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THROMBOLYTIC THERAPY FOR ACUTE MYOCARDIAL INFARCTION BY EMERGENCY CARE PRACTITIONERS

Raveen Naidoo

A dissertation submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfillment of the requirements for the degree of

Master of Science in Medicine

Johannesburg, 2014

DECLARATION

I, Raveen Naidoo, declare that this dissertation is my own work. It is submitted for the degree of Master of Science in Medicine at the University of the Witwatersrand, Johannesburg.



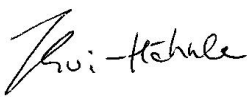
Candidate: _____ Date: 25 July 2014

I hereby certify that the studies contained in this dissertation have the approval of the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg.

Human Research Ethics Committee Protocol Number: M080822



Candidate: _____ Date: 25 July 2014



Supervisor: _____ Date: 25 July 2014

ABSTRACT

Background:

The earliest possible initiation of reperfusion therapy is necessary to reduce morbidity and mortality from acute STEMI. Therefore improving the time to thrombolysis where percutaneous coronary interventional facilities are limited or do not exist is critical. The most effective system would integrate three key components to deliver continuous patient care, including: 1) from time of call for help through to emergency response; 2) transportation to and admission to hospital; 3) assessment and initiation of thrombolytic therapy. The purpose of this prospective study is: to develop a chest pain awareness education programme appropriate for the South African context; to assess safe initiation of thrombolytic therapy by emergency care practitioners for STEMI; and to compare the performance of emergency care practitioner thrombolysis with historical control data.

Methods:

A document study was undertaken on existing chest pain awareness programmes (in international settings) that led to the development of a culturally sensitive and affordable chest pain awareness programme. An investigation was conducted in two international settings, where pre-hospital thrombolysis is within the scope of practice of advanced life support paramedics. This led to the development of best practice guidelines for pre-hospital thrombolysis in South Africa. The study population consisted of two groups of STEMI patients, namely: 20 patients

thrombolysed by the researcher (ECPT group); historical data obtained from previous research on 78 patients who were thrombolysed in-hospital by doctors (IHDT group). Demographic data and time to treatment complications encountered during hospital stay and at day 30 were recorded from patients' ambulance report forms, hospital records and 30-day telephonic patient interviews.

Results:

A poster, an information booklet and a video on heart attack awareness were developed after studying documentation from the United Kingdom, Canada, Australia and South Africa. The study population of 98 (100%) patients comprised 20 patients in the ECPT group and 78 patients in the IHDT group (73.5% of whom were males). The median age of the study population was 57.8 years, with a clear male dominance (73.5%). The majority of patients were of Indian origin (82.7%). Common conventional risk factors evident in all patients included smoking (56.1%), hypertension (52%) and diabetes (41.8%). The mean time from symptom on-set to thrombolysis for the ECPT group was 272 ± 79 minutes; the mean time from symptom on-set to thrombolysis for the IHDT group was 486 ± 373 minutes ($p = 0.055$). The mean door-to-needle time for the ECPT group was 124.9 ± 58.64 minutes; the mean door-to-needle time for the IHDT group was 288.01 ± 261.44 minutes ($p = 0.003$). The most common complications observed between the ECPT and IHDT groups during hospital stay and at 30-day follow-up included: cardiac failure (10.2% versus 12.2%); death (9.2% versus 7.1%); recurrence of angina (10.2% versus 6.1%); and recurrent myocardial infarction (1% versus 3.1%).

Conclusion:

If the goal for the future is defined as effective myocardial reperfusion within two hours of symptom on-set in all patients with STEMI, attempts to change the actions of individuals experiencing AMI symptoms should continue. While thrombolysis by emergency care practitioners offers a significant improvement in reducing symptom-to-needle time in treating STEMI, systems to facilitate various approaches need to be implemented. Prompt recognition of STEMI and shortening the time from first patient contact to initiation of thrombolytic drug therapy will most likely improve survival.

Keywords:

Acute myocardial infarction, heart attack, ST-elevation myocardial infarction, fibrinolysis, thrombolysis, pre-hospital thrombolysis.

DEDICATION

This dissertation is dedicated to all patients who willingly and selflessly participated in this study, despite their unfortunate circumstances.

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PUBLICATIONS AND PRESENTATIONS RELATED TO THIS STUDY

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OTHER PRESENTATIONS

Naidoo, R. 2009. Management of AMI in KwaZulu-Natal. KZN: Health Pietermaritzburg HOC Meeting.

Naidoo R. 2009. Heart Attack – Time is Heart Muscle KZN: College of Emergency Care & eThekwini Paramedic Guild. ALS Forum Meeting.

Naidoo, R. 2009. Heart Attack – Time is Heart Muscle. North Durban Doctors Guild, Mount Edgecombe Hospital.

Naidoo, R. 2009. Heart Attack – Time is Heart Muscle. Doctors' Clinical Forum, Wentworth Hospital.

Naidoo, R. 2009. Heart Attack – Time is Heart Muscle. Doctors Clinical Forum, McCords Hospital.

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CHAPTER IN BOOK

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NOMENCLATURE

1. Acute coronary syndrome (ACS)

Symptoms related to the obstruction of the coronary arteries.

2. Acute myocardial infarction (AMI)

Commonly known as a heart attack; it results from interruption of blood supply to a part of the heart and often results in myocardial death.

3. Advanced life support (ALS)

Provision of advanced life-saving emergency medical care that typically involves invasive techniques (such as advanced airway, ventilation and circulatory management).

4. Alert Voice Pain Unresponsive (AVPU)

The AVPU scale is a system by which a health care provider can measure and record a patient's responsiveness and which indicates the level of consciousness.

5. Aspirin (ASA)

Also known as acetylsalicylic acid, it is used: as an analgesic to relieve minor aches and pains; as an anti-pyretic to reduce fever; as an anti-inflammatory medication. It has an anti-platelet effect.

6. Baccalaureus Technologiae: Emergency Medical Care

A four-year degree qualification for advanced life support emergency care practitioners in South Africa.

7. Blood pressure (BP)

The pressure exerted on the walls of blood vessels by circulating blood - one of the principal vital signs.

8. Coronary care unit (CCU)

A specialised intensive care hospital ward dedicated to the care of cardiac patients.

9. Culturally sensitive

The South African population is made up of many different race groups, cultures, linguistic groups and ethnic groups. All require slightly different approaches to health care. To deliver complete health care requires awareness of these cultural differences: culturally sensitive care targets the entire person not just the physical ailment.

10. “call-to-needle” time

The time from on-set of pain to the time the patient is thrombolysed.

11. “door-to-needle” time

The time taken from the time the patient arrives at the hospital to the time of thrombolysis.

12. Electrocardiogram (ECG)

Electrical activity of the heart recorded by an external device over a period of time; it is detected by electrodes attached to the outer surface of the skin on the chest.

13. Emergency care practitioner (ECP)

Baccalaureus Technologiae: Emergency Medical Care (a four year degree). Qualified persons are registered with the HPCSA in the designated registration category Emergency Care Practitioner.

14. Emergency medical services (EMS)

A broad term for an emergency service dedicated to providing out-of-hospital acute medical care, transport to definitive care and other medical transport to patients with illnesses and injuries that prevent patients from transporting themselves.

15. Emergency Medical Rescue Services (EMRS)

The public sector ambulance service that provides an emergency pre-hospital healthcare service.

16. General practitioner (GP)

A medical doctor who provides comprehensive general medical care to patients.

17. Glucose measurement (GM)

Measurement of glucose levels using a blood or urine sample.

18. Glyceryl Trinitrate (GTN)

A drug used for the treatment of angina, acute myocardial infarction and severe hypertension.

19. Health Professions Council of South Africa (HPCSA)

The statutory body responsible for regulating health care professionals in South Africa.

20. Inkosi Albert Luthuli Central Hospital (IALCH)

A tertiary level hospital located in the Ethekwini Health District.

21. In-hospital

All activities undertaken after a patient is admitted to hospital.

22. Mahatma Gandhi Memorial Hospital (MGMH)

A district level hospital located in the northern sub-district of Phoenix, in the Ethekwini Health District.

23. Non-ST-elevation myocardial infarction (NSTEMI)

Acute myocardial infarction that does not present with ST segment elevation on an electrocardiograph monitor.

24. Paramedic

A Critical Care Assistant or someone with a National Diploma: Emergency Medical Care (3-year qualification). These are qualified persons registered with the HPCSA

in the designated registration category of Paramedic; they practice within the advanced life support scope of practice.

25. Phoenix (PHX)

A northern sub-district in the Ethekwini Health District.

26. Pre-hospital

All activities involving the patient outside the hospital environment.

27. Pre-hospital thrombolysis (PHT)

Thrombolytic therapy undertaken outside the hospital environment.

28. Primary hospital

The initial hospital the patient attends for medical treatment – usually within the same health district (district hospital).

29. Primary percutaneous coronary intervention (PPCI)

A surgical procedure that involves insertion of a catheter into a coronary artery.

30. Professional Board for Emergency Care (PBEC)

The professional board of the HPCSA responsible for the regulation of emergency care providers in South Africa.

31. Referral hospital

The hospital that the patient is referred to for further medical attention within the same health district (regional hospital).

32. Streptokinase (STK)

A first generation, effective and inexpensive thrombolytic agent used for acute STEMI and pulmonary embolism.

33. ST-elevation myocardial infarction (STEMI)

A myocardial infarction involving the full thickness of the heart muscle seen on an electrocardiograph monitor by ST segment elevation.

34. Subcutaneous (SC)

A subcutaneous injection is an injection in which a needle is inserted just under the skin.

35. Tenecteplase (TNK)

An enzyme used as a fibrin specific thrombolytic agent.

36. Thrombolytic / fibrinolytic agent

A pharmacological agent intended to breakdown fibrin with the use of enzymes.

37. Thrombolysis

The process of destroying or breaking up of a blood clot – thrombus.

38. Wentworth Hospital (WW)

A district level hospital located in the southern sub-district Wentworth of the Ethekwini Health District.

39. 30-day follow-up

The follow-up done on a patient 30-days after the patient has been discharged from hospital.

CHAPTER 1

BACKGROUND AND LITERATURE REVIEW

1.1 Introduction

1.1.1 Global burden of coronary heart disease

The World Health Organisation (WHO) reported that cardio-vascular diseases (mainly heart disease and stroke) cause approximately 17 million (30%) of the 58 million deaths that occur worldwide annually. Cardiovascular disease death rates (per 100 000) in the middle-age category (30-69 years) are: low in developed countries such as Canada (120) and United Kingdom (180); and high in developing countries like Brazil (320), China (280), Pakistan (400), Nigeria (410), Russia (680) and India (405) (1).

Coronary heart disease (CHD) is one of the leading causes of death internationally, with more than 60% of the global burden of CHD occurring in developing countries. CHD is decreasing in many developed countries, but is increasing in developing and transitional countries, partly as a result of increasing lifespan, urbanisation and lifestyle modification (2). WHO has predicted that heart disease and stroke will become the leading cause of death and disability worldwide, with the number of fatalities increasing to over 20 million per annum and to over 24 million per annum by 2030 (2). WHO statistics have also shown that CHD has the: highest mortality rates in high income countries (1.33 million,

16.3%); second highest rates in middle income countries (3.4 million, 13.9 %); is lowest in low income countries (2.47 million, 9.4%) (3).

1.1.2 South African burden of coronary heart disease

According the Medical Research Council (MRC) of South Africa, cardiovascular disease is the second leading cause of death (17%) in the list of ten leading causes of death in South Africa (4). Death from cardiovascular disease accounts for 15% of total deaths in KwaZulu-Natal (5). About 195 South Africans die each day from heart disease. Of these, acute myocardial infarction (AMI) is responsible for approximately 33 deaths per day and it is twice as prevalent in men as it is in women (6).

CHD has reached epidemic proportions amongst the White and Indian populations in South Africa (7). An analysis of CHD mortality for the period 1978 to 1982 showed markedly different rates for the Indian, White and Coloured population groups, namely: 780 per 100 000 for Indians; 688 per 100 000 for Whites; and 419 per 100 000 for Coloureds (8). Blacks were excluded from the analysis because of a lack of reliable data for this ethnic group (9).

In a study conducted on 2290 Indians admitted with acute coronary syndromes (ACS) to the R. K. Khan Hospital during a 6-year period (1996 to 2002), significant differences in risk factor status were found between genders as well as for different age groups (10). Twenty percent of these patients were $\leq$ 45 years old.

In addition, these patients revealed aggressive disease on angiographic studies, with 48% having triple vessel disease (TVD).

1.1.3 Epidemiological transition

In a recent study undertaken in KwaZulu-Natal, although the proportion of African patients was relatively low, 10 of 120 (8.3%), the data may herald the emergence of a new epidemic of coronary disease in the Black African population: 8.3% of the study cohort represents Black South African patients with STEMI only (11). Previous statistics reported at least 3 identified patients per annum approximately 50 years ago. This number increased to 5 about 25 years ago. The annual incidence of ACS among Black Africans in Soweto has increased rapidly. Between 1975 and 1980, 54 patients were diagnosed with AMI at Chris Hani Baragwanath Hospital in Soweto: in 2004 there were 64 new cases diagnosed with acute coronary syndromes (12-14). In a community awareness project conducted at several taxi ranks in Soweto involving 1691 participants, 78% of the so called 'healthy population' had more than one major risk factor for heart disease (15).

The recently published "The Heart of Soweto Study" reports 4 162 patients with cardiovascular disease presenting to the cardiology outpatient department and coronary care unit at Chris Hani Baragwanath Hospital during 2006. Of the 1 593 de novo cases, CHD occurred in 6% of the Black African population. Also in this registry, however, the prevalence of risk factors for CHD was high, with 87% having one risk factor or more (16). The INTERHEART investigators evaluated risk

factors for acute myocardial infarction in nine sub-Saharan countries and showed: the risk factors for myocardial infarction are the same, regardless of ethnic origin (17). However, Black Africans suffering myocardial infarction: were younger; had a lower rate of family history; had more single coronary artery disease; and the risk with hypertension and abdominal obesity was higher. This was in comparison with the overall INTERHEART group. The strongest risk factors were smoking and stress. The risk for myocardial infarction in Black Africans with a higher education and higher income increased - in contrast to the risk in Coloureds, Indians and Whites.

These observations raise the question of an epidemiological transition amongst the African population in a post-apartheid era (16). This is possibly due to urbanisation, change in the traditional Black African diet to a consumption of “fast food” (high in saturated fats) and the effect of emerging affluence due to economic growth in South Africa. This continued trend implies an additional burden on an already over-burdened health system.

1.1.4 Delays to definitive treatment

Prompt restoration of blood flow is the primary treatment goal in acute STEMI. It has been known for more than 20 years that a delay (between symptom on-set and treatment) of less than 60 minutes is ideal (18). There are three key components to the initiation of prompt and effective reperfusion therapy. Addressing patient delay would result in the overall symptom-to-needle time being

significantly reduced, e.g. by improving patient and bystander knowledge of symptoms, increasing utilisation of the ambulance service and addressing prolonged in-hospital treatment delays. The patient is probably the most important factor in the time delay between on-set of AMI and the start of reperfusion treatment. Patient delays have proven to be difficult to challenge as it requires a continuous education programme. Interventions to reduce delays have been met with limited success (19).

1.1.5 Reperfusion treatment for STEMI

Reperfusion therapy is a cornerstone of treatment for patients with acute STEMI (20). Several studies have demonstrated that acute STEMI can be aborted if reperfusion of the occluded coronary artery is achieved before the heart muscle is irreversibly damaged (21). Reperfusion is accomplished either: mechanically, by primary percutaneous coronary intervention (PPCI); or pharmacologically, by administration of a thrombolytic agent as soon as possible after diagnosis of STEMI (20, 22). Both methods: have been shown to be successful in the treatment of acute STEMI; have contributed significantly to a reduction in mortality; and have a Class IA recommendation from the European Society of Cardiology (22, 23).

Many randomised clinical trials have shown that PPCI is superior to thrombolytic therapy in the treatment of patients with STEMI (24). However, PPCI has several limitations, the most important of which is that it must be performed by an

experienced interventionist less than 2 hours from presentation of chest pain (25). Therefore, PPCI is typically offered only at specialist centers. Such facilities are not common in South Africa, especially in public sector hospitals.

Due to the limited availability of PPCI, pharmacological reperfusion therapy using thrombolytic agents remains an important therapeutic modality in the management of acute STEMI.

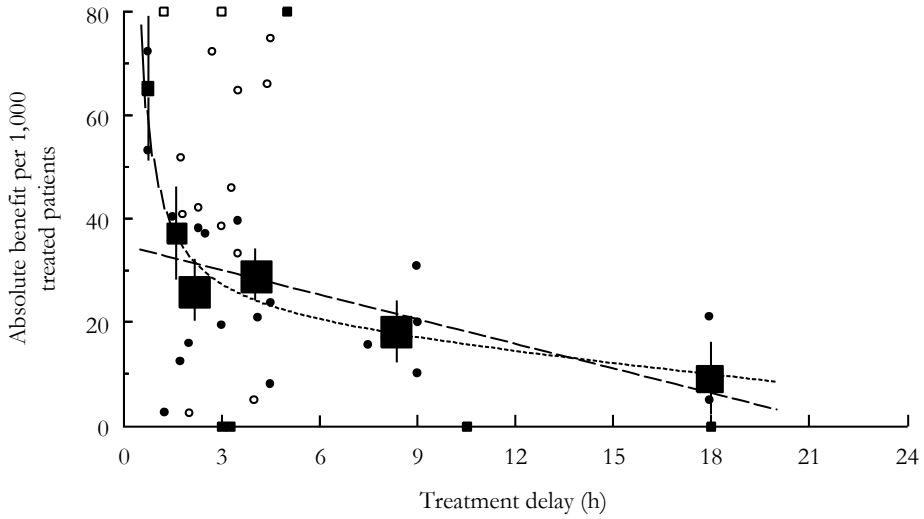


Figure 1: Time benefit curve

Source: (26)

Thrombolytic drugs must be administered rapidly after the infarction has started, as the benefit of treatment decreases rapidly as the time from clot formation increases. An overview of early randomised trials has shown that 65 lives can be saved per 1 000 patients treated if treatment is administered in the first hour ("the golden hour") after symptom on-set. This benefit is reduced to 29 lives and 20

lives saved for every 1 000 patients treated between 3-6 hour and 7-12 hour intervals after symptom on-set, respectively (Figure 1 above) (26).

Therefore, improving the time to thrombolysis is critical in the management of acute STEMI in order to reduce morbidity and mortality. Although many hospitals have improved their “door-to-needle” time to a practical minimum in recent years, further reduction in the “call-to-needle” time are essential to minimise the time to thrombolysis.

1.1.6 Justification of the study – South African context

There is currently limited data describing awareness, delays and application of definitive treatment for acute STEMI within South Africa. A study was conducted by the researcher as part of a Master of Science in Cardiology degree to assess the time interval from first patient contact to initiation of thrombolytic treatment and possible reasons for treatment delay in patients presenting with acute STEMI. The study population comprised 120 patients with acute STEMI, presenting to 20 different hospitals in Durban and surrounding regions during the period August to December 2006. Demographic data, time to treatment, reasons for non-treatment and complications encountered during hospital stay and at day 30 were also obtained from hospital records and patient interviews.

This study showed that of the 120 patients: 65% were thrombolysed; at least 45% of these patients being thrombolysed within 6 hours of on-set of symptoms. The

time to definitive treatment from symptom on-set for all patients was: 55 (45.8%) treated within 6 hours; 85 (70.8%) treated within 12 hours; and 35 (29.2%) treated in the greater than 12 hour category. This suggests an overall delay in treatment of patients. In a sub-group analysis, the treatment time frame for patients thrombolysed 78 (65%) was: 42 (35%) up to 6 hours; 60 (50%) up to 12 hours; and 18 (15%) in the greater than 12 hours category. These proportions are not in keeping with trends in other settings: the United Kingdom Myocardial Infarct National Audit Plan database shows: more than 75% of patients were treated within 6 hours; approximately 7% of patients treated in the category 'greater than 12 hours' from symptom on-set (27). It is a Class I recommendation that thrombolytic therapy be initiated within 12 hours, although it may be appropriate to initiate thrombolysis after 12 hours (Class IIa) (especially in young patients and patients with persistent chest pain that indicates the possibility of a collateral blood supply in the infarcted area or ante-grade flow (20, 28-30)). In the Second International Study of Infarct Survival, Streptokinase reduced mortality when given 13 to 24 hours after the on-set of pain (31). Furthermore, of the 120 patients, 42 (35%) were not thrombolysed and of these 37 (88.1%) were outside treatment time for thrombolytic therapy. The mean time to definitive treatment from symptom on-set was 8.36 ± 5.57 hours, which constitutes a major delay when compared to the symptom-to-needle time recommendation of less than 60 minutes (22).

The patient delay often constitutes the longest period to delay to treatment (32). The mean time taken for the patients to summon help was 3.32 ± 5.26 hours, as shown in the researcher's previous study (11). Many patients reported that they

were not sure was causing the pain and did not think that it was serious. General practitioner referral to hospital of a total of 30 (25%) patients took a mean of 0.37 ± 1.31 hours. None of these patients were thrombolysed by the general practitioners. The mean time taken to transfer patients to a regional hospital by the primary hospital was 7.05 ± 4.58 hours. It took a mean time of 5.18 ± 6.36 hours for patients to receive definitive treatment at a regional hospital. This delay is unacceptable, considering that the international recommendation for time to thrombolysis in hospital is less than 30 minutes (30).

While the reasons for delay to treatment within the hospital environment are not within the scope of this study, most patients reported long waiting periods in the emergency department. The ambulance transport and private vehicle transport times were not analysed because this data was not always recorded. It would have been beneficial to assess: mean time of ambulance arrival from time of ambulance notification; mean ambulance transport time from patient pick up point to hospital; and the contribution of these times to treatment delay. This could be especially important in rural areas where there are lengthy transportation times.

The majority of patients that were not thrombolysed were in the ‘greater than 12 hours’ category (17 (14.2%)), with a further 12 (10%) of patients being in the 6 to 12 hour category. The main reason why patients did not receive thrombolysis was patients being outside the treatment period.

A retrospective review of case notes was conducted by Roshan et al (33) from January 2008 to July 2010 of all patients receiving thrombolytics for AMI in the emergency centres of three Cape Town hospitals. The total door-to-needle time was calculated and the following analysed: patient demographics and presentation, physician qualification, clinical symptomology and reasons for delays in thrombolytic administration.

The findings of this study showed that of 161 acute STEMI patients, the median door-to-needle time achieved was 54 minutes (range 13 - 553 minutes). Also seen was: door-to-needle time of 30 minutes or less achieved in 33 (20.5%) patients; 51.3% of patients arrived by ambulance; 34% of patients had a pre-hospital 12-lead ECG; and 88.8% had typical symptoms of myocardial infarction. This study concluded that a significant number of patients were not thrombolysed within 30 minutes of presentation.

The findings of these South African studies show there is a prolonged time to treatment in each component, that is: the patient, the general practitioner, the primary hospital and the regional hospital. This results in either non-thrombolysis or delayed thrombolysis.

From the findings of these studies it can be extrapolated that one possible strategy to reduce symptom-to-needle time would be to implement thrombolysis by emergency care providers and utilise emergency medical services. The overall

symptom-to-needle time could be significantly reduced in all components, affecting definitive treatment with effective use of the emergency medical services.

1.1.7 Purpose of this study

The purpose of this prospective study is to develop a chest pain awareness education programme through document analysis and to safely initiate thrombolytic therapy by ECPs in order to help reduce morbidity and mortality from acute STEMI.

1.1.8 Objectives of this study

The objectives of this study are to:

1. Develop a culturally sensitive and affordable chest pain awareness education programme.
2. Plan, design, implement and evaluate thrombolysis for acute STEMI by emergency care practitioners.
3. Assess the performance of a developed treatment algorithm in 20 patients and compare this to own historical control data.

1.1.9 Critical questions answered by this research

1. What chest pain awareness education programmes exist nationally and internationally?

Through a literature search and document analysis, this question aims: to determine if such programmes do exist; and to seek guidelines from existing material to inform the development of a programme that will be sensitive to South African needs.

2. What education programmes exist nationally and internationally for pre-hospital management of acute STEMI (with particular emphasis on thrombolysis)?

   The aim of this question is to determine whether South African education programmes for the management of acute STEMI are of adequate levels compared to established international programmes. This will lead to the development of an educational programme and an evidence-based protocol for implementation within South Africa.

3. How long does it take for a patient to call for help from the on-set of symptoms?

   This question aims to determine the influence of patient awareness on time to definitive treatment.

4. How long does it take for the patient to receive definitive treatment?

   The aim is to determine the extent to which location, transportation and in-hospital factors impact on time to definitive treatment.

5. What is the impact of ECP thrombolysis on 30-day morbidity and mortality outcomes?

   The aim is assess the impact of ECP thrombolysis on patient morbidity and mortality outcomes at 30 days post-acute STEMI.

1.2 Literature review

1.2.1 Delays to definitive treatment

Delay time is usually defined as the total time taken from first awareness of symptoms to initiation of definitive treatment; it is divided into three phases of delay: patient/bystander recognition; pre-hospital; and in-hospital. The total pre-hospital delay period consists of two components: time taken by patients to recognise that their symptoms are serious and to contact medical help (decision time); and the time taken from requesting help to hospital admission (home-to-hospital delay). Various factors may affect the recognition of symptoms and time taken to hospital admission (34). Pre-hospital delays, however, remain unacceptably long with median intervals averaging 2 to 4 hours (35-38).

Patient-associated delays from on-set of symptoms (suggestive of AMI) to hospital arrival affect the timely receipt of reperfusion interventions and (potentially) the post-discharge outcomes associated with AMI. The following are some of the numerous studies done on time from symptom on-set to hospital arrival, which have reported considerable variation.

The REACT trial was a multi-centre, randomised community-based trial designed to reduce patient delay (during a baseline period from December 1995 to March 1996). Data from 3 783 hospital records of patients hospitalised for AMI symptoms in 20 communities were analysed. The median pre-hospital delay in patients

hospitalised for evaluation of heart attack symptoms was 2.0 hours, with 25% of patients delaying longer than 5.2 hours. Delay was: longer for Blacks than for Whites; longer in older age groups; and shorter in patients who were transported to hospital by ambulance. The findings of this trial supported the notion that demographic, cultural and socio-economic barriers impact on timely hospital presentation (39).

The results of the Worcester Heart Attack Study (35) (a population based study) suggest that a large proportion of patients with AMI continue to exhibit prolonged delay. This longitudinal study of 3 837 residents with AMI in Worcester examined trends in time to hospital presentation and the factors associated with prolonged delay. The mean, median and distribution of delay times showed either inconsistent or no changes over the study period. In 1986, the mean and median pre-hospital delay was 4.1 and 2.2 hours respectively. Just over a decade later (in 1997) these times were 4.3 and 2.0 hours respectively. No significant differences were noted over the study period. Approximately 44% of these patients presented to hospital within 2 hours of on-set of symptoms of AMI. In the 1997 study year, a delay of more than 2 hours was associated with increasing age, pre-existing angina or diabetes and on-set of symptoms in the afternoon or evening. While the socio-demographic characteristics of this study generally represented the population of the United States, the results could not be generalised as the majority of the population in the Worcester Study were White.

A study done in Glasgow in the United Kingdom sought to determine: reasons for delay in calling for help during AMI; and reasons for choice of first medical contact. The study involved a review of medical records and one-to-one semi-structured interviews. Of the 313 patients included in the study: 25% called for help within one hour of symptoms; 41% did so within two hours; 60% did so within four hours; 20% delayed calling for help for more than four hours; while 12% of the patients exceeded 24 hours i.t.o. time to summon help. The most common reasons for the delay were: patients did not recognise the pain as cardiac in origin; they did not regard the pain as serious and thought that it would go away. Only 25% of patients made the first call for medical help to the ambulance services; 55% called their general practitioner; and 20% of patients self-presented to the nearest hospital emergency department (40). The study was done in an area where there was an established general practitioner service. The data collection methods were reasonable and the inclusion of a semi-structured interview made provision for data that might have been missing in patient records.

A number of other United States of America and European studies published between 1969 and 1987 found that median pre-hospital delay times ranged from 2.5 hours to 7 hours (41). In different registries of patients with STEMI, the time from symptom on-set to hospital presentation was ≥ 4 hours in 50% - a value that has changed very little from 1987 to 2000 (38).

Perkins-Porras et al (42) collected patient delay data on 228 patients with ACS from patient hospital records and through semi-structured interviews. The results

of the study showed that shorter total pre-hospital delays and decision times were associated with STEMI, early recognition of symptoms as cardiac in origin, being married, symptom on-set outside the home and the presence of a bystander. Shorter home to hospital delays were more likely among: younger patients; those experiencing STEMI; and patients with a greater number of symptoms. Shorter delays and decision times were also noticed for patients who utilised the emergency medical service. This study corroborated the findings of other studies in that various factors were associated with shorter times in the decision time and in the home to hospital components (43). The study concluded that greater understanding of these factors may help target interventions more effectively to reduce pre-hospital delays.

There is currently limited data describing delays and the application of definitive treatment for acute STEMI within Africa. In a study done in Morocco, an analysis of a register for 2 566 patients admitted with unstable angina or AMI showed that the mean time from on-set of chest pain to hospital admission was 111 ± 38 hours. This study identified problems relating to transportation from home to hospital; concluding that patient awareness of chest pain, organised transportation and reducing waiting time in the emergency room were central to national policy development to shorten time to definitive treatment (44). In a multi-national survey involving 3 North African countries (Algeria, Morocco and Tunisia) 42% (419/989) of acute STEMI patients did not receive any form of reperfusion therapy (45). The study did not assess the reasons for non-initiation of reperfusion therapy.

In a local study undertaken in KwaZulu-Natal (11), significant delays were noted in overall symptom-to-treatment time with delays in all components, i.e.: time taken for patients to call for help' time taken by the general practitioner to refer a patient to hospital; time taken by the primary hospital to transfer a patient to a regional hospital; and time taken for patients to receive definitive treatment at a regional hospital; however, this study did not assess the reasons for delay in the individual components.

In a more recent retrospective analysis done in Cape Town, South Africa on 238 eligible acute STEMI patient records: 77 (32%) did not receive thrombolysis; of which 49 (64%) missed the thrombolytic window. Only 33 (20.5%) of the 161 patients thrombolysed were treated within the recommended 30 minutes door-to-needle time due to: a lack of senior doctors; difficulty in interpreting ECGs; atypical presentation; and system delays (33).

1.2.2 Patient delay in symptom recognition

Many patients may not be aware that they are having a heart attack and often dismiss the symptoms as indigestion or heartburn (46, 47). A number of factors were associated with the patients' decision time, including: the type of acute coronary syndrome; the nature and localisation of the symptoms; the area where the symptoms occurred; the patient's interpretation of symptoms; and knowledge of AMI (48). Many patients believe that the AMI starts suddenly and dramatically with severe chest pain (49).

In a telephone interview of 2 316 patients conducted in King County, Washington, the main reasons for delay were because: the patient thought the symptoms would go away; the symptoms were not severe enough; and the patient thought that the symptoms were caused by another illness (50).

In a study conducted by Perry et al (36), the pre-hospital delay time was closely related to the mismatch between expected and experienced symptoms. Delay was reduced when the patient conversed with someone about the symptoms during symptom on-set. The data from this study suggested the need for a public education programme on symptoms of AMI - not only to individuals at risk, but also to the general public, given the critical role of another person in facilitating the decision to seek help timeously.

Another study, conducted from September 2004 to March 2005, aimed to obtain a deeper understanding of how AMI patients and their relatives think and act during and after on-set of symptoms; this through six focus group interviews. The results revealed that AMI patients experienced a variety of symptoms and both patients and their relatives were unsure about the origin of the symptoms. Both parties interpreted the symptoms as being less serious and tried to self-remedy the discomfort. Patients sought the assistance of family members only when the symptoms persisted. An important recommendation from this study was that the

public and AMI patients and their relatives should be given information about AMI symptoms and the recommended action to be taken (51).

1.2.3 Impact of age, gender, socio-economic factors, existing clinical conditions and ethnic group on patient delay

Delay is greatest in: the elderly; the low socio-economic and ethnic minority groups; and in those whose symptoms occur between 6 pm and 6 am (39, 52).

While some studies have shown that increased age is associated with longer pre-hospital delay (53, 54), others did not find any statistical significance of the influence of age on delay (49, 55). Early explanations for delay in presentation by women were related to perceptions of the prevalence of coronary heart disease in women in general (56). More recent studies have shown that there is no major gender difference in pre-hospital delay or type of symptoms; but musculo-skeletal symptoms, the experience of symptoms and how these are interpreted and assessed have a stronger impact on men than on women (57-59).

Data obtained from the Northern Sweden MONICA myocardial infarction registry also showed that older patients (65-74 years) - and more prominently women - had a longer delay and less typical symptoms (59). Data was used from the Cooperative Cardiovascular Project, which involved beneficiaries of a funded medical system who were: aged > 65 years; hospitalised with a confirmed AMI between January 1994 and February 1996. This was to identify patients who

presented “late” to hospital, that is, ≥ 6 hours after symptom on-set. Of 102 339 patients, 30 087 (29.4%) arrived late, while 11 905 (11.6%) presented within 6 to 12 hours and 18 213 (17.8%) arrived after 12 hours. Significant predictors of late arrival included diabetes, and a history of angina; prior AMI, angioplasty, bypass surgery and cardiac arrest predicted early presentation. In addition, initial evaluation at a clinic and presentation during the day predicted late arrival. Other risk factors for delay were female gender and Black ethnic group. (54). This study reported that poverty was a significant determinant of prolonged pre-hospital delay. Similarly, Okhravi (60) found that patients who delay for more than six hours from symptom on-set had a low income and low education level.

Data on impact of age, gender, socio-economic factors, existing clinical conditions, race and ethnic group on patient delay in South Africa is not available, as this is an under-researched area. The South African population is made up of many different race groups, cultures, linguistic groups and ethnic groups, which may require slightly different approaches to health care in general. To deliver complete health care, and more specifically, to address reasons for patient delay, sensitivity to these factors must be considered when designing and implementing awareness programmes.

1.2.4 Transport delay

International guidelines suggest activation of emergency medical services (EMS) by patients or bystanders for patients with symptoms consistent with AMI (61).

Activating the EMS is a rapid and effective means of obtaining medical care.

The use of EMS:

1. Leads to faster receipt of initial reperfusion interventions (62).
2. Facilitates early alerting of the receiving hospital. This results in shorter treatment delay as clinical decisions to treatment and preparation thereof can be made more effectively (63, 64).
3. Most ambulances or EMS systems are equipped with defibrillators and paramedics who are trained to advanced life support levels, thereby increasing the chances of survival should cardiac arrest or life-threatening arrhythmias occur (61).
4. Reduces long waiting periods in queues at the presenting hospital when the patient self-presents. With the use of EMS, the patient is handed over from one health care professional to another (65, 66) .

Despite these advantages, only 40% to 60% of patients with AMI choose to initiate emergency medical care by using EMS (38, 67, 68). In the National Registry of Myocardial Infarction 2, just over half (53%) of patients with STEMI were transported to the hospital by ambulance (62). In KwaZulu-Natal, EMS use is even lower. In a study undertaken by the researcher (11), the majority of patients (105 (87.5%)) were transported to hospital privately, while only 12 (10%) utilised ambulance services. This figure is low compared to other studies (38, 68). This local study also demonstrated that time to treatment for the ambulance group

resulted in quicker initiation of definitive care - on average 2 hours and 45 minutes. These findings are similar to those of a study undertaken by Hutchings et al (65), where transportation by EMS resulted in shorter elapsed time to thrombolytic administration compared with patients using private transportation. The door-to-needle time to definitive treatment in the EMS transported group versus private transportation was 32 versus 49 minutes respectively ($p = 0.01$); and the time from decision to seek care until definitive treatment was 75 versus 92 minutes respectively ($p = 0.042$) (65).

