygrok and Dr Ryan Howard for clinical advisement throughout our second and third investigations.

Family and Friends

The most important people to acknowledge are my close family and friends who have supported and believed in me throughout this journey, especially my parents Ralph and Evar Davis, my sister Catherine and my parents-in-law Ken and Helen Turner. However, the one person to whom I am most grateful to is my wife Caroline. Without her support, none of this would have been possible. This thesis is dedicated to her and my two daughters, Keira and Mikaela.

Ethical, Locality and Institutional Approval

Ethics approval for the three studies presented in this thesis was granted by the Auckland University of Technology Ethics Committee (AUTEC) and the Health and Disability Commission Ethics Committee (HDEC).

Study One

Are New Zealand paramedics ready for an autonomous fibrinolysis protocol in the management of STEMI?

1. AUTEC reference 12/94 approved on the 15th of May 2012 (Appendix A).
2. HDEC Multi-region reference 12/EXP/025 approved on the 24th of February 2012 (Appendix B).

All participants in this study were required to sign a consent form (Appendix C) prior to their involvement and they participated on a voluntary basis. Participants were also free to withdraw from the study at any time. Locality and research approval was granted by the St John Research Advisory Board on the 29th of June 2012 (Appendix D).

Study Two

Paramedic-delivered fibrinolysis in the management of STEMI: Comparison of a physician-authorised versus autonomous paramedic approach.

1. AUTEC reference 15/03 approved on the 10th of February 2015 (Appendix E).
2. HDEC Northern A reference 14/NTA/112 approved on the 2nd of December 2014 (Appendix F).

Locality and institutional approval was granted by the St John Research Advisory Board on the 12th of January 2015, reference 0044 (Appendix G), the Northland District Health Board on the 11th of October 2014, reference 2014-28 (Appendix H) and the Hawke's Bay District Health Board on the 18th of November 2014, reference 13/11/181 (Appendix I).

Study Three

Paramedic-initiated helivac to tertiary hospital for primary PCI: A new strategy for improving treatment delivery times.

1. AUTEC reference 15/04 approved on the 29th of January 2015 (Appendix J).

2. HDEC Northern A reference 14/NTA/221 approved on the 24th of December 2014 (Appendix K).

Locality and institutional approval was granted by the St John Research Advisory Board on the 12th of January 2015, reference 0043 (Appendix L), the Northland District Health Board on the 11th of October 2014, reference 2014-28 (Appendix H) and the Auckland District Health Board on the 29th of December 2014, reference A+ 6476 (14/NTA/221 (Appendix M).

Chapter One: Introduction

1.1 Background

The incidence, prevalence and impact of cardiovascular disease (CVD) within New Zealand is significant: it remains one of our country's leading causes of morbidity, mortality and hospitalisation (Ministry of Health, 2015a). Recent national figures show that almost one in 20 adults have been diagnosed with heart disease – approximately 169,000 New Zealanders – and that one adult dies from the condition every 90 minutes (Ministry of Health, 2015a, 2015b). Although a decrease in age-standardised mortality for heart disease has been well-publicised over the last three decades, it continues to account for 30% of all deaths in New Zealand annually (Ministry of Health, 2015a). The cost of this burden of disease is considerable: to the individuals and their families, to the healthcare system, and to our society (J. Ellis & Richards, 2005). Indeed, some societal groupings carry a disproportionate share of this burden, for example Māori (Bramley et al., 2004). Yet there is also abundant evidence that more proactive and early treatment strategies can ameliorate clinical outcomes and improve prognosis, particularly for those patients suffering an acute coronary syndrome (ACS) event (J. Ellis & Richards, 2005).

A subgroup of CVD, ACS sits at the severe end of the disease spectrum and is an acute presentation of ischaemic heart disease (IHD) encompassing three clinical conditions: unstable angina pectoris (UAP), non-ST-elevation myocardial infarction (NSTEMI) and ST-elevation myocardial infarction (STEMI). The most serious and time-critical of these is STEMI, which occurs primarily as a result of an occluded epicardial artery on the surface of the heart secondary to atherosclerotic plaque disruption within the tunica intima, causing dynamic thrombosis and often with associated vasospasm (Montecucco, Carbone, & Schindler, 2016). Only by unblocking the occluded artery can the myocardial tissue be saved, and this must be done promptly. The condition of STEMI is a medical emergency, potentially life threatening and requiring expedient treatment and management. The ultimate therapeutic goal for this patient subgroup is timely reperfusion of the affected area of myocardium, with time elapsed between symptom onset and treatment delivery being a crucial determinant of the degree of myocardial salvage (De Luca et al., 2003; Verheugt, Gersh, & Armstrong, 2006). Therefore, early treatment confers the greatest clinical benefit. Prompt restoration of sufficient coronary blood flow and perfusion can preserve left ventricular function and enhance both early and long-term

survival (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013).

The two primary reperfusion strategies for the treatment of STEMI are the mechanical option of percutaneous coronary intervention (PCI) and the pharmacologic option of fibrinolysis (also referred to as thrombolysis). Of these two strategies, PCI is the preferred and more superior option due to attainment of higher patency rates within the culprit artery, resulting in greater reductions in both morbidity and mortality (Keeley, Boura, & Grines, 2003). In addition, PCI offers a lower risk of haemorrhagic incident such as stroke (Henriques et al., 2006). However, outside metropolitan settings in New Zealand, access to onsite interventional cardiology services does not exist. Due to their geographical location, many STEMI patients are unable to reach the cardiac catheterisation laboratory (CCL), where PCI is performed, within mandated timeframes (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013).

Optimal management of STEMI is challenging and reliant on efficient and contemporary systems of care, which incorporate appropriate clinical knowledge and expedient non-obstructive treatment and logistical processes over the entire continuum of the patient's clinical journey. This path commences from the time of patient symptom onset to the time by which they receive reperfusion therapy. Other important elements of a successful system include clear triage and treatment protocols and effective audit and quality control measures, as well as leadership and ownership of the established system. Strong relationships between key stakeholders, such as ambulance providers and district health boards (DHBs) working in unison, are also essential to achieving these objectives of patient care and system performance. However, from a national perspective, the most recent audits suggest poor resource utilisation with numerous disparities in service delivery among these groups, despite best practice standards being promulgated in local guidelines (C. Ellis et al., 2010a, 2010b; C. Ellis et al., 2013). In particular, for those patients that present at non-interventional hospitals unable to perform PCI, there are often significant delays in accessing planned invasive assessment (C. Ellis et al., 2013). It has also been established that approximately 27% of patients fail to receive any form of reperfusion therapy within New Zealand despite being eligible (C. Ellis et al., 2013).

Given the significant prognostic value of early treatment for this patient subgroup, specific paramedic-based systems of care have assisted in addressing this time-to-

reperfusion imperative. Paramedics are often the first health practitioners to attend patients experiencing an ACS event, and thus are well positioned to expedite the process of STEMI recognition and acute treatment/management (P. Kelly, 2003; A. M. Smith, Hardy, Sandler, & Cooke, 2011). As a result, the delivery of fibrinolysis in the out-of-hospital setting by trained paramedics has been conceptualised as a means to bringing the treatment to the patient and reducing total ischaemic time. Commonly referred to as pre-hospital thrombolysis (PHT), this approach both nationally and abroad has achieved significant reductions in overall morbidity and mortality rates among STEMI patients, especially compared to those who receive the treatment in hospital (Björklund et al., 2006; McCaul, Lourens, & Kredo, 2014; Ranchord, Prasad, Matsis, & Harding, 2009). Moreover, the development of new triage systems in those centres able to perform PCI has enabled paramedics to pre-alert the CCL from the field and subsequently transfer STEMI patients to these facilities directly. These pathways which bypass the hospital emergency department (ED) can significantly improve PCI delivery times, yielding more positive patient outcomes (Brown, Mahmud, Dunford, & Ben-Yehuda, 2008; Garvey et al., 2012; Lee, Van Gelder, & Cone, 2010; Savage et al., 2014).

1.2 Statement of the Problem

Despite the advancements discussed, and unlike many other countries, New Zealand has yet to develop or refine its own paramedic-based systems of care for STEMI patients. In some regions, no specific systems are in place, while others utilise a physician-authorised telemetry-based model. Here, paramedics attend the patient and transmit a 12-lead electrocardiogram (ECG) via cardiac monitor from the scene to a hospital-based physician. Then, following phone consultation, the physician may (or may not) authorise the paramedics to either provide fibrinolysis or transport the patient directly to the CCL via the ED. This is the most commonly used approach by ambulance providers internationally (Danchin, Durand, & Blanchard, 2008). However, evidence shows that these telemetry-based systems are not only costly and inherently time consuming, but also problematic, particularly due to technological failings such as transmission issues and poor mobile phone coverage, especially in rural areas (P. Davis, 2014; Keeling, Hughes, Price, Shaw, & Barton, 2003; McLean, Egan, Connor, & Flapan, 2008). As an example, a retrospective audit of a pilot paramedic fibrinolysis programme in the regions of Northland and Hawke's Bay, New Zealand, revealed that transmission delays occurred a

third of the time, and that 28 out of 124 patients (22%) could not receive fibrinolytic therapy from paramedics because of complete transmission failure (P. Davis, 2014).

A possible solution is to remove both physician consultation and the need for ECG transmission from the process. Paramedics assess the patient and make an independent clinical decision to determine if either fibrinolysis is indicated or activation and direct transfer to the CCL should occur, dependent on location. Having already been trialled in several countries such as Australia, England, Wales, the Netherlands and the United States, this autonomous paramedic model of care has proven to be both safe and effective (Cheskes et al., 2011; Grijseels et al., 1995; Keeling et al., 2003; Pitt, 2002; Savage et al., 2014). Moreover, within New Zealand, in all other areas of clinical practice paramedics make independent decisions without direct physician oversight and treat patients according to written protocols, a form of 'standing orders'. Therefore, adopting an autonomous decision-making model for STEMI management would not only bring this component of paramedic practice into a familiar domain, it may conceivably improve patient outcomes.

1.3 Statement of Purpose

This doctoral research comprises three individual investigations which seek to answer one primary overarching question: Can an autonomous paramedic model of care in the treatment and management of STEMI be implemented successfully within New Zealand? Sub-questions to this are:

1. Can New Zealand paramedics accurately and independently identify patients eligible to receive fibrinolysis and then provide this treatment safely and autonomously in the field without physician oversight and authorisation? (Studies One and Two, Chapters Three and Four).
2. Can New Zealand paramedics accurately and independently identify patients eligible to undergo PCI and activate CCL facilities appropriately from the field without physician authorisation, thereby transferring patients directly to the CCL, with bypass of the ED? (Study Three, Chapter Five).
3. Does an autonomous paramedic approach to both the provision of fibrinolysis and activation of the CCL improve reperfusion times for STEMI patients compared to physician-authorised telemetry-based systems, and if so, does this result in improved

patient outcomes and reduced hospital admission times? (Studies Two and Three, Chapters Four and Five).

1.4 The Necessity for this Research

The clinical and health system benefits of expedited paramedic-initiated out-of-hospital management pathways for STEMI patients are widely proven and well-documented. However, this doctoral research is unique in that it is the first to explore autonomous paramedic-based systems of care specific to this patient subgroup within New Zealand, and the first internationally to compare these approaches with the more commonly utilised physician-assisted telemetry-based models. This has been identified as one of several high priority subjects for research in paramedic practice (Snooks, Evans, Wells, Peconi, & Thomas, 2008). Moreover, paramedicine is still an emerging discipline that is critically under-researched (O'Meara, Maguire, Jennings, & Simpson, 2015; G. Smith & Eastwood, 2009). The paucity of evidence to inform paramedic practice often necessitates generalising from other areas of healthcare practice such as medicine or nursing, albeit considered in a de-contextualized manner (O'Meara et al., 2015; G. Smith & Eastwood, 2009). However, the domain of paramedics in the out-of-hospital environment is both unique and challenging, requiring specific attention to produce truly meaningful research findings. In addition, fundamental differences exist in paramedic practice between New Zealand versus other countries, especially with regards to education and training. These differences likely impact on the generalisability of overseas research findings to New Zealand.

This doctoral research has provided an opportunity to work in collaboration with New Zealand's largest ambulance provider, St John, three DHBs (Northland, Auckland and Hawke's Bay) and one of the country's leading interventional cardiology departments at Auckland City Hospital. It has encouraged interdisciplinary research activity and served to promote the important role of paramedics in the acute out-of-hospital setting, while providing opportunities to build research capacity and lead to research workforce development within the field of paramedicine in New Zealand. The relationships formed between other researchers, academics, practitioners and key stakeholders in health will hopefully encourage future research initiatives.

1.5 The Potential Impact of this Research on Māori Health

It is vital that research is designed to be relevant to and address priority health care issues for Māori. This research project is in line with calls for healthcare initiatives by Māori themselves "to improve Māori cardiovascular health and to remove inequalities in cardiovascular disease outcomes between Māori and non-Māori" (Bramley et al., 2004, p. 3). We believe this research project, which sought to determine if autonomous paramedic-based STEMI management systems may improve reperfusion times and subsequent patient outcomes, has in part contributed to these objectives. While these new approaches are likely to benefit all New Zealanders, they have the potential to particularly benefit Māori, given their higher incidence of IHD. Furthermore, for each of the investigations detailed in this thesis, a comprehensive education and training package was constructed and delivered to paramedic staff. This served as a means of raising awareness of Māori health issues among the ambulance work force. Our research proposal was also reviewed in June 2014 by the Kawa Whakaruruhau Komiti, a Māori advisory group within the School of Health Care Practice at AUT. Health research at AUT is informed by the Te Ara Tika – Guidelines for Māori Research Ethics 22.

Throughout our investigations opportunities were sought to move the whakapapa from consultation to engagement and kaitiaki. Although the tika/arotahinga is mainstream, this research has identified several areas where improvements in treatment access for Māori patients suffering STEMI may lead to reduced morbidity and mortality rates. St John's national Māori advisor also endorsed this research project (Appendix N) following consultation in June 2014. Further discussion on Māori health (specifically CVD) is presented in Chapter Three.

1.6 EAS Provision and the Role of Paramedics Within New Zealand

Emergency ambulance services (EAS) within New Zealand comprise of two service providers: St John, which covers approximately 95% of the country, and Wellington Free Ambulance, which oversees the Wellington and Kapiti Coast area. Both groups are charitable organisations that rely on payment of part charges and donations to cover 30% of their operating costs, while the remaining 70% is funded by contracts with the Ministry of Health, the Accident Compensation Corporation (ACC) and DHBs. In addition, there are 13 independent helicopter rescue services operating throughout the regions that are also managed by charitable trusts and with paramedic crews seconded

from the ambulance providers. Both ambulance and helicopter dispatch are coordinated by joint clinical communications centres (CCC) located in Auckland, Wellington and Christchurch. Within New Zealand, paramedics are dedicated to providing independent acute care to patients in the out-of-hospital setting and to transporting these patients to appropriate centres for more definitive treatment and management if required. In many instances, this will be a hospital ED or similar facility.

In recent years, St John and Wellington Free Ambulance Service have transitioned towards standardised practice levels and common clinical procedures for their officers, a move promoted by the government-funded National Ambulance Sector Office (NASO) and the New Zealand Standards Authority NZS 8156:2008 'Ambulance and Paramedic Services' (National Ambulance Sector Office, 2009; New Zealand Standards Authority, 2008). Currently, three national-based practice levels exist: emergency medical technician (EMT), the lowest practice level, followed by paramedic and intensive care paramedic (ICP). Table 1.1 outlines these current New Zealand EAS practice levels and their corresponding delegated scope of practice.

In terms of the topic of this thesis, New Zealand paramedic-based systems of care for STEMI patients, there are still vast differences between New Zealand and services overseas in terms of the delegated scope of practice aligned with each of the practice levels mentioned. Variation may even occur within a single country, i.e. the United States. In addition, in other countries, the term 'paramedic' often refers to an officer trained to an advanced life support (ALS) level. In New Zealand, only ICPs are trained to this equivalent, while paramedics are trained to an intermediate life support (ILS) level and EMTs to a basic life support (BSL) level. For the three investigations detailed in this thesis, the term 'paramedic' refers to both New Zealand paramedics and ICPs.

Table 1.1 ***New Zealand Emergency Ambulance Service Practice Levels and Delegated Scope of Practice***

	Delegated Scope of Practice		
Clinical Practice Level	Skills	Pharmacotherapy	Devices
EMT	Automated defibrillation 12-lead ECG acquisition IM injection Laryngoscopy (airway obstruction) Urinary catheter troubleshooting	Adrenaline IM, IN, nebulised and topical Aspirin PO Entonox inhaled Glucagon IM GTN SL Ibuprofen PO Ipratropium nebulised Loratadine PO Methoxyflurane inhaled Ondansetron PO Paracetamol PO Prednisone PO Salbutamol nebulised Tramadol PO	Nasopharyngeal airway Oropharyngeal airway Laryngeal mask airway PEEP Tourniquet

Note: EMT = emergency medical technician; ECG = electrocardiogram; IM = intramuscular; PO = per oral; PEEP = positive end expiry pressure; IN = intranasal; GTN = glyceryl trinitrate; SL = sublingual; IV = intravenous; SC = subcutaneous; ICP = intensive care paramedic; IO = intraosseous. Adapted from "Authority to practice and practice levels" by St John Ambulance Service, 2016, Clinical Procedures and Guidelines: Comprehensive edition 2016-2018, p. 8-9. Copyright 2016 by St John Ambulance Service.

Table 1.1 (continued)

Delegated Scope of Practice			
Clinical Practice Level	Skills	Pharmacotherapy	Devices
Paramedic	All of the above plus: Manual defibrillation Synchronised cardioversion 12-lead ECG interpretation IV cannulation SC injection	All of the above plus: Adrenaline IV (cardiac arrest only) Amiodarone IV (cardiac arrest only) Amoxicillin/clavulanic acid IM or IV Clopidogrel PO Enoxaparin SC Fentanyl IM & IV Gentamicin IV Glucose IV Heparin IV Lignocaine SC Metoprolol IV Midazolam IM (seizures or agitated delirium only) Midazolam IV (seizures only) Morphine IM & IV Naloxone IM & IV Olanzapine PO Ondansetron IM & IV Oxytocin IM 0.9% sodium chloride IV Tenecteplase IV Valproate IV	All of the above

Note: EMT = emergency medical technician; ECG = electrocardiogram; IM = intramuscular; PO = per oral; PEEP = positive end expiry pressure; IN = intranasal; GTN = glyceryl trinitrate; SL = sublingual; IV = intravenous; SC = subcutaneous; ICP = intensive care paramedic; IO = intraosseous. Adapted from "Authority to practice and practice levels," by St John Ambulance Service, 2016, Clinical Procedures and Guidelines: Comprehensive edition 2016-2018, p. 8-9. Copyright 2016 by St John Ambulance Service.

Table 1.1 (continued)

	Delegated Scope of Practice		
Clinical Practice Level	Skills	Pharmacotherapy	Devices
ICP	All of the above plus: Capnography Chest decompression Cricothyrotomy IO access Endotracheal intubation Finger thoracostomy Laryngoscopy Transcutaneous pacing	All of the above plus: Adenosine IV Adrenaline (all routes) Amiodarone IV Atropine IV Calcium chloride IV Ketamine (all routes) 1% Lignocaine (all routes) Magnesium IV Midazolam IV Rocuronium IV 8.4% Sodium bicarbonate IV Suxamethonium IV (RSI endorsed personnel only) Valproate IV	All of the above plus: Endotracheal tube Magill forceps Trocar needle

Note: EMT = emergency medical technician; ECG = electrocardiogram; IM = intramuscular; PO = per oral; PEEP = positive end expiry pressure; IN = intranasal; GTN = glyceryl trinitrate; SL = sublingual; IV = intravenous; SC = subcutaneous; ICP = intensive care paramedic; IO = intraosseous. Adapted from "Authority to practice and practice levels," by St John Ambulance Service, 2016, Clinical Procedures and Guidelines: Comprehensive edition 2016-2018, p. 8-9.

Both New Zealand EAS providers have a combined clinical governance committee that governs all clinical matters within their respective services. This includes development and oversight of the clinical practice guidelines (CPGs), under which all operational staff work according to their practice level and delegated scope of practice. The implementation of national standardisation in this area was a requirement for contractual obligations between the two services, the Ministry of Health, ACC and the various DHBs. It was also seen as a necessary prerequisite in the move towards registration of EAS personnel, specifically those at a practice level of paramedic and above. Unfortunately, registration has not yet been achieved, meaning that unlike many other health professionals, New Zealand EMTs, paramedics and ICPs are not recognised under key legislation such as the Health Practitioners' Competence Assurance Act 2003. Instead, medico-legal requirements are fulfilled by officers working under the registration of their appointed medical directors and within their delegated scope of practice. These directors are senior physicians within the clinical governance committee. However, staff must still adhere to such legislation as the Medicines (Standing Order) Regulation 2002 (New Zealand Parliamentary Counsel Office, 2016).

From an international perspective, the level of clinical autonomy bestowed upon New Zealand EAS personnel, particularly our paramedics, is reasonably significant, as many overseas services require their officers to consult with a designated physician prior to initiating most treatments. This level of autonomy, coupled with an expanding scope of practice, reflects the evolution of EMS from a practice model of simple response, delivery of first aid and transport, to having a fully integrated and integral role within the emergency health care system (Council of Ambulance Authorities, 2008). This is further evidenced by the recent implementation of several nationally standardised paramedic-based out-of-hospital patient care pathways for the pathology of stroke, major burns, spinal cord injury and major trauma (Major Trauma National Clinical Network, 2016; Ministry of Health, 2014b; St John Ambulance Service, 2016).

1.7 EMS Education Within New Zealand

A key component among the three studies presented in this thesis is the current standard of paramedic education and training within New Zealand. To correctly provide fibrinolytic therapy or activate CCL facilities independently in the field and without physician oversight, paramedics must possess a variety of prerequisite skills and

knowledge. The overarching hypothesis within this body of research is that the current national standards meet this objective.

Emergency medical services (EMS) education within New Zealand has developed considerably in recent years, coinciding with increasing complexities in patient care. This can be attributed to the advancing age of our population, who exhibit greater co-morbidities and increased levels of prescribed pharmacotherapy. This is in stark contrast to the pre-1970s, when ambulance officers (a single practice level) were only trained in basic first aid and equipped with little more than oxygen, splints and bandages (Swarbrick, 2016). The concept at the time of 'load and go' was focussed on patient retrieval and transport to hospital where definitive medical treatment could then be provided. However, during the mid-1970s, service providers came under increasing pressure due to greater workload demands, along with criticism from both the public and government in respect to national inconsistencies with the standards of treatment delivery. As a result, proceeds from New Zealand's first national telethon in 1975 contributed to the development of the National Ambulance Officers Training School (NAOTS), which opened in Auckland in 1978 (Hunt, 2009; Wright-St. Clair, 1977). International changes in EMS care at the time, particularly in the United States and the United Kingdom, were also influential on New Zealand.

During this same period, various practice levels were subsequently developed by the ambulance sector, these being ambulance officer, intermediate care officer and paramedic, with NAOTS as the main private training establishment (PTE). The duration of the education courses ranged from six weeks to six months and reflected international trends in a broadening clinical scope of practice for EMS personnel. Countries such as the United States and the United Kingdom made efforts to focus on training paramedics in advanced resuscitative care and the treatment of ACS, and this formed the basis of paramedic training in New Zealand (B. Costa-Scorse, personal communication, September 19, 2014). However, recommendations from an independent review conducted in 1984, which in part examined our EMS education, highlighted the need for an affiliation between NAOTS and a tertiary education provider, enabling the delivery of more formalised paramedical education and training (Ambulance Transport Advisory Board, 1984; Walton & Offenberger, 1984). As a result, in 1986 NAOTS aligned with the Auckland Institute of Technology (AIT) within the Faculty of Health Sciences. This partnership continued until 1999, at which time the Ambulance Education Council (AEC) prompted the disestablishment of the single industry-funded training school (NAOTS) in

favour of transitioning towards a model of multiple education providers approved by the New Zealand Qualifications Authority (NZQA) (Costa-Scorse, 2008).

The two ambulance services are currently recognised as PTEs and have their own clinical education and training departments that deliver a post-employment course for the practice level of EMT only. This practice level was previously referred to as 'ambulance officer' and is the entry practice level for those personnel working in the emergency ambulance context (New Zealand Qualifications Authority, 2016). The EMT course follows a national standardised format that is NZQA-aligned and overseen by the Electro Technology Industry Training Organisation (ETITO), the registered standards setting body for unit standard-based education within the New Zealand ambulance sector (Electro-technology Industry Technology Organisation, 2012). The EMT course is a level five national diploma qualification referred to as the National Diploma in Ambulance Practice (NDAP) and is delivered following a symptom-based approach to clinical management and integrated clinical practice (New Zealand Qualifications Authority, 2016). The course duration may spread over six months for full-time employees, comprising of block periods of classroom time, e-learning modules, a written portfolio of patient cases and ambulance road shifts (P. Bradley, personal communication, September 20, 2014).

The practice level of paramedic requires the completion of a three-year Bachelor of Health Science (BHSc) undergraduate degree endorsed in paramedicine, a stipulation that has only been in place since early 2016. Two programmes are currently offered within New Zealand by the Auckland University of Technology (AUT) and Whitireia Community Polytechnic based in Wellington (supported by Victoria University, Melbourne). Although paramedic-based degree programmes have existed as early as the mid-1990s in countries such as Australia and the United Kingdom, they have only been on offer within New Zealand since 2002, marking the ambulance sector's transition to a pre-employment education model. Over the course duration students are required to complete a variety of core health science papers as well as those specific to paramedic practice and to a level of ILS. This study is supplemented by clinical placements and mentoring on road ambulances and in hospital departments such as the ED, operating theatre and coronary care unit (CCU). In addition, the practice level of ICP requires completion of a Postgraduate Certificate in Specialty Care (Advanced Paramedic Practice), a further one year of full-time study focussed at ALS level (T. Smith, personal communication, August 19, 2016). Previously, the undergraduate degree programme

included the ALS component. However, it was recognised that students needed more time to consolidate their knowledge and skills prior to embarking on advanced paramedic education and training (P. Davey, personal communication, August 23, 2016).

Once students have completed their education course and gained employment within either of the two EAS providers, they are placed into an internship programme and allocated a preceptor to guide and assist them in working towards gaining authority to practice (ATP). This is a formal medico-legal term which recognises that staff have fulfilled key requirements and have been granted authority to work at a given practice level by the service's medical director and under his or her medical registration.

Within New Zealand paramedic practice there also exist two sub-specialities: aero-medical retrieval, for those working as flight medics in one of our numerous helicopter rescue services, and the extended care paramedic (ECP) role. The latter involves a single responder car-based paramedic or ICP who is designated to attend emergency ambulance calls triaged as low acuity. The ECP receives skills enhancement and training not normally included in conventional paramedic education programmes. This allows them to treat patients for a range of common medical issues in their home or surrounds and with a capacity to then refer these patients on to other community-based healthcare providers such as GPs if required (Hoyle, Swain, Fake, & Larsen, 2012). This process negates the need for transport by conventional ambulance to the ED. Although a service standard has been produced for these two sub-specialities, an agreed education programme has yet to be determined (Ambulance New Zealand, 2013; Hoyle et al., 2012).

1.8 Paramedic Clinical Decision Making

With the provision of more comprehensive clinical education and training and the subsequent expansion of delegated scopes of practice, the extent to which New Zealand paramedics must exercise independent clinical judgement and decision making has also grown. However, given the unpredictability and often uncontrolled nature of the out-of-hospital environment, paramedics are regularly required to make their decisions in situations non-existent in other clinical settings and with limited diagnostic support (Jensen, Croskerry, & Travers, 2009). These factors are all highly relevant when we consider a move towards new systems of practice where paramedics are given greater influence over the patient's treatment trajectory.

An increase in independent clinical decision making also corresponds with an increase in accountability. This merges with greater public expectations around the quality of care and educational standards of those within EMS (Shaban, Smith, & Cumming, 2004). However, like many of their counterparts overseas, New Zealand EMS personnel make clinical decisions and provide treatment according to written protocols, a form of 'standing orders' referred to as the clinical procedures and guidelines (CPGs). This is a single document developed by a joint national ambulance sector clinical working group and exists in two forms: a pocket version required to be carried by all personnel while on duty, and a larger, more comprehensive version kept in ambulance vehicles and in stations for further reference.

Interestingly, for the care of STEMI patients, the provision of fibrinolysis and activation of the CCL remain the only areas within New Zealand paramedic practice where physician consultation and authorisation is required. This has remained despite paramedics being granted autonomy in many other treatment and referral pathways for the high acuity patient. Therefore, through the trial and examination of paramedic-based STEMI management programmes occurring without physician oversight, this doctoral research project has brought STEMI care into a familiar domain for paramedics while examining their decision-making processes.

1.9 Chapter Summary

Ischaemic heart disease still places a significant burden on our society, with large inequalities observed among key ethnic groups, and despite advances in public health surveillance with improved treatment and management strategies (Ministry of Health, 2015b; Tobias, Sexton, Mann, & Sharp, 2006; Wells, Broad, & Jackson, 2006). Although this issue is multifactorial, for those patients at the acute end of the disease spectrum suffering STEMI, rates of morbidity and mortality can be significantly reduced if prompt access to reperfusion therapy occurs (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013). These outcomes would likely be of greater benefit to Māori, for whom the incidence and prevalence of IHD is significantly higher compared to non-Māori (Ministry of Health, 2014a, 2015a). Two of the main stakeholders in contributing towards reaching this objective are the EAS providers and their paramedic workforce, who are often the first health professionals to encounter this patient subgroup. Paramedics are now emerging as clinicians in their own right, reflected by their current education, training and

scope of practice, as well as their level of autonomy. In a role where they are often required to make time-critical decisions in stressful environments regarding the treatment and care of high acuity patients, the importance of their strategic position within the community is gaining greater recognition by the medical profession.

Unlike other countries such as Australia, the United Kingdom and the United States, New Zealand has yet to adopt and/or refine its own paramedic-based systems of care for STEMI patients. In some regions, no specific systems are currently in place, and where they are, a physician-authorised telemetry-based model is utilised – often exposed to technological failings and with high start-up costs. Therefore, this current national situation provides an opportunity to explore a new autonomous paramedic approach, such as those implemented successfully in some services overseas, but in the context of New Zealand paramedic practice.

1.10 Thesis Structure

This thesis comprises six chapters that present research undertaken within the St John Ambulance Service, the country's largest EAS provider. It examines an autonomous paramedic model for both the delivery of fibrinolytic therapy and CCL referral from the field for the care and management of STEMI patients. The results of this research are then compared to previously utilised telemetry and hospital-based systems with physician oversight. Chapter One has introduced several background themes to support the direction and aims of the investigations. As a context for the research, Chapter Two provides a comprehensive review of the relevant literature. Chapter Three details a formative preliminary investigation that determined if New Zealand paramedics possessed the prerequisite skills and knowledge necessary to permit autonomous decision making for fibrinolysis, under protocol guidance. Specifically, these included accurate 12-lead ECG interpretation skills, and a sufficient understanding of both acute cardiac pathology and principles of pharmacology. Associations between paramedic groups' clinical decision-making abilities and key demographic characteristics were also examined. This investigation serves to inform the remaining two studies discussed in the following chapters.

Chapter Four details a second investigation where the transition from theory to practice was made. This was a 24-month clinical trial of autonomous paramedic-delivered fibrinolysis in the management of STEMI, conducted in the regions of Northland and

Hawke's Bay. The trial involved over 100 paramedic staff in total, servicing a combined population of 328,000 people across two DHBs. Before the trial started, a review was conducted via a patient records audit of the previous physician-authorised telemetry-based programmes within each region. At the completion of the trial period, the accuracy of paramedic diagnosis was examined, specifically paramedics' ability to determine those patients who were either eligible or ineligible to receive the fibrinolytic therapy. A measure of key treatment time intervals and patient outcomes was also undertaken with comparisons made to results of the previous programmes.

Chapter Five details a third and final investigation, a second 48-month clinical trial based in the city of Whangarei in Northland. It focussed on paramedic-initiated helivac of STEMI patients directly from the field to Auckland City Hospital (ACH) CCL for PPCI, a process that bypassed the local receiving hospital. Whangarei's Northland Base Hospital (NBH) is the region's sole tertiary centre and does not provide interventional cardiology services. The trial involved over 25 paramedic staff in total servicing a city population of around 83,000 people. The Northland Emergency Services Trust (NEST) was the aircraft provider, utilising Sikorsky S-76 airframes with a transport distance to Auckland of 155 km direct. Prior to commencement of the trial, STEMI patients attended to by ambulance within the Whangarei City area were transported to NBH in the first instance, before urgent inter-hospital helicopter transfer to ACH was arranged. This hospital-based referral pathway served as a trial comparison. Again, at the completion of the study, the accuracy of paramedic diagnosis was examined, specifically paramedics' ability to determine those patients who were either eligible or ineligible for transfer to the CCL to receive PPCI. A measure of key treatment time intervals and patient outcomes was also undertaken, with comparisons made with results of the previous hospital-based referral pathway.

Chapter Six provides a general discussion and summary of the research findings across the chapters, followed by their significance and contributions, regional and national policy implications, and strengths and limitations. The chapter concludes with recommendations for future inquiry. Auxiliary information to support the information presented in this thesis is included as appendices, rather than in the main text of the chapters.

Chapter Two: Review of the Literature

2.1 Introduction

This chapter is divided into several sections, beginning with a description of the search strategy utilised to identify the literature in the review. Key themes and topics central to this study are then examined and contextualised in relation to New Zealand paramedic practice. These include: the benefits of out-of-hospital fibrinolysis and paramedic models of delivery; the various fibrinolytic agents and adjunctive drug therapy regimes utilised; patient eligibility for treatment and complications encountered; financial considerations and barriers to paramedic programme implementation; and comparison of out-of-hospital fibrinolytic therapy to PPCI. Paramedic-initiated field activation of the CCL with direct patient transfer is then discussed, as well as the method of aeromedical transfer. The chapter concludes with a brief review of Māori cardiovascular health and its relevance to the research presented in this thesis.

2.2 Literature Search Process

A systematic search of the literature was undertaken between October and December 2014 to identify studies investigating and relevant to both paramedic-delivered fibrinolysis and CCL referral from the field in the care and management of STEMI patients. This search was then repeated in October 2017 to retrieve the most recent literature. Figure 2.1 provides an overview of the literature search process, including but not limited to databases accessed, search terms utilised and the study inclusion criteria, one of which was studies published since 1987. This was the time when the first studies emerged, exploring the concept of out-of-hospital fibrinolysis for STEMI. The practice of paramedic referral of STEMI patients from the field direct to the CCL was not developed internationally until the late 1990s.

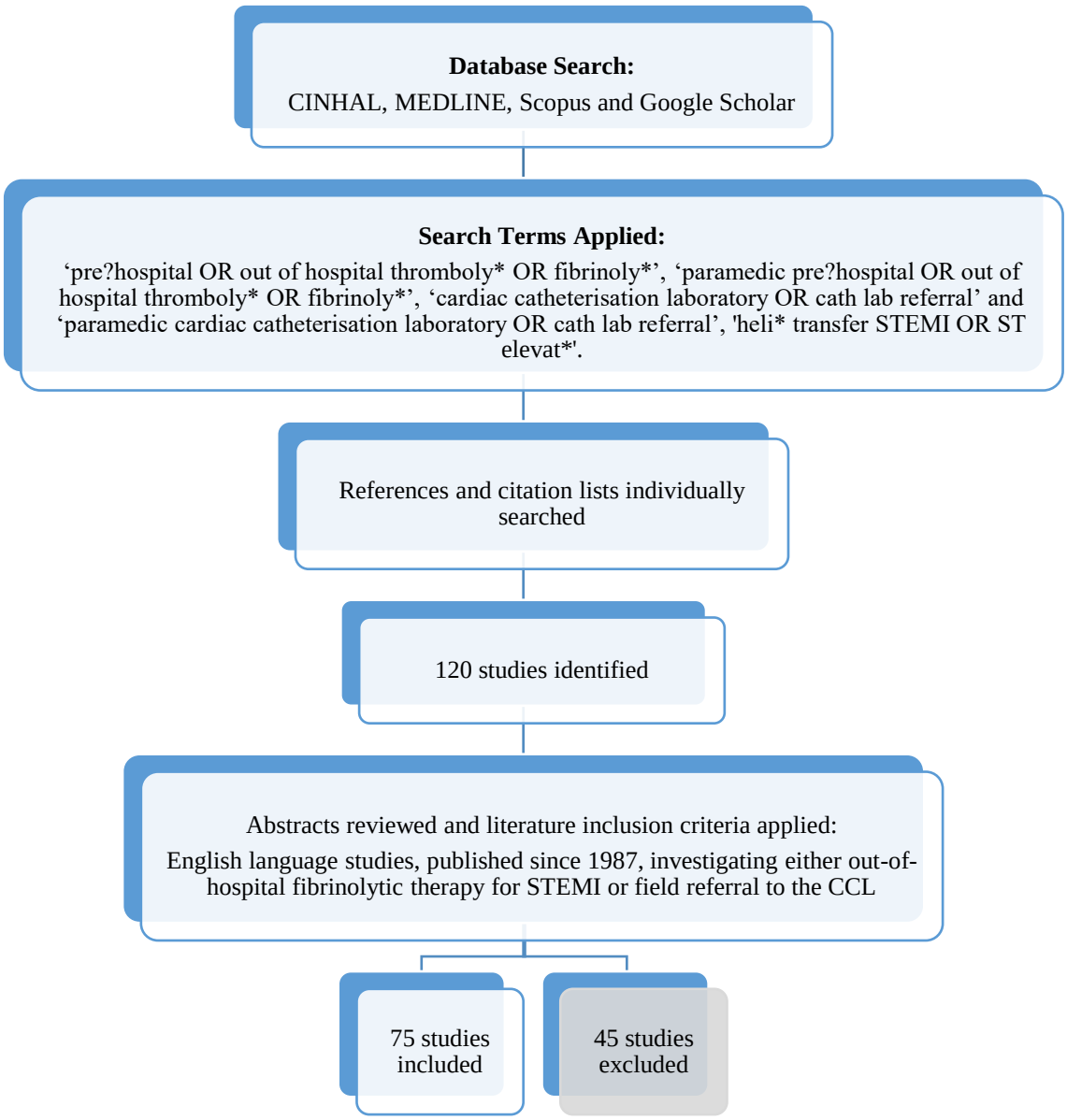


Figure 2.1 **Flowchart of Literature Search Strategy**

Note: STEMI = ST-elevation myocardial infarction; CCL = cardiac catheterisation laboratory

2.3 Out-of-Hospital Fibrinolysis in Perspective

The greatest potential for fibrinolysis to achieve reperfusion of the infarct-related artery and to optimise outcomes in the management of STEMI is with early administration following patient symptom onset (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013; F. Van de Werf et al., 2008). It has been suggested that this is likely due to the treatment having greater effect on breaking down 'fresh' thrombi that have not undergone more extensive polymerisation and through restoring arterial patency early after symptom

onset, at which time the potential for myocardial salvage is at its greatest (Bongard et al., 2009; Morrison, Verbeek, McDonald, Sawadsky, & Cook, 2000). This concept aligns with the well accepted open artery hypothesis, which recognises the clinical benefit of promptly re-establishing anterograde blood flow through the occluded coronary artery (Franzosi et al., 1998). It has also been the central driver internationally in developing systems of care that enable fibrinolytic therapy to reach the patient at the earliest possible juncture and prior to arrival at hospital. Such systems primarily utilise EMS as they are the most appropriately equipped and strategically placed within the community to achieve this key objective.

It was demonstrated in the Thrombolysis in Myocardial Infarction (TIMI) 2 trial that there was an increase in mortality by 1% for every hour fibrinolysis was delayed (C.P Cannon, Antman, Walls, & Braunwald, 1994). This finding was similar to that identified in the mega-trial, Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) (n = 41,021) (Topol, Califf, Van de Werf, & Armstrong, 1993). In addition, Boersma, Mass, Deckers and Simoons (1996) demonstrated the case for early fibrinolysis through the evaluation of 22 randomised control trials covering a ten-year period, comparing the treatment with placebos or controls in the hospital setting. A non-linear relationship was demonstrated between the time of fibrinolysis and the saving of life. It was established that 65–80 additional lives per 1000 patients were saved at 30 days post-STEMI if the treatment was provided within the first hour of symptom onset. This figure fell dramatically to 37 lives if the treatment was provided within the second hour, and to 29 lives if provided between three and six hours. The quantity of heart muscle that may be salvaged during a STEMI is inversely related to the duration of occlusion in the infarct-related artery up to approximately five hours, after which time myocardial ischaemia becomes irreversible (Weaver, 1995). However, the general consensus is that a net benefit is apparent for those patients treated up to 12 hours from symptom onset, principally from improved healing of the affected area (Fibrinolytic Therapy Trialists' Collaborative Group, 1994). After 12 hours fibrinolysis ceases to have any clinical benefit compared with control, and may even contribute to long-term mortality (Fibrinolytic Therapy Trialists' Collaborative Group, 1994).

Because of these empirical findings, several well-defined and internationally recognised treatment time service standards have been established. For example, it is

recommended that fibrinolysis be provided within the first 60 minutes from when the patient seeks medical assistance, referred to as the call-to-needle (CTN) time (Department of Health, 2002; ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013). The term 'pain-to-needle' (PTN) refers to the time from onset of the patient's symptoms to receiving fibrinolysis. Although it is recommended that this also be within 60 minutes, it is primarily dependant on the time it takes the patient to seek professional help. Lastly, eligible patients should receive fibrinolysis within 30 minutes of arrival at hospital, referred to as the door-to-needle (DTN) time. When applied to the out-of-hospital setting, the term EMS contact-to-needle (ETN) time is used instead. This time also has a target of less than 30 minutes and starts from when EMS personnel first make direct contact with the patient (Department of Health, 2002; ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013).

There are many influencing factors that contribute to the time in which STEMI patients receive reperfusion therapy, whatever the modality, and delays are often considerable and multifactorial (Tanner, Larsen, Lever, & Galletly, 2006). These influencing factors include the patient's geographical location, communications access and distance to hospital, as well as hospital and EMS resources and EMS response time (if called upon). However, the main delay often lies with the patients who fail to react quickly and appropriately from the time of their symptom onset (Weaver, 1995). In the New Zealand context, Tanner et al. (2006) reported on the behaviour of 100 ACS patients prior to hospital admission, establishing that it took a median time of 90 minutes before they made contact with any health professional from the time of their symptom onset. In addition, the median time in which they arrived at hospital from the time of their symptom onset was 223 minutes. This occurred despite most patients (62%) correctly assuming their symptoms were resulting from their heart. Weaver (1995) also showed that ACS patients who seek alternative means of transport to hospital, such as with family or friends, on average add 60 minutes to their arrival time at the ED compared with transportation by ambulance.

The time taken to access EMS has been shown to be a key predictor of mortality for those patients suffering out-of-hospital STEMI or other ACS events (Fox, 2004; ISIS-2 Collaborative Group, 1988). It is estimated that 50% of those patients who die from an ACS event do so within the first hour of symptom onset, and that delays as short as 30

minutes in seeking EMS assistance significantly increase mortality at one year (De Luca, Suryapranata, Ottervanger, & Antman, 2004; Newby et al., 1996; Zipes & Wellens, 1998). Paramedic-delivered fibrinolysis not only addresses the goal of providing more timely reperfusion, but also enables patients to have faster access to additional advanced care and defibrillation if required, which may limit arrhythmic death (Tanner et al., 2006).

In New Zealand, fibrinolysis provided by paramedics in the field has been used exclusively when transport times to hospital are prolonged (i.e. more than 30 minutes), which predominantly occurs in rural areas. In addition, it has been used exclusively within those regions where the receiving hospital is non-PCI capable. However, international evidence has provided a persuasive case for the treatment's provision by EMS in urban locations (Dussoix, Reuille, Verin, Gaspoz, & Unger, 2003; Svensson et al., 2003). The main advantages include elimination of unnecessary reassessment and triage of the patient in the ED, further prolonging both PTN and CTN times, often well beyond the 60-minute target timeframe (Benger, 2002; Chamberlain, Penny, & Fisher, 2001). In one randomised trial in the city of Geneva, Switzerland, a comparison between urban paramedic-delivered fibrinolytic therapy and the treatment's provision in hospital (n = 96) demonstrated a significantly reduced median CTN time of 26 minutes versus 94 minutes (p = 0.0004) in favour of the urban paramedic approach (Dussoix et al., 2003).

The two primary groups of health practitioners who deliver out-of-hospital fibrinolysis, from both a national and international perspective, are rural general practitioners (GPs) and EMS personnel; often an ALS qualified paramedic or, in New Zealand, an ILS paramedic or above. The rural GP will either initiate the treatment autonomously or following phone consultation with a hospital-based specialist, e.g. a cardiologist or emergency physician. An ambulance may then be requested to transport the patient to hospital for further management and care. For paramedics, two primary models of treatment delivery exist internationally, as discussed previously in the thesis introduction. These include the physician-authorised telemetry-based approach (the most commonly used) and the autonomous approach.

2.4 The Benefits of Out-of-Hospital Fibrinolysis Versus In-Hospital Fibrinolysis

Relevant evidence supporting the benefits of out-of-hospital fibrinolysis has come from studies involving both paramedics and out-of-hospital physicians and in which the

outcomes of the treatment were compared to its provision in the hospital setting. The primary differences between the two patient groups are: the time in which the treatment was delivered; the medical professional providing the treatment, i.e. paramedic or out-of-hospital physician versus in-hospital physician; and the type of fibrinolytic agent used. This comparative study design has provided a reliable quantitative estimate of the treatment's true clinical benefit when provided in the field (Boersma et al., 1996). Some studies exclusively involving paramedic-delivered fibrinolysis have failed to produce statistically or clinically significant results in terms of both morbidity and mortality. The reasons for this are complex and various, although study size and subsequent power are major influencing factors. Inclusion criteria and contraindications for paramedic treatment were also commonly more rigid than for physicians in both the out-of-hospital and in-hospital setting. This is reflective of the differences in experience, education and training between the two health practitioner groups, but these differences may complicate comparative studies. For example, in some studies, STEMI patients were not candidates for paramedic-delivered fibrinolysis, but went on to receive the treatment in hospital. This will be discussed further in section 2.7.

Compared with its provision in the hospital setting, out-of-hospital fibrinolysis consistently demonstrates markedly reduced PTN and CTN times, as well as clinically significant reductions in complications such as heart failure and major arrhythmias (McCaul et al., 2014). However, when comparing these outcomes between the two settings, it is important to also look at other treatments patients may receive in hospital. In many studies, it is not reported how many post-fibrinolysis patients go on to receive rescue PCI (PCI intervention due to failed fibrinolysis). This would undoubtedly impact on mortality figures, as the results may not be due to fibrinolytic therapy alone (Danchin et al., 2008). In this section, the paramedic-delivered fibrinolysis studies discussed all utilise the physician-authorised telemetry-based approach.

A meta-analysis of six randomised trials conducted by Morrison, Verbeek, McDonald, Sawadsky and Cook (2000) compared out-of-hospital fibrinolytic therapy with in-hospital, with a combined patient total of 6434. These trials involved both paramedics and physicians providing treatment in the field. The collective results showed an average of 58 minutes was saved in time-to-treatment in favour of out-of-hospital care, and a significant reduction in mortality was demonstrated with an odds ratio of 0.83 (95% CI 0.70–0.98). It was also established that there was no difference in clinical outcomes between patients who received treatment out-of-hospital from paramedics and those

treated by physicians. Previously, concerns had been raised regarding the safety of treatment provision by paramedics. However, both the safety and feasibility of this approach have been well established and supported (C. P. Cannon & Braunwald, 1996; Keeling et al., 2003; Pitt, 2002; Ranchord et al., 2009). In addition, the Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT-3 PLUS) trial (n = 1639) demonstrated a longer delay in treatment delivery in the field when provided by physicians compared to that of paramedics (Welsh et al., 2004). It was also shown in the Grampian Region Early Anistreplase trial (one of the principal studies in the meta-analysis by Morrison and colleagues), that with every 30 minutes of time saved in the first three hours from symptom onset, one additional year of life resulted for the patient (Rawles, 1994, 2003).

The Myocardial Infarction Triage and Intervention (MITI) trial was one of the first large multi-centre randomised control trials incorporating paramedic-delivered fibrinolysis, with 360 patients randomised to receive treatment either in the field or in hospital (Weaver et al., 1993). Results showed a PTN time saving of 33 minutes in favour of out-of-hospital care (110 versus 77 minutes; $p < 0.001$), as well as a greater proportion of the same cohort being pain-free on admission (23% versus 7%; $p < 0.001$). Despite these findings, there was no statistical or clinical significance in patient outcome between groups. However, it was established that if fibrinolysis was administered within 70 minutes of onset of symptoms (either in the field or in hospital), there was an 80% relative reduction in 30-day mortality, which translated to a lowering in mortality from 8.7% to 1.2% ($p = 0.03$). It was also observed that treatment within this timeframe resulted in a significant reduction in left ventricle infarct territory from 11.2% to 4.9% ($p < 0.01$).

In terms of mortality benefit, the findings produced by Morrison et al. (2000) are supported by a French study that prospectively analysed a large nationwide registry of STEMI patients (n = 1992) admitted to 369 hospitals during the year 2000 (Danchin et al., 2004). The patients reviewed were categorised into four cohorts according to the reperfusion strategy utilised, i.e. fibrinolysis in field (approximately 180; 9% provided by physicians), fibrinolysis in hospital, PPCI or no reperfusion treatment. The results showed that in-hospital death between the treatment groups was 3.3%, 8.0%, 6.7% and 12.2% respectively, while one-year survival was 94%, 89%, 89%, and 79%. In addition, for those patients in the out-of-hospital cohort that were admitted within 3.5 hours, in-hospital mortality was 0% and one-year survival was 99%. Collectively, these findings demonstrate the net benefit of early reperfusion.

The advantage of analysing mortality rates as a study outcome is that they are often easier to define. However, advancements in the treatment and management of STEMI patients have meant that patient mortality is becoming a less common event, with the current short-term mortality rate in STEMI trials (i.e. up to six months) sitting at around 5% (Jackson, Kendall, & Castle, 2009; Welsh et al., 2004). In addition, the in-hospital mortality rate for AMI has fallen over the last three decades from 16% in the pre-reperfusion era to 6–8% with the use of fibrinolytic agents, anti-thrombotic therapy and PCI (F. Van de Werf et al., 2008). Confounding mortality analysis in trials involving out-of-hospital fibrinolysis, those patients experiencing a large infarct with a subsequent worse prognosis also tend to seek medical assistance earlier (Rawles, 1994). Lamfers et al. (2003a) have therefore suggested that drawing comparisons between treatment groups without utilising a procedure of randomisation (e.g. for out-of-hospital versus in-hospital fibrinolysis) may result in out-of-hospital treatment groups consisting of patients with larger infarcts and subsequently higher mortality rates. Mortality may then be considered a doubtful indicator of the efficacy of out-of-hospital care (Lamfers et al., 2003a).

For these reasons, some researchers have elected to assess the occurrence of aborted MI following reperfusion therapy. Aborted MI means the AMI was averted as a result of the treatment and is commonly defined as: 'ST-segment resolution on ECG of greater than 50% at 90 minutes from the level at presentation; resolution of symptoms; plus an associated rise in the assayed cardiac biomarkers of less than twice the upper limit of normal' (Jackson et al., 2009; Lamfers et al., 2003a). Aborted MI is associated with an improved prognosis, with one year mortality rates being considerably lower than for Established MI (Lamfers et al., 2003a).

Through retrospective analysis Lamfers et al. (2003a) were the first to examine this outcome relative to out-of-hospital fibrinolysis. They reviewed the incidence and patient characteristics of aborted MI among STEMI patients who had received fibrinolysis by paramedics in the field (n = 468) versus those who had received the treatment in hospital (n = 264). Patients in the out-of-hospital group received either anistreplase (86%) or reteplase (14%) as the fibrinolytic agent, both administered as a double intravenous (IV) bolus. Patients in the hospital group received either a streptokinase infusion administered over one hour or an IV bolus of recombinant tissue plasminogen activator (rtPA). Approximately 17.1% of the out-of-hospital group and 4.5% of the in-hospital group met the criteria for aborted MI with no differences identified in risk factors, characteristics at presentation, infarct location or findings on coronary

angiography. The PTN time was shorter among those patients with an aborted MI (86 versus 123 minutes, $p = 0.05$), and 12-month mortality was significantly less in the aborted MI group than the group with established MI (2.2% versus 11.6%, $p = 0.03$). These results demonstrated a fourfold increase in aborted MI with out-of-hospital treatment versus in-hospital and a shorter time to treatment as a predictor of this outcome. However, no mortality benefit was shown with out-of-hospital fibrinolysis.

Contrary to these findings, in a similar study evaluating the incidence of aborted MI among STEMI patients who had received fibrinolysis as the primary reperfusion strategy, Jackson et al. (2009) failed to produce significant results. Again, through retrospective analysis the authors compared outcomes between patients who had received fibrinolysis by paramedics in the field ($n = 119$) versus those who had received the treatment in hospital ($n = 335$). However, multiple differences in patient characteristics were identified between the groups. Those patients who received out-of-hospital care were significantly younger (mean age 62.0 versus 68.1 years, $p < 0.001$) and a greater proportion of the group were male (74% versus 67%, $p = 0.003$). Despite 69% of the out-of-hospital cohort obtaining a PTN time of two hours or less compared to 40.4% of the in-hospital cohort ($p < 0.001$), the incidence of aborted MI between groups was not statistically significant (11.8% versus 18.2%, $p = 0.124$). Moreover, one potential confounding variable not discussed was the more limited treatment inclusion criteria paramedics were required to apply in the field compared to those utilised by physicians in the hospital setting. In addition, the fibrinolytic agent/s utilised in the study was/were not specified.

Taher et al. (2004) have provided one of the most comprehensive systematic analyses of aborted MI to date, as a sub-study to the ASSENT-3 trial. Although the study did not evaluate the provision of fibrinolysis in the field, its findings do support those observed by Lamfers et al. (2003a) in terms of the benefits of timely treatment. This was a prospective hospital-based randomised control trial evaluating three different anti-thrombotic strategies in conjunction with single bolus IV tenecteplase in the treatment of STEMI. From a pool of 6095 patients, the incidence of aborted infarction was 13.3%, providing a cohort of 721 patients for review. The highest incidence of aborted MI was observed among those patients who received fibrinolysis within one hour from onset of symptoms, a finding that closely parallels the concept of the ‘golden hour’ established and promoted by Boersma et al. (1996). In addition, ECG analysis was more comprehensive than in other studies reporting on aborted MI, and therefore new insights

were provided. For example, those patients with complete ST-segment resolution at 60 minutes following treatment delivery had improved clinical outcomes.

Following reperfusion therapy, the degree of blood flow through the coronary arteries to the microvasculature at the myocardial cell level is also important. Therefore, the efficacy of out-of-hospital fibrinolysis has also been demonstrated through utilisation of the thrombolysis in myocardial infarction (TIMI) flow grade system. This is an angiographic examination following treatment that evaluates infarct artery patency and the degree of arterial blood flow by means of contrast material. The grading system ranges from 0, being no antegrade flow beyond the point of occlusion, to the optimal score of 3, indicating complete perfusion, i.e. antegrade flow into the coronary bed distal to the obstruction that occurs as promptly as antegrade flow into the bed proximal to the obstruction (Gibson et al., 1999).

The Orientation of Patients Treated for Myocardial Infarction after Lysis (OPTIMAL) study sought to identify predictors of early epicardial coronary patency in STEMI patients (as judged by a TIMI flow grade of 3) following fibrinolysis in the field ($n = 997$) (Bongard et al., 2009). This was a large, multi-centred observational prospective study in which fibrinolysis was provided by physicians crewing ambulance vehicles. Only those patients who received treatment within six hours of symptom onset and who underwent angiography within six hours of time of treatment were included in the study. Approximately 82% of patients received fibrinolysis (single bolus IV tenecteplase) within three hours of symptom onset and with a median PTN time of 110 minutes – interquartile range (IQR) of 75–165 minutes. In addition, just over half of the study's total patient population (51%) had a TIMI flow grade of 3 on angiography following treatment. Among this group of patients, in-hospital mortality rates were lower compared to all other patients with a lesser TIMI flow grade (2.8% versus 5.4%, $p = 0.039$), as was the occurrence of shock (4.0% versus 10.2%, $p < 0.001$). The independent predictors of a TIMI flow grade of 3 prior to fibrinolysis that were identified included: a Killip class I; current or past smoking; and five or fewer ECG leads showing ST-elevation. The Killip classification is a system that assesses the presence and severity of heart failure by physical examination among patients suffering AMI to predict and stratify the patient's risk of short and long-term mortality (Miller, Scott, Grill, & Kopecky, 2000). The system has shown to provide strong prognostic value and ranges from class I (no clinical signs of heart failure) to class IV (evidence of cardiogenic shock) (Miller et al., 2000; Wu, Parsons, Every, & Bates, 2002).

These results by Bongard et al. (2009) may assist out-of-hospital clinicians in determining which patients are more likely to respond to fibrinolysis versus those who may not and subsequently require rapid transfer to a PCI centre for further care, i.e. rescue PCI. Moreover, these results are supported by Cannon and Braunwald (1996) who established that there was an almost linear correlation between higher rates of early TIMI flow grade 3 and improved survival among STEMI patients post-fibrinolysis. Unsurprisingly, a TIMI flow grade of 3 has also shown to result in reduced size of infarction and improved left ventricular function (Braunwald, 1989).

2.5 Paramedic-Delivered Fibrinolysis Within New Zealand

In 2003, the Wellington Free Ambulance Service in conjunction with the Capital and Coast DHB, was the first to introduce a paramedic-delivered fibrinolysis programme for STEMI patients within New Zealand. The programme was implemented specifically within the Kapiti Coast area, where ambulance transport times are prolonged, and utilised the physician-authorised telemetry-based approach. Prior to the three studies presented in this thesis, Ranchord et al. (2009) were the first and only authors to examine paramedic-delivered fibrinolysis in the New Zealand context, through retrospective analysis of the Kapiti Coast programme. In their study, they compared clinical outcomes between two cohorts of STEMI patients: those who had received fibrinolysis in the field by paramedics (n = 50) versus an historic control group who had received the treatment in hospital following ambulance transport to the ED (n = 50). Similar baseline demographic and clinical characteristics were observed between groups, and the fibrinolytic agent used was reteplase, administered through two IV bolus injections 30 minutes apart. An improved difference in median patient contact-to-needle time in the out-of-hospital cohort was observed (44 versus 133 minutes, $p < 0.0001$), coupled with a lower incidence of developing heart failure (10% versus 28%, $p = 0.04$). However, there was no statistical difference between groups in mortality at 30 days. This was likely due to the study's sample size providing insufficient power to detect differences in this clinical outcome.

Following implementation of the Kapiti Coast programme, the St John Ambulance Service introduced its own programme in Northland and Hawke's Bay in 2008 and in Nelson/Marlborough in 2015. Again, these programmes were implemented in conjunction with the local DHBs, and up until 2015 all utilised the physician-authorised telemetry-based approach (P. Davis, 2014).

2.6 Autonomous Paramedic-delivered Fibrinolysis

The UK Joint Royal Colleges Ambulance Liaison Committee (JRCALC) and Ambulance Services Association (ASA) have acknowledged that out-of-hospital fibrinolysis provided on the initiative of paramedics without mandatory telemetry and physician consultation is the most time-efficient approach to treatment delivery (Chamberlain et al., 2001). This model has subsequently been in practice in many UK ambulance services for well over a decade, with out-of-hospital fibrinolysis constituting 18% of all treatment cases throughout the country each year (Cooke, 2007). However, there remains a distinct paucity of research or inquiry that examines this subject, with only four relevant studies identified in the literature. In addition, given the fundamental differences between paramedic services worldwide as previously discussed in Chapter One, Section 1.4, the generalisability of the findings within these four studies warrants closer scrutiny.