The belief that self-transport is faster or the perception that symptoms are not serious enough is the response that leads people not to choose an ambulance (50, 67).

In Sweden, a national observational study was conducted in 11 hospitals between April 2001 and February 2003 to define the factors influencing the use of an ambulance by patients with AMI. A little more than half ($n = 958$) of the patients went to hospital by ambulance. Symptoms, patient characteristics, ACS characteristics, and perceptions and knowledge were associated with ambulance use in AMI. Patients who did not call for an ambulance thought self-transportation would be faster and did not believe that they were sick enough (69). A substantial number of patients do not call for an ambulance as their first medical contact after on-set of symptoms of AMI. A public education programme on the benefits of ambulance transportation and early treatment is required.

1.2.5 General practitioner delay / primary hospital delay

Further delays in time to reperfusion treatment occur when patients seek help from general practitioners and at local clinics and local hospitals that do not provide thrombolytic therapy (11, 70, 71). In-hospital delays are due to: lack of capacity; delay by the doctor; delay with acquisition of the drug; and overall system admission to treatment delays.

A study was conducted at Vancouver General Hospital to evaluate in-hospital door-to-needle time for thrombolysis for acute STEMI and the factors associated with time prolongation through a retrospective chart review. 140 patients were included in the study. A door-to-needle time of less than: 30 minutes was achieved in 24.3% of patients; 30 to 40 minutes in 24.3%; 40 to 60 minutes in 22.1%; and > 60 minutes in 29.3%. A number of in-hospital factors identified that further delayed the time to delivery of thrombolytic therapy included: delay from arrival to patient admission; delay from time of admission to initial evaluation of patient; delay from time of obtaining and interpreting the electrocardiogram to ordering the drug; and delay from time of ordering the drug to administration of the thrombolytic agent (66).

The South African District Health System (72) lends itself to significant delays in receiving reperfusion treatment as: most of the district level hospitals initiate

thrombolytic treatment inconsistently; all district and regional hospitals do not have PPCI facilities.

1.2.6 Public awareness education programmes for AMI

Based on an understanding of the factors that influence pre-hospital delay, it is important to implement public awareness programmes that focus on the importance of early symptom recognition and quick call for assistance. Early attempts to change the actions of individuals experiencing AMI symptoms did not produce encouraging results. Despite several expensive public education media campaigns to reduce delay, individuals suffering AMI symptoms still delay their decision to seek treatment (19, 73, 74). A study conducted by Ho et al (73) showed that a short-duration education campaign may increase knowledge of AMI, but does not significantly shorten patient delay in seeking care. However, individual education and counselling programmes aimed at those at high risk for AMI, or those who have had an AMI, have produced more positive results in changing health behaviour (75-77). Randomised control trials, designed to test whether an intervention designed specifically for patients with ACS via a one-on-one delivery mode, found that the education and counselling intervention did not lead to reduced pre-hospital delay or increased ambulance use (78, 79). As the aim of such programmes is a reduction in delays and promoting appropriate management for AMI, programme content should focus on: awareness and recognition of symptoms; the importance of seeking help quickly by calling for an ambulance or notifying a family member (80).

Studies aimed at increasing public knowledge of warning signs of stroke have shown that high intensity programs and use of television rather than newspapers increased knowledge and the need to call emergency medical services for specific symptoms (81, 82).

In South Africa, awareness programs driven by non-governmental organizations like September Heart Awareness Month and Think RED campaigns focus on risks and prevention of cardiovascular disease. Some programmes like those on the National Department of Health website brief ly mention symptoms of heart attacks, lacks the action to be taken by the individual and the use of EMS. However a program that focuses on awareness and recognition of symptoms; the importance of seeking help quickly by calling for an ambulance or notifying a family member and use of emergency number is non-existent. Almost two decades of political transition in South Africa has seen a rise in non-communicable diseases like cardiovascular disease, type 2 diabetes, cancer, chronic lung disease and depression. Prevention and treatment of non-communicable diseases are currently marginalised in South Africa, possibly due to the overwhelming prevalence and increase in communicable diseases like HIV, AIDS and tuberculosis (4, 83).

1.2.7 Reperfusion therapy

Several studies have demonstrated that acute STEMI can be aborted if reperfusion of the occluded coronary artery is achieved before the heart muscle is irreversibly damaged (21, 84). Injured but viable myocytes are potentially salvageable if an adequate blood supply can be re-established after acute coronary occlusion. The goals of reperfusion therapy, therefore, would be to limit the infarct size and prevent future infarctions - and thereby improve patient survival (85). Reperfusion is accomplished either mechanically (by percutaneous coronary interventions (PCI)) or pharmacologically (by the administration of a thrombolytic agent) as soon as possible after confirmation of diagnosis of STEMI (Figure 2) (22). Regardless of mode of reperfusion, early treatment, especially within the first 'golden hour', has a significant mortality benefit (22, 86, 87).

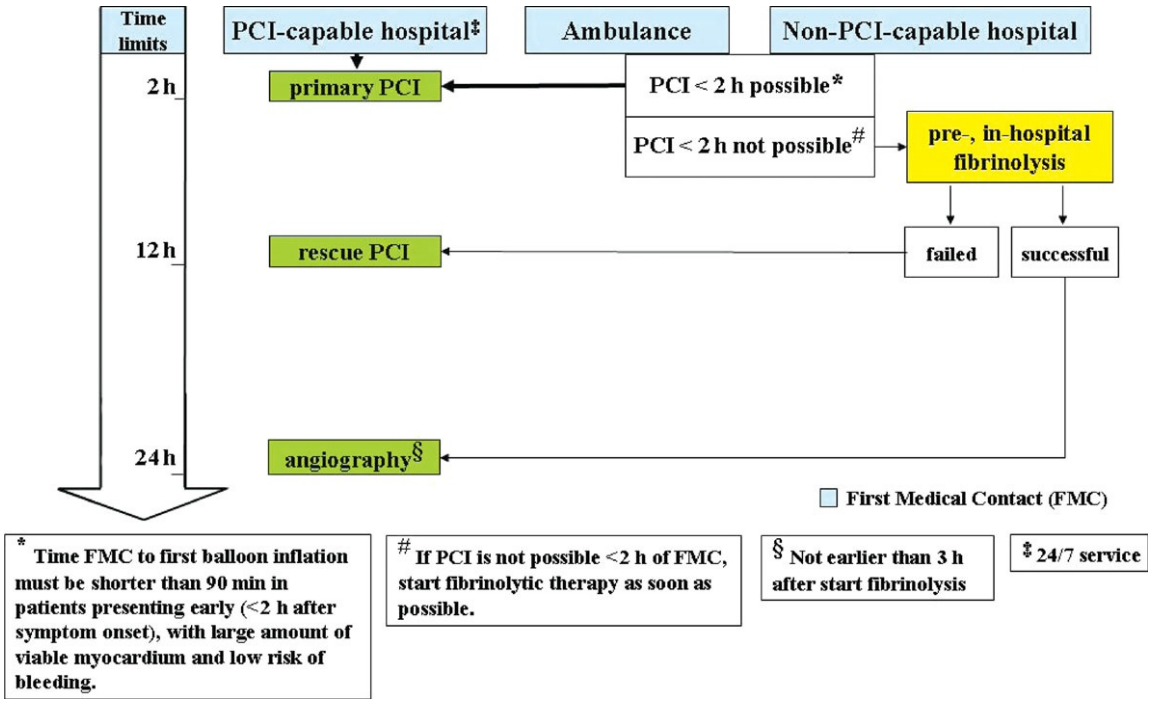


Figure 2: Reperfusion strategies

Source: (22)

1.2.7.1 Percutaneous coronary interventions

The role of PCI during the first hours of management of acute STEMI can be divided into: primary PCI; PCI combined with pharmacological reperfusion therapy; and “rescue PCI” after failed pharmacological reperfusion (88). Primary PCI is the preferred therapeutic option when it can be performed by an experienced team within two hours (25, 89).

A meta-analysis of 23 randomised trials undertaken by Keeley (87), which assigned 7 739 thrombolytic-eligible patients with STEMI to either primary PCI or thrombolytic medication, revealed that primary PCI was better than thrombolytic therapy at reducing: overall short-term (4-6 weeks) death (9.3% versus 7.0%, $p = 0.0002$); non-fatal re-infarction (6.8% versus 2.5%, $p < 0.0001$); total stroke (2.0 versus 1.0%, $p = 0.0004$); and the combined endpoints of death, non-fatal re-infarction and stroke (14.5 versus 8.2%, $p<0.0001$). During long-term follow-up (6-18 months), the results seen with primary PCI remained better than those seen with thrombolytic therapy with: 12.8% versus 9.6% for death; 10.0% versus 4.8% for non-fatal AMI; and 19% versus 12% for the combined endpoints of death, non-fatal re-infarction and stroke.

However, primary PCI has several limitations, the most important of which is that it must be performed by an experienced team timeously after presentation of chest

pain. An experienced team not only includes interventional cardiologists, but also skilled support staff (89). Other limitations include: major bleeding from the femoral artery access site; the need for vascular repair; and acute renal failure (87).

Therefore, primary PCI is typically restricted to hospitals with established interventional cardiac specialist centers that use primary PCI as a routine treatment option for patients presenting with signs and symptoms that suggest acute STEMI. Centres with a high volume of PCI procedures have demonstrated lower mortality rates (90, 91). Fewer than 1 in 5 hospitals in the United States and 1 in 10 hospitals in Europe have cardiac catheterisation facilities; and even fewer hospitals are equipped to perform primary PCI on a full-time emergency basis (24).

Such facilities are lacking in South Africa, especially in public sector hospitals. As an example, the province of KwaZulu-Natal has just one public sector hospital (Inkosi Albert Luthuli Academic Hospital (IALAH)) with such facilities. KwaZulu-Natal is an area of approximately 94 500 square kilometres, with a population of approximately 9 924 000, i.e. a population density of approximately 105 people per square kilometre (92). According to the latest mid-year estimates released by Statistics South Africa in 2011 (93), KwaZulu-Natal has the second largest share of the South African population: 10.8 million (21.4%) of 50.5 million. IALAH is a referral hospital and it is conceivable that a patient requiring PCI may only be attended to after 24 hours of first symptoms.

1.2.7.2 Pharmacological reperfusion

Due to the limited availability of PPCI, pharmacological reperfusion therapy using thrombolytic agents remains the most important therapeutic modality and the most utilised form of reperfusion therapy worldwide in the management of acute STEMI. Timely thrombolytic therapy can re-establish coronary flow and salvage jeopardised myocardium. Thrombolytic drugs must be administered rapidly after the infarction has started, since the benefit of treatment decreases rapidly as the time from clot formation increases.

The introduction of thrombolytic therapy in the late 1950's was a major advance in treatment of acute STEMI. It was not until a meta-analysis of smaller studies undertaken in the 1980's that a significant mortality benefit was suggested (94). Interest in thrombolytic therapy developed in the mid-1980's, when it became possible to assess the effectiveness of thrombolytic therapy with angiography (95-97).

Large randomised clinical trials have clearly demonstrated a statistically significant mortality benefit with thrombolytic therapy. The first large scale trial, GISSI -1 Trial (18), conducted over 17 months, randomly assigned 11 712 patients suspected of acute STEMI within 12 hours of symptoms, to either Streptokinase (STK) or standard treatment. In-hospital mortality at 21 days was: 10.7% in the STK group and 13% in the control group - a 17.6% risk reduction ($p = 0.0002$, RR = 0.81). A

follow-up study demonstrated that improved survival was sustained at 1 - 2 years. The large sample size (drawn from more than 175 coronary care units) makes the results of this study statistically significant and generalisable; however, this was not a blind study, which may have led to treatment bias.

The Fibrinolytic Therapy Trialists (FTT) Collaborative Group (98) undertook a meta-analysis of nine major randomised trials that had more than 1 000 patients each (totalling 58 600 patients), with a view to determining the safety and benefit of thrombolytic therapy in a wide variety of patient sub-groups. The results showed that treatment was helpful regardless of the following: gender; if systolic blood pressure was less than 180 mm Hg; previous AMI; or diabetes mellitus. Therapeutic benefit was noted when administration was initiated for up to 12 hours after first symptoms, but was greatest when administered within 3 hours. Approximately 30 early deaths were prevented per 1 000 patients treated; and if treated between 7 and 12 hours after symptom on-set, 20 deaths were prevented per 1 000 patients treated. The FTT Group found a 'straight-line relationship' between absolute mortality and time to treatment from on-set of symptoms. The large size of the FTT Collaborative Group database provided the statistical strength to analyse the benefits of thrombolysis in sub-sets of patients.

An overview of 22 randomised trials undertaken between 1983 and 1993, which included 50 246 patients, showed that 65 lives per 1000 patients treated can be saved if treatment is administered in the first hour after symptom on-set ("the golden hour"). This benefit is reduced to 29 lives and 20 lives saved for every 1

000 patients treated at the first 3 – 6 hours and 7 - 12 hour intervals after symptom on-set, respectively (26). This study demonstrated that the benefit/time regression line was non-linear: steep to start and then tapering off after 2 hours. Furthermore, twice as many lives were saved when thrombolytic therapy was started within the first hour of on-set of symptoms, in comparison with the 7 to 12 hours (44% versus 20%).

The GUSTO-I study (99) comprised four treatment groups with approximately 10 000 patients in each. The trial was designed to compare new thrombolytic regimes, consisting of the use of: Streptokinase and subcutaneous Heparin; Streptokinase and intravenous Heparin; accelerated tissue plasminogen activator (t-PA); and intravenous Heparin or a combination of Streptokinase plus t-PA. Regardless of thrombolytic strategy used, the study demonstrated the importance of early thrombolysis on the 30-day mortality primary end-point of the study. When thrombolytic agents were given less than 2 hours after on-set of pain, there was a 30-day reduction in mortality of 5,5%, as opposed to 9% if administration was delayed for more than four hours.

More than 50 000 patients have been randomised in trials comparing various thrombolytic agents to a placebo or control and it was shown in the meta-analysis that when these agents are administered early, the benefit is substantially higher (26). Therefore, improving time to thrombolysis is critical in the management of acute STEMI in order to reduce morbidity and mortality. Although many hospitals have, in recent years, improved their “door-to-needle” time to a practical minimum,

further reductions in “call-to-needle” time are essential to minimise the time to thrombolysis.

1.2.8 Pre-hospital thrombolysis

Pre-hospital thrombolysis is well-established in developed settings internationally. Research in pre-hospital thrombolysis is on-going. A large international pharmaceutical company is currently conducting a study called STREAM (Strategic Reperfusion Early After Myocardial Infarction) in 112 locations worldwide. This study aims at evaluating (in a proof of concept approach) the outcome of pre-hospital patients presenting with acute STEMI within 3 hours of symptom on-set. Following randomisation, a treatment strategy of early (pre-hospital) Tenecteplase and additional anti-platelet and anti-thrombin therapy, followed by catheterisation within 6-24 hours, with timely coronary intervention as appropriate (or by rescue coronary intervention if required) in Group A, will be compared to PPCI performed according to local standards in Group B (http://clinical trials.gov.show/NCT00623623). Pre-hospital thrombolysis is a Class IIa therapy recommended for acute STEMI by leading international cardiology societies (89).

The following trials are just some of the numerous thrombolytic trials conducted in the pre-hospital environment that demonstrate the potential value of pre-hospital thrombolysis on morbidity and mortality.

The first published study of pre-hospital thrombolysis was undertaken in 1985; it involved intravenous administration of 750,000 units of Streptokinase by physicians to 53 patients (9 treated at home and 44 in-hospital). This study demonstrated that patients treated in less than 1.5 hours after on-set of pain revealed the following in comparison with patients receiving treatment between 1.5 to 4 hours from the on-set of pain: a significantly higher ejection fraction (56 ± 15 versus 47 ± 14 %; $p < 0.05$); improved infarct-related regional ejection fraction (51 ± 19 versus 34 ± 20 %; $p < 0.01$); and a lower QRS score (5.6 ± 4.9 versus 8.6 ± 5.5; $p < 0.01$). Patients in the pre-hospital group of the study also had better-preserved left ventricular function than patients treated in the hospital. The study concluded that thrombolytic therapy with Streptokinase is most effective when administered within 1.5 hours of on-set of symptoms of AMI. Although this study produced positive results, it lacked statistical power (due to a small sample size), but it served to highlight the importance of timely thrombolysis (100).

The Grampian Region Early Anistreplase Trial (GREAT) is the most influential pre-hospital thrombolysis based study. The aim of GREAT was to determine the time saved by thrombolysis when initiated at home by trained general practitioners / family physicians, compared to thrombolysis in-hospital. The general practitioners randomly assigned thrombolytic therapy to 311 patients with suspected AMI who had been divided into two treatment groups: pre-hospital thrombolysis; and thrombolysis after arrival at the hospital. GPs selected patients on the basis of history of chest pain, from 20 minutes to 4 hours, with treatment initiated within 6 hours of on-set of pain. Patients in the pre-hospital treatment group received

thrombolysis up to 130 minutes earlier than patients at hospital (101 minutes versus 240 minutes from on-set of symptoms), with a 50% reduction in mortality in the pre-hospital group: 17 (10.4%) versus 32 (21.6%). The greatest saving of time was seen in the rural environment and in areas where there were significant in-hospital treatment delays (101). Importantly during the GREAT study, pre-hospital thrombolysis was undertaken using a single bolus thrombolytic agent.

Patients enrolled into the GREAT study were followed up at five years and investigators noted that 25% of the pre-hospital treatment group had died, compared to 36% in the in-hospital treatment group (102). The GREAT study re-confirmed the negative impact of time delays by demonstrating that delaying thrombolysis by one hour increased the hazard ratio of death by 20%, with an equivalent loss of 43 lives per 1000 patients treated at five years. In a sub-set analysis of GREAT patients, who met current ECG criteria for thrombolysis undertaken after 10 ten years, a 16% difference in mortality was maintained between the two groups (103). The benefits seen in GREAT were significantly higher than those seen in any other thrombolysis study. The long-term mortality patterns have not been replicated in other long-term (in-hospital) follow-up studies, like ISIS-2 (31) or GUSTO-1 (99).

Although general practitioners (GP) did ECG recordings, it was not a requirement for trial admission. Trial admission was by strong clinical suspicion of AMI, allowing for the possibility of either an inclusion or exclusion bias. Selection bias was mitigated against in the GREAT study by adopting a randomised controlled

double-blind method, which involved random administration from an ampoule labelled either “home injection” or “hospital injection.” However, there are some challenges with generalising data from the GREAT study: administration of a thrombolytic agent is never undertaken on clinical suspicion of acute STEMI alone and the role of a GP is not typical of current emergency medical systems.

The European Myocardial Infarction Project (EMIP) (104) is the largest double-blind randomised multi-national study (5469) to compare pre-hospital with in-hospital administration of Anistreplase. Patients were included based on on-set of symptoms within six hours and a qualifying 12-lead ECG. Patients treated in the pre-hospital group by emergency medical personnel received treatment a mean 55 minutes sooner than those in the hospital group. A non-significant reduction in mortality at 30-day follow-up was seen: 9.7% versus 11.1%; 95% CI: -0.1% - 3.1%; p = 0.08. The strengths of this trial lie in the sample size (over 5 000 patients) and in it being a multi-national study. A significant point of this study was the overall reduction of 15 minutes to thrombolysis in participants of the hospital group, which reduced the added benefit effects of pre-hospital thrombolysis in the comparative analysis with the pre-hospital call-to-needle time.

The Myocardial Infarction Triage and Intervention (MITI) trial was a much smaller one (n = 360) done in an urban setting that had a well-established history of excellent emergency cardiac care. The purpose of the study was to determine the long-term influence of early thrombolysis for acute STEMI. As in EMIP, in-hospital treatment times were significantly reduced (40 minutes); however, both the

treatment groups had similar outcomes. No significant improvement was noted when thrombolysis was initiated out of hospital. Patients who were treated less than 70 minutes after on-set of symptoms had a 98% 2-year survival rate, compared to 88% when treated later ($p = 0.12$). At 2 years, the event free survival rate was 65% for patients in the early treatment group and 59% for those treated after 70 minutes ($p = 0.8$). The findings of this study were not generalisable, however, because thrombolysis by paramedics could only be undertaken after remote assessment of ECG results and clinical assessment by doctors, which introduced an the element of selection bias. In addition, the study was conducted in an urban setting with well-established cardiac care facilities. These results can only be compared to studies in similar settings (105).

These three trials and three other randomised trials were combined in a meta-analysis undertaken by Morrison et al (106). The primary objective of this meta-analysis was to critically appraise and summarise all randomised controlled trials of pre-hospital versus in-hospital thrombolysis for acute STEMI. The primary outcome was all-cause hospital mortality and the secondary outcomes, amongst others, symptom to treatment time and adverse events. The individual trials failed to demonstrate a statistically significant difference in all cause in-hospital mortality. This meta-analysis (involving 6434 patients) showed: a pooled benefit in that pre-hospital thrombolysis reduced time to thrombolysis by approximately 60 minutes ($p = 0.07$), compared to in-hospital thrombolysis (104 versus 162 minutes); and reduced all-cause hospital mortality by 17%. Perhaps the major criticism of the meta-analysis was the use of trials in which a variety of thrombolytic drugs were

used. However, Morrison et al (106) considered it reasonable to group the trials together, regardless of this variation, on the grounds of their broad clinical similarities.

A clinical trial was undertaken in Helsinki, Finland by Voipio (107), to investigate the safety and efficacy of thrombolytic therapy for an acute myocardial infarction immediately after out-of hospital cardiac arrest. Of the 68 patients treated, an accurate diagnosis was made in 64 patients. Reperfusion was achieved in 71% of patients. Sixty-three patients (93%) were admitted alive to hospital, with 36 eventually surviving to discharge. Although this was a retrospective study, which lends itself to missing data and other inaccuracies, the results are generalisable, on the grounds that the reporting method used to establish the database is an established international collection tool that may have contributed to accurate and consistent reporting of all patients. All patients in the study could be followed up with details of their responses to thrombolysis.

Björklund et al (108) evaluated treatment delays and outcome in a large cohort of acute STEMI patients transported by ambulance and who were either thrombolysed by paramedics in the pre-hospital environment or thrombolysed in-hospital. Importantly, Björklund et al utilised data from the Swedish Register of Cardiac Intensive Care, drawing data from 75 hospitals. Although register-based data lacks the scientific controls seen within clinical trials, it is arguably more reflective of ‘real life’ clinical care. Following this study, Björklund et al were able to conclude that pre-hospital thrombolysis by paramedics in ambulances was

associated with reduced time to thrombolysis of almost 1 hour and reduced adjusted 1-year mortality by 30%.

1.2.8.1 Paramedic-led pre-hospital thrombolysis

The efficacy and safety of pre-hospital thrombolysis depends on several pre-requisites (104, 108-110), i.e.:

1. Ambulance personnel being trained to recognise symptoms and management of STEMI and its early complications.
2. Diagnoses of STEMI using a 12 lead ECG that adds a few minutes delay time with or without computer assistance.
3. Intravenous access to be established and the administration of reperfusion therapy to be initiated within strict treatment directives.
4. During transportation, rhythm monitoring and advanced cardiac life support are mandatory.
5. Early contact with the referring hospital by electronic transmission of the 12 lead ECG appears to be necessary, allowing early preparation of further care that will also contribute to improving outcome.
6. Availability of a consultant cardiologist for clinical support when required.
7. On-going quality assurance.

These and other trials help to confirm the feasibility and safety of pre-hospital thrombolysis in a wide variety of circumstances and settings, ranging from

traditional ambulance services through to use by ship-based medical teams (cruise ships) and deployed military medicine.

1.2.8.2 Pre-hospital thrombolysis supported by early intervention

There are a number of reperfusion strategies for acute STEMI, namely:

1. Pre-hospital thrombolysis supported by rescue PCI for failed thrombolytic reperfusion.
2. Pre-hospital thrombolysis plus pre-discharge or symptom/ischaemia driven PCI for those who evidence reperfusion.
3. Facilitated PCI (reduced dose thrombolysis with planned PCI).
4. Primary PCI.

The ASSENT-4 PCI (111) study demonstrated that facilitated PCI, that is, thrombolysis immediately followed by PCI, has proven to be an unsuccessful intervention.

The WEST study (112) investigated the use of a number of different reperfusion strategies: immediate pre-hospital thrombolysis plus usual in-hospital care (excluding routine PCI); pre-hospital thrombolysis with compulsory rescue PCI for failed thrombolysis against a primary PCI strategy. Key findings of the WEST study were: a lower incidence of cardiogenic shock in patients who received thrombolysis early (within 3 hours); and the importance of pre-hospital triage/decisions for reperfusion with delays to definitive treatment being shorter

when a decision was made in the pre-hospital setting. The WEST study also highlighted that thrombolysis used timeously remains an important treatment modality in early management of acute STEMI.

The larger CAPTIM study (113) used a similar design to the WEST study, utilising pre-hospital decision/triage to pre-hospital thrombolysis (this time supported by compulsory rescue PCI) with pre-discharge coronary intervention compared to PPCI. The long-term 5-year follow-up of the CAPTIM study confirmed a significant reduction in mortality when thrombolysis was administered within 2 hours in the pre-hospital group, compared with primary angioplasty. The relationship between reperfusion strategy and time from symptom on-set on 1 year mortality was examined in a pooled analysis of patients from the CAPTIM and WEST studies. A reduction in 1 year mortality was observed when thrombolytic treatment was initiated within 2 hours, compared to PPCI (2.8% versus 6.9%, p= 0.021, hazard ratio 0.43, 95% CI 0.20-0.91). However, no difference in mortality was observed between the two groups when thrombolytic treatment was initiated after two hours (6.9% versus 6.0%; p= 0.529; hazard ratio 1.23; CI 0.61-2.46)(114). The optimal design of a hybrid reperfusion service is yet to be determined, but the data from WEST and CAPTIM would support pre-hospital thrombolysis within the first three hours, as long as all patients were delivered to a receiving hospital with intervention cardiology capability.

Pre-hospital thrombolysis can be initiated earlier than in-hospital thrombolysis or PPCI and it can be performed with limited equipment. The same minimum

equipment is required to perform pre-hospital thrombolysis as is required to identify pre-hospital patients requiring direct admission for PPCI. Data from WEST (paramedic decision-makers), CAPTIM (doctor decision-makers) and projected findings from STREAM (paramedic/nurse/doctor decision-makers) are intended to inform the debate as to whether a hybrid reperfusion system is appropriate within developed countries. Regardless of the reperfusion strategy put into place, empowering the pre-hospital emergency care provider is a pivotal strategy to success.

1.2.8.3 Risk benefit and hazard considerations for pre-hospital thrombolysis

Although thrombolysis has been determined to be a relatively safe procedure, the treatment is associated with risks and complications. Even with appropriate use, thrombolytic agents can have serious adverse effects; however the risks are off-set by the considerable overall reduction in morbidity and mortality. Many patients with recognised vulnerability to the known hazards are treated in the hospital setting on the basis of a favourable risk-benefit ratio. Pre-hospital thrombolysis should, therefore, always be the result of a risk benefit calculation of: the acute STEMI, thrombolysis risks and PPCI availability. Thus, the emergency care practitioner should carefully consider the risk benefit ratio and consult with the receiving cardiologist as to the most appropriate treatment option (115).

The hazards of thrombolytic therapy relate to:

- Haemorrhage due to the dissolution of haemostatic plugs and old thrombus outside the coronary arteries. The greatest risk is from cerebral haemorrhage, which occurs with a rate of 0.5% to 1%. This risk is minimised by avoiding treatment in the presence of hypertension, known or suspected cerebral tumours, history of cerebro-vascular accident, symptomatic cerebro-vascular disease, old age and recent trauma. Other contra-indications relating to internal or external bleeding include: mistaken diagnosis of pericarditis or dissecting aneurysm; recent surgery; peptic ulceration; known bleeding tendency (including anti-coagulant treatment); and prolonged chest compression from cardio-pulmonary resuscitation. Bleeding is usually minor and occurs at the sites of vascular puncture (70%) (116).
- Complications that follow successful reperfusion of ischaemic tissue, resulting in life-threatening ventricular arrhythmias that may require immediate defibrillation (116).
- Allergy and induced hypotension (particularly for Streptokinase). Allergy is rarely life-threatening and severe hypotension can usually be avoided by withholding treatment if blood pressure is already low (117).
- Administration of a thrombolytic for patients without the patient having an acute STEMI may also lead to complications (118).

1.2.8.4 Ideal pre-hospital thrombolytic agent

There are a number of thrombolytic agents available; however Tenecteplase (TNK) is the only single-use bolus agent available, making it most suitable for pre-hospital use. Nevertheless, an ideal thrombolytic agent currently does not exist.

The characteristics of an “ideal thrombolytic agent” are as follows:

- Rapid reperfusion (15 - 30 minutes)
- 100% efficacy at achieving 100% TIMI 3 in 30 minutes
- Administered as a single intravenous bolus
- Lower incidence of intra-cranial haemorrhage
- Lower incidence of systemic bleeding and other complications
- Specific for recent thrombi
- Lower incidence for re-occlusion
- Long-term sustained patency
- No antigenicity
- No negative interaction with adjunctive therapy
- Affordable

Table 1: Characteristics of commonly used thrombolytic agents

Adapted from Opie (119).

	Streptokinase (STK)	**Alteplase (tPA)**	**Reteplase (rtPA)**	**Tenecteplase (TNK)**
Fibrin selective	No	Yes	Yes	Yes
Plasminogen binding	Indirect	Direct	Direct	Direct
Duration of infusion (minutes)	60	90	10 + 10	5-10 seconds
Half-life (minutes)	23	<5	13-16	20
Fibrinogen breakdown	4+	1-2+	Not known	> tPA
Early Heparin	Yes	Yes	Yes	Yes
Hypotension	Yes	No	No	No
Allergic reactions	Yes	No	No	No
Approximate cost/dose	R957/1.5 MU	R6884/100 mg	R7197/20 unit kit	R5762/50 mg
TIMI re-flow grade 3 at 90 minutes	32	45-54	60	> tPA
Recommended use	Up to 12 hours	Up to 12 hours	Up to 12 hours	Up to 6 hours (typically used up to 12 hours)

The GUSTO trial (99) demonstrated the superiority of an accelerated regimen of tissue plasminogen activator (tPA, Alteplase) over STK, although there was a slightly greater risk of intra-cranial haemorrhage, especially in female patients over the age of 75 years. However, stroke after thrombolysis is a known risk; and in the GUSTO trial the stroke rate with STK was 1.19%, compared to 1.55% with tPA (120). The issue of stroke is an important consideration, as denying thrombolysis

does not decrease the stroke rate. This is because STEMI is an independent risk factor for stroke that is unrelated to thrombolysis, which is due to higher incidence of atrial fibrillation (AF) and poor left ventricular (LV) function caused by STEMI. Therefore, early treatment of STEMI with reperfusion, which reduces the incidence of AF and LV dysfunction, is an important aspect of stroke and morbidity reduction.

Single bolus TNK is now the most widely used thrombolytic agent in developed countries, partly due to its improved efficacy, but also because of ease of administration and variable dosing. TNK and Alteplase are equivalent with regard to 30-day mortality, but non-cerebral bleeding and blood transfusions are fewer with TNK.

The dose of TNK is weight adjusted and administered in a single bolus over 5 seconds; compared to 90 minutes of variable rate infusion with tPA, or a 30-60 minute infusion of STK. Although a 30 minute infusion regime for STK exists, this is associated with increased risk of hypotension; however, by slowing the infusion rate of STK, the incidence of hypotension tends to decrease. Reteplase is a more fibrin-specific agent administered as a 10-unit twin bolus given 30 minutes apart. However, the time sensitive nature of the twin bolus administration of Reteplase can be problematic. Reteplase is equivalent to Alteplase in terms of reduction in mortality and haemorrhage rates.

The major benefit of bolus agents lies in ease of administration and in a simplified dosing regimen that reduces the risk of dosing errors. However, the cost of TNK and its manufacturer's recommendation for use up to 6 hours makes the cheaper STK a more practical drug choice for use in the developing world. Thus, as for every one patient treated with TNK, five patients could be treated with STK (Table 1) (121). Its use as a pre-hospital thrombolytic is worth consideration, particularly in remote health care settings, although its requirement for an infusion plus the incidence of hypotension makes it more labour intensive.

The comparison of STK and TNK treatment regimes are summarised in Table 2. There are two key considerations for the use of STK in the pre-hospital environment. The first is duration of infusion and the requirement for an expensive infusion pump. Although an infusion pump offers better control of drug delivery, this is less of an issue with STK, as the delivery of STK is less time sensitive, compared to tPA. In static medical care environments (e.g. remote medical center) the infusion can be completed before hospital transfer, as STK can be delivered safely without an infusion pump using either: a small intravenous bag (100-250ml 0.9% saline); or a paediatric burette supported by close clinician supervision. The use of a paediatric burette or a 100/250ml bag of saline is not an option for administration during ambulance transfer, as the low ceiling in an ambulance does not have the height to ensure fluid flow; this is further aggravated by ambulance movement. Novel techniques involving the use of low cost drip counters (that restrict flow through drip administration set), supported by a pressure infusion bag

to maintain constant pressure through the drip counter, are feasible, but yet to be proven.

Table 2: Comparison of STK and TNK treatment regimes

Streptokinase	Tenecteplase
1.5 mega units over 30-60 minutes (requires an infusion pump)	Single weight adjusted bolus
Aspirin 300mg	Aspirin 300mg
Clopidogrel age adjusted (75-300mg)	Clopidogrel age adjusted (75-300mg)
No Heparin (local policy may vary)	Weight adjusted Heparin bolus followed by infusion or weight adjusted sub-cutaneous injection of Heparin: 4000 unfractionated Heparin bolus followed by infusion (an infusion pump is mandatory) Age adjusted Enoxaparin
Bradycardia (common) reversed by atropine	Bradycardia (less common than STK) reversed by atropine
High risk of drug induced hypotension responsive to fluid challenge stopping/slowing infusion	No specific drug induced hypotension
Labour intensive	Not labour intensive
Affordable (if no infusion pump is used)	Expensive

The second consideration is a much higher incidence of hypotension and bradycardia. This is due to the release of bradykinin; it is not (as commonly thought) an allergic reaction and although anaphylaxis is more common with STK, it remains rare. Therefore, the treatment of hypotension consists of slowing or stopping the infusion and the administration of a 250-500ml crystalloid bolus. The

routine use of intravenous steroids and anti-histamines offers no clinical benefit and in the case of intravenous steroids use may adversely affect patient outcome by affecting myocardial scar tissue formation, thereby potentially increasing the risk of myocardial rupture.

1.2.9 Adjunctive drug treatment

1.2.9.1 Oxygen

Oxygen is commonly administered during the management of patients during thrombolysis. Its routine use in patients with a pulse oximetry above 95% has been questioned, primarily due to the possibility of vaso-constriction and limited evidence of any benefit (122). Oxygen remains an important adjunctive therapy in the presence of left ventricular failure, although it is better provided as part of continuous positive airway pressure. Oxygen should routinely be administered in the presence of arrhythmias (e.g. ventricular tachycardia) (123), hypotension / hypo-perfusion and any post-cardiac arrest.

1.2.9.2 Analgesia

Analgesia is a priority therapy in the management of STEMI and intravenous opiates (morphine, diamorphine or fentanyl) that offer the most effective analgesia. However, the legal framework for administration of these drugs can be problematic, resulting in drugs such as Tramadol or Nubain being used if legal barriers to opiates do exist. The use of inhaled nitrous oxide (Entonox™) remains

a useful supplementary analgesic (or primary analgesic if pre-hospital opiates are not available), providing both supplementary oxygen and analgesia; the use of Pentrane (common in Australia), is also a useful inhaled analgesic that allows a higher percentage of inhaled oxygen if required. Thrombolysis also represents effective analgesia, as the restoration of myocardial blood flow results in pain relief, reflecting successful reperfusion.

Non-pharmacological interventions (re-assurance, calm professional manner of the health-care provider) are important aspects of pain relief. The use of rapid road transfer with lights and sirens may induce greater patient anxiety (as well as the risk of traffic collision). However, if pre-hospital thrombolysis has been administered (with appropriate adjunctive therapy), there is little to be gained from rapid transfer to hospital.

1.2.9.3 Nitrates

Although there is no survival benefit to be gained from nitroglycerin, it remains a common early therapy that reduces ischaemia - and therefore angina - by reducing the pre-load and after-load of the left ventricle, thereby reducing wall stress and decreasing oxygen consumption. Nitroglycerin (0.4mg) is typically administered sub-lingually, although intravenous nitrates are also used: to manage on-going ischaemic chest discomfort; control hypertension; and for the management of pulmonary oedema. (Nitrates are a Class I recommendation for LVF). Nitrates: should not be administered to patients who have received

phosphodiesterase inhibitors within 24 to 48 hours; and should be administered with care in patients with suspected right ventricular infarction, as it may induce marked hypotension. Despite this, nitrates are safe drugs for use by pre-hospital clinicians and it must be remembered that known cardiac patients may have already treated themselves with varying doses of nitrates prior to arrival of the pre-hospital clinician.

1.2.9.4 Anti-platelet agents: Aspirin and Clopidogrel

Anti-platelets are vital in the management of all acute coronary syndromes (unstable angina, non-STEMI and STEMI). Within the context of STEMI management, anti-platelet therapy is as important as thrombolytic therapy. This is because: the intra-coronary thrombus responsible for re-infarction tends to be platelet rich; and thrombolysis may raise the possibility of thrombolytic-induced platelet aggregation (124).

All patients with suspected ACS (unstable angina, non-STEMI and acute STEMI), should be considered for pre-hospital Aspirin treatment as there are relatively few contra-indications to a single dose of Aspirin (Class I recommendation). Despite this, Aspirin is often withheld due to concerns about: allergy; adverse drug interactions (e.g. Warfarin); confusion due to chronic on-going use of Aspirin; or uncertainty of diagnosis. Typically, unless a patient has a known documented allergic reaction (not just gastric irritation) to Aspirin or is actively bleeding from a gastro-intestinal tract ulcer, Aspirin at the 300mg dose should be given. The

choice of 300mg is typically the dose of a single Aspirin, with administration being initiated as early as possible and consideration being given to emergency call-takers being empowered to recommend Aspirin before the arrival of emergency care providers (Class IIb recommendation).

The benefit of Aspirin was established in the ISIS 2 trial (31), where 162.5 mg Aspirin resulted in 25 lives saved per 1 000 patients, primarily by: reducing the incidence of re-infarctions (10 non-fatal re-infarctions per 1 000); as well as preventing 3 non-fatal strokes per 1000 patients. The results from ISIS 2 trial highlighted that: the effectiveness of Aspirin alone was nearly as effective as STK without Aspirin (23% versus 25%); and that by combining Aspirin with STK, the magnitude of benefit was highly significant (42%). It is noteworthy that Aspirin administration during the ISIS 2 trial was anytime within the first 24 hours; but a meta-analysis by Freimark et al (125) demonstrated that early Aspirin administration (before thrombolysis) was an independent factor in patient survival at one year (5% versus 11%; p = 0.002; odds ratio 0.41; 95% CI 0.21-0.74).

The benefits of Aspirin for acute STEMI are attributed to its inhibition of cyclooxygenase dependent platelet activation. The administration of an initial dose of 160-300mg Aspirin, ideally a non-enteric coated formulation that is chewed, is a Class I recommendation for acute STEMI. Intravenous or rectal Aspirin are also acceptable routes of administration.

Clopidogrel is a potent platelet inhibitor and the anti-platelet benefit of Clopidogrel in combination with Aspirin is to reduce ischaemic events in: non-ST-elevation acute coronary syndromes (126); and in patients undergoing percutaneous coronary intervention - PCI CLARITY study (127). The COMMIT-CCS 2 (128) trial, involving more than 45 000 patients (many post thrombolysis), demonstrated that administration of 75mg Clopidogrel daily with 300mg Aspirin and standard treatment, safely reduced mortality and major vascular events. In the CLARITY-TIMI 28 Trial (129), patients 75 years and younger with acute STEMI received: thrombolysis supported by a loading dose of 300mg Clopidogrel; followed by 75mg once daily; and either low molecular weight Heparin (LMWH) or unfractionated Heparin (UFH). The combination of dual anti-platelet therapy (Aspirin/Clopidogrel) with thrombolytic treatment demonstrated more favourable angiographic patency of the infarct related artery and a reduction in mortality. A major contributor to mortality reduction was the reduction in re-infarction rate in those patients receiving dual anti-platelet therapy. This was without an associated increase in the rate of bleeding.

The importance of improved patency and a lower incidence of re-infarction was confirmed in the ECG CLARITY-TIMI 28 Study (129), where the use of Clopidogrel was shown to improve late coronary patency and clinical outcome in patients who achieve ST-segment resolution by preventing re-occlusion of open arteries, rather than by facilitating early reperfusion. The administration of 300mg loading dose of Clopidogrel in association with thrombolysis, to those less than 75 years of age, is a Class IIa recommendation and it is common practice to adjust the dose in the

over 75 year old patients to 75mg based on the COMMIT data. Newer oral anti-platelet drugs, such Prasugrel and Ticagrelor, are now available with potentially improved anti-platelet action, but are yet to be studied in conjunction with thrombolytic therapy.

1.2.9.5 Anti-coagulants

Heparin is considered effective and is routinely given as an adjunct for PCI and thrombolytic therapy, although it is commonly withheld in the first twenty-four hours in those patients receiving STK. The role of Heparin is primarily to reduce re-infarction, but the combination of dual anti-platelet therapy, thrombolysis and Heparin may increase the risk of bleeding. The American Heart Association guidelines call for careful weight-based dosing of Heparin with thrombolytic therapy in STEMI (130).

The timing of Heparin therapy when using fibrin specific thrombolytic agents (tPA, Reteplase and TNK) is an important aspect of patient management**.** In an observational study of the United Kingdom MINAP (131) registry, the frequency of re-infarction during hospital admission after thrombolytic treatment of 35 356 STEMI patients (during 2005–2006) was analysed. Re-infarction rates with in-hospital treatment were similar for Reteplase (6.5%) and TNK (6.4%), but were higher for those patients treated by paramedics in the community. When the interval from pre-hospital treatment to hospital arrival was greater than 30 minutes re-infarction rates were 12.5% for Reteplase, and 11.4% for TNK. For intervals

shorter than 30 minutes, the re-infarction rates were significantly greater for TNK (9.3%) than Reteplase (4.2%). Overall, re-infarction rates were higher after pre-hospital treatment with TNK than Reteplase (9.6% versus 6.6%, p=0.005).

The differences in re-infarction rates were considered primarily due to the different uses of adjunctive anti-thrombotic therapy. The UK paramedic thrombolysis protocols only allowed for a single bolus dose of Heparin prior to thrombolysis, with no on-going heparinisation until arrival in-hospital - compared to in-hospital practice of either an infusion of UFH (800-1000 IU per hour adjusted to aPTT) or weight adjusted LMWH. It was also noted that on arrival at hospital there was often a delay in commencing Heparin therapy, either due to confusion about the pre-hospital protocol or other time related pressures. In addition, Clopidogrel was commonly administered early in association with in-hospital thrombolysis, but only after arrival at hospital for those patients receiving pre-hospital thrombolysis (131). This may also have been a confounding factor, as Keeley et al (124) noted that thrombolysis induced platelet aggregation was a possible cause of re-infarction following thrombolysis.

UFH was regarded as the anti-thrombotic agent of choice in the adjunctive treatment of patients with STEMI, until the introduction of Enoxaparin. The ASSENT-3 PLUS Trial (132) evaluated the feasibility, efficacy and safety of pre-hospital Enoxaparin or UFH with Tenecteplase. There was a reduction in the composite of 30-day mortality, in-hospital re-infarction or in-hospital refractory ischaemia in the Enoxaparin group (14.2% versus 17.4%., p = 0.08). However,

there was a tendency towards higher rates of intra-cranial haemorrhage (ICH) and major bleeding in the Enoxaparin group. The risk for ICH and major bleeding was mainly confined to patients > 75 years old. It must be noted that in the ASSENT-3 PLUS trial, the dose of Enoxaparin was not weight adjusted. The safety concern of Enoxaparin among elderly patients was addressed by the ExTRACT-TIMI-25 Trial (133) that randomised more than 20 000 thrombolysed patients to receive either Enoxaparin or UFH. The ExTRACT-TIMI 25 study (133) was significantly changed from the ASSENT 3 PLUS study, with patients > 75 years of age: not receiving the IV bolus of Enoxaparin; and receiving a reduced dose of sub-cutaneous Enoxaparin (75%) and with a maximum ceiling dose of subcutaneous Enoxaparin for the under 75 year olds being set at 100mg and at 75mg for the over 75 age group. The primary end-point of this study was all-cause mortality or non-fatal re-infarction at 30-days. Treatment with Enoxaparin was found to be superior to UFH, but was associated with an increase in serious bleeding episodes. A telephone follow-up at 1 year showed a sustained reduction in mortality or re-infarction when using the Enoxaparin strategy (134). Data from a meta-analysis from 12 earlier trials (involving more than 49 000 patients) support these results (135). Enoxaparin is administered as an initial dose of 30mg intravenous bolus, followed by 1mg/kg sub-cutaneously within 15 minutes; this is a Class I recommendation.

Enoxaparin offers a number of operational benefits for use with pre-hospital thrombolysis, but primarily in the absence of an infusion pump that is required when administering an infusion of UFH. Two single 100mg dose syringes of

Enoxaparin are adequate to support pre-hospital thrombolysis, with one syringe being used for the 30mg IV dose, followed by a subsequent sub-cutaneous dose (the maximum sub-cutaneous dose of Enoxaparin remains 100mg). The intravenous dose of Enoxaparin can be simply administered by decanting a 100mg dose of Enoxaparin into a 10ml syringe and then diluting with water to a total volume of 10mls for injection purposes - thereby providing 10mg Enoxaparin per ml. A multiple-use vial of Enoxaparin for IV administration is also available.

1.3 Conclusion

Morbidity and mortality from STEMI can be reduced significantly if patients and bystanders recognise symptoms early and/or activate emergency medical services early, which would reduce the time to definitive treatment. Patients and their relatives should be educated on recognising symptoms of a heart attack to reduce time from symptom on-set to calling for help. Patients with symptoms of AMI should ideally be transported by ambulance, rather than by friends or relatives, because of the proven association between ambulance use and early reperfusion therapy.

Given the importance of patients using emergency medical systems for possible ACS all those involved need to have a mutually acceptable emergency protocol to ensure that patients with symptoms would be able to expeditiously access emergency medical services without barriers to timely evaluation and treatment, including: government policy makers, medical communities, health care insurance

providers, emergency medical systems and hospitals. Such protocols would incorporate rapid detection, evaluation and referral/treatment of patients within a regional system of care that would incorporate quality improvement measures for on-going monitoring and process improvement (136).

CHAPTER 2

METHODOLOGY

2.1 Research paradigm

A paradigm is a world view, a general perspective, a way of breaking down the complexity of the real world. It is an interpretative framework that is guided by "a set of beliefs and feelings about the world and how it should be understood and studied." (137). This research was conducted within a pragmatic philosophy. Pragmatism as a research philosophy embraces the mixed methods approach to applied research questions. Pragmatism emphasises that the research question drives the inquiry, design and methods. The pragmatist works from a premise of ordinary experience and the desire for a better world (138). Pragmatists emphasise the practical function of knowledge as an instrument for adapting to reality and controlling it. The pragmatic position was chosen as the researcher believes that the following matters require development of an applicable awareness programme and acknowledgement of challenges to implementation of ECP thrombolysis prior to full roll-out: the problem of awareness of symptoms of acute STEMI by the layman; the appropriate response to these symptoms; and the implementation of emergency care practitioner led thrombolysis. The researcher’s own worldview is a pragmatic one and this fitted well with the chosen research study. It has been the researcher’s long-standing view that thorough understanding of ordinary experiences will lead to adaptation and improvement for a better life.

2.2 Research design

According to Polit and Beck (139), the mixed methods approach enhances a study in a number of respects - mostly because it appears to hold promise for generalisability. This study used mixed methods, employing both qualitative and quantitative research techniques, to produce more complete knowledge needed to inform the theory and practice of acute STEMI. Another strength of the mixed methods approach is that it can answer a broader and more complete range of research questions; this because it does not confine the researcher to only one method or approach. However, as experienced by the researcher, mixed methods research has several weaknesses as well. Some disadvantages noted were: it can be difficult for a single researcher to carry out both techniques concurrently; it is more time consuming; and the researcher has to learn about multiple techniques and how to mix them appropriately (140). However, the limitations of each technique were off-set by integrating both quantitative data with qualitative data in this research.

In this study, the mixed method approach was undertaken in four phases (See Table 3). The first phase (hereafter referred to as Phase One) analysed existing documentation for the purpose of identifying existing awareness programmes and using these findings to develop a comprehensive heart attack awareness programme. In Phase Two, existing documentation was studied (including education programmes, protocols, guidelines, site evaluations and interviews on pre-hospital thrombolysis) in order to produce an emergency care practitioner thrombolysis (ECPT) programme for the South African context. In the subsequent

two phases – Phase Three and Phase Four: the developed ECPT treatment protocol was implemented and reviewed by an expert panel; thereafter ECPT treatment data was compared to historical data.

Table 3: Summary of research methods

PARADIGM	PHASE	DESIGN	METHOD	ACTIVITY
Pragmatism	Phase 1	Qualitative	Document analysis and expert panel validation using the Adapte process	Development of a culturally sensitive and affordable chest pain awareness education programme
	Phase 2	Qualitative	Document analysis, guideline reviews and interviews using the Adapte process	Planning and designing thrombolysis by emergency care practitioners
	Phase 3	Quantitative and Qualitative	Recording of raw data using a data collection tool and expert panel evaluation	Implementation of the thrombolysis protocol
	Phase 4	Quantitative	Comparison of raw data from two databases	Comparison with historical data

2.3 Research instrument

The ADAPTE process (Appendix 14) was used in: Phase 1 – development of a culturally sensitive and affordable chest pain awareness education programme; and Phase 2 – planning and designing thrombolysis by emergency care practitioners. The ADAPTE process was created by the ADAPTE collaboration in partnership with Guidelines International Network. This was created to develop and validate a generic adaptation process to foster valid and high-quality adapted

guidelines and to enhance the users' sense of ownership of the adapted guideline (http://www.adapte.org/www/rubrique/guideline-adaptation.php).

2.4 Phase One: Development of a culturally sensitive and affordable chest pain awareness education programme using the Adapte process

In line with the first objective of this study, a document review was undertaken on existing chest pain or heart attack awareness programmes, in order to gain baseline knowledge of what already exists nationally and internationally.

2.4.1 Literature search for culturally sensitive and affordable chest pain awareness education programmes

An internet literature search was conducted to find appropriate studies with current and best evidence on chest pain awareness programmes. The search began by accessing the Google search engine then progressed to the following databases: MEDLINE, PROQUEST, Pubmed, Science Direct, Cardiosource and Sae-Journal. The Google search engine was utilised extensively. An internet literature search was conducted to find existing chest pain awareness programmes using the Medical Subject Heading (MeSH) terms: *acute myocardial infarction, heart attack, heart attack awareness, heart attack education* and *chest pain*. These databases were initially searched from 1970 through to 2011. Despite an extensive result, the majority of results did not include chest pain awareness education programmes.

2.4.2 Selection criteria and general characteristics of the chest pain awareness programme sought

All programmes were assessed for relevance to public awareness of chest pain, comprehensiveness, simplicity and affordability. Chest pain awareness education programmes from the United Kingdom, Canada and Australia were found to be relevant to the respective research objective and were used to inform the development of the chest pain awareness education programme. These programs used pictures, posters, booklets and various other print forms and were simple and easy to understand. Additional factors that were considered in the selection and design of the programme were that the South African population is made up of many different race groups, cultures, ethnic groups and linguistic groups. To deliver a general awareness programme, these factors will need to be considered, as culturally sensitive care targets the entire person and not just the physical ailment. The aim of the programme was to make all South Africans aware of the symptoms of a heart attack (regardless of race, age, ethnic group, gender, size, shape, or socio-economic status), thereby being culturally sensitive and being cognisant of the political history of South Africa. With this in mind, where applicable, the content of the various aspects of the programme was designed using neutral figures and colours. It is also the intention to translate the programme into isiZulu - the most widely spoken language in South Africa with 10.7 million speakers (23.8%) (141); and thereafter into isiXhosa and Afrikaans, followed by the remaining official languages, as required. With these factors in mind, a poster, booklet and video were developed by the researcher.

2.4.3. Components of the chest pain awareness programme

The components of the chest pain awareness programme presented in Chapter 3 were developed with due consideration taken of the following:

2.4.3.1 Process for the development of the poster

While various countries used mainly text information in pamphlets, only the British Heart Foundation (BHF) focused on symptom awareness through a picture. This poster was adapted with permission from the BHF. The picture used a neutral form of person, i.e. did not differentiate between gender, and it clearly showed the areas of pain in the figure. The adaptations made by the researcher included: changing the colour of the figure to the internationally accepted colour symbol of a person; the written content was adjusted to reflect local requirements.

Specific intentions with the poster were: to ensure the language was simple for ease of understanding and reading; the use of less text and more figures for ease of message translation; and for the poster to be visually appealing. A non-white figure was deliberately used, so as to not infer that the poster only targets the White population of South Africa.

2.4.3.2 Process for the development of the information booklet

Following a literature search, information booklets from the United States of America, Canada, the United Kingdom and Australia were analysed; this led to the

creation and development the “Heart Attack: Time is heart muscle” booklet. Care was taken to keep the booklet short in length, ensure it is visually appealing and to use simple medical language. It is intended that the booklet be made available free of charge to the general South African public. The content of the booklet was determined by the researcher and subsequently approved by the researcher’s supervisor. The dietary guidelines were endorsed by a registered dietician. A qualitative focus group assessment was conducted thereafter, as discussed below.

2.4.3.3 Process for the development of the video

The video was chosen as part of the heart attack awareness programme because there are a number of advantages to be gained from using a video (142). Some of these are:

- It is a moving medium – it is therefore well suited to the topic, as movement is integral to explanations
- It has immediacy and relevance – the layman will be able to immediately identify with the message being screened
- Video programmes can be tailored to meet exact needs
- Videos target a wide audience at minimum cost.

Following a search on YouTube, two short video clips aimed at heart attack awareness were found. These video clips were from the United Kingdom and United States of America. The videos made use of local people and the general

information was appropriate for the local settings in each country and were therefore not suitable for the South African population. A video awareness programmes currently available in South Africa focuses on heart attack prevention and is part of an advertising strategy for a commercially available food product. There are currently no public viewing videos in South Africa that focus on recognition of symptoms and what should be done in response to a heart attack.

The video was created by a production team that consisted of: the researcher as the producer; a third year animation artist student; and the researcher's supervisor, Prof. K. Sliwa. The researcher wrote the script using salient factors identified while undertaking the literature search; this led to conceptualisation and development of the 6 frames for the video. The animation artist provided the technical expertise required for producing the video. The supervisor approved the script and provided intellectual input throughout the development process. The voice-over was done by the researcher. The video was to be restricted to 30 seconds in length in order to keep production costs and screening costs to a bare minimum. The video was also animated so as not to use any specific ethnic group and to eliminate human error factors in the video.

The focus of the video was symptom recognition and action to be to be taken by the patient or bystanders in the event of a heart attack. It included use of the current national EMS toll-free emergency number. In addition, the video showed a clock ticking to emphasise the need for prompt response to a heart attack and to support the catch phrase; "Think quick ... Act fast ... Time is heart muscle ...".

2.4.4 External review of the chest pain awareness education programme by qualitative focus groups

The entire chest pain awareness programme was subjected to validation by expert panels that consisted of cardiac nurses, consultants working in coronary care units and cardiologists from a specialist cardiac unit. An external review by laymen and determination of the impact of the chest pain awareness programme is intended as a follow-up of this study as on-going research.

The first panel consisted of 20 nursing staff from the Soweto Cardiovascular Research, Chris Hani Baragwanath Hospital. A presentation was made of the programme and feedback was obtained through the completion of a questionnaire consisting of open-ended questions.

The second panel consisted of nursing staff, consultants and cardiologists from Addington Hospital and Inkosi Albert Luthuli Central Academic Hospital. Additional evaluations were undertaken by the medical management teams at Wentworth and McCords Hospitals. The heart attack awareness programme was also presented: at the 10th Annual Congress of the South African Heart Association, held at Sun City, South Africa from 22-25 October 2009; and at the 2011 Emergency Care Society of South Africa: Pre-Hospital Emergency Care Conference, held at University of Johannesburg, South Africa from 22-23 September 2011. All comments and input received on the programme were considered and incorporated, where appropriate. All comments and input was

analysed to identify any errors in the presentation, the content and the format and to identify feedback from the various panels in terms of relevance to public awareness of chest pain, comprehensiveness, simplicity and affordability.

2.5 Phase Two: Planning and designing thrombolysis by emergency care practitioners using the Adapte process

In line with the second objective of this study (document review) an on-site evaluation and thrombolysis guideline review was undertaken on acute STEMI and the management thereof in order to provide in-depth knowledge for the design and implementation of emergency care practitioner thrombolysis.

2.5.1 Literature search for thrombolysis guidelines

An internet literature search was conducted to find appropriate studies with current and best evidence on in-hospital and pre-hospital thrombolysis. The search began by accessing the Google search engine and then progressed to the following databases: MEDLINE, PROQUEST, Pubmed, Science Direct, Cardiosource and Sae-Journal. An internet literature search was conducted to find information on thrombolysis using the Medical Subject Heading (MeSH) terms: *acute myocardial infarction, heart attack, acute STEMI, thrombolysis, pre-hospital thrombolysis, fibrinolysis* and *pre-hospital fibrinolysis*. These databases were initially searched from 1980 through to 2011. The search was extended back to 1970 to include the initial small-scale publications on thrombolysis.

A document analysis was conducted by the researcher in two international settings (Australia and UK), where pre-hospital thrombolysis is within the scope of practice of paramedics. In addition, the education and training programme of the three South African universities offering paramedic training were assessed to determine the extent and depth of the academic development of acute STEMI management by the higher educational institutions. Furthermore, the researcher undertook two on-site visits (to South East Coast Ambulance Services in the UK and the emergency medical services in France - Service d'Aide Médicale Urgente (SAMU)), where pre-hospital thrombolysis is undertaken by paramedics and physicians respectively.

2.5.2 Selection criteria of thrombolysis guidelines for acute STEMI management

The education and training programmes were assessed to ensure that: they contained the critical components; were comprehensive; were of adequate academic depth; determined academic and skill competence; and included on-going quality assurance. The equipment and system requirements of the various clinical settings were compared to identify the critical, common equipment and system requirements. Furthermore, the guidelines were reviewed against best practice guidelines for acute STEMI according to the scientific evidence available and endorsement of national and internationally recognised cardiology societies.

2.5.3 Guidelines for emergency care practitioner thrombolysis

The emergency care practitioner thrombolysis educational program and the clinical skill and checklist was based on the European Society of Cardiology Guidelines for Management of Acute STEMI (89); it is presented in Chapter 3.

2.5.4 External review by qualitative focus groups of emergency care practitioner thrombolysis

The thrombolysis protocol was reviewed by cardiac consultants of the two regional hospitals involved in the study and the researcher's supervisor before implementation by the researcher. This was undertaken to ensure that the thrombolysis protocol: is safe; is in line with international best practice guidelines for acute STEMI; and is appropriate for the South African context.

2.6 Phase Three: Implementation of the thrombolysis protocol

The validated thrombolysis protocol was implemented by the researcher as follows:

2.6.1 Study area

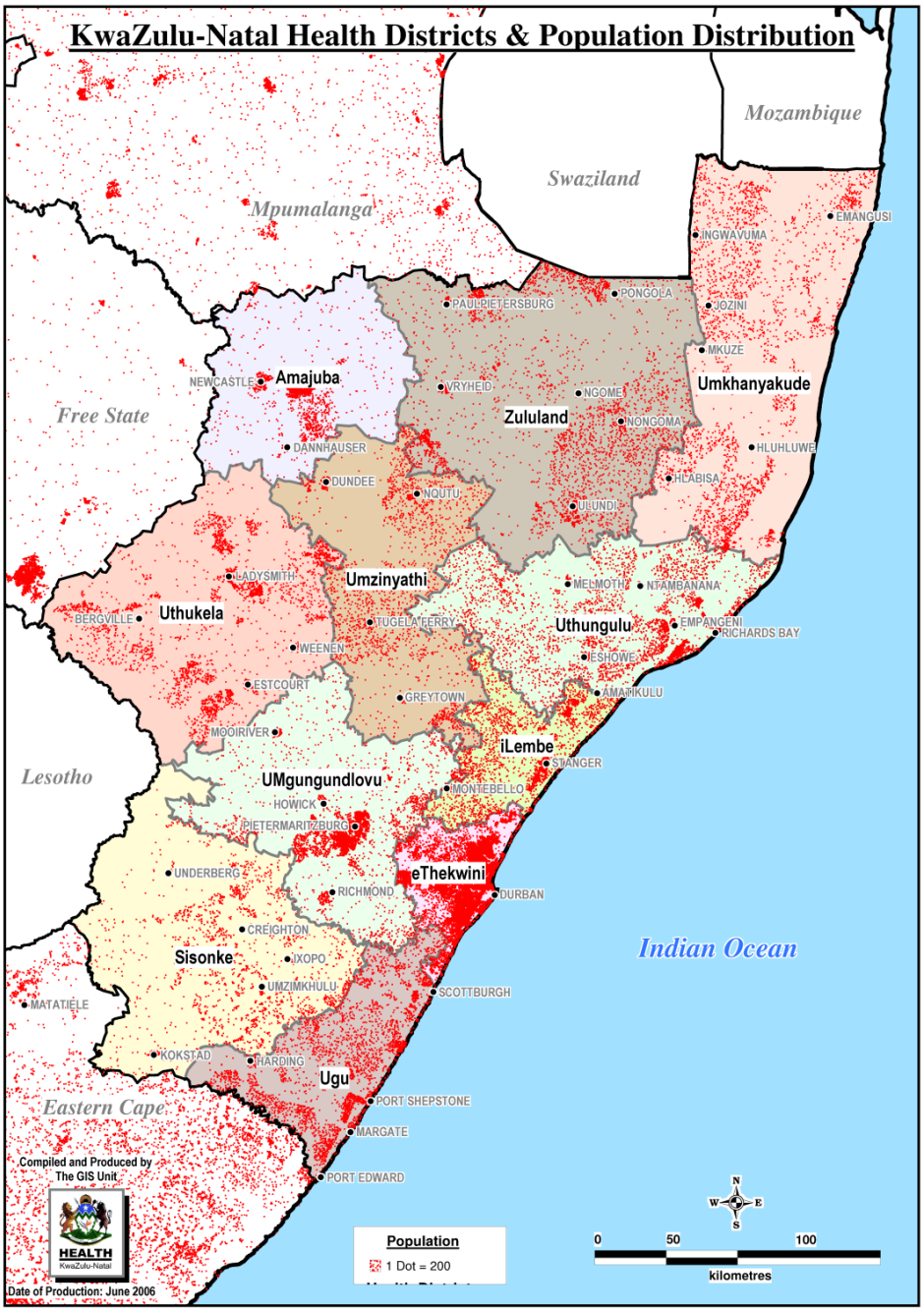


Figure 3: Map of KwaZulu-Natal

Source: (92)

This study was based in KwaZulu-Natal, which is located on the east coast of South Africa. It covers an area of approximately 94 500 square kilometres and is divided into eleven health districts (Figure 3) (92). KwaZulu-Natal has the second largest share of the South African population: 10,8 million of 50.5 million (21,4%). The proportion of urban and rural dwellers is 46% and 54% respectively (93).

The study area was in one of the eleven health districts, namely eThekwini. The population density for eThekwini Health District (which is further categorised into urban and rural population densities) is shown in Table 4. The urban population category comprised urban settlements, informal settlements, recreational areas, industrial areas, institutions and hostels; the rural population category is made up of sparse, tribal settlement, farm and small holding categories. Population distribution by race groups for eThekwini Health District are: Black Africans - 68.3%, Indians - 19.9%, Whites - 9% and Coloureds - 2.8% (143).

2.6.2 KZN: Emergency Medical Rescue Service (EMRS) – eThekwini Health District (EHD)

The EMRS control centre in EHD receives an average of 700 calls during a 24 hour cycle. This district usually operates approximately 38 ambulance units and 3 advance life support (ALS) response units for a population density of more than three million people. Calls received by the emergency control centre are coded by a call-taker, who dispatches an emergency vehicle to the patient; this may include an ALS response vehicle. The dispatch of an ALS is dependent on availability and

nature and coding of the emergency. The qualification of emergency dispatcher varies, with the majority of the personnel holding a four-week basic short course qualification; the remainder have completed an eight-week intermediate life support training programme. The level of experience of the call-taker also varies, with potentially very new and inexperienced personnel taking and triaging the call (144).

2.6.3 Emergency care practitioner scope of practice

Emergency Care Practitioners complete an intensive four-year degree programme that leads to an advanced life support scope of practice, which includes the clinical assessment, diagnosis and management of coronary events like acute STEMI. ECG training includes sessions on 12 lead ECG interpretation and practice sessions. Upon completion of the four-year qualification, the successful graduate is eligible for registration with the Health Professions Council of South Africa (HPCSA) as an Emergency Care Practitioner and is then allowed to practice independently.

The decision to undertake thrombolysis was made in consultation with the cardiac consultant at the receiving regional hospital or at a remote location after normal working hours. The 12 lead ECG was either transmitted via facsimile or via telemetry. Thereafter, the researcher contacted the consultant telephonically to present the patient's details; family history, medical history, clinical presentation and the researcher's interpretation of the 12 lead ECG.

2.6.4 Hospital characteristics

South Africa uses the District Health System (72) to make health care available to all citizens as efficiently as possible. Within each province, there is a referral system in which patients usually attend the local hospital (known as the district hospital) as the first point of contact with the health care system – also referred to as the primary hospital. Thereafter, if the patient requires further management, especially for a higher level of care, the patient is referred to a regional hospital. Each health district usually has at least one regional hospital, but may have additional regional hospitals, depending on the population density of the health district. Regional hospitals may also have district level functions. The eThekwini Health District has two regional hospitals: R. K. Khan Hospital and Addington Hospital. Both regional hospitals participated in the study and the two main district level hospitals that participated were Mahatma Ghandi Memorial Hospital and Wentworth Hospital. Table 4 indicates: the referral status of the hospitals; availability of coronary care and intensive care facilities; total beds and patient population that they service. All other public and private sector hospitals within the eThekwini Health District were also invited to participate in the study.

Table 4: Hospital characteristics

Source: (92)

Health District	Hospital	Type of facility	Bed Status	Patient Population
eThekwini Population density of 3 199 699 (32% of KZN) with a 90% urban and 10% rural population distribution	R. K. Khan (Regional & District Services)	Coronary Care Unit	543	± 850 000
	Addington (Regional & District Services)	Coronary Care Unit	524	± 620 000
	Mahatma Ghandi Memorial (District Service)	No Coronary Care Unit	350	± 1 million
	Wentworth (District Service)	High Care only	220	± 450 000

2.6.5 Population and sampling strategy

The study population consisted of two groups of STEMI patients, being: 20 patients treated by the researcher in his capacity as a registered Emergency Care Practitioner (ECP); this data was compared to historical data (the in-hospital doctor thrombolysed (IHDT) group) obtained from previous research on 78 patients who were thrombolysed in-hospital by doctors (11).

2.6.6 Emergency Care Practitioner Thrombolysis (ECPT) Group

A total of 20 patients, aged 18 years and older, were prospectively recruited by the researcher. These patients either presented with symptoms at home or were admitted with a diagnosis of acute STEMI to district level hospitals in Durban. This was carried out over a 6-month period (August – January 2010). (The statistician involved in this research confirmed that 20 patients would be sufficient for statistical comparison with historical data.) The number of patients included in the study was also limited to 20 due to financial constraints. The cost of the 20 ampoules of Tenecteplase was almost R250 000.00; this was funded by third stream income generation at the researcher's place of employment.

2.6.7 Data collection

Data collection, as detailed below, was undertaken from 2 August 2009 to 6 January 2010.

2.6.8.1 Patient treatment by the ECP

Patients received routine treatment for a confirmed diagnosis of acute STEMI; this involved the administration of morphine, oxygen, nitrates, Aspirin (MONA) and Clopidogrel, as approved by HPCSA: Professional Board for Emergency Care (145). An emergency defibrillator and external pacemaker was always available. The drugs used in the study were previously approved for use by Emergency Care Practitioners by HPCSA: Professional Board for Emergency Care, following extensive consultation with the Medical and Dental Professional Board, the

Resuscitation Council of South Africa and Emergency Medicine Society of South Africa. Final approval was granted by the HPCSA upon conclusion of consultation and consideration of all inputs received.

2.6.8.2 Thrombolytic treatment

The fibrin specific thrombolytic agent used in this study was Tenecteplase (Metalyse). Tenecteplase was given over 5 seconds according to body weight, together with Enoxaparin. Patients received Enoxaparin co-therapy as an intravenous bolus of 30mg, followed by the first sub-cutaneous dose of 1mg/kg about 15 minutes after the administration of Tenecteplase. This treatment strategy is in line with the American Heart Association / European Society of Cardiology guidelines and is also similar to what was done in the STREAM study (http://clinical trials.gov.show/NCT00623623).

2.6.8.3 Electrocardiographic recordings

Emergency Care Practitioners are taught to assess ECGs as part of their four-year program. While this is a skill that is developed and assessed during the course of the four-year degree program, ECPs are encouraged to establish a system of consultation in the area in which they work. As part of the development process towards being able to assess ECGs with confidence, ECPs are required to consult with experienced cardiac consultants/nurses**.** The decision to undertake thrombolysis was made in consultation with the cardiac consultant at the receiving regional hospital or at a remote location after normal working hours. The 12 lead

ECG was either transmitted via facsimile or via telemetry. Thereafter, the researcher contacted the consultant telephonically to present the patient's details; family history, medical history, clinical presentation and the researcher's interpretation of the 12 lead ECG.

Reperfusion, defined as > 50% resolution of the ST segment, was assessed at 90 and 180 minutes post-thrombolysis. The initial plan was for serial 12 lead ECG recordings to be taken at 30-minute intervals. 12 lead ECG recordings were taken: at the initial assessment, upon regional hospital admission, at 90 minutes or at 180 minutes, depending almost entirely on whether it was practically possible to take the recording and usually in accordance with the respective hospital policy. Continuous transportation of the patient to hospital was favoured over stopping the ambulance for additional 12 lead ECG recordings. Stopping the ambulance on the side of the road is generally avoided as it is considered unsafe practice and would delay transportation of the patient to definitive care. Furthermore, the movement of the ambulance or idling of the ambulance engine affected the accuracy of a 12 lead ECG recording, as it caused patient movement that appeared on the ECG as muscular artefacts. Continuous 3 lead ECG monitoring was undertaken to monitor and treat lethal reperfusion arrhythmias if necessary.

2.6.9 In-hospital Doctor Thrombolysis (IHDT) Group

This was an observational study in which 120 patients admitted to 20 hospitals in Durban and surrounding areas with a diagnosis of acute STEMI were

consecutively recruited between August and December 2006. Patients that died during early admission were not included in the study. Of these patients, 78 received thrombolytics by doctors, with the choice of therapy being in accordance with local hospital policy. Two methods of data collection were used: direct patient interviews (primary data) were patients were approached to participate only after the patient's condition had stabilized; and review of hospital records (secondary data). The 30-day follow-up was conducted telephonically. The 20 hospitals in this study group consisted of 5 regional, 9 district and 6 private hospitals - compared to 2 district and 2 private hospitals in the ECPT group. Two regional hospitals and two district hospitals based in the eThekwini Health District also participated in the ECPT Group.