First described by Grijseels et al. (1995) in their prospective observational study entitled Reperfusion in Acute Infarction Rotterdam (REPAIR), autonomous paramedic-delivered fibrinolysis in the management of STEMI has been in practice in Rotterdam since 1988. Shortly thereafter, other parts of the Netherlands and Europe adopted the approach. Conducted over a six-year period from 1988 to 1993, the REPAIR study investigated both time-to-treatment and long-term outcomes between two cohorts of STEMI patients: those who were treated with one of two fibrinolytic agents in the field by either paramedics or GPs (n = 529) versus an historic control group that met the same selection criteria but who received the treatment in hospital (n = 230). Both cohorts received either accelerated rtPA or a streptokinase infusion administered over 60 minutes. In addition, out-of-hospital treatment provided by either paramedics or GPs required both a positive human and device diagnosis of STEMI on 12-lead ECG. This meant that the paramedic or GP had to interpret ST-elevation infarction on the patient's ECG, as did the heart monitor's diagnostic software (termed the automated interpretation). In cases of discordance, fibrinolysis was withheld.

Results of the REPAIR study showed that the overall time gain achieved through the delivery of fibrinolysis in the field was 50 minutes, with the median time from first medical contact to initiation of the treatment being 18 minutes versus 68 minutes for the in-hospital cohort (p = <0.001) (Grijseels et al., 1995). Moreover, the proportion of patients among the out-of-hospital cohort who received treatment within the first hour

from symptom onset increased from 19% initially to 40% over the study's duration. By contrast, this was achieved in only 1% of patients in the control group. The rate of complications among the out-of-hospital cohort was also shown to be exceedingly low, although there was erroneous inclusion of seven patients without STEMI who received fibrinolysis (false positive rate of 1%). This was primarily due to technical issues, i.e. electrocardiographic artefact and subsequent false-positive automated interpretation. Finally, in-hospital mortality among those patients who received treatment in the field was 2%, one-year mortality was 3%, and cumulative survival at five years was 92%. Although this was superior to the 84% five-year survival of the control group, it was not shown to be significant.

The Dutch paramedics in the REPAIR study were all trained nurses with either coronary care or intensive care experience, and had completed six years of education in their respective fields prior to joining the ambulance service (Grijseels et al., 1995). Dedicated university-based paramedic education was non-existent at the time, which suggests that the paramedics' education was predominantly nursing-based and not specific to the out-of-hospital environment. In terms of the study's results, the survival rates among those patients who received out-of-hospital care were impressively high, with approximately 74% of this group receiving treatment within two hours from symptom onset. The number of false positive cases (1%) may also be considered acceptable, although modern ECG technology would be expected to yield more accurate diagnostic decision support.

The second and third identified studies exploring autonomous paramedic-delivered fibrinolysis were both UK-based (Keeling et al., 2003; Pitt, 2002). The first of these was a prospective study involving 19 rural ALS paramedics who underwent additional specialist training to independently provide fibrinolysis in the management of STEMI and according to a strict patient inclusion criteria (Pitt, 2002). The paramedics were required to document the notional time at which they would have provided the treatment to patients they had attended, as well as the 'actual' time the treatment was provided in the ED by the receiving physician. In addition, the receiving ED physician's patient diagnosis served as the standard. In summary, in terms of the accuracy of paramedic selection in determining those patients who were eligible for treatment, specificity was 100% (95% CI, 95.9% to 100%), identifying no errors in case selection. The mean notional CTN time was 25.7 minutes, implying a time saving of 41.2 minutes (95% CI, 25.7 to 56.9 minutes, $p = 0.001$). A wide confidence interval of 24.8% to 69.9%

was also shown around the sensitivity of the paramedics' treatment decision. The study's author attributed this to the small patient sample size (n = 96) and the number of patients eligible for treatment.

The second study by Keeling et al. (2003) involved a larger cohort of 64 ALS paramedics who again were provided additional specialist training in diagnosing STEMI and assessing patient eligibility for fibrinolysis. In contrast, however, the study was superimposed on an existing programme where paramedics alerted the receiving hospital via radio from the field when they were en route with a STEMI patient. Fibrinolysis was only provided by the receiving physician in the ED following patient re-assessment. Prior to notification of the hospital, paramedics were required to document if they believed fibrinolysis was indicated, as well as the notional time at which they would have independently provided the treatment. The receiving ED physicians' diagnosis and the actual CTN time served as the standard. The accuracy of paramedic selection in determining those patients who were eligible for treatment showed a sensitivity score that was much lower in comparison to the ED physicians (71% versus 90%, p = 0.001). However, the paramedics' specificity scores were higher (97% versus 94%, p = 0.001) and the median notional CTN time (the paramedic's decision) was 48 minutes earlier than actual CTN time (when fibrinolysis was provided in hospital).

Although these studies by Pitt (2002) and Keeling et al. (2003) both involved notional times for hypothetical paramedic-delivered fibrinolysis without physician oversight, these notional administrations were intentionally superimposed onto actual real-time ambulance call-outs involving real patients. This enhanced the validity of the experiment. However, although both studies produced compelling results, issues have been raised relative to their methodology. The study by Pitt (2002) shows evidence of paramedic participant selection bias. Of the 40 paramedics contacted to participate, 24 agreed but only 19 (79%) ultimately contributed. These paramedics predominately worked from one of only three rural stations, and therefore the generalisability of the study's findings may be questionable due to the sample group under-representing the greater paramedic population. There may also have been an element of patient selection bias, given the paramedics predominately responded to calls closer to their respective stations. Finally, both studies required the paramedics to document a notional time at which they would have provided fibrinolysis to patients in the field. However, there was no strategy to prevent paramedics from documenting their decision or time in hindsight –

that is, once they had arrived at hospital and after patient assessment by the receiving physician. This would denote a potential measurement bias.

The last research discussed was also a retrospective observational study and was conducted in south-east Scotland over a 20-month period (McLean et al., 2008). These authors reviewed an existing multi-faceted programme for out-of-hospital fibrinolysis involving up to 160 ALS paramedics. The programme directed paramedics to acquire and transmit a 12-lead ECG to the receiving hospital's CCU for all 'potential' cardiac chest pain patients. The transmitted ECG was viewed by either a CCU nurse or junior registrar who would then telephone the paramedic to provide decision support for fibrinolysis if STEMI was present. In the event of transmission failure, the paramedics were encouraged to telephone the CCU and describe the ECG changes. Although this process of collaborative decision making was in place, the paramedics, as autonomous practitioners, could ultimately choose to provide fibrinolysis or not, regardless of the advice given by the CCU staff. Interestingly, this did not occur during the 20-month reporting period. In this study, those patients who received fibrinolysis by paramedics in the field were compared to a second cohort of patients who self-presented to one of the three receiving hospitals over the same time period.

During the study period 544 STEMI patients were attended to by paramedics, of which 146 received fibrinolysis in the field (27%), 247 received the treatment in hospital (45%) and the remaining 151 (28%) were deemed ineligible for treatment (McLean et al., 2008). Of those patients who received treatment in the field, approximately 130 (89%) had a CTN time of less than 60 minutes. When compared to the hospital cohort, there was a significant reduction in CTN time among those patients treated by paramedics (median of 40 minutes versus 86 minutes, $p < 0.001$). This was also the case with PTN time (median of 91 minutes versus 148 minutes, $p < 0.001$). Although the study's authors demonstrated the effectiveness of paramedic-delivered fibrinolysis to expedite early reperfusion, independent decision making by the paramedics without consultation did not occur.

In these four studies, no clear information was provided on the paramedics' clinical rationale or the accuracy of their 12-lead ECG interpretation, both of which are important fundamental components in the diagnosis of STEMI and determining patient eligibility for fibrinolysis. However, other research has demonstrated a high degree of proficiency in 12-lead ECG recognition of STEMI by paramedics, particularly when

compared to physician interpretation (Feldman, Brinsfield, Bernard, White, & Maciejko, 2005; Whitbread, Leah, Bell, & Coats, 2002).

One example was by Feldman et al. (2005) who undertook a prospective study in the US involving 41 metropolitan ALS paramedics who were required to complete a six-hour training course. Course content included both ECG interpretation with an emphasis on the diagnostic characteristics of STEMI, as well as the pathophysiology of ACS. Paramedics were then tasked with obtaining 12-lead ECGs on patients they attended over an eight-month period and with a clinical suspicion of AMI, excluding those patients with left bundle branch block (LBBB) and paced rhythms. Paramedic ECG interpretation was conducted in real-time and recorded on a data collection form. All ECGs collected were later reviewed by an independent emergency physician and cardiologist and without patient clinical data (blinded physician ECG review). A third physician blinded to both the paramedic and physician 12-lead ECG interpretation determined final diagnoses of STEMI utilising the criteria of the World Health Organisation (WHO). A total of 151 patient 12-lead ECGs were selected over the eight-month period with a prevalence of STEMI at 16.6% (95% CI, 11%–25.3%). Paramedic sensitivity was identified at 0.80 (95% CI, 0.64–0.96), specificity was 0.97 (95% CI, 0.94–1.00), the positive predictive value (PPV) was 0.83 (95% CI, 0.68–0.98) and the negative predictive value (NPV) was 0.94 (95% CI, 0.90–0.98). These results were comparative to those of the ED physician and cardiologist, and there was no statistical difference in the overall level of accuracy between the paramedics and two physicians (0.94, 0.93 and 0.95 respectively). The level of agreement between all three paired readings, i.e. paramedic-ED physician, paramedic-cardiologist and ED physician-cardiologist, was also shown to be substantial (k of 0.73, 0.67 and 0.79 respectively).

Hatala, Norman and Brooks (1999) have demonstrated that the provision of patient clinical history accompanying an ECG can improve accuracy of interpretation by 4–12%, depending on the health practitioner's level of expertise. This is why Feldman and colleagues chose to examine the accuracy of the paramedics' ECG interpretation in a real-world out-of-hospital setting, where they clinically assessed the patient as part of their provisional diagnosis. This enhanced the study's validity and provided greater insight into the paramedics' ability to determine candidates for reperfusion therapy. In the New Zealand context, the accuracy of paramedic ECG interpretation and determination of those patients eligible for reperfusion therapy is a key measure among the three studies presented in this thesis and discussed in the following chapters.

Table 2.1 provides a summary of all out-of-hospital versus in-hospital fibrinolysis studies discussed in the preceding sections.

Table 2.1 ***Summary of Out-of-hospital Versus In-hospital Fibrinolysis Studies Reviewed***

Year	Reference	Location	Design	Fibrinolytic Agent	*n*	Out-of-Hospital Treatment Provider	Key Significant Results
1989	(Castaigne et al., 1987)	France	RCT	Anistreplase	100	Physician	Reduced PTN & CTN time with out-of-hospital cohort versus in-hospital (both $p = 0.001$).
1989	(McNeill et al., 1989)	Ireland	Double-blinded RCT	Alteplase	57	Physician	Reduced PTN & CTN time with out-of-hospital cohort versus in-hospital (both $p = 0.0005$) as well as greater infarct-related regional third EF among out-of-hospital cohort (mean value 41 versus 28, $p = 0.05$).
1990	(A. Roth et al., 1990)	Israel	Double-blinded RCT	Alteplase	118	Physician	Reduced PTN time with out-of-hospital cohort versus in-hospital (mean time 94 minutes versus 137, $p = 0.001$) and trend to lower incidence of CHF among out-of-hospital cohort (7% versus 16%, p = NS).
1990	(Schofer et al., 1990)	Germany	Double-blinded RCT	Urokinase	78	Physician	Reduced PTN time with out-of-hospital cohort versus in-hospital (mean time 85 minutes versus 137, $p < 0.0005$). No difference in mortality rates, complications or IRA patency rates between groups.
1992	(McAleer et al., 1992)	Ireland	Double-blinded RCT	Streptokinase	145	Physician	Reduced PTN time with out-of-hospital cohort versus in-hospital (median time 138 minutes versus 172, $p < 0.02$) as well as reduced 14-day, six-month and one-year mortality in favour of out-of-hospital cohort ($p < 0.05$, $p = 0.03$ & $p = 0.04$ respectively).

Note: RCT = randomised control trial; GREAT = Grampian region early anistreplase trial; PTN = pain-to-needle; CTN = call-to-needle; EF = ejection fraction; CHF = congestive heart failure; NS = not significant; IRA = infarct-related artery; RRR = relative risk reduction; CI = confidence interval

Table 2.1 (continued)

Year	Reference	Location	Design	Fibrinolytic Agent	*n*	Out-of-Hospital Treatment Provider	Key Statistically Significant Results
1992	(GREAT Group, 1992)	Scotland	Double-blinded RCT	Anistreplase	311	Physician	Reduced PTN time with out-of-hospital cohort versus in-hospital (median time 101 minutes versus 240, $p < 0.002$), greater RRR of death for out-of-hospital cohort -49% (13/163 (8.0%) versus 23/148 (15.5%); difference −7.6% (95% CI −14.7% to −0.4%), $p = 0.04$), as well as reduced Q wave infarction - 65/122 (53.3%) versus 76/112 (67.9%); difference − 14.6% (95% CI −27.0%) to 2.2% ($p = 0.02$).
1993	(EMIP Group, 1993)	Europe & Canada	Double blinded RCT	Anistreplase	5289	Physician	Reduced PTN time with out-of-hospital cohort versus in-hospital (median time 130 minutes versus 190, $p < 0.003$) as well as a reduction of 17% in overall short-term mortality (95 % CI, 2 to 29%; $p = 0.03$) among those patients treated in the field.
1993	(Weaver et al., 1993)	United States	RCT	Alteplase	357	Paramedic (physician-assisted)	Reduced PTN time with out-of-hospital cohort versus in-hospital (median 77 minutes versus 110, $p < 0.001$) and reduced infarct territory with treatment provision within 70 minutes.
1995	(Grijseels et al., 1995)	The Netherlands	Prospective observational	Alteplase/ Streptokinase	768	Paramedic (autonomous)	Reduced FMCTN time with out-of-hospital cohort versus in-hospital (median 18 minutes versus 68, $p < 0.001$) as well as improved long-term (five-year) survival among out-of-hospital cohort (92% versus 84% survival).
2002	(Pitt, 2002)	United Kingdom	Prospective observational	n/a	96	Paramedic (autonomous)	Notional autonomous paramedic experiment with a potential reduction in CTN time of 41.2 minutes (95% CI 25.7 minutes to 56.9 minutes, $p = 0.001$) in favour of out-of-hospital treatment and with paramedic case selection specificity of 100%.

Note: EMIP = European Myocardial Infarction Project; RCT = randomised control trial; PTN = pain-to-needle; FMCTN = first medical contact-to-needle; CTN = call-to-needle; CI = confidence interval

Table 2.1 (continued)

Year	Reference	Location	Design	Fibrinolytic Agent	*n*	Out-of-Hospital Treatment Provider	Key Statistically Significant Results
2003	(Dussoix et al., 2003)	Sweden	RCT	Tenecteplase	18	Physician	Reduced PTN time with out-of-hospital cohort versus in-hospital (median 152 minutes versus 251, p = 0.0004), as well as FMCTN time (median 26 minutes versus 94, $p < 0.0004$).
2003	(Lamfers et al., 2003a)	The Netherlands	Retrospective controlled observational	Anistreplase/ Retaplase	744	Paramedic (physician-assisted)	Time-to-treatment was shorter among patients with aborted myocardial infarction (median of 86 minutes versus 123, p = 0.05), resulting in a fourfold increase in aborted myocardial infarction among the out-of-hospital cohort versus in-hospital.
2006	(Björklund et al., 2006)	Sweden	Prospective observational	Reteplase	5375	Paramedic (physician-assisted)	Reduced PTN time with out-of-hospital cohort versus in-hospital (median 113 minutes versus 165, p = 0.003) and out-of-hospital treatment was associated with a lower one-year mortality (odds ratio 0.71, 0.55–0.92, p = 0.008).
2008	(McLean et al., 2008)	Scotland	Retrospective observational	Tenecteplase	297	Paramedic (physician/nurse-assisted and autonomous)	Reduced PTN time with out-of-hospital cohort versus in-hospital (median 91 minutes versus 148, p = 0.002) as well as a 1.3% inappropriate treatment rate by paramedics among the out-of-hospital cohort.
2009	(Jackson et al., 2009)	United Kingdom	Retrospective observational	Tenecteplase	454	Paramedic (physician-assisted)	Reduced PTN time with out-of-hospital cohort versus in-hospital and with 69% of patients receiving treatment within two hours or less compared with 40.4% among the in-hospital cohort ($p < 0.001$). Aborted infarction more likely among those patients treated within two hours from symptom onset, although no difference in rates of aborted infarction observed between cohorts.
2009	(Ranchord et al., 2009)	New Zealand	Retrospective observational	Reteplase	100	Paramedic (physician-assisted)	Reduced ETN time among those patients treated in the field versus those transferred to hospital to receive treatment (44 minutes versus 133, $p < 0.0001$). Reduced incidence of CHF among out-of-hospital cohort versus in-hospital (10% vs. 26%, p = 0.04).

Note: PTN = pain-to-needle; CTN = call-to-needle; ETN = emergency medical services contact-to-needle; CHF = congestive heart failure

2.7 Fibrinolytic Agents and Adjunctive Drug Regimes for Paramedic Programmes

In-depth discussion and analysis of the various fibrinolytic agents and adjunctive drug regimens used in the treatment of STEMI is an expansive subject and not within the remit of this thesis. Therefore, this section will provide a brief history and review of the subject before focussing on several topics relevant to the clinical trial undertaken as part of this thesis, presented in Chapter Four. These include: influencing factors in the choice of fibrinolytic agent used specifically by paramedics in the field; fibrinolysis drug regimens currently recommended within Australasian guidelines; and the regimen that was utilised for our clinical trial.

Fletcher, Alkjaersig, Smyrniotis and Sherry (1958) were the first to discuss fibrinolytic therapy in the management of AMI utilising streptokinase (SK), the first drug developed within this class. As a result, a transition from palliative care to treatment of the AMI patient occurred (Sikri & Bardia, 2007). However, this study, along with others over the following two decades, produced equivocal results due to their size and methodology. It was not until the 1980s, through advancements in angiographic imaging coupled with the findings from several large in-hospital RCTs, that the true benefit of fibrinolysis was established by demonstrating significant reductions in mortality (AIMS Trial Study Group, 1988; Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico, 1986; Wilcox et al., 1988).

At the time, the mechanism by which fibrinolytic agents were thought to produce their therapeutic benefit was through reperfusion of the infarct related artery (IRA) following lysis of the occluding thrombus, referred to as the ‘open artery hypothesis’ (Liverpool Reviews and Implementation Group, 2002). This was later confirmed by the Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO-I) trial which compared the use of four fibrinolytic and adjunctive drug therapy regimes (Topol et al., 1993). The trials in the 1980s helped to establish fixed protocols for the use of fibrinolytic agents in the treatment of STEMI, and large multi-centred in-hospital RCTs continued in the 1990s, comparing the efficacy between the various agents (Gruppo Italiano Per Lo Studio Della Sopravvivenza nell'Infarto Miocardico, 1990; The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators, 1997; The International Study Group, 1990).

The comparative efficacy of each fibrinolytic agent in the out-of-hospital setting has not been established and therefore conclusions must be drawn from hospital-based trials. Overall, the evidence shows there is no consistent or significant difference between these various agents in terms of the risk of minor or major bleeding, reinfarction rates or response to drug by age, by time to receiving the treatment or by site of infarct (Liverpool Reviews and Implementation Group, 2002). Mortality rates also seem to be similar, although the GUSTO investigators demonstrated that an accelerated alteplase regimen resulted in lower mortality rates compared to SK (Topol et al., 1993). Unsurprisingly, this group also established that a close correlation existed between culprit artery patency rates and mortality rates (Topol, Califf, & Lee, 1994).

The biological mechanism by which fibrinolytic agents work is through activation of the endogenous fibrinolytic pathway, specifically the conversion of plasminogen into plasmin, a serine protease that acts to dissolve the fibrin mesh of formed thrombi (Ouriel, 2004). The extent to which this process occurs is dependent on how recently the offending thrombus was formed, as older thrombi undergo extensive fibrin polymerisation, making them more resistant to fibrinolysis; hence the importance of timely receipt of treatment (Hoffman et al., 2009). Fibrinolytic agents are categorised as fibrin-specific or non-fibrin-specific. Fibrin-specific agents include alteplase, reteplase and tenecteplase, and are classified as such due to their limited plasminogen conversion in the absence of fibrin, resulting in these agents attaining higher early patency rates in the culprit artery (Hoffman et al., 2009). By contrast, SK and urokinase are non-fibrin-specific agents that catalyse systemic fibrinolysis and degrade systemic fibrinogen, the precursor to fibrin, along with other plasma proteins. This results in the destruction of thrombi existing in other parts of the body and prevents new thrombi from developing (Hoffman et al., 2009; Sikri & Bardia, 2007).

The choice of fibrinolytic agent used by paramedics in the field is driven by several variables, primarily convenience and cost. Fibrin-specific agents are the most practical and preferred by EMS providers as they have a longer shelf life, do not require refrigeration and can be delivered via IV bolus administration. Fibrinolytic agents requiring complex dosing regimens may provide opportunities for dosing errors (C. P. Cannon, Sayah, & Walls, 2000). This was established in the GUSTO-1 trial, where 11.5% of patients treated with alteplase via an initial IV bolus followed by two infusions did not receive the correct drug dose or method of administration (Topol et al., 1993). This resulted in the mortality rate among this group being more than twice that of patients who

received the drug correctly. For administration of drugs via an infusion, the most accurate means of delivery is with the use of a syringe driver. However, these are expensive items of equipment that are not commonly used on road ambulances internationally and are not currently used by either of New Zealand's EAS providers.

Reteplase (rPA) and tenecteplase (TNK) are both delivered via IV bolus administration, rPA is administered as two boluses 30 minutes apart and TNK as a single bolus from a weight-graduated syringe. Use of these bolus-administered agents by paramedics in the field has not only helped to simplify the process, but have also transformed the management of STEMI patients, reducing overall one-month mortality for those who receive timely treatment (Danchin et al., 2008). As a result, despite its greater cost, TNK is the most widely used fibrinolytic agent in the treatment of STEMI throughout the world (including New Zealand) in both the out-of-hospital and in-hospital setting and is recommended as the agent of choice by numerous treatment guideline groups (National Institute of Health & Clinical Excellence, 2002; ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013).

To summarise, Table 2.2 provides detailed characteristics of the three main fibrinolytic agents currently used in the treatment of STEMI within New Zealand.

Table 2.2 ***Characteristics of Fibrinolytic Agents used in the Treatment of STEMI Within New Zealand***

	Fibrinolytic Agent		
	Alteplase	Reteplase	Tenecteplase
Administration	Infusion (weight-based given over 90 minutes)	Bolus (repeated after 30 minutes)	Bolus (weight adjusted)
Fibrin specific	Yes++	Yes+	Yes+++
Systemic fibrinogen depletion	+	++	Minimal
Bleeding (non-cerebral)	++	++	+
Haemorrhagic stroke	++	++	++
Antigenic	No	No	No
Hypotension with administration	No	No	No
TIMI flow grade 3 at 90 minutes	54	60	63
Cost	++	+++	++++

Note: TIMI = time in myocardial infarction. Adapted from "ST-elevation myocardial infarction: New Zealand management guidelines," by ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand branch of the Cardiac Society of Australia and New Zealand, 2005, *The New Zealand Medical Journal*, *118*, p. 9. Copyright 2005 by the New Zealand Medical Association.

In terms of adjunctive drug treatment for use in the out-of-hospital setting among those patients who receive fibrinolysis, Australasian guidelines recommend dual antiplatelet therapy, namely aspirin and clopidogrel, as well as a low molecular weight heparin (LMWH), i.e. enoxaparin (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013). Combined, these agents have been shown to improve pharmacological reperfusion therapy (Patrono, Baigent, Hirsh, & Roth, 2008).

Aspirin is the most widely studied antiplatelet agent and its additive effect in reducing mortality among AMI patients was first established in the second International Study of Infarct Survival trial (ISIS-2) (ISIS-2 Collaborative Group, 1988). This was a 2×2 factorial placebo-controlled trial of aspirin and streptokinase that recruited 17,187 patients. The trial demonstrated that oral aspirin administered alone within the first four hours of symptom onset resulted in a 25% relative risk reduction (RRR) of death. Moreover, a combination of streptokinase and aspirin administered within the same time period resulted in a 53% RRR of death. In a meta-analysis of more than 200 randomised trials, the Antithrombotic Trialists' Collaboration Group (2002) also established that aspirin was found to prevent vascular death by approximately 15% and non-fatal vascular events by around 30% in high-risk patients.

Aspirin's mechanism of action as an antiplatelet agent is to irreversibly acetylate and inactivate cyclo-oxygenase (COX) activity of prostaglandin H-synthase-1 and -2 (also referred to as COX-1 and COX-2) (G. J. Roth & Majerus, 1975). These enzymes are responsible for membrane arachidonic acid conversion, which ultimately leads to the synthesis of prostaglandins such as thromboxane A2 (TXA2) (Patrono et al., 2008). Released by platelets, TXA2 causes platelet aggregation and localised blood vessel constriction as part of the haemostasis and thrombus production process (Patrono, García Rodríguez, Landolfi, & Baigent, 2005). Aspirin's irreversible inhibiting of both platelet release and aggregation lasts the lifespan of the platelet, about eight to 10 days in humans (Loll, Picot, & Garavito, 1995). The current recommended dose of aspirin for all patients receiving fibrinolysis in the management of STEMI is 150 to 300mg per oral (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013). Evidence shows that a dose beyond this recommended range may result in increased bleeding (Yusuf et al., 2001).

There is a consistent finding of a favourable benefit/risk profile of dual antiplatelet therapy provided to patients with ACS, particularly aspirin and clopidgrel (Chen, Jiang, Chen, & Xie, 2005; Sabatine et al., 2005; Yusuf et al., 2001). In terms of utilising these drugs as part of an adjunctive regimen for fibrinolysis in the management of STEMI, Sabatine et al. (2005) were some of the first to establish the combined benefit in the Clopidogrel as Adjunctive Reperfusion Therapy – Thrombolysis in Myocardial Infarction (CLARITY-TIMI) 28 trial. This was a hospital-based RCT that enrolled 3491 patients and established that the addition of clopidogrel versus placebo with aspirin and a standard fibrinolytic regimen resulted in a lower incidence of occluded IRA as the primary endpoint (21.7% in the placebo group versus 15% in the clopidogrel group). In addition to this absolute reduction of 6.7%, a 36% reduction in the odds of the endpoint with clopidogrel therapy was also shown (95% CI, 24 to 47%, $p < 0.001$). Moreover, ischaemic complications were reduced among those patients in the experimental group.

These findings by Sabatine et al. (2005) were also congruent with those of the Clopidogrel and Metoprolol Myocardial Infarction trial (COMMIT) which enlisted 45,852 patients admitted to 1250 hospitals within 24 hours of suspected AMI (Chen et al., 2005). Here it was identified that the allocation of both clopidogrel and aspirin versus aspirin and placebo resulted in a 9% (95% CI, 3 to 14%) proportional reduction in mortality and major vascular events in hospital ($p = 0.002$) without any increased risk of transfused, fatal or cerebral bleeds.

In terms of clopidogrel's mechanism of action, as a prodrug its active metabolite selectively and irreversibly inhibits an adenosine diphosphate (ADP) chemoreceptor on the platelet cell membrane (Coukell & Markham, 1997; Pereillo et al., 2002). This in turn inhibits ADP-mediated activation of the GPIIb/IIIa complex, inhibiting platelet aggregation for the remainder of the cell's lifespan and subsequently impairing thrombus growth (Pereillo et al., 2002). The current recommended dose of clopidogrel for patients receiving fibrinolysis treatment in the management of STEMI is 300mg per oral for those patients under 75 years and 75mg for those patients 75 years or over (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013).

The benefits of early reperfusion therapy in the setting of AMI may be abrogated due to reocclusion of the culprit artery (Prins & Hirsh, 1991). As an anti-thrombotic/anti-coagulant, adjunctive heparin therapy is recommended for administration: a) immediately with fibrin-specific fibrinolytic agents in the treatment of STEMI, and b) as an option with the use of the non-fibrin specific streptokinase due to the increased risk of adverse bleeding (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013; F. Van de Werf et al., 2008). Adjunctive heparin therapy is essential in order to maintain patency of the culprit artery following administration of the fibrinolytic agent as the fissured atherosclerotic plaque surface remains highly thrombogenic (Prins & Hirsh, 1991). Historically, conventional unfractionated heparin (UFH) has been utilised and administered via an infusion. However, following the results of several large clinical trials over the last 10 to 15 years, the LMWH enoxaparin has emerged as the preferred adjunctive anti-thrombotic agent due to its superior clinical effectiveness and ease of administration, i.e. IV and SC bolus (Antman et al., 2006; Welsh et al., 2004).

Investigators within the Assessment of the Safety and Efficacy of a New Thrombolytic 3 (ASSENT 3) trial (n = 6095), an in-hospital RCT, were some of the first to demonstrate the benefits of enoxaparin versus UFH following testing of three drug regimens among STEMI patients presenting within six hours from symptom onset (The Assessment of the Safety Efficacy of a New Thrombolytic Regimen Investigators, 2001). These regimens included: full-dose TNK and enoxaparin for a maximum of seven days (n = 2040); half-dose TNK with weight-adjusted low-dose UFH and a 12-hour infusion of abciximab, a glycoprotein IIb/IIIa receptor antagonist/antiplatelet aggregator (n = 2017); or full-dose TNK with weight-adjusted UFH for 48 hours (n = 2038). The primary

endpoints for the trial were the composites of 30-day mortality, in-hospital reinfarction, or in-hospital refractory ischaemia. The results showed a significant reduction in all three of these components among those patients who received enoxaparin versus UFH – 233/2037 (11.4%) versus 315/2038 (15.4%; relative risk 0.74 [95% CI 0.63-0.87], p = 0.0002) in favour of enoxaparin.

Findings of the ASSENT 3 trial were further supported by the Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment, Thrombolysis in Myocardial Infarction 25 (ExTRACT-TIMI 25) mega-trial (n = 20,479 patients) (Giraldez et al., 2007). Patients suffering STEMI were randomised to a strategy of either enoxaparin or UFH to support fibrinolysis (either TNK or SK). The results showed 30-day death and non-fatal recurrent AMI occurred significantly less among those patients who received enoxaparin: 12.0% in the UFH group versus 9.8% in the enoxaparin group (odds ratio adjusted 0.78; 95% CI 0.70–0.87; $p < 0.001$). Despite the enoxaparin cohort exhibiting an increase in major bleeding rates, including intra-cranial haemorrhage (ICH), the study's collective results demonstrated an overall clinical benefit with adjunctive enoxaparin therapy versus UFH, regardless of the fibrinolytic agent utilised.

In terms of heparin's mechanism of action, it binds to the naturally occurring enzyme inhibitor anti-thrombin III (AT), initiating a conformational change that facilitates AT's activation, and allowing it to then inactivate thrombin and other proteases such as factor Xa essential to thrombus formation (Chuang, Swanson, Raja, & Olson, 2001). When AT is bound with heparin, the enzyme inhibitor's inactivation of proteases involved in the clotting cascade may increase up to 1000-fold (Björk & Lindahl, 1982). In addition, activation of AT via low molecular weight derivatives of heparin, such as enoxaparin, results in greater inhibition of factor Xa, which is responsible for catalysing the conversion of prothrombin to thrombin (Chuang et al., 2001). A more subtle regulation of haemostasis is therefore achieved, coupled with an improved therapeutic index (Petitou et al., 1999).

To conclude, Table 2.3 provides a summary of the current recommended New Zealand out-of-hospital fibrinolysis drug regimen for the management of STEMI. This was also the regimen utilised in the clinical trial discussed in Chapter Four.

Table 2.3 ***New Zealand Out-of-Hospital Fibrinolysis Drug Regimen for the Management of STEMI***

If the patient is under 75 years
▪ 300mg aspirin PO ▪ 300mg clopidogrel PO ▪ 0.5mg/kg of tenecteplase IV (up to a maximum of 100kg) ▪ 30mg of enoxaparin IV ▪ 1mg/kg of enoxaparin SC
If the patient is aged 75 years or over
▪ 300mg aspirin PO ▪ 75mg clopidogrel PO ▪ 0.25mg/kg of tenecteplase IV (up to a maximum of 100kg) ▪ 0.75mg/kg of enoxaparin SC

Note: IV = intravenous; SC = subcutaneous. Adapted from "ST-elevation myocardial infarction: New Zealand management guidelines," by ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013, *The New Zealand Medical Journal*, *126*, p. 133 & 141. Copyright 2013 by the New Zealand Medical Association.

2.8 Patient Eligibility for Paramedic-Delivered Fibrinolysis

Historically, the inclusion and exclusion criteria for paramedic-delivered fibrinolysis in the out-of-hospital setting, regardless of the model of delivery utilised, have been more stringent than for physician-led hospital-based protocols. As a result, fewer patients are eligible to receive the treatment in the field. This conservative approach adopted by ambulance providers is predominantly aimed towards safety, simplifying the procedure and reducing the risk of inappropriate patient selection for the treatment, and is also reflective of paramedic education, training and experience (Grijseels et al., 1995; Keeling et al., 2003; McLean et al., 2008). Of note, the risk of inappropriate treatment tends to raise more concern among ambulance providers than the omission of treatment that is indicated (Pitt, 2002). In addition, EMS personnel often have limited access in the field to accurate patient information that may assist them in their clinical decision making, compared to that which is available to hospital-based physicians through department database systems (Keeling et al., 2003).

Through a retrospective descriptive analysis conducted in the US, Weaver et al. (1990) reviewed the clinical notes of 453 STEMI patients who received fibrinolysis in hospital in order to determine the proportion that would have met local paramedic protocols to receive the treatment in the field. The results identified that only 105 patients (23.9%) were eligible for out-of-hospital treatment. In the UK, Castle, Owen, Vincent and Ineson (2006) undertook an almost identical project reviewing the clinical notes of 126 STEMI patients. Their results showed that even fewer patients (14.2%) met the

established national out-of-hospital treatment criteria. Hyper/hypotension was identified as the most common exclusion factor (50%), followed by onset of symptoms being greater than six hours (41.7%), and patient age greater than 75 years (37%). It was also identified that two or more contraindications to treatment were present with 63.9% of the patients reviewed. These findings were also consistent with that of other UK-based studies (Hanson & Williamson, 2006; Pitt, 2002).

One influencing factor in the provision of out-of-hospital fibrinolysis by paramedics is that cyclic variations in the ST segment during the early stages of an AMI may mean that many patients who are ultimately eligible for the treatment may not present with the necessary ECG criteria in the early stages of infarction (Krucoff et al., 1993). In addition, as previously illustrated by Castle and colleagues, age excludes a number of patients from receiving paramedic treatment, with many protocols excluding those over 75 years old. The basis of this age criteria was first discussed by Thiemann et al. (2000) in a retrospective cohort study (n = 7864) that sought to specifically determine the benefit of fibrinolysis in the elderly. Here the investigators found that among those patients aged 76 to 86 years (33.9%, n = 2673), the treatment was associated with a survival disadvantage due to an increased risk of bleeding (particularly ICH) and with a 30-day mortality hazard ratio of 1.38 (95% CI 1.12 to 1.71, p = 0.003). However, these results were contradictory to those of the Fibrinolytic Trialists Collaborative Group (1994), which reviewed nine randomised trials enlisting a total of 58,600 patients, of which 3300 were over the age of 75 years. Their findings established that fibrinolysis significantly reduced mortality within this group (29.4 to 26.0%, p = 0.03) and that although the risk of serious bleeding for older patients was proportionally higher, the net benefit of the treatment remained acceptable if provided within 12 hours of symptom onset.

White (2000) discussed these disparate reports, highlighting the rigour of randomised trials and their ability to more accurately determine the true benefit of a treatment intervention versus an observational approach. Ayanian and Braunwald (2000) concurred with this opinion. Furthermore, it was established in the ISIS-2 mega-trial that age was not a factor in the degree to which fibrinolytic therapy lysed thrombi within the culprit artery (ISIS-2 Collaborative Group, 1988). Angiographic data from the GUSTO-I trial also identified that post-fibrinolysis, patency of the culprit artery as determined by TIMI grade flow occurred to a similar extent in patients aged above and below 75 years (Topol et al., 1993).

In New Zealand we have an aging population, with an exponential increase in life expectancy calculated each year. Currently the average lifespan is 80 years for males and 83.3 years for females, with a combined average of 81 years (Statistics New Zealand, 2017a). In addition, the overwhelming majority of patients attended to by New Zealand's emergency ambulance services are elderly and present with extensive co-morbidities. Therefore, given all the information provided, there seems little basis for denying fibrinolysis and its potential benefits to elderly patients presenting with STEMI and without contraindications to the treatment.

Expansion of the inclusion and exclusion criteria for paramedic-delivered fibrinolysis that is more closely aligned with hospital-based protocols is likely to occur as EMS education and experience grows. Moreover, increasing confidence in the capabilities of paramedics by EAS medical directors, along with hospital coronary care and ED directors, may also influence advancements/changes in out-of-hospital protocols. Regular re-evaluation of these protocols is therefore essential so that more patients may be eligible to receive the treatment.

The inclusion and exclusion criteria used within this thesis for the paramedic-based clinical trial discussed in Chapter Four are more reflective of the conservative approach adopted previously within New Zealand, but with a greater age limit.

2.9 Clinical Complications Associated with Out-of-Hospital Fibrinolysis

Several studies and reports have reviewed the incidence of clinical complications associated with out-of-hospital fibrinolysis and this consistently appears to be low (Benger, 2002; Chamberlain et al., 2001; Cooke, 2007; P. Davis, 2014; Grijseels et al., 1995; Ranchord et al., 2009). Despite the development of several bioengineered fibrinolytic agents, the primary and most consequential complication of the treatment remains bleeding. Identifying complications that are directly attributed to fibrinolysis beyond minor or major haemorrhaging is difficult, as STEMI patients are often prone to acute deterioration in a variety of ways. As an antigenic bacterial product, SK may incite an allergic response but its use has significantly declined over the last decade in favour of fibrin-specific agents.

Minor haemorrhaging is classified as non-life threatening and may include bleeding from venepuncture sites or the gums (Schulman, Beyth, Kearon, & Levine, 2008). Conversely, major haemorrhage has been variously defined as: intracranial or retroperitoneal haemorrhage; bleeding resulting in death, hospitalisation or the need for a blood infusion (Schulman et al., 2008). Intra-cranial haemorrhage (ICH), the most ominous type of haemorrhage associated with fibrinolysis, has proven to be a rare complication, particularly in the out-of-hospital setting with an overall occurrence of 1–1.5% (Cooke, 2007; Oldgren, Wernroth, & Stenestrand, 2010; Schulman et al., 2008). For patients presenting without any apparent contraindications to fibrinolysis, the greatest independent risk factor for ICH appears to be advanced age, followed by low bodyweight (less than 70kg) and hypertension (Schulman et al., 2008). In a UK national audit of paramedic-delivered fibrinolysis from 2000 to 2006 using rPA and TNK (n = 7005), there were no documented cases of ICH in the field (Cooke, 2007). However, it appears evident that the time taken for the pathology to develop may exceed the period of transportation to hospital by ambulance. Therefore, unless patient follow-up has occurred, the true incidence of ICH associated with out-of-hospital fibrinolysis may not be captured.

In the REPAIR randomised trial involving autonomous paramedic decision making, no significant bleeding or death was reported among those patients who received fibrinolysis in the field (n = 529) and prior to arrival at hospital (Grijseels et al., 1995). Approximately 3% of these patients suffered sudden cardiac arrest (SCA) either prior or during transport, but all were successfully resuscitated by the attending paramedics. From a New Zealand perspective, combined results from both the Kapiti Coast, Northland and Hawke's Bay paramedic fibrinolysis programmes (n = 146) showed that SCA occurred among fifteen patients in the field (10.2%) post-treatment, of which all but one patient was successfully resuscitated (P. Davis, 2014; Ranchord et al., 2009). There were no further documented cases of significant complications (including major bleeding).

In the Swedish study reported by Benger et al. (2002) (n = 98), for those patients who received fibrinolysis in the field, the total rate of complications observed in the acute phase was shown to be almost identical compared to those patients treated in hospital (25% versus 24% respectively). These complications included arrhythmias such as ventricular tachycardia (VT), ventricular fibrillation (VF), bradycardia and asystole. There were no reports of bleeding during this initial treatment period. Rates of VF or VT were shown to be higher among the out-of-hospital cohort (19% versus 9%), but these findings failed to reach statistical significance (p = 0.17), most likely due to the study's

small sample size. However, a comparison of complications in the latter stages of care in hospital for both cohorts showed a 26% increase in complications among those patients who received treatment in hospital (24% to 50%, $p = 0.018$).

Reperfusion arrhythmias are a commonly reported occurrence among patients who have received fibrinolysis but are still poorly understood. Krumholz & Goldberger (1991) suggest that these arrhythmias (which are often ventricular in origin) may develop as a result of complex cellular and humoral reactions accompanying reperfusion therapy. Their occurrence, however, is an insensitive marker of successful reperfusion of the IRA and they are usually brief and intermittent, rarely resulting in physiological compromise of the patient (Hackett et al., 1990; Krumholz & Goldberger, 1991).

Lastly, earlier out-of-hospital fibrinolysis studies utilising streptokinase have reported that administration is associated with a moderate incidence of hypotension and a small incidence of allergic reaction or anaphylaxis (Grijseels et al., 1995; McAleer et al., 1992). These findings are consistent with larger in-hospital trials (Gruppo Italiano Per Lo Studio Della Sopravvivenza nell'Infarto Miocardico, 1990; ISIS-2 Collaborative Group, 1988). However, given almost all EMS providers worldwide now use fibrin-specific non-antigenic fibrinolytic agents, including in New Zealand, these findings can be considered redundant.

2.10 Cost, Cost-Effectiveness and Barriers to Programme Implementation

There are several factors to consider with regards to implementation of paramedic-delivered out-of-hospital fibrinolysis programmes. These relate to the cost and cost-effectiveness of each programme, as well as potential barriers to programme implementation and success. Firstly, the model adopted for each programme is a major determinant of the costs incurred by programme implementation and ongoing facilitation. In addition to staff training, those programmes adopting a physician-authorised telemetry-based model require greater funding for ECG monitor transmission technology upgrades and receiving stations/servers (Chamberlain et al., 2001; Danchin et al., 2008). Further technology expenditures may include ongoing maintenance and licence costs. The choice of drugs utilised within each programme is also a major determinant of cost, particularly the selected fibrinolytic agent, often the most expensive item. Moreover, selecting fibrinolytic agents able to be administered in a bolus capacity and that do not require

special storage such as refrigeration would allow for easier and safer use, while also helping to reduce cost.

The clinical benefits of out-of-hospital fibrinolysis have been well established in the literature, yet few studies have explored the cost effectiveness of the treatment in comparison to either its provision in hospital or to PPCI. However, these two concepts are interlinked, with a health intervention only considered cost-effective if the clinical benefits that it produces justify its cost (Araújo et al., 2008). The cost effectiveness of out-of-hospital fibrinolysis was first discussed in an ancillary study of the Comparison of Angioplasty and Pre-hospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial (Machecourt et al., 2005). The study's aim was to assess the cost-efficacy ratio of PPCI and out-of-hospital fibrinolysis for the treatment of STEMI patients (n = 299) presenting less than six hours from symptom onset and less than 60 minutes' travel time from a PCI centre. Costs during the in-hospital period were shown to be significantly lower among the PPCI cohort ($8287 versus $9170, p = 0.0001). This was largely due to longer hospital admission periods among those patients who received fibrinolysis (10 versus 9.1 days, p = 0.03). Although no difference was observed between the two groups in terms of mortality, non-fatal AMI and stroke, it was established that transport to the CCL for PPCI within 60 minutes from symptom onset was more cost-effective than failed fibrinolysis requiring rescue PCI.

This clinical scenario portrays an ideal situation. However, for many areas of New Zealand expedient transfer of STEMI patients to a CCL facility within an acceptable timeframe is unrealistic. Conversely, although an AMI may be averted with fibrinolysis, especially if provided within the first few hours of symptom onset, many patients go on to receive non-urgent PCI in the hours to days following the event (Bongard et al., 2009; Grijseels et al., 1995; Lamfers et al., 2004). This was one of several findings identified in a registry study conducted in Sweden which utilised data from 26,205 STEMI patients who received either PPCI (n = 7,084), out-of-hospital fibrinolysis (n = 3,078) or in-hospital fibrinolysis (n = 16,043) (Stenestrand, Lindbäck, & Wallentin, 2006). Although the median hospital admission period was one day less among the PPCI cohort compared to those who received out-of-hospital fibrinolysis, nearly 50% of the latter cohort received revascularisation within the following two weeks, and this extended their overall hospital admission time.

However, examining the economic benefits of paramedic-delivered fibrinolysis versus the treatment's provision in hospital has yielded favourable results in support of early paramedic intervention. Utilising a decision-analysis model to compare these two treatment strategies, Araújo et al. (2008) and Scuffham and Tippett (2008) both established that PTN time was a strong predictor of national healthcare system monetary costs. As such, paramedic-delivered fibrinolysis was shown to be the more cost-effective of the two strategies and correlated with an improved average life expectancy. In addition, this improvement was the same across a wide range of ages, supporting the argument that paramedic treatment should not be limited by an age threshold.

Despite the model adopted for programme implementation, staff experience must also be considered. A common dilemma confronting EMS is that staff in more rural and lower socioeconomic areas are often less qualified and experienced (Govindarajan & Schull, 2003). This issue is multifactorial and attributed to such things as a lower work volume and subsequently less exposure to a greater variety of patient presentations. Therefore, as an example, although an autonomous paramedic model would alleviate the financial costs associated with telemetry-based systems, it would undoubtedly require added confidence in the capabilities of rural paramedics from EMS medical directors. To achieve success in such programmes, a robust process of initial staff training, testing and ongoing training would need to be established, coupled with detailed programme audit and quality control measures.

Paramedic perception and attitude towards providing fibrinolysis in the field in terms of benefits versus risks is also an area that has been explored, with potential impact on programme implementation. Key themes to emerge from a UK-based qualitative study included: a belief by paramedics that the treatment was more invasive than it is generally considered to be; that paramedic pay was disproportional to the degree of responsibility involved in providing the treatment; and concerns around adequate training (Price, Keeling, Brown, Hughes, & Barton, 2005). Such countervailing imperatives would need to be addressed at an early juncture to assuage the concerns of those involved.

2.11 Out-of-Hospital Fibrinolysis Versus Primary PCI

Numerous randomised controlled trials comparing in-hospital fibrinolysis with PPCI in the management of STEMI have produced unequivocal results in favour of PPCI as the more superior reperfusion strategy in terms of morbidity, mortality and infarct

artery patency rates (Andersen et al., 2003; A. Kelly, Kerr, Patrick, & Walker, 2003; Weaver et al., 1997). Successful coronary revascularisation with PPCI occurs in more than 90% of cases, compared to 50–60% in patients who receive fibrinolysis (Andersen et al., 2003). In addition, PPCI has shown higher attainment of TIMI flow grade 3 rates (70–90% of cases) while substantially reducing the risk of ICH (Andersen et al., 2003). This superiority has also been consistent when interhospital transfer of patients to a PCI facility has occurred (Aversano et al., 2002; Grines et al., 2002; Widimský et al., 2000; Zijlstra, 2003).

However, the Comparison of Angioplasty and Pre-hospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) trial (n = 834) uncovered an interesting refinement of this broad picture (Steg et al., 2003). When treatment was received within two hours of symptom onset, a lower 30-day mortality rate was observed among those patients who received out-of-hospital fibrinolysis compared with PPCI (2.2% versus 5.7%, p = 0.05). This was also coupled with a lower occurrence of cardiogenic shock among the fibrinolysis cohort (1.3% versus 5.3%, p = 0.032). By contrast, beyond the two-hour boundary a steep decline in therapeutic benefit was observed for fibrinolysis, with improved outcomes among those patients who received PPCI. This impact of time on the efficacy of fibrinolysis mirrors findings by Boersma and colleagues and their appraisal of the ‘golden hour’ for reperfusion therapy (Boersma et al., 1996). Although results of the CAPTIM trial supported a timely pharmaco-invasive strategy, it must be stated that approximately 70% of those patients who received fibrinolysis underwent PCI before day 30, of which 26% required rescue PCI for failed fibrinolysis (Steg et al., 2003).

Observational studies utilising registry data are not considered to have the same methodological strength as randomised controlled trials, but have produced some interesting (though mixed) results (Kalla et al., 2006; McLean, Wild, Connor, & Flapan, 2011; Stenestrand et al., 2006). In two large European STEMI registry studies, out-of-hospital fibrinolysis provided within two hours from symptom onset was also associated with an unchanged or slightly reduced short- and long-term mortality when compared to PPCI (Kalla et al., 2006; McLean et al., 2011). However, as shown in previous studies, the advantage of out-of-hospital treatment was lost as PTN times increased. Conversely, in a cohort of 10,162 STEMI patients, of whom 7084 were treated with PPCI and the remaining 3078 with out-of-hospital fibrinolysis, a slightly lower 30-day and one-year mortality rate in favour of PPCI was observed (Stenestrand et al., 2006).

Despite the overall superiority of PPCI compared to fibrinolysis, numerous barriers exist within major parts of New Zealand and most other countries that impede timely access to interventional centres. These delays subsequently degrade the incremental benefit of the treatment. The most important barrier is prolonged transport times from rural areas. Therefore, in those locations where patient access to a PCI-capable hospital within accepted timeframes is not achievable, the case for early paramedic-delivered fibrinolysis in the field as a primary approach still holds strong merit, albeit contingent on adequate staff training and resources. In addition, it has been identified that more than two-thirds of total ischaemic time among STEMI patients (time from symptom onset to reperfusion) occurs prior to their arrival at hospital (McLean et al., 2008).

Optimally, total ischaemic time should not exceed 180 minutes regardless of the reperfusion strategy, and should be considered the main measure of importance in the treatment and care of STEMI patients (Denktas, Anderson, McCarthy, & Smalling, 2011; Gersh & Antman, 2006; Gersh, Stone, White, & Holmes, 2005). However, a continued disadvantage of fibrinolysis, regardless of where or by whom it is provided, is its numerous contraindications, which exceed those listed for PCI. In addition, there is evidence that the treatment is often less successful among those patients with severe cardiogenic shock, severe congestive heart failure or electrical instability (Chou, Amidon, Ports, & Wolfe, 1996; Levine & Hochman, 1995). Within this thesis, both reperfusion strategies (fibrinolysis and PPCI) are examined under clinical trial.

To summarise: Figure 2.2 illustrates the key timeline metrics for the provision of fibrinolysis and PPCI in the treatment of STEMI, as per current Australasian and European guidelines. Where possible, all STEMI patients attended to by EMS should be transported directly to a PCI-capable hospital, even if fibrinolysis has been provided in the field. Moreover, the time taken by patients to call for help following symptom onset, as well as patient time spent in the ED, are two of the greatest contributing factors to delays in access to PPCI (Savage et al., 2014; Tanner et al., 2006; J. M. White et al., 2012).

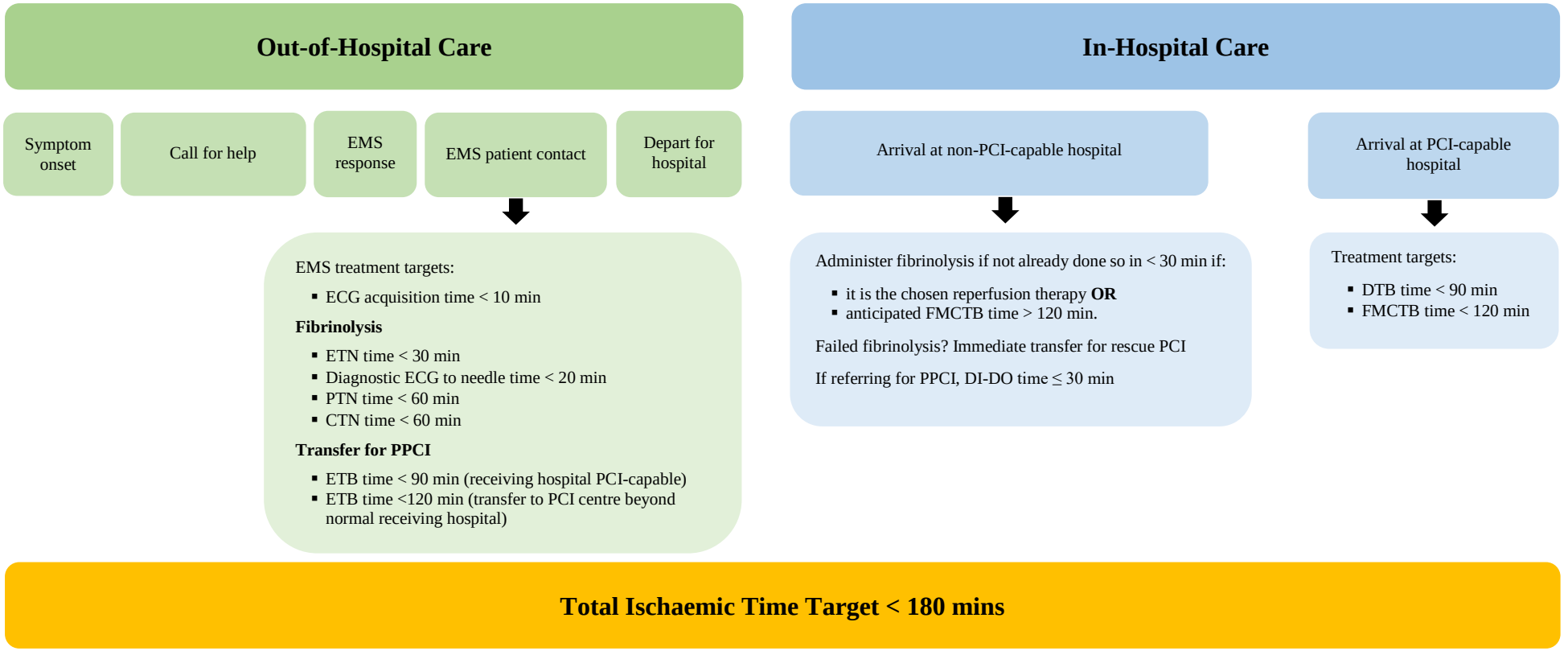


Figure 2.2 **Key Timeline Metrics for the Provision of Fibrinolysis and PCI**

Note: Figure not drawn to scale. Patient-related delays can vary substantially in length. EMS = emergency medical services; ECG = electrocardiogram; ETN = emergency medical services contact-to-needle; PTN = pain-to-needle; CTN = call-to-needle; PPCI = primary percutaneous coronary intervention; ETB = emergency medical services contact-to-balloon; PCI = percutaneous coronary intervention; FMCTB = first medical contact-to-balloon; DI-DO = door in-door out; DTB = door-to-balloon

2.12 Autonomous Paramedic CCL Activation

International guidelines recommend PCI as the preferred treatment modality in the management of STEMI if the time from patient symptom onset is less than 12 hours and the first medical contact-to-balloon (FMCTB) time can be achieved within 120 minutes (King et al., 2008; Steg et al., 2012). This is the time from first clinician contact with the patient to when the patient undergoes PCI and reperfusion of the culprit artery (colloquially known as balloon-time). Thus, the American Heart Association (AHA) has established several recommendations for EMS as a standard of optimal care for patients eligible for PPCI. These include: a paramedic capability of diagnosis and direct transfer to the nearest CCL; emergency medical services contact-to-balloon (ETB) time of less than 90 minutes (unless transporting beyond the normal receiving hospital, in which case the target ETB time is less than 120 minutes); and an ability to achieve these target timeframes for at least 75% of patients transported (Antman et al., 2007).

Another measured key time interval for PCI is the door-to-balloon (DTB) time, which starts from when the patient enters the interventional hospital. Although recommendations suggest a period of less than 90 minutes, the reality, as identified in many international STEMI registries, shows average DTB times of between 135 and 185 minutes (Huber et al., 2005). Further analysis reveals that patient time spent in the ED contributes the most to these delays and that protracted DTB times (as with all subintervals) are associated with both an attenuation of treatment benefit as well as an increase in in-hospital mortality (Clark et al., 2012; Hughes, 2005; McNamara et al., 2006). Moreover, in the Western world PCI is available to only 15–20% of STEMI patients on average, with the exception of 24-hour CCL facilities (Huber et al., 2005).

The rate of eligible patients who receive PCI in New Zealand is poor, as is the treatment's delivery within optimal time frames (C. Ellis et al., 2004). This has been attributed to several factors, including: lack of adequate funding; patient location in relation to a PCI facility; time of day; and in particular, delays within emergency healthcare systems (C. Ellis et al., 2004; Williams, 2007). These findings have provoked development of various strategies in some regions to improve treatment access and reduce delays. For example, a small number of PCI-capable hospitals will accept direct transfer of STEMI patients to the CCL following paramedic ECG telemetry from the field and physician consultation – a process designed to bypass the ED. In Australia, this approach

has significantly improved achievement of key treatment subintervals such as ETB time (1.8% to 19.4% respectively, $p = 0.001$) (Ranasinghe et al., 2012). Similar results have also been achieved in the US (Brown et al., 2008; Diercks et al., 2009; Roe et al., 2010).

However, the most effective strategy to emerge internationally has been one of autonomous paramedic triage and referral. Here, paramedics make an independent decision as to patient eligibility for PPCI before transporting appropriate candidates directly to the CCL, bypassing the ED and without ECG transmission or physician oversight. The limited studies that have investigated this approach have shown markedly improved PCI treatment delivery times overall compared to both previous paramedic models and improved in-hospital strategies (Cheskes et al., 2011; Garvey et al., 2012; Savage et al., 2014). Allowing New Zealand paramedics the same degree of freedom in clinical decision making may yield similar positive results. Study Three of this doctoral project (discussed in Chapter Five) tested this hypothesis in the real world during a 48-month trial period.

Critical to the success of such an approach is the confidence key stakeholders have in paramedics' ability to accurately determine patient eligibility for treatment. The main concern held by interventional cardiology departments around adopting such programmes is the rate of inappropriate CCL activations. In this instance, the referred patient is not a candidate for emergent PCI, often due to ECG misinterpretation. Such occurrences can prove costly and inconvenient, particularly outside of normal working hours when staff are commonly on-call. Within the literature, acceptable rates of inappropriate CCL activation for paramedic-initiated referral pathways range between 5 and 20% (Garvey et al., 2012; Moyer et al., 2007).

Like the subject of autonomous paramedic-delivered fibrinolysis, there remains a distinct paucity of research or inquiry examining systems of paramedic-initiated CCL referral, with only three studies identified within the literature. The first of these was a Canadian prospective observational study ($n = 175$) which sought to determine the proportion of patients who met the benchmark ETB time of less than 90 minutes before and after implementation of an independent paramedic CCL activation protocol (Cheskes et al., 2011). Results showed a 28.4% achievement in the before phase, compared to a 91.3% achievement in the after phase ($p < 0.001$), an approximate improvement of 62.9%. In addition, the rate of the inappropriate CCL activation during the after phase was 12.4%.

Inappropriate activation rates were specifically examined by Garvey et al. (2012) who reviewed 3973 CCL activations across 14 American PCI hospitals over a 12-month period. Approximately 29% of these activations were by autonomous paramedics and the remaining 71% by emergency physicians. The overall combined inappropriate activation rate was 15% (596 patients) with inaccurate ECG interpretation accounting for 72% of this total (427 patients). In addition, rates of inaccurate ECG interpretation were slightly higher among paramedics (6% of all activations) versus emergency physicians (4.6% of all activations), however this difference was not statistically significant. The authors then concluded that the high rate of coronary intervention and relatively low rate of inappropriate activations were evidence of a feasible and accurate autonomous paramedic CCL activation system.

Of closer relevance to New Zealand paramedic practice, Australian authors Savage et al. (2014) examined a paramedic-initiated CCL referral system with a primary focus on DTB times, followed by both 30-day and six-month mortality rates. Utilising a prospective observational approach, a comparison was then made to a second cohort who underwent emergency PCI but without pre-hospital notification of the CCL. A total of 281 cases were reviewed, of which 63 involved pre-hospital paramedic CCL referral. A significant reduction in median DTB times was observed among the pre-notification cohort compared to those without pre-hospital notification (40.4 versus 75.6 minutes, $p = < 0.001$). This difference represented a 47.6% time reduction. Although a numerical trend towards increased 30-day and six-month survival was shown among the pre-notification cohort, this was not found to be significant (1.6 versus 4.3%, $p = 0.307$ and 1.6 versus 6.4%, $p = 0.203$, respectively). Despite this, the study served to validate the overall superiority of a paramedic-initiated referral system in which no inappropriate CCL activations occurred. Moreover, it was also identified that ED assessment was the greatest contributing factor to delays in treatment delivery times.

2.13 Aeromedical Patient Transfer for Primary PCI

Despite the recommended treatment delivery times for PPCI as previously discussed, there is also strong evidence showing that excellent outcomes may still be achieved with inter-hospital transfer of patients for PCI beyond these traditional deadlines versus receiving onsite fibrinolysis (Widimský et al., 2002; Wöhrle et al., 2010); that is, transfer from a non-interventional centre to one with CCL facilities. As such, some guidelines allow for a delay of up to 120 minutes for both the FMCTB time and arrival at

the receiving non-interventional hospital to balloon time (including transport time) (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013; Steg et al., 2012). In this case the additional subinterval of door in-door out (DI-DO) with a goal of less than 30 minutes is measured, i.e. patient arrival at the non-interventional hospital to transfer out towards the PCI centre. Unsurprisingly, achieving this target is associated with shorter reperfusion times and lower in-hospital mortality rates (T. Y. Wang et al., 2011).

Evidence to support longer timeframes for the delivery of PPCI was first presented in the PRAGUE-2 study (Widimský et al., 2002). Patients presenting with STEMI to 41 non-interventional community hospitals and less than 12 hours from symptom onset were randomised to receive either onsite fibrinolysis (n = 421) or rapid road transfer to a hospital with CCL facilities to receive PPCI (n = 429) (maximum road distance of 120km). The average randomisation-to-balloon time among the PPCI cohort was 97 ± 27 minutes. Results showed that mortality rates were significantly less among those patients who underwent PPCI (6% versus 10.4%, $p < 0.05$), with the difference increasing further among those patients randomised more than three hours after symptom onset (n = 299), (6% versus 15.3%, $p <0.02$). Although no mortality difference between treatments was observed among those patients randomised within three hours of symptom onset, the study's combined endpoint of death, reinfarction or stroke at 30 days was in favour of PPCI (8.4% versus 15.2%, $p < 0.003$).

The Danish AMI (DANAMI-2) study (n = 1129) shared an identical design to that of the PRAGUE-2 trial, with similar supportive results (Nielsen et al., 2010). Among those patients randomised to receive PPCI following rapid road transfer from up to 24 non-interventional hospitals, the median time from randomisation to arrival at the CCL was 67 minutes, with 96% of all patients arriving within 120 minutes. The findings showed that rates of reinfarction were considerably less among those patients who received PPCI versus on-site fibrinolytic treatment (13% versus 18.5%; hazard ratio (HR), 0.66; 95% CI, 0.49 to 0.89), as was mortality (26.7% versus 33.3%; HR, 0.78; 95% CI, 0.63 to 0.97).

Within the New Zealand context, the distance between many non-interventional provincial hospitals and the nearest CCL (most of which are in our major cities) precludes road transport as a viable option. As a result, significant disparities exist between our interventional versus non-interventional hospitals in terms of the level of care provided

and patient outcome (Tang, Wong, & Herbison, 2006). However, the use of strategically placed rescue helicopter services may provide a critical link and more expedient transport medium for STEMI patients that could address both challenging geography and the time-to-treatment imperative.

The few studies within the literature that have examined this approach have produced mixed results. In the US, McMullan et al. (2011) undertook a retrospective audit which in part reviewed 140 STEMI patients referred for PPCI from 24 non-interventional hospitals to six receiving hospitals with CCL facilities, and transported via a hospital-based EMS helicopter service. Twenty-nine patients had no device inserted, leaving 111 for review. Among this group, the median DTB time was 131 minutes (IQR 114 to 158 minutes) starting from arrival at the referral hospital, with 97% of these cases exceeding the previously recommended 90-minute target. Failure to consistently meet the 120-minute evidence-based timeframe was not surprising given only two BK117 helicopters were available to service all 24 referral hospitals over a large geographic area (240 sq km). Moreover, despite a median flight time of only 10 minutes (IQR 2 to 28 minutes), time from helicopter request to arrival at the receiving hospital proved the greatest delay, with a median time of 48 minutes (IQR 42 to 58 minutes).

In New Zealand, White et al. (2012) reported on a smaller yet more successful rapid helicopter transfer programme aimed at delivering STEMI patients to a PCI centre approximately 155km from a single non-interventional community hospital and with a standard flight time of 30 to 35 minutes. Aptly named the Northland Code STEMI pathway, the programme utilised a single EMS helicopter service based less than two minutes' flying time from the referral hospital, and targeted a 120-minute DTB time starting from arrival at the referring ED. A total of 57 patients were transferred over a three-year period; only 24 patients (42.1%) received PCI within the target timeframe, although the median time was close at 122 minutes (IQR = 24). The greatest contributor to delay was patient time spent in the ED prior to transfer (median time 52 minutes, IQR = 23). Patient time in the ED contributed 44% of the total time until PPCI was achieved. More interesting was the fact that 32 out of 57 patients (56%) were delivered to the ED via ambulance, and the attending paramedics had already accurately determined the diagnosis of acute STEMI prior to hospital arrival.

Intuitively, given the findings discussed, for those patients who seek ambulance assistance, paramedic-initiated referral to the CCL and helivac direct from the field

(bypassing the local non-interventional receiving hospital) may facilitate substantially improved treatment delivery times. However, the limited studies that have reported on this approach have yielded poor results, for a variety of reasons. The first of these was by Sigmundsson et al. (2010), who undertook a retrospective chart review of 33 STEMI patients flown by air ambulance from remote northern rural areas of Iceland to the nearest interventional hospital in the city of Reykjavik following paramedic referral. The median flight time was 58 minutes (IQR 26) with the aircraft based in Reykjavik. Unsurprisingly, the programme failed to achieve the guideline-mandated FMCTB time for PPCI of less than 120 minutes among all patients, with a median time of 255 minutes. Arguably, this programme was overly ambitious and conceptually flawed from the onset due to the prolonged response and transfer flight times, which left minimal manoeuvrability among other logistical and clinical time components of each case.

However, with the implementation of a strict standard operating procedure (SOP) that includes target times for helicopter request, response, time on scene and transport to the CCL, the provision of PPCI within 120 minutes following paramedic-initiated helivac from the field may well be feasible (Balerdi, Ellis, Grieve, Murray, & Dalby, 2011). Although underpowered (n = 8), the study provided by Balerdi and colleagues reported a median first-medical-contact-to-door (FMCTD) time of 85 minutes (IQR 70 to 95), with average flight times ranging between 18 and 25 minutes. These overall concepts form the basis of the third study presented within this thesis, which is described in Chapter Five. This study was a 48-month clinical trial of autonomous paramedic patient referral to a PCI facility via helivac, conducted within the same provincial city as the Northland Code STEMI pathway (previously discussed and reported by White et al. (2012), allowing a comparison to be made.

2.14 Relevance to Māori Health

Prior to conclusion of the literature review process, it is important to address the relevance to Māori health that paramedic-based STEMI management systems may hold. Ischaemic heart disease is responsible for over half of all CVD-related mortality in New Zealand, and this societal burden falls disproportionately on the Māori population, both men and women (Ministry of Health, 2010). Rates of hospitalisation and death due to IHD are significantly greater among Māori versus their non-Māori counterparts, and Māori are more likely to succumb at younger ages (Ministry of Health, 2010; Tobias et al., 2006; Wells et al., 2006). For example, in middle adulthood (aged 45–64 years) Māori

are almost four times more likely to die from IHD than non-Māori (Ministry of Health, 2010; Tobias et al., 2006). Of greater relevance to this doctoral research, the rates of revascularisation procedures such as PCI and coronary artery bypass grafting (CABG) surgery are also significantly higher among Māori compared to non-Māori (Ministry of Health, 2010).

Despite the national decline in mortality rates for IHD observed over the last 30 years, a strong disparity between Māori and non-Māori still exists in that the rate of decline has not been as rapid for Māori. Moreover, because the Māori population is increasing, with a tendency to live longer, the actual numbers of Māori with active IHD are projected to increase (Tobias et al., 2006; Wells et al., 2006). As a result, the Ministry of Health has prioritised CVD preventative and management strategies for Māori, as outlined in The Guide to He Korowai Oranga: Māori Health Strategy, specifically aimed at reducing health inequalities (Ministry of Health, 2014a; Wells et al., 2006).

Part of the reason for the higher incidence of IHD among Māori is that they also exhibit a greater prevalence of attributable CVD risk factors. For example, the current rate of smoking among Māori women is more than three times that for non-Māori women, while Māori men smoke nearly twice as much as non-Māori males (Ministry of Health, 2011). Cigarette smoking has been identified as the leading preventable risk factor for heart disease among Māori (Ministry of Health, 2011). Diabetes mellitus is another well-documented risk factor for IHD, whose prevalence among Māori is twice that of non-Māori (Joshy & Simmons, 2006). In a 2004 survey of a large rural Māori community, half the adults were found to have diabetes or signs of impaired glucose metabolism, the condition from which diabetes often develops (Tipene-Leach et al., 2004). Similarly, a greater proportion of Māori adults are treated for high blood pressure (both men and women) and are much more likely to be obese (43.2% of Māori compared to 23.2% for European New Zealanders; data is age standardised) (Kerr et al., 2008).

Nearly 15% of New Zealanders self-identify as Māori (Statistics New Zealand, 2014). Like all New Zealanders, most Māori now live in urban settings (nearly one quarter of all Māori live in greater Auckland) while about 16% live in rural areas (Statistics New Zealand, 2017b). In some regions – in Northland, Rotorua/Bay of Plenty, and in East Cape – Māori account for greater than 25% of the total population, and in some districts the proportions are much higher: the Kawerau, Wairoa and Opotiki Districts are each approximately 60% Māori (Statistics New Zealand, 2014). Of note, risk factors for IHD

are higher among rural Māori when compared with urban Māori, and there is a statistical trend (not reaching significance, $p = 0.073$) for an increase in diagnosed IHD among rural Māori compared to those living in urban settings (Cameron et al., 2012). Given that rural residents by definition have greater transport distances to healthcare facilities, they are the most likely to gain benefit from expedited paramedic-based treatment and referral pathways.

2.15 Chapter Summary

Despite the significant continued burden of CVD on our society, New Zealand, unlike many other countries, has yet to adopt and/or refine strategies to improve the treatment and care of those patients presenting at the acute end of the disease spectrum (C. Ellis et al., 2010a). ST-elevation myocardial infarction represents a serious and potentially life-threatening scenario where patient access to timely reperfusion therapy is the greatest determinant of both morbidity and mortality (Boersma et al., 1996; Steg et al., 2003). It is evident from the literature presented in this chapter that EMS worldwide are an integral component in the chain of survival for STEMI patients who seek medical assistance through the emergency call system. With an ability to respond rapidly throughout the community, paramedics are now better educated, trained and equipped to undertake timely assessment, diagnosis and subsequent treatment and transport of this population group. As such, specific paramedic-based systems of care for STEMI patients have emerged as the most logical and efficient approach internationally to achieving the goal of early reperfusion, while consistently meeting evidence-based treatment timeframes (Danchin et al., 2008; Huber et al., 2005). In terms of patient outcomes, these systems have also repeatedly demonstrated their superiority compared to both standard and improved hospital-based strategies, while also providing a strong economic incentive due to reduced patient hospital admission times (Araújo et al., 2008; Machecourt et al., 2005).

Although PCI provides significantly higher rates of revascularisation and with far fewer complications, fibrinolysis remains a valid contemporary reperfusion modality for STEMI, especially where patient access to CCL facilities cannot be achieved within mandated timeframes (McLean et al., 2011). However, its efficacy is determined primarily by the time of administration from point of symptom onset, with the greatest benefit achieved in the early stages of infarction (less than three hours), after which the treatment's clinical gain reduces substantially (Boersma et al., 1996). For this reason,

where appropriate, the literature supports the treatment's provision in the out-of-hospital setting versus in-hospital, due to significant reductions in both PTN and CTN times, resulting in improved short- and long-term mortality figures (Danchin et al., 2004; Frans Van de Werf et al., 2008).

Utilising paramedics to provide fibrinolysis in the field with physician oversight via telemetry-based systems has proven to be safe and feasible, both internationally and in New Zealand (McLean et al., 2008; Ranchord et al., 2009). However, such programmes can also be costly and prone to technological failings (P. Davis, 2014; Keeling et al., 2003). Several countries have successfully trialled and implemented an alternative model of autonomous paramedic treatment provision that alleviates these issues, while potentially expediting needle times even further (Grijseels et al., 1995; Keeling et al., 2003).

The literature highlights the benefit of fibrin-specific agents such as TNK for use in paramedic programmes due to low-cost storage requirements and simpler dosing regimens that mitigate the risk of drug administration error (Danchin et al., 2008; Topol et al., 1993). In addition, these newer agents exhibit fewer complications than those that are older and non-fibrin-specific (Cooke, 2007; Schulman et al., 2008). It must also be acknowledged that for a variety of reasons, paramedic treatment protocols have historically been more stringent than those that are physician-led in the hospital setting, thereby excluding a small yet significant proportion of STEMI patients encountered by EMS within the community (Castle et al., 2006; Weaver et al., 1990). As such, regular re-evaluation of paramedic treatment inclusion and exclusion criteria for fibrinolysis is essential.

For those STEMI patients able to reach an interventional hospital within guideline-mandated times, the evidence is clear that PCI offers greater clinical benefit than that of fibrinolytic treatment alone and is more cost-effective (Stenestrand et al., 2006; Weaver et al., 1997). This is especially the case given most patients who receive fibrinolytic therapy will undergo PCI in the hours to days following their acute event (McLean et al., 2011; Weaver et al., 1997). The literature also recognises and supports the early notification of these hospitals by paramedics to expedite PCI-delivery times, while acknowledging significant hospital-based delays in need of remedy, i.e. patient time spent in the ED (Cheskes et al., 2011; Clark et al., 2012; Savage et al., 2014; J. M. White et al., 2012). Paramedic-initiated patient referral to the CCL with direct transfer

(occurring without physician oversight and bypass of the ED) offers a valid solution to reducing such delays, having been successfully trialled internationally (Cheskes et al., 2011; Savage et al., 2014). Moreover, aeromedical transport utilising EMS helicopter services may potentially enable patients to receive timely PCI, whereas under previous circumstances their location and distance to the CCL would have excluded them from receiving the treatment (J. M. White et al., 2012).

Collectively, these subjects of autonomous paramedic-delivered fibrinolysis and CCL activation from the field have been identified as a high priority for research in Australasian out-of-hospital emergency care (Snooks et al., 2008). Moreover, the paucity of research exploring these subjects invites further investigation, particularly given the differences in paramedic practice between New Zealand and other countries. Specifically, no study has yet to compare the two paramedic STEMI management models of telemetry-based physician-assisted versus autonomous paramedic decision making, to establish the true clinical advantage (if any) of one approach versus the other.

The potential to improve outcomes for STEMI patients through the national implementation of homogeneous, streamlined and accelerated paramedic-based treatment models is congruent with the National Heart Foundation's strategic plan 2015–2018 to stop New Zealanders dying prematurely from heart disease (New Zealand National Heart Foundation, 2016). A primary focus on the broader measure of total ischaemic time versus fixation on less important subintervals would also be beneficial. In addition, since 2009, the New Zealand ambulance sector has worked collaboratively in addressing numerous issues related to service delivery. For example, national standardisation of qualification levels and clinical procedures was implemented in 2011 (National Ambulance Sector Office, 2009). Therefore clinical-based out-of-hospital research within the sector may now have a greater national impact. Research focussed on the ACS patient is also of strong relevance to Māori given their significant inequality in CVD-related conditions.

Chapter Three: Are New Zealand Paramedics Ready for an Autonomous Fibrinolysis Protocol in the Management of STEMI?

3.1 Introduction

This chapter details the first of three studies that form the basis of this thesis – a preliminary investigation to determine if New Zealand paramedics possess the prerequisite skills and knowledge necessary to permit autonomous decision making in the management of STEMI: specifically, the provision of fibrinolysis under protocol guidance. This study was peer reviewed and accepted for publication in the Australasian Journal of Paramedicine in July 2017.

Given no paramedic fibrinolysis programme without physician-oversight had existed in any region of the country prior, field testing was deemed unethical at such an early juncture. Therefore, this study was undertaken in simulation. In addition, for autonomous paramedic-based STEMI management pathways to be established nationally, it is essential that the relevant clinical decision-making abilities of our paramedics are measured. Research conducted in the New Zealand context also provides greater insight and support due to the significant variability in paramedic practice between New Zealand and other countries, as discussed in Chapter One.

Furthermore, this study enabled a comparison to be made between New Zealand's two paramedic education models: the previous post-employment in-house education model and the current pre-employment higher education model, i.e. university-based undergraduate and postgraduate programmes. Associations between the decision-making abilities of paramedic participants and key individual characteristics were also investigated. The study's results have then served to support and inform the educational components of the second and third investigations in this thesis, discussed in Chapters Four and Five respectively.

3.2 Research Questions

1. Do New Zealand paramedics possess the prerequisite skills and knowledge necessary to permit autonomous decision making for the provision of fibrinolysis

in the treatment of STEMI, under protocol guidance? Specifically, this includes accurate 12-lead ECG interpretation skills, and an understanding of both acute cardiac pathology and principles of pharmacology.

2. Do any associations exist between our paramedic groups' clinical decision-making abilities and key characteristics, such as gender, age, practice level, clinical education, length of service and area predominantly worked, i.e. rural or metropolitan?

3.3 Aims

1. To design an inclusion/exclusion protocol that identifies those patients for whom out-of-hospital fibrinolysis is indicated/contraindicated, in conjunction with the St John Ambulance Service.
2. To introduce this protocol to selected New Zealand paramedics and assess their abilities in its application, in simulation.

3.4 Hypotheses

1. Following introduction to the new protocol for identification of those patients for whom fibrinolysis is indicated/contraindicated, paramedics will demonstrate that their current education and training is sufficient to enable them to accurately apply the protocol (in simulation).
2. Those paramedics who are university-educated will demonstrate greater clinical decision-making abilities in protocol application (in simulation), versus those paramedics who are in-house educated.
3. Those paramedics with a clinical practice level of ICP will demonstrate greater clinical decision-making abilities in protocol application (in simulation), versus those paramedics employed at lesser levels of clinical practice.

3.5 Methods

3.5.1 Study Design

This study had a quasi-experimental design of one group post-test only. In addition, the assumption that the accuracy of one's clinical decision making may be measured objectively necessitated a positivist approach. However, it is acknowledged that human participants are complex and that some generalisations may be difficult to apply

(Polit & Beck, 2006). Figure 3.1 summarises the study design process with further detailed discussion provided in the following sections.

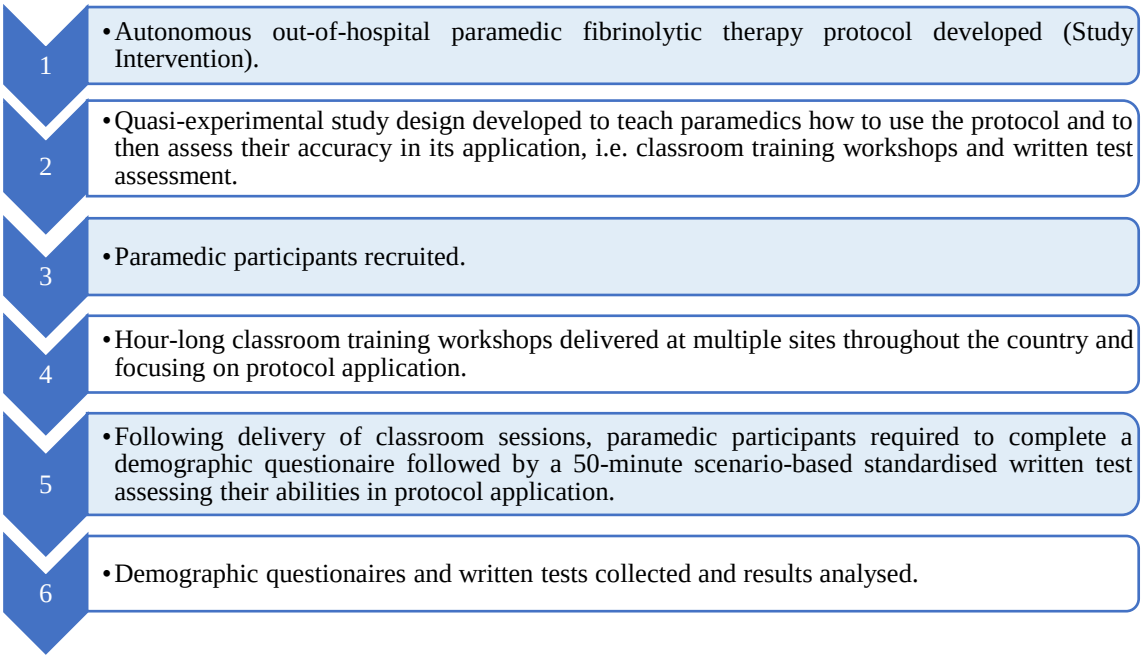


Figure 3.1 **Summary of Study Design Process**

The study intervention was a new autonomous paramedic out-of-hospital fibrinolysis inclusion/exclusion protocol (Appendix O) introduced to participants in a one-hour classroom training workshop. This session provided explanation of all aspects relevant to protocol application, and was delivered by the principal researcher. Class content included

- treatment indications and contraindications
- gaining informed patient consent
- introduction to all drugs administered including preparation, pharmacodynamics, pharmacokinetics and administration procedure
- post-treatment complications
- documentation requirements.

The protocol was constructed by the principal researcher with input from the study supervisors (one of whom was a consultant cardiologist and professor at Auckland Medical School), as well as the St John Ambulance Medical Director. The protocol also aligned with current evidence-based best practice guidelines for the provision of fibrinolytic therapy as stipulated by the New Zealand ST-Elevation Myocardial Infarction Guidelines Group (2013). Correct interpretation of both patient signs and symptoms and

12-lead ECG were essential in applying the protocol and these components were emphasised during the classroom training workshop.

Following delivery of the training workshop, participants were assessed in application of the protocol to patients, in simulation, by means of a scenario-based standardised written test. The outcome (dependent variable) was the paramedic participants' level of accuracy in applying the new protocol, that is, the accuracy of identifying the suitability (inclusion/exclusion) of patients to receive fibrinolysis. Although the study participants had received prior education and training around components directly relevant to the protocol, the actual protocol itself was a new concept that they were unfamiliar with. This negated both a true experimental study design with randomisation and a pre-test/post-test approach. Moreover, quasi-experimental designs have proven useful in evaluating the impact of educational interventions (Shadish, Cook, & Campbell, 2002). However, a common disadvantage associated with the design is threats to internal validity from confounding variables (L. S. Robson, Shannon, Goldenhar, & Hale, 2001). This was reduced through researcher control over both the independent variable (the protocol) and the measurement tool (the standardised written test used to assess protocol application).

3.5.2 Setting

The study was conducted within the St John Ambulance Service with classroom training workshops held at ambulance stations in five different locations throughout the country: Whangarei, Auckland, Tauranga, Nelson and Christchurch, to ensure a north/south, urban/rural spread.

3.5.3 Participants

Eighty-one self-selecting paramedic participants were recruited via advertisements on ambulance station noticeboards and the St John hub website. Inclusion criteria were: employed on front-line ambulances, with current authority to practice (ATP), and educated in 12-lead ECG interpretation by either educational model. That is, educated by either the post-employment in-house system or by the pre-employment university-based system. These criteria meant that participants had completed education and training directly relevant to the provision of fibrinolysis, and had consolidated this learning in a 'real world' out-of-hospital EMS clinical setting. Participants also signed a consent form as per ethical requirements.

3.5.4 Sample Size

To determine the accuracy of paramedic protocol application, it was calculated that 81 participants were required for the study. This number was based on an *a priori* power analysis of data from two previous similar studies that also explored paramedic clinical decision making with regards to the provision of fibrinolysis in the treatment of STEMI (Keeling et al., 2003; Pitt, 2002). This was assuming a sensitivity of 70%, an accuracy measure of +/− 10%, and a statistical significance level of $\alpha = 0.05$, denoting a 95% confidence interval. In addition, our 81 participants made up approximately 7.1% of an actual population size of 1127 St John Ambulance personnel eligible to participate in the study.

3.5.5 Measures

Accuracy of Paramedic Protocol Application (Outcome Variable): The summative criterion-referenced standardised written test provided the means by which the participants' accuracy of protocol application was measured, as per Hypothesis One. Specific measures included the participants' sensitivity and specificity, along with PPV and NPV of diagnosis in determining patient suitability to receive fibrinolysis. Approximately 50 minutes was allocated for participants to complete the test, which consisted of four patient scenarios constructed from actual field cases plus three questions allocated per scenario. Two patients were eligible for fibrinolysis and two were not. In the three questions per scenario participants were required to: 1) interpret the patient's 12-lead ECG and signs and symptoms as supplied in the scenario; 2) make a clinical decision as to whether fibrinolysis was indicated or not; and 3) provide their rationale. The scenarios were then followed by a multiple-choice section consisting of ten questions that further probed acute cardiac and pharmacology knowledge, as well as protocol application.

The patient scenarios in the written test and the correct answers were reviewed and approved by three independent cardiology consultants (experts). This served as the standard against which participants' accuracy in protocol application was measured, and allowed test scoring to be objective. The content validity (face validity) of standardised tests within the medical field has been shown to be high, particularly when expert judgement on the relevance of the test content has been sought, coupled with test content alignment with actual practice requirements (Turnbull, Grey, & MacFadyen, 1998). This test was aligned with nationally recognised indications and contraindications for fibrinolysis. Reliability of the written test was also enhanced due to two main factors: the

reproducibility of the testing material and scoring procedure, and standardisation of conditions including data collection from participants, assessment time, seating and print quality of materials.

Associations between the Accuracy of Paramedics' Protocol Application and Key Characteristics: Participants were also asked to complete a demographic questionnaire (Appendix P). This information was used for several purposes: to statistically describe the sample group; to help determine if any associations existed between the accuracy of paramedics' clinical decision making and key individual characteristics (study question two); and to test Hypotheses Two and Three. Information sought included: sex, age, clinical practice level, clinical education, length of service and area predominately worked (i.e. rural or metropolitan).

3.5.6 Study Implementation Process

Implementation of the study commenced by seeking approval from the relevant ethics committees, before locality and institutional approval was sought from St John's Clinical Audit and Research Team (Appendix D). This also included the use of clinical details from ambulance patient report forms where fibrinolysis was considered, in order to construct the written test. Content for the new protocol, written test and classroom training workshop was then developed and participants were recruited. In addition, participants were informed of the purpose and methods of the study both in writing and verbally. Following delivery of the classroom sessions, participants completed the written test and demographic questionnaire. They were instructed not to write their name on either document, thus protecting their anonymity. These documents were then collected at the end of each session (data collection) and analysis of data occurred once all workshops had been delivered.

3.5.7 Data Management and Processing

Raw data was entered in the Statistical Package for Social Sciences (SPSS) software programme version 19 and screened to ensure no entry errors. A screening of the data for outliers also occurred, with corrections made prior to analysis.

3.5.8 Data Analysis

Key participant characteristics and demographic data was initially analysed as one dataset, and given this data was categorical, frequencies were used to obtain descriptive statistics. Confidence intervals were set at 95% and an alpha level of 0.05 was considered

statistically significant. Non-parametric testing was utilised, given data was dichotomous, categorical or ordinal. The written test case scenarios were categorised as either: *Fully Correct* (correct 12-lead ECG interpretation, correct treatment decision, correct rationale); *Partially Correct* (correct treatment decision, but based on incorrect ECG interpretation and/or only partially correct rationale); or *Misdiagnosis* (incorrect treatment decision, for whatever reason). We calculated overall sensitivity (*Fully Correct* clinical decision making for true positive scenarios) and overall specificity (*Fully Correct* clinical decision making for true negative scenarios). Associations between written test scenario scores and demographic characteristics were analysed using a chi-square test for independence (with Yates's continuity correction when cells had fewer than five observations).

3.5.9 Ethics

Ethical approval for the study was obtained from AUTEC (application number 12/94 – Appendix A) and from HDEC – Multi-region Ethics Committee (MEC/12/EXP/025 – Appendix B).

3.6 Results

3.6.1 Participant Characteristics

Key characteristics of the study participants, including demographic data, are presented in Table 3.1. As shown, the majority were male, less than 40 years of age and with a current practice level of paramedic. Most participants had completed a BHSc paramedic degree programme, had been employed in the ambulance service for between five and ten years and worked predominantly in a metropolitan area. In addition, these figures were concordant with national workforce data (data not shown). Thus this sample was considered representative of the whole.

Table 3.1 ***Participant Characteristics***

Variable	*n*	(%)
Male	47	(58)
Female	34	(42)
Age:		
20 – 29 years	14	(17.3)
30 – 39 years	37	(45.7)
40 – 49 years	15	(18.6)
50 – 59 years	13	(16)
60 years +	2	(2.4)
Clinical Practice Level:		
EMT	8	(9.9)
Paramedic	44	(54.3)
ICP	29	(35.8)
Clinical Education:		
BHSc paramedic degree	44	(54.3)
In-house ambulance service paramedic course	25	(30.9)
In-house ambulance service paramedic course + some university papers	12	(14.8)
Length of Service:		
0 – 5 years	24	(29.6)
6 – 11 years	35	(43.2)
12 – 17 years	10	(12.3)
18 – 23 years	6	(7.4)
24 years +	6	(7.4)
Area Predominantly Worked:		
Rural	32	(39.5)
Metropolitan	49	(60.5)

Note: EMT = emergency medical technician; ICP = intensive care paramedic; BHSc = Bachelor of Health Science

3.6.2 Written Test Scenarios

The raw data for accuracy in clinical decision making in the four case scenarios in the written test is provided in Table 3.2. Participants were least *Fully Correct* in Scenario 2, but withheld treatment when it was indicated most often in Scenario 3. A positive case is one where fibrinolysis was indicated; a negative case is one where fibrinolysis was contraindicated, as per the protocol.

Table 3.2 ***Accuracy of Participant Clinical Decision Making in Written Test Scenarios***

Score	Scenario			
	1 (Positive Case)	2 (Negative Case)	3 (Positive Case)	4 (Negative Case)
Fully Correct	80	66	69	75
Partially Correct	0	9	0	6
Misdiagnosis	1	6	12	0

Note: Positive Case = fibrinolytic therapy indicated; Negative Case = fibrinolytic therapy contraindicated

Sensitivity in clinical decision making was 92.0% (95% CI: 84.8–96.5) and specificity was 95.6% (95% CI: 89.1–98.8). These results were obtained through calculation of *Fully Correct* and *Misdiagnosis* answers only. The main reason for participants failing to be *Fully Correct* in each scenario was failure to interpret the ECG correctly. In Scenario 4, which showed a STEMI ECG, there were two contraindications present. However, six participants were *Partially Correct* because they recognised only one of these. For the above calculations, *Partially Correct* answers were excluded. In addition, there was a total of 324 ECG interpretations in this study (81 participants x four scenarios each). ECG misinterpretation occurred 27 times – this produced an accuracy rate of 91.7%. The more common areas of misinterpretation were bundle branch blocks (BBBs) and left ventricular hypertrophy (LVH) with strain pattern.

3.6.3 Multiple-Choice Questions

Ten multiple-choice questions (MCQs) followed the written test scenarios. Seven questions were correctly answered by all participants, two questions were correctly answered by 96.2% of participants, and one question was correctly answered by 62.9% of participants. All participants correctly answered eight or more of the 10 MCQs, with nearly three-quarters of the group (74%) answering all 10 questions correctly. The average participant score for the 10 MCQs was 9.6.

3.6.4 Associations between *Fully Correct* Written Test Scenarios and Participant Characteristics

There were no significant associations between the number of scenarios that were *Fully Correct* and the participants' sex, age, length of service or area predominantly worked (i.e. metropolitan versus rural) (see Table 3.3). The trend seen for age is toward younger age and number of scenarios *Fully Correct*. However, there was a significant association between the participants' current practice level (as determined by ATP) and the number of *Fully Correct* scenarios. Participants currently practising as ICPs (n = 29)

achieved *Fully Correct* scores for all four written scenarios significantly more often than participants currently practising as either EMTs ($n = 8$) or paramedics ($n = 44$) ($p = 0.006$). See Figure 3.2.

Table 3.3 ***Associations Between Fully Correct Written Test Scenarios and Participant Characteristics***

Demographic Feature (n = 81)	χ^2	df	*p*-Value
Sex	0.31	1	0.57
Age	6.7	1	0.08
Clinical practice level	7.4	1	0.006*
Clinical education (in-house versus university-based)	14.9	1	0.001*
Length of service	0.98	1	0.61
Area predominantly worked (rural versus metropolitan)	0.000	1	1.00

Note: χ^2 = chi-square; df = degrees of freedom
*Significant at $p < 0.05$

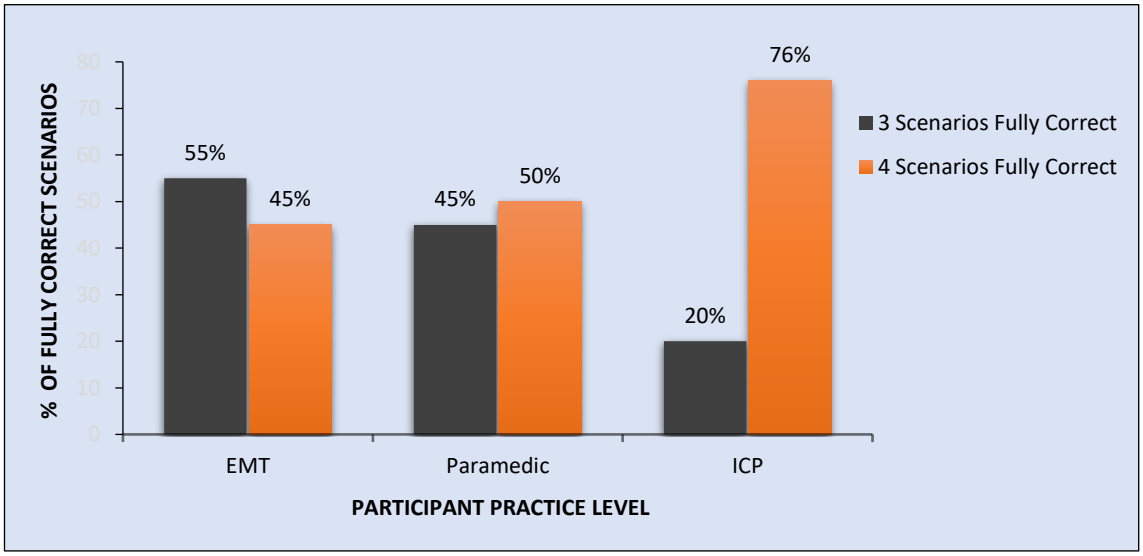


Figure 3.2 **Number of Fully Correct Scenarios by Participant Practice Level**
Note: EMT = emergency medical technician; ICP = intensive care paramedic

A significant association also existed between participants' clinical educational pathway and the number of *Fully Correct* scenarios. Participants who had undergone pre-employment higher education, i.e. paramedic degree graduates ($n = 44$), achieved *Fully Correct* scores for all four Written Test scenarios significantly more often compared to those educated via the post-employment in-house pathway ($n = 37$) ($p = 0.001$). See Figure 3.3.

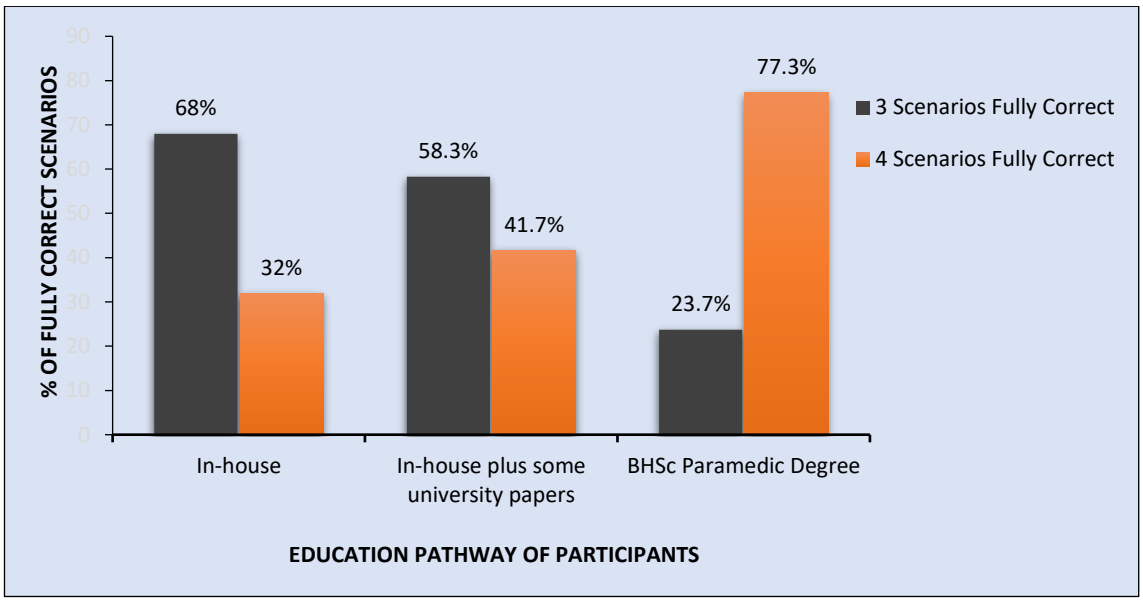


Figure 3.3 **Number of Fully Correct Scenarios by Participant Clinical Education Pathway**

Note: BHSc = Bachelor of Health Science

3.7 Discussion

Our New Zealand paramedic sample demonstrated a high standard of autonomous clinical decision making in application of this fibrinolytic therapy protocol in simulation – sensitivity of 92.0% (95% CI: 84.8–96.5) and specificity of 95.6% (95% CI: 89.1–98.8). Participants could recognise STEMI patients for whom the treatment was indicated, and then apply inclusion and exclusion criteria with a high degree of accuracy. Likewise, patients who were not eligible for fibrinolysis were readily identified. Participants demonstrated sufficient cardiac and pharmacology knowledge on which to base the introduction of a new fibrinolysis procedure. These New Zealand findings are similar to standards of paramedic clinical decision making with regards to fibrinolytic therapy observed in England, Wales and the Netherlands (Grijseels et al., 1995; Keeling et al., 2003; Pitt, 2002). However, differing experimental designs make direct comparisons difficult.

The four scenarios in the written test were constructed from actual field cases carefully selected as being representative of the out-of-hospital setting (Brady, Perron, Martin, Beagle, & Aufderheide, 2001; Feldman et al., 2005). A 12-lead ECG for both anterior and inferior STEMI was used because these are the two most common types of STEMIs (F. Van de Werf et al., 2008). A left bundle branch block (LBBB) was presented: these, along with RBBBs, are a frequent STEMI mimic occurring among non-traumatic

chest pain patients, particularly those with a history of ischaemic heart disease (Go & Barron, 1998). Even one of the negative cases, a patient with multiple contraindications to fibrinolysis, presented with a genuine inferior STEMI. This allowed us to assess the paramedics' protocol adherence beyond a positive ECG finding.

Four scenarios were a realistic number for a 50-minute written test, which also explored rationale and contained additional MCQs. Approximately ten minutes per scenario is realistic for the working environment, where paramedics must interpret the patient's ECG and assimilate further clinical information before reaching a treatment decision. Both the number of scenarios and timeframe for each are consistent with similar studies conducted in England and Wales (Keeling et al., 2003; Pitt, 2002). However, our testing methodology enabled further insight into each participant's clinical rationale, beyond simple accuracy of ECG interpretation. By asking participants further questions to validate their treatment decision, this enabled us to interrogate any correct treatment decisions which were based on flawed clinical analysis and rationale.

12-lead ECG interpretation was largely accurate in the four written scenarios, with sensitivity and specificity values comparable to international studies involving both paramedics and physicians (D. P. Davis et al., 2007; Feldman et al., 2005). However, some areas of common weakness were revealed. Bundle branch blocks were the arrhythmias most often misinterpreted, as was LVH with strain pattern. These have been identified as arrhythmias that often challenge frontline paramedics (Feldman et al., 2005; Ioannidis, Salem, Chew, & Lau, 2001). Therefore, our study uncovered two clear areas of 12-lead ECG interpretation deficit. If an autonomous fibrinolysis protocol for paramedics is to be introduced, these arrhythmias would need to be given specific attention within the developed training package.

Paramedics in this study showed that they could take the new fibrinolysis protocol and apply it to the written scenarios with a high degree of accuracy in clinical decision making. Note that in this study paramedics were not required to memorise the new protocol; the protocol was available for review during testing. This is realistic to the environment in which they work: in New Zealand, paramedics are required to carry a copy of the ambulance clinical procedures and guidelines on their person, and are expected to consult them as necessary. Therefore, it was not surprising that participants answered the written test MCQs on protocol application so well, with 100% success for many questions. However, the questions that were answered less well were revealing.

Twenty-one percent of the participants erroneously believed that AMI was the most common cause of ST-elevation on 12-lead ECG (Question 7). This was the same question that uncovered the paucity of understanding of strain pattern associated with LVH. These knowledge deficits are best addressed by education.

As discussed in the introductory chapter of this thesis, ambulance education has been in transition in New Zealand since 2002, the year university-based degree programmes were first offered. This study provides a unique snapshot of this transition period given our participants came from both older and newer educational pathways, enabling a comparison to be made. Those paramedics who had completed a Bachelor of Health Science paramedic degree scored significantly higher than those whose education was solely in-house industry-based. Those whose education was a mixture of both pathways scored between these two groupings. These results do not denigrate the post-employment in-house education system, but are a validation of the newer pre-employment higher education pathway standards. It is now a requirement within New Zealand's two emergency ambulance services that those staff wanting to practise at either paramedic or ICP level need to complete a university undergraduate paramedic degree programme or higher.

Unsurprisingly, those participants currently practising as ICPs demonstrated significantly higher accuracy in their clinical decision making than those practising at either paramedic or EMT level ($p = 0.006$). Of more interest, this was also found to be the case among degree-qualified participants (even though not all were practising as ICPs) versus those educated via other pathways ($p = 0.001$). In fact, the degree-qualified participants were at all practise levels – EMT, paramedic and ICP. This is because ATP is granted by the ambulance industry, and university graduates begin their employment as EMTs and then progress to paramedic and potentially to ICP. This finding suggests that the higher standard in clinical decision making shown by university-educated participants may be due not so much to their current practice level or associated on-road experience, but more to the greater depth and duration of their education.

Determining patient eligibility for primary PCI has strong similarities to the criteria for fibrinolytic therapy but with far fewer contraindications. Therefore, within New Zealand's main metropolitan centres our results provide support for a model of paramedic-initiated activation of the CCL and direct patient transfer from the field. As discussed in the previous chapters, this approach, which bypasses the hospital ED, has

been shown to significantly reduce PCI delivery times more than telemetry-based models and improved in-hospital strategies, with greater positive effects on both patient morbidity and mortality (Brown et al., 2008; Lee et al., 2010).

3.8 Limitations

Our 81 participants were self-selected and therefore may have been a more proactive, non-representative group. This may limit the generalisability of our results to the greater New Zealand St John Ambulance paramedic workforce, consisting of 1127 paid full-time officers who may be eligible to administer fibrinolytic therapy. Our participants represented 7.2% of this workforce. In addition, protocol application was tested in simulation. Therefore, paramedics were not exposed to real-life factors such as fatigue associated with circadian low points, which may potentially impact on their clinical decision making. However, field testing of our protocol was deemed unethical at such an early juncture without first investigating our paramedics' capabilities in simulation. There was also no lag period between the teaching of our protocol and the testing of its application by participants, meaning that knowledge retention was not examined.

3.9 Conclusion

This study provides evidence of the abilities of a self-selected New Zealand paramedic sample in 12-lead ECG interpretation and clinical decision making with regards to fibrinolysis, and supports recent changes in education and training within the profession. It adds weight to the argument that autonomous paramedic administration of fibrinolysis is an effective strategy to provide this life-saving treatment to STEMI patients. We believe that this study would serve as a useful tool to support and inform a pilot programme of autonomous paramedic-administered fibrinolysis in the New Zealand ambulance services, in terms of staff training and introductory requirements.

Chapter Four:Paramedic-Delivered Fibrinolysis in the Treatment of STEMI: Comparison of a Physician-Assisted Versus Autonomous Paramedic Approach.

4.1 Introduction

In October 2008 the St John Ambulance Service introduced its first paramedic-delivered fibrinolysis pilot programme in Northland and Hawke's Bay. This programme was developed in partnership with each region's DHB and employed a physician-authorised telemetry-based approach (P. Davis, 2014). The technology platform utilised for this programme was the LIFENET STEMI management system produced by Physio Control Inc. (a division of Medtronic, USA). This consisted of an ECG transmission receiving station for each region's main hospital and Vodafone GSM network SIM cards installed in the LIFEPAK® 12 heart monitors carried in all emergency ambulances. This system was subsequently upgraded in 2013, when St John transitioned to use of the Phillips HeartStart MRx monitor.

Under the pilot programme's protocol, when paramedics attended a patient in the field who presented with ischaemic chest discomfort and was located more than 30 minutes transport time from hospital, they would acquire and transmit the patient's 12-lead ECG to the receiving hospital where it would be viewed by an emergency physician. The paramedic would then proceed through a fibrinolysis contraindication checklist with the patient before phoning the hospital-based physician, who would authorise the paramedic to administer the treatment (or not) following discussion of the entire clinical scenario.

Prior to commencement of this physician-authorised programme, ambulance staff with an ATP of paramedic or above were provided a hospital-led two-hour classroom training session introducing them to the new protocol. Class content included a brief revision of ACS pathology and STEMI ECG features, introduction to the fibrinolysis procedure checklist, ECG transmission and physician consultation process, followed by the procedure for drug administration.

Fibrinolysis was and remains the primary reperfusion strategy in the treatment of STEMI within each region, as their main secondary-level hospitals are without cardiac

interventional facilities. For Northland, the nearest PCI centre is based approximately 155km away in the city of Auckland, while for Hawke's Bay, the city of Wellington has the closest PCI centre at 295km. From both a geographic and demographic standpoint, the regions share strong similarities in terms of land area, rural spread and population, of which 24–25% is Māori (Statistics New Zealand, 2013a, 2013b, 2017b).

Many patients were successfully treated with fibrinolysis under the physician-authorised programme. However, technological complications were a relatively common occurrence (P. Davis, 2014). Over a six-year period, transmission delays were experienced a third of the time and approximately 28 out of 127 patients (22%) could not receive fibrinolytic therapy from paramedics because of complete transmission failure. Moreover, the need to transmit an ECG and discuss clinical details with a hospital-based physician was time-consuming in a setting where earlier treatment confers the greatest clinical benefit.

It was these concerns that underpinned the second study in this doctoral project, set up to investigate an alternative model of treatment authorisation. This was a 24-month clinical trial (May 2015 to May 2017) of autonomous paramedic-delivered fibrinolysis in the management of STEMI, occurring without physician oversight and authorisation. This trial was conducted in the same regions of Northland and Hawke's Bay, servicing a combined population of 328,000. In addition, the study is unique: it is the first to compare the two models of paramedic-delivered fibrinolysis, i.e. the physician-authorised telemetry-based model versus the autonomous paramedic model. This study also builds on the foundation of the previous investigation discussed in Chapter Three, taking theory into practice.

4.2 Research Question

1. Are New Zealand paramedics able to accurately identify patients eligible for fibrinolysis in the management of STEMI and provide this treatment safely and autonomously in the field under protocol guidance without physician oversight and authorisation?

4.3 Aims

1. To introduce our previously designed fibrinolysis protocol to selected paramedics and to assess their abilities in its application, in the field.

2. To determine if an autonomous paramedic approach for the provision of fibrinolysis under protocol guidance (compared to a physician-authorised telemetry-based approach) will improve treatment delivery times and patient outcomes, and reduce hospital length of stay (LOS).

4.4 Hypotheses

1. Following education in protocol application, New Zealand paramedics will be able to accurately identify STEMI patients eligible for fibrinolysis and provide this treatment safely and autonomously in the field (under protocol guidance), without physician oversight and authorisation.
2. STEMI patients who receive fibrinolysis from autonomous paramedics (under protocol guidance) will have improved treatment delivery times, clinical outcomes and reduced hospital LOS compared to those who have received the treatment from paramedics under a physician-authorised telemetry-based model.

4.5 Methods

4.5.1 Study Design

Utilising a prospective analysis of differences design, this study made a comparison between two groups of STEMI patients, both of which received fibrinolysis from paramedics but by two different models of treatment authorisation. The first group, an historic retrospective control cohort (referred to as the Pre-Implementation group), were patients who received the treatment from paramedics under the physician-authorised telemetry-based model. In contrast, the second group, our prospective experimental cohort (referred to as the Post-Implementation group), were patients who received the treatment from paramedics who made an autonomous clinical decision under protocol guidance, without physician oversight and authorisation. The difference between these two groups was the intervention – implementation of the new autonomous paramedic fibrinolysis protocol (designed and trialled in the previous study discussed in Chapter Three) that permitted this new independent model of paramedic treatment provision.

The study's prospective approach enabled standardisation of measures used and provided stronger confidence in the findings (Carter, Lubinsky, & Domholdt, 2011; Domholdt, 2005). A true experimental design with randomisation was considered neither ethical nor pragmatic due to the impossibility of blinding the treatment protocol

application, as well as the lengthy timeframe required to reach statistically significant levels of patient numbers. Therefore, the selected design provided a reasonable alternative with efficient use of patient numbers that were available.

Data for the study was collected from patient medical records within the St John Ambulance Service and the receiving hospitals. Medical records provide an abundance of information that can be evaluated in context (Carter et al., 2011). However, inconsistencies may exist and information may be incomplete. For these reasons, data primarily drawn from the records were standard clinical assessment details, of the type routinely gathered for all patients in the context of the STEMI.

The first outcome variable for this trial was the level of paramedic accuracy in identifying patients suitable to receive fibrinolysis (in the post-implementation phase). The second outcome variable was timelines of treatment delivery: the time intervals for patients receiving the treatment from time of symptom onset, from call for ambulance assistance, from first paramedic contact and from first diagnostic STEMI ECG. The third outcome variable was patient outcome at both 30 days and six months post-STEMI (morbidity and mortality), including diagnostic findings and treatment received in hospital. The fourth outcome variable was patient hospital LOS. Additionally, a supplementary investigation examined the incidence of aborted MI following fibrinolysis versus established MI due to failure to reperfuse. This was included within the third outcome variable of patient outcome.

4.5.2 Setting

This clinical trial was conducted within the St John Ambulance Service and in the regions of Northland and Hawke's Bay. The selection of these locations allowed a comparison to be made between the two treatment authorisation models, but also made sense because fibrinolysis drug kits were already carried within each emergency ambulance and staff were trained and experienced in their use. On average, each region undertakes 15–20 fibrinolysis cases per year (P. Davis, 2014). In addition, Northland and Hawke's Bay had a similar number of full-time employed frontline staff (60 and 55 respectively), the majority of whom were qualified as either paramedic or ICP. In terms of DHB services, each region operates four public hospitals, with their main centres being medium-sized secondary-level facilities. Although neither DHB has interventional cardiology services, Hawke's Bay Public Hospital does have coronary angiography facilities.

Table 4.1 provides a comparison of key geographic and demographic features between the two regions, with strong similarities shown. One exception is urban population, with Northland being the country's least urbanised region (Statistics New Zealand, 2017b). Furthermore, from a national perspective, Northland and Hawke's Bay have respectively the second and fourth highest Māori populations, and of the 16 regions in total, are respectively the eighth and ninth most populated (Statistics New Zealand, 2017b).

Table 4.1 ***Comparison of Key Geographic and Demographic Features Between the Regions of Northland and Hawke's Bay***

Geographic / Demographic Feature	Northland	Hawke's Bay
Land area	13,789 km²	14,111 km²
Gross population	171,400	161,500
Percentage of national population	(3.6%)	(3.4%)
Māori population n (%)	43,530 (25%)	38,760 (24%)
Urban population n (%)	85,700 (50%)	130,815 (81%)
Population aged 65+ years n (%)	33,300 (19%)	29,300 (18%)

Note: Adapted from "Subnational population estimates (UA, AU), by age and sex, at 30 June 1996, 2001, 2006–16 (2017 boundary)" by Statistics New Zealand, Retrieved January 9, 2017, from http://nzdotstat.stats.govt.nz/wbos/Index.aspx?DataSetCode=TABLECODE7541. Copyright 2017 by Statistics New Zealand.

4.5.3 Paramedic Participants

Full-time employed ambulance staff from the two regions with an ATP of paramedic or above were automatically enrolled in the trial's education package as part of their employer-based continuing clinical education programme (refer to section 4.5.9 for more detail). To participate in the trial, staff were required to have been enlisted in the previous fibrinolysis programme, i.e. the retrospective pre-implementation phase, and to have successfully completed the education package for the prospective post-implementation phase. This requirement allowed for less confounded comparisons of outcomes between the two groups of STEMI patients observed, and increased equivalence in the characteristics of those paramedics who provided fibrinolysis to the two patient groups. A total of 91 ambulance staff participated in the trial, another eight staff members elected to exclude themselves and a further three failed to complete all requirements of the education package.

4.5.4 Study Population

a) The Pre-Implementation group included all patients who received paramedic-delivered fibrinolysis in the treatment of STEMI within the Northland and

Hawke's Bay regions and under the previous physician-authorised telemetry-based model. This extended over the period from October 2008 to April 2015.

b) The Post-Implementation group included all patients who received fibrinolysis by autonomous paramedics following a diagnosis of STEMI in line with protocol criteria and over the trial's 24-month period from May 2015 to May 2017. In addition, those patients transported by paramedics over the same time period who did not receive fibrinolysis in the field but had a hospital diagnosis of STEMI were also investigated.

4.5.5 Sample Size

To measure all outcomes, based on a previous New Zealand paramedic out-of-hospital fibrinolysis study involving 100 patients by Ranchord et al. (2009) and an *a priori* power analysis using their data, 108 patients were required for this trial: 54 in each of the two observed groups (Faul, Erdfelder, Lang, & Buchner, 2007). This was assuming a sensitivity of 70%, an accuracy measure of +/− 10% and a statistical significance level of $\alpha = 0.05$, denoting a 95% confidence interval.

4.5.6 Criteria for Diagnosis of STEMI

The criteria for diagnosis of STEMI varied slightly between the two groups. For those patients treated in the retrospective pre-implementation phase following physician authorisation, criteria were as per CSANZ guidelines:

- persistent ST-elevation of at least 1mm in two or more contiguous limb leads or at least 2mm in two or more contiguous precordial leads (including posterior leads), or
- new or presumed new LBBB, and
- chest pain less than 12 hours in duration.

Conversely, for those patients treated in the prospective post-implementation phase of the trial by autonomous paramedics, LBBB was considered a contraindication to treatment and the term 'chest pain' was replaced with 'symptoms consistent with myocardial ischaemia'.

4.5.7 Fibrinolysis Drug Regime and Treatment Exclusion Criteria

The fibrinolysis drug regime utilised during both phases of the trial was as per CSANZ guidelines and included single bolus IV tenecteplase, IV bolus enoxaparin (for patients less than 75 years of age only) and SC enoxaparin, as well as oral clopidogrel

and aspirin. Patients in the retrospective pre-implementation phase were considered ineligible for fibrinolysis if they presented with symptoms beyond 12 hours, or had contraindications to the treatment. These exclusion criteria also applied to those patients in the prospective post-implementation phase, with the addition of an age limit of 85 years or older and/or LBBB identified on 12-lead ECG.

4.5.8 Measures

Patient Characteristics: Key demographic data was collected to describe the patient sample population. This included sex, age, ethnicity and body mass index (BMI) score, as well as spatial distribution relative to local population density (per km^2) and the New Zealand socioeconomic deprivation index (NZDep). The NZDep is a measure of socioeconomic deprivation allocated for each meshblock within New Zealand, this being the smallest geographical area defined by Statistics New Zealand, with a population ranging from 60 to 110 people. (Atkinson, Salmond, & Crampton, 2014). The NZDep factors several variables obtained from census data relating to income, home ownership, employment, qualifications, family structure, housing, access to transport and communications (Atkinson et al., 2014). It then places deprivation scores into deciles, where 1 represents the areas that are least socioeconomically deprived and 10 the areas that are most socioeconomically deprived. As has been identified in previous New Zealand ACS-based research, we hypothesised that most patients included in this study would reside in areas allocated a high NZDep score.

In addition, the time interval from patient symptom onset to their 'call for help', i.e. receipt of the 111 emergency call, was measured, and diagnosed patient CVD risk factors and clinical characteristics on presentation were collected. These included key vital signs, Global Registry of Acute Coronary Events (GRACE) 2.0 score, Killip class score, infarct type and automated ECG interpretation. The GRACE 2.0 is a risk-scoring system devised from a large unbiased multinational registry to predict in-patient mortality and post-discharge six-month mortality for the entire spectrum of ACS (Eagle et al., 2004; Mehta et al., 2009). Predictor variables include: age, heart rate (HR), systolic blood pressure (SBP), creatinine level, Killip class of heart failure, cardiac arrest at admission, ST-segment deviation and cardiac enzymes. The scoring system is primarily used at initial hospital presentation to identify those patients most likely to benefit from an invasive treatment strategy.

Like most heart monitors/defibrillators carried by EMS, those that were utilised in the trial have advanced diagnostic software to provide an automated interpretation of acquired 12-lead ECGs, including interpretation of acute STEMI. These automated STEMI algorithms have been widely studied and show high specificity values (89–95%) and moderate sensitivity values (60–68%) (Garvey, Zegre-Hemsey, Gregg, & Studnek, 2016; Ioannidis et al., 2001; Massel, Dawdy, & Melendez, 2000). The automated ECG interpretation was recorded among all patients in the trial who received fibrinolysis. The accuracy of these automated ECG interpretations was then checked against definitive diagnostic measures: the presence of a culprit coronary artery identified on angiography, and/or confirmatory diagnosis of STEMI by the receiving cardiologist, plus a rise in cardiac troponin assays. Note the ambulance heart monitors used in the trial were the Physio-Control LIFEPAK® 12 and LIFEPAK® 15, and the Phillips HeartStart MRx.

First Outcome Variable – Accuracy of Paramedic Diagnosis and Protocol Application: The sensitivity and specificity along with PPV and NPV of the paramedic participants' clinical diagnoses were determined from their identification of patients suitable to receive fibrinolysis or not. This was possible only in the post-implementation phase of the trial. Three independent cardiology consultants (experts) reviewed all cases after the fact, to determine the actual field diagnosis. Accuracy of paramedic protocol application was then assessed accordingly. The rate of *True Positive* and *True Negative* cases, along with *False Positive* and *False Negative* cases, was determined. Each of these categories has been described as a proportion of the total number of clinical decisions made. Causes of *False Positive* and *False Negative* cases were investigated, as were the subgroup of patients excluded from receiving treatment.

Second Outcome Variable – Time to Treatment: Key performance indicator (KPI) targets were established in the prospective post-implementation phase of the trial. These utilised standard target treatment time intervals for fibrinolysis and were monitored as part of the quality assurance process. They included

1. from pain-to-needle (PTN) time and from call-to-needle (CTN) time < 60 minutes, with a target of achieving this time for > 80% of all cases
2. from EMS contact-to-needle (ETN) time of < 30 minutes, with a target of achieving this time for > 80% of all cases
3. from first diagnostic STEMI ECG to needle time < 20 minutes, with a target of achieving this time for > 80% of all cases

4. minimal inappropriate treatment cases, with a target of < 5% of all cases.

The treatment time intervals ('needle times') were also measured and compared between groups, as were operational out-of-hospital time intervals. These included

1. ambulance response time (time from dispatch to arrival at patient)
2. paramedic scene time (arrival at scene to scene departure)
3. first ECG acquisition time (time from arrival at scene to first ECG)
4. ambulance transport time (departure from scene to arrival at hospital).

Treatment time intervals were further measured and compared between regions for both the pre- and post-implementation phases of the trial, to determine any differences.

All the above times were measured in minutes.