2.6.10 Patient eligibility

The inclusion and exclusion criteria are as per Table 5.

Table 5: Study inclusion and exclusion criteria

INCLUSION CRITERIA
• Patients who presented within 12 hours of the on-set of ischaemic chest pain. • ST-segment elevation of at least 0.1mV in two or more limb leads or at least 0.2 mV in two or more contiguous precordial leads, or presumed new on-set left bundle – branch block. • 18 years and older.
EXCLUSION CRITERIA
• An inability to give informed consent; and dementia. • Uncontrolled hypertension [systolic blood pressure of more than 180mmHg, diastolic blood pressure of more than 110mmHg on repeated measurements]; major surgery. • Biopsy of a parenchymal organ or substantial trauma within 2 months. • Any head injury or other trauma occurring after on-set of current myocardial infarction. • Any known history of stroke. • Any known structural damage to the central nervous system. • Current treatment with oral anti-coagulants. • Sustained cardio-pulmonary resuscitation of more than 10 minutes duration.

2.6.11 Demographic data

After obtaining patient consent, demographic data was obtained from all 20 patients. This included: age, gender, ethnic grouping, and information on risk factors such as diabetes mellitus, hypertension, smoking status, dyslipidaemia, a previous history of angina or myocardial infarction, and a family history of vascular disease. All patients were of Black African, Indian, White, or Coloured origin.

Additional information included: a detailed description of the time of on-set of ischaemic chest pain; the transportation times and mode of transport; the duration of time to treatment; and treatment received. Reasons for any delay in the initiation of treatment were also recorded; these may have included: patient delay; lack of transport; and delay at the level of the general practitioner or the primary hospital or referral hospital.

2.6.12 Patient follow-up

In-hospital follow-up was conducted through the study of all patient hospital records, as these contained general information about: the patient, the patient's clinical background, clinical condition and in-hospital clinical treatment. If data required was not clear or missing in the record, the researcher engaged with the attending medical consultant to clarify the matter or provide the information. The

30-day follow-up was conducted via a telephone interview between the researcher and the patient.

2.6.13 Complications from STEMI

All complications encountered during hospital admission and at 30-day telephonic follow-up were also documented. These complications included: recurrence of angina or myocardial infarction, sustained ventricular arrhythmias (ventricular tachycardia / ventricular fibrillation), cardiac failure, cardiogenic shock, pericarditis, complete heart block and death. Re-infarction was defined as recurrent symptoms of ischaemia accompanied by new or recurrent ST-segment elevations of 0.1mV or more in at least two contiguous leads, lasting at least 20 minutes, and further increases in cardiac biomarkers (146). Recurrence of angina was defined as symptoms of ischaemia, with ST-segment deviation or T-wave inversion persisting for at least 10 minutes despite medical management and not fulfilling the diagnosis of re-infarction (147). Cardiac failure was based on the Framingham criteria, which includes: progressive resting dyspnoea associated with clinical signs of pulmonary; and/or peripheral congestion; and requiring treatment with diuretics (148).

2.6.14 Cardiac enzyme laboratory analysis

The cardiac biomarkers used to confirm the diagnosis of STEMI in-hospital were creatinine phosphokinase (CPK), creatinine kinase muscle brain iso-enzyme (CK-MB), and or troponin T/I. Troponin T levels were measured using the Roche

Cardiac T Quantitative test, which is based on the Elisa test principle - the clinical discriminator value for myocardial infarction is 0.1ng/ml (detection range 0.010 – 25.00ng/ml; sensitivity 100% and specificity 83.9% at 24 hours) (149-152).

2.7 Design of data collection tool

For purposes of this study, a data collection tool was developed to collect all clinical data in consultation with the clinical supervisor, Prof Karen Sliwa (Appendix 1). The database (and data collection tool) was designed using Microsoft Access in order to facilitate data collection and transfer of data to a statistical package for analysis.

2.8 Research process

The research process involved EMRS control centre paramedics or operational ALS paramedics alerting the researcher to patients suspected of having acute STEMI. Similarly, doctors at the district level hospitals were requested to alert the researcher when patients were admitted to emergency departments during the study period. The control centre staff and the doctors at district level were advised of their institution's approval and participation in this study by the respective institution's line management. The researcher also followed this up with reminders at the initial stages of the research.

The researcher then responded to the emergency call using Durban University of Technology: Emergency Medical Care and Rescue (DUT: EMCR) operational paramedic response vehicle, Techmed 1. This clinical operational response unit is an existing, well established service arrangement between DUT: EMCR and KZN: EMRS for purposes of augmenting KZN: EMRS paramedic resources during peak periods and providing operational clinical practice for students of DUT: EMCR. Permission was granted to the researcher by the Head of Department of DUT: EMCR to use this operational unit for this research.

Once at the patient's side, the patient was informed about the study. Permission was sought from the patient to administer thrombolysis as per the research protocol provided they met the inclusion. The researcher also obtained permission from the patient to access personal and clinical information from hospital records and to contact the patient or the patient's next of kin 30-days from symptom on-set (this to enquire about their condition and establish early outcomes of treatment). The researcher then provided the initial routine treatment for a confirmed diagnosis of acute STEMI. This involved administration of morphine, oxygen, nitrates, Aspirin (MONA) and Clopidogrel. In some instances, some of these drugs had already been administered by the attending doctor or paramedic, in which case the initial drug treatment was adjusted accordingly. The thrombolytic treatment regime (as outlined above) was then continued.

The study was described to the patient and a Letter of Information given to the patient (Appendix 5). The Letter of Information was translated from English to

isiZulu to accommodate non-English speaking patients (Appendix 6). It must be noted that English and isiZulu are the most commonly spoken languages in KwaZulu-Natal. Patients who were willing to participate in the study were then given an Informed Consent Form to complete (Appendix 7). The Informed Consent Form was also translated into isiZulu (Appendix 8).

All 20 cases in which thrombolysis was instituted by the researcher were subjected to a local expert panel review. The local panel consisted of cardiologists from Inkosi Albert Luthuli Central Academic Hospital Cardiology Department. The purpose of this review was to obtain an external independent review by clinical experts in the field. The panel appraised the clinical summaries of all patients, in conjunction with treatment protocols used within the district health system. Feedback from the panel was intended to revise and improve overall clinical care of acute STEMI patients by emergency care practitioners and this will be discussed in Chapter 4.

2.9 Phase 4: Comparison with historical data

The clinical data for the 20 patients was assessed and compared to the researcher's own historical control data. This historical data was obtained when the researcher undertook a Master of Science (Cardiology) degree through the University of Brighton. This study assessed the use of thrombolytic treatment in the management of patients presenting with acute STEMI in several primary and secondary hospitals in Durban and the surrounding areas. In addition, the study

also addressed possible reasons for delay in the administration of thrombolytic treatment.

2.10 Data documentation

All data was initially captured at the patient's bedside on the data collection tool designed in Microsoft Access Software 2007 after all treatment was administered. Thereafter, the data was entered into the database as the patients presented to the researcher. No editing took place, as the structure of the data collection tool was the same as the database. The data was then converted into Microsoft Excel Software 2007 format for ease of transfer into IBM SPSS Version 20.0.

Errors in the IBM SPSS Version 20.0 database were minimised by a verification audit undertaken by the researcher of all 20 entries (both the original and electronic databases).

2.11 Statistical analysis

Data was analysed using the IBM SPSS Version 21.0 and G Power 3.1. Statistical analysis was performed using the following techniques: descriptive statistics, correlation analysis, multi-variate analysis and measures of association. Descriptive statistics were used to summarise demographic and clinical characteristics. Categorical variables were summarised in terms of frequencies and percentages; and for each continuous variable, the mean and standard

deviation and/or median with minimum time, maximum time and inter-quartile ranges were calculated. In this study, there was no missing data on any of the measures. Descriptive techniques included the presentation of frequency percentage tables, cross-tabulations and graphs (pie, bar and line). Inferential statistics involved testing hypotheses about the means for times. Non-parametric testing procedures were utilized, as the variables were not normally distributed. These tests included Mann-Whitney Test, Wilcoxon Signed Rank Test, Chi-Square Test and Fisher's Exact Test. Results with a $p < 0.05$ were considered significant. Where appropriate, the results are also expressed as mean ± standard deviation or medians with minimum time, maximum time and inter-quartile ranges or as proportions (%).

2.12 Data quality

2.12.1 Trustworthiness of Phase One and Phase Two qualitative data

Lincoln and Guba's (153) criteria for establishing trustworthiness of qualitative data were adopted and are described hereafter:

Credibility – the goal of credibility is to demonstrate that the inquiry was conducted in such a manner as to ensure that the subject was accurately identified and described (154). Furthermore, Lincoln and Guba (153) note that the strength of qualitative study (which is its credibility) is largely dependent on prolonged engagement, which provides scope, persistent observation and depth. In this study, considerable time was invested in data collection activities. This was

necessary to elicit an in-depth understanding of: awareness of heart attacks; the nature of programmes that exist; and also to consider characteristics of the local context. Furthermore, according to Polit and Beck (139), the credibility of a study is enhanced by the use of multiple methods to address a research problem - triangulation. Triangulation was used for the main component of the study (the qualitative evaluation of emergency care practitioner thrombolysis, including a clinical review of the implementation) and a quantitative assessment through descriptive comparison with historical data. The use of qualitative and quantitative research techniques off-set the limitations of each technique used in this study. Another technique for establishing credibility involves external checks on the inquiry. According to Lincoln and Guba (153) this can be achieved through peer presentations and input. Input on the heart attack awareness programme was solicited from cardiac nurses, cardiologists, medical practitioners and the study supervisor, who is an expert in the field of cardiology.

Transferability – in Lincoln and Guba's framework (153), transferability refers to the extent to which findings from data can be transferred to other settings or groups; it is thus similar to the concept of generalisability in quantitative research. The outputs for Phase One and Phase Two provided sufficient rich information to allow the reader to consider applicability to other similar settings.

Confirmability and dependability – confirmability refers to the objectivity or neutrality of the data, such that two or more independent people would agree about the data's relevance or meaning. Dependability refers to data stability over time and across conditions. According to Polit and Beck (139), inquiry audits can

be used to establish both dependability and confirmability. Inquiry audits are usually a systematic collection of documentation that allows an independent auditor to come to conclusions about data. All source documents collected for Phase 1 and Phase 2 were reviewed using an established tool (Adapte process) and were reviewed by the study supervisor to establish confirmability and dependability.

Researcher credibility - Patton (155) mentions that in qualitative studies, the researcher is the data collecting instrument. He or she is also the creator of the analytic process; and therefore the researcher's training, qualifications and experience are important in establishing confidence in the data. The researcher holds a post graduate qualification (MSc in Cardiology) and is a registered emergency care practitioner with HPCSA, with close to 25 years of clinical, academic and research experience. Furthermore, the researcher has an excellent professional working relationship with healthcare professionals in the area, which has developed over a 20-year period. This created an excellent rapport between the researcher and healthcare professionals, thereby facilitating a collegial and friendly, yet respectful, working environment.

2.12.2 Quantitative data quality

2.12.2.1 Pilot study

According to Brink (156) and Kelley *et al* (157), a pilot study, also known as a "preliminary study", is a small scale study conducted to: investigate the feasibility

of the proposed main study; and to detect possible flaws in the research instrument.

The data collection tool used in this study is very similar to an established data collection tool used by the researcher in a previous study. The previous data collection tool was developed from a well-established data collection tool used by a cardiac consultant from a regional hospital involved in this study. This cardiac consultant's data collection tool has been in use for more than 5 years and was also used in the consultant's postgraduate studies. The data collection tool used by the researcher in the previous study contained all aspects of the researcher's current study. The data collection tool used in this study was assessed by the researcher's supervisor and the two consultants at the coronary care units involved in the study in order to test for validity and reliability. These experts were requested to comment on the structure, appropriateness and accuracy of the demographic, risk factor, family history and clinical data. Minor modifications were made to make data capture more efficient (layout) and a few more fields were added to add clarity to information being collected (drugs administered). The pilot study was then conducted in one of the coronary care units involved in the study on one consenting stable pre-discharge post-acute STEMI patient. The results from the pilot test revealed that the data collection tool was structured correctly and that the data fields created were appropriate and accurate.

2.12.2.2 Validity and reliability of the data collection tool

The central question, according to Brink (156), that determines the concept of validity and reliability, is whether or not the researcher yielded data that reflects the truth. The truth is achieved through both reliability and validity, as they share a close relationship. Reliability is the accuracy with which the research instrument measures the responses; whilst validity is the degree to which the instrument measures what it is supposed to measure. Polit and Beck (139) state that the research instrument must fulfil its purpose by collecting the intended data in order to provide the correct information to describe the area of enquiry. To ensure reliability and validity of the research instrument, the researcher applied face and content validity. Face validity, although regarded as a weak measure (156) was used to determine readability and clarity of the variables. Content validity was used to assess how well the research instrument represents all components of the variable to be measured. By applying content validity, the assessment measured overall suitability for use by evaluating what the research instrument measured and also what it did not measure (156). All fields of the research instrument were interrogated: internally by the expert panel; and externally through the pilot study. The data collection tool used for this study was developed from a data collection tool used by the researcher in a previous study, to which the researcher made changes relevant to this study.

2.12.2.3 Internal and external validity of the study

Polit and Beck (139) state that internal validity denotes the degree to which it is possible infer that the independent variable is truly causing or influencing the

dependant variable. Possible threats to the study's internal validity could be selection threat, which encompasses bias when people are not assigned randomly to groups. For this study, participants were sampled through convenience sampling. In addition, data entered into the data collection tool were reviewed randomly and independently by the consultants of the respective coronary care units - this by cross-checking against the patient's ambulance report form and hospital records.

According to Polit and Beck (139), external validity is the degree to which relationships hold true to different people, conditions and settings. Replication is an important concept relevant to external validity, as multiple site studies are powerful and produce more confidence in the generalisability of the results. The diverse sample of the study can test whether study results are replicated in sub-groups. The participants in this study and from the historical data were from 20 hospitals.

2.13 Ethical aspects and approval

An application for the research proposal and ethical approval was submitted to and subsequently approved by the University of the Witwatersrand Research Ethics Committee – Ethical Clearance Number: M080822 (Appendix 2 and Appendix 3). Upon receiving ethical clearance from the University of Witwatersrand, permission to undertake this study was granted by KwaZulu-Natal: Department of Health (Appendix 4). Once this approval was granted from the KwaZulu-Natal Provincial Government, permission was sought from the respective

hospital managers and the manager of Emergency Medical Rescue Services to undertake the study in the respective units. It must be noted that complete documentation had to be submitted to the respective hospitals for further ethical clearance by each hospital's institutional review board.

CHAPTER 3

RESULTS

3.1 A simple, culturally sensitive and affordable chest pain awareness programme for South Africa

Following approval from the respective validation panels, a poster, an information booklet and an animated video on heart attack awareness were finalised as follows:

3.1.1 Poster

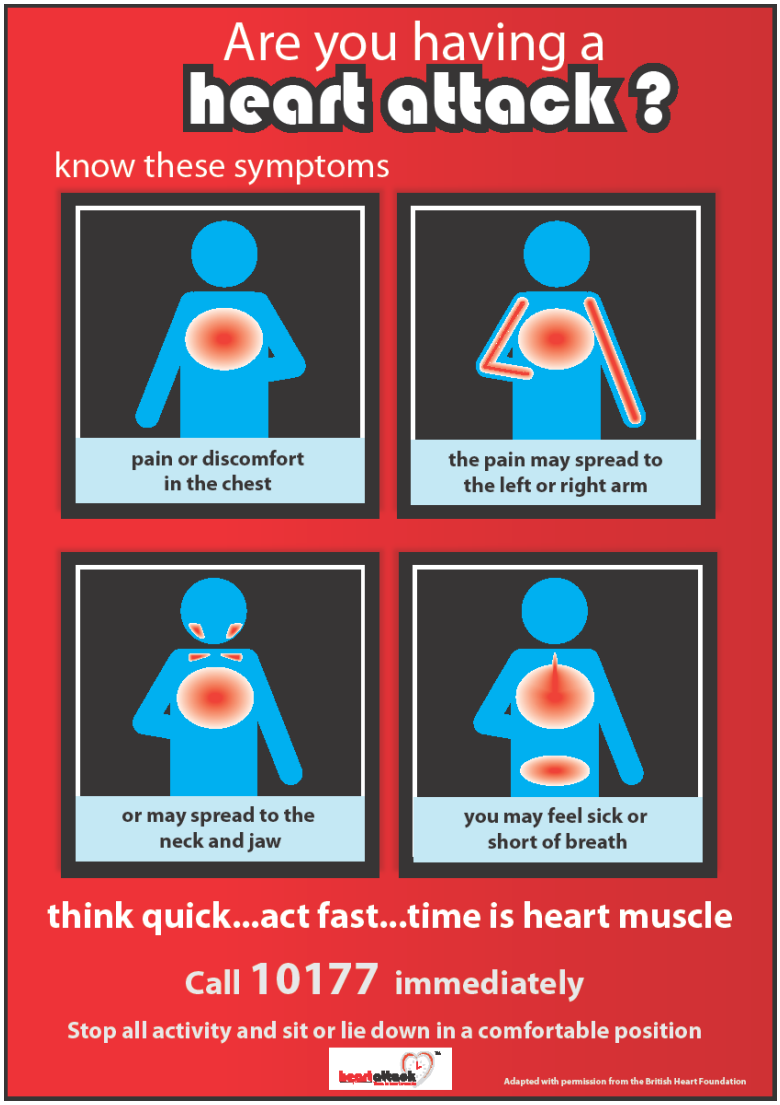


Figure 4: Heart attack poster

The poster is also attached as Appendix 10. While this poster (Figure 4) is designed primarily for dissemination in the public domain, it can be adapted for display in receiving/waiting areas of emergency departments of health establishments.

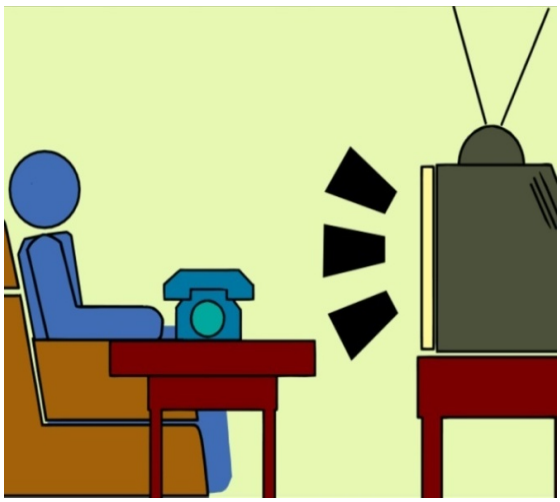
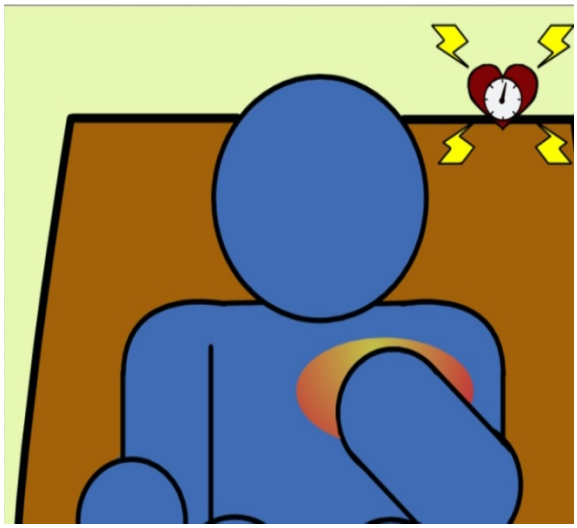
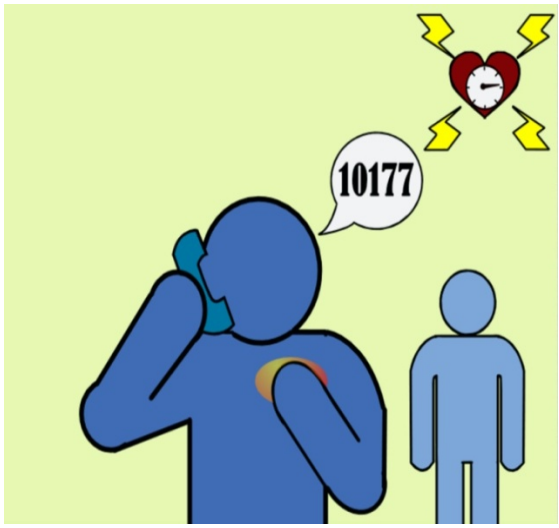
3.1.2 Information booklet

The information booklet is attached as Appendix 10. The contents of the booklet are as follows:

1. What is a heart attack?
2. What causes a heart attack?
3. Are there any warning signs and symptoms of a heart attack?
4. What are the symptoms of a heart attack?
5. How is a heart attack diagnosed?
6. What is an ECG?
7. What to do?
8. What treatment may be administered by paramedics?
9. What treatment may be administered by doctors at hospital?
10. If I have already had a heart attack, can I have another?
11. What brings on a heart attack?
12. What happens to the heart after a heart attack?
13. What are some simple exercise tips for being physically active after a heart attack?
14. What are some general dietary tips for healthy eating after a heart attack?
15. What are some dietary and lifestyle goals for reducing the risk of cardio-vascular disease?
16. Dietary guidelines.
17. Dietary recommendations.

3.1.3 Animated video

The animated video (Figure 5) is attached as Appendix 10. The storyboard of the video is as follows:

<table>
<tr><td>Title page</td><td>Scene 1: Person sitting in lounge, watching television.</td></tr>
<tr><td>
</td><td></td></tr>
<tr><td>Scene 2: Person gets chest pain.</td><td>Scene 3: Person calls for help.</td></tr>
<tr><td></td><td>
</td></tr>
</table>

(The storyboard is continued on the following page.)

(The storyboard continues from the previous page.)

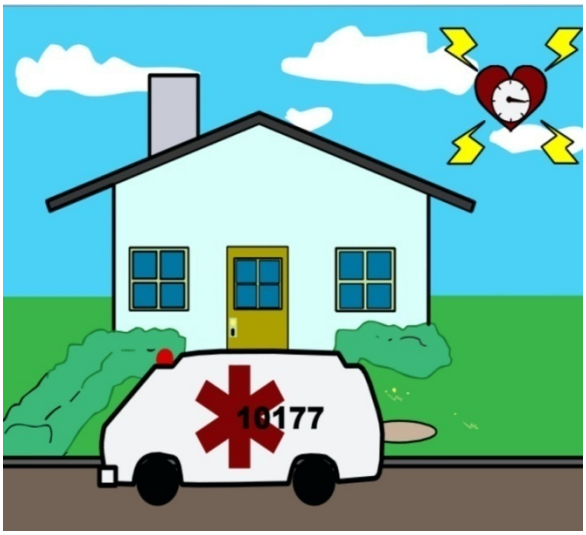
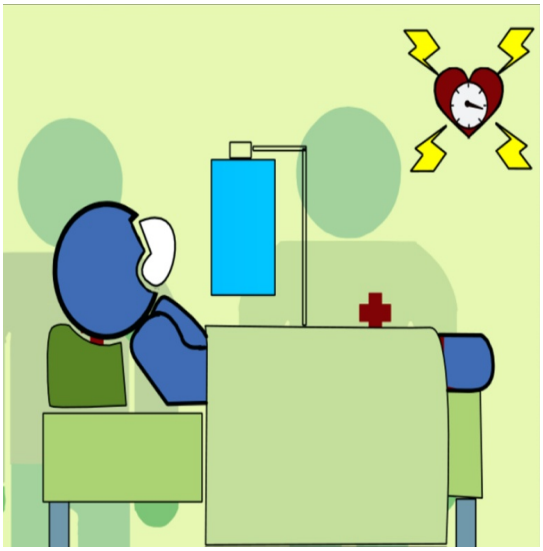
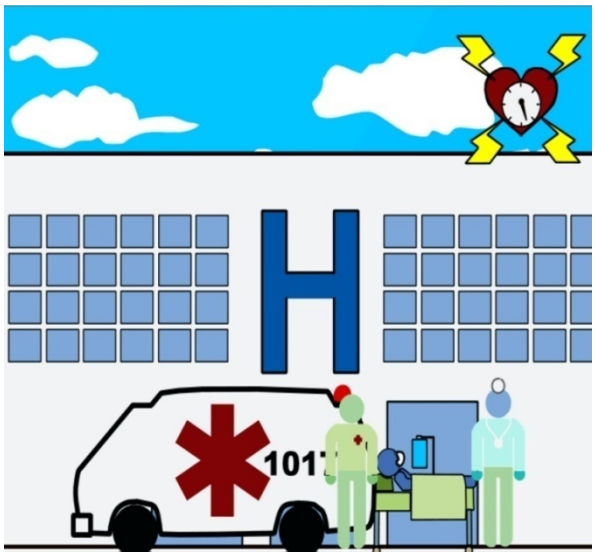
Scene 4: Ambulance arrives at person's house.	**Scene 5:** Ambulance transporting patient to hospital with oxygen, drip and ECG.
	
Scene 6: Ambulance arriving at hospital and handing patient over to doctor.	
	

Figure 5: Storyboard

3.2 Thrombolytic therapy for acute STEMI by emergency care practitioners

3.2.1 Education programme for emergency care practitioner thrombolysis

The foundation theoretical knowledge required for the practice of thrombolysis should begin with an in-depth study of anatomy and physiology of the cardio-vascular system. This should be followed by a study of the patho-physiology of acute coronary syndromes. The complications of acute coronary syndromes, more specifically acute STEMI, must be covered, as this will prepare the emergency care practitioner for complications that may arise during clinical practice. In-depth training will need to be provided on 12 lead ECG analyses, with a focus on recognition of acute STEMI from an ECG. The evidence-based thrombolysis clinical skill (Appendix 15) with supporting drug information (Appendix 13) that has been approved by the HPCSA: Professional Board for Emergency Care, will need to be taught (whilst taking into consideration the operational requirements for practical implementation of the protocol). Classroom practice through the use of simulated clinical patient scenarios for the following will prepare and improve clinical practice: stable angina, unstable angina, infarctions of the various territories including right ventricular infarction, and scenarios where thrombolysis is contra-indicated. This theoretical and practical classroom education and training will need to be supported by clinical exposure in an authentic environment, e.g. coronary care units, cardiac clinics and cardiac catheterisation facilities.

Upon successful completion of the recommended education and training programme, implementation of the skill must be undertaken using the thrombolysis

checklist (Appendix 16). An ECG monitor with data transmission, pacing and defibrillation capabilities, as well as on site access resuscitation drugs, is mandatory; and it is highly recommended that a specialist clinician experienced in acute STEMI management is consulted at the initial implementation of thrombolysis.

An on-going continuous professional development programme, which would incorporate quality improvement measures for on-going monitoring and process improvement, is also mandatory for safe emergency care practitioner thrombolysis.

3.2.2 Clinical skill: Emergency Care Practitioner Thrombolysis Protocol

The developed documents for Emergency Care Practitioner Thrombolysis are provided as appendices: Emergency Care Practitioner Thrombolysis Protocol (Appendix 15), Thrombolysis Checklist (Appendix 16) and Patient Consent Form (Appendix 17).

3.3 Thrombolytic therapy for acute STEMI by emergency care practitioners: Results of a pilot study involving 20 patients compared to historical data

3.3.1 Summary of 20 patients thrombolysed

Implementation of the thrombolysis skill was undertaken as per the expert panel and HPCSA: PBEC approved protocol using the checklist and consent form. A summary of all 20 patients thrombolysed by the researcher is as per Appendix 18:

3.3.2 Demographic data

Table 6: Demographic data

	Total	ECPT Group	IHDT Group	p-Value	Power Analysis
	N (%)	N (%)	N (%)		
	98 (100)	20 (100)	78 (100)		
Gender					
Male	72 (73.5)	15 (75)	57 (73.1)	0.862 [a]	0.054
Female	26 (26.5)	5 (25)	21 (26.9)		
Age					
Median	57.75	57.5	58	-	
30 - 39	5 (5.1)	1 (5)	4 (5.1)	0.488 [b]	0.054
40 - 49	23 (23.5)	7 (35)	16 (20.5)		
50 - 59	25 (25.5)	3 (15)	22 (28.2)		
60 - 69	33 (33.7)	6 (30)	27 (34.6)		
70 -79	10 (10.2)	2 (10)	8 (10.3)		
80 -89	1 (1)	1 (5)	1 (1.3)		
Ethnic Group					
Black	6 (6.1)	1 (5)	5 (6.4)	0.196 [b]	0.053
Coloured	3 (3.1)	2 (10)	1 (1.3)		
Indian	81 (82.7)	15 (75)	66 (84.6)		
White	8 (8.1)	2 (10)	6 (7.7)		
Type of Infarct					
Inferior	57 (58.2)	11 (55)	46 (59)	0.748 [a]	0.058
Posterior	11 (11.2)	7 (35)	4 (5.1)	< 0.001 [b]	0.244
Anteroseptal	27 (27.6)	3 (15)	24 (30.8)	0.159 [a]	0.114
Anterolateral	24 (24.5)	9 (45)	15 (19 .2)	0.038 [b]	0.220
High Lateral	3 (3.1)	0 (0)	3 (3.8)	1.00 [b]	0.053

Key: ECPT – Emergency care practitioner thrombolysis

IHDT – In-hospital doctor thrombolysis

[a] - Pearson Chi-Square Test

[b] - Fisher's Exact Test

The demographic characteristics of all patients are shown in Table 6. The total study population of 98 (100) patients comprised: 20 patients in the ECPT group; and 78 patients in the IHDT group. 73.5% were males. The majority of patients were of Indian origin (82.7%) with a median age of 57.75 years. No statistically significant differences for gender, ethnic group and median age between the groups were noted.

The most common type of infarct was in the inferior territory (58.2%). A statistically significant difference between the two groups for the posterior ($p < 0.001$) and anterolateral ($p = 0.038$) types of infarction were noted.

A family history of premature atherosclerotic coronary heart disease was prevalent in 41.8% of the patients; while 27.6% and 22.4% had a family history of diabetes and hypertension respectively (Table 7). Common conventional risk factors evident in all patients included: smoking (56.1%); hypertension (52%); and 41.8% were diabetics. No statistically significant differences were noted between the groups for family history and risk factors.

Table 7: Family history and risk factors

	Total	ECPT Group	IHDT Group	p-Value	Power Analysis
	N (%)	N (%)	N (%)		
	98 (100)	20 (100)	78 (100)		
Family History of Vascular Diseases					
Premature CHD	41 (41.8)	12 (60)	29 (37.2)	0.065 [a]	0.222
CVA	3 (3.1)	0 (0)	3 (3.8)	1.000 [b]	0.053
Hypertension	22 (22.4)	2 (10)	20 (25.6)	0.228 [b]	0.109
Diabetes Mellitus	27 (27.6)	3 (15)	24 (30.8)	0.159 [a]	0.114
Risk Factors					
MI	17 (17.3)	3 (15)	14 (17.9)	1.000 [b]	0.052
Angina	10 (10.2)	3 (15)	7 (9)	0.426 [b]	0.057
Diabetes Mellitus	41 (41.8)	9 (45)	32 (41)	0.748 [a]	0.055
Hypertension	51 (52)	10 (50)	41 (52.6)	0.838 [a]	0.053
Dyslipidaemia	10 (10.2)	2 (10)	8 (10.3)	1.000 [b]	0.050
Smoker	55 (56.1)	14 (70)	41 (52.6)	0.161 [a]	0.184

Key: ECPT – Emergency care practitioner thrombolysis

IHDT – In-hospital doctor thrombolysis

CHD – Coronary Heart Disease

CVA – Cerebro-vascular Disease

MI – Myocardial Infarction

[a] - Pearson Chi-Square Test

[b] - Fisher's Exact Test

3.3.3 Patient outcomes

The most common complications observed (Table 8) in the two groups during hospital stay and at 30-day follow-up included: cardiac failure (12.2% versus 12.2%); death (9.2% versus 7.1%); recurrence of angina (10.2% versus 6.1%); and recurrent myocardial infarction (1.0% versus 3.1%). Pericarditis was not observed during in-hospital stay and at 30-day follow-up.

Table 8: In-hospital and 30-day complications

	In-hospital Complications					30-day Complications				
	TOTAL	ECPT Group	IHDT Group	p-Value	Power Analysis	TOTAL	ECPT Group	IHDT Group	p-Value	Power Analysis
	N (%)	N (%)	N (%)			N (%)	N (%)	N (%)		
	98 (100)	20 (100)	78 (100)			98 (100)	20 (100)	78 (100)		
Recurrence of angina	10 (10.2)	2 (10.0)	8 (10.2)	0.973 [a]	0.050	6 (6.1)	1 (5.0)	5 (6.4)	0.810 [a]	0.050
Recurrence of infarction	1 (1.0)	0	1 (1.0)	0.498 [a]	0.050	3 (3.1)	0	3 (3.1)	0.238 [a]	0.053
Ventricular arrhythmias	2 (2.0)	1 (5.0)	0	0.073 [a]	0.055	1 (1.0)	0	1 (1.0)	0.498 [a]	0.050
Cardiac failure	12 (12.2)	3 (15.0)	9 (11.5)	0.680 [a]	0.053	12 (12.2)	0	12 (12.2)	0.015 [a]	0.100
Cardiogenic shock	3 (3.0)	3 (15.0)	0	0.002 [a]	0.093	0	0	0	-	-
Pericarditis	0	0	0	-	-	0	0	0	-	-
Complete heart block	4 (4.0)	2 (10.0)	2 (2.5)	0.011 [a]	0.069	0	0	0	-	-
Death	9 (9.2)	4 (20.0)	5 (6.4)	0.085 [a]	0.050	7 (7.1)	1 (5.0)	6 (7.7)	0.664 [a]	0.051

Key: ECPT – Emergency care practitioner thrombolysis

IHDT – In-hospital doctor thrombolysis

[a] - Fisher's Exact Test

3.2.4 Treatment time frame

None of the 20 patients in the ECPT group received thrombolytic treatment within two hours of on-set of symptoms; whilst 35% received thrombolytic treatment within 2 to 4 hours following the commencement of symptoms; and 60% received treatment from 4 to 6 hours. Five percent of the patients received treatment after 6 hours. In the IHDT group, 7 (9%) patients presented to the hospital in less than 2 hours from symptom on-set received thrombolytic treatment; whilst 20.5% received thrombolytic treatment within 2 to 4 hours; 24.4% from 4 to 6 hours; 23.1 % from 6 hours to 12 hours; and 23.1 % after 12 hours (Figure 6).