Third Outcome Variable – Patient Clinical Management and Outcomes: The following data was collected for both observed groups and analysed to determine patient outcomes:

1. clinical complications in the field, i.e. cardiogenic shock, compromising arrhythmia (not including those patients in cardiac arrest) and cardiac arrest
2. rates of aborted MI defined as: ST-segment resolution of greater than 50% from baseline; no new ST depression; and patient pain-free at 60 minutes after the beginning of fibrinolysis (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013, p. 143)
3. inappropriate fibrinolysis cases, i.e. no rise in cardiac biomarkers identified on hospital admission
4. coronary angiography performed and initial findings.
5. rates of those patients who received medical management only during hospital admission
6. rates of PCI performed during hospital admission (including rescue PCI and non-urgent PCI)
7. intra-aortic balloon pump (IABP) required
8. rates of emergent CABG from the CCL and elective CABG performed later during hospital admission
9. PCI procedure complications

10. in-hospital major bleed (excluding ICH)
11. intra-cranial haemorrhage up to discharge
12. in-hospital reinfarction
13. thirty-day and six-month mortality
14. hospital re-admission within six months of an ACS event.

Of the patients who underwent rescue PCI, the proportion who received the treatment within guideline-mandated timeframes was calculated.

Comparison of Aborted MI Patients to Those with Established MI: All previously described measures of patient clinical characteristics, time to treatment, clinical management and outcomes, as well as hospital admission duration were compared between those patients with aborted MI and those with established MI. This process was undertaken to determine factors associated with established MI.

Fourth Outcome Variable – Hospital LOS: Patient hospital LOS is an indicator of costs to the public health care system. It can also indicate that other in-hospital interventions were necessary, for example rescue-PCI following failed fibrinolysis, CABG or other treatment for in-hospital complications. This time period was measured in bed days for both observed groups.

4.5.9 Intervention

Autonomous Paramedic Fibrinolysis Protocol (Independent Variable): The clinical criteria and drug regime applied in the new autonomous paramedic fibrinolysis protocol (Appendix O) was similar to the previous physician-authorised protocol, but with two main exceptions. The first of these was three additional treatment inclusion criteria designed to mitigate the risk of erroneous paramedic ECG interpretation of STEMI. These were:

1. monitor interpretation indicates >>> Acute MI <<< OR ***ACUTE MI SUSPECTED*** OR ***MEETS ST ELEVATION MI CRITERIA*** on two consecutive 12-lead ECGs
2. normal QRS width (≤ 0.12secs) OR right bundle branch block identified on 12-lead ECG
3. heart rate < 130 beats per minute.

Evidence shows that false positive automated interpretation of STEMI commonly occurs due to one or more factors: incorrect lead placement, ECG artefact, tachy-dysrhythmia, and a QRS width beyond normal limits (> 0.12secs) (Garvey et al., 2016). Therefore, the protocol stipulation to obtain two consecutive ECGs with an automated interpretation of STEMI was intended to prompt paramedics to check lead placement and trace quality prior to acquisition of the second ECG.

The second main exception is related to the treatment contraindication checklist. In the new protocol, those patients presenting with a LBBB or aged 85 years or older were excluded from receiving fibrinolysis. Beyond these listed exceptions, the primary difference between the two observed groups was in fact the model of treatment authorisation, i.e. physician-authorised (pre-implementation phase) versus paramedic-authorised (post-implementation phase).

The new paramedic protocol was introduced to ambulance staff as part of an eight-hour education package designed by the principal researcher, with input from academic supervisors, AUT School of Paramedicine and St John. The components of the education package are listed in Table 4.2. Among other things, they sought to address key areas of paramedic knowledge deficit identified by the research team in their previous study discussed in Chapter Three. In particular, this included accurate understanding and interpretation of STEMI-mimics such as bundle branch block patterns and LVH (P. R. Davis, Howie, & Dicker, 2017).

Both the training and refresher workshops were delivered by the principal researcher, alongside several St John education tutors. These sessions were delivered during routine rostered staff training days, where staff attendance was a compulsory requirement of the employer, St John. Furthermore, for the paramedic participants to have fibrinolysis added to their scope of clinical practice and thus be able to provide the treatment autonomously, they were required to complete all components of the education package and obtain a pass mark of 80% or greater within the final written examination.

Table 4.2 ***Paramedic Education Package***

Education Component	Description	Duration
Online ACS and 12-lead ECG refresher module	Revision of ACS pathology and assessment of the ACS patient, as well as STEMI recognition and STEMI-mimic recognition on 12-lead ECG. Completed prior to training workshop attendance.	2hr
Training workshop	In-class teaching session revising all content of the online refresher module followed by introduction of the new autonomous paramedic fibrinolysis protocol.	3hr
Written examination	Summative scenario-based standardised written test undertaken at the completion of the training workshop.	1hr
Refresher workshop	In-class teaching session conducted 12 months after the initial training workshop with presentation and discussion of fibrinolysis cases, attended by staff during the study period to date.	2hr

Note: ACS = acute coronary syndrome; ECG = electrocardiogram; STEMI = ST-elevation myocardial infarction

4.5.10 Study Implementation Process

Before the trial commenced approval was gained from the relevant ethics committees, the St John Ambulance Service and Northland and Hawke's Bay DHBs. Then the trial's education package was fully developed and paramedic participants from the selected regions were identified via their respective line managers. All received details to access the self-directed online refresher module. The training workshops and written examination were then delivered at St John Ambulance stations in Kerikeri, Whangarei, Napier and Hastings. Following completion of each workshop, staff members who successfully passed the written examination were permitted to provide fibrinolysis autonomously, utilising the new protocol, effective immediately. This new addition to their existing scope of clinical practice was authorised by means of a 'standing order' by the St John Medical Director. This point also marked the start of patient data collection for the prospective cohort from both ambulance and hospital records. After the first 12-month period from when the trial commenced, refresher workshops were conducted for all staff at the same locations previously discussed.

4.5.11 Data Management and Processing

Raw data was entered in the SPSS software programme version 24 and screened to ensure no entry errors. A screening of the data for outliers also occurred with corrections made prior to analysis. The significance level was set at 0.05.

4.5.12 Data Analysis

Initial analysis of data was primarily descriptive, producing frequencies, means and standard deviations, or medians and interquartile ranges where relevant, and testing for normal distributions of continuous measures, e.g. time between events. Where normality was not achieved, transformations such as the log of measure were examined. To test Hypothesis One, the rates of *True Positive* and *True Negative* along with *False Positive* and *False Negative* cases were identified, and the sensitivity, specificity, PPV and NPV of paramedic protocol application were then calculated. This was achieved by use of a frequency score and subsequent presentation of results utilising a frequency distribution table, with comparison of scores against the standard (a dummy variable) as determined by three independent cardiologists (experts).

To test Hypothesis Two, both observed groups were initially compared using (where relevant) chi-square tests for independence or independent-sample t-tests. Comparison of medians was made using Mann-Whitney U tests. Variables such as time to treatment, time to hospital, patient demographics and time of day were examined, as were patient presentation characteristics before receiving fibrinolysis (e.g. vital signs, GRACE 2.0 and Killip score, symptoms and ECG findings). Where significant differences were present, those characteristics were added as covariates to the model after examination for potential correlations. Logistic regression was used to examine associations between these same objective measures and the outcome of established MI.

4.5.13 Geographic Information System Data and Map Reference

To present patient spatial distribution throughout the Northland and Hawke's Bay regions and relative to both the NZDep and regional population density, geographical information system (GIS) data was obtained from each regional council and the national census database for 2013 (the closet census to the study dates). All maps are presented in the GCS_NZGD_2000 geographic coordinate system and the New Zealand Transverse Mercator projected coordinate system.

4.5.14 Ethics

Ethical approval for the trial was obtained from HDEC Northern A (14/NTA112 – Appendix F), and from AUTEC (application number 15/03 – Appendix E). Locality and institutional approval was obtained from St John's Clinical Audit and Research Group (Appendix G), as well as Northland and Hawke's Bay DHBs (Appendix H and I respectively).

4.5.15 Criteria for Trial Termination and Management of Pre-Hospital Adverse Events

As a stipulation of the trial's locality and institutional approval, the research team was required to provide an update to the St John Ambulance Service and both the Northland and Hawke's Bay DHBs biannually by means of a variance report. Each party had the capacity to terminate the trial at any stage and for any reason. One example may have been an excessive number of inappropriate treatment cases, i.e. patients administered fibrinolysis by autonomous paramedics when the treatment should have been withheld. In addition, treating paramedics were required to submit the ambulance electronic patient report form (ePRF) via email to the trial's lead investigator immediately following each job. This provided for any pre-hospital adverse events (including inappropriate treatment cases) to be identified and addressed promptly, in line with existing St John Ambulance standard operating procedures (SOPs). Furthermore, as a requirement of the trial's ethics approval by HDEC, an independent safety monitoring group was established to oversee all clinical aspects of the trial and provide feedback where appropriate. This group consisted of three independent cardiologists who received a copy of each patient audit form upon completion.

4.6 Results

4.6.1 Patient Characteristics

A total of 174 patients were included in the study – 96 patients in the Pre-Implementation group and 78 patients in the Post-Implementation group. All data points were complete.

Table 4.3 reports on patient demographics and CVD risk factors. These were similar overall between the two observed groups. Most patients were male (combined average age of 64 years, SD ± 11.2), of European ethnicity and residing in more socioeconomically deprived areas (as measured by the NZDep). Smoking and a family history of ACS were the most prominent risk factors identified.

Maps showing the spatial distribution of geo-coded residential addresses for all patients with a confirmed diagnosis of STEMI, and relative to regional population density, are presented in Figure 4.1 and 4.2. As shown, in both regions STEMI patients were encountered more frequently in the more highly populated areas. In Northland, the main cluster of patients was observed in the Kerikeri area, while for Hawke's Bay, two

large clusters were observed in the Napier and Hastings city areas. The same spatial distribution overlay for confirmed STEMI patients is presented relative to the NZDep in Figure 4.3 and Figure 4.4, reconfirming the previous findings identified in Table 4.3.

Clinical characteristics of patients on initial presentation are presented in Table 4.4. These include mean heart rate, blood pressure, arterial oxygen saturation and GRACE 2.0 score, as well as Killip scores of II to IV and infarct type. These were all similar between the two groups. Furthermore, chest, neck or arm discomfort formed part of the symptomology among all patients treated as well as those with a confirmed diagnosis of STEMI (n = 196). This figure includes those STEMI patients excluded from receiving fibrinolysis in the post-implementation phase (Figure 4.5). In addition, 78% (153/196) of STEMI patients stated that their discomfort was a first-time occurrence.

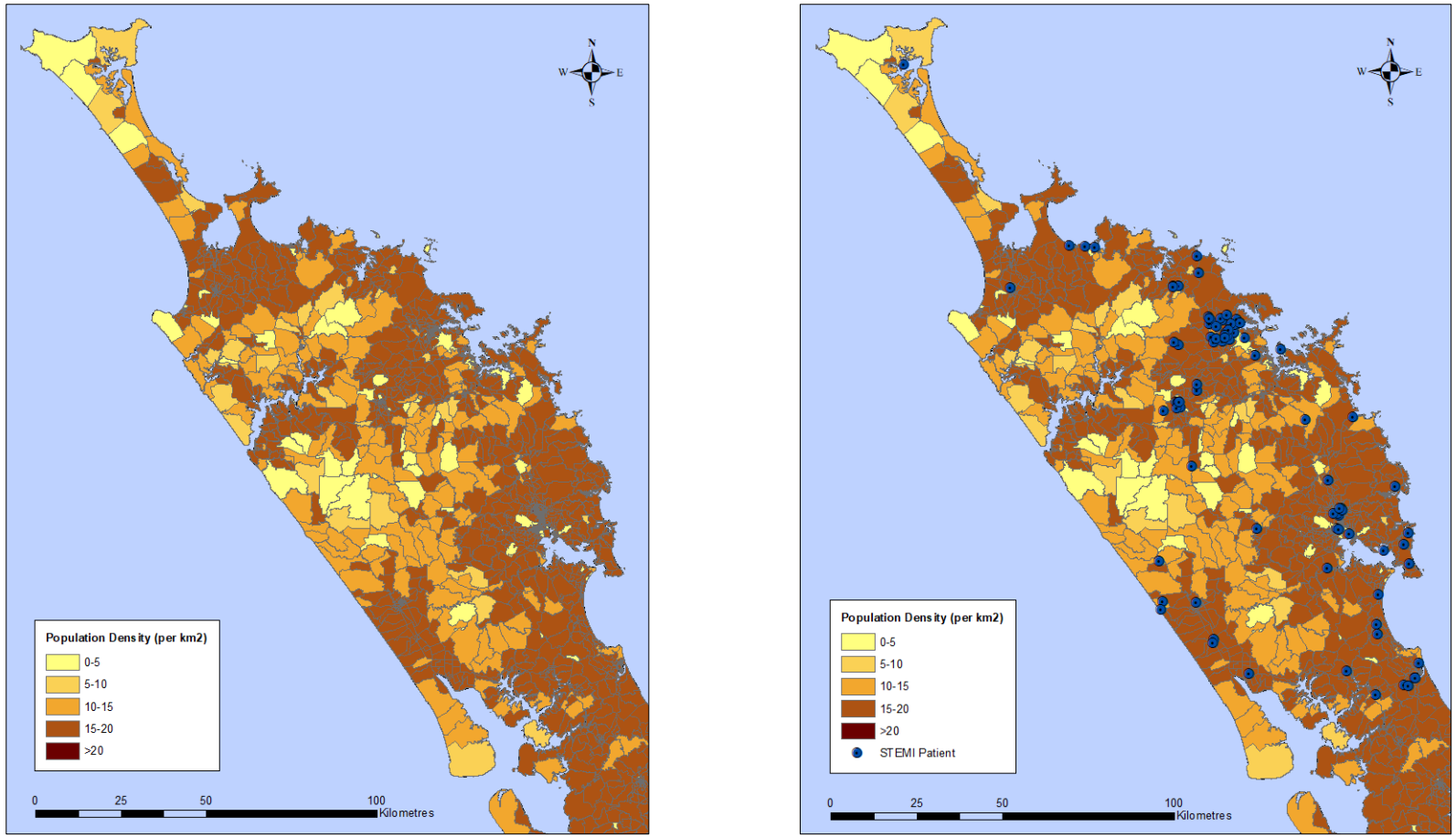
Within the Pre-Implementation group, 89/96 patients (93%) had a positive automated interpretation of STEMI on their diagnostic 12-lead ECG, compared with all 76 patients (100%) in the Post-Implementation group. (However, note that this was a protocol requirement for the provision of fibrinolysis in the post-implementation phase.) In all but nine of these cases (165/174 – 95% combined total), this finding corresponded with a culprit lesion identified on coronary angiography and/or a confirmatory diagnosis of STEMI by the receiving cardiologist along with a positive rise in cardiac troponin assays.

No significant difference was identified between groups in terms of the time lapse between patient symptom onset and phoning 111 for ambulance assistance (median time 34 minutes, 95% CI 28–101, [IQR 65] Pre-, versus 26 minutes, 95% CI 22–97, [IQR 48] Post-Implementation, $p = 0.41$ – 2-tailed). The combined median time for this subinterval was 28 minutes (95% CI 25–92). Sixty-one percent of all patients presented during normal working hours, i.e. between 9am and 5pm.

Table 4.3 ***Demographics and Cardiovascular Disease Risk Factors: Comparison of the Pre- Versus Post-Implementation Group***

Variable		Pre-Implementation Group (n = 96) n (%)	Post-Implementation Group (n = 78) n (%)	Test Statistic	p-Value
Sex	- Male	68 (71)	53 (68)		
	- Female	28 (29)	25 (32)	$\chi^2(1) = 0.169$	0.68
Mean age in years (±SD)		**63 (±11.1)**	**64 (±11.5)**	t (172) = 0.21	0.82 (2-tailed)
Ethnicity	- European	81 (84)	64 (82)		
	- Māori	12 (13)	11 (14)		
	- Pacific peoples	3 (3)	3 (4)	FET	0.90
NZDep score 1-5		15 (16)	19 (24)		
NZDep score 6-10		81 (84)	59 (66)	$\chi^2(1) = 1.569$	0.21
CVD Risk factors	- HTN	52 (54)	51 (65)	$\chi^2(1) = 1.366$	0.24
	- Diabetes	17 (18)	10 (13)	$\chi^2(1) = 0.456$	0.50
	- Hyperlipidaemia	47 (49)	35 (45)	$\chi^2(1) = 0.148$	0.70
	- Increased BMI	34 (36)	31 (40)	$\chi^2(1) = 0.184$	0.66
	- Current Smoker	61 (63)	54 (69)	$\chi^2(1) = 0.394$	0.53
	- Family history of ACS	67 (70)	48 (61)	$\chi^2(1) = 0.966$	0.32
	- IHD	36 (38)	23 (29)	$\chi^2(1) = 0.901$	0.34
	- Previous AMI	10 (11)	12 (15)	$\chi^2(1) = 0.564$	0.45
	- Previous PCI	13 (14)	9 (11)	$\chi^2(1) = 0.028$	0.86
	- Previous CABG	3 (3)	3 (4)	FET	1.00

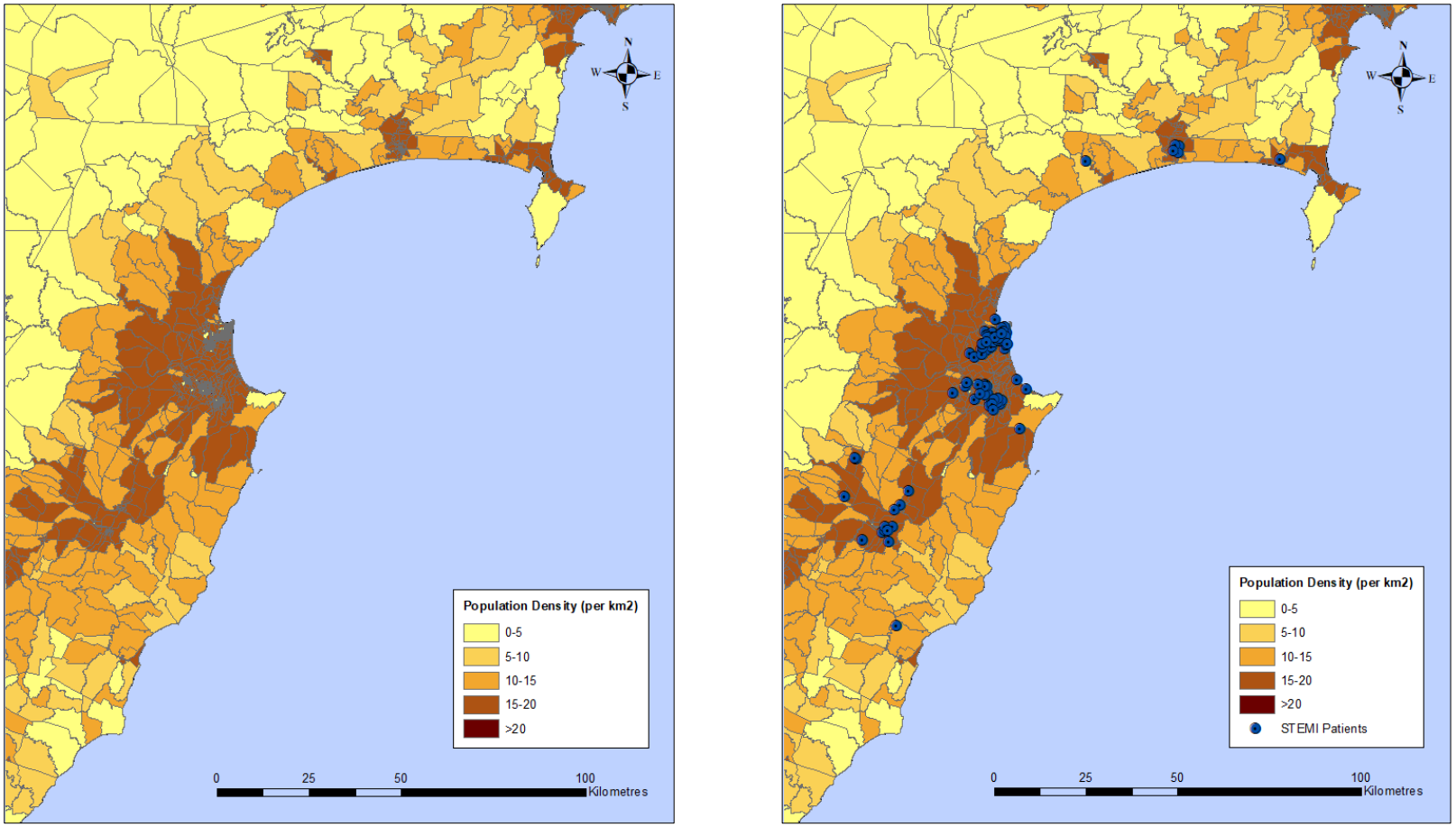
Note: χ^2 = chi-square; SD = standard deviation; t = t-test value; FET = Fisher's exact test; NZDep = New Zealand Socioeconomic Deprivation Index; CVD = cardiovascular disease; HTN = hypertension; BMI = body mass index; ACS = acute coronary syndrome; IHD = ischaemic heart disease; AMI = acute myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting



(A) (B)

Figure 4.1 **Population Density of Northland with STEMI Patient Overlay**

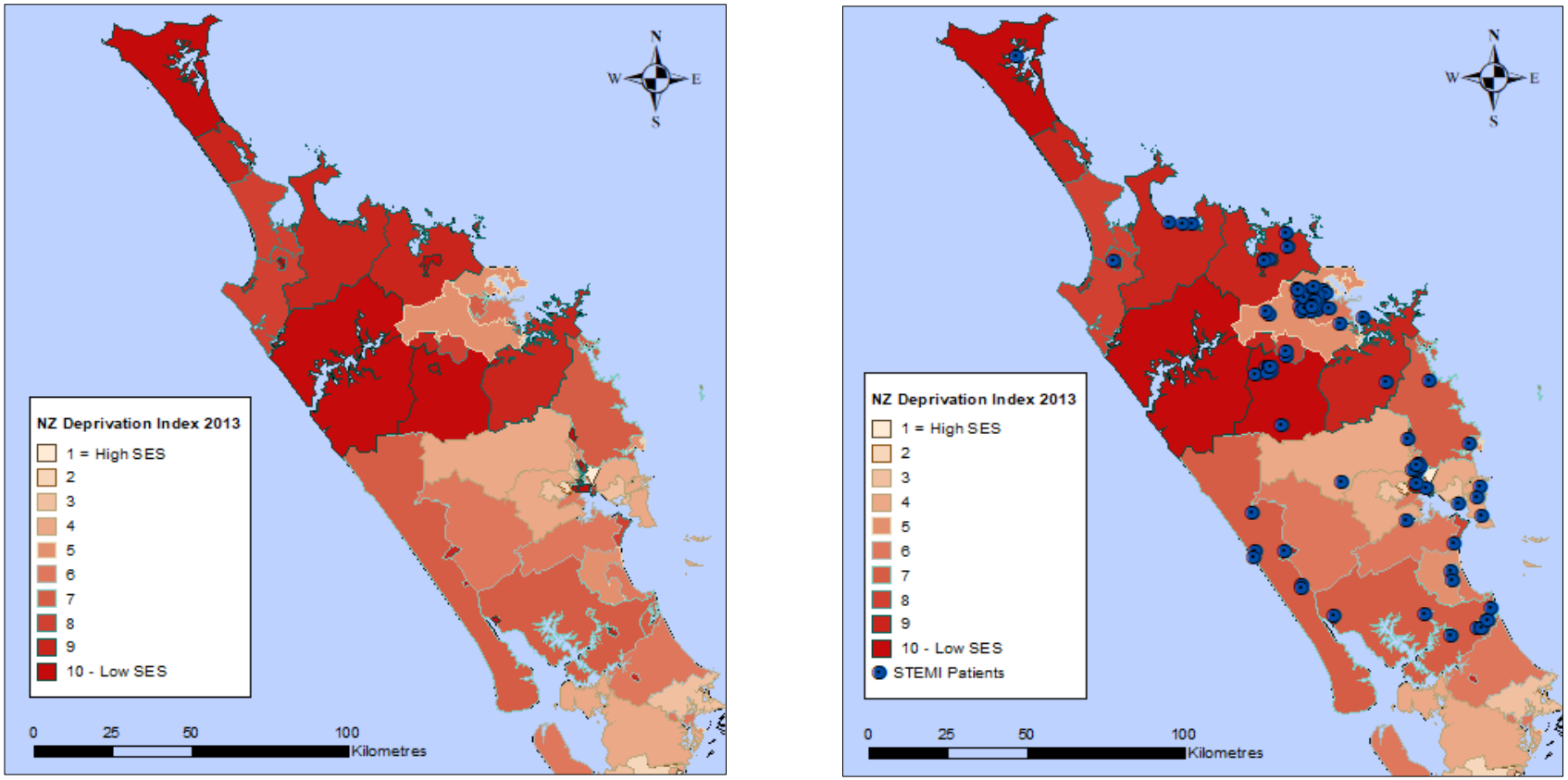
(A) Population density (number of people per km^2) calculated from NZ census (2013) by meshblock
(B) Population density by meshblock with confirmed STEMI patients' addresses overlaid



(A) (B)

Figure 4.2 **Population Density of Hawke's Bay with STEMI Patient Overlay**

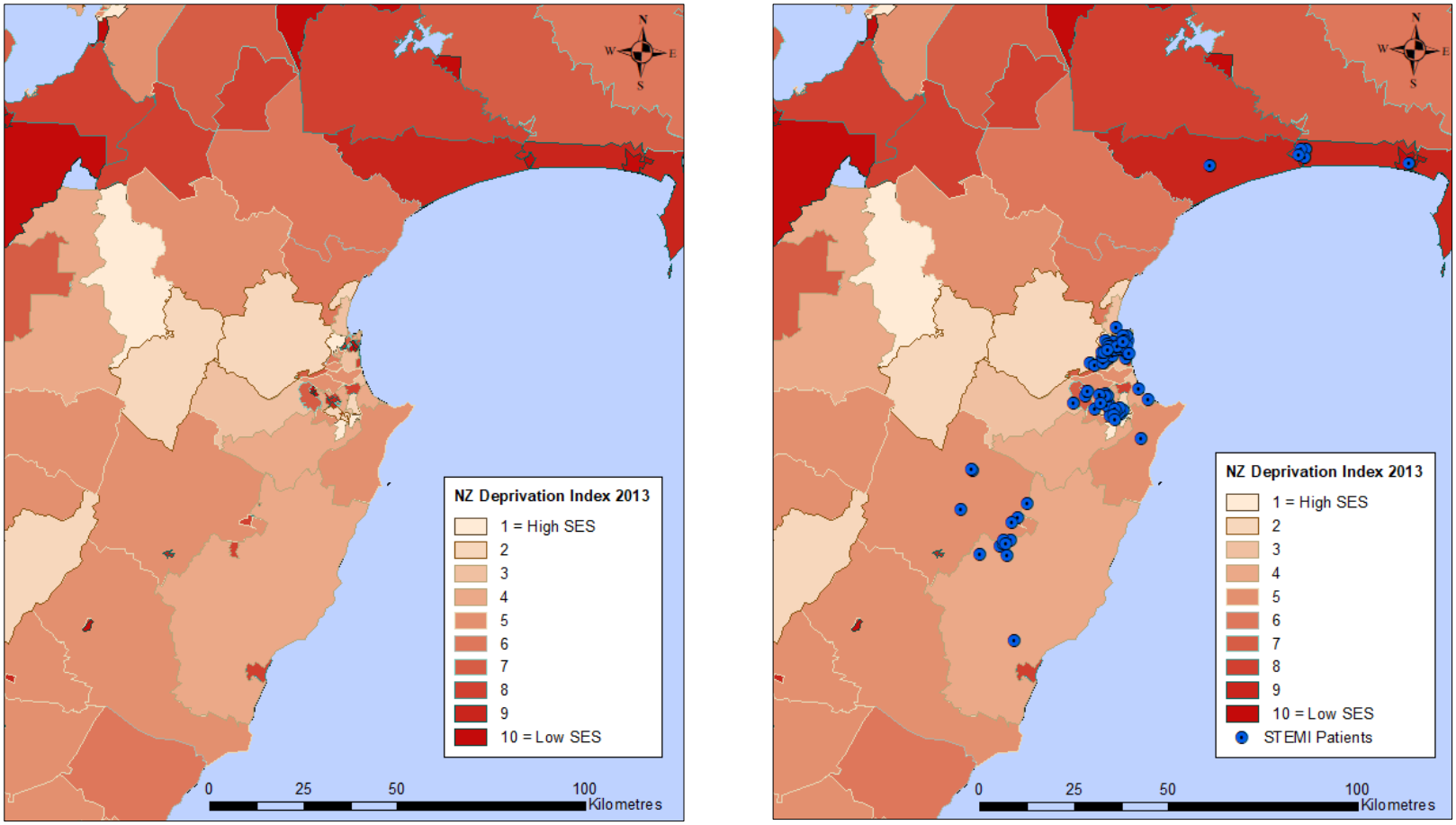
(A) Population density (number of people per km2) calculated from NZ census (2013) by meshblock
(B) Population density by meshblock with confirmed STEMI patients' addresses overlaid



(A) (B)

Figure 4.3 **New Zealand Deprivation Index in Northland with STEMI Patient Overlay**

(A) New Zealand Deprivation Indices calculated from NZ census (2013) by meshblock
(B) New Zealand Deprivation Indices by meshblock with confirmed STEMI patients' addresses overlaid



(A) (B)

Figure 4.4 **New Zealand Deprivation Index in Hawke's Bay with STEMI Patient Overlay**

(A) New Zealand deprivation indices calculated from NZ census (2013) by meshblock
(B) New Zealand deprivation indices by meshblock with confirmed STEMI patients' addresses overlaid

Table 4.4 ***Clinical Characteristics on Initial Presentation: Comparison of the Pre- Versus Post-Implementation Group***

Clinical Characteristic	Pre-Implementation Group (*n* = 96) *n* (%)	Post-Implementation Group (*n* = 78) *n* (%)	Test Statistic	*p*-Value
Mean HR - beats/min (±SD)[a]	70 (±10.5)	71 (±11.4)	*t* (172) = 0.21	0.65 (2-tailed)
Mean SBP -mmHg (±SD)[a]	128 (±27.7)	127 (±28.7)	*t* (172) = 0.25	0.79 (2-tailed)
Mean SpO_2 -% (±SD)[a]	96 (±2.6)	97 (±2.8)	*t* (172) = 0.46	0.64 (2-tailed)
Mean GRACE 2.0 score (±SD)[b]	122 (±38.9)	115 (±34.8)	*t* (172) = 1.22	0.22 (2-tailed)
Killip class II-IV[b]	8 (8)	6 (7)	$\chi^2(1) = 0.023$	0.87
Infarct type[b] - Anterior	38 (39)	35 (45)	$\chi^2(1) = 0.494$	0.48
- Inferior	47 (49)	36 (46)	$\chi^2(1) = 0.135$	0.71
- Other	5 (5)	4 (5)	FET	1.00
- Mimic	6 (7)	3 (4)	FET	0.73

Note: HR = heart rate; SD = standard deviation; *t* = t-test value; SBP = systolic blood pressure; SpO_2 = percentage of arterial oxygen saturation; GRACE = Global Registry of Acute Coronary Events; χ^2 = chi-square; FET = Fisher's exact test

[a]HR, SBP and SpO_2 recorded on first paramedic assessment in the field

[b]GRACE score, Killip class and infarct type recorded on patient presentation at hospital

4.6.2 Inappropriate Fibrinolysis Cases

Of the 174 patients who received fibrinolysis among both observed groups, nine patients (5.1%) showed no rise in cardiac biomarkers. Retrospective review of these nine cases, examining patient presentation, history of events leading to ambulance request and combined ECG, showed that six were inconsistent with myocardial ischaemia. Of the nine patients, six were treated in the Pre-Implementation group following physician authorisation and the remaining three in the Post-Implementation group by autonomous paramedics (6.2% Pre- versus 3.8% Post-Implementation, p = 0.73). None of these patients developed complications from fibrinolysis and all have been excluded from analysis of patient outcomes. Table 4.5 provides a diagnostic summary of these cases.

Table 4.5 ***Inappropriate Fibrinolysis Cases and Final Diagnoses***

Case and Final Diagnosis	*N*	(%)
Pericarditis	3	(33.3)
Upper respiratory tract infection with non-specific ST-elevation	1	(11.1)
Cardiomyopathy / apical ballooning syndrome	2	(22.3)
Costochondritis with early repolarisation	1	(22.3)
Upper respiratory tract infection with previous left ventricular aneurysm	1	(11.1)
Intra-cranial haemorrhage with raised intracranial pressure	1	(11.1)
Total	**9**	**(100)**

4.6.3 Accuracy of Paramedic Diagnosis and Protocol Application

During the prospective post-implementation phase of the trial, 116 patients were assessed for their suitability to receive fibrinolysis by autonomous paramedics. Seventy-eight of these patients were deemed eligible and received the treatment; the remaining 38 patients were deemed ineligible and did not receive the treatment. Of the 78 patients who received fibrinolysis, three cases (3.8%) were later identified as inappropriate treatment decisions. The overall accuracy of paramedic diagnosis and protocol application is presented in Table 4.6, and a summary of cases excluded for fibrinolysis is presented in Figure 4.5.

Among the 38 excluded cases, 24 patients presented with a contraindication to fibrinolysis. The most common encountered contraindication was uncontrolled hypertension (6/24), defined as an initial systolic blood pressure > 180mmHg or diastolic blood pressure > 110mmHg. The second most common contraindication was the patient currently medicated with an anticoagulant (5/24), i.e. warfarin or dabigatran. In all 24

cases where treatment was contraindicated, the patient had a hospital diagnosis of STEMI. Among those patients presenting with a STEMI-mimic on 12-lead ECG, the most common mimic identified was LVH (3/7), followed by LBBB (2/7). For the two cases where treatment was indicated but withheld, the attending paramedic accurately diagnosed STEMI but elected not to proceed with the fibrinolysis procedure.

Table 4.6 ***Accuracy of Paramedic Ability to Independently Determine Patient Eligible for Fibrinolysis (Post-Implementation Group, n = 78)***

Accuracy Value	(%)	[95% CI]
Sensitivity	(96)	[89–99]
Specificity	(91)	[76–98]
Positive predictive value (PPV)	(96)	[90–99]
Negative predictive value (NPV)	(91)	[77–97]

Note: CI = confidence interval

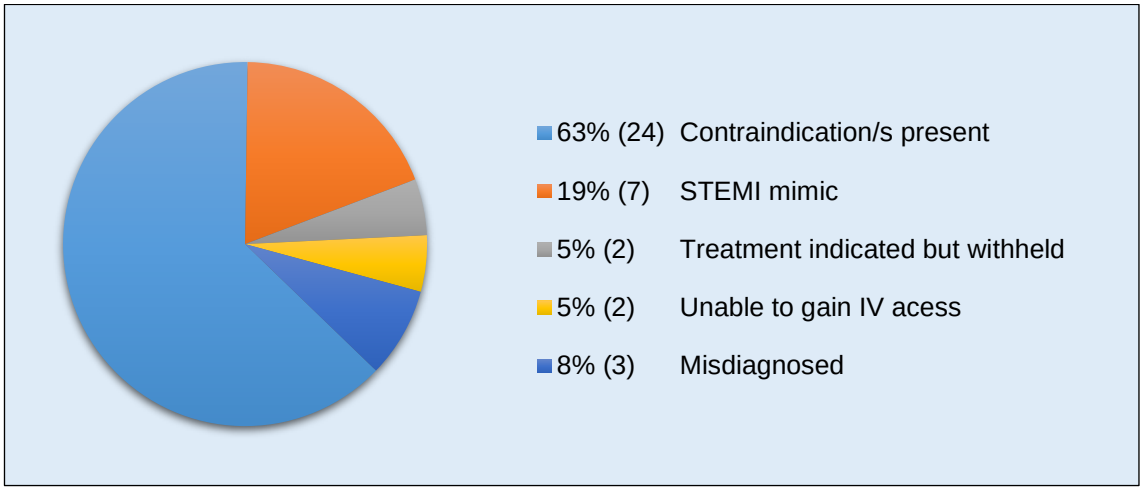


Figure 4.5 **Summary of Cases Excluded from Receiving Fibrinolysis by Autonomous Paramedics in the Post-Implementation Phase (*n* = 38)**

Note: STEMI = ST-elevation myocardial infarction; IV = intravenous

4.6.4 Time to Treatment

Key performance indicator (KPI) target results for the autonomous paramedic fibrinolysis programme in the post-implementation phase are presented in Table 4.7. All targets were achieved except for a PTN time of less than 60 minutes for greater than 80% of cases. Table 4.8 provides a comparison of key treatment time intervals between the two observed groups, excluding those cases of inappropriate fibrinolysis. For all measures, a significant improvement in time was demonstrated in favour of the post-implementation group. Figure 4.6 compares the distribution of ETN times between groups. In the Pre-Implementation group only 28% of patients received treatment within

the mandated target time of less than 30 minutes. Conversely, in the Post-Implementation group, this time was achieved for approximately 93% of cases – a more than three-fold improvement.

Table 4.9 provides a comparison of additional operational and clinical times between the two observed groups. A significant improvement in both first ECG acquisition time (commenced from first contact with the patient) and ambulance transport time (departure from scene to arrival at hospital) was shown in favour of the Post-Implementation group.

Table 4.10 provides a comparison of the key treatment time intervals between the Northland and Hawke's Bay regions during the pre-implementation phase of the trial. All measures were found to be significantly shorter among those patients who received treatment in Hawke's Bay. Conversely, when comparing the same intervals, no significant differences were observed between the two regions during the post-implementation phase of the trial (Table 4.11).

Table 4.7 ***Key Performance Indicators, Targets and Results: Autonomous Paramedic Fibrinolysis Programme (Post-Implementation Phase)***

KPI Measure	Target (% of Total Cases)	*N*	Result (%)
From pain-to-needle (PTN) time ≤ 60 minutes[a]	(>80)	75	(44)
From call-to-needle (CTN) time ≤ 60 minutes[a]	(>80)	75	(92)
From EMS contact-to-needle (ETN) time ≤ 30 minutes[a]	(>80)	75	(93)
From first diagnostic STEMI ECG to needle time ≤ 20 minutes[a]	(>80)	75	(92)
Minimal inappropriate treatment cases	(<5)	3/78	(4)

Note: KPI = key performance indicator; EMS = emergency medical services; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram
[a] Excludes cases of inappropriate fibrinolysis (*n* = 3)

Table 4.8 ***Comparison of Key Treatment Time Intervals in Minutes (Median Values and Interquartile Ranges): Pre- Versus Post-Implementation Group***

	Pre-Implementation Group (*n* = 90)			Post-Implementation Group (*n* = 75)			
Treatment Time Interval	Median	[95% CI]	IQR	Median	[95% CI]	IQR	*p*-Value
From pain-to-needle (PTN) time[a]	87	[82, 138]	58	65	[60, 110]	41	0.007* (2-tailed)
From call-to-needle (CTN) time[a]	52	[49, 62]	30	36	[33, 42]	10	<0.001* (2-tailed)
From EMS contact-to-needle (ETN) time[a]	37	[34, 45]	30	20	[17, 23]	8	<0.001* (2-tailed)
From first diagnostic STEMI ECG to needle time[a]	24	[24, 31]	24	16	[14, 17]	9	<0.001* (2-tailed)

Note: EMS = emergency medical services; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram; CI = confidence interval; IQR = interquartile range. All comparisons between groups were made using Mann-Whitney U tests.
*Significant at $p < 0.05$
[a] Excludes cases of inappropriate fibrinolysis (*n* = 9)

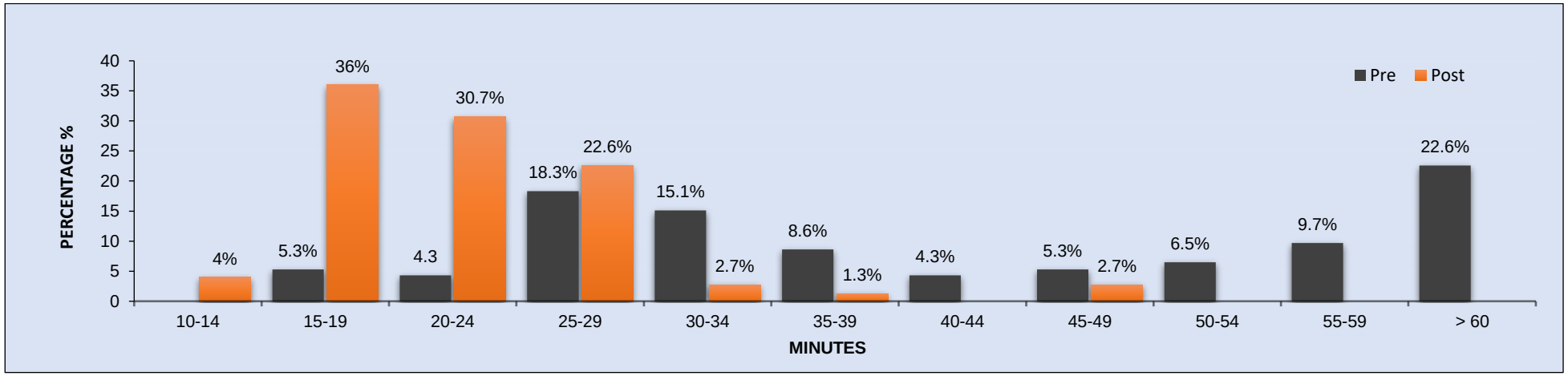


Figure 4.6 **Distribution and Comparison of ETN Times: Pre- Versus Post-Implementation Group**

Note: ETN = emergency medical services contact-to-needle. The target time for this subinterval is < 30 minutes. This figure excludes those cases of inappropriate fibrinolysis (n = 9).

Table 4.9 ***Comparison of Additional Operational and Clinical Times in Minutes (Median Values and Interquartile Ranges): Pre- Versus Post-Implementation Group***

	Pre-Implementation Group (n = 96)			Post-Implementation Group (n = 78)			
Time Measure	Median	[95% CI]	IQR	Median	[95% CI]	IQR	p-Value
Ambulance response time	10	[9, 16]	14	11	[10, 17]	10	0.39 (2-tailed)
Ambulance scene time	35	[35, 45]	20	33	[31, 36]	10	0.34 (2-tailed)
First ECG acquisition time[a]	10	[10, 15]	11	4	[4, 6]	3	<0.001* (2-tailed)
Ambulance transport time	42	[41, 55]	57	18	[16, 30]	18	<0.001* (2-tailed)

Note: CI = confidence interval; IQR = interquartile range; ECG = electrocardiogram. All comparisons between groups were made using Mann-Whitney U tests.
[a] ECG acquisition time commenced from time of first paramedic contact with patient
*Significant at $p < 0.05$

Table 4.10 ***Comparison of Key Treatment Time Intervals (Median Values and Interquartile Ranges): Hawke's Bay Versus Northland Pre-Implementation Groups***

	Northland (*n* = 46)			Hawkes Bay (*n* = 44)			
Treatment Time Interval	Median	[95% CI]	IQR	Median	[95% CI]	IQR	*p*-Value
From pain-to-needle (PTN) time[a]	101	[97, 148]	71	80	[75, 146]	47	0.07 (2-tailed)
From call-to-needle (CTN) time[a]	62	[57, 72]	32	45	[42, 54]	28	0.001* (2-tailed)
From EMS contact-to-needle (ETN) time[a]	49	[41, 52]	33	31	[30, 41]	22	0.004* (2-tailed)
From first diagnostic STEMI ECG to needle time[a]	29	[28, 37]	27	19	[18, 26]	15	0.001* (2-tailed)

Note: EMS = emergency medical services; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram; CI = confidence interval; IQR = interquartile range. All comparisons between groups were made using Mann-Whitney U tests.
*Significant at $p < 0.05$
[a] Excludes cases of inappropriate fibrinolysis ($n = 6$)

Table 4.11 ***Comparison of Key Time Intervals in Minutes (Median Values and Interquartile Ranges): Hawke's Bay Versus Northland Post-Implementation Groups***

	Northland (*n* = 29)			Hawkes Bay (*n* = 46)			
Treatment Time Interval	Median	[95% CI]	IQR	Median	[95% CI]	IQR	p-Value
From pain-to-needle (PTN) time[a]	70	[60, 122]	52	62	[54, 115]	55	0.07 (2-tailed)
From call-to-needle (CTN) time[a]	39	[34, 48]	12	35	[32, 46]	12	0.16 (2-tailed)
From EMS contact-to-needle (ETN) time[a]	20	[17, 25]	7	21	[18, 23]	6	0.74 (2-tailed)
From first diagnostic STEMI ECG to needle time[a]	17	[14, 19]	6	15	[13, 16]	5	0.28 (2-tailed)

Note: EMS = emergency medical services; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram; CI = confidence interval; IQR = interquartile range. All comparisons between groups were made using Mann-Whitney U tests.
[a] Excludes cases of inappropriate fibrinolysis ($n = 3$)

4.6.5 Patient Clinical Management and Outcomes

Out-of-hospital complications and coronary angiographic findings were found to be similar overall between both observed groups (Table 4.12). This included most patients presenting with single vessel disease. However, a significantly higher proportion of patients in the Post-Implementation group had both a coronary angiogram performed and presented with a culprit RCA. Referral for coronary angiogram was at the discretion of the treating physician in the ED during both study phases.

Table 4.13 summarises ongoing clinical management and outcomes across both observed groups. No significant difference in the rates of aborted MI between groups was identified. However, 30-day mortality was found to be significantly lower among patients in the Post-Implementation group. For those patients who underwent rescue PCI among both observed groups (40 in total), the average time from arrival at the referral hospital to balloon inflation was 182 minutes (SD ± 13).

Table 4.12 ***Out-of-Hospital Complications and Angiographic Findings: Comparison of the Pre- Versus Post-Implementation Group***

Variable	Pre-Implementation Group (*n* = 90) *n* (%)	Post-Implementation Group (*n* = 75) *n* (%)	Test Statistic	*p*-Value
Out-of-hospital complications:				
- Cardiogenic shock	15 (17)	8 (11)	$\chi^2(1) = 1.227$	0.26
- Compromising arrhythmia (excluding SCA)	8 (9)	8 (11)	$\chi^2(1) = 0.147$	0.70
- Cardiac arrest	10 (11)	7 (9)	$\chi^2(1) = 0.139$	0.70
- Death	1 (1)	-	-	-
Coronary angiography performed	77 (85)	72 (96)	$\chi^2(1) = 5.096$	0.02*
Angiographic findings:				
- No significant lesion > 50%	3 (4)	5 (7)	FET	0.48
- 1 vessel disease	60 (78)	54 (72)	$\chi^2(1) = 0.176$	0.67
- 2 vessel disease	6 (8)	5 (7)	FET	0.10
- 3 vessel disease	7 (9)	8 (11)	$\chi^2(1) = 0.167$	0.68
- Left main stem stenosis	1 (1)	-	-	-
Culprit artery (excluding cases of no significant VD)**:**				
- Left anterior descending	25 (34)	24 (36)	$\chi^2(1) = 0.064$	0.79
- Left circumflex	11 (15)	4 (6)	FET	0.10
- Right	27 (36)	37 (55)	$\chi^2(1) = 6.440$	0.01*
- Left main stem	3 (4)	-	-	-
- Other	8 (11)	2 (3)	FET	0.10

Note: SCA = sudden cardiac arrest; χ^2 = chi-square; FET = Fisher's exact test; VD = vessel disease. Table excludes cases of inappropriate fibrinolysis.
* Significant at $p < 0.05$

Table 4.13 ***Ongoing Clinical Management and Outcomes: Comparison of the Pre- Versus Post-Implementation Group***

Variable	Pre-Implementation Group (*n* = 90) *n* (%)	Post-Implementation Group (*n* = 75) *n* (%)	Test Statistic	*p*-Value
Aborted MI	60 (66)	53 (70)	$\chi^2(1) = 0.303$	0.58
Hospital treatment:				
- Medical management only	22 (24)	10 (13)	$\chi^2(1) = 3.231$	0.07
- PCI				
Rescue PCI	20 (22)	20 (26)	$\chi^2(1) = 0.440$	0.50
Non-urgent PCI	42 (46)	42 (56)	$\chi^2(1) = 1.426$	0.23
PCI procedure complications	4 (5)	4 (5)	FET	1.00
- IABP required	1 (1)	-	-	-
- Emergent CABG from CCL	1 (1)	-	-	-
- Elective CABG	5 (6)	4 (5)	FET	1.00
In-hospital major bleed (excluding ICH)	-	-	-	-
ICH up to discharge	2 (2)	-	-	-
In-hospital reinfarction	-	-	-	-
Mortality at 30 days	8 (9)	1 (1)	FET	0.04*
Mortality at 6 months	10 (11)	2 (3)	FET	0.06
Re-admission for an ACS event within 6 months	10 (11)	4 (5)	FET	0.26

Note: MI = myocardial infarction; χ^2 = chi-square; PCI = percutaneous coronary intervention; FET = Fisher's exact test; IABP = intra-aortic balloon pump; CABG = coronary artery bypass grafting; CCL = cardiac catheterisation laboratory; ICH = intracranial haemorrhage; ACS = acute coronary syndrome. Table excludes cases of inappropriate fibrinolysis (*n* = 9).
*Significant at $p < 0.05$

4.6.6 Hospital Length of Stay

For those patients who were admitted to hospital (excluding cases of inappropriate fibrinolysis), patients in the Post-Implementation group were found to have significantly shorter hospital LOS (measured in bed days) (median = 4 days, IQR = 2) compared to those in the Pre-Implementation group (median = 5 days, IQR = 3, p = <0.001, 2-tailed). Raw data from both groups is presented graphically for comparison in Figure 4.7.

4.6.7 Comparison of those Patients with an Outcome of Aborted MI Versus Established MI

The incidence of aborted MI among our combined cohorts was 68%. Patient demographics and CVD risk factors were found to be similar overall between those patients with an outcome of aborted MI versus established MI (Table 4.14). In terms of clinical characteristics on presentation, significantly more patients among the Established MI group presented with a Killip class of II to IV, as well as anterior STEMI, whereas significantly more patients in the Aborted MI group presented with inferior STEMI (Table 4.15). For key treatment time intervals, there were no significant differences observed between groups (Table 4.16).

Table 4.17 reports out-of-hospital complications and angiographic findings, comparing those patients with an outcome of aborted MI versus established MI. There were no differences in out-of-hospital complications between the two groups. For those patients who underwent coronary angiography, results showed that 8% of the Aborted MI group had no significant lesion greater than 50% (so-called 'no significant vessel disease') whereas no patient in the Established MI group exhibited this finding. There was also a significantly greater percentage of patients with both single vessel disease and a culprit LAD in the Established MI group (p = 0.02 and p = 0.03 respectively). This corresponded with that group's finding of significantly higher rates of anterior STEMI, which was reported in Table 4.15. Furthermore, significantly more patients among the Aborted MI group presented with a culprit RCA (p = 0.02), corresponding with that group's finding of significantly higher rates of inferior STEMI, also reported in Table 4.15.

Rates of procedural complications for PCI (rescue and non-urgent) were significantly higher among the Established MI group (p = 0.01), as was 30-day and six-month mortality (p = <0.001 respectively) and rates of re-admission for an ACS event

within six months post-discharge (p = <0.001) (Table 4.18). No significant difference in the median hospital LOS (measured in bed days) was observed between groups (Aborted MI group – median of 4 days, IQR – 3, versus Established MI group – median of 4 days, IQR – 4, p = 0.09-tailed).

Bivariate analysis presented in Table 4.19 demonstrated a significant association between family history of ACS and established MI (p = 0.007), as well as anterior STEMI and established MI (p = 0.006). Conversely, inferior STEMI was shown to have a significant association in favour of aborted MI (p = 0.01). Table 4.20 presents multiple logistic regression models examining the joint effect of family history of ACS, anterior STEMI and a PTN time greater than 120 minutes for the development of established MI. Again, statistical significance was demonstrated for the first two variables, but not with regards to PTN time (p = 0.08).

Table 4.14 ***Demographics and Cardiovascular Disease Risk Factors: Comparison of the Aborted MI Group Versus Established MI Group***

Variable		Aborted MI Group (*n* = 113) *n* (%)	Established MI Group (*n* = 52) *n* (%)	Test Statistic	*p*-Value
Sex	- Male	80 (71)	37 (71)		
	- Female	33 (29)	15 (29)	$\chi^2(1) = 0.002$	0.96
Mean age in years (±SD)		**64 (±10.7)**	**63 (±12.4)**	$t\ (163) = 0.52$	0.60 (2-tailed)
Ethnicity	- European	97 (86)	44 (85)		
	- Māori	13 (11)	6 (11)		
	- Pacific peoples	3 (3)	2 (4)	FET	0.62
NZDep score 1-5		25 (22)	10 (19)		
NZDep score 6-10		88 (78)	42 (81)	$\chi^2(1) = 0.470$	0.49
CVD Risk factors - HTN		62 (55)	33 (63)	$\chi^2(1) = 1.076$	0.29
	- Diabetes	15 (13)	8 (15)	$\chi^2(1) = 0.132$	0.71
	- Hyperlipidemia	48 (42)	27 (52)	$\chi^2(1) = 1.281$	0.25
	- Increased BMI	40 (35)	23 (44)	$\chi^2(1) = 1.177$	0.27
	- Current smoker	74 (65)	34 (65)	$\chi^2(1) = 0.000$	0.98
	- Family history of ACS	69 (61)	38 (73)	$\chi^2(1) = 2.255$	0.13
	- IHD	34 (30)	18 (35)	$\chi^2(1) = 0.338$	0.56
	- Previous AMI	12 (11)	6 (11)	$\chi^2(1) = 0.030$	0.86
	- Previous PCI	13 (11)	7 (13)	$\chi^2(1) = 0.128$	0.72
	- Previous CABG	3 (3)	2 (4)	FET	0.65

Note: MI = myocardial infarction; χ^2 = chi-square; SD = standard deviation; *t* = t-test value; FET = Fisher's exact test; NZDep = New Zealand socioeconomic deprivation index; CVD = cardiovascular disease; HTN = hypertension; BMI = body mass index; ACS = acute coronary syndrome; IHD = ischaemic heart disease; AMI = acute myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting

Table 4.15 ***Clinical Characteristics on Presentation: Comparison of the Aborted MI Group Versus Established MI Group***

Clinical Characteristic	Aborted MI Group (*n* = 113) *n* (%)	Established MI Group (*n* = 52) *n* (%)	Test Statistic	*p*-Value
Mean HR - beats/min (±SD)[a]	70 (±13.1)	68 (±14)	*t* (163) = 1.16	0.24 (2-tailed)
Mean SBP - mmHg (±SD)[a]	130 (±26.1)	130 (±28.6)	*t* (163) = 0.05	0.95 (2-tailed)
Mean SpO_2 -% (±SD)[a]	96 (±2.4)	96 (±3)	*t* (163) = 0.26	0.79 (2-tailed)
Mean GRACE 2.0 score (±SD)[b]	123 (±28.5)	118 (±39.7)	*t* (163) = 0.90	0.36 (2-tailed)
Killip class II-IV[b]	5 (4)	9 (17)	$\chi^2(1) = 7.611$	0.05*
Infarct type[b] - Anterior	42 (37)	31 (60)		
- Inferior	64 (57)	19 (36)		
- Other	7 (6)	2 (4)	FET	0.002*

Note: MI = myocardial infarction; HR = heart rate; SD = standard deviation; *t* = t-test value; SBP = systolic blood pressure; SpO_2 = percentage of arterial oxygen saturation; GRACE = Global Registry of Acute Coronary Events; χ^2 = chi-square

[a] HR, SBP and SpO_2 recorded on initial paramedic assessment in the field

[b] GRACE score, Killip class and infarct type recorded on patient presentation at hospital

*Significant at $p < 0.05$

Table 4.16 ***Comparison of Key Treatment Time Intervals in Minutes (Median Values and Interquartile Ranges): Aborted MI Group Versus Established MI Group***

	Aborted MI Group (*n* = 113)			Established MI Group (*n* = 52)			
Treatment Time Interval	Median	[95% CI]	IQR	Median	[95% CI]	IQR	*p*-Value
From pain-to-needle (PTN) time	76	[71, 132]	50	83	[81, 135]	53	0.74 (2-tailed)
From call-to-needle (CTN) time	42	[38, 52]	24	42	[42, 55]	28	0.86 (2-tailed)
From EMS contact-to-needle (ETN) time	26	[24, 35]	17	28	[26, 39]	20	0.50 (2-tailed)
From first diagnostic STEMI ECG to needle time	18	[17, 24]	11	22	[20, 28]	14	0.15 (2-tailed)

Note: MI = myocardial infarction; CI = confidence interval; IQR = interquartile range; EMS = emergency medical services; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram. All comparisons between groups were made using Mann-Whitney U tests.

Table 4.17 ***Out-of-Hospital Complications and Angiographic Findings: Comparison of the Aborted MI Group Versus Established MI Group***

Variable	Aborted MI Group (*n* = 113) *n* (%)	Established MI Group (*n* = 52) *n* (%)	Test Statistic	*p*-Value
Out-of-hospital complications:				
- Cardiogenic shock	14 (12)	9 (17)	$\chi^2(1) = 0.718$	0.39
- Compromising arrhythmia (excluding SCA)	10 (9)	6 (11)	$\chi^2(1) = 0.294$	0.58
- Cardiac arrest	9 (8)	8 (15)	$\chi^2(1) = 2.121$	0.14
- Death	-	1 (2)	-	-
Coronary angiography performed	105 (93)	44 (85)	$\chi^2(1) = 2.805$	0.09
Angiographic findings:				
- No significant lesion > 50%	8 (8)	-	-	-
- 1 vessel disease	75 (71)	39 (89)	$\chi^2(1) = 5.108$	0.02*
- 2 vessel disease	10 (10)	1 (2)	FET	0.17
- 3 vessel disease	12 (11)	3 (7)	FET	0.55
- Left main stem stenosis	-	1 (2)	-	-
Culprit artery (excluding cases of no significant VD)**:**				
- Left anterior descending	26 (27)	23 (52)	$\chi^2(1) = 7.662$	<0.001*
- Left circumflex	13 (14)	2 (5)	FET	0.14
- Right	50 (51)	14 (32)	$\chi^2(1) = 4.993$	0.02*
- Left main stem	2 (2)	1 (2)	FET	1.00
- Other	6 (6)	4 (9)	FET	0.72

Note: MI = myocardial infarction; χ^2 = chi-square; SCA = sudden cardiac arrest; FET = Fisher's exact test; VD = vessel disease
*Significant at $p < 0.05$

.

Table 4.18 ***Ongoing Clinical Management and Outcomes: Comparison of the Aborted MI Group Versus Established MI Group***

Variable	Aborted MI Group (*n* = 113) *n* (%)	Established MI Group (*n* = 52) *n* (%)	Test Statistic	*p*-Value
Hospital treatment:				
- Medical management only	22 (20)	10 (19)	$\chi^2(1) = 0.001$	0.97
- PCI	83 (73)	41 (79)	$\chi^2(1) = 0.555$	0.45
PCI procedure complications	2 (2)	6 (11)	FET	0.01*
- IABP required	-	1 (2)	-	-
- Emergent CABG from CCL	-	1 (2)	-	-
- Elective CABG	6 (5)	3 (6)	FET	1.00
In-hospital major bleed (excluding ICH)	-	-	-	-
ICH up to discharge	-	2 (4)	-	-
In-hospital reinfarction	-	-	-	-
Mortality at 30 days	1 (1)	8 (15)	FET	<0.001*
Mortality at 6 months	2 (2)	10 (19)	FET	<0.001*
ACS re-admission within 6 months	5 (4)	9 (17)	$\chi^2(1) = 7.611$	<0.001*

Note: MI = myocardial infarction; χ^2 = chi-square; PCI = percutaneous coronary intervention; FET = Fisher's exact test; IABP = intra-aortic balloon pump; CABG = coronary artery bypass grafting; CCL = cardiac catheterisation laboratory; ICH = intracranial haemorrhage; ACS = acute coronary syndrome.
*Significant at $p < 0.05$

Table 4.19 ***Bivariate Analysis Examining Associations Between Key Patient Features and Established MI***

Variable	Total Group	Outcome of Established MI		Odds Ratio	(95% CI)	*p*-Value
	N	*N*	(%)			
Age:						
Less than 65 years	81	26	(32)	1.02	(0.53, 1,97)	0.94
Greater than 65 years	84	26	(31)	1.00	-	-
Sex:						
Female	51	15	(29)	0.86	(0.42, 1.77)	0.69
Male	114	37	(32)	1.00	-	-
CVD risk factors:						
HTN						
- Yes	96	33	(34)	1.00		
- No	69	19	(28)	0.72	(0.36,1.42)	0.35
Diabetes					-	-
- Yes	24	8	(33)	1.00		
- No	141	44	(31)	0.90	(0.36, 2.27)	0.83
Hyperlipidemia					-	-
- Yes	75	27	(36)	1.00		
- No	90	25	(28)	0.68	(0.35, 1.32)	0.25
Increased BMI					-	-
- Yes	60	24	(40)	1.00		
- No	105	28	(26)	0.54	(0.27, 1.07)	0.07
Current smoker					-	-
- Yes	109	34	(31)	1.00		
- No	56	18	(32)	1.04	(0.52, 2.08)	0.90

Note: MI = myocardial infarction; CI = confidence interval; CVD = cardiovascular disease; HTN = hypertension; BMI = body mass index.
*Significant at $p < 0.05$

Table 4.19 *Continued*

Variable	Total Group	Outcome of Established MI		Odds Ratio	(95% CI)	*p*-Value
	N	*N*	(%)			
Family history of ACS						
- Yes	105	41	(39)	1.00		
- No	60	11	(18)	0.35	(0.16, 0.75)	0.007*
IHD						
- Yes	52	18	(35)	1.00	-	-
- No	113	34	(30)	0.92	(0.45, 1.86)	0.82
Previous AMI						
- Yes	18	6	(33)	1.00	-	-
- No	147	46	(31)	0.99	(0.35, 2.78)	0.99
Previous PCI						
- Yes	20	7	(35)	1.00	-	-
- No	145	45	(31)	0.90	(0.34, 2.40)	0.84
Previous CABG						
- Yes	5	2	(40)	1.00	-	-
- No	160	50	(31)	0.68	(0.11, 4.20)	0.68
Infarct type:						
Anterior						
- Yes	73	31	(42)	1.00	-	-
- No	92	21	(23)	0.38	(0.19, 0.75)	0.006*
Inferior						
- Yes	83	19	(23)	1.00	-	-
- No	82	33	(40)	2.43	(1.23, 4.80)	0.01*

Note: MI = myocardial infarction; CI = confidence interval; ACS = acute coronary syndrome; IHD = ischaemic heart disease; AMI = acute myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting.
*Significant at $p < 0.05$

Table 4.19 ***Continued***

Variable	Total Group	Outcome of Established MI		Odds Ratio	(95% CI)	*p*-Value
	N	*N*	(%)			
Other						
- Yes	9	2	(22)	1.00	-	-
- No	156	50	(32)	1.40	(0.27, 7.19)	0.68
PTN time > 120 minutes						
- Yes	41	16	(39)	1.56	(0.74, 3.27)	0.23
- No	124	36	(29)	1.00	-	-
CTN time > 60 minutes						
- Yes	43	38	(88)	1.00	-	-
- No	122	14	(11)	0.92	(0.43, 1.96)	0.83
ETN time > 30 minutes						
- Yes	66	23	(35)	1.29	(0.66, 2.51)	0.45
- No	99	29	(29)	1.00	-	-
1st STEMI ECG to needle time > 30 minutes						
- Yes	33	14	(42)	1.71	(0.78, 3.73)	0.17
- No	132	38	(29)	1.00	-	-

Note: MI = myocardial infarction; CI = confidence interval; PTN = pain-to-needle; CTN = call-to-needle; ETN = emergency medical services contact-to-needle; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram.
*Significant at $p < 0.05$

Table 4.20 ***Multiple Logistic Regression Models Examining the Joint Effects of Patient Characteristics and Implementation of Treatment on the Outcome of Established MI***

		Patient Characteristics Model 1			Patient Characteristics and Implementation of Treatment Model 2		
		OR	(95% CI)	*p*-Value	OR	(95% CI)	*p*-Value
Family history of ACS	No	1.00	-		1.00	-	-
	Yes	0.40	(0.18, 0.88)	0.02*	0.36	(0.16, 0.81)	0.01*
Anterior STEMI	No	1.00	-		1.00	-	-
	Yes	0.44	(0.22, 0.88)	0.02*	0.43	(0.21, 0.87)	0.02*
Pain-to-needle time greater than 120 minutes	No				1.00	-	-
	Yes				2.01	(0.90, 4.47)	0.08

Note: MI = myocardial infarction; OR = odds ratio; CI = confidence interval; ACS = acute coronary syndrome; STEMI = ST-elevation myocardial infarction.
*Significant at $p < 0.05$

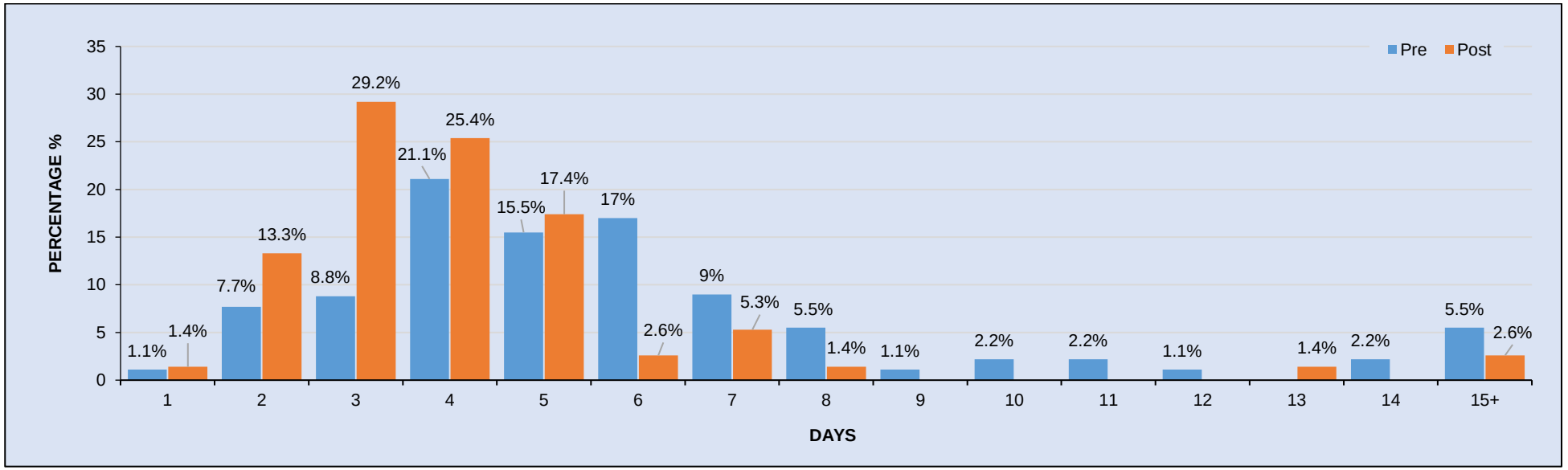


Figure 4.7 **Comparison of Hospital Length of Stay Measured in Bed Days Between the Pre- and Post-Implementation Groups**

4.7 Discussion

This study is the first to compare two distinct models of paramedic-delivered fibrinolysis within a national-based ambulance service. Authorisation of the treatment was the main distinction between the two models – physician-authorised versus autonomous paramedic decision making – and this study has demonstrated significant time-saving in treatment delivery in favour of the autonomous paramedic model. Compared to the physician-assisted telemetry-based approach utilised in the Pre-Implementation phase, there was a 22-minute reduction in the median PTN time in the Post-Implementation group (p = <0.001). Moreover, a significant increase was demonstrated in the proportion of patients who received fibrinolysis within benchmark timeframes (as stipulated by CSANZ and AHA Guidelines).

The ETN time goal of less than 30 minutes was achieved among only 28% of Pre-Implementation cases versus 93% of Post-Implementation cases, a greater than three-fold increase (p = <0.001). Similarly, there was a significant reduction in 30-day mortality (p = 0.04) and hospital LOS (p = <0.001) in favour of the autonomous paramedic decision-making model. Of note, there were no significant differences in demographic features, CVD risk factors or clinical presentation between the two experimental groups that would account for these differences in both treatment times and outcomes.

For those patients with a diagnosis of STEMI and residing in areas where timely access to a PCI-capable centre is not feasible, paramedic-delivered fibrinolysis offers the most viable option for early reperfusion, particularly when compared to the treatment's provision in the hospital-based emergency department (Danchin et al., 2004; McCaul et al., 2014; Weaver, 1995). Time between patient symptom onset and treatment delivery is a crucial determinant of the degree of myocardial salvage (De Luca, Biondi-Zoccai, & Marino, 2008; Gersh et al., 2005; Verheugt et al., 2006). Therefore, early treatment confers the greatest clinical benefit, while also influencing the likely success of fibrinolysis (Boersma et al., 1996). However, despite demonstrating its safety and feasibility, the current New Zealand paramedic treatment model of telemetry-assisted physician-authorised fibrinolysis has at times been problematic due to technological failings, which have led to prolonged treatment-delivery times (P. Davis, 2014). This study has demonstrated that the simplified model of autonomous paramedic decision making can minimise delays to treatment delivery and result in improved patient

outcomes. These results are consistent with those of previous studies from England, Wales and the Netherlands (Grijseels et al., 1995; Keeling et al., 2003; Pitt, 2002). This study recommends that the autonomous paramedic approach be adopted nationwide in New Zealand.

Although the risks associated with fibrinolysis are relatively low, when administered to patients with existing contraindications there is a significant exponential increase in the likelihood of harm (Fibrinolytic Therapy Trialists' Collaborative Group, 1994; Oldgren et al., 2010; Schulman et al., 2008). Therefore, it is crucial that paramedics accurately determine patient eligibility for treatment. Within our trial there were approximately nine inappropriate treatment cases (false positives): 6/96 cases in the Pre-Implementation group following physician authorisation, and 3/78 cases in the Post-Implementation group following autonomous paramedic decision making (6.2% Pre- versus 3.8% Post-Implementation, $p = 0.73$).

In all cases inappropriate treatment was primarily due to ECG misinterpretation. Among the three cases within the Post-Implementation group, the first two patients were later diagnosed with pericarditis while the third was diagnosed with non-specific ST-elevation and an URTI. None of these three patients developed complications from fibrinolysis, as was the case among the six patients in the Pre-Implementation group. These results, in part, serve to validate the study's protocol for autonomous paramedic-delivered fibrinolysis, which included a more stringent list of indication/contraindication criteria, designed to mitigate the risk of misdiagnosis. Applying this protocol after a relatively small amount of additional training, our autonomous paramedic participants demonstrated highly accurate STEMI diagnosis and treatment decision making with a sensitivity of 96% (95% CI: 89–99) and specificity of 91% (95% CI: 76–98). Moreover, these results link with previous evidence showing the accuracy of paramedic ECG interpretation of STEMI to be comparable to that of physicians (Feldman et al., 2005; Whitbread et al., 2002).

One potential limitation of our autonomous paramedic fibrinolysis protocol was the exclusion of more complex ECG criteria for STEMI, that is, the new or presumed new LBBB. These patients were excluded because determining a new or presumed new LBBB in the field is difficult, often with little or no access to any form of patient medical records, coupled with the criteria being less sensitive and specific for the diagnosis (Jain et al., 2011; Kontos et al., 2011). However, this study has demonstrated that New Zealand

paramedics can determine patient eligibility for treatment (including ECG interpretation) with a high degree of accuracy. This supports the idea of broadening the ECG criteria for STEMI among the New Zealand paramedic workforce, something which has recently occurred within the latest St John and Wellington Free Ambulance CPGs (National Ambulance Sector Clinical Working Group, 2016). Of note, there was one patient in the Post-Implementation phase of the trial who presented with ECG evidence of inferior STEMI and co-existing LBBB. Attending paramedics accurately diagnosed the patient but withheld fibrinolysis as per the new treatment protocol.

A positive automated interpretation of STEMI was mandated in the autonomous paramedic protocol, to provide decision support. If the treating paramedic disagreed with the automated interpretation (whether to treat or not to treat – termed 'discordance'), fibrinolysis was to be withheld. Among the 116 patients in total assessed for suitability to receive fibrinolysis in the post-implementation phase, all presented with a positive automated interpretation of STEMI. Of this number, 106 patients (91.3%) showed evidence of a culprit lesion on angiography and/or had a confirmatory diagnosis of STEMI by the receiving cardiologist, along with a rise in cardiac troponin assays. Seventy-five of these patients received fibrinolysis by autonomous paramedics and 24 presented with treatment contraindications. In addition, attending paramedics misdiagnosed 3 patients, were unable to obtain IV access in 2 patients and elected not provide fibrinolysis in a further 2 cases, despite identifying the treatment was indicated. The remaining 10/116 patients presented with ECG evidence of a STEMI-mimic (false positives), of which 3 were erroneously diagnosed by autonomous paramedics as true STEMI cases and received fibrinolysis.

Overall, these combined figures are consistent with previous evidence detailing both the sensitivity and specificity of the diagnostic software incorporated within the ambulance service heart monitors (Garvey et al., 2016; Ioannidis et al., 2001; Massel et al., 2000). They also demonstrate the utility of this software in providing decision support, while emphasising the necessity for clinician over-read prior to decision making regarding patient treatment and management.

Both study cohorts failed to consistently achieve the mandated PTN target time of less than 60 minutes. A significant improvement in this treatment sub-interval was shown among patients in the post-implementation phase ($p = <0.001$), but the target of less than 60 minutes was still only achieved in 44% of cases. Various factors influence the PTN

time, including the patient's geographical location and subsequent ambulance response time, as well as patient communications access. However, for both our study cohorts, the main contributing factor was simple failure of the patients to promptly call for ambulance assistance as soon as possible after their symptom onset. The median time from onset of symptoms to calling for an ambulance was 28 minutes (95% CI 20-92, n = 165, combined data from Pre- and Post-Implementation groups, excluding cases of inappropriate fibrinolysis), with a minimum time of one minute and a maximum time of 640 minutes. In the New Zealand context, Tanner et al. (2006) reported a median time of 90 minutes for this sub-interval among 100 ACS patients, despite the majority (62%) correctly assuming their symptoms were resulting from their heart. The simplest way to directly reduce PTN times is for patients to ring for ambulance assistance as soon as symptoms are experienced. Continued public awareness and education on this matter is needed. Specifically, it would be important to address the reasons why ACS patients fail to seek help early after symptom onset, while also encouraging these patients to call for ambulance assistance immediately. This is to endeavour to bring all reperfusion times to within guideline targets.

Introduction of the new treatment model also saw a significant improvement in both ECG acquisition time and ambulance transport time. Under the new model, paramedics were strongly encouraged to prioritise ECG acquisition during their initial patient assessment, with a target acquisition time of less than 5 minutes from time of patient contact. The significantly shorter transport times can likely be attributed to removal of both the ECG transmission and physician consultation process. In the previous model, many crews needed several attempts to complete these processes (often due to poor mobile phone coverage) and would commonly elect to begin transport to hospital before stopping and making further attempts en route. Furthermore, part of the treatment criteria within the previous model was that only those patients located more than 30-minutes' transport time from the nearest hospital were eligible. This requirement was removed from the study's post-implementation protocol on the basis that earlier fibrinolysis confers greater clinical benefit whereas transporting an eligible STEMI patient to hospital only leads to treatment delays associated with reassessment and re-triage in the ED (Dussoix et al., 2003).

When comparing the Northland and Hawke's Bay regions during the pre-implementation phase of the trial, significantly shorter treatment times were observed among those patients who received fibrinolysis in the Hawke's Bay. This is most likely

attributed to the majority of patients in Hawke's Bay residing in residential locations (coinciding with the region's higher urban population), meaning shorter ambulance response times. However, no significant differences were observed between the two regions during the post-implementation phase of the trial. This finding serves to reinforce the statement that a simplified model of autonomous paramedic decision making can minimise delays to treatment delivery.

For those patients who failed to reperfuse following fibrinolysis and subsequently underwent rescue PCI, our study showed prolonged delays at the referral hospital before transfer to the CCL and balloon inflation (average time from patient arrival at the referral hospital to rescue balloon inflation 182 minutes, SD ± 13). Therefore, considering that revascularisation should ideally occur within 120 minutes from time of symptom onset to achieve significant myocardial salvage, rescue PCI within our study was universally performed beyond the period of optimal benefit. In addition, current CSANZ guidelines recommend immediate patient transfer to a PCI-capable centre for those patients who remain symptomatic and who fail to show greater than 50% ST-segment resolution or new ST depression at 60 minutes post-fibrinolysis (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013).

Considering that a large proportion of this 60-minute time period will likely occur prior to hospital arrival among those patients treated by paramedics, prompt recognition of failed fibrinolysis, anticipation of time delays and arranged rapid transfer to the CCL are essential elements for ED staff to consider. Moreover, recently developed New Zealand guidelines propose direct patient transfer to a PCI-capable hospital for those who receive out-of-hospital fibrinolysis, regardless of whether reperfusion is achieved or not (New Zealand National Cardiac Network, 2016). This strategy is more in the patients' best interests in that it provides greater capacity to further reduce time delays to rescue PCI and allow revascularisation to occur within the time period of optimal benefit. Moreover, it ensures patients are delivered directly to hospitals more equipped to deal with potential complications.

Previous investigations have reported that up to 25–50% of AMI patients do not present with any form of chest discomfort or other anginal equivalents, a process termed silent myocardial ischaemia (SMI) (Cohn, Fox, & Daly, 2003; Kannel, Cupples, & Gagnon, 1990). While the underlying mechanisms preventing an effective anginal

warning signal have not been firmly elucidated, many population-based clinical studies have shown the prevalence of SMI to be variably influenced by certain risk profiles among patients (Nehme & Boyle, 2008). For example, a greater incidence of SMI and poorer prognostic outcomes have been found among those with diabetes, hypertension, a family history of premature CAD, smokers, the elderly and women (Anand, Lim, Raval, Lipkin, & Lahiri, 2004; Cohn et al., 2003; Sheifer, Manolio, & Gersh, 2001; Zellweger et al., 2004).

However, for patients presenting at the extreme end of the ischaemic spectrum, i.e. those with acute STEMI, the incidence and prevalence of SMI is less well-known. Eagle et al. (2002) suggest that as many as 30% of patients eligible for reperfusion therapy have treatment withheld due to the absence of typical chest discomfort accompanying their ECG changes. In our study, it was revealed that chest, neck or arm discomfort formed part of the symptomology among all patients with a confirmed diagnosis of STEMI. Moreover, approximately 78% (153/196) of these patients stated that their discomfort was a first-time occurrence. Although an extensive evaluation of these findings is beyond our study's remit, they serve to support the quantitative theory of SMI, suggesting that the presence or absence of clinically detectable myocardial ischaemia correlates to the size or extent of the ischaemia experienced.

Significantly more patients in the post-implementation phase had a coronary angiogram performed during their hospital admission ($p = 0.02$). The reason for this is unclear, but is likely attributable to an improved focus by DHBs over the last few years on achieving best practice standards for this patient subgroup as detailed within current CSANZ guidelines.

Advancements in the treatment and management of STEMI patients have meant that patient mortality is becoming a less common event, with the current short-term mortality rates in STEMI trials (i.e. up to 6 months) sitting at around 5% (Jackson et al., 2009; Welsh et al., 2004). In addition, in-hospital mortality rates for AMI have fallen over the last 3 decades from 16% in the pre-reperfusion era to 6–8% with the use of fibrinolytic agents, anti-thrombotic therapy and PCI (F. Van de Werf et al., 2008). Confounding mortality analysis in trials involving out-of-hospital fibrinolysis, those patients experiencing a large infarct with a subsequent worse prognosis also tend to seek medical assistance earlier (Rawles, 1994). Lamfers et al. (2003a) have therefore suggested that drawing comparisons between treatment groups without utilising a procedure of

randomisation (e.g. for out-of-hospital versus in-hospital fibrinolysis) may quite well result in out-of-hospital treatment groups consisting of patients with larger infarcts and subsequently higher mortality rates. Mortality may then be considered a doubtful indicator in terms of the efficacy of out-of-hospital care (Lamfers et al., 2003a). For these reasons, some researchers have elected to assess the occurrence of aborted MI following fibrinolysis.

Our study is not only unique for being the first to compare two different models for paramedic-delivered fibrinolysis, but also for undertaking a secondary investigation examining and comparing patients with aborted MI versus established MI, and where all patients reviewed were treated by paramedics in the pre-hospital setting. Previously, Lamfers et al. (2003a) demonstrated a fourfold increase of aborted MI among patients who received pre-hospital fibrinolysis compared with in-hospital. This corresponded with significantly shorter treatment delivery times among the pre-hospital cohort, as well as improved survival rates at 12 months. A sub-study to the ASSENT-3 trial (n = 5470) showed similar benefit with prompt delivery of fibrinolysis among hospital-based patients (Taher et al., 2004). Our study, however, has not demonstrated a significant increase in the number of aborted MI cases among the Post-Implementation group compared to the Pre-Implementation group (p = 0.58), despite the significant improvement in treatment delivery times. This finding might suggest that there is a limit to the efficacy of early fibrinolysis, as the median PTN times among both our pre-hospital cohorts (Pre- 87 minutes versus Post- 65 minutes) were less than or similar to those reported for aborted MI patients among other larger studies. These median times range from 86 to 171 minutes and with patient sample sizes ranging from 472 to 5470 (Jackson et al., 2009; Lamfers et al., 2004; Taher et al., 2004).

The incidence of aborted MI in our study (68%) exceeds those previously reported across other trials (16.5%, 12.6% 12.3% and 23.3%) (Jackson et al., 2009; Lamfers et al., 2003b; Lamfers et al., 2004; Taher et al., 2004). This is undoubtedly due to our criteria for aborted MI excluding measure of cardiac biomarkers and based on resolution of patient symptoms and ECG changes only. Within current CSANZ guidelines, these are the two components assessed to determine urgent patient referral for coronary angiogram and consideration for rescue PCI. The GREAT sub-study (n = 131) applied a similar criteria and reported a 46% incidence of aborted MI in total, comparing patients treated both pre- and in-hospital (Trent, Adams, & Rawles, 1994). However, with a significantly shorter median PTN time (100 versus 240 minutes, p = <0.001), the proportion of aborted

MI patients among the pre-hospital cohort was significantly higher (pre- 60% versus in-hospital 34%, $p = 0.003$), aligning more closely with our trial's figure.

Although our trial did not show a significant difference in treatment delivery times between those patients with aborted MI versus established MI, several differences were observed between the two groups that might partly explain these two clinical outcomes. Patients among the Established MI group presented with significantly higher rates of Killip class II to IV ($p = 0.05$), anterior STEMI ($p = 0.002$), PCI procedural complications ($p = 0.01$), 30-day and six-month mortality ($p = <0.0001$), as well as re-admissions for an ACS event within 6 months post-discharge ($p = <0.0001$). These findings correspond with previous evidence showing anterior STEMI to be less amenable to fibrinolysis and associated with significantly higher rates of both in-hospital morbidity and mortality compared to other types of AMI (Fibrinolytic Therapy Trialists' Collaborative Group, 1994; Stone et al., 1988). We were also able to demonstrate through multiple logistic regression models that those patients who present with a family history of ACS and anterior STEMI were less likely to achieve reperfusion following fibrinolysis i.e. develop an Established MI. Previous studies have shown prolonged PTN times (i.e. greater than 120 minutes) to also contribute towards this outcome (Lamfers et al., 2003a; Taher et al., 2004). However, our study was unable to replicate this finding ($p = 0.08$).

Eight paramedics in the post-implementation phase excluded themselves from enrolling in the education package and participating in the trial. A further two paramedics who did participate elected to withhold fibrinolysis on two separate occasions despite correctly diagnosing STEMI and determining the treatment was indicated. For all 10 staff, follow-up discussion identified several underlying themes: lack of self-confidence; concerns with their level of training being inadequate; and an overestimated view on the clinical risks associated with fibrinolysis, particularly ICH. These are similar themes previously reported among paramedics in both the United Kingdom and Saudi Arabia (Abdullah, Qais, & Nawfal, 2014; Humphrey, Walker, & Hassan, 2005; Price et al., 2005). To address these countervailing imperatives and assuage their concerns, additional training was provided for the two paramedics who withheld treatment. For those who elected not to participate, introduction of this new procedure within the ambulance CPGs (outside of a trial setting) would require their engagement or result in demotion to a lesser practice level.

4.8 Limitations

This study was not randomised and there were several differences in the fibrinolysis protocol (indication/contraindication criteria) between the Pre- and Post-Implementation groups. However, both patient groups were demographically similar and had similar clinical characteristics on initial presentation, so were considered comparable. A cost efficacy analysis was beyond the remit of this study, but it would certainly be of interest to compare ultimate costs of the two models of treatment authorisation. Examples include the purchase and upkeep of telemetry systems (physician-assisted model) versus additional paramedic training requirements (autonomous paramedic model), as well as patient hospital admission duration. It may also be felt that our autonomous paramedic participants were more adept at determining patient eligibility for fibrinolysis due to their experience under the previous physician-assisted telemetry-based programme within their respective regions. Therefore, our results may not be considered truly representative of the wider New Zealand paramedic workforce.

4.9 Conclusion

The provision of fibrinolysis in the out-of-hospital setting by autonomous paramedics without physician oversight is a safe and feasible strategy for the treatment of STEMI. Moreover, this approach provides a significant time-saving advantage for treatment delivery compared to the more commonly utilised physician-authorised telemetry-based model, resulting in improved 30-day mortality rates, as well as reduced hospital LOS. Among patients who received fibrinolysis by paramedics in the field, those that present with a family history of ACS and anterior STEMI are also less likely to achieve reperfusion following the treatment. Continued public education campaigns that address the reasons why ACS patients fail to seek help early after symptom onset, and which encourage these patients to call for ambulance assistance immediately, are required. This is in an endeavour to bring PTN times to within guideline targets. Further investigation into causes of hospital-based time delays for urgent referral of STEMI patients to PCI centres in the New Zealand setting is warranted.

Chapter Five: Paramedic-Initiated Helivac to Tertiary Hospital for Primary PCI: A Strategy for Improving Treatment Delivery Times.

5.1 Introduction

The yearly rate of STEMI patients in the region of Northland, New Zealand, continues to rise. With an estimated population of 171,400, District Health Board records show that during the 2014 calendar year, approximately 121 STEMI patients presented throughout the region, increasing to 152 patients in 2015 and 184 patients in 2016 (S. Vallancey, personal communication, March 19, 2017). However, as discussed in the previous chapter, like many provincial centres throughout the country, there are no CCL facilities based in Northland. The closest hospital able to perform PCI is located 155km away in the city of Auckland. Therefore, fibrinolysis was and remains the region's sole treatment modality in the management of STEMI.

However, in June 2010, Whangarei Hospital ED, based in the city of Whangarei (Northland's main metropolitan centre), commenced a rapid helicopter transfer protocol for STEMI patients to Auckland City Hospital Cardiac Intervention Unit (ACH-CIU) for PPCI. This was termed the Northland Code STEMI Programme, a multi-agency and multi-department venture which also involved both the St John Ambulance and Northland Rescue Helicopter (NRH) services. The programme had numerous specific features which made it potentially viable in terms of ensuring patients received PPCI within optimal timeframes, primarily within 120 minutes of arrival at Whangarei Hospital ED (the non-interventional centre). These included

- Northland's established EMS helicopter service, operating 24/7, utilising Sikorsky-S76 airframes and based within two minutes' flying time of the Whangarei Hospital helipad
- the helipad being situated on the roof, with lift access directly from the ED
- the average flight time from Whangarei to Auckland of 30 minutes
- the helipad at ACH also being located on the roof, where the patient could be conveyed directly to the CCL on the helicopter stretcher within a few minutes of landing

- ACH-CIU being a high-volume facility operating 24/7 and able to have team members assembled faster than the flight time from Whangarei to Auckland.

The programme continued for three years (June 2010 to July 2013) with 57 patients transferred in total. However, despite its favourable features, the programme failed to consistently achieve its target treatment-delivery time. Only 24 patients (42.1%) received PPCI within the target 120 minutes, although the median time was close at 122 minutes (IQR = 24) (J. M. White et al., 2012). The greatest contributor to delay was patient time spent in the ED prior to transfer (median time 52 minutes, IQR = 23). Patient time in ED contributed 44% of the total time until PPCI was achieved. More interesting was the fact that 32/57 patients (56%) were delivered to the ED via ambulance, and the attending paramedics had already accurately determined the diagnosis of acute STEMI, prior to hospital arrival.

It is these findings that underpin the third and final investigation in this doctoral project and detailed in this chapter. This was a 48-month clinical trial (June 2013 to June 2017) of paramedic-initiated helivac of STEMI patients directly from the field in the Whangarei City area to ACH-CIU for PPCI. Termed the Whangarei Paramedic STEMI Bypass Programme, the trial serviced a city population of 56,400. In contrast to the previous Northland Code STEMI programme, patients attended by St John Ambulance paramedics and who met specific protocol criteria were transported directly to the NRH helipad, bypassing the Whangarei Hospital ED. At the helipad, the duty flight ICP would reassess the patient before phoning the on-call interventional cardiologist at ACH-CIU, to have the patient accepted for transfer. Upon acceptance, the patient was then flown directly to Auckland. This local initiative sought to reduce the time interval to PPCI.

This study is unique: it is the first to compare two models of STEMI patient referral. The referral is from a non-interventional region via helivac to the CCL for PPCI. The two models are hospital-based physician referral versus pre-hospital-based paramedic referral. This study builds on the foundation of the previous two studies, expanding theory further into practice.

5.2 Research Question

1. Are New Zealand paramedics able to accurately identify those patients eligible for PPCI and activate CCL facilities appropriately from the field under protocol guidance without physician oversight and authorisation?

5.3 Aims

1. To design a protocol that identifies those patients for whom CCL activation and referral from the field is indicated / contraindicated, in conjunction with the St John Ambulance Service and Northland and Auckland DHBs.
2. To introduce this protocol to selected paramedics and to assess their abilities in its application, in the field.
3. To determine if application of the new protocol (compared to a previous hospital-based physician referral system) will improve PCI delivery times and patient outcomes, and reduce hospital LOS.

5.4 Hypotheses

1. Following education in protocol application, New Zealand paramedics will be able to accurately identify those patients eligible for PPCI and activate CCL facilities appropriately and autonomously from the field (under protocol guidance), without physician oversight and authorisation.
2. Patients who undergo PPCI following paramedic-initiated CCL activation and referral from the field (under application of the new protocol) will have reduced treatment delivery times, improved clinical outcomes and shorter hospital LOS compared to patients referred and treated under the previous hospital-based system.

5.5 Methods

5.5.1 Study Design

Utilising a prospective analysis of differences design, this study made a primary comparison between three groups of STEMI patients, all of whom received PPCI but following two different models of patient identification and referral to the CCL. The first group, an historic retrospective control cohort in the trial's pre-implementation phase, were STEMI patients initially attended and diagnosed by paramedics in the field, prior to

being transported to the ED. These patients went on to receive PPCI under a hospital-based system where referral to the CCL was made by the treating emergency physician. This cohort is referred to as Pre-Group One. The second group was also an historic retrospective control cohort in the trial's pre-implementation phase, and is referred to as Pre-Group Two. These were patients who self-presented to the ED prior to being referred to the CCL under the same hospital-based system. Conversely, the third group, a prospective experimental cohort in the trial's post-implementation phase, referred to as the Post-Group, received PPCI following identification and direct referral to the CCL from the field by independent attending paramedics. This process bypassed the ED and occurred without physician oversight. For all three groups, the patients came from Whangarei City and all were transported to the same PCI centre via the region's sole rescue helicopter service. The primary difference between both Pre-Groups combined and the Post-Group was the intervention – the implementation of an autonomous paramedic CCL activation protocol that permitted the paramedic-initiated referral process. Figure 5.1 provides a visual presentation and description of the three groups.

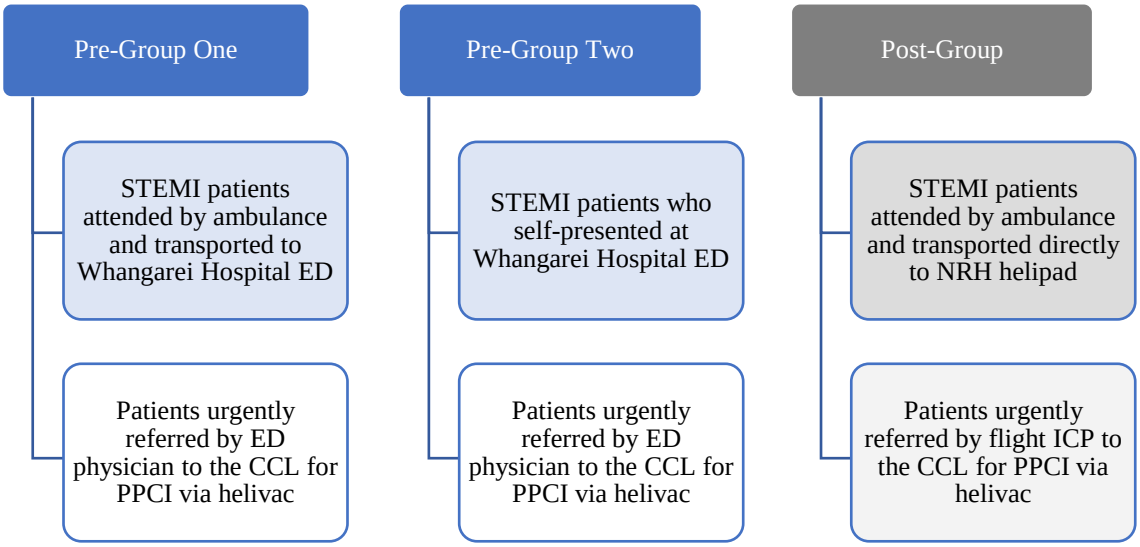


Figure 5.1 **Description of Patient Groups for Comparison**

Note: STEMI = ST-elevation myocardial infarction; ED = emergency department; NRH = Northland Rescue Helicopter; CCL = cardiac catheterisation laboratory; PPCI = primary percutaneous coronary intervention; ICP = intensive care paramedic

The study's prospective approach enabled standardisation of measures used, providing stronger confidence in the findings (Carter et al., 2011; Domholdt, 2005). A true experimental design with randomisation was considered neither ethical nor pragmatic due to the impossibility of blinding the treatment protocol application, as well as the lengthy timeframe required to reach statistically significant levels of patient numbers.

Therefore, the selected study design provided a reasonable alternative with efficient use of the patient numbers available.

Data for the study was collected from patient medical records from the St John Ambulance Service and the receiving hospitals. Medical records provide an abundance of information that can be evaluated in context (Carter et al., 2011). However, inconsistencies may exist and information may be incomplete. For these reasons, data primarily drawn from the records comprised standard clinical assessment details of the type routinely gathered for all patients in the context of STEMI.

The first outcome variable for this trial was the level of paramedic accuracy in identifying those patients eligible for direct admission to CCL, as well as appropriate field activation of the CCL facility in the post-implementation phase. The second outcome variable was timelines of treatment delivery: the time intervals for patients receiving PPCI from symptom onset; from first contact with medical personnel; from first diagnostic STEMI ECG; and from arrival at the CCL. The third outcome variable was patient outcome at both 30 days and six months post-STEMI (morbidity and mortality), including diagnostic findings and post-CCL treatment received in hospital. Finally, the fourth outcome variable was patient hospital LOS.

5.5.2 Setting

This clinical trial was conducted within the city of Whangarei, the main metropolitan centre for the region of Northland, New Zealand. The selection of this location allowed a comparison to be made between the two treatment referral models. The city has a population of 56,400 (increasing to 85,900 for the wider Whangarei area) and is serviced by a single 246-bed, secondary-level public hospital (the trial's referral hospital). The city's ambulance service has one centrally located station operating two double-crewed emergency ambulances 24/7 and a third operating between the hours of 9am and 6pm, Monday to Friday.

The trial's receiving hospital, ACH, is a 1000-plus-bed, quaternary-level public hospital and the largest in New Zealand. Furthermore, the hospital's CIU is one of three transregional cardiac centres that provide PCI services for the country's mid and upper North Island. The centre provides 24/7 coverage, 365 days a year, with three CCLs and 11 interventional cardiologists contributing to the PCI roster. Staff members are in house from 8am to 5pm during weekdays, and outside of this timeframe are expected to be on

site within 30 minutes of laboratory activation. During the 2016 calendar year, the unit performed approximately 988 PCI procedures, of which 349 (35%) were acute primary.

Throughout the trial, helicopter patient transfer between Whangarei City and the receiving hospital in Auckland was undertaken by the NRH service, the region's sole air ambulance operator, which utilises two Sikorsky S-76 airframes available 24/7, 365 days a year. The NRH aircraft hangars are located directly adjacent to the city's ambulance station and within two minutes' flying time from Whangarei Hospital. Crew configuration for the helicopters consists of two pilots and one flight ICP. Figure 5.2 illustrates the helicopter flight path used for this clinical trial.

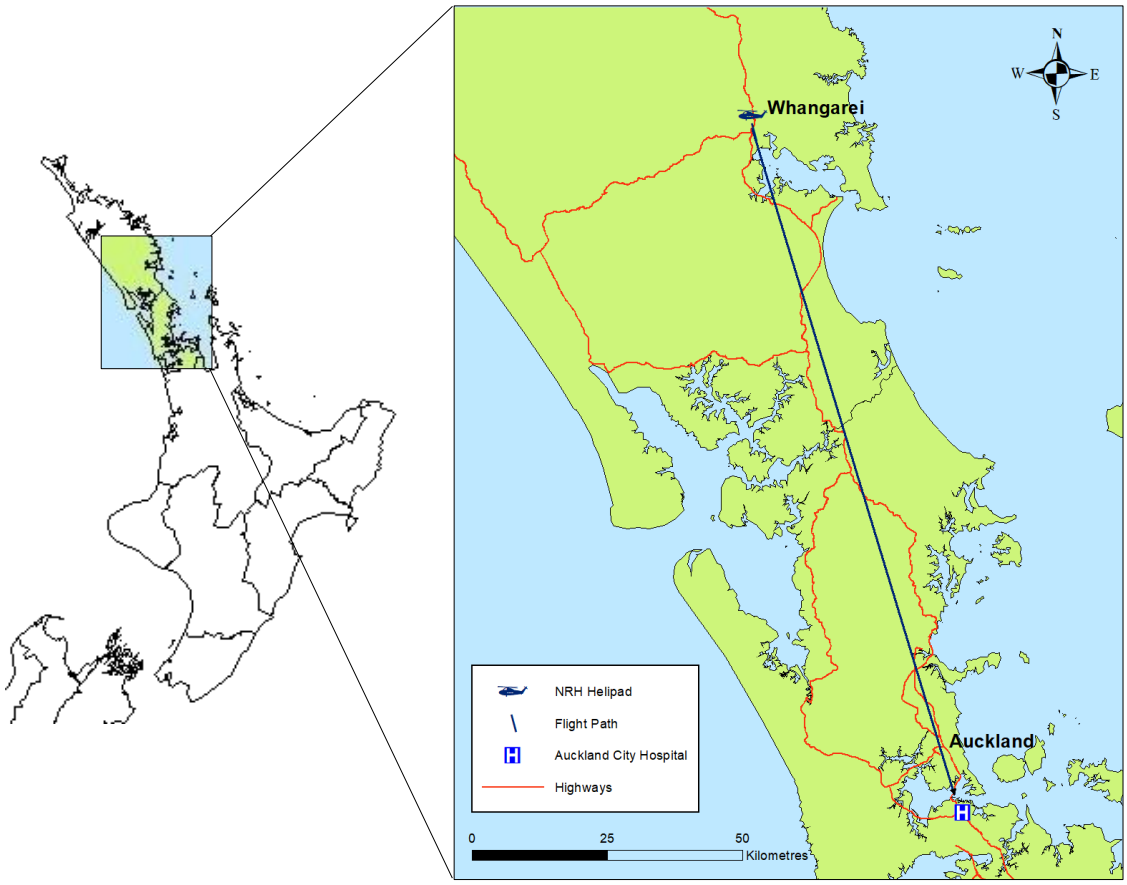


Figure 5.2 **Helicopter Patient Transfer Flight Path**

Note: The designated flight path is an approximate distance of 155km with an average duration of 30 minutes.

5.5.3 Paramedic Participants

Full-time Whangarei ambulance staff with an ATP of paramedic or above were automatically enrolled in the trial's education package in the post-implementation phase as part of their employer-based continuing clinical education programme (refer to section 5.5.8 for more detail). To participate in the trial, staff were required to successfully complete all components of the education package. This was achieved by all eligible staff – 25 in total, consisting of eight flight ICPs and 17 road-based paramedics.

5.5.4 Study Population

a) The Pre-Implementation groups (Pre-Group One and Pre-Group Two) included all patients of the previous Northland Code STEMI Programme who were urgently referred and transported by air ambulance from Whangarei Hospital ED to ACH-CIU with a diagnosis of STEMI. This extended over the period from June 2010 to June 2013.

b) The Post-Implementation group (Post-Group) included all patients attended by paramedics in the Whangarei City area with a diagnosis of STEMI and helivaced

directly from the NRH helipad to ACH-CIU as part of the Whangarei Paramedic STEMI Bypass Programme. This extended over the period from June 2013 to June 2016.

In addition, those patients transported by road-based paramedics to the NRH helipad during the post-implementation phase of the trial, but who were deemed ineligible for helivac to ACH-CIU by the duty flight ICP, were also investigated.

5.5.5 Sample Size

To measure the primary outcomes of accuracy of paramedic diagnosis and time to treatment, 60 patients were required for the trial's main comparison between ambulance cohorts, i.e. Pre-Group One and the Post-Group (Faul et al., 2007). This was based on a previous autonomous paramedic PPCI referral study involving 175 patients by Cheskes et al. (2011) and an *a priori* power analysis using their data. This was assuming a sensitivity of 70%, an accuracy measure of +/− 10%, and a statistical significance level of $\alpha = 0.05$, denoting a 95% confidence interval.

5.5.6 Patient Eligibility for Helicopter Transfer in the Post-Implementation Phase

To ensure key target time intervals were achieved following commencement of the Whangarei Paramedic STEMI Bypass Programme in the trial's post-implementation phase, a catchment area was established. This was dictated primarily by the average ambulance transport time to the NRH helipad, with outer boundaries of the catchment area within a 20-minute road travel timeframe (Figure 5.3). The central location of the helicopter base coupled with the city's road system allowed for expedient access and retrieval of patients located in all city suburbs and many fringe settlements by responding ambulance crews. Beyond this catchment area, those patients attended to by ambulance crews with a diagnosis of STEMI were assessed as to their suitability for receiving fibrinolysis. This also applied in cases of aircraft unavailability for those patients within the designated catchment area. Further patient inclusion and exclusion criteria for the trial's post-implementation phase are outlined in Table 5.1.

Figure 5.3 **Catchment Area for the Whangarei Paramedic STEMI Bypass Programme (Post-Implementation Phase)**

Note: The inner circular frame represents the catchment area. STEMI = ST-elevation myocardial infarction; NRH = Northland Rescue Helicopter.

5.5.7 Measures

Patient Characteristics: Key demographic data was collected to describe the patient sample. This included sex, age, ethnicity and BMI score, as well as each group's spatial distribution relative to the post-implementation phase catchment area and the New Zealand socioeconomic deprivation index (NZDep). The time interval from patient symptom onset to their 'call for help', i.e. calling for ambulance assistance or self-presenting at hospital, was also measured, along with the time of day. Diagnosed patient CVD risk factors were collected, as were clinical characteristics on presentation. These included key vital signs, GRACE 2.0 score, Killip class score, infarct type and automated ECG interpretation. The automated ECG interpretation was recorded for all ambulance patients within the trial, i.e. who were diagnosed with STEMI and helivaced to ACH-CIU

to receive PPCI. The ambulance patients with automated ECG interpretations occurred in two cohorts: Pre-Group One and the Post-Group. The accuracy of these automated ECG interpretations was then checked against definitive diagnostic measures: the presence of a culprit coronary artery identified on angiography, and/or confirmatory diagnosis of STEMI by the receiving cardiologist, plus a rise in cardiac troponin assays. Note the ambulance heart monitors used in the trial were the Physio-Control LIFEPAK ® 12 and LIFEPAK ® 15, and the Phillips HeartStart MRx.

First Outcome Variable – Accuracy of Paramedic Diagnosis and Protocol Application: The sensitivity and specificity along with PPV and NPV of the paramedics' clinical diagnoses and protocol application were determined from their identification of patients suitable for PPCI or not, and their activation or non-activation of the CCL. This was possible only in the post-implementation phase of the trial. Three independent cardiology consultants (experts) reviewed all cases after the fact, to determine actual field diagnosis and patient suitability for PPCI referral. Accuracy of paramedic protocol application was then assessed accordingly. The rate of True Positive and True Negative cases, along with False Positive and False Negative cases, was determined. Each of these categories has been described as a proportion of the total number of clinical decisions made.

Causes of False Positive cases, i.e. inappropriate activation of the CCL, and False Negative cases, i.e. missed CCL activations, were investigated among all patients in both the trial's pre- and post-implementation phases. Inappropriate activation of the CCL was defined by patient ECG features being inconsistent with STEMI, i.e. misinterpreted and/or no culprit lesion identified on angiography and no rise in cardiac troponin assays.

Second Outcome Variable – Time to Treatment and Factors that Incurred Delays: Key performance indicators (KPIs) were established in the post-implementation phase of the trial for the Paramedic STEMI Bypass Programme. These utilised standard treatment time intervals for PPCI and were monitored as part of the quality assurance process. They included

1. from EMS patient contact to arrival at the CCL < 90 minutes, with a target of achieving this time > 80% of all cases
2. from EMS patient contact to balloon inflation < 120 minutes, with a target of achieving this time > 80% of all cases

3. arrival at the referral centre (NRH helipad) to balloon inflation < 90 minutes, with a target of achieving this time > 80% of all cases
4. minimal inappropriate activations of the CCL, with a target of < 5% of all cases.

Treatment-related time intervals were also measured for all three observed groups where applicable. These included

1. from EMS patient contact to arrival at the CCL (ETD)
2. from EMS patient contact to balloon inflation (ETB)
3. from patient arrival at the referral centre to balloon inflation (either Whangarei Hospital in the trial's pre-implementation phase, or the NRH helipad in the trial's post-implementation phase)
4. from first medical contact to balloon inflation (FMCTB)
5. from first diagnostic STEMI ECG to balloon inflation
6. from patient arrival at the receiving hospital to balloon inflation (DTB)
7. from patient arrival at the CCL to balloon inflation
8. from patient symptom onset to balloon inflation (total ischaemic time).

For those patients with a FMCTB time of greater than 120 minutes, an analysis of each case was conducted to determine the cause/s contributing to treatment delay.

Additional operational time intervals and other features were collected and calculated among all three groups where applicable. These included

1. ambulance response time (time from dispatch to arrival at patient)
2. paramedic scene time (arrival at scene to scene departure)
3. ambulance transport time (departure from scene to arrival at referral centre)
4. helicopter flight time
5. pilot use of visual flight rules (VFR) or instrument flight rules (IFR).

All the above time intervals were measured in minutes.

Third Outcome Variable – Patient Clinical Management and Outcomes: The following data was collected for all three groups (pre- and post-implementation phases) and analysed to determine patient outcomes:

1. clinical complications prior to undergoing PPCI, i.e. cardiogenic shock, compromising arrhythmia (not including those patients in cardiac arrest) and cardiac arrest
2. initial findings on coronary angiography
3. culprit artery
4. misdiagnosis and inappropriate activation of the CCL
5. intra-aortic balloon pump (IABP) required
6. PCI procedural complications
7. TIMI flow grade post-PCI
8. rates of emergent CABG from the CCL
9. rates of repeat PCI performed later during hospital admission
10. rates of elective CABG performed later during hospital admission
11. no intervention (medical management only)
12. in-hospital reinfarction
13. 30-day and six-month mortality
14. hospital re-admission within six months for an ACS event.

Fourth Outcome Variable – Hospital LOS: Patient hospital LOS is an indicator of costs to the public healthcare system. It can also indicate that other hospital interventions were necessary, for example further PCI, CABG or other treatment for in-hospital complications. This time period was measured in bed days for all three observed groups.

5.5.8 Intervention

Autonomous Paramedic CCL Activation Protocol (Independent Variable): Table 5.1 details the new paramedic protocol (criteria for STEMI diagnosis and PPCI referral) applied in the post-implementation phase of the trial. These listed criteria differ from those within the CSANZ guidelines and used by the emergency physicians in the trial's Pre-Implementation phase. To mitigate the risk of erroneous paramedic ECG interpretation of STEMI, inclusion criteria 2 to 4 and exclusion criterion 1 were added when the protocol was designed.

As discussed in the previous study in Chapter Four, false positive automated interpretation of STEMI commonly occurs due to one or more factors: incorrect lead placement, artefact, tachy-dysrhythmia, and a QRS width beyond normal limits (> 0.12secs) (Garvey et al., 2016). Therefore, the protocol stipulation to obtain two consecutive ECGs with an automated interpretation of STEMI was intended to prompt

paramedics to check lead placement and trace quality prior to acquisition of the second ECG. Beyond these listed exceptions, the primary difference between the two Pre-Groups combined and the Post-Group was in fact the model of PPCI referral authorisation, i.e. physician-authorised (pre-implementation phase) versus paramedic-authorised (post-implementation phase).

Table 5.1 ***Autonomous Paramedic CCL Activation Protocol (Inclusion and Exclusion Criteria)***

Inclusion Criteria
1. ECG with persistent ST-elevation ≥ 1mm in two or more contiguous limbs leads or ≥ 2mm in two or more contiguous precordial leads (including posterior leads)
2. Heart monitor interpretation indicates >>> Acute MI <<< or ***ACUTE MI SUSPECTED*** on two consecutive ECGs
3. Normal QRS width (≤ 0.12secs) or right bundle branch block identified on 12-lead ECG
4. Heart rate <130 beats per minute
5. Symptoms consistent with myocardial ischaemia of < 12 hours in duration
6. Ambulance transport time to helicopter base < 20 minutes
Exclusion Criteria
1. Left bundle branch block identified on 12-lead ECG
2. History of serious systemic disease, e.g. advanced / terminal cancer, severe liver or kidney disease
3. Severe dementia
4. Severe dependent living, i.e. resident of an aged care facility requiring significant assistance with activities of daily living
5. Ongoing cardiac arrest requiring repeated CPR

Note: ECG = electrocardiogram; MI = myocardial infarction; CPR = cardiopulmonary resuscitation

The new paramedic protocol was introduced to all flight ICPs and ambulance staff as part of a two-hour classroom-based training workshop designed by the principal researcher, with input from academic supervisors, AUT School of Paramedicine and St John. Session content included revision of assessment of the ACS patient, as well as STEMI and STEMI-mimic recognition on 12-lead ECG. This sought to address key areas of paramedic knowledge deficit identified by the research team in their previous study, discussed in Chapter Three. In particular, this included accurate understanding and interpretation of common STEMI-mimics such as bundle branch block patterns and LVH (P. R. Davis et al., 2017). The training workshops were repeated after 12 months, serving as refresher sessions for all staff.

The training workshops were delivered solely by the principal researcher and during routine rostered staff training days, at which staff attendance was a compulsory requirement of the employer, St John. In addition, both Northland ambulance dispatchers and NRH pilots were briefed on the new referral pathway with key components relevant to their role highlighted. For example, dispatchers were required to page the duty flight crew with a generic 'STEMI Bypass' message to avoid confusion with other types of jobs, while pilots were required to have the aircraft prepared in a 'standby and ready state' upon receipt of pager message. This meant having the aircraft placed on the helipad with pre-flight checks completed prior to patient arrival by ambulance.

5.5.9 Study Implementation Procedure

Before the trial commenced approval was gained from the relevant ethics committees, the St John Ambulance Service and the Northland and Auckland DHBs. Then the trial's education package was fully developed and classroom training workshops were delivered. Following completion of each workshop, flight ICPs were permitted to autonomously activate and refer patients to the CCL via helivac, utilising the new protocol effective immediately. This new addition to their existing scope of clinical practice was authorised by means of a 'standing order' by the St John Medical Director. This point also marked the commencement of patient data collection for the prospective Post-Group, from both ambulance and hospital records. After every 12-month period, refresher workshops were conducted for all staff.

Figure 5.4 details the sequence of events for paramedic-initiated referral of STEMI patients to the CCL in the trial's Post-Implementation phase. As shown, ultimately it was the duty flight ICP who made the final decision as to whether a patient was eligible for helivac to ACH-CIU. In cases where transfer was indicated, the flight ICP made direct contact with the on-call interventional cardiologist via a dedicated 0800 mobile telephone number. However, if the flight ICP deemed a patient ineligible for transfer, the ambulance crew were directed to continue transporting the patient via road to Whangarei Hospital ED.

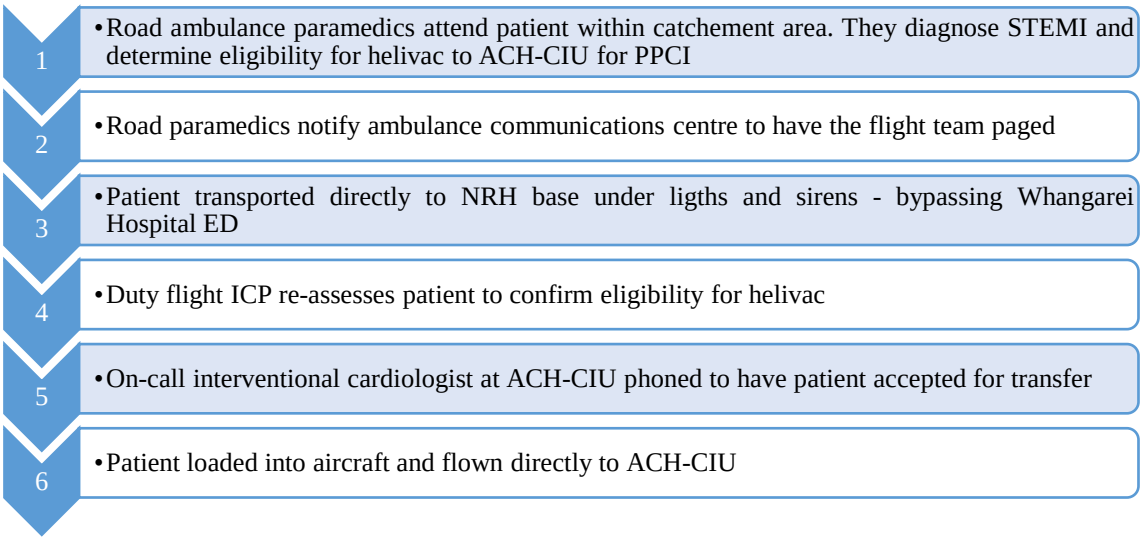


Figure 5.4 **Whangarei Paramedic STEMI Bypass Programme – Transfer Sequence**

Note: STEMI = ST-elevation myocardial infarction; ACH-CIU = Auckland City Hospital Cardiac Interventional Unit; PPCI = primary percutaneous coronary intervention; NRH = Northland Rescue Helicopter; ED = emergency department

5.5.10 Data Management and Processing

Raw data was entered in the SPSS software programme version 24 and screened to ensure no entry errors. A screening of the data for outliers also occurred with corrections made prior to analysis. The significance level was set at 0.05.

5.5.11 Data Analysis

Initial analysis of data was primarily descriptive, producing frequencies, means and standard deviations, or medians and interquartile ranges where relevant, and testing for normal distributions of continuous measures, e.g. time between events. Where normality was not achieved, transformations such as the log of measure were examined. To test Hypothesis One, the rates of True Positive and True Negative and False Positive and False Negative cases were identified, and the sensitivity, specificity, PPV and NPV of paramedic protocol application were then calculated. This was achieved by use of a frequency score and subsequent presentation of results utilising a frequency distribution table, with comparison of scores to the standard (a dummy variable) as determined by three independent cardiologists (experts).

To test Hypothesis Two, observed groups were initially compared using where relevant: chi-square tests for independence, one-way analysis of variance (ANOVA) or independent-sample t-tests. Comparisons of medians were made using Mann-Whitney U tests and Kruskal-Wallis tests. For dichotomous outcome measures such as mortality, groups were compared using logistic regression, whereas for continuous measures such

as length of hospital stay, general linear models were utilised. Variables such as time to treatment, time to hospital, patient demographics and time of day were examined, as were patient presentation characteristics before receiving PPCI (e.g. vital signs, GRACE 2.0 and Killip score, symptoms and ECG findings). Where significant differences were present, those characteristics were added as covariates to the model after examination for potential correlations.

5.5.12 Geographic Information System Data and Map Reference

To present patient spatial distribution throughout the Whangarei City area relative to the post-implementation phase catchment area and the NZDep, GIS data was obtained from Whangarei District Council and the national census database for 2013 (the closet census to the study dates). All maps are presented in the GCS_NZGD_2000 geographic coordinate system and the New Zealand Transverse Mercator projected coordinate system.

5.5.13 Ethical Approval

Ethical approval for the trial was obtained from HDEC Northern A (14/NTA221 – Appendix K), and from AUTEC (application number 15/04 – Appendix J). Locality and institutional approval was obtained from St John's Clinical Audit and Research Group (Appendix M), as well as Northland and Auckland DHBs (Appendix H and M respectively).

5.5.14 Criteria for Trial Termination and Management of Pre-Hospital Adverse Events

As a stipulation of the trial's locality and institutional approval, the research team were required to provide an update to the St John Ambulance Service and to Northland and Auckland DHBs biannually by means of a variance report. All parties had the capacity to terminate the trial at any stage and for any reason. One example may have been an excessive number of inappropriate activations of the CCL by autonomous paramedics in the Post-Implementation phase, where the cost and inconvenience outweighed the potential benefits of all appropriate referrals. In addition, the duty flight ICP was required to submit the ambulance ePRF via email to the trial's lead investigator immediately following each job. This allowed for any pre-hospital adverse events to be identified and addressed promptly, in line with existing St John Ambulance Standard Operating Procedures (SOPs).

5.6 Results

5.6.1 Patient Characteristics

A total of 92 patients were included in the study: 32 patients in Pre-Group One, 25 in Pre-Group Two, and 35 in the Post-Group. All data points were complete.

Table 5.2 reports patient demographics and CVD risk factors. These were similar overall between the three observed groups. Most patients were male (combined average age of 64 years SD ± 10.3), of European ethnicity and residing in more socioeconomically deprived areas or suburbs (as determined by the NZDep). When compared to other New Zealand ethnic population groups, as a percentage of the parent population Māori were over-represented within all three observed groups (22%, 20% and 23% respectively). Smoking, increased BMI and a family history of ACS were the most prominent risk factors identified.

A map showing the spatial distribution of geo-coded residential addresses for all patients helivaced to ACH-CIU is presented in Figure 5.5. This includes patients in all three observed groups and is presented relative to the designated catchment area in the post-implementation phase of the trial. As is shown, all bar one patient from the pre-implementation phase are clustered within this boundary. The same spatial distribution overlay is presented relative to the NZDep in Figure 5.6, reconfirming the findings identified in Table 5.2.

Clinical characteristics of patients on initial presentation are presented in Table 5.3. These include mean heart rate, blood pressure, arterial oxygen saturation and GRACE 2.0 score, as well as Killip scores of II to IV and infarct type. These were all similar between groups. Furthermore, chest, neck or arm discomfort formed part of the symptomology among all patients treated, with 68.4% (63/92) stating that their discomfort was a first-time occurrence.

Only one patient out of 67 (2%) in the combined ambulance patient groups (i.e. Pre-Group One and the Post-Group) lacked a positive automated interpretation of STEMI on their diagnostic 12-lead ECG. (However, note that a positive automated interpretation was a protocol requirement for paramedic-initiated patient referral to the CCL in the post-implementation phase.) All 66 cases of positive automated interpretation corresponded with a culprit lesion identified on coronary angiography and a confirmatory diagnosis of STEMI by the receiving cardiologist along with a positive rise in cardiac troponin assays.

No significant difference was identified between groups in terms of the time lapse between patient symptom onset and phoning 111 for ambulance assistance or self-presenting at hospital (p = 0.36). The combined median time for this subinterval was 72 minutes (95% CI 67−121). Sixty-eight percent of all patients presented during normal working hours, i.e. between 9am and 5pm.