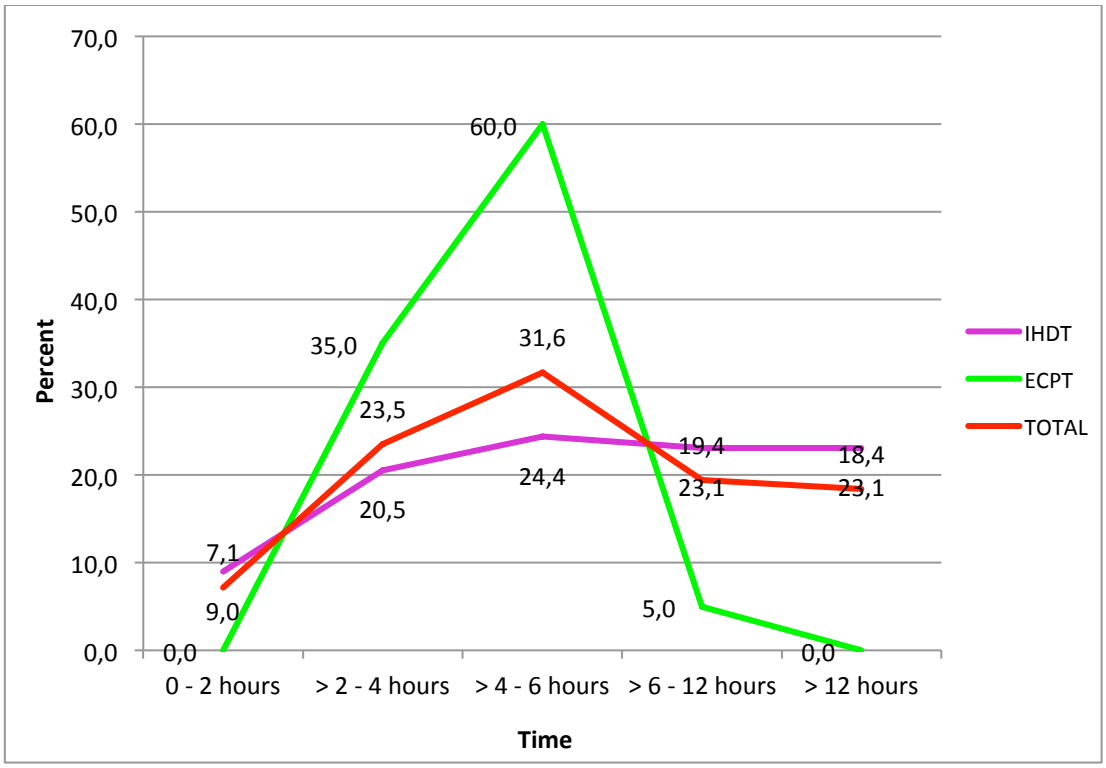


Figure 6: Treatment time frames

The median time differences to treatment are shown in Figure 7. For the ECPT patient group, the median time to calling for help from symptom on-set was 3 minutes (range 0 – 255; IQR 86). The median time taken for transportation of patient, that is, the time taken from calling for help to hospital presentation, was 95 minutes (range 20 – 245; IQR 102); while the door-to-needle median time was 140 minutes (range 30 – 265; IQR 97). For the IHDT patient group, the median time to calling for help from symptom on-set was 18 minutes (range 0 – 810; IQR 150). The median time taken for transportation of patient, that is, the time taken from calling for help to hospital presentation was 30 minutes (range 0 – 860; IQR 105); while the door-to-needle median time was 188 minutes (range 25 – 1250; IQR 275)

The median time from symptom on-set to thrombolysis for the ECPT group was 280 minutes (Range 145 – 400; IQR 146); while the median time from symptom on-set to thrombolysis for the IHDT group was 338 minutes (Range 45 – 1785; IQR 466). The mean time from symptom on-set to thrombolysis for the ECPT group was 272 ± 79 minutes; while the mean time from symptom on-set to thrombolysis for the IHDT group was 486. ± 373 minutes ($p = 0.055$ – calculated using Mann-Whitney Test). The power calculation using G Power 3.1 = 0.593.

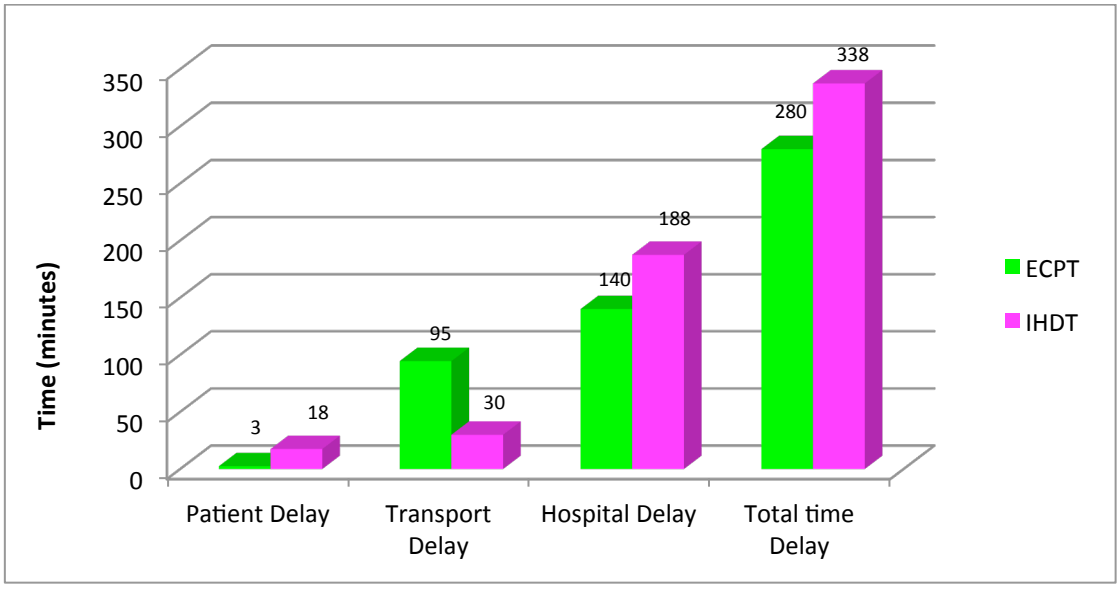


Figure 7: Median time differences to treatment

3.2.5 Transportation of patients

The use of the ambulance service was 12.2% versus private transportation of 87.8% by patient group (p = 0.070). The ECPT group comprised 5 (25%), with the majority of patients choosing private transport (15 (75%)); while the use of ambulances in the IHDT group was 7 (9%), with the majority of patients also choosing private transport - 71 (91%) (Table 9).

Table 9: Patient mode of transport

	Total	ECPT Group	IHDT Group
	N (%)	N (%)	N (%)
	98 (100)	20 (100)	78 (100)
Ambulance	12 (12.2)	5 (25)	7 (9)
Private	86 (87.8)	15 (75)	71 (91)
p-Value	0.070 [a]	N/S	N/S
Power Analysis	0.496		

Key: [a] - Fisher's Exact Test

Utilisation of ambulance transportation resulted in thrombolytic therapy being administered in a mean time of 119 ± 46.60 minutes; while the mean time for those using private transport was 127 ± 118.60 for the ECPT group. The median times were 141 minutes (Range 46 - 163; IQR 22) and 140 minutes (range 30 - 265; IQR 50) respectively. Utilisation of ambulance transportation resulted in thrombolytic therapy being administered in a mean time of 273.29 ± 175.05 minutes; while the mean time for those using private transport was 289 ± 269.33 in the IHDT group. The median times were 227 minutes (range 60 - 585; IQR 108) and 180 minutes (range 25 - 1250; IQR 138) respectively.

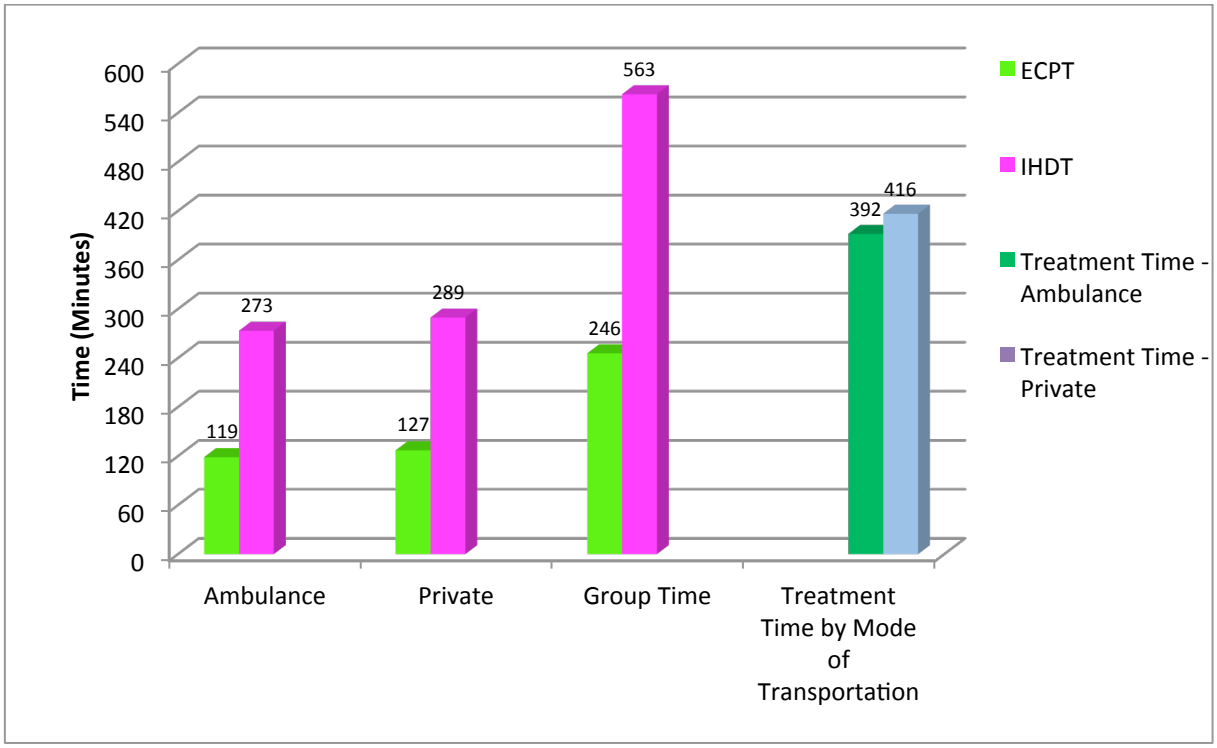


Figure 8: Transport mode and time to treatment

However: the mean door-to-needle time for the ECPT group was 124.9 ± 58.64 minutes; while the mean door-to-needle time for the IHDT group was 288.01 ± 261.44 minutes (p = 0.003 - calculated using Wilcoxon Signed Ranks Test) (Figure 8). The power calculation using G Power 3.1 = 0.056.

CHAPTER 4

DISCUSSION

4.1 Heart attack awareness programme

The development of this simple, culturally-sensitive and affordable chest pain awareness programme for South Africa has highlighted the paucity of programmes aimed at symptom recognition and action to be taken when experiencing a heart attack. The general lack of recognition of a serious medical event among populations in the developing world (resulting in prolonged delay to treatment) is well documented (35).

The developed poster (intended for general public display) could also be adapted for in-hospital waiting areas. The average waiting time for treatment at an emergency department of major hospitals in a developing country is often prolonged prior to triage and treatment (158, 159). The developed poster and instructional video could utilise patients' waiting time for educational purposes, as identified in Nigeria and Saudi Arabia (158, 159). The poster and instructional video are simple, bold and eye-catching, which would encourage patients to take notice of this aspect of the heart attack awareness programme. Furthermore, broad strategies - like the use of billboards and national television prime time viewing, as well as talk show programmes like '3 Talk with Noleen' - are essential for dissemination of this information. Video interventions may be helpful at teaching poorly educated, illiterate populations about health issues in the developing world (160). The patient encounter with the doctor is often rushed, with

many doctors being unable to spend time during the patient encounter to convey basic health concepts and preventative knowledge. The information booklet produced would offer information in simple layman's language about heart attack and heart attack prevention. This booklet can also be disseminated through primary health care centres and ischaemic heart clinics, as it is designed to be used by all heath care professionals and not only by doctors.

Knowledge of the nature of ACS and the importance of calling the emergency medical services system is necessary, but it may not be sufficient to reduce patient delay. It has been shown that even patients who have had a previous MI do not reduce delay time (43). The heart attack awareness programme addresses these concerns partially, as it contains basic information on symptoms of a heart attack and what actions to be taken for a heart attack. Dissemination of information to patients in the developing world has been an on-going public health struggle, due to limited health access and illiteracy (19, 39, 50, 74). It is for these reasons that the poster and video used animation and simple language. In addition to patient education, Moser et al (43) recommend that: the social, cognitive and emotional factors that contribute to delay need to be examined; new interventions that target high risk populations need to be tested. This is to systematically apply empirical knowledge to the education of patients who are at risk for ACS and to focus on previously under-studied and under-served populations. The impact of the heart attack awareness programme on patient education would also need to be assessed through scientific research processes.

4.2 Emergency care practitioner thrombolysis

4.2.1 Feedback from clinical expert panel

The clinical notes of all 20 patients thrombolysed by the researcher were critically assessed by an expert panel of cardiologists from Albert Luthuli Central Academic Hospital. Two main concerns were raised by the expert panel, the first being the lack of risk stratification of the patients. The expert panel pointed out that a number of the patients were high risk patients and should have been transferred directly to a specialist facility for further management. The second point revolved around clarification as to why the researcher, an emergency care practitioner, would have to go into hospitals to thrombolyse patients where doctors with the necessary drugs were available and that waiting for the researcher may have delayed definitive treatment. Other points raised by the expert panel were related to missing clinical information, assessment of reperfusion and unclear reporting of the symptom to definitive time categories. These points were corrected immediately.

In terms of risk stratification of patients, for the intention of direct admission to a tertiary level hospital, this was not considered in the planning and implementation of emergency care practitioner thrombolysis. The researcher complied with the referral patterns of the District Health System (DHS), which requires that patients be transferred primarily to the regional hospital within the designated catchment area. In terms of the DHS, EMS personnel are not allowed to deviate from this patient drainage system (72). Risk stratification must be included in the education programme as part of the initial assessment of the patient (Appendix 14); and

operational arrangements will need to be made with the respective tertiary level hospital for direct admission of high risk patients for possible cardiac catheterisation of patients thrombolysed by emergency care practitioners (64). Early risk stratification into low, intermediate and high risk categories to identify which acute STEMI patients will benefit from early coronary intervention. Several risk scores have been developed to classify acute STEMI risk like the widely known TIMI and GRACE risk scores (161, 162). However, these scores are not applicable to the pre-hospital environment, as these risk models are bedside scores used in hospital. A simple risk score, based on age, heart rate and systolic blood pressure (developed by Morrow et al (163)), is the only risk score for acute STEMI appropriate for the pre-hospital phase. Furthermore, a simple system of 90 minute post-thrombolysis ST segment resolution (> 50%), for assessing post thrombolysis reperfusion (164-166), must be included in the education and training programme and in the thrombolysis protocol for emergency care practitioners (Appendix 14). This 90 minute post-thrombolysis assessment is essential for identifying failed thrombolysis, thereby further triaging patients into those who would require rescue PCI (115).

To address the concern with regard to the researcher undertaking thrombolysis in the hospital, the following points were discussed with the expert panel of cardiologists from Albert Luthuli Central Academic Hospital:

1. From previous research undertaken (11), it was seen that at least 50% of patients who presented to district level hospitals received thrombolysis, which meant a delay in definitive treatment for the balance of the patients.

2. Some doctors revealed inexperience and required assistance at times as they lacked the ability to interpret the ECG. This was also seen in the research undertaken in Cape Town by Maharaj et al (33), where delays to thrombolysis were found: 28.6% due to consultation with a senior doctor; and 18.6% due to difficulty in interpreting the ECG. On five occasions, the researcher was called by junior doctors to treat patients who did not require thrombolysis. Some doctors were reluctant to use Streptokinase due to their lack of experience in the administration process of the agent. It was observed that this scenario became worse during the start of new rotations of doctors between hospitals or departments within the hospital.
3. Some of the hospitals did not have a thrombolytic agent available or ran out of stock and therefore called the researcher to thrombolyse and transfer the patient to the regional hospital. District level hospitals that do thrombolyse use Streptokinase only, due to its affordability.
4. The researcher observed that there was no apparent in-hospital triage for chest pain in the participating hospitals. In addition, given the workload and the administrative challenges, it appeared as though there was little to no emphasis on “time is heart muscle” by attending doctors in-hospital. The South African Triage Score (a scoring system recommended and tested in the South African context), if implemented, will ensure appropriate prioritisation of patients in emergency departments. According to the South African Triage Score, chest pain requires an urgent response (i.e. less than 10 minutes), with clear clinical management guidelines given by the receiving medical team (167, 168).

5. The focus of attending doctors appeared to be obtaining a bed in a regional hospital and getting permission from the regional hospital to transfer the patient, rather than to thrombolyse the patient. Doctors at primary hospitals will not thrombolyse a patient unless permitted to do so by the receiving regional hospital.
6. The researcher was also called to assist with the first patient at the district hospital, because: there were no beds available for the patient at the receiving regional hospital; and the referring hospital did not have Streptokinase. This patient was admitted to the emergency centre of the district hospital within 1 hour of symptom on-set and therefore could have potentially been thrombolysed within recommended guidelines (89). If the researcher did not respond to the district hospital, the patient would have been admitted to the ward in the district hospital without the benefit of thrombolysis.
7. The researcher's involvement started to speed up the in-hospital processes, as door-to-needle median time was 140 minutes (Range 30 – 265). While doctors were liaising with regional hospitals to obtain a bed, the researcher travelled to the district hospital and usually administered TNK within 10 minutes of arrival - the travel time to the participating hospitals did not exceed 15 minutes. Previous research in the South African context has shown that the median door-to-needle time in Durban and its surrounding areas was 188 minutes (Range 25 – 1250) (11).
8. Except for Patient 2, who was initially assessed by a paramedic at the patient's home, all other patients presented to a district level hospital first. The EMS dispatch to this patient was for an attempted hijacking. The

patient was shot at. Fortunately the bullet missed the patient, who then suffered a heart attack.

9. The process of confirmation of acceptance of the patient at the regional hospital (after sending the 12 lead ECG and clinical notes) needs to be reviewed. This is usually exacerbated by personality differences between transferring and receiving doctors, and access to the receiving doctor outside normal working hours. Doctors at district level hospitals need to be encouraged to focus on clinical management and stabilisation of the patient as a priority and to thereafter concentrate on arrangements for admission and transfer to a regional hospital.
10. Ideally all patients thrombolysed by an emergency care practitioner should have direct access to tertiary facilities, especially for patients with complications from acute STEMI.

4.2.2 Some specific patient related observations

In keeping with other studies, which showed that 40 to 60% of AMI patients use EMS for transportation to hospital (38, 62, 67), there was limited use of EMS by the patients in this study: most patients preferred to use private transportation, as they felt it would be quicker. There appears to be a general expectation of delayed arrival of the local public sector emergency medical services. In addition, most patients reported that they did not realise they were having a heart attack, as they did not recognise the symptoms. This is not unusual, as most patients are not

aware of typical symptoms of AMI (39, 46, 48). Furthermore, registries have shown that at least 30% of patients present with atypical symptoms (169).

4.2.3 Some specific EMS related observations

Despite recommendations for pre-hospital use of EMS for the diagnosis, triage and treatment for acute STEMI, the following observations were noted (115, 170, 171).

- There was no evidence that medical advice was given by the receiving call taker.
- Advanced life support paramedics were not routinely dispatched to patients who did activate EMS; except for one patient, which was initially dispatched as a gunshot to the body.
- Furthermore, there was no evidence in the ambulance patient report form that ALS assistance was requested for chest pain, nor whether or not Aspirin was administered and whether or not the hospitals were pre-alerted to the patient, despite the ambulance crew making a provisional diagnosis of chest pain of cardiac origin.

4.3 Comparative analysis of acute STEMI patients thrombolysed

This study found a high proportion of the Indian population with AMI - 82 (82.75%), which does not fit the ethnic group profile of South Africa. Currently, Indians make up just 2.46% of the South African population and 8.47% of people in KwaZulu-

Natal (93). Furthermore, it also does not fit the ethnic group profile within the study area, eThekwini Health District, which is: Black Africans - 68.3%; Indian - 19.9%; White - 8.98%; and Coloured - 2.82% (143). In a study conducted at R. K. Khan Hospital (172), it was reported that cardiac disease has reached epidemic proportions in South African Indians. The high proportion of Indians in the study therefore cannot be generalized to the rest of South Africa.

While the incidence of acute myocardial infarction in the Black African population in this study is relatively low 6 (6.1%), this data may herald the emergence of a new epidemic of coronary disease in the Black African population. This was previously reported as being quite uncommon (12-14). These observations raise the question of an epidemiological transition due, possibly, to: urbanisation, changes in the traditional Black African diet to a “fast food” one – high in saturated fats - and the effect of emerging affluence due to economic growth in South Africa. The most prevalent risk factor identified by Tibazarwa et al (15) was obesity (43%), with significantly more obese women than men (55% versus 23%, or 1.76 95% CI 1.62 to 1.91: $p < 0.001$).

The most common type of infarct was in the inferior territory (58.2%). Although a statistically significant difference between the two groups for the posterior ($p < 0.001$, power calculation = 0.0244) and anterolateral ($p = 0.038$, power calculation = 0.220) types of infarction were noted, these results need to be interpreted cautiously due to the small number of patients in each group which may have resulted in a Type II error.

A family history of premature coronary heart disease, diabetes mellitus and hypertension accounted for almost one-third of the study population (41.8%, 27.6% and 22.4% respectively) (See Table 7). The high incidence of premature coronary heart disease (41.8%) is consistent with the findings of Ranjith et al (10). The mean age of all patients (57.8 years) is also very young.

Smoking and hypertension risk factors were present in more than 50% of the patients (56.1% and 52% respectively), while 41.8% were diabetic; these are well-known risk factors (173). While only 10.2% of patients were reported to have dyslipidaemia, this data must be interpreted cautiously, as some patients were not aware of their cholesterol status.

A key benefit of prompt reperfusion therapy is the improvement in morbidity, typically reducing the incidence of heart failure and arrhythmias. It must be noted that patients in this study generally had a higher incidence of heart failure. By 6 hours there is limited viable myocardium and the impact of thrombolytic therapy is greatly reduced despite having a clinical impact on patient outcome up to 12 hours from symptom on-set (29). While the ECPT group had a higher mortality rate (4 of 20 (20%) in-hospital, compared to 5 of 79 (6.4%) in the IHDT group), these results need to be interpreted with caution, due to the small number in the ECPT group. Furthermore, the in-hospital group did not include patients that died in the acute phase of acute STEMI simply because the ethical provisions of the study only

allowed the researcher to approach patients for consent to participate in the study when the patient was in a clinically stable condition.

The mean symptom-to-needle time of 272 ± 79 minutes and 486 ± 373 minutes for the ECPT and IHDT groups respectively constitutes a major delay, compared to the symptom-to-needle time recommendation of less than 60 minutes (22). While the symptom to treatment time was reduced in the ECPT group ($p = 0.055$), further reductions are critical to realise the goals of reduced morbidity and mortality from STEMI. However, concentrating on delivery of thrombolytic therapy at point of patient presentation to a health care facility/professional would have a significant impact on treatment delay. To achieve point-of-contact thrombolytic therapy, the emergency care practitioner needs to be at the patient's side within at least 15 minutes from activation of the emergency medical services; district and regional hospital emergency departments need to be able to initiate reperfusion therapy within 30 minutes of arrival at hospital (22).

Patient delay often constitutes the longest period of delay to treatment (32) and should not be longer than 15 minutes, according the European Society of Cardiology (22). The mean time taken for patients to call for help was: 48 ± 77 minutes for the ECPT group; and 109 ± 59 minutes for the IHDT group. Many patients reported that they were not sure of the pain and did not think that it was serious. A number of factors were associated with patient's decision time, including: the type of acute coronary syndrome, the nature and localisation of symptoms, the place where symptoms occurred, the patient's interpretation of

symptoms and knowledge (48). Various registries of patients with AMI have shown that the time from symptom on-set to hospital presentation was: ≥ 4 hours in 50% of the patients; > 6 hours in 40%; and > 12 hours in 9 – 31% (38). Internationally, patient delays have proven to be difficult to reduce as this requires a continuous education programme (35).

The majority of patients were transported privately to hospital 86 (87.8%); while only 12 (12.2%) utilised the ambulance service; this is low compared to other published data (38, 68). It must be noted that only 1 of the 5 patients transported by ambulance was treated by the emergency care practitioner at home; therefore, greater time saving could have been achieved if thrombolysis was initiated in the pre-hospital environment by EMS. Despite informing the control center of the study and delivering repeated presentations to staff and the officers in charge, the researcher was not informed of calls received about patients with chest pain of cardiac origin. The converse also applied sporadically, the researcher was advised of all calls received, without proper screening, e.g. the researcher was informed of patients with chest pain secondary to tuberculosis. The researcher was also not informed by the ambulance crew about the 5 patients transported. These patients had a provisional diagnosis of chest pain of cardiac origin at the patient's home. The ambulance crews elected to transport the patients directly to hospital. Although there was a marginal difference in time to treatment between ambulance and private transportation, in-hospital treatment is usually faster when patients are transported by ambulance (62). The results of this study must also be interpreted

with caution, as the study was conducted mainly in an urban setting and not in a rural setting where there are prolonged transportation times.

There was a clear indication of significant delays in the treatment of STEMI at the receiving hospital: 125 ± 59 minutes in the ECPT group; and 288 ± 261 minutes in the IHDT group. The significant delays at hospital were due to: non-triage (not assessed) of patients with chest pain; non-availability of a thrombolytic agent; lack of sufficient; and appropriate acute care training by the attending medical officer. There were also indications that some district hospitals have the resources to initiate thrombolysis but it was not being applied consistently. The focus of the attending medical officer appeared to be on securing a bed for the patient in the respective coronary care unit and obtaining permission to initiate thrombolysis. Further research needs to be undertaken to identify the reasons for under-utilisation of thrombolysis at district level hospitals. Local medical officers need to be encouraged to initiate thrombolytic treatment before referral and confirmation of a bed at regional hospital coronary care units. This delay is unacceptable, considering the international recommendation for time to thrombolysis within the hospital is within 30 minutes (30). While the reasons for delay to treatment within the hospital environment were not the scope of this study, most patients reported long waiting periods within the emergency department. Door-to-needle time was significantly reduced when thrombolysis was initiated by the emergency care practitioner ($p < 0.003$). A recent study undertaken by Maharaj et al (33) at three regional hospitals in Cape Town concluded that a significant number of patients were not thrombolysed within 30 minutes of presentation due to: a lack of senior

doctors (28.6%); difficulty in interpreting ECGs (18.6%); atypical presentation (12.9%); patients going into cardiac arrest (11.4%); hypertension 7.1%; shift change (7.1%); obtaining a chest X-ray (4.3%); fibrinolytics agent not available in emergency centre (4.3%); and other system challenges (5.7%).

When comparing the results of the treatment timeframes with the United Kingdom MINAP database (where more than 75% of patients were treated within 6 hours from symptom on-set (27)) the South African performance i.t.o. delivery of reperfusion therapy requires urgent review - despite the reduction in call-to-needle time by emergency care practitioner involvement. Within the United Kingdom, a national 'treatment target' of 'door-to-needle' (DTNT) (and more recently 'call-to-needle time' (CTNT)) has been enforced since 2000. The timeframe of DTNT of < 30 minutes and CTNT of < 60 minutes represent guidance from the European Cardiac Society. There has been a significant improvement in time to delivery of reperfusion therapy, with: > 85% of patients now receiving thrombolysis within 30 minutes of arrival in-hospital; and > 60% receiving therapy in under 60 minutes after calling for professional help. In comparison, performance in Durban was poor (174). Key to the success achieved in United Kingdom has been: clinical audit, training of medical/nursing/paramedics, and publication of individual hospital performance to "name and shame" poor-performing hospitals (175).

4.4 Limitations of the study

Several limitations of this study have been identified. Being a feasibility study, the results from ECPT group cannot be generalised; and no statistically significant conclusions can be made due to the small number of patients treated. Furthermore, comparisons made between the two groups may be flawed as the ECPT group involved just 2 district hospitals, while the IHDT group included 20 hospitals of various types (this group included regional hospitals, district hospitals and private hospitals). Apart from varying in type, the hospital's policies, facilities and equipment varied as well. No provision was made in this study for chance or participant bias for the generally improved time to ECP thrombolysis. A further reduction in symptom to treatment could have been achieved if patient recruitment was primarily at the site where the patient initially had the chest pains, i.e. at home or work - as is intended by emergency care practitioner thrombolysis. A limited number of district level hospitals participated in the ECPT group. Data from the IHDT group has shown that several hospitals without PCI capabilities do not consistently initiate thrombolytic treatment for confirmed acute STEMI patients, resulting in significant treatment delays. The emergency care practitioner's response time to the patient was not recorded. Although every attempt was made to limit the response time and time to lyses to the bare minimum when at the patient's side, the actual times would have been beneficial, if they had been recorded. Inferences from the results of this study cannot be generalised to private sector hospitals in the research area. It must be noted that some private sector hospitals have PCI facilities and that management strategies for acute STEMI vary considerably from one private hospital to another. While serial 12 lead ECG recordings were planned to be undertaken at 30 minute intervals to assess for

reperfusion, this was not always practically possible, e.g. the patient may have been in the process of transferring from hospital into the ambulance or vice versa or in transit from one hospital to another. The most practical time for following thrombolysis for a 12 lead ECG recording was found to be during admission at the receiving CCU.

CHAPTER 5

CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

South Africa is a developing nation that is experiencing economic growth, urbanisation and general improvement in basic services. The net benefit of this is contributing to higher disposable income, which in turn leads to behaviour changes that promote a sedentary lifestyle, increase in smoking and changes to diets to mimic that of the Western world. It is, therefore, critical to ensure the earliest possible initiation of treatment to reduce morbidity and mortality from AMI. The most effective system will integrate key components to deliver continuous patient care, that is: reduce the time to making the call for help from symptom on-set; reduce transportation time to hospital using a well-resourced emergency medical services; and overall reduction of door-to-needle or door-to-balloon time at hospital.

ECP thrombolysis resulted in a statistically significant reduction in symptom-to-needle time and door–to-needle time. The findings of this study clearly demonstrate that there is prolonged time to definitive treatment in each component (that is: the patient, transportation and in-hospital treatment), resulting in delayed thrombolysis.

5.2 Recommendations

5.2.1 Prevention

Government public awareness initiatives should be aimed at emphasising prevention and reducing the risks of cardio-vascular diseases. National government needs to play an active role in promoting a healthy life style, which involves healthy eating and exercise. The issue of obesity, especially amongst teenagers, and dependency on convenience foods also needs to be addressed. Major risk factors for the development of coronary heart disease, (smoking, family history, adverse lipid profiles and hypertension) are well established, therefore more educational programmes (through schools, prime time television screening, clinics) need to be introduced to reduce ignorance and rectify misconceptions and stereo typical thinking about cardio-vascular diseases.

Some of these initiatives may be achieved through health policies endorsing healthy products and banning harmful products e.g. smoking. Community health workers should be trained on disease prevention as part of their primary health care responsibilities. Other specific initiatives include a structured cardiovascular disease awareness programme, such as September Heart Awareness Month. More specific to this study, further research needs to be undertaken to examine AMI awareness in a group randomised to the chest pain awareness programme or not, with comparison to probable action in the short to long-term.

Given the alarmingly high incidence of AMI amongst the Indian population group, carefully monitored intervention strategies aimed at reduction needs to be implemented as soon as possible. Furthermore, a multi-centred prospective study is necessary to determine the emergence of acute coronary syndromes in the Black African population; and preventative interventional strategies need to be implemented to limit the deleterious lifestyle changes associated with socio-economic improvements in South Africa.

5.2.2 Cardiac care network

A network for acute STEMI management should be developed at national and regional levels by government, health care professionals, health care insurance providers, hospitals and emergency medical services. The network needs to have a mutually acceptable emergency protocol to ensure that patients with cardiac symptoms are able to access emergency medical services without barriers to timely evaluation and treatment. External surveillance registries, like MINAP and the Swiss registries and cardiac care networks like the Vienna STEMI (176) and Bologna (177) networks, would provide valuable information on trends for both pre-hospital and in-hospital management of acute STEMI; they should therefore be established and used to reduce treatment timeframes and improve clinical outcomes.

5.2.3 Patient delay and transportation

Patients and bystanders should be educated to ensure they are able to recognise symptoms early, activate the emergency medical services early - and thereby reduce the time to reperfusion treatment. Patients with chest pain should also ideally be transported by ambulance, rather than by friends or relatives because of the proven association between arrival at the hospital emergency department and early reperfusion therapy.

5.2.4 Pre-hospital management

EMS providers should be encouraged to make a pre-hospital diagnosis to allow for preparation before arrival of the patient at the emergency department, which may result in an important improvement in the delivery time of thrombolysis. There is a need for a well-structured educational programme to ensure safe early acute STEMI diagnosis with 12-lead ECG at home or in the ambulance by emergency care practitioners. A system of consultation and 12-lead ECG transmission with CCU nurses or a senior paramedic or specialist clinician who is experienced in STEMI management is highly recommended at initial implementation of thrombolysis and for on-going clinical support in difficult cases. Furthermore, paramedics could fast-track acute STEMI patients to CCU by by-passing the developing emergency departments and by-passing local hospitals to deliver the patient to a hospital with an on-site catheterisation laboratory for either rescue angioplasty or pre-discharge angioplasty.

An on-going continuous professional development programme that incorporates quality improvement measures obtained by on-going monitoring of pre-hospital thrombolysis via clinical audit and feedback must be mandatory for continued safe pre-hospital thrombolysis and staff development. A clinical review team, incorporating all role players, would need to meet regularly to appraise all cases of pre-hospital thrombolysis. In settings where the frequency of performance of thrombolysis is low, an on-going programme of refresher training would be essential to maintain skill competence. Furthermore, pre-hospital thrombolysis should be done within a prospective research project to measure the effects of early initiation of treatment on acute STEMI within the South African context.

5.2.5 In-hospital management

All hospitals need to develop a guideline-based protocol for triaging and managing patients presenting to the emergency department with acute STEMI. The delay, from patient arrival time at the emergency department (either by self-presentation or by emergency care providers) to initiation of thrombolytic treatment, should ideally be less than 30 minutes to be in line with evidence-based best practice guidelines. Patients with chest pain must be triaged immediately to reduce the reported long waiting periods in queues by patients. The poster designed by the researcher, which is aimed at the general public, can be modified to alert patients with chest pain in the hospital queues to seek help from the nurse or doctor in charge of the emergency department. Frontline doctors or nurses should undergo continuous professional development programmes to encourage prompt thrombolytic therapy independently and with confidence. Better co-operation will

need to be fostered between prehospital emergency care providers and emergency medicine specialists in the emergency department. “Fast tracking” to CCU, when emergency departments are not operationally ready for thrombolysis, may be a necessary option to reduce delays. A system of consultation and 12-lead ECG transmission with CCU nurses or a specialist clinician experienced in STEMI management (and for on-going clinical support in difficult cases) is also recommended for inexperienced, junior doctors and nurses in emergency departments.

Every attempt must be made to reduce the in-hospital drug acquisition and administration delays to thrombolysis. The use of Tenecteplase, which can be administered by bolus injection, could be another way of reducing time to thrombolysis. Regardless of the agent used, the drug could be kept in the emergency department. The hospital’s performance should be continually monitored as part of the strategy to shorten in-hospital delays; and if the average delay is longer than 30 minutes for patients, the process must be examined and improved.

While thrombolysis by ECPs offers a significant improvement in reducing symptom-to-needle time in treating acute STEMI, systems to facilitate various approaches need to be implemented. Until reperfusion strategies are delivered effectively, the promise of reduced morbidity and mortality from AMI will not be realised. This, however, can be realised by re-organisation of the respective components of the current South African health care system.