Table 5.2 ***Demographic Features and Cardiovascular Disease Risk Factors: Comparison of Pre-Implementation Groups versus Post-Implementation Group***

Variable		Pre-Group One (*n* = 32) *n* (%)	Pre-Group Two (*n* = 25) *n* (%)	Post-Group (*n* = 35) *n* (%)	Test Statistic	*p*-Value
Sex	- Male	24 (75)	19 (76)	24 (68)		
	- Female	8 (25)	6 (24)	11 (31)	$\chi^2(2) = 0.524$	0.77
Mean age in years (±SD)		**65 (±10.4)**	**63 (±8.7)**	**65 (±13.3)**	F (2, 89) = 0.33	0.72
Ethnicity	- European	24 (75)	19 (76)	26 (74)		
	- Māori	7 (22)	5 (20)	8 (23)		
	- Asian	1 (3)	1 (4)	1 (3)	$\chi^2(4) = 0.122$	0.98
NZDep score 1-5		7 (22)	5 (20)	5 (15)		
NZDep score 6-10		25 (78)	20 (80)	30 (85)	$\chi^2(2) = 1.383$	0.96
CVD Risk factors	- HTN	13 (40)	8 (32)	13 (37)	$\chi^2(2) = 0.449$	0.80
	- Diabetes	6 (18)	4 (16)	4 (12)	$\chi^2(2) = 0.711$	0.70
	- Hyperlipidaemia	12 (37)	10 (40)	12 (34)	$\chi^2(2) = 0.211$	0.90
	- Increased BMI	13 (40)	8 (32)	16 (45)	$\chi^2(2) = 1.144$	0.56
	- Current smoker	15 (47)	11 (42)	14 (40)	$\chi^2(2) = 0.325$	0.85
	- Family history of ACS	20 (62)	16 (64)	20 (57)	$\chi^2(2) = 0.343$	0.84
	- IHD	11 (34)	5 (20)	11 (32)	$\chi^2(2) = 1.517$	0.47
	- Previous AMI	3 (9)	2 (8)	4 (11)	FET	0.90
	- Previous PCI	3 (9)	1 (4)	3 (8)	FET	0.72
	- Previous CABG	1 (3)	-	-	-	-

Note: χ^2 = chi-square; F = F-test for analysis of variance; SD = standard deviation; FET = Fisher's exact test; NZDep = New Zealand socioeconomic deprivation index; CVD = cardiovascular disease; HTN = hypertension; BMI = body mass index; IHD = ischaemic heart disease; AMI = acute myocardial infarction; PCI = percutaneous coronary intervention; CABG = coronary artery bypass grafting

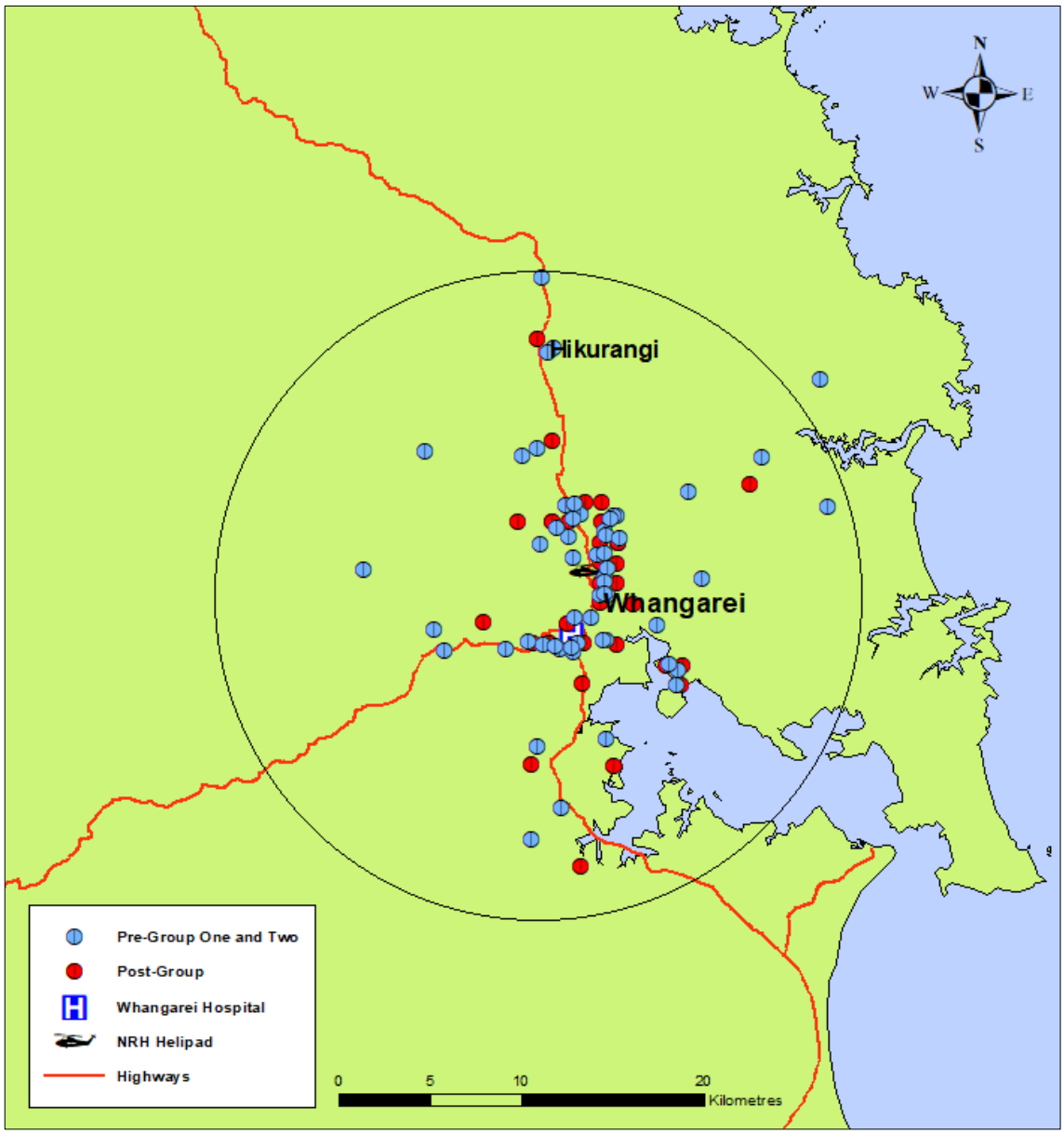
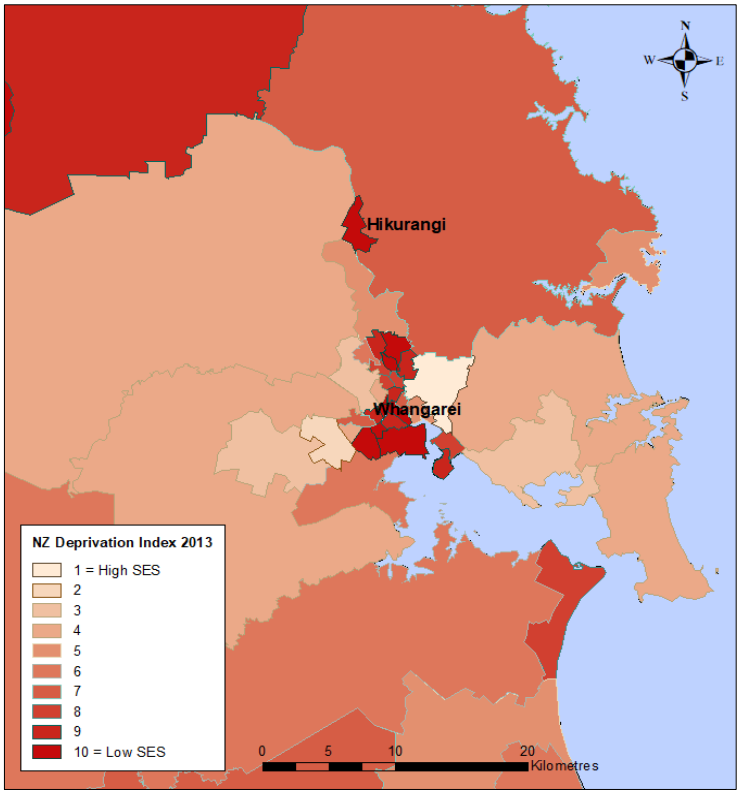
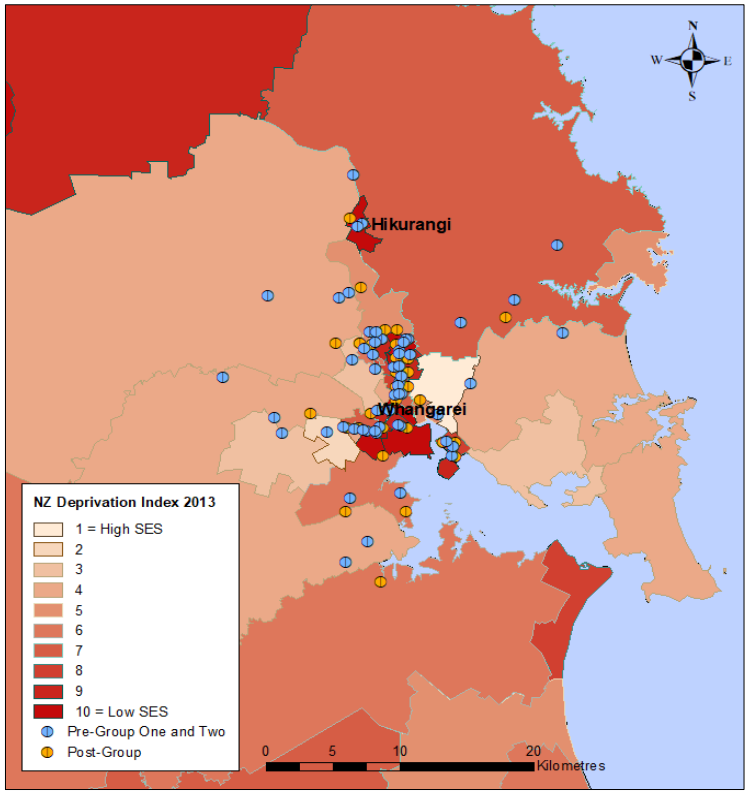


Figure 5.5 **Spatial Distribution of all Patients Helivaced to ACH-CIU: Pre- and Post-Implementation Phases**

Note: Patient spatial distribution is shown relative to the catchment area boundary in the trial's post-implementation phase.



(A)



(B)

Figure 5.6 **New Zealand Deprivation Index in the Whangarei City Area with Patient Overlay**

(A) New Zealand deprivation indices calculated from NZ census (2013) by meshblock
(B) New Zealand deprivation indices by meshblock with patients' addresses overlaid

Table 5.3 ***Clinical Characteristics on Initial Presentation: Comparison of Pre-Implementation Groups versus Post-Implementation Group***

Clinical Characteristic	Pre-Group One (*n* = 32) *n* (%)	Pre-Group Two (*n* = 25) *n* (%)	Post-Group (*n* = 35) *n* (%)	Test Statistic	p-Value
Mean HR - beats/min (±SD)[a]	70 (±12)	73 (±8)	71 (±11)	F (2, 89) = 0.90	0.40
Mean SBP – mmHg (±SD)[a]	131 (±18)	133 (±20)	125 (±24)	F (2, 89) = 0.67	0.51
Mean SpO_2 - % (±SD)[a]	96 (±2)	96 (±2)	97 (±2)	F (2, 89) = 0.21	0.80
Mean GRACE 2.0 score (±SD)[b]	129 (±39)	117 (±25)	124 (±40)	F (2, 89) = 0.85	0.43
Killip class II-IV[b]	6 (18)	4 (16)	6 (17)	$\chi^2(2) = 0.076$	0.96
Infarct type[b] - Anterior	16 (50)	13 (52)	15 (43)		
- Inferior	14 (44)	10 (40)	18 (51)		
- Other	2 (6)	2 (8)	2 (6)	$\chi^2(2) = 0.881$	0.92

Note: HR = heart rate; SD = standard deviation; F = F-test for analysis of variance; SBP = systolic blood pressure; SpO_2 = arterial oxygen saturation; GRACE = Global Registry of Acute Coronary Events; FET = Fisher's exact test; $\chi 2$ = chi-square

[a]HR, SBP and SpO_2 recorded on initial paramedic assessment in the field (Pre-Group One and Post-Group), or on initial hospital assessment in the emergency department (Pre-Group Two)

[b]GRACE score, Killip class and infarct type recorded on patient presentation at hospital

5.6.2 Accuracy of Paramedic Diagnosis and Protocol Application

During the prospective post-implementation phase of the trial, 57 patients were transported by ambulance paramedics to the NRH helipad for further assessment by the duty flight ICP as to their suitability for helivac to ACH-CIU for PPCI. Thirty-five of these patients (61%) were deemed eligible for transfer and were subsequently flown to Auckland; the remaining 22/57 patients (39%) were deemed ineligible and redirected to Whangarei Hospital ED. Following audit review, none of the 35 helivac cases were deemed as inappropriate activations of the CCL. However, among the 22 patients excluded, one was misdiagnosed by the flight ICP and did meet criteria for helivac (false negative). The overall accuracy of paramedic diagnosis and protocol application is presented in Table 5.4, and a summary of all cases excluded for helivac is presented in Figure 5.7.

Table 5.4 ***Accuracy of Paramedic Diagnosis and Protocol Application (Post-Implementation Group, n = 57)***

Value	(%)	[95% CI]
Sensitivity	(97)	[85-99]
Specificity	(100)	[84-100]
Positive predictive value (PPV)	(100)	[85-100]
Negative predictive value (NPV)	(95)	[84-99]

Note: CI = confidence interval

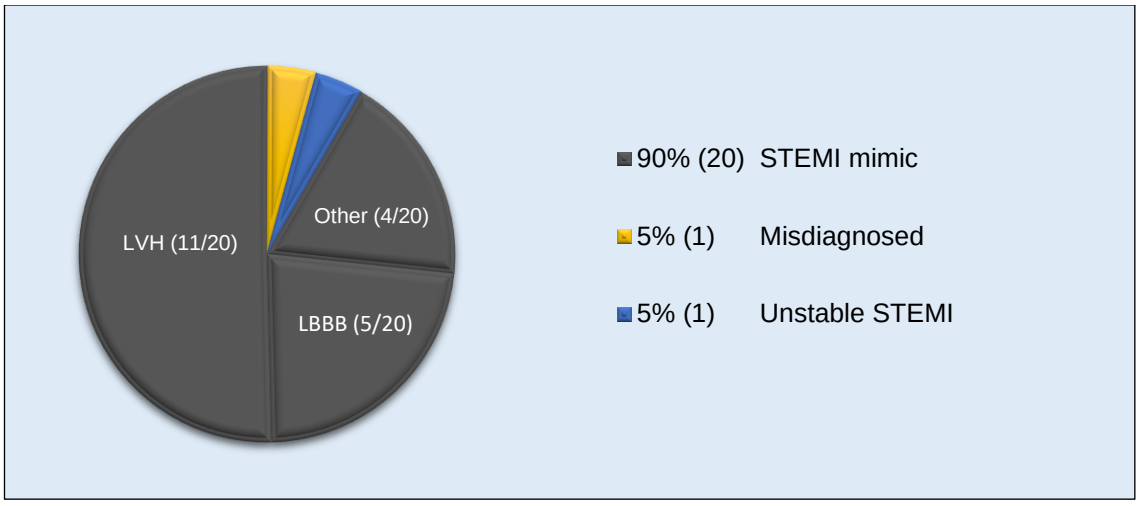


Figure 5.7 **Summary of Cases Excluded for Helivac (Post-Implementation Phase, *n* = 22)**

Note: STEMI = ST-elevation myocardial infarction; LVH = left ventricular hypertrophy; LBBB = left bundle branch block

Among the 22 excluded cases, the majority of patients presented with a STEMI-mimic on 12-lead ECG (false positives). The most common STEMI-mimic was LVH (11/20), followed by LBBB (5/20). Approximately 90% of these false positive cases (18/20) occurred within the first 12 months of the trial. The single patient who was misdiagnosed received fibrinolysis in Whangarei Hospital ED before being referred to ACH-CIU for rescue PCI via helicopter transfer. In addition, despite being correctly diagnosed, one patient was deemed too unstable for helivac due to repeated episodes of cardiac arrest requiring CPR and defibrillation – one of the exclusion criteria within the new paramedic referral protocol. This patient was later flown from Whangarei Hospital ED to ACH-CIU as an ICU transfer.

During the course of the trial's post-implementation phase, an additional thirteen STEMI patients eligible for helivac were transported directly to Whangarei Hospital ED by attending paramedics due to aircraft unavailability. In all cases, the duty aircraft was already tasked with an inter-hospital transfer. Figure 5.8 provides a summary of these cases. Of the 13 patients, four were flown directly to ACH-CIU for PPCI. The other nine were initially treated with fibrinolysis, but only one patient achieved reperfusion by this method. The other eight were eventually flown to ACH-CIU for rescue PCI.

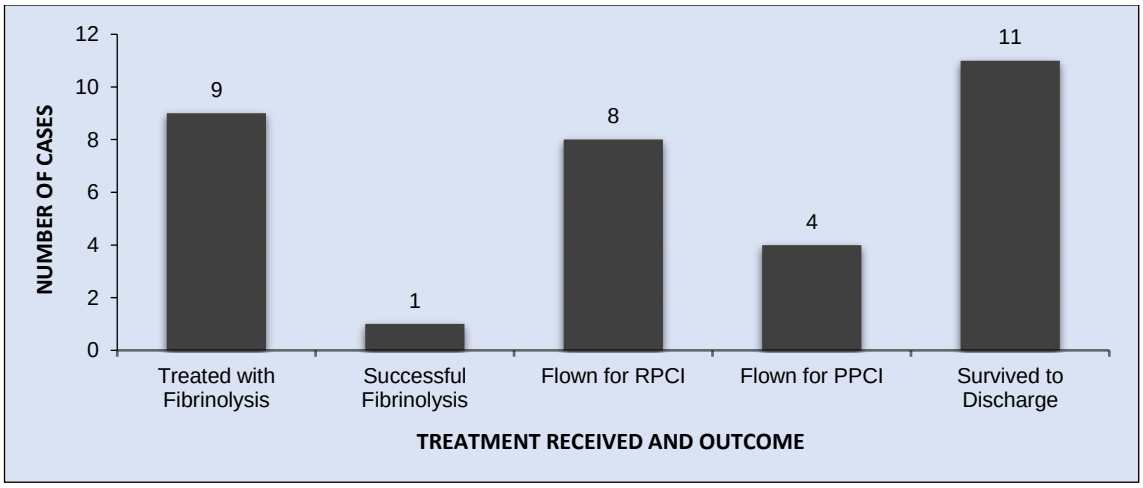


Figure 5.8 **Summary of Cases for Aircraft Unavailability in the Trial's Post-Implementation Phase (*n* = 13)**

Note: RPCI = rescue percutaneous coronary intervention; PPCI = primary percutaneous coronary intervention

5.6.3 Time to Treatment and Factors that Incurred Delays

Key performance indicator (KPI) target results for the Paramedic STEMI Bypass Programme in the post-implementation phase are presented in Table 5.5. All pre-hospital targets were achieved. Table 5.6 provides a comparison of key treatment time intervals

between the two groups that were attended to by ambulance paramedics, i.e. Pre-Group One versus the Post-Group. Note that balloon inflation times and the total ischaemic time exclude one patient in the Pre-Group One and two patients in the Post-Group. This was due to no device being inserted because of anatomy which precluded stent placement.

For all measures, a significant improvement in time was demonstrated in favour of the Post-Group, except for 'From arrival at referral centre to balloon inflation' and 'From arrival at CCL to balloon inflation', where no difference between groups was observed. Figure 5.9 compares the spread of ETB times between groups. In Pre-Group One, only 3% of patients received treatment within the mandated target time of less than 120 minutes. Conversely, in the Post-Group, this time was achieved for 91% of cases – an almost 30-fold improvement.

Table 5.7 provides a comparison of key treatment time intervals between all three observed groups, excluding initial paramedic-based values previously shown, given Pre-Group Two comprised patients who self-presented at the referral centre. Again, a significant improvement in time was demonstrated in favour of the Post-Group, except for 'From arrival at referral centre to balloon inflation' and 'From arrival at CCL to balloon inflation', where no difference between groups was observed. In addition, for Pre-Group Two (self-presentation), the FMCTB time equates to the additional sub-interval of 'door-to-device', that is, patient presentation at the referral hospital to balloon inflation. The median time shown exceeds the benchmark standard of less than 120 minutes, with only 6/25 patients (24%) receiving treatment within this time period.

Table 5.8 provides a comparison of additional operational and clinical times between the two observed ambulance groups, i.e. Pre-Group One and the Post-Group. A significant reduction in ambulance scene time, ECG acquisition time and transport time was shown in favour of the Post-Group, while ambulance response time and helicopter flight time were similar between groups.

For all three groups combined, no significant difference in time-to-treatment (commencing from patient arrival at the referral location) was observed between those patients that presented during normal working hours (8am–5pm) versus outside of normal working hours (5pm–8am) (p = 0.48, 2-tailed). This was also the case for those flights flown under VFR versus IFR (p = 0.72, 2-tailed).

Among those patients who received PPCI with a FMCTB time exceeding 120 minutes, the causes for delays are summarised in Table 5.9. Prolonged emergency department assessment was the most common cause for delay, evident in more than three-quarters of all cases. The CCL being already occupied upon patient arrival was the second most common cause of delay, occurring in 9% of cases. Among the 56 patients in total who received PPCI within the hospital-based referral system (i.e. Pre-Group One and Pre-group Two), 50/56 patients (89.3%) had a FMCTB time exceeding 120 minutes. Emergency department assessment time contributed to 82% of these delays.

Table 5.5 ***Key Performance Indicators, Targets and Results: Paramedic STEMI Bypass Programme (Post-Implementation Phase)***

Key Performance Indicator (KPI) Measure	Target (% of Total Cases)	*N*	Result (%)
From paramedic contact to arrival at CCL (ETD) ≤ 90 minutes	(>80)	35	(100)
From paramedic contact to balloon inflation (ETB) ≤ 120 minutes[a]	(>80)	33	(91)
From arrival at referral centre (helipad) to balloon inflation ≤ 90 minutes[a]	(>80)	33	(88)
Minimal inappropriate activations	(<5)	0/35	(0)

Note: STEMI = ST-elevation myocardial infarction; ETD = emergency medical services contact-to-door; ETB = emergency medical services contact-to-balloon
[a]Balloon inflation times exclude two patients, due to no device being inserted because of anatomy which precluded stent placement.

Table 5.6 ***Comparison of Key Treatment Time Intervals in Minutes (Median Values and Interquartile Ranges) Between Ambulance Groups: Pre-Group One versus Post-Group***

	Pre-Group One				Post-Group				
Treatment Time Interval	*N*	Median	[95% CI]	IQR	*N*	Median	[95% CI]	IQR	*p*-Value
From paramedic contact to arrival at CCL (goal < 90 minutes)	32	125	[119, 134]	22	35	67	[66, 72]	9	<0.001* (2-tailed)
From paramedic contact to balloon inflation[a] (goal < 120 minutes)	31	155	[149, 164]	27	33	102	[89, 110]	16	<0.001* (2-tailed)
From arrival at referral centre[b] to balloon inflation[a] (goal < 120 minutes)	31	116	[109, 125]	30	33	82	[70, 89]	17	<0.001* (2-tailed)
From first diagnostic STEMI ECG to balloon inflation[a] (goal < 120 minutes)	31	151	[142, 156]	26	33	100	[88, 109]	17	<0.001* (2-tailed)
From land at receiving hospital to balloon inflation[a] (goal < 30 minutes)	31	34	[33, 40]	8	33	36	[32, 47]	18	0.47 (2-tailed)
From arrival at CCL to balloon inflation[a] (goal < 30 minutes)	31	28	[26, 33]	7	33	31	[27, 41]	17	0.23 (2-tailed)
Total ischaemic time[a] (goal < 180 minutes)	31	256	[236, 327]	139	33	150	[148, 234]	108	<0.001* (2-tailed)

Note: CI = confidence interval; IQR = interquartile range; CCL = cardiac catheterisation laboratory; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram. All comparisons between groups were made using Mann-Whitney U tests.
[a]All balloon inflation times and the total ischaemic time exclude one patient in the Pre-Group One and two patients in the Post-Group. This was due to no device being inserted because of anatomy which precluded stent placement.
[b]Referral centre = Whangarei Hospital in Pre-Group One and the Northland Rescue Helicopter helipad in the Post-Group
*Significant at $p < 0.05$

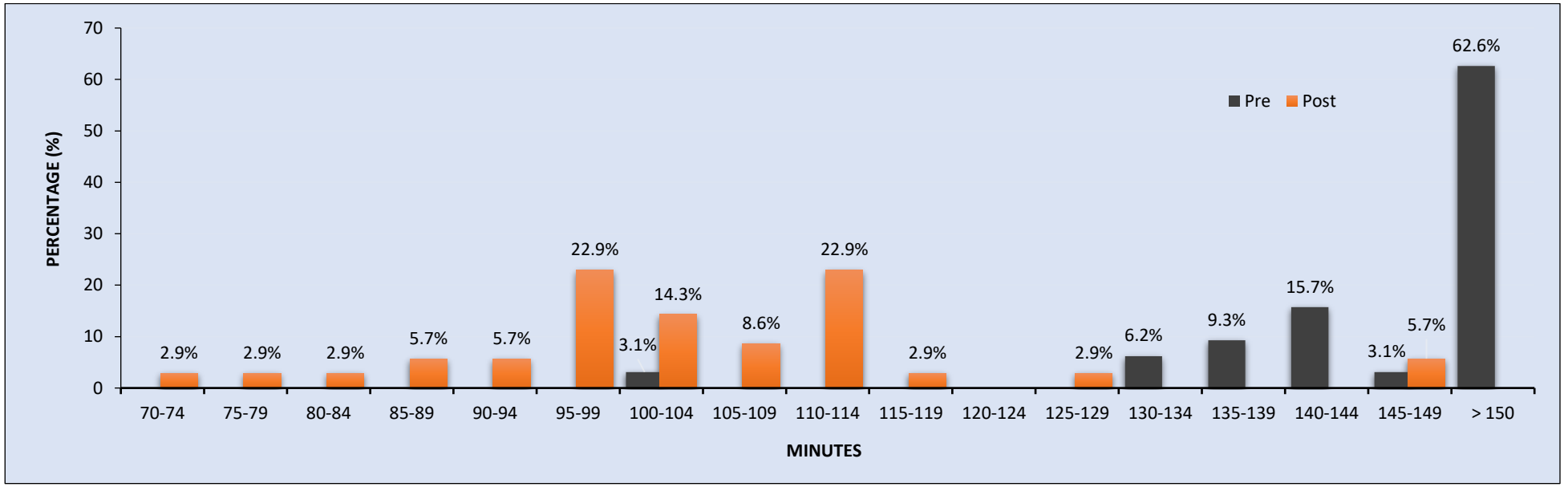


Figure 5.9 **Distribution and Comparison of ETB Times Between Ambulance Groups: Pre-Group One versus Post-Group**

Note: ETB = emergency medical services (paramedic) contact-to-balloon. The mandated target time for this sub-interval is less than 120 minutes.

Table 5.7 ***Comparison of Key Treatment Time Intervals in Minutes (Median Values and Interquartile Ranges): Pre-Implementation Groups versus Post-Implementation Group***

	Pre-Group One (*n* = 31)			Pre-Group Two (*n* = 25)			Post-Group (*n* = 33)				
Treatment Time Interval	Median	[95% CI]	IQR	Median	[95% CI]	IQR	Median	[95% CI]	IQR	Test Statistic	*p*-Value
From arrival at referral centre to balloon inflation[ab]	116	[109, 125]	30	124	[115, 161]	52	82	[70, 89]	17	$\chi^2(2, n = 92) = 52.38$	<0.001*
From first medical contact to balloon inflation	155	[149, 164]	27	124	[115, 161]	52	102	[89, 110]	16	$\chi^2(2, n = 92) = 49.53$	<0.001*
From first diagnostic STEMI ECG to balloon inflation[a]	151	[142, 156]	26	130	[121, 175]	51	100	[88, 109]	17	$\chi^2(2, n = 92) = 47.61$	<0.001*
From landing at receiving hospital to balloon inflation[a]	34	[33, 40]	8	35	[33, 42]	13	36	[32, 47]	18	$\chi^2(2, n = 92) = .473$	0.79
From arrival at CCL to balloon inflation[a]	28	[26, 33]	7	29	[26, 34]	13	31	[27, 41]	17	$\chi^2(2, n = 92) = 1.442$	0.48
Total ischaemic time[a]	256	[236, 327]	139	209	[185, 278]	110	150	[148, 234]	108	$\chi^2(2, n = 92) = 52.38$	<0.001*

Note: CI = confidence interval; IQR = interquartile range; χ^2 = chi-square; STEMI = ST-elevation myocardial infarction; ECG = electrocardiogram; CCL = cardiac catheterisation laboratory. All comparisons between groups were made using Kruskal-Wallis tests.
[a]All treatment time intervals exclude one patient in Pre-Group One and two patients in the Post-Group. This was due to no device being inserted because of anatomy which precluded stent placement.
[b]Referral centre = Whangarei Hospital for both Pre-Group One and Two, and the Northland Rescue Helicopter helipad for the Post-Group
*Significant at $p < 0.05$

Table 5.8 ***Comparison of Additional Operational and Clinical Times in Minutes Between Ambulance Groups: Pre-Group One versus Post-Group***

Time Measure	Pre-Group One (*n* = 32)	Post-Group (*n* = 35)	Test Statistic	*p*-Value
Mean ambulance response time (±SD)	8 (±3)	7 (±2)	$t(65) = 1.7$	0.08 (2-tailed)
Mean ambulance scene time (±SD)	26 (±6)	14 (±4)	$t(53) = 8.9$	<0.001* (2-tailed)
Mean ECG acquisition time[a] (±SD)	8 (±2)	4 (±2)	$t(65) = 8.1$	<0.001* (2-tailed)
Mean ambulance transport time (±SD)	13 (6)	7 (±2)	$t(40) = 5.2$	0.001* (2-tailed)
Mean helicopter flight time (±SD)	31 (±1)	31 (±2)	$t(65) = 0.3$	0.71 (2-tailed)

Note: SD = standard deviation; *t* = t-test value; ECG = electrocardiogram.
[a] ECG acquisition time commenced from time of first contact with patient.
*Significant at $p < 0.05$

Table 5.9 ***Causes of Delays where FMCTB Time Exceeded 120 minutes (n=53)***

Cause of Delay	*N*	(%)
ED assessment	41	(77)
Diagnosis	2	(4)
Aircraft availability	2	(4)
CCL occupied	5	(9)
Procedural complication	2	(4)
Resuscitation	1	(2)

Note: FMCTB = first medical contact-to-balloon; ED = emergency department; CCL = cardiac catheterisation laboratory

5.6.4 Patient Clinical Management and Outcomes

Table 5.10 summarises the PCI procedural characteristics for all patients. No significant differences between groups were identified. Clinical complications prior to the intervention included cardiogenic shock, compromising arrhythmia (not including those patients in cardiac arrest) and cardiac arrest. Among the 92 patients in total (both Pre- and Post-Implementation Groups), no deaths occurred during helicopter transfer and only one patient required resuscitation with defibrillation in flight.

Table 5.11 summarises further clinical management and outcomes across all groups. Despite the significant reductions in time-to-treatment demonstrated in favour of the Post-Group, this did not result in a significant reduction in either 30-day or six-month mortality or hospital re-admissions for an ACS event within six months post-discharge.

5.6.5 Hospital Length of Stay

Patients in the Post-Group were found to have significantly shorter hospital LOS (measured in bed days) compared to those in both the Pre-Implementation Groups (Pre-Group One – median of 4.5 days, IQR - 3, Pre-Group Two – median of 4 days, IQR - 3, and the Post-Group – median of 3 days, IQR - 3, χ^2 (2, n = 92) = 8.45, p = 0.01). Raw data from the three groups is presented graphically for comparison in Figure 5.10.

Table 5.10 ***PCI Procedural Characteristics: Comparison of Pre-Implementation Groups Versus Post-Implementation Group***

Variable	Pre-Group One (*n* = 32) n (%)	Pre-Group Two (*n* = 25) n (%)	Post-Group (*n* = 35) n (%)	Test Statistic	*p*-Value
Clinical complications prior to PCI[a]	6 (18)	3 (12)	6 (17)	$\chi^2(2) = 0.492$	0.78
Angiographic findings:					
- 1 vessel disease	18 (56)	12 (48)	22 (62)		
- 2 vessel disease	8 (25)	8 (32)	9 (26)		
- 3 vessel disease	5 (16)	4 (16)	3 (9)		
- Left main stem stenosis	1 (3)	1 (4)	1 (3)	$\chi^2(2) = 1.796$	0.93
Culprit artery:					
- Left anterior descending	17 (53)	15 (60)	16 (46)		
- Left circumflex	1 (3)	1 (4)	1 (3)		
- Right	13 (41)	8 (32)	17 (48)		
- Left main stem	1 (3)	1 (4)	1 (3)	$\chi^2(2) = 1.676$	0.94
Inappropriate CCL activation	-	-	-	-	-
IABP required	-	-	1 (3)	-	-
Procedural complications	4 (12)	3 (12)	5 (15)	$\chi^2(2) = 0.810$	0.96
TIMI flow post-PCI:					
- 3	28 (87)	23 (92)	31 (88)		
- 0 – 2	4 (12)	2 (8)	4 (12)	$\chi^2(2) = 0.311$	0.85

Note: PCI = percutaneous coronary intervention; χ^2 = chi-square; CCL = cardiac catheterisation laboratory; IABP = intra-aortic balloon pump; TIMI – thrombolysis in myocardial infarction flow grade.
[a]Clinical complications prior to PCI included cardiogenic shock, compromising arrhythmia (not including those patients in cardiac arrest) and cardiac arrest.

Table 5.11 ***Further Clinical Management and Outcomes: Comparison of Pre-Implementation Groups Versus Post-Implementation Group***

Variable	Pre-Group One (*n* = 32) *n* (%)	Pre-Group Two (*n* = 25) *n* (%)	Post-Group (*n* = 35) *n* (%)	Test Statistic	*p*-Value
Emergent CABG from the CCL	-	-	-	-	-
Repeat PCI to culprit artery	-	-	-	-	-
Repeat PCI to non-culprit artery	2 (6)	2 (8)	3 (9)	FET	0.99
Elective CABG	3 (9)	-	1 (3)	-	-
No intervention[a]	-	-	-	-	-
In-hospital reinfarction	-	-	-	-	-
Mortality at 30 days	1 (3)	-	1 (3)	-	-
Mortality at 6 months	1 (3)	1 (4)	1 (3)	FET	0.99
Re-admission for an ACS event within 6 months	5 (15)	4 (16)	1 (3)	FET	0.15

Note: CABG = coronary artery bypass grafting; CCL = cardiac catheterisation laboratory; PCI = percutaneous coronary intervention; FET = Fisher's exact test; ACS = acute coronary syndrome

[a]No intervention refers to patients who did not receive any invasive treatment, i.e. PCI or CABG.

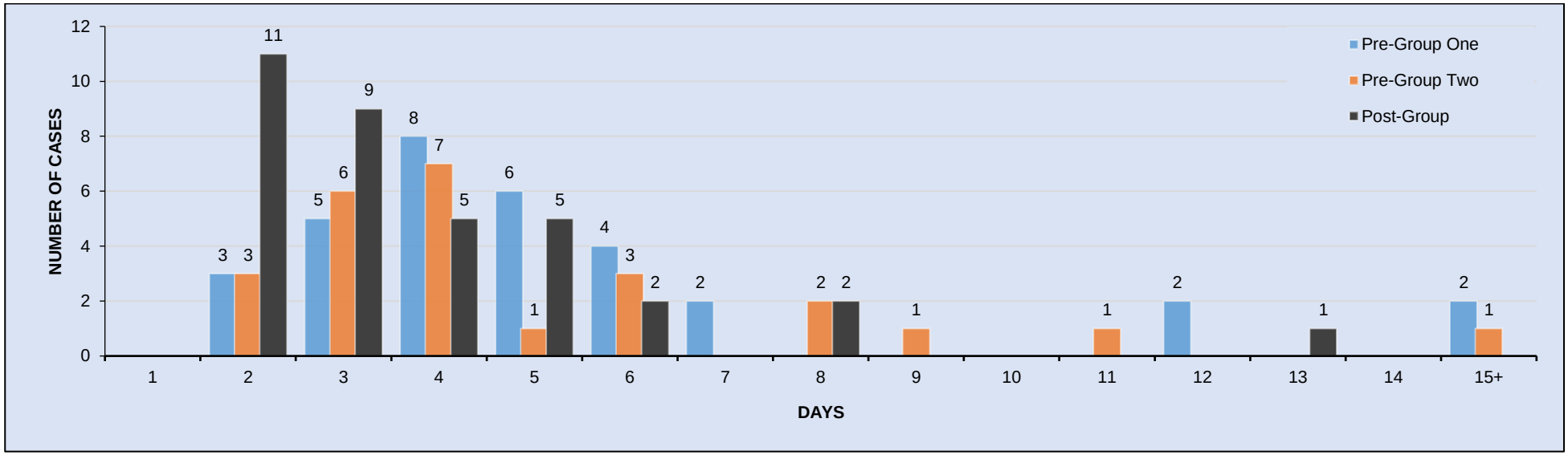


Figure 5.10 **Comparison of Patient Hospital Length of Stay Measured in Bed Days Between Groups**

5.7 Discussion

This study is the first to compare two distinct models of CCL activation and referral of acute STEMI patients for PPCI via helivac. Authorisation of this activation and referral process was the main distinction between the two models: physician-authorised versus autonomous paramedic decision making. Despite modest numbers, this study has demonstrated a significant time saving in treatment delivery in favour of the autonomous paramedic model. Compared to the physician-authorised approach, there was a 34-minute reduction in the median FMCTB time when autonomous paramedics initiated patient referral to the CCL (Pre-Groups – combined median time 136 minutes, IQR 55, versus Post-Group – 102 minutes, IQR 16, $p = <0.0001$). Moreover, there was a significant increase in the proportion of patients who received treatment within benchmark timeframes (as stipulated by CSANZ and AHA Guidelines). The ETB time goal of less than 120 minutes was achieved among only 3% of relevant pre-implementation cases versus 91% of post-implementation cases, a 30-fold improvement ($p = <0.0001$). The total ischaemic time goal of less than 180 minutes was achieved in only 16–18% of pre-implementation cases versus 60% of post-implementation cases, a more than three-fold improvement ($p = <0.0001$).

These results compare favourably with similar aeromedical transfer pathways reported in the literature, including those that were physician-led, and/or inter-hospital based (Grines et al., 2002; McMullan et al., 2011; Sigmundsson et al., 2010). They were also associated with a significant reduction in patient hospital admission times in favour of our autonomous paramedic model ($p = 0.01$). Of note, there were no significant differences in demographic features, CVD risk factors or clinical presentations between the three experimental groups that would account for these differences in treatment times. Although significant reductions in both treatment delivery times and hospital LOS were demonstrated, the study was underpowered to show mortality benefit at 30 days and six months, as well as reduced re-admission rates for an ACS event at six months.

A variety of strategies designed to expedite PPCI delivery have been proposed within the literature, as many studies have shown that failure to meet evidence-based treatment times may diminish the relative benefits of the intervention and its superiority over on-site fibrinolysis (Pinto et al., 2006). This is particularly the case when patient transfer is required due to local centres being without interventional cardiology services.

Among these proposed strategies, internationally, paramedic-initiated referral and direct patient transport from the field to the CCL has yielded the most promising results. The limited studies that have investigated this more streamlined approach have shown markedly improved PCI delivery times compared to both physician-assisted paramedic models and improved in-hospital strategies (Cheskes et al., 2011; Clark et al., 2012; Garvey et al., 2012). Not only has our study reaffirmed this in the New Zealand context, it has done so with patient transport occurring over a greater distance (155km) than that reported in similar trials (De Luca et al., 2008; Grines et al., 2002; Widimský et al., 2003; Widimský et al., 2000).

Critical to the success of paramedic-initiated referral pathways for PPCI, is the confidence key stakeholders must have in paramedics' ability to accurately identify those patients eligible for treatment and referral. The main concern interventional cardiology departments have with adopting such programmes is the rate of inappropriate CCL activations. Such occurrences can prove costly and inconvenient, particularly outside of normal working hours when staff are commonly on-call. Within the literature, acceptable rates of inappropriate activation by autonomous paramedics range between five and 20 percent (Garvey et al., 2012; Moyer et al., 2007). For our four-year 57-case trial, there were no inappropriate activations and all patients referred to the CCL by the flight ICPs were accepted by the on-call interventional cardiologists. However, it must be stated that without this process of patient reassessment by the flight ICPs, as many as 20 patients would have been referred inappropriately by road paramedics. This result, in part, serves to validate the study's autonomous paramedic protocol, which included a stringent list of indication/contraindication criteria designed to mitigate the risk of misdiagnosis. In applying this new protocol after a relatively small amount of additional training, our autonomous flight ICPs demonstrated highly accurate STEMI diagnosis and clinical decision making with a sensitivity of 97% (95% CI: 85–99) and specificity of 100% (95% CI: 84–100). For the one false negative case that occurred, the patient received fibrinolysis in the ED before eventually being flown to the CCL as an inter-hospital transfer.

Similar to the protocol utilised in the previous study detailed in Chapter Four, one potential limitation of our new autonomous paramedic CCL activation protocol was the exclusion of more complex ECG criteria for STEMI, that is, the new or presumed new LBBB. These patients were excluded because determining a new or presumed new LBBB in the field is difficult, with often little or no access to any form of patient medical records,

coupled with the criteria being less sensitive and specific for the diagnosis (Jain et al., 2011; Kontos et al., 2011). However, this study has demonstrated that New Zealand paramedics can determine patient eligibility for urgent PPCI referral (including ECG interpretation) with a high degree of accuracy. This supports the idea of broadening the ECG criteria for STEMI among the New Zealand paramedic workforce, something which has recently occurred within the latest St John and Wellington Free Ambulance CPGs (National Ambulance Sector Clinical Working Group, 2016). Notably, however, of the 57 patients assessed in the Post-Implementation phase of the trial, none presented with ECG evidence of either a new or presumed new LBBB.

A positive automated interpretation of STEMI was mandated in the indications list for the autonomous paramedic CCL activation protocol, to provide decision support. If the duty flight ICP disagreed with the automated interpretation (termed 'discordance'), the patient and attending ambulance crew were redirected by road to the local receiving hospital. All of the 57 patients assessed by the duty flight ICP for suitability to undergo urgent PPCI in the Post-Implementation phase presented with a positive automated interpretation of STEMI. Of this number, 37 patients (64.9%) showed evidence of a culprit lesion on angiography and received PPCI. Thirty-five of these patients were referred to the CCL by the duty flight ICP. As for the two patients who weren't referred, one was misdiagnosed and one presented at the helipad suffering repeated cardiac arrest requiring CPR and defibrillation and exclusion criteria for helivac within the new paramedic referral protocol. The remaining 20/57 patients presented with ECG evidence of a STEMI-mimic (false positives).

In part, this false positive number is reflective of the fact that during the trial road paramedics were encouraged to transport patients to the helipad (for re-assessment by the flight ICP) if they presented with a positive automated interpretation but if the paramedic was unsure of a STEMI diagnosis. This process served to reduce the likelihood of patients eligible for helivac being transported to the local receiving hospital, denying them access to timely PPCI. As was previously discussed, 90% of these false positive cases (18/20) presented within the first 12 months of the trial. This demonstrated that as time progressed, road paramedic selection of patients improved substantially, which is likely attributable to greater familiarity with the new protocol as well as staff feedback as part of the trial's quality assurance process.

Among the ambulance patients that made up Pre-Group One (referred for urgent PPCI by ED physicians at Whangarei Hospital), 31/32 presented with a positive automated interpretation of STEMI on their initial ambulance ECG and all showed evidence of a culprit lesion on angiography. However, of note, we were unable to collect and examine false positive cases which would have accompanied this group. Overall, these combined figures are consistent with previous evidence detailing both the sensitivity and specificity of the diagnostic software incorporated within the ambulance service heart monitors (Garvey et al., 2016; Ioannidis et al., 2001; Massel et al., 2000). They also demonstrate the utility of this software in providing decision support, while emphasising the necessity for clinician over-read prior to decision making regarding patient treatment and management. Our Flight ICPs successfully filtered 56/57 patients (98%), determining true STEMI cases from false STEMI cases.

Among all patients in the trial's pre- and post-implementation phase (n = 92), the median time from onset of symptoms to seeking medical assistance (i.e. calling 111 to request an ambulance or self-presenting at hospital) was 72 minutes (95% CI 67–121). The minimum time was three minutes and the maximum time was 536 minutes. In the New Zealand context, Tanner et al. (2006) reported a median time of 90 minutes for this sub-interval among 100 ACS patients, despite the majority (62%) correctly assuming their symptoms were heart related. Weaver (1995) showed that ACS patients who seek alternative means of transport to hospital, such as with family or friends, on average add 60 minutes to their arrival time at the ED, compared with transportation by ambulance. For the STEMI patient, any delay in seeking medical assistance greatly impacts on the time taken to receive reperfusion therapy (whatever the modality) and on the subsequent outcome. In most cases, requesting ambulance assistance provides the fastest means by which diagnosis and treatment access can occur. Continued public awareness and education on this matter is needed. Specifically, it would be important to address the reasons why ACS patients fail to seek help early after symptom onset, while also encouraging these patients to call for ambulance assistance immediately. This is in an endeavour to bring all reperfusion times to within guideline targets.

Among patients in the trial's post-implementation phase, significantly shorter hospital admission periods were observed (Pre-Group One – median of 4.5 days, Pre-Group Two – median of 4 days and the Post-Group – median of 3 days, χ^2 (2, n = 92) = 8.45, p = 0.01). This finding is likely attributable to the time-saving advantage demonstrated by our paramedic-initiated referral pathway, as the benefits of PPCI are

directly proportional to total ischaemic time, i.e. time from symptom onset to reperfusion (McNamara et al., 2006; Steg et al., 2003). This finding suggests there may be an economic benefit to our new paramedic-initiated CCL referral pathway; however, our study's patient sample size is too small to be definitive.

Compared to the ambulance cohort in the trial's pre-implementation phase (Pre-Group One), introduction of our new paramedic protocol also showed significant improvements in key operational times, i.e. ambulance scene and transport time, as well as first ECG acquisition time. This is not surprising given ambulance crews were provided with clear target goals for each time interval. These included: an ECG acquisition time of less than five minutes; a scene time of less than fifteen minutes; and a transport time to the helicopter pad of less than twenty minutes under lights and sirens. Improvements in these areas contributed greatly to achieving the international benchmark treatment timeframes for PPCI, while also highlighting the benefit of a targeted approach over the entire continuum of patient care, both pre- and in-hospital.

The primary deficiency of the earlier Code STEMI Programme in the trial's pre-implementation phase was the excessive time that patients spent in the ED prior to transfer: median time 52 minutes (95% CI: 50–67). The international benchmark for this sub-interval of 'door in-door out' (DIDO) is less than 30 minutes (Moyer et al., 2007). Among the 56 patients in total who received PPCI within this hospital-based referral system, the overwhelming majority (89.3%) had a FMCTB time exceeding 120 minutes. Emergency department assessment time contributed to 82% of these delays. Although numerous potential factors may account for this, i.e. patients who were unstable, inadequate staffing levels or ECG interpretation skills, there were no comparable delays observed among patients in the study's post-implementation phase. By excluding transport to the ED and activating the CCL team from the first point of care, our paramedic-initiated referral pathway not only achieved significantly shorter times to treatment, but also proved to be safe and feasible with no additional risk to the patient. Moreover, prior CCL notification coupled with an average flight time of 30 minutes provided adequate time for CCL staff to assemble and prepare for patient arrival, including outside of normal working hours.

As detailed in Chapter Two: Review of the Literature, numerous randomised controlled trials comparing fibrinolysis with PPCI in the management of STEMI have produced unequivocal results in favour of PPCI as the more superior reperfusion strategy

in terms of morbidity, mortality and infarct artery patency rates (Andersen et al., 2003; A. Kelly et al., 2003; Weaver et al., 1997). This superiority has also been consistent when inter-hospital transfer of patients to a PCI facility has occurred (Aversano et al., 2002; Grines et al., 2002; Widimský et al., 2000; Zijlstra, 2003). However, the rates of those patients who receive PCI, and within optimal timeframes, is poor in New Zealand (C. Ellis et al., 2004). This has been attributed to several factors, including: lack of adequate funding; patient location in relation to a PCI facility; time of day; and in particular, delays within emergency healthcare systems (C. Ellis et al., 2004; Williams, 2007). The paramedic-based model of care presented in our study offers a viable strategy to address many of these issues.

Twelve eligible patients presenting in the study's post-implementation phase were unable to be transferred directly to the CCL due to aircraft unavailability. In all cases, patients were immediately assessed as to their suitability to receive fibrinolysis by the attending paramedics, and eight were deemed eligible. This additional component of care within our autonomous paramedic model provides further alignment with current evidence-based best practice guidelines (ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand, 2013). Numerous studies have demonstrated the clear superiority of pre-hospital versus in-hospital fibrinolysis in terms of significantly improved treatment delivery times, and with associated reductions in both morbidity and mortality (Boersma et al., 1996; Morrison et al., 2000). Interestingly, up until late 2017, only a few regions throughout New Zealand had any form of paramedic-based pre-hospital STEMI management programme (including fibrinolysis). This is despite the overwhelming evidence in support of paramedic inclusion within STEMI management systems (P. Kelly, 2003; A. M. Smith et al., 2011).

As per our previous clinical trial discussed in Chapter Four, this investigation explored the topic of SMI in the setting of STEMI and revealed similar results. We identified that chest, neck or arm discomfort formed part of the symptomology among all patients with a confirmed diagnosis of STEMI and that approximately 68.4% (63/92) of these patients stated that their discomfort was a first-time occurrence. Again, these findings serve to support the quantitative theory of SMI, suggesting that the presence or absence of clinically detectable myocardial ischaemia correlates to the size or extent of the ischaemia experienced.

Current population statistics show that 15% of New Zealanders self-identify as Māori (Statistics New Zealand, 2017b). Therefore, within each of our study's three observed groups, Māori were over-represented (22%, 20% and 23% respectively). However, this is likely due to the fact that the Northland region has the country's highest Māori population at 25%, and that the Whangarei District has a Māori population of 28% (Statistics New Zealand, 2017b; Whangarei District Council, 2015). Also to be considered is that the prevalence of IHD is significantly higher among Māori than non-Māori, and higher overall within Northland compared to other regions of the country (Ministry of Health, 2014a; Northland District Health Board, 2007). Although further continued efforts are needed to address this well-known health inequality for Māori at both local and government level, our study's programme has enabled a large Māori population to have timely access to optimal STEMI care.

Within our paramedic-initiated referral pathway, detailed audit and quality assurance measures were vital to establishing an optimal system. At the completion of each transfer, duty flight ICPs were required to submit the ambulance ePRF to the trial's lead investigator. This process not only enabled the timely collection of key demographic, clinical and logistical data, it also provided the means by which any issues could be addressed immediately. One common example was incorrect job details being paged to the flight crew by the ambulance communications centre in the post-implementation phase of the trial. This overall approach enabled consistency and repeatability of a service focussed on patient outcome.

5.8 Limitations

This study was not randomised and there were several differences in the PPCI referral protocols (indication/contraindication criteria) between the Pre-Implementation Groups and the Post-Implementation Group. However, all patient groups were demographically similar and had similar clinical characteristics on initial presentation, so were considered comparable. A cost efficacy analysis was beyond the remit of this study, but it would certainly be of interest to compare ultimate costs of the two models of referral. One notable example is the significantly shorter hospital admissions times associated with the autonomous paramedic referral programme. Certain features of our local setting may impact on the generalisability of the study's results to other regions of New Zealand. These include geography and distance to the nearest CCL, population, ambulance crew qualifications and available EMS helicopter services. However, this

experience may serve as a benchmark which invites other regions to utilise the trial's key concepts and develop similar pathways tailored to their own local setting. This would especially be the case in regional areas where the local receiving hospital is reliant on a parent tertiary centre to provide CCL services.

5.9 Conclusion

Paramedic-initiated patient referral and helivac to the CCL for PPCI is a safe and feasible strategy for the treatment of STEMI, a process that bypasses the ED and occurs without physician oversight. This approach provided a significant time-saving advantage for treatment delivery compared to an older inter-hospital helicopter transfer model with physician referral. Moreover, time-to-treatment came within international best practice guidelines. As a result, a significant reduction in hospital LOS was demonstrated. The paramedics in our study demonstrated a high level of accurate clinical decision making with no inappropriate CCL referrals occurring. These findings have now allowed for routine consideration of PCI as a primary reperfusion strategy in a population whose local receiving hospital is without interventional cardiology services and where distance to the nearest CCL precludes road transfer. Continued public education campaigns that address the reasons why ACS patients fail to seek help early after symptom onset, and which encourage these patients to call for ambulance assistance immediately, are required. This is in an endeavour to bring all reperfusion times to within guideline targets. Further investigation into causes of hospital-based time delays for urgent referral of STEMI patients to PCI centres in the New Zealand setting is also warranted.

Chapter Six: General Discussion and Conclusion

6.1 Introduction

This chapter is divided into several sections, the first of which seeks to both summarise and synthesise the research undertaken within this thesis in terms of its value both nationally and abroad. The research's significance and contribution to paramedicine and the greater emergency health care sector are then discussed, followed by potential implications for both regional and national health care system policies. Contributions towards Māori health are also discussed, and the project's strengths and limitations are explored. The chapter concludes with recommendations for future inquiry.

6.2 Thesis Summary

6.2.1 General

ST-elevation myocardial infarction remains a widely prevalent and acute pathology within our society, and has serious and potentially life-threatening implications (J. Ellis & Richards, 2005). However, the evidence shows that efficient contemporary systems of care with timely patient diagnosis and access to reperfusion therapy improves patient outcomes – both morbidity and mortality (Cheskes et al., 2011; Moyer et al., 2007; Steg et al., 2003). Despite this, results from the most recent national audits have demonstrated several inadequacies in our current health care system in providing optimal STEMI management pathways (C. Ellis et al., 2013). Key findings were as follows:

- There was poor resource utilisation with numerous disparities in service delivery among DHBs, despite best practice standards being promulgated in local guidelines.
- Significant delays for accessing planned invasive assessment were observed among patients presenting at non-interventional hospitals unable to perform PCI.
- Approximately 27% of patients failed to receive any form of reperfusion therapy, despite being eligible.

To better improve system performance, the international literature provides an overwhelming body of evidence in support of paramedic utilisation. The strategic position of paramedics within our communities mean they are often the first health practitioners to encounter the ACS patient, and thus expedite the process of STEMI recognition and

acute treatment/management (P. Kelly, 2003; A. M. Smith et al., 2011). As a result, compared to solely hospital-based processes, paramedic-inclusive systems of care have demonstrated significant reductions among all treatment timeline metrics, and reduced patient morbidity and mortality rates (Björklund et al., 2006; Cheskes et al., 2011; Moyer et al., 2007; Weaver et al., 1993). However, historically there has been a distinct under-utilisation of the paramedic workforce within New Zealand to assist in achieving similar outcomes. Although some select regions have incorporated telemetry-based paramedic programmes with physician oversight, cost concerns and evidence of treatment delays due to technological failings invite strategies for improvement (P. Davis, 2014). Potential new strategies are possible because of advances in New Zealand paramedic practice over the last two decades, particularly in the areas of educational standards and scope of clinical practice (Council of Ambulance Authorities, 2008).

An autonomous paramedic model of care is one specific approach supported by a small body of international research that alleviates many of the issues encountered in other models (Cheskes et al., 2011; Garvey et al., 2012; Grijseels et al., 1995; Keeling et al., 2003; Moyer et al., 2007; Pitt, 2002). However, there are fundamental differences in paramedic practice between New Zealand and other countries, which are likely to impact on the generalisability of overseas research findings to New Zealand. Therefore, the overarching aim of the research presented in this thesis was to examine an autonomous paramedic model of care in the treatment and management of STEMI within the New Zealand context, and to compare this approach with previous strategies. This was achieved by conducting several investigations focussed on: (1) the clinical knowledge and independent decision-making abilities of a New Zealand paramedic sample group in simulation; (2) implementation of an autonomous paramedic model for the provision of fibrinolysis via clinical trial with comparison made to a physician-assisted telemetry-based approach; and (3) implementation of a paramedic-initiated CCL activation and direct patient transfer pathway via clinical trial with comparison made to that of a hospital-based referral process. This research is unique, not only for being the first to explore these concepts within New Zealand, but also for being the first internationally to compare two differing paramedic-based STEMI management systems.

In Chapter Three the first preliminary investigation was detailed. Utilising a quasi-experimental design of one group post-test only, this simulation-based study enabled us to gain critical insight into several key areas prior to progressing to clinical trial. These included: the clinical knowledge and independent decision-making abilities of our

paramedic sample relative to the provision of fibrinolysis under protocol guidance; comparison of New Zealand's two paramedic education pathways; and associations between our paramedics' clinical decision-making abilities and key individual characteristics.

Results from the testing phase showed highly accurate STEMI diagnosis and treatment decision making overall among our paramedic sample – sensitivity of 92.0% (95% CI: 84.8–96.5) and specificity of 95.6% (95% CI: 89.1–98.8). This demonstrated that our participants possessed sufficient clinical knowledge, i.e. cardiac and pharmacology, on which to base the introduction of a new paramedic-initiated STEMI management system that excludes the requirement for physician consultation. We were also able to demonstrate a greater level of accuracy among two subgroups. These included those at a practice level of ICP, as well as those who had completed a BHSc undergraduate paramedic degree (p = 0.006 and p = 0.001 respectively). The latter finding served to validate recent educational changes within New Zealand paramedicine, i.e. the transition from a post-employment in-house education model to that of a pre-employment university-based model. Furthermore, despite ECG interpretation across the entire group being largely accurate, two areas of interpretation deficit were revealed regarding STEMI-mimics. Although the study's paramedic participants were not randomly selected, collectively these findings served to support and inform our second and third investigation, in terms of staff training and introductory requirements.

Chapter Four marked the transition from theory to practice and detailed the first of our two clinical trials. Over a 24-month period an autonomous paramedic fibrinolysis programme was implemented in the regions of Northland and Hawke's Bay, both regions having previously trialled a physician-authorised telemetry-based programme. This enabled a comparison to be made between the two models, utilising a prospective analysis of differences study design. Key findings from the trial included the following:

- Autonomous paramedic participants demonstrated highly accurate STEMI diagnosis and treatment decision making with a sensitivity of 96% (95% CI: 89–99) and specificity of 91% (95% CI: 76–98).
- A significant time-saving improvement was demonstrated across all treatment timeline metrics in favour of the autonomous paramedic model, as was the proportion of patients who received treatment within benchmark timeframes.

- These findings were associated with a significant reduction in both 30-day patient mortality and hospital LOS (p = 0.04 and p = <0.001 respectively).

The proportion of inappropriate treatment cases (false positives) was also found to be lower among those patients treated by autonomous paramedics versus those treated following physician authorisation. In all cases this was primarily due to ECG misinterpretation. Although this difference was not significant, it served to validate both the accuracy of independent paramedic diagnosis and treatment decision making, as well as the more stringent protocol developed and utilised. Moreover, it links with previous evidence showing the accuracy of paramedic ECG interpretation of STEMI to be comparable to that of physicians (Feldman et al., 2005; Whitbread et al., 2002).

A secondary investigation within this trial examined and compared cases of aborted MI versus established MI. This was also an international first in that all patients reviewed were treated by paramedics in the pre-hospital setting. The 68% incidence of aborted MI in our study exceeded that previously reported across other trials (16.5%, 12.6%, 12.3% and 23.3%) and was likely due to differing criteria and shorter median PTN times (Jackson et al., 2009; Lamfers et al., 2003b; Lamfers et al., 2004; Taher et al., 2004). Interestingly, unlike previous studies, no significant difference in treatment-delivery times emerged between groups. However, our Established MI group presented with several significant differences, which in part might explain this finding. These included

- more patients presenting with a Killip class II to IV as well as anterior STEMI (p = 0.05 and p = 0.002 respectively)
- higher rates of PCI procedural complications (p = 0.01)
- higher rates of 30-day and six-month mortality (p = <0.0001)
- higher re-admission rates for an ACS event within six months post-discharge (p = <0.0001).