APPENDICES

Appendix 1: Data Collection Tool

PERSONAL DETAILS

ID: 1

Date:

Sumame

Name

Gender:

Address

Area

DOB

Age 0

Race

Telephone 1:

Telephone 2:

SYMPTOM TO CALL

Symptoms experienced:

Symptom 1:

Symptom 2:

Symptom 3:

Date of onset:

Time of onset:

Date called for help:

Time called for help:

MODE OF TRANSPORT

TIME

Ambulance ☐

Public ☐

Private ☐

Other

GP/HOSPITAL TIME FRAME

Time of arrival at GP

Referral to hospital by GP? ☐

Time of referral by GP

Time of arrival at primary/district hospital

Primary/district hospital

Time transferred from primary facility:

Time arrived at regional /referral hospital:

Name of regional/referral hospital

EMERGENCY CARE PRACTITIONER TREATMENT

TIME

Oxygen ☐

Aspirin ☐

Clopidogrel ☐

Glyceryl Trinitrate ☐

Morphine Sulphate ☐

Tenecteplase ☐

Time thrombolysed:

Unfractioned Heparin ☐

Reason for non-thrombolysis

Patient refused thrombolysis ☐

Known contra-indication ☐

Outside treatment time ☐

Other_____ ☐

SYMPTOM TO NEEDLE TIME FRAME

Symptom to needle time:

Reason for delay (if > 2 hours to definitive treatment):

Patient Unawareness ☐ Doctor Delay ☐

Delay at receving hospital ☐ Primary Hospital Delay ☐

Transport Delay ☐ Other_____ ☐

SITE OF INFARCTION

Inferior ☐

Posterior ☐

Anteroseptal ☐

Anterolateral ☐

☐ High Lateral

Q Wave infarct ☐

FAMILY HISTORY

Premature CHD ☐
Male < 55, Female <65

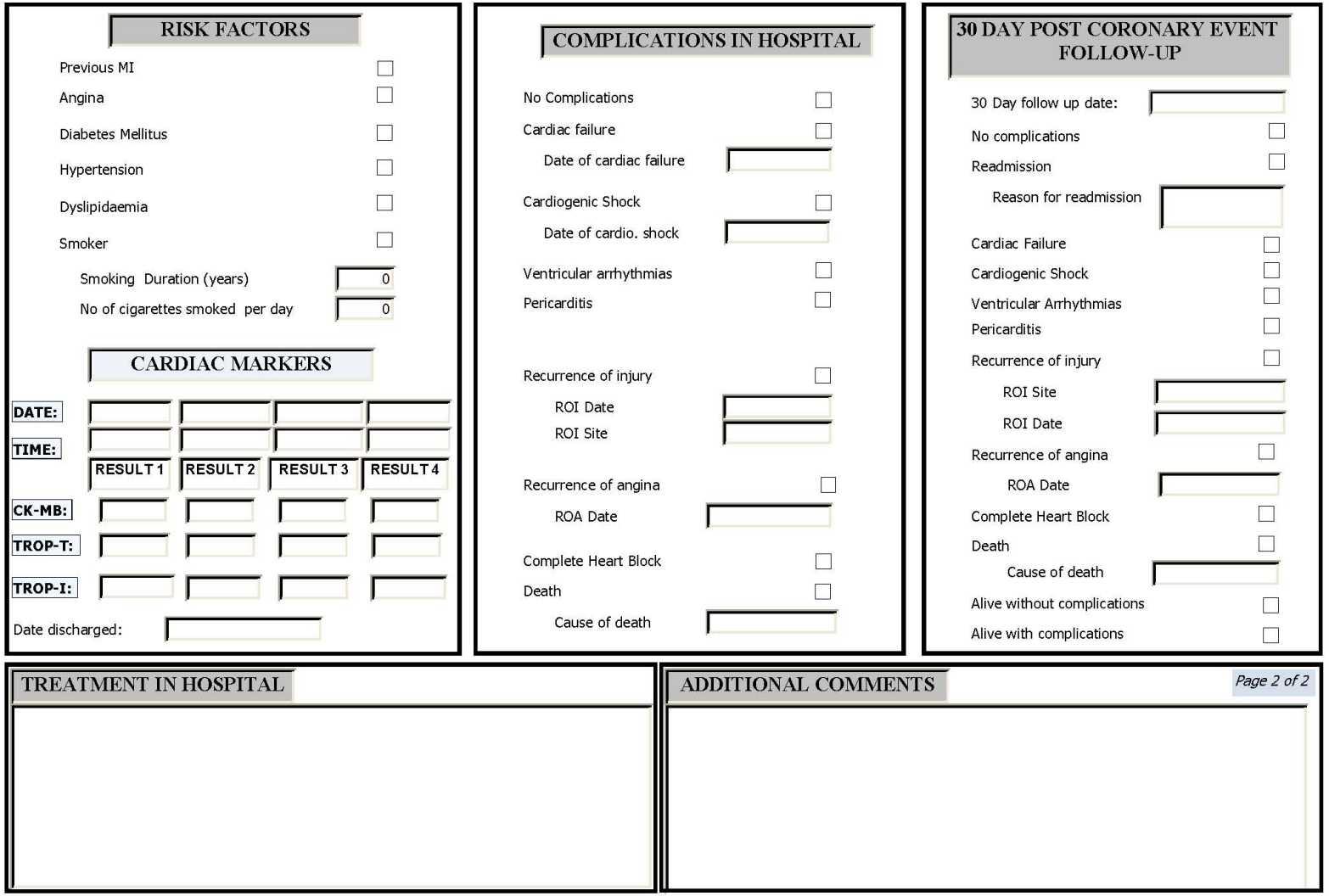
CVA Father ☐

CVA Mother ☐

Hypertension ☐

Diabetes ☐

Page 1 of 2



RISK FACTORS

Previous MI ☐
Angina ☐
Diabetes Mellitus ☐
Hypertension ☐
Dyslipidaemia ☐
Smoker ☐
Smoking Duration (years) 0
No of cigarettes smoked per day 0

CARDIAC MARKERS

	RESULT 1	RESULT 2	RESULT 3	RESULT 4
DATE:				
TIME:				
CK-MB:				
TROP-T:				
TROP-I:				

Date discharged:

COMPLICATIONS IN HOSPITAL

No Complications ☐
Cardiac failure ☐
Date of cardiac failure
Cardiogenic Shock ☐
Date of cardio. shock
Ventricular arrhythmias ☐
Pericarditis ☐
Recurrence of injury ☐
ROI Date
ROI Site
Recurrence of angina ☐
ROA Date
Complete Heart Block ☐
Death ☐
Cause of death

30 DAY POST CORONARY EVENT FOLLOW-UP

30 Day follow up date:
No complications ☐
Readmission ☐
Reason for readmission
Cardiac Failure ☐
Cardiogenic Shock ☐
Ventricular Arrhythmias ☐
Pericarditis ☐
Recurrence of injury ☐
ROI Site
ROI Date
Recurrence of angina ☐
ROA Date
Complete Heart Block ☐
Death ☐
Cause of death
Alive without complications ☐
Alive with complications ☐

TREATMENT IN HOSPITAL

ADDITIONAL COMMENTS

Page 2 of 2

Appendix 2: Research Proposal Approval – University of the Witwatersrand

Faculty of Health Sciences
Medical School, 7 York Road, Parktown, 2193
Fax: (011) 717-2119
Tel: (011) 717-2745

Reference: Ms Tania Van Leeve
E-mail: tania.vanleeve@wits.ac.za
07 October 2008
Person No: 326438
PAG

Mr R Naidoo
28 Clark Road
Queensburgh
Kwazulu-Natal
4093
South Africa

Dear Mr Naidoo

Doctor of Philosophy: Approval of Title

We have pleasure in advising that your proposal entitled "*Thrombolytic therapy for acute myocardial infarction by emergency care practitioners*" has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 3: Human Research Ethics Committee Approval – University of the Witwatersrand

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Naidoo

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M080822**
PROJECT	Thrombolytic Therapy for Acute Myocardial Infarction by Emergency Care Practitioners
INVESTIGATORS	Mr R Naidoo
DEPARTMENT	Medicine and Cardiology
DATE CONSIDERED	08.08.29
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 08.11.28 **CHAIRPERSON** .....
(Professor P E Cleaton Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof K Sliwa-Hanle

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

Appendix 4: Ethical Approval – KwaZulu-Natal Health Department

HEALTH
KwaZulu-Natal

Health Research & Knowledge Management sub-component
10 – 103 Natalia Building, 330 Langalibalele Street
Private Bag x9051
Pietermaritzburg
3200
Tel.: 033 – 3953189
Fax.: 033 – 394 3782
Email.: hrkm@kznhealth.gov.za
www.kznhealth.gov.za

Reference : HRKM102/08
Enquiries : Mrs G Khumalo
Telephone : 033 – 3953189

18 December 2008

Dear Mr Naidoo

Subject: Approval of a Research Proposal

1. The research proposal titled **'Thrombolytic therapy for acute myocardial infarction (AMI) by emergency care practitioners'** was reviewed by the KwaZulu-Natal Department of Health. The proposal is hereby **approved** for research to be undertaken at eThekwini District.
2. You are requested to undertake the following:
   a. Make the necessary arrangement with identified facility before commencing with your research project.
   b. Provide an interim progress report and final report (electronic and hard copies) when your research is complete.
3. Your final report must be posted to **HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200** and e-mail an electronic copy to hrkm@kznhealth.gov.za

For any additional information please contact Mrs G Khumalo on 033-3953189.

Yours Sincerely

L. Sipies

Dr. S.S.S. Buthelezi
Chairperson: Provincial Health Research Committee
KwaZulu-Natal Department of Health

Appendix 5: Patient Information Document – English

PARTICIPANT INFORMATION DOCUMENT

Study title: Thrombolytic therapy for acute myocardial infarction by emergency care practitioners.

Greeting: Hello Sir / Madam. My name is Raveen Naidoo and I am doing research that involves early treatment of heart attack patients by emergency care practitioners (paramedics).

Introduction:

You are being invited to take part in this research study. Research is just the way to learn the answer to a question. Before you decide whether or not to participate, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask me if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Why have I been chosen?

You have been chosen because you are a patient who has suffered a heart attack.

In this study we want to learn about safe initiation of thrombolytic treatment for heart attack patients by emergency care practitioners (paramedics) in the South African context, in particular, in Durban and the surrounding areas. The procedure known as “thrombolysis” involves administration of a drug that will break down a dangerous clot in the blood vessels of the heart. The earliest possible time for starting thrombolysis is critical to lower the effects of a heart attack. Thrombolysis is a well-established method of treatment for heart attacks in-hospital; however, unlike in other countries, it does not occur outside hospital in South Africa. In this part of the study, we would like to find out: how long did it take for the heart attack patient to receive thrombolytic treatment by an emergency care practitioner; and what is the overall effect of this treatment on the patient. The results of this study will provide valuable information and will guide the national roll-out of emergency care practitioner-led thrombolysis in South Africa.

What is involved in the study?

I need your permission to give you the thrombolytic agent, i.e. the drug that will break down the clot in your heart. I will also need your permission to read your patient file later at the hospital to obtain information relevant to the study and to contact you or your next of kin in a month's time to follow-up on your well-being. I will make every effort not to cause any discomfort or distress to you or your family. The information I require is specific information about your clinical treatment and some laboratory results.

What are the possible risks of taking part?

There are some risks to you as a patient, because the treatment being offered to you, although well established treatment regime undertaken in the hospital environment, is not without side effects and complications. Some patients have reported experiencing side effects such as bleeding - predominantly at the injection site. Successful treatment with the thrombolytic agent may be accompanied by arrhythmias. Your blood pressure may also drop. You may be nauseas and may experience vomiting. You may also have mild pain, swelling and mild local irritation of the skin from the injection given.

What are the procedures for handling adverse events and what arrangements have been made for compensation?

Most of these complications do not need further treatment; however, should treatment be necessary, this will first be provided by me in my capacity as a paramedic and then by the doctor in charge at your hospital. Compensation is provided through professional indemnity, student indemnity cover and in-hospital provisions.

What are the possible benefits of taking part?

Research has already shown that earlier administration of thrombolytic agents improves patient outcome after a heart attack, which may be a direct benefit to you. In addition, the information obtained through your participation will be useful i.t.o. future care of heart attack patients. The information obtained from this study will provide guidance to health care professionals (especially paramedics) on how to start the thrombolysis procedure outside hospital. It may provide guidance to government officials on how to improve cardiac care.

Are there alternative procedures or courses of treatment that might be advantageous to me?

There is no alternative treatment.

Do I have to take part?

No; your participation is entirely voluntary. Your routine treatment will not be affected in any way if you decide not to take part in the study or if you decide to withdraw from it.

Are there reimbursements for "out of pocket" expenses?

You will not be paid to participate in this study and there will not be any reimbursements, as this is not applicable in this study.

Will my taking part in this study be kept confidential?

All participant information will be kept confidential. All information will be stored electronically and will be password-protected for a period of five years. After that, all information will be deleted. Only the researcher and the researcher's supervisor will have access to the information. All information will be coded and will not be made public. The findings of the study will be used for research purposes only. However, absolute confidentiality cannot be guaranteed as personal information may be disclosed if required by law, or organisations may inspect and/or copy your research records for quality assurance and data analysis. These organisations may include groups such as the Research Ethics Committee and the Medicines Control Council.

What will happen to the results of the study?

The results of the study will hopefully be published in a peer-reviewed journal and will be made available to relevant professional boards and government departments. The results will also be made available to participants upon request. You have the right to be informed of any new findings that are made if you request such information.

Who has reviewed the study?

This research project has been reviewed and approved by the University of the Witwatersrand Research Ethics Committee. In addition, permission to undertake the study has been granted by: KZN Health Department; KZN Emergency Medical Rescue Services; and the Hospital Manager of your hospital.

You are welcome to contact me or my supervisor if you have any questions to which you would like answers or to report any study related adverse effects. If you are not satisfied with any area of the study, please feel free to forward any concerns to my supervisors. The name of the Research Ethics Committee (REC) administrator and chair are provided below for purposes of reporting complaints or problems.

Contact for further information

Name of Researcher:

Mr Raveen Naidoo

Director: Postgraduate Development and Support (Acting)

Durban University of Technology

Tel: 031 3732846

Name of Supervisor:

Prof K. Sliwa

Director: Soweto Cardiovascular Research Unit

Associate Professor of Medicine and Cardiology

Department of Cardiology

CH Baragwanath Hospital

University of the Witwatersrand

Tel: 011 9338197

Name of REC Administrator and Chair: Prof P. E. Cleaton Jones.

Appendix 6: Patient Information Document – isiZulu

IPHESHANA LOKWAZISA KOZOBAMBA IQHAZA NEMVUME YOKUBAMBA IQHAZA

Isihloko socwaningo: Ukwelashwa ngendlela yokuncibilikiswa kwehluli legazi elihambisana nesifo senhliziyo ngabasebenzi bosizo oluphuthumayo.

Isibingelelo: Sawubona, igama lami ngingu Raveen Naidoo ngenza ucwaningo oluhambisana nokwelashwa ngokushesha kokuhlaselwa isifo senhliziyo ngabasebenzi bosizo oluphuthumayo.

Isendlalelo:

Uyamenywa ukuthi ubambe iqhaza kulolucwaningo. Ucwaningo luyindlela yokuthola impendulo yombuzo othile. Ngaphambi kokuba uthathe isinqumo kubalulekile ukuthi uqonde kahle isizathu socwaningo nokuthi yini elindelekile. Ngicela uthathe isikhathi sakho ufunde leminingwane elandelayo ngokucophelela futhi ukhulumisane nabanye uma ufisa ukwenze njalo. Ungangibuza uma kukhona okungacacile noma ufuna eminye iminingwane. Zinikeze isikhathi sokuthi wenze isinqumo sokuthi uyalibamba iqhaza yini kulolucwaningo noma qha.

Kungani ngikhethiwe?

Ukhethwe ngoba uke waphathwa isifo senhliziyo ngaphambilini.

Kulolucwaningo sifuna ukufunda ngesikhathi esiphephile sokuqalisa ukwelapha okuvimbela ukwakheka kwamahluli egazi kulezoziguli eziphethwe isifo senhliziyo uma zelashwa abosizo oluphuthumayo eNingizimu Afrika, ikakhulukazi eThekwini namaphethelo. Indlela yokwelapha ebizwa ngokuthi i”thrombolysis” (ukuncibilikiswa kwegazi) isebenzisa uhlobo lwemithi encibilikisa amahluli ayingozi emithanjeni yegazi esenhlizweni.

Ukuqalisa ukwelapha ngokushesha kusetshenziswa ukuncibilikiswa kwegazi kubalulekile ekwehliseni imiphumela engemihle yesifo senhliziyo. Ukwelapha ngokuncibilkisa igazi indlela yokwelapha eyamukelekile esetshenziswa esibhedlela, kodwa eNingizimu Afrika akufani nakwamanye amazwe ngoba lendlela yokwelapha ayisetshenziswa ngaphandle kwesibhedlela.

Ngalolucwaningo sifisa ukuthola ukuthi kuthathe isikhathi esingakanani ukuthi isiguli esihlaselwe isifo senhliziyo sithole ukwelashwa ngokuncibilkiswa kwegazi abosizo oluphuthumayo. Sifuna nokuthola ukuthi ukuthi ithini imiphumela yokwelashwa ngaloluhlobo. Imiphumela yalolucwaningo izonikeza ulwazi olubalulekile oluyosiza ekunikezeni umhlahlandlela ekwethulweni kokwelapha ngaloluhlobo ngabezimo eziphuthumayo lapha eNingizimu Afrika.

Ngabe lolucwaningo luqhutshwa kanjani?

Ngidinga ukuthi unginikeze igunya lokuthi ngikunikeze umuthi wokwelapha ngokuncibilikisa igazi i.e. umshanguzo uzobulala amahluli egazini. Ngizodinga ukuthi unginikeze igunya lokuthi ngihlole izincwadi zakho zasesibhedlela ukuze ngithole imininingwane eqondene nocwaningo negunya lokuthi ngixhumane nomunye wezihlobo zakho ukuze ngithole ukuthi uqhuba kanjani. Imininingwane engiyidingayo ileyo eqondene ngqo nokwelashwa kwakho esibhedlela neminye yemiphumela yokuhlolwa kwakho.

Ingabe yibuphi ubungozi obuhambisana nokubamba iqhaza?

Kukhona ubungozi obhekene nabo wena njengesiguli esibambe iqhaza kulolucwaningo ngenxa yokuthi yize umshanguzo ozonikezwa wona ujwayelekile ukusetshenziswa esibhedlela, kodwa lomshanguzo unakho ukungaziphathi kahle eziguli. Ezinye iziguli kuyenzeka zibike imiphumela engemihle yalomshanguzo, lemimiphumela okubalwa kuyo ukopha ikakhulukazi lapho kungene khona umjovo. Ukulashwa okuyimpumelelo kungahambisana nokushaya kwenhliziyo ngendlela engejwayelekile. Kungenzeka futhi wehlelwe umfutho wegazi (blood pressure). Ungaba nenhliziyo encane ehambisana noma ingahambisani nokuphalaza. Kungenzeka ube nobuhlungu kanye nokuvuvukala lapho ujovwe khona.

Ingabe iziphi izindlela zokuvikela imiphumela engemihle futhi iziphi izinhlelo ezilungiselelwe ukunxephezela labo ababambe iqhaza?

Isikhathi esiningi lemiphumela engemihle ayidingi okunye ukwelashwa kodwa uma kwenzeka kube nesidingo sokwelashwa, lokhu kwelashwa kuyonikezwa yimina njengomsebenzi wezimo eziphuthumayo bese welashwa nawudokotela wasesibhedlela sakho. Ukunxephezelwa kulungiselelwe ngokomsebenzi engiwenzayo, ukuba umfundi kwami kanye nezimiso zasesibhedlela.

Ingabe ikhona yini inzuzo ngokubamba iqhaza kulolucwaningo?

Ucwaningo lwangaphambilini luye lwakuveza ukuthi ukusheshe kunikezwe imishanguzo yokuncibilikisa igazi emva kokuhlaselwa isifo senhliziyo kunikeza imiphumela emihle. Ngaphezulu kwalokho, ulwazi oluyotholakala ngokubamba kwakho iqhaza kulolucwaningo luyosiza ekunakekelweni kweziguli ezihlaselwa isifo senhliziyo esikhathini esizayo. Ulwazi oluyotholakala kulolucwaningo luyosetshenziswa njengomhlahlandlela kazwelonke kubasebenzi bezempilo, ikakhulukazi abezimo eziphuthumayo, mayelana nokuthi kuqaliswa kanjani ukulashwa ngalendlela yethrombolysis ngaphambi kokuba isiguli sifike esibhedlela.

Ingabe zikhona yini ezinye izindlela ezingasetshenziswa ezingangisebenzela kangcono?

Ayikho enye indlela yokwelapha engasetshenziswa.

Ngiphoqelekile yini ukuthi ngibambe iqhaza?

Qha, ukubamba kwakho iqhaza ukwenza ngokuzikhethela wena. Indlela yakho ojwayele ukwelashwa ngayo angeke iphazamiseke uma uthatha isinqumo sokubamba iqhaza kulolucwaningo noma ungalibambi iqhaza.

Ingabe kukhona yini ukunxeshezelwa mayelana nezindleko zami?

Angeke ukhokhelwe ngokubamba iqhaza kulolucwaningo futhi angeke kube khona ukunxeshezelwa ngoba lokhu akudinengekile kuloluhlobo locwaningo.

Ingabe ukubamba kwami iqhaza kulolucwanigno kuyogcinwa kuyimfihlo?

Yonke imininingwane yababambe iqhaza iyogcinwa iyimfihlo. Yonke imininingwane iyogcinwa kwicomputer eyovikelwa ngamagama ayimfihlo isikhathi esiyiminyaka emihlanu. Emva kwalokho yonke imininingwane iyokwesulwa. Umcwaningi kanye nombheki wakhe kuphela abayokwazi ukuhlola noma ukubheka imininingwane. Yonke imininingwane ngeke isebenzise amagama eziguli futhi ngeke yaziswe emphakathini. Imiphumela yocwaningo iyosetshenziselwa lolucwaningo kuphela. Nomakunjalo, angeke sinikezwe ngokuphelele isiqiseko sokugcinwa kwemininingwane iyimfihlo ngoba kungenzeka kube nesidingo sokwazisa imininingwane ngokomthetho noma kubenezinhlangano ezifuna ukuhlola imininingwane ukuze ziqinisekise ukuthi ucwaningo luqhutshwe ngendlela efanele. Lezi zinhlangano zingafaka izinhlangano ezifana nekomidi elebhekelela ubulungiswa bocwaningo (Research Ethics Committee) nenhlangano elawula ukusetshenziswa kwemithi (Medicines Control Council).

Kuyokwenzekani ngemiphumela yocwaningo?

Kunethemba lokuthi imiphumela yalolucwaningo iyokwaziswa ngokhishwa emabhukwini ezemfundo noma aqondene nocwaningo futhi iyokwaziswa kubaqondisi babasebenzi abathintekayo kanye nohulumeni. Imiphumela iyokwaziswa futhi nakulabo abambe iqhaza uma benze isicelo. Unelungelo lokwaziswa ngemiphumela etholakalayo uma wenza isicelo sokwaziswa.

Ingabe ubani ohlolisise uhlelo lwalolucwaningo?

Lolucwaningo lubhekisiswe futhi lwahlolwa ikomidi elibhekene nocwaningo enyuvesi yaseWitwatersrand. Ngaphuzulu kwalokho igunya lokwenza lolucwaningo linikezwe umnyango wezempilo waKwaZulu-Natal, umnyango wabosizo oluphuthumayo KwaZululu-Natal kanye nomphathi wesibhedlela olashwa kuso.

Wamukelekile ukuthi uxhumane kanye nami okanye umbheki walolucwaningo uma unemibuzo odinga ukuthi iphenduleke noma ufuna ukubika okungahambi kahle ngocwaningo. Uma unganelisekile noma ngani kulolucwaningo, ungadlulisela ukngeneliseki kwakho kumbheki wocwaningo. Igama likamabhalane wekomidi elbhekele ucwanigno lifakiwe lapha ngezansi ukuze ukwazi ukuthintana naye uma kukhona udinga ukukubika.

Mayelana neminye imininingwane ungathintana nalaba:

Igama lomcwaningi:

Mr Raveen Naidoo

Director: Postgraduate Development and Support (Acting)

Durban University of Technology

Tel: 031 3732846

Igama lombheki wocwaningo:

Prof K. Sliwa

Director: Soweto Cardiovascular Research Unit

Associate Professor of Medicine and Cardiology

Department of Cardiology

CH Baragwanath Hospital
University of the Witwatersrand
Tel: 011 9338197

Igama lomqondisi wekomidi lobulungiswa bocwaningo nosihlalo welelikomidi.

Appendix 7: Informed Consent Form – English

CONSENT FORM

- I hereby confirm that I have been informed by the researcher, Raveen Naidoo, about the nature, conduct, benefits and risks of this study - Protocol Number: M080822, Title: Thrombolytic therapy for acute myocardial infarction by emergency care practitioners.
- I have also received, read and understood the above written information (Participant Information Document) regarding the study.
- I am aware that the results of the study, including personal details regarding my gender, age, date of birth, initials and diagnosis will be anonymously processed into a study report.
- In view of the requirements of the research, I agree that the data collected during this study can be processed by the researcher using a computer system.
- I may, at any stage, withdraw my consent and participation in the study without prejudice,.
- I have had sufficient opportunity to ask questions and (of my own free will) declare myself prepared to participate in the study.
- I understand that significant new findings developed during the course of this research, which may relate to my participation, will be made available to me.

_____	_____	_____
Name of Participant	Date / Time	Signature / Thumbprint

I, Raveen Naidoo, herewith confirm that the above participant has been fully informed about the nature, conduct and risks of the above study.

_____	_____	_____
Name of Researcher	Date / Time	Signature / Thumbprint

Appendix 8: Informed Consent Form – isiZulu

IMVUME YOKUBAMBA IQHAZA OCWANINGWENI

- Ngiyaqinisekisa ukuthi umcwaningi uRaveen Naidoo ungazisile ngohlobo locwaningo, indlela oluzoqhutshwa ngayo, usizo olungatholakala ngalo nobungozi obuhambisana nalolucwaningo. Inombolo yocwaningo: M080822 Ishihloko socwaningo: Ukwelashwa ngendlela yokuncibilikiswa kwehluli legazi elihambisana nesifo senhliziyo ngabasebenzi bosizo oluphuthumayo.
- Ngiyitholile, ngayifunda futhi ngayiqonda imininingwane ebhalwe lapha ngenhla mayelana nalolucwaningo.
- Ngiyaqonda ukuthi imiphumela yalolucwaningo, kuhlangene nemininingwane eqondene nami, ubulili, ubudala / iminyaka yami, usuku lokuzalwa, nohlobo lokugula kwami kuyovezwa ngaphandle kokwazisa igama lami kulolucwaningo.
- Ngiyavumelana nokuthi yonke imininingwane eqondene nalolucwaningo umcwaningi ayihlaziye ngecomputer njengokumiselwe lolucwaningo.
- Ngiyaqonda futhi ukuthi ngivumelekile ukuthi ngingakuhoxisa ukubamba kwami iqhaza kulolucwaningo noma yini ngaphandle kokuthi ngibandlululwe ngandlela thile.
- Ngithole ithuba elanele lokubuza imibuzo futhi ngokuzikhethela kwami ngizobamba iqhaza kulolucwaningo.
- Ngiyaqonda ukuthi ulwazi olusha nolubalulekile oluyovela kulolucwaningo olumayelana nokubamba kwami iqhaza ngiyokwaziswa ngalo.

_____	_____	_____
Igama lobambe iqhaza	Usuku	Isignature

Mina Raveen Naidoo ngiyaqinisekisa ukuthi lona obambe iqhaza kulolucwaningo ngimazise ngokuphelele ngohlobo locwaningo, indlela oluzoqhutshwa ngayo kanye nobungozi obuhambisana nocwaningo.

_____	_____	_____
Igama lomcwaningi	Usuku	Isignature

Appendix 9: Registered Trademark

Application Number: 2010 / 11215



Appendix 10: Heart Attack: Time is Heart Muscle Poster, Booklet & Video

The compact disc contains the poster, booklet and video. The software required to play the video has also been loaded onto the compact disc.

Appendix 11: Published Conference Proceedings

Spring 2009
Volume 6 • Number 4
sa heart

An awareness programme to help reduce patient delays in acute myocardial infarction

Raveen Naidoo* and Karen Sliwa#

*Department of Emergency Medical Care and Rescue, Durban University of Technology, South Africa
#Department of Cardiology, Chris Hani Baragwanath Hospital, University of the Witwatersrand, Johannesburg, South Africa

Introduction: Definitive treatment for heart attack is early reperfusion by either primary angioplasty or thrombolytic therapy. The time elapsed from the onset of symptoms to reperfusion is directly related to patient outcomes as demonstrated in the GISSI trial more than 20 years ago. Reperfusion is a time-related intervention. There are three key components to prompt and effective reperfusion therapy: addressing patient delay, increasing utilisation of the ambulance service and addressing the prolonged in-hospital treatment delays would significantly reduce pain-to-needle times. The patient is most probably the most important factor involved in the delay between the onset of AMI and the start of reperfusion treatment. A number of factors, including the type of acute coronary syndrome, the nature and localisation of the symptoms, the place where the symptoms occurred, the patients interpretation of symptoms and knowledge were associated with the patients decision time (Herlitz, Thuresson et al. 2009). Various registries of patients with acute myocardial infarction have shown that the time from symptom onset to hospital presentation was ≥ 4 hours in 50%, > 6 hours in 40% and > 12 hours in 9 – 31%. A study in South Africa has shown that the patient took a mean time of 3:32 ± 5:26 hours to call for help and that only 10% (12) patients utilised an ambulance service. This implies that for maximum effectiveness, the public should be trained to recognise symptoms early and activate the emergency medical services early through a health awareness program via mass media to reduce delay times. The purpose of this study was to develop a culturally sensitive and affordable chest pain education program.

Methods: A document study was undertaken on existing chest pain awareness programs in international settings that led to the development of a culturally sensitive and affordable chest pain awareness program.

Ethics: Ethical approval was granted by the Human Research Ethics Committee - University of Witwatersrand.

Results: A poster, an information booklet and a video on heart attack awareness were developed after studying documentation from United Kingdom, Canada, Australia and South Africa.

Conclusion: Attempts to change the actions of individuals experiencing AMI symptoms on an ongoing basis must and should continue. Structures to facilitate various approaches need to be established for coordination and implementation. Until reperfusion strategies are delivered effectively, the promise of reduced morbidity and mortality from AMI will not be realised.

Impact of time to treatment with fibrinolytic drugs in patients presenting with ST- elevation myocardial infarction

R. Naidoo*, N. Ranjith#, D. Singh* and N. Castle*

*Department of Emergency Medical Care and Rescue, Durban University of Technology, KwaZulu-Natal, South Africa
#Department of Medicine, Coronary Care Unit, R K Khan Hospital, Durban, KwaZulu-Natal, South Africa

Aims: The prompt restoration of myocardial blood flow is vital to myocardial salvage and mortality reduction after ST- elevation myocardial infarction [STEMI]. Reperfusion is achieved with primary percutaneous coronary intervention (PPCI) or fibrinolytic agents. Due to the limited availability of PPCI, fibrinolytic therapy still remains an important treatment modality in managing STEMI. The aims of this study were to address the time interval from first patient contact to initiation of fibrinolytic treatment, possible reasons for treatment delay, and complications arising in those with and without treatment.

Methods: The study population comprised 120 patients with STEMI presenting to 20 different hospitals in Durban and surrounding regions between August to December 2006. Demographic data, time to treatment, reasons for non-treatment, and complications encountered during hospital stay and at day 30 were obtained from hospital records and patient interviews.

Appendix 12: Chapter in Book

Pre-hospital Thrombolysis: It's all a Matter of Time *in* Ischemic Heart Disease

STATEMENT OF ORIGINALITY

NAME	RESPONSIBILITY
Raveen Naidoo University of Witwatersrand Durban University of Technology	Principal author in the dissertation. Involved in chapter writing and review.
Nicholas Castle Durban University of Technology	Involved in chapter writing and editing.
CANDIDATE: I declare that this work is wholly my own, except where acknowledged as being the work of others (as listed above). I also acknowledge the contribution of others (as listed above) to this work in this STATEMENT OF ORIGINALITY. Raveen Naidoo	**SUPERVISOR:** I hereby certify that all-co-authors have provided their consent for inclusion of the manuscripts in the dissertation and that the co-authors accept the candidate's contribution to the paper, as described in this STATEMENT OF ORIGINALITY. Professor Karen Sliwa

Appendix 13: Medications

(117); (178)

Tenecteplase (TNK)

DESCRIPTION:
- Classification : Enzymatic preparation
- Trade name : Metalyse®
- Schedule : 4

PHARMACOLOGICAL ACTION:
- Tenecteplase is a recombinant fibrin-specific plasminogen activator.
- The molecule differs from the native tissue-type plasminogen activator (t-Pa) by modifications at three sites of the protein structure, thus increasing its fibrin specificity and resistance and inactivation by its endogenous inhibitor.
- It binds to the fibrin component of the thrombus and selectively converts thrombus bound plasminogen to plasmin, which degrades the fibrin matrix of the thrombus.

PHARMACOKINETICS:
- Dominant half-life: 24 $\pm$ 5,5 minutes (18 to 30 minutes).
- Terminal half-life: 129 $\pm$ 87 minutes (40 minutes to 4 hours).

INDICATIONS:
- Thrombolytic therapy for acute phase of myocardial infarction.

ADVERSE EFFECTS:
- Haemorrhage: Predominantly at the injection site, gastro-intestinal, genito-urinary or gingival bleeding occurred occasionally. Haemo-pericardium, retro-peritoneal bleeding, cerebral haemorrhage and epistaxis have been observed.
- Cardiovascular: Successful reperfusion for AMI is often accompanied by arrhythmias. Hypotension may also occur. Tenecteplase therapy may lead to cholesterol crystal embolisation or thrombotic embolism (in rare cases).
- Anaphylactoid reaction: Anaphylactoid reactions (e.g. rash, urticaria, bronchospasm, laryngeal oedema) have been reported.
- Other: Nausea, and/or vomiting and fever were the most frequently reported remaining adverse events.

CONTRA-INDICATIONS:
- Uncontrolled hypertension [systolic blood pressure of more than 180mmHg, diastolic blood pressure of more than 110mmHg on repeated measurements];
- Major surgery: biopsy of a parenchymal organ, substantial trauma within 2 months;
- Any head injury or other trauma occurring after on-set of current myocardial infarction;
- Any known history of stroke;

- Bleeding tendency;
- Any known structural damage to the central nervous system;
- Current treatment with oral anti-coagulants;
- Sustained cardio-pulmonary resuscitation of more than 10 minutes' duration;
- Active peptic ulceration within the last 6 months;
- Pregnancy; nor has the patient delivered within the last 2 weeks.

PRECAUTIONS:
- There might be complications if Tenecteplase is given without the patient having an infarct (but had pneumonia).

PACKAGING:
- Metalyse® 8 000 U: 1 vial contains 8 000 units (40mg) Tenecteplase. 1 pre-filled syringe (Metalyse® solvent) contains 8 ml of water for injection.
- Metalyse® 10 000 U: 1 vial contains 10 000 units (50mg) Tenecteplase. 1 pre-filled syringe (Metalyse® solvent) contains 10 ml of water for injection.

DOSAGE AND ADMINISTRATION:
- Tenecteplase should not be administered in a line containing dextrose.
- Any unused solution should be discarded.
- Tenecteplase is to be administered IVI over 5 to 10 seconds according to body weight as per the table below.

Patient's weight (kg)	Corresponding volume of reconstituted solution (ml)	Tenecteplase (U)	Tenecteplase (mg)
< 60	6	6 000	30
60 – 69	7	7 000	35
70 – 79	8	8 000	40
80 – 89	9	9 000	45
≥ 90	10	10 000	50

Streptokinase (STK)

DESCRIPTION:

- Classification : Enzymatic preparation
- Trade name : Streptase®
- Schedule : 4

PHARMACOLOGICAL ACTION:

- Anti-thrombotic enzymes convert plasminogen to plasmin, which in turn degrades fibrin thrombi and fibrinogen.
- Streptokinase is antigenic and will induce antibody formation.
- Generally reperfusion of occluded arteries will occur within 20 minutes to 2 hours of initiation of therapy (average is 45 minutes). The hyper-fibrinolytic state will disappear within a few hours after discontinuation of administration.
- Streptase® is highly purified Streptokinase derived from the culture filtrate of beta-haemolytic streptococci.

PHARMACOKINETICS:

- Half-life: 23 minutes.

INDICATIONS:

- Thrombolytic therapy for acute phase of myocardial infarction in adults.

ADVERSE EFFECTS:

- Early reactions: Headaches, pain in the back and allergic-anaphylactic reaction with flushing and dyspnoea may occur. Allergic reactions can be avoided by giving the intravenous infusion slowly.
- Pyrexia, chills and rashes: Chills with or without pyrexia may occur during treatment.
- Haemorrhage: Predominantly at the injection site.
- Hypotension: Streptokinase can induce hypotension when given too rapidly. The infusion should run over a 1-hour period (400-500 IU/kg/minute).

CONTRA-INDICATIONS:

- Known hypersensitivity to Streptokinase.
- Existing or recent haemorrhage:
    - all forms of reduced blood coagulation
    - local lesions with risk of bleeding
    - recent operations
    - recent abortion or delivery
    - diseases of the urogenital tract with existing or potential sources of bleeding.
- Recent streptococcal infections.
- Endocarditis.

- Uncontrolled hypertension [systolic blood pressure of more than 180mmHg, diastolic blood pressure of more than 110mmHg on repeated measurements].
- Impaired liver or kidney function.
- Recent stroke or cerebro-vascular abnormalities.
- Pulmonary diseases with cavitation (e.g. open tuberculosis) or severe bronchitis.
- Acute pancreatitis or proliferative diabetic retinopathy.
- Advanced age with arteriosclerotic cerebral disease.

PRECAUTIONS:
- Should not be given during the first 18 weeks of pregnancy unless absolutely necessary.
- Caution is necessary with patients with mitral valve defect or fibrillation because of the danger of cerebral embolisation.

PACKAGING:
- Freeze-dried white powder sealed in a single dose in a clear glass vial. In reconstitution, a colourless, clear to opalescent solution for intravenous use is obtained.
- One vial of 1 500 000 IU Streptokinase in individual cartons.
- One vial of 750 000 IU Streptokinase in individual cartons.

DOSAGE AND ADMINISTRATION:
- Streptokinase should not be administered between 5 days and (a minimum of) 2 years following initial treatment as antibodies persist for at least 2 years.
- Streptokinase does not contain any preservatives; therefore it should be reconstituted immediately before use.
- Do not add any other medication to the container with Streptokinase.
- Slowly add 5ml sodium chloride injection or dextrose 5% injection to the Streptokinase vial, directing the diluent to the side of the vacuum-packed vial rather than into the drug powder.
- Roll and tilt the vial gently to reconstitute. Avoid shaking (shaking may cause foaming).
- Withdraw the entire reconstituted contents of the vial; slowly and carefully dilute further into 200ml normal saline.
- Infuse the 1 500 000 IU solution intravenously within 60 minutes.

Enoxaparin

DESCRIPTION:

- Classification : Anti-coagulant
- Trade name : Clexane®
- Schedule : 4

PHARMACOLOGICAL ACTION:

- Enoxaparin is a low molecular weight Heparin that has a greater anti-thrombotic activity (anti-factor Xa) than a thrombolytic effect (anti-factor IIa activity) *in vivo.*
- It is well absorbed after sub-cutaneous injection.

PHARMACOKINETICS:

- Half-life: 4,5 hours. This is increased to 6,7 hours in the elderly.

INDICATIONS:

- Enoxaparin is indicated as co-therapy to Tenecteplase for thrombolytic therapy for acute phase of myocardial infarction by Emergency Care Practitioners.

ADVERSE EFFECTS:

- Haemorrhage: During Enoxaparin therapy, bleeding may occur in the presence of associated risk factors, such as organic lesions liable to bleed, invasive procedures or the use of medications affecting haemostasis.
- Thrombocytopenia: Transient asymptomatic thrombocytopenia has been reported during the first days of therapy. Rare cases of immune-allergenic thrombocytopenia (with or without thrombosis) have been reported.
- Local reactions: Pain, haematoma and mild local irritation may follow sub-cutaneous injection of Enoxaparin. Rarely, hard inflammatory nodules have been observed at the injection site. Cases of skin necrosis have also been reported.
- Others: Cutaneous or systemic allergic reactions may occur. Asymptomatic and reversible increases in platelet counts and lever enzyme levels have been reported.
- Enoxaparin co-therapy should be discontinued should bleeding occur.

CONTRA-INDICATIONS:

- Hypersensitivity to Enoxaparin, Heparin or its derivatives, including other low molecular weight Heparins.
- Patients who are haemorrhaging (normal menstruation excluded).
- Patients at risk of haemorrhage: haemorrhagic blood disorders, thrombocytopenia, peptic ulcers, cerebro-vascular disorders, bacterial endocarditis and severe hypertension.

PACKAGING:

- Clexane 40: Enoxaparin 40mg per 0,4ml

- Clexane 60: Enoxaparin 60mg per 0,6ml
- Clexane 80: Enoxaparin 80mg per 0,8ml
- Clexane 100: Enoxaparin 100mg per 1,0ml
- Clexane 300: Per multi-dose vial. Enoxaparin sodium 300mg, benzyl alcohol (preservative) 1, 5%m/v, water for injection to 3, 0ml.

DOSAGE AND ADMINISTRATION:

- Patients will receive Enoxaparin co-therapy as an intravenous bolus of 30mg, followed by the first sub-cutaneous dose of 1mg/kg about 15 minutes after the administration of Tenecteplase.

Heparin

DESCRIPTION:

- Classification : Anti-thrombotic agent
- Trade name : Intramed Heparin Sodium®, Heparin Novo®
- Schedule : 4

PHARMACOLOGICAL ACTION:

- Unfractionated Heparin is a heterogenous mixture of strongly acidic mucopolysaccharide and has molecular weights varying from 3 000 to 30 000.
- It is a direct anti-coagulant that prevents the formation of venous thrombi and the extension of existing thrombi.
- It acts by potentiating the inhibitory effect of anti-thrombin III (Heparin co-factor) on the activated forms of clotting factors XII, XI, IX, X and thrombin.
- Low molecular weight Heparins are manufactured chemically from unfractionated Heparin and have average molecular weights between 4000 and 5000.

PHARMACOKINETICS:

- Half-life: 1 – 6 hours (average 1.5 hours) – dependent on dose, route and patient variability.
- It is best given by continuous infusion for sustained effect.
- Heparin is administered sub-cutaneously or intravenously; on-set of action is immediate after IV injection and usually within 1-2 hours when given sub-cutaneously.

INDICATIONS:

- Co-therapy for acute phase of myocardial infarction.

ADVERSE EFFECTS:

- Risk of bleeding increases with dose (less when given by continuous infusion than by intermittent bolus injection).
- Hypersensitivity reactions include fever, chills, urticaria and anaphylactic shock.
- Mild thrombocytopenia is common, but is mostly transient and harmless.
- Skin necrosis may occur at the injection site.

ABSOLUTE CONTRA-INDICATION:

- Known hypersensitivity.

RELATIVE CONTRA-INDICATION:

- Impaired coagulation
- Thrombocytopenia
- Severe hepatic disease
- Active intestinal bleeding
- Suspected intra-cranial bleeding

- Cerebral aneurysm
- Threatened abortion
- Visceral carcinoma
- Bacterial endocarditis
- Active cavitating tuberculosis
- During or after eye, brain or spinal cord surgery
- Prior to lumbar puncture or regional anaesthetic block

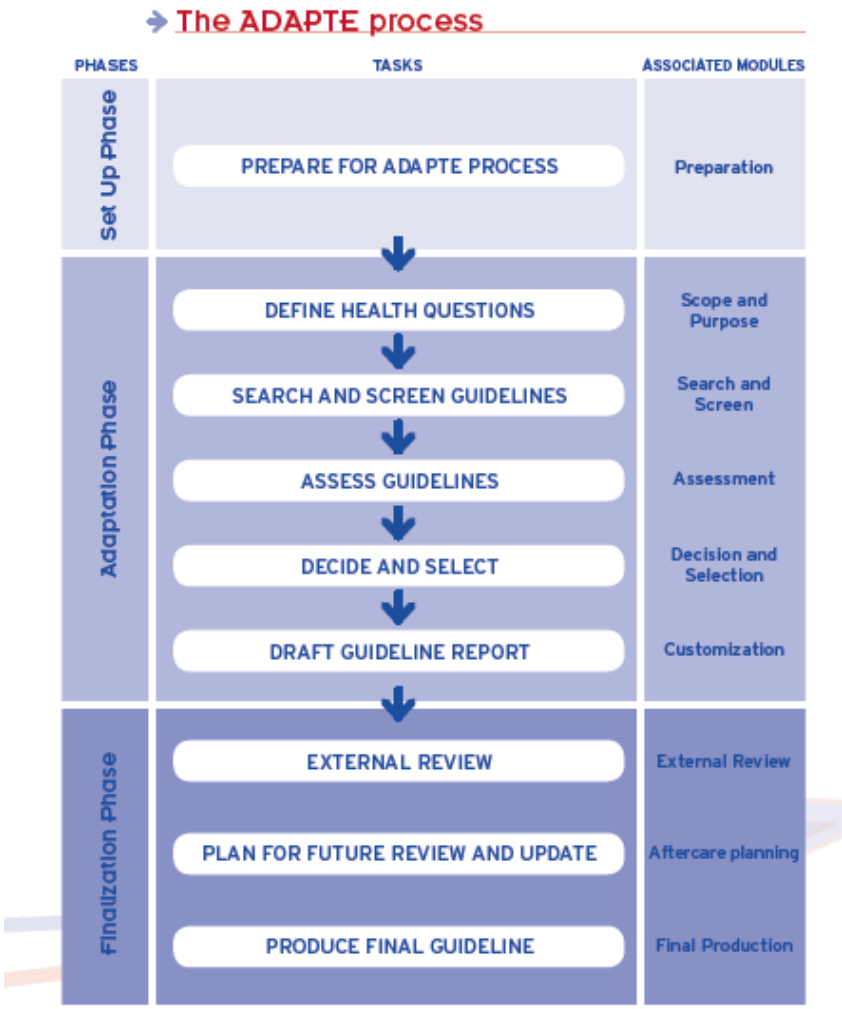
PACKAGING:

- Intramed Heparin Sodium®
  Injection, 1000 IU, 5000 IU, 12 500 IU, 25 000 IU/ml.
- Heparin Novo®
  Injection, 5000 IU/ml

DOSAGE AND ADMINISTRATION:

- Administer 5000 units of Heparin IVI. Reduce to 4000 units for initial bolus for patients weighing < 67kg.

Appendix 14: Adapte Process



Appendix 15: Emergency Care Practitioner Thrombolysis

CLINICAL SKILL: THROMBOLYSIS

Procedure

1. Take universal precautions, including protective gloves, facemask and eyewear.
2. Calm, reassure and place patient in a comfortable position.
3. Undertake a full clinical and 12 lead ECG assessment of the patient.
4. Consider direct transfer of high risk patients to PCI facility.
5. Undertake a 12 LEAD ECG within 10 minutes; thereafter every 15 minutes for the first hour if not continuous.
6. Manage patient according to **MONA** mnemonic (morphine; oxygen; nitrates; Aspirin).
1. Administer Clopidogrel (300mg for < 75 years; 75mg > 75 years).
7. Determine if thrombolysis is indicated.
8. Exclude the contra-indications for thrombolysis:
9. Explain the procedure and its risks to the patient and obtain consent.
10. Establish a large-bore IV line in a large peripheral vein.
11. Following consultation with your local receiving physician (as applicable), administer thrombolytic agent using one of the following regimens:

    11.1. Tenecteplase

    Single weight-adjusted dose IV bolus:

Patient's weight (kg)	Corresponding volume of reconstituted solution (ml)	Tenecteplase (U)	Tenecteplase (mg)
< 60	6	6 000	30
60 – 69	7	7 000	35
70 – 79	8	8 000	40
80 – 89	9	9 000	45
≥ 90	10	10 000	50

    or

    11.2. Streptokinase

    Infusion of 1.5 million units of Streptokinase over 60 minutes (via syringe driver) in solution with 0.9% normal saline, 5% D/W or Ringer's Lactate. (In the event of hypotension, halve the infusion rate or terminate infusion, as appropriate).

12. Initiate anti-thrombotic co-therapy.
    12.1. Enoxaparin

    Administer Enoxaparin 30mg IV bolus, followed by the first sub-cutaneous dose of 1mg/kg about 15 minutes after the administration of Tenecteplase. If patient's age is > 75 years, no IV bolus and start with reduced sub-cutaneous dose.

    or

    12.2. Heparin

    Administer 5000 units of Heparin IVI. Reduce to 4000 units for initial bolus for patients weighing < 67kg.

13. Pre-alert receiving hospital and assess the patient regularly en route to hospital.
14. Undertake a clinical re-assessment (pain reduction) and 90-minute post lysis ECG (> 50% reduction of ST segment) to assess for successful reperfusion.
15. If ST segment resolution is less than 50%, consider transfer of patient to PCI facility for Rescue PCI.

Appendix 16: Thrombolysis Checklist

Indications: Acute ST-elevation myocardial infarction within 12* hours of on-set of symptoms.

	Primary assessment: Can you confirm the following?	Yes	No
1	The patient is conscious and coherent and able to understand that clot dissolving drugs will be used?		
2	The patient has symptoms that are characteristic of a heart attack (severe, continuous pain in a typical distribution of 15 minutes duration or more without remission?)		
3	The symptoms started less than 12 hours ago? **NOTE:** Consider "stuttering start" MI – many infarcts start this way.		
4	The pain built up over seconds and minutes, rather than starting abruptly?		
5	Breathing does **not** influence the severity of the pain?		
6	**Systolic** blood pressure is more than 80mmHg and less than 180mmHg and **diastolic** is below 110mmHg despite treatment? i.e. Analgesia & GTN for blood pressure and fluid challenge / atropine for hypotension).		
7	The electrocardiogram (ECG) shows abnormal ST-elevation of 2mm or more in at least 2 standard leads or in at least 2 adjacent pre-cordial leads, not including V1. **NOTE:** ST-elevation can sometimes be normal in V1 and V2.		
8	The QRS width is 0.16 seconds (4 small squares) or less, and the left bundle branch block is absent from the tracing? **NOTE:** RBBB is permitted only with qualifying ST elevation. LBBB = QRS 140 ms or greater; small narrow R wave in V1 & V2 with big S wave; tall upright monophasic R in standard Lead 1 and V6.		
	Secondary assessment (contra-indications): Can you confirm the following?	**Yes**	**No**
9	The patient is not likely to be pregnant, nor has delivered within the last 2 weeks?		
10	The patient has not had an active peptic ulcer within the last 6 months?		
11	The patient has not had a stroke of any sort within the last 12 months and does not have any permanent disability from a previous stroke?		
12	The patient: has no diagnosed bleeding tendency. has had no recent blood loss (except normal menstruation); and is not taking Warfarin (anti-coagulant) therapy?		
13	The patient has not had any surgical operation, tooth extractions, significant trauma, or head injury within the last 4 weeks?		
14	The patient has not been recently treated for any other serious head or brain condition?		
15	The patient is not being treated for liver failure, renal failure, or any other severe systemic illness?		

If all answers are YES ... Thrombolysis should commence.

Appendix 17: Patient Consent Form

PATIENT CONSENT

NOTE:

Many patients with acute myocardial infarction (AMI) may not be legally 'competent' to give informed consent, and the EMERGENCY CARE PRACTITIONER must act in the individual patient's best interest. Prior to administration, you must ensure the patient understands the risk and benefits of thrombolysis, as set out below.

Initial Consent

"It is likely that you are having a heart attack and the best treatment available to you is a clot dissolving drug called **Tenecteplase/Streptokinase**. The quicker you receive this drug, the lower the risks of a heart attack, which is why doctors recommend that the treatment is started as soon as possible. These drugs can cause serious side effects in a small minority of patients, which I can explain to you in more detail if you so wish; but the risks attached to this treatment are very much less than the likely benefit. Would you like me to give you the injection or would you prefer to be given more details?"

I hereby consent to the treatment:

_____	_____/_____	_____
Name of patient	Date / Time	Signature / Thumbprint

In the unlikely event that the patient does want more information, the following information should be provided:

Further information

"Treatment at this stage saves the lives of about 1 in every 25 patients treated. But, it can sometimes cause serious bleeding. The biggest risk is stroke, which affects about 1 patient in every 200 treated. Some patients also have an allergic reaction and other side-effects that do not usually cause any major problems. Would you like me to give you the injection?"

If the patient refuses treatment at this stage, please record this on the patient record, transport the patient to hospital as quickly as possible and hand the patient over to the doctor -in charge.

Appendix 18: Summary of 20 patients thrombolysed

Patient Number: 1 - 020809

Ethnic group	C	**Gender**	M	**Age**	49
Respiration	20	**Pulse**	91		
HGT	7.4	**BP**	140/90		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Nil	
Risk Factors	Smoker	
ECG:	Initial: Inferior, lateral, posterior. ECG @ 90 minutes: Reperfusion arrhythmias.	
Treatment	At district hospital: Oxygen; ASA. Raveen Naidoo: Clopidogrel (300mg), Morphine7.5mg), TNK (7000U), Enoxaparin (30mg IVI, 70mg SC).	
Timeframes	**Symptom to call for help**	Notified wife immediately.
	Transportation time (from time call received to patient drop-off at hospital)	01H27 by ambulance
	GP time	N/A
	Primary hospital time	02H43
	Symptom to definitive treatment	04H10
In-hospital Outcome	No complications – discharged 06/08/09.	
30-day Outcome	No complications.	
Researcher Reflective Practice	Patient's notified wife timeously. From time of EMS notification to admission > 1hour. (EMS crew recognised that patient was having AMI). Time at district hospital with basic treatment - almost 3 hours. Symptom-to-needle could have been reduced further by: 1. On-scene thrombolysis – within 1 hour. 2. Quicker dispatch, response, on-scene time and transportation by ambulance services. 3. Pre-alerting hospital by ambulance crew. 4. Earlier in-hospital thrombolysis activation– within 30 minutes of arrival. Points to note: 1. No medical advice given by EMS control centre. 2. No ALS dispatch by EMS control centre. 3. No ASA administration by EMS ambulance crew. 4. No request for ALS assistance by EMS ambulance crew. 5. No pre-alerting of receiving hospital. 6. The importance of a cardiac care network was highlighted – direct admission to CCU, a system of consultation essential for safe ECP thrombolysis.	

Patient Number: 2 - 220809

Ethnic group	I	**Gender**	M	**Age**	47
Respiration	14	**Pulse**	103		
HGT	11	**BP**	140/80		
AVPU	Alert	**Symptom/s**	Severe central chest pain		

Family History	Unknown	
Risk Factors	Diabetic, Smoker	
ECG	Initial: Anterior infarct. ECG @ 90 minutes: Resolving ST-elevation.	
Treatment	At district hospital: Oxygen; ASA, GTN, Morphine (2mg) Raveen Naidoo: Clopidogrel (300mg), Morphine(3mg), TNK (9000U), Enoxaparin (30mg IVI, 80mg SC).	
Timeframes	**Symptom to call for help**	4H15
	Transportation time	20min – privately
	GP time	30min – treated for ulcer prior to severe chest pain.
	Primary hospital time	1H23
	Symptom to definitive treatment	05H58
In-hospital Outcome	No complications – discharged 28/08/09.	
30-day Outcome	No complications.	
Researcher Reflective Practice	Patient had intermittent pain from the day before (20/09/09). Saw GP at 17H15 on 21/08/09 and was treated for ulcers and sent home. Patient delayed at home on the basis that he had ulcers. Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Notification and use of EMS. 3. Accurate GP diagnosis. 4. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. The importance of an awareness programme as well accuracy of GP diagnosis.	

Patient Number: 3 - 220809

Ethnic group	I	**Gender**	M	**Age**	47
Respiration	24	**Pulse**	99		
HGT	15.5	**BP**	196/120		
AVPU	Alert	**Symptom/s**	Central chest discomfort/pain		

Family History	Diabetes	
Risk Factors	Diabetic, Hypertension, Dyslipidaemia, Smoker	
ECG	Initial: anterolateral infarct ECG @ 90 minutes: reperfusion noted.	
Treatment	Raveen Naidoo: Oxygen; ASA, GTN, Clopidogrel (300mg), Morphine(4mg), TNK (8000U), Enoxaparin (30mg IVI, 80mg SC).	
Timeframes	**Symptom to call for help**	00H00
	Transportation time (From time call received to patient drop off at hospital)	01H49min by ALS and ambulance.
	GP time	N/A
	Primary hospital time	N/A
	Symptom to definitive treatment	CCU time 46 min. Total time: 02H25
In-hospital Outcome:	No complications – discharged 26/08/09.	
30-day Outcome:	No complications.	
Researcher Reflective Practice	Patient could not be lysed on scene, as the BP was above permissible parameters. Following consultation with Dr Ranjith telephonically, the patient was admitted directly to CCU. Nitrocine infusion was commenced. Raveen Naidoo thrombolysed patient when BP dropped below 180/110 mmHg in CCU. Symptom-to-needle could have been reduced further by: 1. ECP use of Nitrocine Points to note: 1. Nitrocine should be included in the scope of practice of ECP (pain and reduction of BP). Paramedics are currently undertaking inter-hospital patient transfers with nitrocine infusion, when paramedics are trained on the use of nitrates (GTN).	

Patient Number: 4 - 270809

Ethnic group	I	**Gender**	F	**Age**	66
Respiration	16	**Pulse**	72		
HGT	14.3	**BP**	88/45		
AVPU	Voice	**Symptom/s**	Central chest pain		

Family History	Brother died at a young age of heart problems.	
Risk Factors	Diabetic, Hypertension	
ECG	Initial: Inferior, Anterolateral infarct. ECG @ 90 minutes: Not done; patient in cardiac arrest at ADD 60 minutes later.	
Treatment	At hospital: Mount Edgecombe - Nitrocine infusion, Clopidogrel (75mg); ASA. At hospital: MGMH – Oxygen; stopped Nitrate infusion and commenced Dobutamine infusion (20mls/hr). Raveen Naidoo: TNK (8000U), Enoxaparin (30mg IVI, 70mg SC).	
Timeframes	**Symptom to call for help**	03H00
	Transportation time	20 minutes – privately.
	GP time	Initial private hospital 01H10
	Primary hospital time	01H00
	Symptom to definitive treatment	05H30
In-hospital Outcome	Patient went into cardiac arrest upon arrival at regional hospital CCU. CPR and ALS management was undertaken for 15 minutes. Resuscitation attempt terminated at 04H30.	
30-day Outcome	Not applicable.	
Researcher Reflective Practice	Administration of TNK delayed by 30 minutes, as the patient was in cardiogenic shock. Symptom-to-needle could have been reduced further by: 1. Reducing patient decision time. 2. Administration of TNK at private hospital. 3. Quicker commencement of inotropic support. Points to note: 1. Inotropic support (Dobutamine) should be included in the scope of practice of ECP. Paramedics are currently undertaking inter-hospital patient transfers with inotropic infusions and are trained on its use. 2. Only 75mg Clopidogrel (as opposed to the minimum of 300mg) given at private facility. 3. Need additional ALS crew assistance to optimise management when transferring critically ill patients.	

Patient Number: 5 - 060909

Ethnic group	I	**Gender**	M	**Age**	66
Respiration	18	**Pulse**	105		
HGT	20	**BP**	120/85		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Unknown	
Risk Factors	Diabetic, Hypertension, Smoker	
ECG	Initial: Anterolateral infarct. ECG @ 90 minutes: 12 lead not done as patient went in cardiac arrest en route to regional hospital.	
Treatment	At hospital: Mount Edgecombe – No treatment. At hospital: MGMH – Oxygen, ASA, Actrapid. Raveen Naidoo: Clopidogrel (300mg), Morphine (2mg),GTN, TNK (9000U), Enoxaparin (30mg IVI, 80mg SC)	
Timeframes	**Symptom to call for help**	0H30
	Transportation time	2H00 patient waited for private transport.
	GP time	Initial private hospital 02H00
	Primary hospital time	0H35
	Symptom to definitive treatment	05H05
In-hospital Outcome	Patient went into cardiac arrest en route to regional hospital; re-routed CPR in progress back to district hospital. CPR and ALS management undertaken for 45 minutes. Resuscitation attempt terminated at 21H55.	
30-day Outcome	Not applicable.	
Researcher Reflective Practice	Patient kept saying that he was going to die. Symptom-to-needle could have been reduced further by: 1. Reducing patient decision time, 2. Administration of TNK at private hospital, Points to note: 1. Had to call for additional ALS support when patient went into cardiac arrest. 2. Sudden cardiac arrest after approx 30 second convulsion; PEA – VF-Asystole. 3. Need additional personnel to optimise cardiac arrest management in the back of an ambulance.	

Patient Number: 6 - 170909

Ethnic group	W	**Gender**	M	**Age**	44
Respiration	18	**Pulse**	96		
HGT	6	**BP**	140/80		
AVPU	Alert	**Symptom/s**	Severe central chest pain		

Family History	Mother CABG	
Risk Factors	Smoker	
ECG	Initial: Infero-Anterolateral infarct. ECG @ 90 minutes: Reperfusion noted.	
Treatment	At hospital: WW – Oxygen, ASA, Morphine (4mg), Nitrate infusion (3mls/hr). Raveen Naidoo: Clopidogrel (300mg), Morphine (4mg), TNK (8000U), Enoxaparin (30mg IVI, 75mg SC).	
Timeframes	**Symptom to call for help**	0H00
	Transportation time (from time call received to patient drop off at hospital)	42 minutes; patient walked to pick-up point. 1H10 minutes
	GP time	N/A
	Primary hospital time	01H40
	Symptom to definitive treatment	03H25
In-hospital Outcome	No complications – transferred to tertiary hospital for angiogram, EF 35%.	
30-day Outcome	Angina on stress and physical exertion; relieved by rest. TVD, booked for CABG.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Reducing EMS activation time. 2. Reducing EMS on scene time. 3. EMS activation of ECP for on scene thrombolysis. 4. EMS pre-alerting receiving hospital. 5. Administration of TNK at private hospital. 6. Earlier in-hospital thrombolysis activation– delivery within 30 minutes of patient arrival. Points to note: 1. No medical advice given by EMS communications centre. 2. No ASA administration by EMS ambulance crew. 3. No request for ALS assistance by EMS ambulance crew. 4. No pre-alerting of receiving hospital. 5. ECP in-hospital TNK administration delayed due to referring doctor's interest in PHT and the lack of in-hospital casualty fax facilities.	

Patient Number: 7 - 250909

Ethnic group	W	**Gender**	F	**Age**	74
Respiration	12	**Pulse**	96		
HGT	5.7	**BP**	165/95		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Parents died of MI; Mother (57); Father (62).	
Risk Factors	Previous MI, Hypertension, Smoker	
ECG	Initial: Inferior Infarct. ECG @ 90 minutes: No ECG changes.	
Treatment	At hospital: Oxygen, ASA, GTN, Morphine Raveen Naidoo: Enoxaparin (40mg SC) Clopidogrel (300mg), TNK (8000U).	
Timeframes	**Symptom to call for help**	0H30
	Transportation time	02H30 minutes transport delay Private
	GP time	N/A
	Primary hospital time	02H27
	Symptom to definitive treatment	05H27
In-hospital Outcome	No complications – Patient discharged on 28/09/09, 3 days later, no elevation of cardiac enzymes.	
30-day Outcome	Patient had chest pains one week later and had a CABG the day after in Vereeniging. Patient fine thereafter.	
Researcher Reflective Practice	Patient was initially planned to be transferred to a private hospital for TNK but could not due to lack of medical benefits. Symptom-to-needle could have been reduced further by: 1. Reducing transportation time. 2. Administration of TNK at private hospital/ 3. Earlier in-hospital thrombolysis activation– delivery within 30 minutes of patient arrival/ Points to note: 1. The patient did not infarct as evidenced by the normal cardiac enzymes during in-hospital stay. 2. ST elevation in inferior leads incorrectly diagnosed and missed by all - RBBB. 3. Patient diagnosis – unstable angina.	

Patient Number: 8 - 250909

Ethnic group	I	**Gender**	M	**Age**	36
Respiration	28	**Pulse**	68		
HGT	5.7	**BP**	70/50		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Mother and father AMI, deceased @ 57 and 62 respectively.	
Risk Factors	? Previous MI was treated for ulcers beginning of May 2009.	
ECG:	Initial: Inferior Posterior Infarct. ECG @ 65 minutes: Reperfusion noted. ECG @ 90 minutes: Not done.	
Treatment:	At hospital: Oxygen, ASA, GTN (2 puffs), Voluven (500mls X2), Dobutrex (10mls/hour). Raveen Naidoo: Clopidogrel (300mg), TNK (9000U), Enoxaparin (30mg IVI, 80mg SC).	
Timeframes:	**Symptom to call for help**	00H00
	Transportation time	01H30 minutes waited for transport – private. 30 minutes travel time.
	GP time	N/A
	Primary hospital time	01H40
	Symptom to definitive treatment	03H40
In-hospital Outcome:	Patient died approximately 01H30 after admission to CCU. LVF.	
30-day Outcome:	N/A	
Researcher Reflective Practice	Patient was hypotensive and was given Voluven to increase BP at hospital. BP remained below 80mmHg after 1 liter of Voluven. Dobutrex commenced thereafter. TNK administered 20 minutes later (12H20) BP at this stage 91/58 mmHg. Patient developed pulmonary oedema approx 25 minutes later – sudden on-set, positive pressure ventilated to CCU (O2 sats 92%). Symptom-to-needle could have been reduced further by: 1. Reducing transportation time. 2. Inotropic support commenced earlier. 3. Earlier in-hospital thrombolysis activation– delivery within 30 minutes of patient arrival. Points to note: 1. The use of Voluven (colloid) for hypotension is questionable. 2. My management had to be defended. 3. Pulmonary oedema possibly due to fluid over-load. 4. Infero-posterior MI and sudden on-set = ?papillary muscle rupture.	

Patient Number: 9 - 091009

Ethnic group	I	**Gender**	M	**Age**	60
Respiration	20	**Pulse**	54		
HGT	10	**BP**	97/64		
AVPU	Alert	**Symptom/s**	Mild central chest pain		

Family History	Nil	
Risk Factors	Smoker	
ECG	Initial: Inferior Posterior Infarct. ECG @ 120 minutes: Reperfusion noted.	
Treatment	At district hospital: Oxygen; ASA. Raveen Naidoo: Clopidogrel (300mg), GTN (3 tabs), TNK (8000U), Enoxaparin (30mg IVI, 75mg SC).	
Timeframes	**Symptom to call for help**	03H00
	Transportation time	00H25 – Private
	GP time	00H05
	Primary hospital time	03H10
	Symptom to definitive treatment	06H40 1H10min delay due to discussions with receiving hospital.
In-hospital Outcome	No complications – discharged 13/10/09	
30-day Outcome	081109. No complications	
Researcher Reflective Practice	Several delays occurred at the district hospital that were related to admission to CCU. Had to wait for confirmation at receiving hospital of acceptance of patient by medical registrar, who then requested that the patient be lysed and post lyses ECG be faxed, before confirmation of admission to CCU – resulted in a 1h10 minute delay. Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Notification and use of EMS. 3. Earlier in-hospital thrombolysis activation– within 30 minutes of arrival 4. Easy access to consultant after hours. Points to note: 1. Patient had active bleeding haemorrhoids mid September. This delayed thrombolyses, as I wished to discuss this with a consultant. Go ahead given by Dr Bayat for lyses regardless of 40 minutes outside 6 hour cut off. 2. Access to specialist essential for consultation of PHT – especially in early stages of PHT. Solution may be access to cardiologist on call at IALAH.	

Patient Number: 10 - 250909

Ethnic group	I	**Gender**	F	**Age**	60
Respiration	24	**Pulse**	44 - 92		
HGT	17.1	**BP**	100/60		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Sister and brother died of a heart attack within last year.	
Risk Factors	Unstable angina since 2007, Diabetes, Hypertension, Dyslipidaemia, Smoker.	
ECG	Initial: Inferior Infarct with first degree block. ECG @ 90 minutes: Not done; patient arrested at Addington Hospital.	
Treatment	At hospital: Oxygen, ASA. Raveen Naidoo: Clopidogrel (300mg), GTN (2 puffs), TNK (9000U), Enoxaparin (30mg IVI, 80mg SC).	
Timeframes	**Symptom to call for help**	00H05
	Transportation time (From time call received to patient drop off at hospital)	35 minutes by **ambulance to** clinic. 5 minutes by son's car from clinic to MGMH.
	GP time	2H05 minute delay at Phoenix Clinic
	Primary hospital time	02H23
	Symptom to definitive treatment	05H53
In-hospital Outcome	Patient died approximately 22H55; approximately 50 minutes after admission to CCU.	
30-day Outcome	N/A	
Researcher Reflective Practice	Patient was initially hypotensive and was started on Voluven IV by hospital staff – stopped after 10mls by Raveen Naidoo (BP 100/60). Patient developed pulmonary oedema at CCU upon admission - went into cardiac arrest, resuscitated and then arrested again. Symptom-to-needle could have been reduced further by: 1. EMS activation of ALS. 2. EMS admission to district hospital rather than clinic. 3. Pre-alerting receiving hospital. 4. Earlier in-hospital thrombolysis activation– delivery within 30 minutes of patient arrival. Points to note: 1. No medical advice given by EMS control centre. 2. No ALS dispatch by EMS control centre. 3. No ASA administration by ambulance crew. 4. Consulted with Dr Harku re recent tooth extraction. Extraction was well healed, uninfected, compressible area and not a deep-root canal. 5. Reperfusion noted en route to hospital on Lead II, III. 6. 12 lead ECG monitor failure- Called for operational Paramedic. Lysed on hospital ECG.	

Patient Number: 11 - 161009

Ethnic group	C	**Gender**	F	**Age**	80
Respiration	18	**Pulse**	86		
HGT	6	**BP**	168/91		
AVPU	Alert	**Symptom/s**	Discomfort/mild central chest pain		

Family History	Unknown	
Risk Factors	Hypertension, Asthmatic, Mild CVA 1986.	
ECG	Initial: Inferior, anterolateral Infarct. ECG @ 60 minutes: Reperfused.	
Treatment	At private clinic: Oxygen; ASA, GTN, Morphine (6mg). Raveen Naidoo: Clopidogrel (75mg), GTN (3 tabs), TNK (6000U), Enoxaparin (40 mg SC).	
Timeframes	**Symptom to call for help**	00H15
	Transportation time	00H45 – waited for private transportation. Transportation time: 15 minutes
	GP time	N/A
	Primary hospital time	01H15
	Symptom to definitive treatment	02H30
In-hospital Outcome	No complications – discharged 20/10/09.	
30-day Outcome	15/11/09. No complications	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Quicker transportation. 2. Earlier in-hospital thrombolysis activation– within 30 minutes of arrival. Points to note: 1. Pleasing outcome.	

Patient Number: 12 - 261009

Ethnic group	Black African	**Gender**	M	**Age**	51
Respiration	18	**Pulse**	107		
HGT	11	**BP**	164/109		
AVPU	Alert	**Symptom/s**	Severe central chest pain		

Family History	Unknown	
Risk Factors	Possibly undiagnosed Hypertension, Diabetic	
ECG	Initial: Inferior, posterior lateral Infarct. ECG @ 90 minutes: Reperfused.	
Treatment	At district hospital: Oxygen; ASA, Nitrate infusion (5mls/hr), Morphine (2mg). Raveen Naidoo: Clopidogrel (300mg), GTN (2 tabs), Morphine (10mg), Metoclopramide (10mg), TNK (10000U), Enoxaparin (30mg IVI, 80 mg SC).	
Timeframes	**Symptom to call for help**	00H00
	Transportation time	00H35 – Private (waited 30 minutes)
	GP time	
	Primary hospital time	02H20
	Symptom to definitive treatment	02H55
In-hospital Outcome	Patient discharged on 021109. No complications. Patient diagnosed as hypertensive.	
30-day Outcome	251109. No complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Notification and use of EMS. 3. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Patient pain free and comfortable upon admission to CCU.	