These findings corresponded with previous evidence showing anterior STEMI to be less amenable to fibrinolysis and associated with significantly higher rates of both in-hospital morbidity and mortality compared to other types of AMI (Fibrinolytic Therapy Trialists' Collaborative Group, 1994; Stone et al., 1988). Moreover, we were also able to demonstrate through multiple logistic regression models that those patients who presented with a family history of ACS and anterior STEMI were less likely to achieve reperfusion following fibrinolysis, i.e. develop an established MI. Overall, the results of this study

supported our tested hypotheses, demonstrating the superiority of an autonomous paramedic model in the provision of fibrinolysis, while alleviating safety and feasibility concerns.

The third and final investigation was detailed in Chapter Five: a second clinical trial of 48 months' duration and examining a programme of paramedic-initiated CCL activation with direct patient transfer from the field via helivac. This was a relatively ambitious project undertaken in a regional metropolitan centre without interventional cardiology services, and covering a transport distance much greater than those reported in previous similar trials. Again, utilising a prospective analysis of differences study design, a comparison was made against the regional centre's previous hospital-based programme for urgent CCL referral utilising the same aeromedical transfer service. The project's key findings were similar to those of the previous trial: highly accurate autonomous paramedic diagnosis and treatment decision making; a significant time-saving improvement demonstrated among all treatment timeline metrics in favour of the new paramedic referral model; and the proportion of patients who received treatment within benchmark timeframes. While the study was underpowered to show a mortality-benefit associated with the improved treatment times, it was observed that patients among the paramedic referral cohort had significantly shorter hospital LOS (p = 0.01). Moreover, the safety, feasibility and superiority of our paramedic-initiated referral pathway was well established.

6.2.2 Additional Findings

Our two clinical trials also yielded several additional common findings. Firstly, we reported on the time it took patients to seek medical assistance from the time of symptom onset. The median values for this subinterval showed large variability and ranged from 28 to 72 minutes (both trials combined). Although these figures were less than previously reported in the New Zealand context, they still represented a period of delay that contributed greatly to the time taken before STEMI patients received reperfusion therapy. Further public education campaigns that address the reasons why ACS patients fail to seek help early after symptom onset, and which also encourage these patients to call for ambulance assistance immediately, are warranted. This is in an endeavour to bring reperfusion times to within guideline targets.

Patient symptomology was also examined between trials. For those with a confirmed diagnosis of STEMI, all experienced chest, neck or arm discomfort on

presentation, with the majority stating that it was a first-time occurrence. These findings serve to provide further insight into the topic of SMI with reference to STEMI, of which there is a paucity of inquiry. Moreover, they suggest that the presence or absence of clinically detectable myocardial ischaemia correlates to the size or extent of the ischaemia experienced, as postulated in the quantitative theory of SMI.

Both trials reported on the overall accuracy of the automated ECG interpretation of STEMI by the ambulance heart monitors. This was achieved through confirmatory diagnosis via multiple means. A positive automated interpretation was mandated within each of the trial's autonomous paramedic protocols to provide decision support. Our combined results were consistent with previous evidence detailing both the sensitivity and specificity of the diagnostic software incorporated within the heart monitors (Garvey et al., 2016; Ioannidis et al., 2001; Massel et al., 2000). They also served to demonstrate the utility of this software in providing decision support, while emphasising the necessity for clinician over-read prior to decision making regarding patient treatment and management.

Patient demographics and clinical characteristics on initial presentation were largely similar across trials. However, although patients who received fibrinolysis were treated sooner, collectively they presented with more complications in the field and had worse mortality outcomes compared to those who underwent PPCI. These findings may be attributed to two primary factors. Firstly, between 30 and 34% of patients failed to achieve reperfusion following fibrinolysis, versus 8–13% of patients who underwent PPCI (as measured by a TIMI 3 flow grade post-treatment). Secondly, total ischaemic times were likely much longer among fibrinolysis patients given reperfusion is not immediate with successful treatment, as is the case with successful PPCI. These findings are consistent with evidence discussed in the literature review chapter, supporting the superiority of PPCI in the treatment of STEMI in terms of infarct artery patency rates, as well as morbidity and mortality outcomes.

When we examine patient mortality outcomes and six-month hospital re-admission rates across trials, the results of those patients treated or referred exclusively by autonomous paramedics are almost identical. However, for those who received fibrinolysis, approximately 82% also underwent PCI during the same hospital admission period, either rescue or non-urgent. Therefore, improved outcomes among this cohort cannot be attributed to fibrinolysis alone.

6.3 Research Significance and Contribution

6.3.1 General

The current international body of research on autonomous paramedic-based STEMI management systems is small and highly variable. For these reasons and despite favourable results in support of this approach, further investigation was warranted, especially within Australasia (Snooks et al., 2008). The research presented in this thesis has made several significant and original contributions to this knowledge pool.

Our out-of-hospital paramedic fibrinolysis trial was the first internationally to compare the more commonly utilised physician-authorised telemetry-based model with that of an autonomous paramedic model. In doing so, we demonstrated the true extent of treatment time delay associated with the process of ECG transmission and physician consultation, and the subsequent deleterious effect this has on patient outcome. These findings add weight to the validity of previous reports highlighting the inefficiencies of this approach (P. Davis, 2014; Keeling et al., 2003; McLean et al., 2008). Moreover, our results confirm the safety and feasibility of an independent paramedic decision-making system for the treatment and management of STEMI, while demonstrating the model's ability to improve all performance measures.

The secondary investigation within this trial that examined and compared patients with aborted MI versus established MI was also unique. It was the first internationally to compare two separate pre-hospital patient cohorts treated by paramedics and under two different treatment authorisation models. The results of this inquiry confirmed the efficacy of early fibrinolysis, as reported in previous studies (Jackson et al., 2009; Lamfers et al., 2003b; Taher et al., 2004; Trent et al., 1994). It also provided new insights into clinical predictors of established MI with explanatory differences between the two groups.

The comparison of a hospital-based versus pre-hospital-based patient referral system for PPCI via helivac and involving autonomous paramedics (trial two) was also an international first. Previous evidence has shown significant treatment delays associated with transfer of patients to non-interventional centres in the first instance, as well as time spent in the ED (Clark et al., 2012; Hughes, 2005; McNamara et al., 2006; J. M. White et al., 2012). Like other studies, we demonstrated that exclusion of these factors, with direct patient transfer to the CCL from the field (the first point of care) resulted in

significant improvements in all treatment timeline metrics. However, our trial presented new evidence demonstrating the achievability of an autonomous paramedic model in meeting mandated PCI delivery times with transport distances well beyond those previously reported (Cheskes et al., 2011; McMullan et al., 2011; Nielsen et al., 2010; Savage et al., 2014; Widimský et al., 2002). This provides a template for interventional centres supported by EMS helicopter services to expand their PPCI catchment area. This would then allow for routine consideration of PCI as a primary reperfusion strategy in populations whose local receiving hospital is without interventional cardiology services and/or where distance to the nearest CCL precludes road transfer.

In context of these clinical trials, several relevant sub-topics were also investigated, providing additional new insights. These included paramedic education, patient symptomology and automated ECG interpretation. Furthermore, our two clinical trials incorporated detailed paramedic education packages and quality assurance measures with clinical KPIs. These two components contributed greatly to each trial's success, and may provide a generic template for future paramedic-based clinical programmes.

Within Australasia, paramedicine is still an emerging discipline and one that is critically under-researched (O'Meara et al., 2015; G. Smith & Eastwood, 2009). As a result, the paucity of evidence to inform paramedic practice often necessitates generalising from other areas of healthcare practice such as medicine or nursing, albeit considered in a de-contextualized manner (O'Meara et al., 2015). However, with paramedic registration in New Zealand on the horizon, it is important that paramedicine builds and strengthens its own self-led research base, in line with other healthcare professions, to further enhance the group's professional credibility. This has been an important motivation for undertaking the research presented in this doctoral thesis. This research has contributed to addressing these issues while providing multiple new insights into contemporary paramedic practice in the New Zealand context, and achieved within a real-world setting.

6.3.2 Regional and National Policy Implications

Given their successes, both the autonomous paramedic programmes trialled and presented within this thesis have now been accepted for continued implementation by St John and the three relevant DHBs, i.e. Northland, Auckland and Hawke's Bay. These programmes serve as a benchmark that invites other regions to develop similar systems

tailored to their own local setting and adhering to the same concepts and standards. The programmes also link strongly with section 2.1 of the St John Integrated Business Plan 2013–2018: "To improve outcomes for patients who are critically ill or injured, including the development of STEMI pathways" (St John Ambulance Service, 2015, p. 2).

However, in May 2016, during the later stages of this doctoral project, the New Zealand National Cardiac Network in conjunction with the ambulance sector presented a draft proposal for a national out-of-hospital STEMI pathway, intended to take effect in mid-to-late 2018. Once introduced, it is likely that this system will replace our existing autonomous paramedic programmes within their respective regions (T. Smith, personal communication, August 4, 2017). Developed primarily for emergency ambulance staff, the goal of this pathway is to ensure STEMI patients throughout the country receive timely reperfusion therapy (either fibrinolysis or PPCI) in a consistent manner (New Zealand National Cardiac Network, 2016). This is to be achieved utilising a physician-assisted telemetry-based model, employing designated regional specialists (primarily cardiologists) to coordinate activities, and with whom EMS staff are to consult from the field.

This pathway represents the first standardised and coherent national strategy for out-of-hospital STEMI care and follows the recent implementation of similar expedited EMS pathways for major trauma, stroke, burns and spinal cord injury (Major Trauma National Clinical Network, 2016; Ministry of Health, 2014b; St John Ambulance Service, 2016). Moreover, it will provide a formal STEMI pathway within multiple regions where none has previously existed.

However, applying a blanket national approach to out-of-hospital STEMI care that fails to take into consideration the unique elements of each region may be problematic. These include differences in ambulance crew clinical practice levels and their regional dispersion, availability and capability of EMS helicopter services, patient transport distances and hospital care capabilities. Although the concepts outlined in the proposed pathway are consistent with Australasian guidelines, for these to be effectively translated in the field, procedural variations for some regions may need to occur.

In the first instance, utilisation of a physician-assisted telemetry-based model within the proposed pathway is an ideal first step, as it will provide an opportunity for ambulance staff to gain experience with both the fibrinolysis procedure and PPCI referral

process. However, given the evidence presented in this thesis supporting the overall effectiveness of an autonomous paramedic model, intuitively a goal of transitioning towards this approach sometime in the future would make sense.

6.4 Contribution to Māori Health

Although the tika/arotahinga of this research is mainstream, the higher incidence of IHD among Māori compared to non-Māori means that they as a societal group have the potential to benefit more from improved paramedic-based STEMI management systems such as those trialled and presented in this thesis. Furthermore, via our paramedic education and training programmes, this research has contributed to raising awareness of Māori health amongst the ambulance work force, specifically the higher cumulative burden of disease and comorbidity in Māori, requiring greater consideration in the acute clinical setting.

A prominent claim among some Māori health researchers is the existence of a healthcare system that is inequitable towards Māori, especially for those requiring invasive cardiovascular procedures such as PCI and CABG surgery (Curtis, 2013; Curtis et al., 2010; B. Robson & Harris, 2007). They consider the very structure of the healthcare system to be a form of institutional racism and the driving force of this inequity, but they acknowledge that clinician bias may also be a factor (Curtis, 2013; Curtis et al., 2010; Hill et al., 2010; B. Robson & Harris, 2007). There is a countervailing viewpoint that Māori are not treated differently in terms of quality of care and that their poorer outcomes are likely attributable to their greater prevalence in CVD risk factors and other comorbidities, as well as delays in presentation and subsequent diagnosis (Stewart & White, 2007; T. Wang et al., 2013; H. White, Wang, Ramanathan, & Stewart, 2010). Numerous government health strategies have been developed especially for Māori, as a commitment to improving these inequalities (Ministry of Health, 2014a; New Zealand Guidelines Group, 2012; Wells et al., 2006).

Emergency ambulance services are free and available to all New Zealanders, i.e. regardless of age, sex, ethnicity, location or socioeconomic status. Within both our clinical trials Māori patients were encountered by paramedics and received treatment and care as per written protocols and indistinguishable from that which was provided to their non-Māori counterparts. This finding aligns with the current Māori health strategy for the St John Ambulance Service, which aims to contribute to Te Ara Hato Hone, the

government strategy for enhancing Māori health outcomes ("Copyright A2 - Chan, Theodore C," 2005). Moreover, it provides further support for the existence of an equitable pre-hospital emergency care system within New Zealand.

6.5 Strengths and Limitations

The research presented in this thesis was undertaken within New Zealand's largest emergency ambulance service, St John, and was supported by the organisation's clinical audit and research team. This provided greater capacity for our research findings to influence the country's paramedic workforce in terms of clinical training, education, procedure and policy. As an example, much of the paramedic education and training package developed in our fibrinolysis trial was adopted by St John and taught to all ambulance staff throughout the country as part of the 2016 continued clinical education programme. Moreover, given that the regions selected to undertake our two clinical trials had previously utilised physician-authorised models of care, this allowed comparisons to be made with our new autonomous paramedic programmes and greater control over potential confounding variables. The two trials were undertaken in a real-world setting with an immediate and measurable impact on patient care and outcome. They also utilised a large and representative number of the New Zealand paramedic workforce.

In Chapters Four and Five, patient data collected and analysed was primarily drawn from standard clinical assessment records, routinely gathered for all patients in the context of ACS. This alleviated the likelihood of inconsistences and information being incomplete, a recognised advantage of this type of medical documentation (Carter et al., 2011). Moreover, linking of ambulance and hospital records allowed for cross-referencing to occur, providing additional means of addressing data inconsistencies, as well as reconfirming key information sought.

Part of the success of both clinical trials discussed in Chapters Four and Five can be attributed to the prompt ambulance data collection process in the prospective phases. This allowed for stronger oversight of each trial where any operational issues could be addressed immediately and paramedics could receive timely educational feedback.

In terms of research limitations, the paramedic participants in our initial investigation discussed in Chapter Three were self-selected and therefore may have been a more proactive, non-representative group. This may have limited the generalisability of our results to the greater St John Ambulance paramedic workforce (the group represented

7.2% of personnel eligible to participate). Application of the experimental protocol was also tested in simulation, meaning paramedics were not exposed to real-life factors, such as fatigue associated with circadian low points, which may potentially impact on their clinical decision making. However, protocol field testing was deemed unethical at such an early juncture of our investigations without first identifying the capabilities of our paramedics in a safer and more controlled setting. There was also no lag period between the teaching of our protocol and the testing of its application by participants, meaning that knowledge retention was not examined.

In Chapters Four and Five, a true experimental design with randomisation would have provided a stronger and more direct comparison between the two treatment models examined in both our clinical trials. However, this approach was considered neither ethical nor pragmatic due to the impossibility of blinding the treatment protocol application, as well as the lengthy timeframe required to reach statistically significant levels of patient numbers. Therefore, the selected study design in each case provided a reasonable alternative with efficient use of available patient numbers. The prospective approach also enabled standardisation of measures used, providing stronger confidence in the study design (Carter et al., 2011; Domholdt, 2005).

Furthermore, in both our clinical trials several differences existed in the treatment protocol and the referral protocol between the control and experimental groups, impacting on the strength of comparison. These differences were primarily additional ECG criteria for our autonomous paramedics, designed and implemented to mitigate the risk of misdiagnosis and in recognition of their lesser experience and education compared to that of emergency physicians. However, all patient groups were found to be demographically similar and had similar clinical characteristics on initial presentation, so were considered comparable. The modest patient numbers obtained in our PCI referral study discussed in Chapter Five must also be recognised as a limitation.

6.6 Future Recommendations

6.6.1 Future Research Recommendations

Our initial investigation discussed in Chapter Three produced favourable results in support of the pre-employment paramedic education model. However, our analysis was small and limited, inviting further research to evaluate the benefits of pre-employment education towards contemporary paramedic practice within New Zealand. Currently,

paramedic education is provided via four sources: two tertiary institutions which deliver undergraduate and postgraduate programmes, and the country's two emergency ambulance services, which provide continued clinical education packages several times throughout the year. What is yet to be established is the compatibility of these four groups in terms of their teaching objectives and how this may impact on the knowledge and performance of emergency ambulance personnel.

In Chapter Four, in order to test our hypotheses we compared STEMI patients who received fibrinolysis by autonomous paramedics to a second historic pre-hospital treatment cohort. However, further insights as to the benefits or otherwise of this new model of care would have been gained from a third comparison; specifically, a comparison versus those patients treated with fibrinolysis at the same local receiving hospitals, following self-presentation at the ED.

The benefits of direct patient transfer from the field to a facility able to provide more definitive treatment were demonstrated in Chapter Five with our paramedic-initiated PCI referral programme. Similar expedited EMS pathways focussing on optimal patient destination have recently been implemented nationally for major trauma (including burns), spinal cord injury and stroke patients. A prospective review of these new destination-focussed programmes, with comparison to the previous systems in terms of time-to-treatment and patient outcome, would provide useful insights on pathway performance and paramedic decision-making processes.

6.6.2 General Recommendations

In Chapter Five we demonstrated the efficiency of patient helivac utilising an established local EMS helicopter service. Within New Zealand this process plays a vital role in the care of many critical patients. A recent national shift has occurred in the emergency healthcare sector, whereby greater focus is now placed on these patients being transported to the most appropriate hospital that is better equipped to meet their treatment needs. In many cases this would be one of the country's quaternary-level hospitals based in one of the main metropolitan centres. However, several factors often preclude patient transport via road, placing reliance on EMS helicopter services. These factors include patient location, acuity, transport distance and the importance of timely definitive treatment in terms of patient outcome.

Currently there are 13 independent EMS helicopter service providers operating throughout the country, all of which are managed by charitable trusts. Variability among these services is significant, meaning that our successes (demonstrated in Chapter Five) may not be easily replicated within other regions. These differences include the operator base location relative to main centres, operating aircraft type and performance capability, crew configuration and qualifications and standard operating procedures. This variability also has implications for national patient destination pathways both current and future, in terms of meeting key objectives. To improve system performance, there is a strong requirement for central government to take the lead in helping establish a nationally standardised EMS helicopter network with reliable revenue. Internationally, an effective strategy in achieving this goal has been government contracting of a single private EMS helicopter service provider (Pre-Hospital Emergency Care Council, 2017). Investing in such a project would arguably be a considerable cost saving, compared with attempts to increase treatment services available in smaller regional hospitals. This is an approach adopted by several similar-sized OECD countries including Poland, Ireland and Israel (European Aeronautic Defence and Space, 2008; Israeli Homeland Security, 2014; Pre-Hospital Emergency Care Council, 2017)

In Chapters Four and Five, a key finding within both trials was that for patients suffering STEMI, much of the delay between symptom onset and reperfusion therapy was attributed to the patient themselves failing to seek help earlier. This finding was consistent with other studies, demonstrating that continued public awareness and education on the matter is needed (Tanner et al., 2006; Weaver, 1995). In 2015, the New Zealand Heart Foundation undertook the first heart attack awareness campaign in New Zealand in over 40 years, which directly addressed this issue (New Zealand Heart Foundation, 2017). The campaign focussed on people 45 years and older, in lower socioeconomic areas, with heart disease. From an international perspective this was a comprehensive campaign delivered via multiple media platforms, as well as mail drops, posters and leaflets. Moreover, it included nationwide community and health sector activities of engagement involving general practices, PHOs, DHBs, community groups, pharmacies, workplaces and marae.

While post-campaign survey findings showed that over 50% of the target audience saw the campaign and 78% were able to recall the key message, a large national increase in emergency calls to the ambulance service for non-traumatic chest pain was observed during and after the campaign period (Devlin et al., 2016). Reasons for delays in seeking

help were also surveyed and dichotomised between those living in socioeconomically deprived areas versus non-deprived areas, providing further valuable insights. These included several prominent themes emerging across both groups such as denial, uncertainty, concern about being wrong and cost implications, the latter being of most concern among those residing in the more deprived areas. However, surprisingly, no change in the time to first medical contact among STEMI patients was observed during or after the campaign period. Intuitively, future campaigns might achieve this main objective by addressing the reasons for delays in seeking help as discussed.

The clinical trials presented in this thesis also yielded two additional findings which may be of benefit in future campaigns. Firstly, we encountered numerous STEMI patients that did not fit within the standard coronary candidacy framework, suggesting that expansion of target audiences may be warranted. This included patients less than 45 years of age, as well those without any obvious or formally diagnosed CVD risk-factors, including a family history of ACS. Secondly, from a public educational standpoint, not only did all STEMI patients we encountered present with some form of chest discomfort or other anginal equivalent, but the majority (78%), claimed the symptom was a first-time occurrence.

6.7 Conclusion

ST-elevation myocardial infarction represents a serious and potentially life-threatening medical emergency experienced by several thousand New Zealanders each year. To optimise patient outcomes, efficient and contemporary systems of care are required with a primary focus on timely diagnosis and access to reperfusion therapy. This PhD research has provided evidence in support of the crucial role autonomous paramedics can play within our communities to achieve this key objective, using clinical strategies not previously employed in New Zealand. These findings have served to address several failings within our current healthcare system towards the treatment and management of STEMI patients, while also demonstrating an expanded potential and capability for paramedics as autonomous clinicians in time-critical settings. This thesis contributes to the scope and growth of paramedic practice, both nationally and abroad. The results of this research have the capacity to inform multidisciplinary policies and bring about meaningful clinical practice change within New Zealand.

References

Abdullah, F. A., Qais, S. A., & Nawfal, A. A. (2014). Paramedics beliefs and attitudes towards pre-hospital thrombolysis. *International Journal of Applied Basic Medical Research, 4*(1), 11-15. doi: 10.4103/2229-516X.125672

AIMS Trial Study Group. (1988). Effect of Intraveous APSAC on Mortality after Acute Myocardial Infarction: Preliminary report of a placebo-controlled clinical trial. *The Lancet, 331*(8585), 545-549. doi: 10.1016/S0140-6736(88)91350-5

Ambulance New Zealand. (2013). Air ambulance / air search and rescue service standard. Version 2.0: 2013. Wellington: Ambulance New Zealand

Ambulance Transport Advisory Board. (1984). *Proposal for a New Zealand Ambulance Authority*. Wellington, New Zealand: Ambulance Transport Advisory Board.

Anand, D. V., Lim, E., Raval, U., Lipkin, D., & Lahiri, A. (2004). Prevalence of silent myocardial ischemia in asymptomatic individuals with subclinical atherosclerosis detected by electron beam tomography. *Journal of Nuclear Cardiology, 11*(4), 450-457. doi: 10.1016/j.nuclcard.2004.06.125

Andersen, H. R., Nielsen, T. T., Rasmussen, K., Thuesen, L., Kelbaek, H., Thayssen, P., . . . Mortensen, L. S. (2003). A Comparison of Coronary Angioplasty with Fibrinolytic Therapy in Acute Myocardial Infarction. *New England Journal of Medicine, 349*(8), 733-742. doi: 10.1056/NEJMoa025142

Antithrombotic Trialists' Collaboration Group. (2002). Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ, 324*(7329), 71. doi: 10.1136/bmj.324.7329.71

Antman, E. M., Hand, M., Armstrong, P. W., Bates, E. R., Green, L. A., Halasyamani, L. K., . . . Smith, S. C. (2007). 2007 Focused update of the ACC/AHA 2004 Guidelines for the Management of Patients With ST-Elevation Myocardial Infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. doi: 10.1161/circulationaha.107.188209

Antman, E. M., Morrow, D. A., McCabe, C. H., Murphy, S. A., Ruda, M., Sadowski, Z., . . . Braunwald, E. (2006). Enoxaparin versus Unfractionated Heparin with Fibrinolysis for ST-Elevation Myocardial Infarction. *New England Journal of Medicine, 354*(14), 1477-1488. doi: 10.1056/NEJMoa060898

Appleby, P., Baigent, C., Collins, R., Flather, M., & et al. (1994). Indications for fibrinolytic therapy in suspected acute myocardial infarction: Collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *The Lancet, 343*(8893), 311.

Araújo, D. V., Tura, B. R., Brasileiro, A. L., Luz Neto, H., Pavão, A. L. B., & Teich, V. (2008). Cost-effectiveness of prehospital versus inhospital thrombolysis in acute myocardial infarction. *Arquivos Brasileiros De Cardiologia, 90*(2), 91-98. http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=18392380&site=ehost-live

Atkinson, J., Salmond, C., & Crampton, P. (2014). *NZDep2013 Index of Deprivation*. Retrieved from University of Otago, Department of Public Health website: http://www.otago.ac.nz/wellington/otago069936.pdf.

Aversano, T., Aversano, L. T., Passamani, E., Knatterud, G. L., Terrin, M. L., Williams, D. O., & Forman, S. A. (2002). Thrombolytic Therapy vs Primary Percutaneous Coronary Intervention for Myocardial Infarction in Patients Presenting to Hospitals Without On-site Cardiac Surgery. *The Journal of the American Medical Association, 287*(15), 1943-1951. doi: 10.1001/jama.287.15.1943

Ayanian, J. Z., & Braunwald, E. (2000). Thrombolytic Therapy for Patients With Myocardial Infarction Who Are Older Than 75 Years : Do the Risks Outweigh the Benefits? *Circulation, 101*(19), 2224-2226. doi: 10.1161/01.cir.101.19.2224

Balerdi, M., Ellis, D. Y., Grieve, P., Murray, P., & Dalby, M. (2011). Aeromedical transfer to reduce delay in primary angioplasty. *Resuscitation, 82*(7), 947-950. doi: 10.1016/j.resuscitation.2011.02.031

Benger, J. R. (2002). The case for urban prehospital thrombolysis. *Emergency Medicine Journal: EMJ, 19*(5), 441-443. http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=12205002&site=ehost-live

Björk, I., & Lindahl, U. (1982). Mechanism of the anticoagulant action of heparin. *Molecular and Cellular Biochemistry, 48*(3), 161-182. doi: 10.1007/bf00421226

Björklund, E., Stenestrand, U., Lindbäck, J., Svensson, L., Wallentin, L., & Lindahl, B. (2006). Pre-hospital thrombolysis delivered by paramedics is associated with reduced time delay and mortality in ambulance-transported real-life patients with ST-elevation myocardial infarction. *European Heart Journal, 27*(10), 1146.

Boersma, E., Maas, A. C. P., Deckers, J. W., & Simoons, M. L. (1996). Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *The Lancet, 348*(9030), 771-775. doi: 10.1016/s0140-6736(96)02514-7

Bongard, V., Puel, J., Savary, D., Belle, L., Charpentier, S., Cottin, Y., . . . Steg, P. G. (2009). Predictors of infarct artery patency after prehospital thrombolysis: the multicentre, prospective, observational OPTIMAL study. *Heart, 95*(10), 799-806. doi: 10.1136/hrt.2008.152504

Brady, W. J., Perron, A. D., Martin, M. L., Beagle, C., & Aufderheide, T. P. (2001). Cause of ST segment abnormality in ED chest pain patients. *The American Journal of Emergency Medicine, 19*(1), 25-28. doi: 10.1053/ajem.2001.18029

Bramley, D., Riddell, T., Crengle, S., Curtis, E., Harwood, M., Nehua, D., & Reid, P. (2004). Call to action on Maori cardiovascular health. *The New Zealand Medical Journal, 117*(1197), 1-7.

Braunwald, E. (1989). Myocardial reperfusion, limitation of infarct size, reduction of left ventricular dysfunction, and improved survival. Should the paradigm be expanded? *Circulation, 79*(2), 441-444. doi: 10.1161/01.cir.79.2.441

Brown, J. P., Mahmud, E., Dunford, J. V., & Ben-Yehuda, O. (2008). Effect of Prehospital 12-Lead Electrocardiogram on Activation of the Cardiac Catheterization Laboratory and Door-to-Balloon Time in ST-Segment Elevation Acute Myocardial Infarction. *The American Journal Of Cardiology, 101*(2), 158-161. doi: 10.1016/j.amjcard.2007.07.082

Cameron, V. A., Faatoese, A. F., Gillies, M. W., Robertson, P. J., Huria, T. M., Doughty, R. N., . . . Pitama, S. G. (2012). A cohort study comparing cardiovascular risk factors in rural Māori, urban Māori and non-Māori communities in New Zealand. *BMJ Open, 2*(3). doi: 10.1136/bmjopen-2011-000799

Cannon, C. P., Antman, E. M., Walls, R., & Braunwald, E. (1994). Time as an adjunctive agent to thrombolytic therapy. *Journal of Thrombosis and Thrombolysis, 1*, 27-33. doi: 10.1007/BF01061992

Cannon, C. P., & Braunwald, E. (1996). Time to reperfusion: The critical modulator in thrombolysis and primary angioplasty. *Journal of Thrombosis and Thrombolysis, 3*(2), 117-125. doi: 10.1007/bf00132404

Cannon, C. P., Sayah, A. J., & Walls, R. M. (2000). ER TIMI-19: testing the reality of prehospital thrombolysis. *The Journal Of Emergency Medicine, 19*(3, Supplement 1), S21-S25. doi: 10.1016/s0736-4679(00)00251-1

Carter, R., Lubinsky, J., & Domholdt, E. (2011). *Rehabilitation Research: Principles and Applications* (4th ed.). St Louis, MI, USA: Elsevier Saunders

Castaigne, A. D., Duval, A. M., Dubois-Rande, J. L., Herve, C., Jan, F., & Louvard, Y. (1987). Prehospital administration of anisoylated plasminogen streptokinase activator complex in acute myocardial infarction. *Drugs, 33 Suppl 3*, 231-234.

Castle, N., Owen, R., Vincent, R., & Ineson, N. (2006). What percentages of patients are suitable for prehospital thrombolysis? *Emergency Medicine Journal, 23*(6), 444-445. doi: 10.1136/emj.2005.026450

Chamberlain, D., Penny, L., & Fisher, J. (2001). Pre-Hospital Thrombolysis: Combined submission from The Joint Royal Colleges Ambulance Liason Committee and The Ambulance Services Association (pp. 1-23). London, United Kingdom: The National Institute for Clinical Excellence.

Chen, Z. M., Jiang, L. X., Chen, Y. P., & Xie, J. X. (2005). Addition of clopidogrel to aspirin in 45 852 patients with acute myocardial infarction: randomised placebo-controlled trial. *The Lancet, 366*(9497), 1607-1621.

Cheskes, S., Turner, L., Foggett, R., Huiskamp, M., Popov, D., Thomson, S., . . . Verbeek, R. (2011). Paramedic Contact to Balloon in Less than 90 Minutes: A Successful Strategy for St-Segment Elevation Myocardial Infarction Bypass to Primary Percutaneous Coronary Intervention in a Canadian Emergency Medical System. *Prehospital Emergency Care, 15*(4), 490-498. doi: 10.3109/10903127.2011.598613

Chou, T. M., Amidon, T. M., Ports, T. A., & Wolfe, C. L. (1996). Cardiogenic Shock: Thrombolysis or Angioplasty? *Journal of Intensive Care Medicine, 11*(1), 37-48. doi: 10.1177/088506669601100106

Chuang, Y., Swanson, R., Raja, S. M., & Olson, S. T. (2001). Heparin Enhances the Specificity of Antithrombin for Thrombin and Factor Xa Independent of the Reactive Center Loop Sequence. *Journal of Biological Chemistry, 276*(18), 14961-14971. doi: 10.1074/jbc.M011550200

Clark, C. L., Berman, A. D., McHugh, A., Roe, E. J., Boura, J., & Swor, R. A. (2012). Hospital Process Intervals, not Ems Time Intervals, are the Most Important Predictors of Rapid Reperfusion in Ems Patients with St-Segment Elevation Myocardial Infarction. *Prehospital Emergency Care, 16*(1), 115-120. doi: 10.3109/10903127.2011.615012

Cohn, P. F., Fox, K. M., & Daly, C. (2003). Silent Myocardial Ischemia. *Circulation, 108*(10), 1263. doi: 10.1161/01.CIR.0000088001.59265.EE

Cooke, M. E. (2007). Pre-Hospital Thrombolysis (England and Wales). London: Ambulance Services Association.

Copyright A2 - Chan, Theodore C. (2005). In W. J. Brady, R. A. Harrigan, J. P. Ornato & P. Rosen (Eds.), *ECG in Emergency Medicine and Acute Care* (pp. iv). Philadelphia: Mosby.

Costa-Scorse, B. (2008). Submission on the Inquiry into the provision of Ambulance Services in New Zealand. http://www.jephc.com/full_article.cfm?content_id=492

Coukell, A. J., & Markham, A. (1997). Clopidogrel. *Drugs, 54*(5), 745-750. doi: 10.2165/00003495-199754050-00006

Council of Ambulance Authorities. (2008). *Expanding roles: An Australasian overview of emerging paramedic models of care*. Adelaide: Council of Ambulance Authorities.

Curtis, E. (2013). Deserving of more: framing of Māori inequities in cardiovascular care remains a challenge. *New Zealand Medical Journal, 126*(1379).

Curtis, E., Harwood, M., Riddell, T., Robson, B., Harris, R., Mills, C., & Reid, P. (2010). Access and Society as Determinants of Ischaemic Heart Disease in Indigenous Populations. *Heart, Lung and Circulation, 19*(5–6), 316-324. doi: 10.1016/j.hlc.2010.04.129

Danchin, N., Blanchard, D., Steg, P. G., Sauval, P., Hanania, G., Goldstein, P., . . . Lablanche, J. (2004). Impact of Prehospital Thrombolysis for Acute Myocardial Infarction on 1-Year Outcome. *Circulation, 110*(14), 1909-1915. doi: 10.1161/01.cir.0000143144.82338.36

Danchin, N., Durand, E., & Blanchard, D. (2008). Pre-hospital thrombolysis in perspective. *European Heart Journal, 29*(23), 2835-2842. doi: 10.1093/eurheartj/ehn462

Davis, D. P., Graydon, C., Stein, R., Wilson, S., Buesch, B., Berthiaume, S., . . . Leahy, D. R. (2007). The Positive Predictive Value of Paramedic Versus Emergency Physician Interpretation of the Prehospital 12-Lead Electrocardiogram. *Prehospital Emergency Care, 11*(4), 399-402. doi: 10.1080/10903120701536784

Davis, P. (2014). Northland and Hawkes Bay Pre-Hospital Paramedic Fibrinolysis Program: Audit Report 2014 (pp. 1-21). Whangarei, New Zealand: St John

Davis, P. R., Howie, G. J., & Dicker, B. (2017). New Zealand Paramedics are ready for an autonomous pre-hospital thrombolysis protocol. *Australasian Journal of Paramedicine, 14*(3), 1-8.

De Luca, G., Biondi-Zoccai, G., & Marino, P. (2008). Transferring Patients With ST-Segment Elevation Myocardial Infarction for Mechanical Reperfusion: A Meta-Regression Analysis of Randomized Trials. *Annals of Emergency Medicine, 52*(6), 665-676. doi: 10.1016/j.annemergmed.2008.08.033

De Luca, G., Suryapranata, H., Zijlstra, F., van't Hof, A. W. J., Hoorntje, J. C. A., Gosselink, A. T. M., . . . de Boer, M. (2003). Symptom-onset-to-balloon time and mortality in patients with acute myocardial infarction treated by primary angioplasty. *Journal of the American College of Cardiology, 42*(6), 991-997. doi: 10.1016/S0735-1097(03)00919-7

De Luca, G., Suryapranata, H. M., Ottervanger, J. P., & Antman, E. M. (2004). Time Delay to Treatment and Mortality in Primary Angioplasty for Acute Myocardial Infarction: Every Minute of Delay Counts. *Circulation, 109*(10), 1223-1225.

Denktas, A. E., Anderson, H. V., McCarthy, J., & Smalling, R. W. (2011). Total Ischemic Time: The Correct Focus of Attention for Optimal ST-Segment Elevation Myocardial Infarction Care. *JACC: Cardiovascular Interventions, 4*(6), 599-604. doi: 10.1016/j.jcin.2011.02.012

Department of Health. (2002). *Review of early thrombolysis: Faster and better treatment for heart attack patients*. London, United Kingdom: Department of Health Retrieved from http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4068251.pdf.

Devlin, G., Arcus, K., Williams, G., De Silva, S., Alexander, J., Winning, V., & Duncan, T. (2016). A heat attack is not as dramatic as you think: Results of a public awareness campaign in New Zealand. Auckland, New Zealand: National Heart Foundation.

Diercks, D. B., Kontos, M. C., Chen, A. Y., Pollack Jr, C. V., Wiviott, S. D., Rumsfeld, J. S., . . . Roe, M. T. (2009). Utilization and Impact of Pre-Hospital Electrocardiograms for Patients With Acute ST-Segment Elevation Myocardial Infarction: Data From the NCDR (National Cardiovascular Data Registry) ACTION (Acute Coronary Treatment and Intervention Outcomes Network) Registry. *Journal of the American College of Cardiology, 53*(2), 161-166. doi: 10.1016/j.jacc.2008.09.030

Domholdt, E. (2005). *Rehabilitation Research: Principles and Applications* (3rd ed.). St Louis, MI, USA: Elsevier Saunders.

Dussoix, P., Reuille, O., Verin, V., Gaspoz, J. M., & Unger, P. F. (2003). *Time savings with prehospital thrombolysis in an urban area* Vol. 10. *European Journal of Emergency Medicine* (pp. 2-5). Retrieved from http://journals.lww.com/euro-emergencymed/Fulltext/2003/03000/Time_savings_with_prehospital_thrombolysis_in_an.2.aspx

Eagle, K. A., Goodman, S. G., Avezum, Á., Budaj, A., Sullivan, C. M., & López-Sendón, J. (2002). Practice variation and missed opportunities for reperfusion in ST-segment-elevation myocardial infarction: findings from the Global Registry of Acute Coronary Events (GRACE). *The Lancet, 359*(9304), 373-377. doi: 10.1016/S0140-6736(02)07595-5

Eagle, K. A., Lim, M. J., Dabbous, O. H., Pieper, K. S., Goldberg, R. J., Van de Werf, F., . . . for the GRACE Investigators. (2004). A validated prediction model for all forms of acute coronary syndrome: Estimating the risk of 6-month postdischarge death in an international registry. *JAMA, 291*(22), 2727-2733. doi: 10.1001/jama.291.22.2727

Electro-technology Industry Technology Organisation. (2012). How national qualifications training works. from http://www.etito.co.nz/how-national-qualifications-training-works-16/

Ellis, C., Devlin, G., Elliott, J., Matsis, P., Williams, M., Gamble, G., . . . for the New Zealand Acute Coronary Syndromes (NZACS) Audit Group. (2010a). ACS patients in New Zealand experience significant delays to access cardiac investigations and revascularisation treatment especially when admitted to non-interventional centres: results of the second comprehensive national audit of ACS patients. *The New Zealand Medical Journal, 123*(1319), 44-60.

Ellis, C., Devlin, G., Elliott, J., Matsis, P., Williams, M., Gamble, G., . . . for the New Zealand Acute Coronary Syndromes (NZACS) Audit Group. (2010b). Patients admitted with an acute coronary syndrome in New Zealand in 2007: results of a second comprehensive nationwide audit and a comparison with the first audit from 2002. *The New Zealand Medical Journal, 123*(1319), 44-60.

Ellis, C., Devlin, G., Matsis, P., Elliott, J., Willliams, M., Gamble, G., . . . White, H. (2004). Acute Coronary Syndrome patients in New Zealand receive less invasive management when admitted to hospitals without invasive facilitie. *New Zealand Medical Journal, 117*(1917), 1-16.

Ellis, C., Gamble, G., Devlin, G., Elliott, J., Hamer, A., Williams, M., . . . for the New Zealand Acute Coronary Syndromes (NZACS) 'SNAPSHOT' Audit Group. (2013). The management of acute coronary syndrome patients across New Zealand in 2012: results of a third comprehensive nationwide audit and observations of current interventional care. *The New Zealand Medical Journal, 126*(1387), 36-68.

Ellis, J., & Richards, M. (2005). Heart attacks and unstable angina (acute coronary syndromes) have doubled in New Zealand since 1989: How do we best manage the epidemic? http://journal.nzma.org.nz/journal/118-1223/1674/

EMIP Group. (1993). Prehospital Thrombolytic Therapy in Patients with Suspected Acute Myocardial Infarction. *New England Journal of Medicine, 329*(6), 383-389. doi: doi:10.1056/NEJM199308053290602

European Aeronautic Defence and Space. (2008). Poland's Ministry of Health orders 23 Eurocopter EC135s for Nationwide Emergency Medical Services. Retrieved August 14, 2017, from https://web.archive.org/web/20080828181558/http://www.eads.com/1024/en/pressdb/pressdb/Eurocopter/20080630_ec_poland_ec135.html

Faul, F., Erdfelder, E., Lang, A., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*(2), 175-191. doi: 10.3758/BF03193146

Feldman, J. A., Brinsfield, K., Bernard, S., White, D., & Maciejko, T. (2005). Real-time paramedic compared with blinded physician identification of ST-segment elevation myocardial infarction: results of an observational study. *The American Journal of Emergency Medicine, 23*(4), 443-448. doi: 10.1016/j.ajem.2004.10 .011

Fibrinolytic Therapy Trialists' Collaborative Group. (1994). Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet, 343*(8893), 311.

Fletcher, A. P., Alkjaersig, N., Smyrniotis, F. E., & Sherry, S. (1958). The treatment of patients suffering from early myocardial infarction with massive and prolonged streptokinase therapy. *Transactions of the Association of American Physicians, 71*, 287-295.

Fox, K. A. A. (2004). Management of acute coronary syndromes: an update. *Heart, 90*(6), 698-706. doi: 10.1136/hrt.2003.020321

Franzosi, M. G., Santoro, E., De Vita, C., Geraci, E., Lotto, A., Maggioni, A., . . . Tognoni, G. (1998). Ten-Year Follow-Up of the First Megatrial Testing Thrombolytic Therapy in Patients With Acute Myocardial Infarction: Results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto-1 Study. *Circulation, 98*(24), 2659-2665.

Garvey, J. L., Monk, L., Granger, C. B., Studnek, J. R., Roettig, M. L., Corbett, C. C., & Jollis, J. G. (2012). Rates of Cardiac Catheterization Cancelation for ST-Segment Elevation Myocardial Infarction After Activation by Emergency Medical Services or Emergency Physicians: Results From the North Carolina Catheterization Laboratory Activation Registry. *Circulation, 125*(2), 308-313. doi: 10.1161/CIRCULATIONAHA.110.007039

Garvey, J. L., Zegre-Hemsey, J., Gregg, R., & Studnek, J. R. (2016). Electrocardiographic diagnosis of ST segment elevation myocardial infarction: An evaluation of three automated interpretation algorithms. *Journal of Electrocardiology, 49*(5), 728-732. doi: 10.1016/j.jelectrocard.2016.04.010

Gersh, B. J., & Antman, E. M. (2006). Selection of the optimal reperfusion strategy for STEMI: does time matter? *European Heart Journal, 27*(7), 761. doi: 10.1093/eurheartj/ehi775 761

Gersh, B. J., Stone, G. W., White, H. D., & Holmes, D. R. (2005). Pharmacological facilitation of primary percutaneous coronary intervention for acute myocardial infarction: Is the slope of the curve the shape of the future? *JAMA, 293*(8), 979-986. doi: 10.1001/jama.293.8.979

Gibson, M. C., Ryan, K. A., Kelley, M., Rizzo, M. J., Mesley, R., Murphy, S., . . . Antman, E. M. (1999). Methodologic drift in the assessment of TIMI grade 3 flow and its implications with respect to the reporting of angiographic trial results. *American Heart Journal, 137*(6), 1179-1184. doi: 10.1016/S0002-8703(99)70380-7

Giraldez, R. R., Nicolau, J. C., Corbalan, R., Gurfinkel, E. P., Juarez, U., Lopez-Sendon, J., . . . Antman, E. M. (2007). Enoxaparin is superior to unfractionated heparin in patients with ST elevation myocardial infarction undergoing fibrinolysis regardless of the choice of lytic: an ExTRACT-TIMI 25 analysis. *European Heart Journal, 28*(13), 1566-1573. doi: 10.1093/eurheartj/ehm179

Go, A. S., & Barron, H. V. (1998). Bundle-branch block and in-hospital mortality in acute myocardial infarction. *Annals of Internal Medicine, 129*(9), 690.

Govindarajan, A., & Schull, M. (2003). Effect of socioeconomic status on out-of-hospital transport delays of patients with chest pain. *Annals of Emergency Medicine, 41*(4), 481-490. doi: 10.1067/mem.2003.108

GREAT Group. (1992). Feasibility, Safety, And Efficacy Of Domiciliary Thrombolysis By General Practitioners: Grampian Region Early Anistreplase Trial. *British Medical Journal, 305*(6853), 548-553.

Grijseels, E. W. M., Bouten, M. J. M., Lenderink, T., Deckers, J. W., Hoes, A. W., Hartman, J. A. M., . . . Simoons, M. L. (1995). Pre-hospital thrombolytic therapy with either alteplase or streptokinase. *European Heart Journal, 16*(12), 1833-1838. http://eurheartj.oxfordjournals.org/content/16/12/1833.abstract

Grines, C. L., Westerhausen, D. R., Grines, L. L., Hanlon, J. T., Logemann, T. L., Niemela, M., . . . Balestrini, C. (2002). A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: The air primary angioplasty in myocardial infarction study. *Journal of the American College of Cardiology, 39*(11), 1713-1719. doi: 10.1016/s0735-1097(02)01870-3

Gruppo Italiano Per Lo Studio Della Sopravvivenza nell'Infarto Miocardico. (1990). MEDICAL SCIENCE: GISSI-2: A factorial randomised trial of alteplase versus streptokinase and heparin versus no heparin among 12 490 patients with acute myocardial infarction. *The Lancet, 336*(8707), 65-71. doi: 10.1016/0140-6736(90)91589-3

Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico. (1986). Effectiveness of Intravenous Thrombolytic Treatment in Acute Myocardial Infarction *The Lancet, 327*(8478), 397-402. doi: 10.1016/S0140-6736(86)92368-8

Hackett, D., McKenna, W., Davies, G., Maseri, A., Lowe, T., & Aber, V. (1990). Reperfusion arrhythmias are rare during acute myocardial infarction and thrombolysis in man. *International Journal of Cardiology, 29*(2), 205-213. doi: 10.1016/0167-5273(90)90223-r

Hanson, T. C., & Williamson, D. (2006). Identifying barriers to prehospital thrombolysis in the treatment of acute myocardial infarction. *Emergency Medicine Journal, 23*(8), 650-653. doi: 10.1136/emj.2005.033993

Hatala, R., Norman, G., & Brooks, L. (1999). Impact of a clinical scenario on accuracy of electrocardiogram interpretation. *Journal of General Internal Medicine, 14*(2), 126-129. doi: 10.1046/j.1525-1497.1999.00298.x

Henriques, J. P. S., Zijlstra, F., van 't Hof, A. W. J., de Boer, M. J., Dambrink, J. H. E., Gosselink, A. T. M., . . . Suryapranata, H. (2006). Primary percutaneous coronary intervention versus thrombolytic treatment: long term follow up according to infarct location. *Heart, 92*(1), 75-79. doi: 10.1136/hrt.2005.060152

Hill, S., Sarfati, D., Blakely, T., Robson, B., Purdie, G., Chen, J., . . . Kawachi, I. (2010). Survival disparities in Indigenous and non-Indigenous New Zealanders with colon cancer: the role of patient comorbidity, treatment and health service factors. *Journal of Epidemiology and Community Health, 64*(2), 117. doi: 10.1136/jech.2008.083816

Hoffman, R., Benz, E. J., Shattil, S. J., Furie, B., Cohen, H. J., Silberstein, L. E., & McGlave, P. (Eds.). (2009). *Hematology: Basic Principles and Practice.* (5th ed.).Philadelphia: Elsevier.

Hoyle, S., Swain, A. H., Fake, P., & Larsen, P. D. (2012). Introduction of an extended care paramedic model in New Zealand. *Emergency Medicine Australasia, 24*(6), 652-656. doi: 10.1111/j.1742-6723.2012.01608.x

Huber, K., Caterina, R., Kristensen, S. D., Verheugt, F. W. A., Montalescot, G., Maestro, L. B., & Van de Werf, F. (2005). Pre-hospital reperfusion therapy: a strategy to improve therapeutic outcome in patients with ST-elevation myocardial infarction. *European Heart Journal, 26*(19), 2063-2074. doi: 10.1093/eurheartj/ehi413

Hughes, S. (2005). Speeding up the treatment of MI: Is prehospital thrombolysis or expanded primary PCI the answer? Retrieved from Medscape website: http://www.medscape.com/viewarticle/787281

Humphrey, J., Walker, A., & Hassan, T. B. (2005). What are the beliefs and attitudes of paramedics to prehospital thrombolysis? A questionnaire study. *Emergency Medicine Journal, 22*(6), 450. doi: 10.1136/emj.2004.016998

Hunt, G. J. (2009). *First to care: 125 years of the Order of St John in New Zealand 1885-2010*. Auckland, New Zealand: Libro International and Waddington Press Ltd.

Ioannidis, J. P., Salem, D., Chew, P. W., & Lau, J. (2001). Accuracy and clinical effect of out-of-hospital electrocardiography in the diagnosis of acute cardiac ischemia: a meta-analysis. *Annals of Emergency Medicine, 37*(5), 461-470. doi: 10.1067/mem.2001.114904

ISIS-2 Collaborative Group. (1988). Randomised trial of intravenous streptokinase, oral aspirin, both or neither among 17 187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet, 332*(8607), 349-360. doi: 10.1016/S0140-6736(88)92833-4

Israeli Homeland Security. (2014). Israeli Airborne Rescue: The MDA Helicopters. Retrieved August 14, 2017, from http://i-hls.com/archives/29637

Jackson, L., Kendall, J., & Castle, N. (2009). Does prehospital thrombolysis increase the proportion of patients who have an aborted myocardial infarction? *Emergency Medicine Journal, 26*(3), 206-209. doi: 10.1136/emj.2008.061564

Jain, S., Ting, H. T., Bell, M., Bjerke, C. M., Lennon, R. J., Gersh, B. J., . . . Prasad, A. (2011). Utility of Left Bundle Branch Block as a Diagnostic Criterion for Acute Myocardial Infarction. *American Journal of Cardiology, 107*(8), 1111-1116. doi: 10.1016/j.amjcard.2010.12.007

Jensen, J. L., Croskerry, P., & Travers, A. H. (2009). Paramedic clinical decision making during high acuity emergency calls: Design and methodology of a Delphi study. *BMC Emergency Medicine, 9*(1), 17. doi: 10.1186/1471-227X-9-17

Joshy, G., & Simmons, D. (2006). Epidemiology of diabetes in New Zealand: revisit to a changing landscape. *The New Zealand Medical Journal, 119*(1235).

Kalla, K., Christ, G., Karnik, R., Malzer, R., Norman, G., Prachar, H., . . . Huber, K. (2006). Implementation of Guidelines Improves the Standard of Care. *Circulation, 113*(20), 2398-2405. doi: 10.1161/circulationaha.105.586198

Kannel, W. B., Cupples, L. A., & Gagnon, D. R. (1990). Incidence, precursors and prognosis of unrecognized myocardial infarction. *Advances in Cardiology, 37*, 202-214.

Keeley, E. C., Boura, J. A., & Grines, C. L. (2003). Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *The Lancet, 361*(9351), 13-20. doi: 10.1016/S0140-6736(03)12113-7

Keeling, P., Hughes, D., Price, L., Shaw, S., & Barton, A. (2003). Safety and feasibility of prehospital thrombolysis carried out by paramedics. *British Medical Journal, 327*, 27-28. doi: 10.1136/bmj.327.7405.27

Kelly, A., Kerr, D., Patrick, I., & Walker, T. (2003). Call-to-needle times for thrombolysis in acute myocardial infarction in Victoria. *The Medical Journal Of Australia, 178*(8), 381-385. http://search.ebscohost.com/login.aspx?direct=true&db=cmedm&AN=12697009&site=ehost-live

Kelly, P. (2003). Thrombolysis in the Pre-Hospital Setting: Importance of Effective Care Pathways and Protocols. *The British Journal of Cardiology, 10*(5), 395-398. http://bjcardio.co.uk/2003/09/thrombolysis-in-the-pre-hospital-setting/

Kerr, A., J , McLachlan, A., Furness, S., Broad, J., Riddell, T., Jackson, R., & Wells, S. (2008). The burden of modifiable cardiovascular risk factors in the coronary care unit by age, ethnicity, and socioeconomic status—PREDICT CVD-9 *The New Zealand Medical Journal, 121*(1285), 21-34.

King, S. B., Smith Jr, S. C., Hirshfeld Jr, J. W., Jacobs, A. K., Morrison, D. A., & Williams, D. O. (2008). 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. *Journal of the American College of Cardiology, 51*(2), 172-209. doi: 10.1016/j.jacc.2007.10.002

Kontos, M. C., Aziz, H. A., Chau, V. Q., Roberts, C. S., Ornato, J. P., & Vetrovec, G. W. (2011). Outcomes in patients with chronicity of left bundle-branch block with possible acute myocardial infarction. *American Heart Journal, 161*(4), 698-704. doi: 10.1016/j.ahj.2011.01.008

Krucoff, M. W., Croll, M. A., Pope, J. E., Pieper, K. S., Kanani, P. M., Granger, C. B., . . . Califf, R. M. (1993). Continuously updated 12-lead ST-segment recovery analysis for myocardial infarct artery patency assessment and its correlation with multiple simultaneous early angiographic observations. *The American Journal Of Cardiology, 71*(2), 145-151. doi: 10.1016/0002-9149(93)90729-V

Krumholz, H. M., & Goldberger, A. L. (1991). Reperfusion arrhythmias after thrombolysis. Electrophysiologic tempest, or much ado about nothing. *Chest, 99*(4), 135S-140S. doi: 10.1378/chest.99.4.135S

Lamfers, E. J. P., Hooghoudt, T. E. H., Hertzberger, D. P., Schut, A., Stolwijk, P. W. J., & Verheugt, F. W. A. (2003a). Abortion of acute ST segment elevation myocardial infarction after reperfusion: incidence, patients' characteristics, and prognosis. *Heart, 89*(5), 496-501. doi: 10.1136/heart.89.5.496

Lamfers, E. J. P., Hooghoudt, T. E. H., Hertzberger, D. P., Schut, A., Stolwijk, P. W. J., & Verheugt, F. W. A. (2003b). Abortion of acute ST segment elevation myocardial infarction after reperfusion: incidence, patients' characteristics, and prognosis. *Heart, 89*(5), 496. doi: 10.1136/heart.89.5.496

Lamfers, E. J. P., Schut, A., Hertzberger, D. P., Hooghoudt, T. E. H., Stolwijk, P. W. J., Boersma, E., . . . Verheugt, F. W. A. (2004). Prehospital versus hospital fibrinolytic therapy using automated versus cardiologist electrocardiographic diagnosis of myocardial infarction: abortion of myocardial infarction and unjustified fibrinolytic therapy. *American Heart Journal, 147*(3), 509-515. doi: 10.1016/j.ahj.2003.10.007

Lee, C. H., Van Gelder, C. M., & Cone, D. C. (2010). Early Cardiac Catheterization Laboratory Activation by Paramedics for Patients with ST-segment Elevation Myocardial Infarction on Prehospital 12-Lead Electrocardiograms. *Prehospital Emergency Care, 14*(2), 153-158.

Levine, G. N., & Hochman, J. S. (1995). Thrombolysis in acute myocardial infarction complicated by cardiogenic shock. *Journal of Thrombosis and Thrombolysis, 2*(1), 11-20. doi: 10.1007/bf01063156

Liverpool Reviews and Implementation Group. (2002). Early Thrombolysis for the Treatment of Acute Myocardial Infarction. Liverpool: The National Institute for Clinical Excellence.

Loll, P. J., Picot, D., & Garavito, M. R. (1995). The structural basis of aspirin activity inferred from the crystal structure of inactivated prostaglandin H2 synthase. *Nature Structural Biology 2*, 637 - 643. doi: 10.1038/nsb0895-637

Machecourt, J., Bonnefoy, E., Vanzetto, G., Motreff, P., Marliere, S., Leizorovicz, A., . . . Touboul, P. (2005). Primary angioplasty is cost-minimizing compared with pre-hospital thrombolysis for patients within 60 min of a percutaneous coronary intervention center: The Comparison of Angioplasty and Pre-hospital Thrombolysis in Acute Myocardial Infarction (CAPTIM) cost-efficacy sub-study. *J Am Coll Cardiol, 45*(4), 515-524. doi: 10.1016/j.jacc.2004.11.031

Major Trauma National Clinical Network. (2016). *New Zealand Major Trauma Registry & National Clinical Network: Annual Report 2015-2016*. Wellington, New Zealand: Retrieved from http://docs.wixstatic.com/ugd/bbebfb_28543150b87246fd959b10af996bb1ac.pdf.

Massel, D., Dawdy, J. A., & Melendez, L. J. (2000). Strict reliance on a computer algorithm or measurable ST segment criteria may lead to errors in thrombolytic therapy eligibility. *American Heart Journal, 140*(2), 221-226. doi: 10.1067/mhj.2000.108240

McAleer, B., Ruane, B., Burke, E., Cathcart, M., Costello, A., Dalton, G., . . . Varma, M. P. S. (1992). Prehospital thrombolysis in a rural community: Short- and long-term survival. *Cardiovascular Drugs and Therapy, 6*(4), 369-372. doi: 10.1007/bf00054183

McCaul, M., Lourens, A., & Kredo, T. (2014). Pre-hospital versus in-hospital thrombolysis for ST-elevation myocardial infarction. *Cochrane Database of Systematic Reviews*(9). doi: 10.1002/14651858.CD010191.pub2

McLean, S., Egan, G., Connor, P., & Flapan, A. D. (2008). Collaborative decision-making between paramedics and CCU nurses based on 12-lead ECG telemetry expedites the delivery of thrombolysis in ST elevation myocardial infarction. *Emergency Medicine Journal, 25*(6), 370-374. doi: 10.1136/emj.2007.052746

McLean, S., Wild, S., Connor, P., & Flapan, A. D. (2011). Treating ST elevation myocardial infarction by primary percutaneous coronary intervention, in-hospital thrombolysis and prehospital thrombolysis. An observational study of timelines and outcomes in 625 patients. *Emergency Medicine Journal, 28*(3), 230-236. doi: 10.1136/emj.2009.086066

McMullan, J. T., Hinckley, W., Bentley, J., Davis, T., Fermann, G. J., Gunderman, M., . . . Gibler, W. B. (2011). Reperfusion Is Delayed Beyond Guideline Recommendations in Patients Requiring Interhospital Helicopter Transfer for Treatment of ST-segment Elevation Myocardial Infarction. *Annals of Emergency Medicine, 57*(3), 213-220.e211. doi: 10.1016/j.annemergmed.2010.08.031

McNamara, R. L., Wang, Y., Herrin, J., Curtis, J. P., Bradley, E. H., Magid, D. J., . . . Krumholz, H. M. (2006). Effect of Door-to-Balloon Time on Mortality in Patients With ST-Segment Elevation Myocardial Infarction. *Journal of the American College of Cardiology, 47*(11), 2180-2186. doi: 10.1016/j.jacc.2005.12.072

McNeill, A. J., Cunningham, S. R., Flannery, D. J., Dalzell, G. W., Wilson, C. M., Campbell, N. P., . . . Adgey, A. A. (1989). A double blind placebo controlled study of early and late administration of recombinant tissue plasminogen activator in acute myocardial infarction. *British Heart Journal, 61*(4), 316-321. doi: 10.1136/hrt.61.4.316

Mehta, S. R., Granger, C. B., Boden, W. E., Steg, P. G., Bassand, J., Faxon, D. P., . . . Yusuf, S. (2009). Early versus Delayed Invasive Intervention in Acute Coronary Syndromes. *The New England Journal of Medicine, 360*(21), 2165-2175. doi: 10.1056/NEJMoa0807986

Miller, W. L., Scott, W. R., Grill, J. P., & Kopecky, S. L. (2000). Improved survival after acute myocardial infarction in patients with advanced killip class. *Clinical Cardiology, 23*(10), 751-758. doi: 10.1002/clc.4960231012

Ministry of Health. (2010). Tatau Kahukura: Māori health statistics 2010. Wellington: Ministry of Health.
Ministry of Health. (2011). Māori Smoking and Tobacco Use. Wellington.
Ministry of Health. (2014a). The Guide to He Korowai Oranga – Māori Health Strategy. Wellington.
Ministry of Health. (2014b). *New Zealand Spinal Cord Impairment Action Plan 2014–2019*. Wellington, New Zealand: Ministry of Health Retrieved from http://www.health.govt.nz/publication/new-zealand-spinal-cord-impairment-action-plan-2014-2019.
Ministry of Health. (2015a). Annual Update of Key Results 2014/15: New Zealand Health Survey. Wellington.
Ministry of Health. (2015b). Mortality and Demographic data 2013 (provisional). Wellington.
Montecucco, F., Carbone, F., & Schindler, T. H. (2016). Pathophysiology of ST-segment elevation myocardial infarction: novel mechanisms and treatments. *European Heart Journal, 37*(16), 1268-1283. doi: 10.1093/eurheartj/ehv592
Morrison, L. J., Verbeek, R. P., McDonald, A. C., Sawadsky, B. V., & Cook, D. J. (2000). Mortality and Prehospital Thrombolysis for Acute Myocardial Infarction. *JAMA: The Journal of the American Medical Association, 283*(20), 2686-2692. doi: 10.1001/jama.283.20.2686
Moyer, P., Ornato, J. P., Brady, W. J., Davis, L. L., Ghaemmaghami, C. A., Gibler, W. B., . . . Zane, R. D. (2007). Development of Systems of Care for ST-Elevation Myocardial Infarction Patients: The Emergency Medical Services and Emergency Department Perspective. *Circulation, 116*(2), e43-e48. doi: 10.1161/CIRCULATIONAHA.107.184047
National Ambulance Sector Clinical Working Group. (2016). *Clinical Procedures and Guidelines: Comprehensive edition*. Auckland, New Zealand: St John.
National Ambulance Sector Office. (2009). The New Zealand Ambulance Service Strategy: The first line of mobile emergency intervention in the continuum of health care (N. A. S. Office, Trans.). Wellington, New Zealand
National Institute of Health & Clinical Excellence. (2002). *Guidance on the use of drugs for early thrombolysis in the treatment of acute myocardial infarction*. National Institute of Health and Clinical Excellence Retrieved from https://www.nice.org.uk/guidance/ta52/resources/guidance-on-the-use-of-drugs-for-early-thrombolysis-in-the-treatment-of-acute-myocardial-infarction-2294634226885.
Nehme, Z., & Boyle, M. (2008). Silent Myocardial Ischaemia: A Review of the Literature for Prehospital Care Providers. *Australasian Journal of Paramedicine, 6*(1), 1-19.
New Zealand Guidelines Group. (2012). *New Zealand Primary Care Handbook 2012* (3rd ed.). Wellington: New Zealand Guidelines Group for the Ministry of Health.
New Zealand Heart Foundation. (2017). Heart attack warning signs. Retrieved September 1, 2017, from https://www.heartfoundation.org.nz/your-heart/heart-attack-warning-signs
New Zealand National Cardiac Network. (2016). *New Zealand Out-of-Hospital STEMI pathway*. Wellington, New Zealand: New Zealand Ministry of Health.
New Zealand National Heart Foundation. (2016). *Strategic Plan 2015-2018*. Wellington: National Heart Foundation Retrieved from http://assets.heartfoundation.org.nz/documents/marketing/about-us/heart-foundation-strategic-plan.pdf.
New Zealand Parliamentary Counsel Office. (2016). *Medicines (Standing Order) Regulations 2002*. Wellington, New Zealand: New Zealand Parliamentary Counsel Office Retrieved from http://www.legislation.govt.nz/regulation/public/2002/0373/latest/DLM170107.html.

New Zealand Qualifications Authority. (2016). *National Diploma in Ambulance Practice (Level 5)*. Wellington: New Zealand Qualifications Authority Retrieved from http://www.nzqa.govt.nz/nqfdocs/quals/pdf/1408.pdf.

New Zealand Standards Authority. (2008). NS 8156: 2008 Ambulance and paramedic services. Wellington, New Zealand.

Newby, K. L., Rutsch, W. R., Califf, R. M., Simoons, M. L., Aylward, P. E., Armstrong, P. W., . . . Van de Werf, F. (1996). Time from symptom onset to treatment and outcomes after thrombolytic therapy. *Journal of the American College of Cardiology, 27*(7), 1646-1655. doi: 10.1016/0735-1097(96)00053-8

Nielsen, P. H., Maeng, M., Busk, M., Mortensen, L. S., Kristensen, S. D., Nielsen, T. T., & Andersen, H. R. (2010). Primary Angioplasty Versus Fibrinolysis in Acute Myocardial Infarction. *Circulation, 121*(13), 1484. doi: 10.1161/CIRCULATIONAHA.109.873224

Northland District Health Board. (2007). *Cardiovascular Disease Strategic Action Plan*. Whangarei, New Zealand: Retrieved from http://www.northlanddhb.org.nz/Portals/0/Communications/Publications/cvd-strategic-action-plan-adopted-july-2007.pdf.

O'Meara, P., Maguire, B., Jennings, P., & Simpson, P. (2015). Building an Australasian paramedicine research agenda: a narrative review. *Health Research Policy and Systems, 13*, 79. doi: 10.1186/s12961-015-0065-0

Oldgren, J., Wernroth, L., & Stenestrand, U. (2010). Fibrinolytic therapy and bleeding complications: risk predictors from RIKS-HIA. *Heart*. doi: 10.1136/hrt.2009.188243

Ouriel, K. (2004). A History of Thrombolytic Therapy. *Journal of Endovascular Therapy, 11*(6 suppl), II-128-II-133. doi: 10.1177/15266028040110s614

Patrono, C., Baigent, C., Hirsh, J., & Roth, G. (2008). Antiplatelet drugs*: American college of chest physicians evidence-based clinical practice guidelines (8th edition). *Chest, 133*(6_suppl), 199S-233S. doi: 10.1378/chest.08-0672

Patrono, C., García Rodríguez, L. A., Landolfi, R., & Baigent, C. (2005). Low-Dose Aspirin for the Prevention of Atherothrombosis. *New England Journal of Medicine, 353*(22), 2373-2383. doi: 10.1056/NEJMra052717

Pereillo, J. M., Maftouh, M., Andrieu, A., Uzabiaga, M. F., Fedeli, O., Savi, P., . . . Picard, C. (2002). Structure and Stereochemistry of the Active Metabolite of Clopidogrel. *Drug Metabolism and Disposition, 30*(11), 1288. doi: 10.1124/dmd.30.11.1288

Petitou, M., Herault, J., Bernat, A., Driguez, P., Duchaussoy, P., Lormeau, J., & Herbert, J. (1999). Synthesis of thrombin-inhibiting heparin mimetics without side effects. *Nature, 398*(6726), 417-422. doi: 10.1038/18877

Pinto, D. S., Kirtane, A. J., Nallamothu, B. K., Murphy, S. A., Cohen, D. J., Laham, R. J., . . . Gibson, C. M. (2006). Hospital Delays in Reperfusion for ST-Elevation Myocardial Infarction: Implications When Selecting a Reperfusion Strategy. *Circulation, 114*(19), 2019-2025. doi: 10.1161/CIRCULATIONAHA.106.638353

Pitt, K. (2002). Prehospital selection of patients for thrombolysis by paramedics. *Emergency Medicine Journal, 19*(3), 260-263. doi: 10.1136/emj.19.3.260

Polit, D. F., & Beck, C. T. (2006). *Essentials of nursing research. Methods, appraisal and utilization* (6 ed.). Philadelphia: Lippincott, Williams & Wilkins.

Pre-Hospital Emergency Care Council. (2017). Ireland's First Emergency Aeromedical Service. Retrieved August 14, 2017, from http://www.phecit.ie/PHECC/Publications_and_Resources/Newsletters/Newsletter_Itmes/Winter_2012/Ireland_s_First_Emergency_Aeromedical_Service.aspx

Price, L., Keeling, P., Brown, G., Hughes, D., & Barton, A. (2005). A qualitative study of paramedics' attitudes to providing prehospital thrombolysis. *Emergency Medicine Journal, 22*(10), 738-741. doi: 10.1136/emj.2005.025536

Prins, M. H., & Hirsh, J. (1991). Heparin as an adjunctive treatment after thrombolytic therapy for acute myocardial infarction. *The American Journal Of Cardiology, 67*(3), 3-11. doi: 10.1016/0002-9149(91)90082-v

Ranasinghe, I., Turnbull, F., Tonkin, A., Clark, R. A., Coffee, N., & Brieger, D. (2012). Comparative Effectiveness of Population Interventions to Improve Access to Reperfusion for ST-Segment–Elevation Myocardial Infarction in Australia. *Circulation: Cardiovascular Quality and Outcomes, 5*(4), 429. doi: 10.1161/CIRCOUTCOMES.112.965111

Ranchord, A. M., Prasad, S., Matsis, P., & Harding, S. A. (2009). Paramedic-administered prehospital thrombolysis is safe and reduces time to treatment. *New Zealand Medical Journal, 122*(1302), 47-53. http://www.ncbi.nlm.nih.gov/pubmed/19834522

Rawles, J. (1994). Having of mortality at 1 year by domiciliary thrombolysis in the grampian region early anistreplase trial (GREAT). *Journal of the American College of Cardiology, 23*(1), 1-5. doi: 10.1016/0735-1097(94)90494-4

Rawles, J. (2003). GREAT: 10 year survival of patients with suspected acute myocardial infarction in a randomised comparison of prehospital and hospital thrombolysis. *Heart, 89*(5), 563-564. www.cinahl.com/cgi-bin/refsvc?jid=1526&accno=2003155426

Robson, B., & Harris, R. (2007). *Hauora: Māori Standards of Health IV. A study of the years 2000-2005*. Wellington, New Zealand: Te Rōpū Rangahau Hauora a Eru Pōmare.

Robson, L. S., Shannon, H. S., Goldenhar, L. M., & Hale, A. R. (2001). *Guide to Evaluating the Effectiveness of Strategies for Preventing Work Injuries: How to Show Whether a Safety Intervention Really Works*. Cincinnati, OH: National Institute for Occupational Safety and Health Retrieved from https://www.iwh.on.ca/system/files/documents/evaluation_guide_2001b.pdf.

Roe, M. T., Messenger, J. C., Weintraub, W. S., Cannon, C. P., Fonarow, G. C., Dai, D., . . . Rumsfeld, J. S. (2010). Treatments, Trends, and Outcomes of Acute Myocardial Infarction and Percutaneous Coronary Intervention. *Journal of the American College of Cardiology, 56*(4), 254-263. doi: 10.1016/j.jacc.2010.05.008

Roth, A., Barbash, G. I., Hod, H., Miller, H. I., Rath, S., Modan, M., . . . Kaplinsky, E. (1990). Should thrombolytic therapy be administered in the mobile intensive care unit in patients with evolving myocardial infarction? A pilot study. *J Am Coll Cardiol, 15*(5), 932-936. http://content.onlinejacc.org/cgi/content/abstract/15/5/932

Roth, G. J., & Majerus, P. W. (1975). The mechanism of the effect of aspirin on human platelets. I. Acetylation of a particulate fraction protein. *Journal of Clinical Investigation, 56*(3), 624-632. doi: 10.1172/JCI108132

Sabatine, M. S., Cannon, C. P., Gibson, C. M., López-Sendón, J. L., Montalescot, G., Theroux, P., . . . Braunwald, E. (2005). Addition of Clopidogrel to Aspirin and Fibrinolytic Therapy for Myocardial Infarction with ST-Segment Elevation. *The New England Journal of Medicine, 352*(12), 1179-1189.

Savage, M. L., Poon, K. K. C., Johnston, E. M., Raffel, O. C., Incani, A., Bryant, J., . . . Walters, D. L. (2014). Pre-Hospital Ambulance Notification and Initiation of Treatment of ST Elevation Myocardial Infarction is Associated with Significant Reduction in Door-to-Balloon Time for Primary PCI. *Heart, Lung and Circulation, 23*(5), 435-443. doi: 10.1016/j.hlc.2013.11.015

Schofer, J., Büttner, J., Geng, G., Gutschmidt, K., Herden, H. N., Mathey, D. G., . . . Voelz, P. (1990). Prehospital thrombolysis in acute myocardial infarction. *The American Journal Of Cardiology, 66*(20), 1429-1433. doi: 10.1016/0002-9149(90)90528-9

Schulman, S. P., Beyth, R. J., Kearon, C., & Levine, M. N. (2008). Hemorrhagic Complications of Anticoagulant and Thrombolytic Treatment*. *Chest, 133*(6 suppl), 257S-298S. doi: 10.1378/chest.08-0674

Scuffham, P. A., & Tippett, V. (2008). The cost-effectiveness of thrombolysis administered by paramedics*. *Current Medical Research and Opinion, 24*(7), 2045-2058. doi: 10.1185/03007990802224762

Shaban, R. Z., Smith, C. M. W., & Cumming, J. J. (2004). Uncertainty, error and risk in human clinical judgement: introductory theoretical frameworks in paramedic practice. *Journal Of Emergency Primary Health Care, 2*(1-2), 12-12.

Shadish, W. R., Cook, T. D., & Campbell, D. (2002). *Experimental and Quasi-Experimental Designs for Generalized Causal Inference*. New York: Houghton Mifflin Company.

Sheifer, S. E., Manolio, T. A., & Gersh, B. J. (2001). Unrecognized myocardial infarction. *Annals of Internal Medicine, 135*(9), 801-811. doi: 10.7326/0003-4819-135-9-200111060-00010

Sigmundsson, T. S., Gannarsson, B., Benediktsson, S., Gunnarsson, G. T., Duason, S., & Thorgeirsson, G. (2010). Management of patients with STEMI transported with air-ambulance to Landspitali University Hospital in Reykjavik. *Laeknabladid, 96*(3), 159-165.

Sikri, N., & Bardia, A. (2007). A History of Streptokinase Use in Acute Myocardial Infarction. *Texas Heart Institute Journal, 34*(3), 318-327. http://www.ncbi.nlm.nih.gov.ezproxy.aut.ac.nz/pmc/articles/PMC1995058/

Smith, A. M., Hardy, P. J., Sandler, D. A., & Cooke, J. (2011). Paramedic decision making: prehospital thrombolysis and beyond. *Emergency Medicine Journal, 28*(8), 700-702. doi: 10.1136/emj.2009.083766

Smith, G., & Eastwood, K. (2009). Reflections in the research pool: A paramedic experience in clinical research and the Master of Emergency Health degree. http://www.jephc.com/uploads/GS990342.pdf

Snooks, H., Evans, A., Wells, B., Peconi, J., & Thomas, M. (2008). What are the highest priorities for research in pre-hospital care? Results of a review and Delphi consultation exercise. http://www.jephc.com/uploads/990319HS.pdf

ST-Elevation Myocardial Infarction Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand. (2013). ST-elevation myocardial infarction: New Zealand management guidelines, 2013. *The New Zealand Medical Journal, 126*(1387), 127-164.

St John Ambulance Service. (2015). St John Integrated Business Plan Summary 2013−2018: Goals, Objectives, Deliverables and Outcomes. from https://thehub.stjohn.org.nz/theplan/Documents/IBP%20Strategy%20Summary%20Feb%202014.pdf

St John Ambulance Service. (2016). *Clinical Procedures and Guidelines: Comprehensive edition 2016-2018*. Wellington, New Zealand: St John.

Statistics New Zealand. (2013a). 2013 Census QuickStats about a place: Hawke's Bay Region. Retrieved January 9, 2017, from http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/quickstats-about-a-place.aspx?request_value=14018&tabname=

Statistics New Zealand. (2013b). 2013 Census QuickStats about a place: Northland Region. Retrieved January 9, 2017, from http://www.stats.govt.nz/Census/2013-census/profile-and-summary-reports/quickstats-about-a-place.aspx?request_value=13068&tabname=

Statistics New Zealand. (2014). Population estimates tables at 30 June 1996, 2001, 2006, and 2013. from http://www.stats.govt.nz/tools_and_services/nzdotstat/tables-by-subject/population-estimates-tables-30-jun-96-01-06-13.aspx

Statistics New Zealand. (2017a). New Zealand Period Life Tables: 2012–14. Retrieved March 2nd, 2017, from http://www.stats.govt.nz/browse_for_stats/health/life_expectancy.aspx

Statistics New Zealand. (2017b). Subnational population estimates (UA, AU), by age and sex, at 30 June 1996, 2001, 2006-16 (2017 boundary). Retrieved January 9, 2017, from http://nzdotstat.stats.govt.nz/wbos/Index.aspx?DataSetCode=TABLECODE7541

Steg, P. G., Bonnefoy, E., Chabaud, S., Lapostolle, F., Dubien, P., Cristofini, P., . . . Touboul, P. (2003). Impact of Time to Treatment on Mortality After Prehospital Fibrinolysis or Primary Angioplasty. *Circulation, 108*(23), 2851-2856. doi: 10.1161/01.cir.0000103122.10021.f2

Steg, P. G., James, S. K., Atar, D., Badano, L. P., Lundqvist, C. B., Borger, M. A., . . . Wallentin, L. (2012). ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *European Heart Journal, 33*(20), 2569-2619. doi: 10.1093/eurheartj/ehs215

Stenestrand, U., Lindbäck, J., & Wallentin, L. (2006). Long-term Outcome of Primary Percutaneous Coronary Intervention vs Prehospital and In-Hospital Thrombolysis for Patients With ST-Elevation Myocardial Infarction. *The Journal of the American Medical Association, 296*(14), 1749-1756. doi: 10.1001/jama.296.14.1749

Stewart, R. A., & White, H. D. (2007). Reducing the lifetime cardiovascular risk of New Zealanders. *New Zealand Medical Journal, 120*(1261), 5-7.

Stone, P. H., Raabe, D. S., Jaffe, A. S., Gustafson, N., Muller, J. E., Turi, Z. G., . . . Braunwald, E. (1988). Prognostic significance of location and type of myocardial infarction: Independent adverse outcome associated with anterior location. *Journal of the American College of Cardiology, 11*(3), 453-463. doi: 10.1016/0735-1097(88)91517-3

Svensson, L., Karlsson, T., Nordlander, R., Wahlin, M., Zedigh, C., & Herlitz, J. (2003). Safety and delay time in prehospital thrombolysis of acute myocardial infarction in urban and rural areas in sweden. *The American Journal of Emergency Medicine, 21*(4), 263-270. doi: 10.1016/S0735-6757(03)00040-8

Swarbrick, N. (2016). Ambulance services - Ambulance crew. Retrieved 20th of May, 2016, from http://www.teara.govt.nz/en/ambulance-services/3

Taher, T., Fu, Y., Wagner, G. S., Goodman, S. G., Fresco, C., Granger, C. B., . . . Armstrong, P. W. (2004). Aborted myocardial infarction in patients with ST-segment elevation: Insights from the assessment of the safety and efficacy of a new thrombolytic regimen-3 trial electrocardiographic substudy. *J Am Coll Cardiol, 44*(1), 38-43. doi: 10.1016/j.jacc.2004.03.041

Tang, E. W., Wong, C. K., & Herbison, P. (2006). Community hospital versus tertiary hospital comparison in the treatment and outcome of patients with acute coronary syndrome: a New Zealand experience. *New Zealand Medical Journal, 119*(1238), 36-48.

Tanner, H., Larsen, P., Lever, N., & Galletly, D. (2006). Early recognition and early access for acute coronary syndromes in New Zealand: key links in the chain of survival. *The New Zealand Medical Journal, 119*(1232), 38-46.

The Assessment of the Safety Efficacy of a New Thrombolytic Regimen Investigators. (2001). Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. *The Lancet, 358*(9282), 605-613. doi: http://dx.doi.org /10.1016/S0140-6736(01)05775-0

The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO III) Investigators. (1997). A Comparison of Reteplase with Alteplase for Acute Myocardial Infarction. *New England Journal of Medicine, 337*(16), 1118-1123. doi: 10.1056/NEJM199710163371603

The International Study Group. (1990). In-hospital mortality and clinical course of 20 891 patients with suspected acute myocardial infarction randomised between alteplase and streptokinase with or without heparin. *The Lancet, 336*(8707), 71-75. doi: 10.1016/0140-6736(90)91590-7

Thiemann, D. R., Coresh, J., Schulman, S. P., Gerstenblith, G., Oetgen, W. J., & Powe, N. R. (2000). Lack of Benefit for Intravenous Thrombolysis in Patients With Myocardial Infarction Who Are Older Than 75 Years. *Circulation, 101*(19), 2239-2246. doi: 10.1161/01.cir.101.19.2239

Tipene-Leach, D., Pahau, H., Joseph, N., Coppell, K., McAuley, K., Booker, C., . . . Mann, J. (2004). Insulin resistance in a rural Maori communit. *The New Zealand Medical Journal, 117*(1207), 1-11.

Tobias, M., Sexton, K., Mann, S., & Sharp, N. (2006). How long can it go? Projecting ischemic heart disease mortality in New Zealand to 2015. *The New Zealand Medical Journal*. http://journal.nzma.org.nz/journal/122-1288/3433/content.pdf

Topol, E. J., Califf, R. M., & Lee, K. L. (1994). More on the GUSTO Trial. *New England Journal of Medicine, 331*(4), 277-278. doi: 10.1056/NEJM199407283310418

Topol, E. J., Califf, R. M., Van de Werf, F., & Armstrong, P. W. (1993). An International Randomized Trial Comparing Four Thrombolytic Strategies for Acute Myocardial Infarction. *New England Journal of Medicine, 329*(10), 673-682. doi: 10.1056/NEJM199309023291001

Trent, R., Adams, J., & Rawles, J. (1994). Electrocardiographic evidence of reperfusion occurring before hospital admissionA Grampian Region Early Anistreplase Trial (GREAT) sub-study. *European Heart Journal, 15*(7), 895-897. doi:10. 1093/oxfordjournals.eurheartj.a060607

Turnbull, J., Grey, J., & MacFadyen, J. (1998). Improving in-training evaluation programmes. *Journal of General Internal Medicine, 13*, 317-323. doi: 10.1046/j.1525-1497.1998.00097.x

Van de Werf, F., Bax, J., Betriu, A., Blomstrom-Lundqvist, C., Crea, F., Falk, V., . . . Weis, M. (2008). Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. *European Heart Journal, 29*(23), 2909-2945. doi: 10.1093/eurheartj/ehn416

Van de Werf, F., Bax, J., Betriu, A., Blomstrom-Lundqvist, C., Crea, F., Falk, V., . . . Rutten, F. (2008). Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. *European Heart Journal, 29*(23), 2909-2945. doi: 10.1093/eurheartj/ehn416

Verheugt, F. W. A., Gersh, B. J., & Armstrong, P. W. (2006). Aborted myocardial infarction: a new target for reperfusion therapy. *European Heart Journal, 27*(8), 901-904. doi: 10.1093/eurheartj/ehi829

Walton, R., & Offenberger, H. (1984). *Review of ambulance officer training*. Wellington, New Zealand: Department of Health.

Wang, T., Ramanathan, T., Stewart, R., Crengle, S., Gamble, G., & White, H. (2013). Māori have worse outcomes after coronary artery bypass grafting than Europeans in New Zealand. *New Zealand Medical Journal, 126*(1379).

Wang, T. Y., Nallamothu, B. K., Krumholz, H. M., Li, S., Roe, M. T., Jollis, J. G., . . . Ting, H. H. (2011). ASsociation of door-in to door-out time with reperfusion delays and outcomes among patients transferred for primary percutaneous coronary intervention. *JAMA, 305*(24), 2540-2547. doi: 10.1001/jama.2011.862

Weaver, D. W. (1995). Time to thrombolytic treatment: Factors affecting delay and their influence on outcome. *Journal of the American College of Cardiology, 25*(7, Supplement), S3-S9. doi: http://dx.doi.org/10.1016/0735-1097(95)00108-G

Weaver, D. W., Cerqueira, M., Hallstrom, A. P., Litwin, P. E., Martin, J. S., Kudenchuk, P. J., & Eisenberg, M. (1993). Prehospital-Initiated vs Hospital-Initiated Thrombolytic Therapy. *The Journal of the American Medical Association, 270*(10), 1211-1216. doi: 10.1001/jama.1993.03510100061033

Weaver, D. W., Eisenberg, M. S., Martin, J. S., Litwin, P. E., Shaeffer, S. M., Ho, M. T., . . . Ritchie, J. L. (1990). Myocardial infarction triage and intervention project—Phase I: Patient characteristics and feasibility of prehospital initiation of thrombolytic therapy. *Journal of the American College of Cardiology, 15*(5), 925-931. doi: 10.1016/0735-1097(90)90218-E

Weaver, D. W., Simes, R. J., Betriu, A., Grines, C. L., Zijlstra, F., Garcia, E., . . . Ribichini, F. (1997). Comparison of Primary Coronary Angioplasty and Intravenous Thrombolytic Therapy for Acute Myocardial Infarction. *JAMA: The Journal of the American Medical Association, 278*(23), 2093-2098. doi: 10.1001/jama.1997.03550230069040

Wells, S., Broad, J., & Jackson, R. (2006). Estimated prevalence of cardiovascular disease and distribution of cardiovascular risk in New Zealanders: data for healthcare planners, funders, and providers. *New Zealand Medical Journal, 119*(1232), 1-8.

Welsh, R. C., Goldstein, P., Adgey, J., Verheugt, F., Bestilny, S. A., Wallentin, L., . . . Armstrong, P. W. (2004). Variations in pre-hospital fibrinolysis process of care: insights from the Assessment of the Safety and Efficacy of a New Thrombolytic 3 Plus international acute myocardial infarction pre-hospital care survey. *European Journal of Emergency Medicine, 11*(3), 134-140. http://journals.lww.com/euro-emergencymed/Fulltext/2004/06000/Variations_in_pre_hospital_fibrinolysis_process_of.4.aspx

Whangarei District Council. (2015). *Demographic Profile for the Whangarei District June 2013*. Whangarei, New Zealand: Retrieved from http://www.wdc.govt.nz/PlansPoliciesandBylaws/Plans/SustainableFutures/Documents/Sustainable%20Society%20and%20Culture/Demographic-Profile-of-the-Whangarei-District.pdf.

Whitbread, M., Leah, V., Bell, T., & Coats, T. J. (2002). Recognition of ST elevation by paramedics. *Emergency Medicine Journal, 19*(1), 66-67. doi: 10.1136/emj.19.1.66

White, H., Wang, T., Ramanathan, T., & Stewart, R. (2010). Response to NZMJ editorial by Dr Elana Curtis entitled Deserving of more: framing of Māori inequities in cardiovascular care remain a challenge. *New Zealand Medical Journal, 126*(1382).

White, H. D. (2000). Thrombolytic therapy in the elderly. *The Lancet, 356*(9247), 2028-2030. doi: http://dx.doi.org/10.1016/S0140-6736(00)03397-3

White, J. M., Howard, R., Goldsmith, R., Harrison, N., Johanson, S. P., Webster, M. W. I., . . . Ruygrok, N. (2012). Safety and feasibility of patient transfer by helicopter for primary percutaneous coronary intervention. *New Zealand Medical Journal, 125*(1362), 47-59.

Widimský, P., Budešínský, T., Voráč, D., Groch, L., Želízko, M., Aschermann, M., . . . Formánek, P. (2003). Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. *European Heart Journal, 24*(1), 94-104. doi: 10.1016/s0195-668x(02)00468-2

Widimský, P., Budešínský, T., Voráč, D., Groch, L., Želízko, M., Aschermann, M., . . . Formánek, P. (2002). Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. *European Heart Journal, 24*(1), 94. doi: 10.1016/S0195-668X(02)00468-2

Widimský, P., Groch, L., Zelízko, M., Aschermann, M., Bednář, F., & Suryapranata, H. (2000). Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE Study. *European Heart Journal, 21*(10), 823-831. doi: 10.1053/euhj.1999.1993

Wilcox, R. G., Olsson, C. G., Skene, A. M., Von Der Lippe, G., Jensen, G., & Hampton, J. R. (1988). Trial of Tissue Plasminogen Activator for Mortality Reduction in Acute Myocardial Infarction *The Lancet, 332*(8610), 525-530. doi: 10.1016/S0140-6736(88)92656-6

Williams, M. (2007). Percutaneous coronary intervention in New Zealand. *New Zealand Medical Journal, 120*(1248), 10-11.

Wöhrle, J., Desaga, M., Metzger, C., Huber, K., Suryapranata, H., Guetta, V., . . . Stone, G. W. (2010). Impact of Transfer for Primary Percutaneous Coronary Intervention on Survival and Clinical Outcomes (from the HORIZONS-AMI Trial). *The American Journal Of Cardiology, 106*(9), 1218-1224. doi: 10.1016/j.amjcard. 2010.06.049

Wright-St. Clair, R. E. (1977). *The Order of St John in New Zealand*. Trentham, New Zealand: The Priory in New Zealand of the Order of St John.

Wu, A. H., Parsons, L., Every, N. R., & Bates, E. R. (2002). Hospital outcomes in patients presenting with congestive heart failure complicating acute myocardial infarction: A report from the Second National Registry of Myocardial Infarction (NRMI-2). *Journal of the American College of Cardiology, 40*(8), 1389-1394. doi: 10.1016/S0735-1097(02)02173-3

Yusuf, S., Zhao, F., Mehta, S. R., Chrolavicius, S., Tognoni, G., & Fox, K. K. (2001). Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. *The New England Journal of Medicine, 345*(7), 494-502.

Zellweger, M. J., Hachamovitch, R., Kang, X., Hayes, S. W., Friedman, J. D., Germano, G., . . . Berman, D. S. (2004). Prognostic relevance of symptoms versus objective evidence of coronary artery disease in diabetic patients. *European Heart Journal, 25*(7), 543-550. doi: 10.1016/j.ehj.2004.02.013

Zijlstra, F. (2003). Angioplasty vs thrombolysis for acute myocardial infarction: a quantitative overview of the effects of interhospital transportation. *European Heart Journal, 24*(1), 21-23. doi: 10.1016/s0195-668x(02)00693-0

Zipes, D. P., & Wellens, H. J. (1998). Sudden Cardiac Death. *Circulation, 98*(21), 2334-2351.

Appendices

Appendix A:AUTEC Approval Letter – Study One

AUT UNIVERSITY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

MEMORANDUM

Auckland University of Technology Ethics Committee (AUTEC)

To: Bronwyn Tunnage
From: **Dr Rosemary Godbold** Executive Secretary, AUTEC
Date: 15 May 2012
Subject: Ethics Application Number 12/94 **The accuracy of New Zealand intensive care paramedics' clinical decision-making applied to Autonomous Pre-Hospital Thrombolysis.**

Dear Bronwyn

Thank you for providing written evidence as requested. I am pleased to advise that it satisfies the points raised by the Auckland University of Technology Ethics Committee (AUTEC) at their meeting on 30 April 2012 and 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 28 May 2012.

Your ethics application is approved for a period of three years until 15 May 2015.

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 15 May 2015;
- 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 15 May 2015 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 participants. 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 AUTEC 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.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all written and verbal correspondence with us. Should you have any further enquiries regarding this matter, you are welcome to contact me by email at ethics@aut.ac.nz or by telephone on 921 9999 at extension 6902. Alternatively you may contact your AUTEC Faculty Representative (a list with contact details may be found in the Ethics Knowledge Base at http://www.aut.ac.nz/research/research-ethics/ethics).

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

Yours sincerely

Dr Rosemary Godbold
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Paul Davis team_davis@windowslive.com

Appendix B: HDEC Approval Letter – Study One

Health and Disability Ethics Committees

Multi-region Ethics Committee
c/- Ministry of Health
PO Box 5013
1 the Terrace
Wellington
Phone: (04) 816 2655
Fax: (04) 496 2343
Email: multiregion_ethicscommittee@moh.govt.nz

27 February 2012

Mr Paul Davis
St John Ambulance
39C Ketenikau Road
Kamo
Whangarei 0112

Dear Mr Davis

Ethics ref: **MEC/12/EXP/025** (please quote in all correspondence)
Study title: The Accuracy of New Zealand Intensive Care Paramedics' Clinical Decision-making applied to Autonomous Pre-Hospital Thrombolysis

This expedited study was given ethical approval by the Chairperson of the Multi-region Ethics Committee on **24 February 2012**.

This approval is valid until **01 March 2013**, provided that Annual Progress Reports are submitted (see below).

Amendments and Protocol Deviations

All significant amendments to this proposal must receive prior approval from the Committee. Significant amendments include (but are not limited to) changes to:

- the researcher responsible for the conduct of the study at a study site
- the addition of an extra study site
- the design or duration of the study
- the method of recruitment
- information sheets and informed consent procedures.

Significant deviations from the approved protocol must be reported to the Committee as soon as possible.

Annual Progress Reports and Final Reports

The first Annual Progress Report for this study is due to the Committee by **24 February 2013**. The Annual Report Form that should be used is available at www.ethicscommittees.health.govt.nz. Please note that if you do not provide a progress report by this date, ethical approval may be withdrawn.

A Final Report is also required at the conclusion of the study. The Final Report Form is also available at www.ethicscommittees.health.govt.nz.

We wish you all the best with your study.

Yours sincerely

AWHINA RANGIWAI
ADMINISTRATOR
Multi Regional Ethics Committee

Appendix C: Participant Consent Form – Study One

Participant Consent Form

Project Title: The accuracy of New Zealand Paramedics' clinical decision-making in the application of an autonomous pre-hospital thrombolysis protocol.

- ☐ I have read and understood the information provided for this study in the Participant Information Sheet dated 20th March 2012.
- ☐ I have had an opportunity to ask questions about this study and I am satisfied with the answers I have been given.
- ☐ I understand that taking part in this study is voluntary and that I may withdraw myself or any information that I have provided for this study at any time prior to the completion of data collection without being disadvantaged in any way.
- ☐ I meet the first inclusion criteria for this study - *I have successfully completed the university based educational requirements needed to obtain authority to practice as an Intensive Care Paramedic within New Zealand* OR
- ☐ I meet the second inclusion criteria for this study - *I have successfully completed the current ILS paramedic course* OR
- ☐ I meet the third inclusion criteria for this study - *I am a current practicing paramedic and have successfully completed a paramedic-based tertiary level 7 cardiology paper* AND
- ☐ I meet the fourth inclusion criteria for this study - *I am currently employed within a New Zealand EMS group i.e. ambulance service or aero-medical helicopter/fixed wing operation.*
- ☐ I understand that my participation in this study is confidential and that no material that could identify me will be used in any reports on this study.
- ☐ I agree to allow the answers from my written test and demographic questionnaire to be used for this study for publication.
- ☐ I have had sufficient time to consider whether to take part in the study.
- ☐ I agree to take part in this study.

I wish to receive an email of the final report for this study (please tick one):

☐ Yes ☐ No

Participant's email address if requesting a copy of the final report:

.....

.....

Participant's signature: ..... **Date:** .....

*Note: The participant should retain a copy of this form.

Project Explained By: Paul Davis (Primary Researcher)
Phone: (09) 921 9999 extension 7088
Email: ap_phtstudy@live.com

Appendix D:St John Locality Approval Letter – Study One

St John
first to care

29 June 2012

Paul Davis
St John
PO Box 8011
Kensington
Whangarei 0112
New Zealand

Study title: The Accuracy of New Zealand Intensive Care Paramedics' Clinical Decision-making applied to Autonomous Pre-Hospital Thrombolysis

St John reference: 0001

Dear Mr Davis,

I am pleased to inform you that your data access request has been reviewed by St John and that the outcome of this review is that data access for the study "*The accuracy of New Zealand Intensive Care Paramedics' clinical decision-making applied to autonomous pre-hospital thrombolysis*" is approved and your study may go ahead subject to conditions set out below.

Conditions of data access:

1. When cold calling for recruitment of participants it will be made clear that their personal details were obtained from an AUT source and not from the St John phone list/database.

2. When the study is advertised within ambulance stations the branding must be AUT and not St John.

3. The timetable for delivery of the study is designed so that all participants will undertake the course and testing in their own time and not during work time, there will be no cost to St John for implementation of the study.

4. At the end of the training/testing period the participants must be clear that the despite having done the proposed course that they are in no way to administer PHT without telemetry and that it does not alter the current St John pre-hospital thrombolysis protocols. There must be a statement to this effect prior to the release of the participants at the end of the testing period.

THE ORDER OF ST JOHN

Dr. Bridget Dicker, PhD | Clinical Research Coordinator
T 09 5260527 ext 8771 | M 027 705 2617 | E bridget.dicker@stjohn.org.nz
Private Bag 14902 I Mt Wellington I New Zealand | www.stjohn.org.nz

5. The course teaching and testing materials are to be St John branded and not AUT branded. The teaching resources to be used will be generated by St John and tailored to fit the project purpose though joint meetings and collaboration with both Paul Davis, his current AUT supervisor(s) and members of the St John Clinical Development team.

6. All researchers involved in the study are required to complete a copy of the *St John data access protocol*.

7. Study reporting is required on a on a 3 monthly basis and at completion of the study. Use the *St John Research Status Report* for report submission.

Regards,

Dr. Bridget Dicker

Clinical Research Coordinator

CC Dr. Graham Howie
Bronwyn Tunnage

Attachments St John Data Access Protocol
St John Research Status Report

Appendix E: AUTEC Approval Letter – Study Two

AUT UNIVERSITY
TE WĀNANGA ARONUI O TAMAKI MAKAU RAU

AUTEC SECRETARIAT

10 February 2015

Graham Howie
Faculty of Health and Environmental Sciences

Dear Graham

Re Ethics Application: **15/03 Autonomous paramedic delivered pre-hospital thrombolysis: A new approach in the treatment of ST_Elevation myocardial infarction patients.**

Thank you for providing evidence as requested.

Your ethics application has been approved for three years until 10 February 2018.

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/researchethics. When necessary this form may also be used to request an extension of the approval at least one month prior to its expiry on 10 February 2018;
- A brief report on the status of the project using form EA3, which is available online through http://www.aut.ac.nz/researchethics. This report is to be submitted either when the approval expires on 10 February 2018 or on completion of the project.

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 participants. You are responsible for ensuring that research undertaken under this approval occurs within the parameters outlined in the approved application.

AUTEC grants ethical approval only. If you require management approval from an institution or organisation for your research, then you will need to obtain this.

To enable us to provide you with efficient service, please use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

All the very best with your research,

Kate O'Connor
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Paul Davis paul.davis@stjohn.org.nz

Appendix F: HDEC Approval Letter – Study Two

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
C/- MEDSAFE, Level 6, Deloitte House
10 Brandon Street
PO Box 5013
Wellington
6011

0800 4 ETHICS
hdecs@moh.govt.nz

02 December 2014

Mr Paul Davis
39C Ketenikau Road
Kamo
Whangarei 0112

Dear Mr Davis

Re:	**Ethics ref:**	**14/NTA/112**
	Study title:	Autonomous Paramedic Delivered Pre-Hospital Thrombolysis: A new Approach in the Treatment of ST-Elevation Myocardial Infarction Patients

I am pleased to advise that this application has been *approved* by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Northern A Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at *a given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

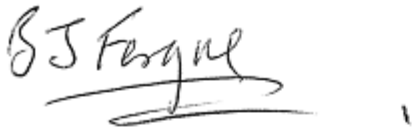
After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your **next progress report** is due by **01 December 2015.**

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,



Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix G: St John Locality Approval Letter – Study Two

12 January 2015

Paul Davis
39C Ketenikau Rd,
Kamo
Whangarei 0112

St John
first to care

Study title: Autonomous Paramedic Delivered Pre-Hospital Thrombolysis: A new Approach in the Treatment of ST-Elevation Myocardial Infarction Patients.
St John reference: 0044

Dear Paul,

Your research study has undergone a locality review by St John, and I am pleased to inform you that your study is now authorised to go ahead subject to the conditions set out below.

Conditions
All final teaching material and assessment processes are required to be reviewed and authorised by either the Head of Clinical Practice (Dan Ohs) or the St John National Clinical Planning manager (Sarah Werner) prior to delivery.
Project reports must be submitted to St John on the following dates:

- 30 June 2015 Interim Progress Report #1
- 30 June 2016 Interim Progress Report #2
- 30 June 2017 Final Report
- The final report should be submitted at the completion of the study. This should be returned to St John within four weeks of the project completion. The date stated above is the anticipated final report date for this project. If this is to be extended please state this in the Interim Progress Report #1 and our records will be amended. The final report should provide a synopsis outlining the results and conclusions from the study.
- Please use the *OMF 4.9.8 Research Status Report* for report submissions.
- All researchers involved in the study are required to complete a copy of the *OMF 4.9.7 Research Memorandum of Understanding*.

Yours sincerely

Bridget Dicker

Dr Bridget Dicker, PhD
Clinical Research Fellow
National Headquarters

Attachments OMF 4.9.8 Research Status Report
OMF 4.9.7 Research Memorandum of Understanding

Appendix H: NDHB Locality Approval Letter – Study Two and Study Three

Locality Assessment by Northland District Health Board

Locality Assessment No : 2014-28

Locality Assessment Sign Off

All research conducted in the Northland DHB must be conducted with the knowledge of the Northland DHB, and must meet all the requirements of the Health & Disability Ethics Committees (HDECs), though not all research will require HDEC review.

A locality assessment must be undertaken to review all research conducted at Northland District Health Board. Locality Assessments will consider resource implications, suitability of the local researcher and research environment, and cultural issues.

Part One: General

Full project title:	Paramedic based systems of care for STEMI patients within Northland
Short project title:	Paramedic based systems of care for STEMI patients within Northland
Locality to be assessed:	Northland
Brief outline of study:	**Study One** In partnership with the NDHB, St John have run a pre-hospital thrombolysis (PHT) programme in Northland since 2008. This programme utilises a physician-authorised telemetry model. Here our paramedics attend the patient in the field and transmit a 12-lead ECG from the scene to NBHED where it is viewed by a physician, who may (or may not) authorise the paramedic to administer thrombolysis following phone communication. Our proposed interventional study would like to trial a new approach which removes both physician consultation and the need for ECG transmission from the process: paramedics assess the patient and make an independent clinical decision as to whether or not thrombolysis is indicated under strict protocol guidance. Having already been trialled in several countries such as England, Wales and the Netherlands, this autonomous paramedic model is thought to be the most time efficient approach to PHT delivery. The written proposal for this study has been peer reviewed by both the AUT Post-Graduate Board and St John's Clinical Audit and Research Group who both give their full support. **Study Two** In partnership with the NDHB and Auckland City Hospital Interventional Cardiology Department, St John have developed a Whangarei-based paramedic-initiated pathway for the referral of STEMI patients from the field direct to the cardiac catheterisation lab in Auckland for primary PCI via EMS helicopter transfer. Named the *STEMI Bypass* programme and having now run for just over a year, this programme was preceded by a pathway where ambulance STEMI patients were firstly routed through the ED at NBH and the decision for transfer on to Auckland was made by the receiving physician. For our second proposed study we would simply like to compare patient outcomes from the old programme with that of the new programme. This

	project is still currently in the planning phase and we anticipate an ethics application being submitted within the next two months.
Principal investigator (for this locality):	Paul Davis, St. John Northern Region
Contact details:	Tel : 021 295 0951 Email : paul.davis@stjohn.org.nz PO Box 8011, Kensington, Whangarei 0110
Other local investigators (list all at this site):	
Contact details:	

Part Two: Locality Issues

Identify any local issues and specify how these issues **will** be addressed.

1. **Suitability of local researcher**

   For example, are all roles for the investigator(s) at the local site appropriate (for example, has any conflict the investigator might have between her or his local roles in research and in patient care been adequately resolved)? [X] Yes [ ] No

2. **Suitability of the local research environment**

   a) Are all the resources (other than funding that is conditional on ethical approval) and/or facilities that the study requires appropriate and available (for example, is staffing adequate? Is this site accessible for mobility-impaired people where necessary)? [X] Yes [ ] No

   b) Have all potentially affected managers of resources such as clinical records or laboratory managers been notified? [X] Yes [ ] No

3. **Have issues such as cultural issues specific to this locality or to people being recruited at this locality been addressed?** [X] Yes [ ] No

4. **Have the local investigator contact details and other important contact details been provided to the locality organisation for checking?** [X] Yes [ ] No

Part Three: Declaration by locality organisation

I am authorised to complete locality approval on behalf of this locality organisation. I understand that I may withdraw locality approval if any significant local concerns arise. I agree to advise the principal investigator and then the relevant ethics committee should this occur. I confirm the organisation has sufficient indemnity insurance to compensate participants for harm that does not qualify for compensation under the Injury Prevention, Rehabilitation and Compensation Act 2001.

Signature:	M. Roberts	Date:	11/9/14
Name:	Dr Michael Roberts	Position:	Chief Medical Officer
Contact details:	Northland District Health Board, Private Bag 9742, Whangarei 0148		

Appendix I: HBDHB Locality Approval Letter – Study Two

Health Services

WHAKAWATEATIA

HAWKE'S BAY
District Health Board

18 November 2014

Institutional Approval

Mr Paul Davis
39C Ketenikau Road
Kamo
Whangarei 0112

Dear Paul

RE: Hawke's Bay District Health Board Research Application - Reference 13/11/181

Thank you for your application to conduct research within the Hawke's Bay District Health Board. The Research Office has had the opportunity to review your study and has given approval for your research project to be conducted within HBDHB.

This Institutional Approval is dependant on the Research Office having up-to-date information and documentation relating to your research and being kept informed of any changes to your study.

It is your responsibility to ensure you have kept Ethical Committees (as required) and the Research Office up to date and have the appropriate approvals. HBDHB approval may be withdrawn for your study if you do not keep the Research Office informed of the following:

- Any amendment to study documentation
- Study completion, suspension of cancellation

Conclusion of your Research
At the conclusion of your research you will be required to provide a written report of your research findings to the HBDHB Research Office.

Please find enclosed a signed copy of your application. Should you have any queries during your research, please do not hesitate to contact me during normal working hours.

Regards

Sally Houliston RN, BN, MN
Nurse Consultant
On behalf of the
HBDHB Research Office

Appendix J:AUTEC Approval Letter – Study Three

AUTEC
SECRETARIAT

29 January 2015

Graham Howie
Faculty of Health and Environmental Sciences

Dear Graham

Ethics Application: **15/04 Paramedic initiated helivac to tertiary hospital for primary percutaneous coronary intervention: A new approach in the treatment of ST-Elevation myocardial infarction patients.**

Thank you for submitting your application for ethical review to the Auckland University of Technology Ethics Committee (AUTEC). I am pleased to advise that the Chair and I have approved your ethics application subject to the following conditions:

1. Provision of authorizing signature for section F.3 of the application;
2. Provision of the evidence of St Johns support for the study.

Please provide me with a response to the points raised in these conditions, indicating either how you have satisfied these points or proposing an alternative approach. AUTEC also requires copies of any altered documents, such as Information Sheets, surveys etc. Once your response is received and confirmed as satisfying the Committee's points, you will be notified of the full approval of your ethics application. Full approval is not effective until all the conditions have been met. Data collection may not commence until full approval has been confirmed. If these conditions are not met within six months, your application may be closed and a new application will be required if you wish to continue with this research.

To enable us to provide you with efficient service, we ask that you use the application number and study title in all correspondence with us. If you have any enquiries about this application, or anything else, please do contact us at ethics@aut.ac.nz.

I look forward to hearing from you,

Yours sincerely

Kate O'Connor
Executive Secretary
Auckland University of Technology Ethics Committee

Cc: Paul Davis paul.davis@stjohn.org.nz

Appendix K: HDEC Approval Letter – Study Three

Health and Disability Ethics Committees

Health and Disability Ethics Committees
Ministry of Health
C/- MEDSAFE, Level 6, Deloitte House
10 Brandon Street
PO Box 5013
Wellington
6011

0800 4 ETHICS
hdecs@moh.govt.nz

23 December 2014

Mr Paul Davis
39C Ketenikau Road
Kamo
Whangarei 0112

Dear Mr Davis

Re:	**Ethics ref:**	**14/NTA/221**
	Study title:	Paramedic Initiated Helivac to Tertiary Hospital for Primary Percutaneous Coronary Intervention: A new Approach in the Management of ST-Elevation Myocardial Infarction Patients

I am pleased to advise that this application has been *approved* by the Northern A Health and Disability Ethics Committee. This decision was made through the HDEC-Expedited Review pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study's sponsor, to ensure that these conditions are met. No further review by the Northern A Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at *any* locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at *a given* locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

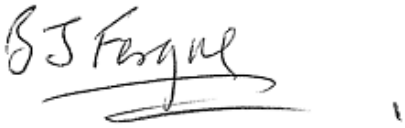
After HDEC review

Please refer to the *Standard Operating Procedures for Health and Disability Ethics Committees* (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your **next progress report** is due by **22 December 2015**.

Please don't hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,



Dr Brian Fergus
Chairperson
Northern A Health and Disability Ethics Committee

Encl: appendix A: documents submitted
appendix B: statement of compliance and list of members

Appendix L: St John Locality Approval Letter – Study Three

12 January 2015

Paul Davis
39C Ketenikau Rd,
Kamo
Whangarei 0112

St John
first to care

Study title: Paramedic Initiated Helivac to Tertiary Hospital for Primary Percutaneous Coronary Intervention: A new Approach in the Management of ST-Elevation Myocardial Infarction Patients.
St John reference: 0043

Dear Paul,

Your research study has undergone a locality review by St John, and I am pleased to inform you that your study is now authorised to go ahead subject to the conditions set out below.

Conditions
All final teaching material and assessment processes are required to be reviewed and authorised by either the Head of Clinical Practice (Dan Ohs) or the St John National Clinical Planning manager (Sarah Werner) prior to delivery.
Project reports must be submitted to St John on the following dates:

- 30 June 2015 Interim Progress Report #1
- 30 June 2016 Interim Progress Report #2
- 30 June 2017 Final Report
- The final report should be submitted at the completion of the study. This should be returned to St John within four weeks of the project completion. The date stated above is the anticipated final report date for this project. If this is to be extended please state this in the Interim Progress Report #1 and our records will be amended. The final report should provide a synopsis outlining the results and conclusions from the study.
- Please use the *OMF 4.9.8 Research Status Report* for report submissions.
- All researchers involved in the study are required to complete a copy of the *OMF 4.9.7 Research Memorandum of Understanding*.

Yours sincerely

Bridget Dicker

Dr Bridget Dicker, PhD
Clinical Research Fellow
National Headquarters

Appendix M:ADHB Locality Approval Letter – Study Three

Research Office
Level 14, Support Bldg
Auckland City Hospital
PB 92024, Grafton, Auckland
Phone: 64 9 307 4949 Extn. 23854
Fax: 64 9 307 8913
Email: mwoodnorth@adhb.govt.nz
Website: www.adhb.govt.nz/ResearchOffice

29th December 2014

Institutional Approval

Paul Davis
39C Ketenikau Road
Kamo
Whangarei 0112

Dear Paul

RE: Research project A+ 6476 (14/NTA/221) - Paramedic Initiated Helivac to Tertiary Hospital for Primary Percutaneous Coronary Intervention: A new Approach in the Management of ST-Elevation Myocardial Infarction Patients

The Auckland DHB Research Review Committee (ADHB-RRC) would like to thank you for the opportunity to review your study and has given approval for your research project.

Your Institutional approval is dependant on the Research Office having up-to-date information and documentation relating to your research and being kept informed of any changes to your study. It is your responsibility to ensure you have kept the Research Office up to date and have the appropriate approvals. ADHB approval may be withdrawn for your study if you do not keep the Research Office informed of the following:

- Any amendment to study documentation
- Any change to the ethical approval of the study
- Study completion, suspension or cancellation

More detailed information is included on the following page. If you have any questions please do not hesitate to contact the Research Office.

Yours sincerely

On behalf of the ADHB Research Review Committee
Dr Mary-Anne Woodnorth
Manager, Research
ADHB

c.c. Peter Ruygrok, Jim Stewart

Appendix N: Māori Consultation and Approval Letter

17 June 2014

To whom it may concern

Tena Koutou

Study Proposal:

New Zealand Paramedic-Based Systems of Care for ST-Elevation Myocardial Infarction Patients: Autonomous Delivery of Fibrinolytic Treatment and Cardiac Catheterisation Laboratory Referral.

I was appointed by the Chief Executive of St John in 2010 as Kaitohutohu (National Maori Advisor) to assist the organisation to provide culturally appropriate services to Maori. In this capacity, I have reviewed the above study proposal, discussed these with the principle researcher, Paul Davis, and provided advice on communication within Maori communities. The research will also be informed by Kawa Whakaruruhau Komiti at AUT University.

An initial study was completed by Mr Davis to assess whether or not New Zealand paramedics possess the pre-requisite skills and knowledge to permit autonomous decision-making for the delivery of fibrinolytic treatment under protocol guidance. The proposed study will design protocols, train paramedics and introduce new proactive approaches and strategies to facilitate early treatment for heart attack patients. The study will collect and analyse data on the treatment strategies and patient outcomes. It is likely that the new approaches will have positive and significant impacts for Maori who have the poorest cardiovascular health outcomes in New Zealand.

The study will collect ethnicity data, and the principles of the Treaty of Waitangi have been taken into account in the research methodology. The principle researcher will continue to draw on advice with and across St John on the Treaty of Waitangi and cultural matters as required to support his study. In addition, the researcher is reporting in early July to the Hui Whakapiripiri (sponsored by the Health Research Council) on the findings of his completed initial study. He will also provide a brief outline of his proposed study topics at the hui. Mr Davis plans to report the findings of the proposed study to Maori communities on their completion.

I fully support the proposed study and look forward to assisting Mr Davis on any Maori matters associated with his work program.

Hei kona ra

Miriama Evans

Miriama Evans

Kaitohutohu

Appendix O: Autonomous Paramedic Fibrinolytic Therapy Protocol

Attach NHI sticker here

St John

Autonomous Paramedic Fibrinolytic Therapy Form

Complete **ALL** sections of this form if fibrinolytic therapy is provided. Email the ACS code, ambulance job number, job date and patient surname to paul.davis@stjohn.org.nz within 24hrs. Ensure a photo is taken of this form within the ePRF, as well as photos of all 12-lead ECGs acquired.

1. Job Details			
Date		Patient's estimated weight (kg)	
Job number		Time of symptom onset	
Patient's surname		Time first 12-lead ECG acquired	
Patient's NHI number		Time of diagnostic STEMI ECG	
Patient's ethnicity		Time of fibrinolytic therapy	

2. Indications If the answer is **NO** or **UNSURE** to **ANY** of the following, do **NOT** administer the patient clopidogrel, enoxaparin or tenecteplase	**Yes**	**No**	**Unsure**
• 12-lead ECG with persistent ST-elevation ≥ 1mm in two or more contiguous limbs leads (I, II, III, aVL or aVF) **AND/OR** ST-elevation ≥ 2mm in two or more contiguous chest leads (V1-V6) as well as posterior leads (V7-V9)			
• Monitor interpretation indicates >>> Acute MI <<< **OR** ***ACUTE MI SUSPECTED*** **OR** ***MEETS ST ELEVATION MI CRITERIA*** on **two consecutive** 12-lead ECGs			
• Normal QRS width (≤ 0.12secs) **OR** Right Bundle Branch Block identified on 12-lead ECG			
• Heart Rate **<** 130 bpm			
• GCS 15			
• Symptoms consistent with myocardial ischemia of **<** 12 hours in duration			
• Patient located **> 60 minutes** transport time to a PCI-capable hospital from time of diagnostic ECG			

3. Contraindications If the answer is **YES** or **UNSURE** to **ANY** of the following, do **NOT** administer the patient clopidogrel, enoxaparin or tenecteplase	**Yes**	**No**	**Unsure**
• ≥ 85 years of age			
• Left Bundle Branch Block identified on 12-lead ECG			
• Prior intracranial haemorrhage or history of stroke			
• Uncontrolled hypertension - systolic BP > 180mmHg **AND/OR** diastolic BP > 110mmHg at any stage during current acute episode			
• Transient Ischemic Attack (TIA) within the last 3 months			
• Bleeding or clotting disorder (e.g. haemophilia)			
• Known cerebral disease, in particular - a malignant intracranial neoplasm, aneurysm or arteriovenous malformation (AVM)			
• Suspected aortic dissection (including new neurological symptoms)			
• History of significant closed head or facial trauma within the last 3 months			
• History of major trauma or surgery (including laser eye surgery) within the last 6 weeks			
• Internal bleeding (e.g. GI / urinary tract bleed) within last the 6 weeks (excluding menses)			
• Current use of anticoagulants (e.g. warfarin or dabigatran)			
• Prolonged (> 10 minutes) CPR			
• History of serious systemic disease (e.g. advanced / terminal cancer, severe liver or kidney disease)			
• Known to be pregnant or delivered within the last 2 weeks			
• Severe dependant living i.e. resident of an aged care facility requiring significant assistance with activities of daily living			

Attach NHI sticker here

4. Patient Consent

Formal written consent is not required for fibrinolytic therapy. However, the patient does need to be informed of the potential risks and benefits of fibrinolysis if you decide that the treatment is indicated. Inform the patient that they are having a 'heart attack'. Tell them that;

- This is due to a clot blocking one of the blood vessels that supplies part of their heart.
- We now want to administer a 'clot busting' drug.
- This clot busting drug is being given in an attempt to dissolve the clot. Dissolving the clot reduces the chance that they will die or be left with permanent heart damage.
- The earlier this clot busting drug is given, the more likely it is that it will work.
- Rarely this clot busting drug can cause bleeding, for example from wounds, into the bowel or into the brain. Very rarely this bleeding can cause death.
- There is good evidence that clot busting drugs are more likely to help the patient than to harm them.

5. Miscellaneous

For those patients less than 35 years of age, increased scrutiny should be applied due to the greater likelihood of STEMI mimics such as pericarditis or BER. **Extreme** caution should be exercised and if doubt exists regarding the suitability of fibrinolytic therapy - do not proceed with the treatment.

6. Paramedic Confirmation

I confirm that I have completed the indications and contraindications checklist for fibrinolytic therapy as outlined. Indications for the treatment are present and no contraindications to the treatment have been identified. I have read the patient consent section to the patient and they have verbally agreed to receive the treatment.

Name		**Officer Number**		**Signature**	

7. Treatment Procedure

Assuming standard care has been given as per the MYOCARDIAL ISCHEMIA section of the CPGs including aspirin:

Determine patient's age and weight

Age less than 75yrs

- Clopidogrel 300mg PO (4 x 75mg tablets)
- Tenecteplase IV (dose as per below)
- Enoxaparin 30mg IV (yellow pre-filled syringe)
- Enoxaparin SC (dose as per below)

	Tenecteplase IV		**Enoxaparin SC**	
Weight	Dose	Volume	Dose	Volume
< 60kg	30mg	6ml	60mg	0.6ml
60-69kg	35mg	7ml	70mg	0.7ml
70-79kg	40mg	8ml	80mg	0.8ml
80-89kg	45mg	9ml	90mg	0.9ml
>90kg	50mg	10ml	100mg	1ml

Age 75yrs or over

- Clopidogrel 75mg PO
- Tenecteplase IV (dose as per below)
- Enoxaparin SC (dose as per below)

	Tenecteplase IV		**Enoxaparin SC**	
Weight	Dose	Volume	Dose	Volume
< 60kg	15mg	3ml	45mg	0.45ml
60-69kg	17.5mg	3.5ml	50mg	0.5ml
70-79kg	20mg	4ml	60mg	0.6ml
80-89kg	22.5mg	4.5ml	70mg	0.7ml
>90kg	25mg	5ml	75mg	0.75ml

If you wish to seek advice for whatever reason, phone the St John clinical desk to speak to the on-call doctor.

8. Further Data

What is your interpretation of the patient's 12-lead ECG?

Were there any complications / issues encountered pre-hospital? If so, please describe.

Appendix P: Participant Demographic Questionnaire – Study One

Participant Demographic Questionnaire

Please complete the following questions by circling the correct answer:

1. **What is your sex?**

   Male / Female

2. **Which of the following age brackets do you fall within?**

   20-24 / 25-29 / 30-34 / 35-39 / 40-44 / 45-49 / 50-54 / 55+

3. **What is your current length of full-time paid employment service with New Zealand EMS?**

   0-5 years / 6-11 years / 12-17 years / 18-23 years / 24+ years

4. **What is your current clinical practice level?**

   EMT / BLS-Paramedic / ILS-Paramedic / Intensive Care Paramedic

5. **Which type of area do you predominately work in?**

   Metropolitan / Rural

6. **Have you successfully completed one of the recognised university based programmes required to obtain authority to practice as an ICP within New Zealand?**

   Yes / No

7. **Have you successfully completed the current ILS paramedic course?**

   Yes / No

8. **Are you a current practicing paramedic and have you successfully completed a paramedic-based tertiary level-7 cardiology paper?**

   Yes / No

9. **Have you successfully completed a BHSc paramedic degree programme?**

   Yes / No

Approved by the Auckland University of Technology Ethics Committee (AUTEC) on the 15/05/2012, AUTEC Reference Number 1294