Patient Number: 13 - 311009

Ethnic group	I	**Gender**	M	**Age**	57
Respiration	24	**Pulse**	40		
HGT	17,4	**BP**	92/54		
AVPU	Alert	**Symptom/s**	Severe central chest pain		

Family History	Brother died of MI at 52	
Risk Factors	Diabetes, Hypertension, Smoker	
ECG	Initial: Inferior Infarct; Complete heart block. ECG @ 120 minutes: Reperfused, but patient in complete block.	
Treatment	At district hospital: Oxygen; ASA, Nitrate infusion (5mls/hr). Raveen Naidoo: Clopidogrel (300mg), Morphine (7.5mg), Metoclopramide (10mg), TNK (10000U), Enoxaparin (30mg IVI, 80 mg SC).	
Timeframes	**Symptom to call for help**	00H00
	Transportation time	01H15 – Private
	GP time	
	Primary hospital time	02H55
	Symptom to definitive treatment	04H10
In-hospital Outcome	Patient discharged on 061109. Patient had to be externally paced and put on double inotropic support at CCU.	
30-day Outcome	Patient stable at 30-day follow-up. Patient in first degree block – no further complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Notification and use of EMS. 2. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Direct admission to IALAH should have been considered. 2. Patients pulse and BP increase to 55 and 102/56 en route to hospital.	

Patient Number: 14 - 021109

Ethnic group	I	**Gender**	F	**Age**	58
Respiration	18	**Pulse**	76		
HGT	11	**BP**	165/95		
AVPU	Alert	**Symptom/s**	Severe central chest pain		

Family History	Parents and siblings.	
Risk Factors	Angina, Diabetes, Hypertension	
ECG	Initial: Anterolateral Infarct. ECG @ 180 minutes: Reperfused.	
Treatment	At district hospital: Oxygen Raveen Naidoo: ASA, Clopidogrel (300mg), GTN (1 tabs), TNK (7000U), Enoxaparin (30mg IVI, 65 mg SC).	
Timeframes	**Symptom to call for help**	00H48
	Transportation time (From time call received to patient drop off at hospital)	01H27 via ambulance
	GP time	
	Primary hospital time	02H10
	Symptom to definitive treatment	04H25
In-hospital Outcome	No complications. Patient discharged on 06/11/09.	
30-day Outcome	051209 – No complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. (Differentiate between angina and AMI.) 2. EMS activation of ECP. 3. Pre-alerting receiving hospital. 4. Earlier in-hospital thrombolysis activation– delivery within 30 minutes of patient arrival. Points to note: 1. No medical advice given by EMS control centre. 2. No ALS dispatch by EMS control centre – this was considered but the local operational ALS unit was not available. 3. No ASA administration by Ambulance crew. 4. Patient pain free and comfortable upon admission to CCU.	

Patient Number: 15 - 051109

Ethnic group	I	**Gender**	M	**Age**	63
Respiration	12	**Pulse**	80		
HGT	11	**BP**	111/77		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Unknown	
Risk Factors	None	
ECG	Initial: Inferior with posterior extension. ECG @ 90 minutes: Complete reperfusion.	
Treatment	At district hospital: Oxygen, ASA Raveen Naidoo: Clopidogrel (300mg), Morphine (2.5mg), TNK (7000U), Enoxaparin (30mg IVI, 65 mg SC), Metoclopramide (10mg), Atropine (0.25mg).	
Timeframes	**Symptom to call for help**	0H30
	Transportation time	00H05 – Private to PHX Clinic. 00H05 to MGMH
	GP time	00H55
	Primary hospital time	01H15
	Symptom to definitive treatment	02H50
In-hospital Outcome	No complications. Patient discharged on 09/11/09.	
30-day Outcome	051209 – No complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Notification and use of EMS. 3. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Mild pain and comfortable upon admission to CCU. 2. Time to ECP activation and in-hospital treatment time reduced. 3. Reperfusion changes occurred within 10 minutes of TNK. Bradycardia with severe pain experienced. Bradycardia (46) responded to 0.5mg Atropine.	

Patient Number: 16 - 111109

Ethnic group	I	**Gender**	M	**Age**	70
Respiration	16	**Pulse**	115		
HGT	14	**BP**	80/60		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Siblings	
Risk Factors	Hypertension, Smoker	
ECG	Initial: Anterior Infarct. ECG @ 180 minutes: Some perfusion.	
Treatment	At district hospital: Oxygen, ASA, Dobutrex infusion Raveen Naidoo: Clopidogrel (300mg), TNK (8000U), Enoxaparin (30mg IVI, 80mg SC)	
Timeframes	**Symptom to call for help**	02H00
	Transportation time	02H45 – Private; patient delayed at home.
	GP time	
	Primary hospital time	1H10 minutes
	Symptom to definitive treatment	05H55
In-hospital Outcome	Developed pulmonary oedema at Add CCU, transferred to IALAH, triple inotropic support, weaned off. TVD (Triple stent) – for CABG. Patient discharged on 171109 from IALAH	
30-day Outcome	Patient died on 301109 – Patient collapsed suddenly at 21H00. Patient was diagnosed of a gastric ulcer the same day at IALAH. Declared dead by Raveen Naidoo at 21H15.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Notification and use of EMS. 3. Earlier in-hospital thrombolysis activation– delivery within 30 minutes of patient arrival. Points to note: 1. Patient had differing pulse and BP. 2. Time to ECP activation and in-hospital treatment time reduced. 3. Overall improvement in time to treatment for patient in all health sectors.	

Patient Number: 17 - 161109

Ethnic group	I	**Gender**	M	**Age**	49
Respiration	16	**Pulse**	91		
HGT	13.5	**BP**	131/86		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Mother – Cardiac	
Risk Factors	Smoker	
ECG	Initial: Anteroseptal Infarct. ECG @ 60 minutes: No change. ECG @ 4 hours later: Resolution noted.	
Treatment	At district hospital: Oxygen, ASA, GTN X 2 tablets. Raveen Naidoo: Clopidogrel (300mg), TNK (7000U), Enoxaparin (30mg IVI, 65mg SC), GTN X 2 tablets.	
Timeframes	**Symptom to call for help**	0H00
	Transportation time	02H25 Patient delayed transportation
	GP time	0H05 PHX Clinic
	Primary hospital time	03H00
	Symptom to definitive treatment	05H30
In-hospital Outcome	Nitrate infusion started due to on-going mild central chest pain. No complications. Patient discharged on 20/11/09.	
30-day Outcome	15/12/09 – No complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Patient had pain for more than two weeks, self-medicated for ulcers. 2. Q waves in septal territory with hyperacute ST changes and ongoing chest pain. 3. Pain subsided after initial pain @ 03H00; therefore, patient went home after clinic. Went to MGMH when pain started again @ 05H25.	

Patient Number: 18 - 171109

Ethnic group	I	**Gender**	M	**Age**	49
Respiration	16	**Pulse**	89		
HGT	11.3	**BP**	143/97		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Brother – Cardiac	
Risk Factors	Smoker	
ECG	Initial: Anteroseptal Infarct. ECG @ 60 minutes: No reperfusion. ECG @ 160 minutes: No reperfusion.	
Treatment	At district hospital: Oxygen, ASA, Nitrocine infusion, Enoxaparin (80mg SC). Raveen Naidoo: Clopidogrel (300mg), TNK (6000U), Enoxaparin (30mg IVI), GTN X 2 tablets, Morphine (2.5mg), Metoclopramide (10mg).	
Timeframes	**Symptom to call for help**	02H00
	Transportation time	01H00 Waited for employer's help.
	GP time	Initial private hospital 50 minutes
	Primary hospital time	2H20
	Symptom to definitive treatment	06H10
In-hospital Outcome	Complete AV block night of admission at Addington. Temporary external pacemaker. Cardiac arrest and VT when temporary internal pacemaker attempted at Addington. Transferred to Albert Luthuli Hospital Stent inserted in LAD. On IABP and inotropic support. Off pump 23/11/09. Patient discharged on 02/12/09. Failed lyses?	
30-day Outcome	15/12/09 – No complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time. 2. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Q waves in septal territory with hyper-acute ST changes and ongoing chest pain.	

Patient Number: 19 - 191109

Ethnic group	I	**Gender**	M	**Age**	68
Respiration	18	**Pulse**	75		
HGT	Not done	**BP**	110/59		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Mother – Cardiac	
Risk Factors	Smoker	
ECG	Initial: Anteroseptal Infarct. ECG @ 90 minutes: Reperfused. ECG @ 180 minutes: Reperfused.	
Treatment	At district hospital: Oxygen, ASA, Enoxaparin (40mg SC). Raveen Naidoo: Clopidogrel (300mg), TNK (7000U), Enoxaparin (30mg IVI, 30mg SC), GTN X 1 tablet, Morphine (2.5mg), Metoclopramide (10mg).	
Timeframes	**Symptom to call for help**	0H00
	Transportation time	00H30
	GP time	
	Primary hospital time	4H25
	Symptom to definitive treatment	4H55
In-hospital Outcome	Nitrate infusion started due to on-going mild central chest pain. No complications. Patient discharged on 23/11/09.	
30-day Outcome	18/12/09 – No complications, patient still smoking 5 cigarettes a day.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Nil.	

Patient Number: 20 - 061209

Ethnic group	I	**Gender**	M	**Age**	46
Respiration	12	**Pulse**	125		
HGT		**BP**	149/107		
AVPU	Alert	**Symptom/s**	Central chest pain		

Family History	Mother – Cardiac, died at 68; Father – Cardiac, died at 50.	
Risk Factors	Diabetic	
ECG	Initial: Anterolateral Infarct. ECG @ 90 minutes: Did not reperfuse.	
Treatment	At district hospital: Oxygen, ASA, GTN X 1 spray Raveen Naidoo: Clopidogrel (300mg), TNK (7000U), Enoxaparin (30mg IVI, 730mg SC)	
Timeframes	**Symptom to call for help**	0H00
	Transportation time	00H25 – patient waited for private transport.
	GP time	
	Primary hospital time	2H55
	Symptom to definitive treatment	3H20
In-hospital Outcome	No complications. Patient discharged on 10/12/09. Patient diagnosed with a laminated thrombus in apex via echo. No increase in CPK, but elevated Trop I. Patient did not benefit from TNK.	
30-day Outcome	05/01/10. No complications.	
Researcher Reflective Practice	Symptom-to-needle could have been reduced further by: 1. Earlier patient symptom recognition and decision time - Influence of diabetes on pain? 2. Earlier in-hospital thrombolysis activation – delivery within 30 minutes of patient arrival. Points to note: 1. Initial pain started at 05H00 the same day, but subsided. Although patient did not delay when pain became severe at 20H00, patient could have sought medical help much earlier. 2. Given the benefit administration of STK up to 12 hours, the administration of STK should have been considered.	

REFERENCES

1. World Health Organisation. Preventing Chronic Disease: A Vital Investment. Geneva; 2005.
2. World Health Organisation. The atlas of heart disease and stroke. Mackay J, Mensah G, editors. Geneva: World Health Organization; 2004.
3. World Health Organisation. The Top Ten Causes of Death. Geneva; 2008.
4. Bradshaw D, Groenewald P, Laubscher R, Nannan N, Nojilana B, Norman R, et al. Initial estimates from the South African National Burden of Disease Study, 2000. MRC Policy Brief. 2003;1.
5. Bradshaw D, Groenewald P, Laubscher R, Nannan N, Nojilana B, Norman R, et al. Provincial mortality in South Africa, 2000 - Priority-setting for now and a benchmark for the future. South African Medical Journal. 2005;95(7):496.
6. Steyn K. Heart disease in South Africa. Cape Town: Medical Research Council; 2007.
7. Seedat YK. Ethnicity, hypertension, coronary heart disease and renal diseases in South Africa. Ethnicity Health. 1996(1):349-57.
8. Derry CW, Bourne DE, Sayed AR. Variations in mortality of the Coloured, White and Asian population groups in the RSA, 1978-1982. Part VI. Ischaemic heart disease. South African Medical Journal. 1987;72:698-700.
9. Botha JL, Bradshaw D. African vital statistics - a black hole. South African Medical Journal. 1985;67:977-82.
10. Ranjith N, Pegoraro RJ, Naidoo DP. Demographic data and outcome of acute coronary syndrome in the South African Asian Indian population. Cardiovascular Journal of South Africa. 2005;16(1):48-54.
11. Naidoo R. Thrombolytic therapy for acute myocardial infarction and early patient

outcomes in Durban and surrounding areas in South Africa. Brighton: University of Brighton; 2007.

12. Seftel HC, Keeley KJ, Walker ARP. Characteristics of South African Bantu who have suffered myocardial infarction. American Journal of Cardiology 1963;12:148-56.

13. Di Bisceglie AM, Miler MT, Blumsohn D. Myocardial infarction in an intensive care unit for Blacks. South African Medical Journal. 1982;61:902-4.

14. Amira C, Ntyintyane L, Wilkinson D, Stewart S, Becker A, Libhaber E, et al. Emerging epidemic of cardiovascular disease among urban Africans. SA Heart. 2006:7-11.

15. Tibazarwa K, Ntyintyane L, Sliwa K, Gerntholtz T, Carrington M, Wilkinson D, et al. A time bomb of cardiovascular risk factors in South Africa: Results from the Heart of Soweto Study "Heart Awareness Days". International Journal of Cardiology. 2009;132(2):233-9.

16. Sliwa K, Wilkinson D, Hansen C, Ntyintyane L, Tibazarwa K, Becker A, et al. Spectrum of heart disease and risk factors in a black urban population in South Africa (the Heart of Soweto Study): A cohort study. The Lancet. 2008;371(9616):915.

17. Steyn K, Sliwa K, Hawken S, Commerford P, Onen C, Damasceno A, et al. Risk factors associated with myocardial infarction in Africa: The INTERHEART Africa Study. Circulation. 2005;112(23):3554-61.

18. GISSI Group. Effectiveness of intravenous thrombolytic treatment in acute myocardial infarction. Lancet. 1986;1:397-402.

19. Kainth A, Hewitt A, Sowden A. Systematic review of interventions to reduce delay in patients with suspected heart attack. Emergency Medicine Journal. 2004;21:506-8.

20. American Heart Association. Part 8: Stabilization of the patient with acute coronary

syndromes. Circulation 2005;112(24 Supplement):IV-89-IV-110.

21. Robinson NM, Timmis AD. Reperfusion in acute myocardial infarction. British Medical Journal. 2000;320(7246):1354-5.

22. European Society of Cardiology. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology. European Heart Journal. 2008;29(23):2909-45.

23. Townend JN, Doshi SN. Reducing mortality in myocardial infarction. British Medical Journal. 2005;330(7496):856-7.

24. Ryan TJ, Antman EM. 1999 Update: ACC/AHA Guidelines for the management of patients with acute myocardial infarction: Executive Summary and Recommendations: A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Management of Acute Myocardial Infarction). Circulation. 1999;100(9):1016-30.

25. Van de Werf F, Ardissino D. The Task Force on the Management of Acute Myocardial Infarction of the European Society of Cardiology: Management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal. 2003;24(1):28-66.

26. Boersma E, Maas A, Deckers J. Early thrombolytic treatment in acute myocardial infarction: Re-appraisal of the golden hour. Lancet. 1996;348:771.

27. Birkhead JS. MINAP. National audit of myocardial infarction; 2004.

28. Brodie B, Stuckey T, Hansen C. Benefit of late coronary reperfusion in patients with acute myocardial infarction and persistent ischaemic pain. American Journal of Cardiology 1994;74:538-43.

29. Becker RC, Charlesworth A, Wilcox RG, Hamptom J, Skene A, Gore JM, et al.

Cardiac Rupture Associated with Thrombolytic Therapy: Impact of time to Treatrment in the Late Assessment of Thrombolytic Efficacy (LATE) Study. Journal of American College of Cardiology 1995;25:1063-8.

30. Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, et al. ACC/AHA 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 (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). Journal of American College of Cardiology. 2004;44(3):E1-E211.

31. ISIS-2 Group. Randomised Trial Of Intravenous Streptokinase, Oral Aspirin, Both, Or Neither Among 17 187 Cases Of Suspected Acute Myocardial Infarction: ISIS-2. Lancet. 1988;332(8607):349.

32. Nallamothu B, Bates E. Times to Treatment in Transfer Patients Undergoing Primary Percutaneous Coronary Intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 Analysis. Circulation. 2005;111(6):761-7.

33. Maharaj RC, Geduld, H., Wallis, L.A. Door-to-needle time for administration of fibrinolytics in acute myocardial infarction in Capte Town. South African Medical Journal. 2012;102(4).

34. Ottesen M, Dixen U, Torp-Pedersen C. Pre-hospital delay in acute coronary syndrome - an analysis of the components of delay. International Journal of Cardiology. 2004;961:97-103.

35. Goldberg RJ, Yarzebski J, Lessard D, Gore JM. Decade-Long Trends and Factors Associated With Time to Hospital Presentation in Patients With Acute Myocardial Infarction: The Worcester Heart Attack Study. Arch Intern Med. 2000;160(21):3217-23.

36. Perry K, Petrie KJ, Ellis CJ. Symptom expectations and delay in acute myocardial infarction patients. Heart. 2001;86:91-3.

37. Goldberg RJ, Steg PG, Sadiq I. Extent of, and factors associated with, delay to hospital presentation in patients with acute coronary disease (the GRACE registry). American Journal Cardiology. 2002;89:791-6.

38. McGinn AP, Rosamond WD, Goff JDC, Taylor HA, Miles JS, Chambless L. Trends in pre-hospital delay time and use of emergency medical services for acute myocardial infarction: Experience in 4 US communities from 1987-2000. American Heart Journal. 2005;150(3):392-400.

39. Goff DC, Feldman HA, McGovern G, Goldberg RJ, Simons-Morton DG, Cornell CE, et al. Pre-hospital delay in patients hospitalized with heart attack symptoms in the United States: The REACT trial. American Heart Journal. 1999;138(6):1046-57.

40. Leslie WS, Urie A, Hooper J, Morrison CE. Delay in calling for help during myocardial infarction: reasons for the delay and subsequent pattern of accessing care. Heart. 2000;84(2):137-41.

41. Yarzebski J, Goldberg RJ, Gore JM, Alpert JS. Temporal trends and factors associated with extent of delay to hospital arrival in patients with acute myocardial infarction: the Worcester Heart Attack Study. American Heart Journal. 1994;128:255-63.

42. Perkins-Porras L, Whitehead DL, Strike PC, Steptoe A. Pre-hospital delay in patients with acute coronary syndrome: Factors associated with patient decision time and home-to-hospital delay. European Journal of Cardiovascular Nursing. 2009;8(1):26-33.

43. Moser DK, Kimble LP, Alberts MJ, Alonzo A, Croft JB, Dracup K, et al. Reducing Delay in Seeking Treatment by Patients With Acute Coronary Syndrome and Stroke. Circulation. 2006;114(2):168-82.

44. Abdelkhirane C, Naji, A., Adnan, K. How to improve the management of pre-hospital AMI patients in North Africa. Atherosclerosis. 2009;10(2):Supplement.

45. Moustaghfir A, Haddak M, Mechmeche R. Management of acute coronary syndromes in Maghreb countries: The ACCESS (ACute Coronary Events – a multi-national Survey of current management Strategies) registry. Archives of Cardiovascular Diseases. 2012; 105:566-577.

46. Dracup K, McKinley S, Moser DK. Australian patients' delay in response to heart attack symptoms. Medical Journal of Australia. 1997;166:233-6.

47. Elliot J. Why I ignored my heart attack. In: Reporter H, editor. BBC News. United Kingdom; 2006.

48. Herlitz J, Thuresson M, Svensson L, Lindqvist J, Lindahl B, Zedigh C, et al. Factors of importance for patients' decision time in acute coronary syndrome. International Journal of Cardiology. 2010;141(3):236-42.

49. Horne R, James D, Petrie K, Weinman J, Vincent R. Patients' interpretation of symptoms as a cause of delay in reaching hospital during acute myocardial infarction. Heart. 2000;83(4):388-93.

50. Meischke H, Ho MT, Heisenberg MS, Schaeffer SM, Larsen MP. Reasons patients with chest pain delay or do not call 911. Annals of Emergency Medicine. 1995;25(2):193-7.

51. Henriksson C, Lindahl B, Larsson M. Patients' and relatives' thoughts and actions during and after symptom presentation for an acute myocardial infarction. European Journal of Cardiovascular Nursing. 2007;6(4):280-6.

52. Gurwitz JH, McLaughlin TJ, Willison DJ, Guadagnol E, Hauptman PJ, Gao X, et al. Delayed hospital presentation in patients who have had acute myocardial infarction. Annals of Internal Medicine. 1997;126(8):593-9.

53. McKinley S, Moser DK, Dracup K. Treatment-seeking behavior for acute

myocardial infarction symptoms in North America and Australia. Heart & Lung: The Journal of Acute and Critical Care. 2000;29(4):237-47.

54. Sheifer SE, Rathore SS, Gersh BJ, Weinfurt KP, Oetgen WJ, Breall JA, et al. Time to presentation with acute myocardial infarction in the elderly. Circulation. 2000;102:1651-6.

55. Banks AD, Dracup K. Factors Associated With Prolonged Pre-hospital Delay of African Americans With Acute Myocardial Infarction. American Journal of Critical Care. 2006;15(2):149-57.

56. Douglas P. Coronary artery disease in women. In: Braunwald E, editor. Heart Disease: A Textbook of Cardiovascular Medicine. Philidelphia: WB Saunders Co.; 1997. p. 1704-14.

57. King KB, McGuire MA. Symptom presentation and time to seek care in women and men with acute myocardial infarction. Heart & Lung: The Journal of Acute and Critical Care. 2007;36(4):235-43.

58. Lovlien M, Schei B, Hole T. Pre-hospital delay, contributing aspects and responses to symptoms among Norwegian women and men with first time acute myocardial infarction. European Journal of Cardiovascular Nursing. 2007;6:308-13.

59. Isaksson R-M, Holmgren L, Lundblad D, Brulin C, Eliasson M. Time trends in symptoms and pre-hospital delay time in women vs. men with myocardial infarction over a 15-year period. The Northern Sweden MONICA Study. European Journal of Cardiovascular Nursing. 2008;7(2):152.

60. Okhravi M. Causes for Pre-hospital and in-hospital delays in acute myocardial infarction at Tehran teaching hospitals. Australian Emergency Nursing Journal. 2002;5(1):21-6.

61. Arntz HR, Bossaert LL, Danchin N, Nikolaou NI. European Resuscitation Council

Guidelines for Resuscitation 2010 Section 5. Initial management of acute coronary syndromes. Resuscitation. 2010;81(10):1353-63.

62. Canto JG, Zalenski RJ, Ornato JP, Rogers WJ, Kiefe CI, Magid D, et al. Use of Emergency Medical Services in Acute Myocardial Infarction and Subsequent Quality of Care. Circulation. 2002;106(24):3018-23.

63. Afolabi BA, Novaro GM, Pinski SL, Fromkin KR, Bush HS. Use of the pre-hospital ECG improves door-to-balloon times in ST segment elevation myocardial infarction, irrespective of time of day or day of week. Emergency Medicine Journal. 2007;24(8):588-91.

64. Van 't Hof AWJ, Rasoul S, Van de Wetering H, Ernst N, Suryapranata H, Hoorntje JCA, et al. Feasibility and benefit of pre-hospital diagnosis, triage and therapy by paramedics only in patients who are candidates for primary angioplasty for acute myocardial infarction. American Heart Journal. 2006;151(6):1255.e1-.e5.

65. Hutchings CB, Mann NC, Daya M, Jui J, Goldberg JR, Cooper L, et al. Patients with chest pain calling 9-1-1 or self-transporting to reach definitive care: Which mode is quicker? American Heart Journal. 2004;147:35-41.

66. Zed PJ, Abu-Laban RB, Cadieu TM, Purssell RA, Filiatrault L. Fibrinolytic administration for acute myocardial infarction in a tertiary ED: factors associated with an increased door-to-needle time. The American Journal of Emergency Medicine. 2004;22(3):192-6.

67. Johansson I, Stromberg A, Swahn E. Ambulance Use in Patients With Acute Myocardial Infarction. Journal of Cardiovascular Nursing. 2004;19(1):5-12.

68. Kerr D, Holden D, Smith J, Kelly A-M, Bunker S. Predictors of ambulance use in patients with acute myocardial infarction in Australia. Emergency Medicine Journal. 2006;23(12):948-52.

69. Thuresson M, Jarlöv MB, Lindahl B, Svensson L, Zedigh C, Herlitz J. Factors that

influence the use of an ambulance in acute coronary syndrome. American Heart Journal. 2008;156(1):170.

70. Rogers WJ, Canto JG, Barron HV, Boscarino JA, Shoultz DA, Every NR. Treatment and outcome of myocardial infarction in hospitals with and without invasive capability. Investigaters in the national registry of myocardial infarction. Journal of American College of Cardiology 2000;35(2):371-9.

71. Fukuoka Y, Dracup K, Kobayashi F, Froelicher ES, Rankin SH, Ohno M, et al. Trajectory of pre-hospital delay in patients with acute myocardial infarction in the Japanese health care system. International Journal of Cardiology. 2006;107(2):188-93.

72. Department of Health. White Paper for the Transformation of the Health System in South Africa. Pretoria; 1997.

73. Mary TH, Mickey SE, Paul EL, Sharon MS, Susan KD. Delay between onset of chest pain and seeking medical care: The effect of public education. Annals of Emergency Medicine. 1989;18(7):727-31.

74. Luepker RV, Raczynski JM, Osganian S, Goldberg RJ, Finnegan JR, Jr, Hedges JR, et al. Effect of a Community Intervention on Patient Delay and Emergency Medical Service Use in Acute Coronary Heart Disease: The Rapid Early Action for Coronary Treatment (REACT) Trial. JAMA. 2000;284(1):60-7.

75. Moore SM. The effects of discharge information intervention on recovery outcomes following coronary artery bypass surgery. International Journal of Nursing Studies. 1996;33(2):181-9.

76. Dracup K, McKinley S, Riegel B, Mieschke H, Doering LV, Moser DK. A Nursing

Intervention to Reduce Pre-hospital Delay in Acute Coronary Syndrome: A Randomized Clinical Trial. Journal of Cardiovascular Nursing. 2006;21(3):186-93.

77. Buckley T, McKinley S, Gallagher R, Dracup K, Moser DK, Aitken LM. The effect of education and counselling on knowledge, attitudes and beliefs about responses to acute myocardial infarction symptoms. European Journal of Cardiovascular Nursing. 2007;6(2):105-11.

78. Dracup K, McKinley, S, Riegel, B, Moser, DK, Meischke, H, Doering, LV, Davidson, P, Paul, SM, Baker, H, Pelter, M. A randomized clinical trial to reduce patient pre-hospital delay to treatment in acute coronary syndrome. Circ Cardiovasc Qual Outcomes. 2009;2(6):524-32.

79. McKinley S, Dracup, K, Moser, DK, Riegel, B, Doering, LV, Meischke, H, Aitken, LM, Buckley, T, Marshall, A, Pelter, M. The effect of short one-on-one nursing intervention on knowledge, attitudes and beliefs related to response to acute coronary syndrome in people with coronary heart disease: a randomized controlled trial. International Journal for Nursing Studies. 2009;46(6):1037-46.

80. Khraim FM, Carey MG. Predictors of pre-hospital delay among patients with acute myocardial infarction. Patient Education and Counseling. 2009;75:155-61.

81. Silver FL, Rubini, F, Black, D, Hodgson, CS Advertising strategies to increase public knowledge of the warning signs of stroke. Stroke. 2003;34(8):1965-8.

82. Fogle CC, Oser, CS, McNamara, MJ, Helgerson, SD, Gohdes, D, Harwell, TS. Impact of media on community awareness of stroke warning signs: a comparison study. Journal of Stroke and Cerebrovascular Disease. 2010;19(5):370-5.

83. Mayosi B, Flisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D. The burden of

non-communicable diseases in South Africa. The Lancet. 2009;374(9693).

84. White HD, Chew DP. Acute myocardial infarction. The Lancet. 2008;372(9638):570.

85. Libby P. Current concepts of the pathogenesis of the acute coronary syndromes. Circulation. 2001;104:365-72.

86. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. European Heart Journal. 2006;27(7):779-88.

87. Keeley EC, Boura, JA, Grines, CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet. 2003;361:13-20.

88. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, et al. Guidelines on myocardial re-vascularization. European Heart Journal. 2010;31(20):2501-55.

89. Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. European Heart Journal. 2008;29(23):2909-45.

90. Canto JG, Every NR, Magid DJ, Rogers WJ, Malmgren JA, Frederick PD, et al. The Volume of Primary Angioplasty Procedures and Survival after Acute Myocardial Infarction. New England Journal of Medicine. 2000;342(21):1573-80.

91. Spaulding C, Morice M-C, Lancelin B, El Haddad S, Lepage E, Bataille S, et al. Is the volume-outcome relation still an issue in the era of PCI with systematic stenting? Results of the greater Paris area PCI registry. European Heart Journal. 2006;27(9):1054-60.

92. Department of Health. KwaZulu-Natal Health. 2009 [[01 July 2009]; Available from: http://www.kznhealth.gov.za.

93. Statistics South Africa. Mid-year population estimates. In: Africa SS, editor. Pretoria; 2011.

94. Yusuf S, Collins R, Peto R, Furberg C, Stampfer MJ, Goldhaber SZ, et al. Intravenous and intracoronary fibrinolytic therapy in acute myocardial infarction: Overview of results on mortality, reinfarction and side-effects from 33 randomized controlled trials. European Heart Journal. 1985;6(7):556-85.

95. Rogers W, Mantle J, Hood W, Baxley W, Whitlow P, Reeves R, et al. Prospective randomized trial of intravenous and intracoronary Streptokinase in acute myocardial infarction. Circulation. 1983 November 1, 1983;68(5):1051-61.

96. Schroder R, Biamino G, Von Leitner ER, Linderer T, Bruggemann T, Heitz J, et al. Intravenous short-term infusion of Sstreptokinase in acute myocardial infarction. Circulation. 1983;67(3):536-48.

97. Anderson JL, Marshall HW, Askins JC, Lutz JR, Sorensen SG, Menlove RL, et al. A randomized trial of intravenous and intracoronary Streptokinase in patients with acute myocardial infarction. Circulation. 1984;70(4):606-18.

98. Fibrinolytic Therapy Trialists' Collaborative Group. 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. 1994;343(8893):311-22.

99. GUSTO Group. An International Randomized Trial Comparing Four Thrombolytic Strategies for Acute Myocardial Infarction. New England Journal of Medicine. 1993;329(10):673-82.

100. Koren G, Weiss AT, Hasin Y, Appelbaum D, Welber S, Rozenman Y, et al.

Prevention of Myocardial Damage in Acute Myocardial Ischemia by Early Treatment with Intravenous Streptokinase. New England Journal of Medicine. 1985;313(22):1384-9.

101. Rawles J. Halving of mortality at 1 year by domiciliary thrombolysis in the Grampian Region Early Anistreplase Trial (GREAT). Journal of American College of Cardiology. 1994;23(1):1-5.

102. Rawles JM. Quantification of the Benefit of Earlier Thrombolytic Therapy: Five-Year Results of the Grampian Region Early Anistreplase Trial (GREAT). Journal of the American College of Cardiology. 1997;30(5):1181-6.

103. Rawles J. GREAT: 10 year survival of patients with suspected acute myocardial infarction in a randomised comparison of prehospital and hospital thrombolysis. Heart. 2003;89(5):563-4.

104. EMIP Group. Pre-hospital thrombolytic therapy in patients with suspected acute myocardial infarction. New England Journal of Medicine. 1993;329:383-90.

105. Brouwer MA, Martin JS, Maynard C, Wirkus M, Litwin PE, Verheugt FWA, et al. Influence of early pre-hospital thrombolysis on mortality and event-free survival (The Myocardial Infarction Triage and Intervention [MITI] Randomized Trial). The American Journal of Cardiology. 1996;78(5):497-502.

106. Morrison LJ, Verbeek PR, McDonald AC, Sawadsky BV, Cook DJ. Mortality and Pre-hospital Thrombolysis for Acute Myocardial Infarction. JAMA: The Journal of the American Medical Association. 2000;283(20):2686-92.

107. Voipio V, Kuisma M, Alaspää A, Mänttäri M, Rosenberg P. Thrombolytic treatment of acute myocardial infarction after out-of-hospital cardiac arrest. Resuscitation. 2001;49(3):251-8.

108. Björklund E, Stenestrand U, Lindbäck J, Svensson L, Wallentin L, Lindahl B. 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. 2006;27(10):1146-52.

109. Welsh RC, Travers A, Senaratne M, Williams R, Armstrong PW. Feasibility and applicability of paramedic-based pre-hospital fibrinolysis in a large North American center. American Heart Journal. 2006;152(6):1007.

110. Weaver WD, J SR, Betriu A, Grines CL, Zijistra F, Garcia E, et al. Comparison of primary coronary angioplasty and intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review. Journal of American Medical Association 1997;278(23):2093-8.

111. Van de Werf P, Ross A, Armstrong P, Granger C. Primary versus Tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. The Lancet. 2006;367(9510):569-78.

112. Armstrong PW. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. European Heart Journal. 2006;27(13):1530-8.

113. Bonnefoy E, Steg PG, Boutitie F, Dubien P-Y, Lapostolle F, Roncalli J, et al. Comparison of primary angioplasty and pre-hospital fibrinolysis in acute myocardial infarction (CAPTIM) trial: a 5-year follow-up. European Heart Journal. 2009:ehp156.

114. Westerhout CM, Bonnefoy E, Welsh RC, Steg PG, Boutitie F, Armstrong PW. The influence of time from symptom onset and reperfusion strategy on 1-year survival in ST-elevation myocardial infarction: A pooled analysis of an early

fibrinolytic strategy versus primary percutaneous coronary intervention from CAPTIM and WEST. American Heart Journal. 2011;161(2):283-90.

115. Steg PG, James SK, Atar D, Badano LP, Lundqvist CB, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). European Heart Journal. 2012 October 1, 2012;33(20):2569-619.

116. Gersh BJ, Rahimtoola SH, editors. Acute Myocardial Infarction. Second ed. New York: Chapman & Hall; 1997.

117. MIMS Desk Reference. Freitas Nd, editor: MIMS; 2006/7.

118. Adams JN, Jamieson M, Trent RJ, Rawles J, Jennings KP. The risks of thrombolysis in patients without acute myocardial infarction. International Journal of Cardiology. 1995;51(2):177-81.

119. Opie LH, Gersh BJ. Drugs for the heart. 7th ed. Philadelphia: Saunders Elsevier; 2009.

120. Gore JM, Granger CB, Simoons ML, Sloan MA, Weaver WD, White HD, et al. Stroke After Thrombolysis : Mortality and Functional Outcomes in the GUSTO-I Trial. Circulation. 1995;92(10):2811-8.

121. British National Formulary. London: BMJ Group; 2011.

122. O'Driscoll BR, Howard LS, Davison AG. Guidelines for emergency oxygen use in adults: On behalf of the British Thoracic Society Emergency Oxygen Guidelines Development Group. Thorax. 2008;63(Supplement VI):VI 1-VI 73.

123. Neumar RW, Otto CW, Link MS, Kronick SL, Shuster M, Callaway CW, et al. Part 8: Adult Cardiovascular Life Support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Care. Circulation. 2010;Vol 122(Supplement):S729-S67.

124. Keeley EC, Boura JA, Grines CL. Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials. The Lancet. 2006;367(9510):579-88.

125. Freimark D, Matetzky S, Leor J, Boyto V. Timing of Aspirin administration as a determinant of survival of patients with acute myocardial infarction treated with thrombolysis. American Journal of Cardiology. 2002;89:381-5.

126. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of Clopidogrel in Addition to Aspirin in Patients with Acute Coronary Syndromes without ST-Segment Elevation. New England Journal of Medicine. 2001;345(7):494-502.

127. Sabatine MS, Cannon CP, Gibson CM, López-Sendón JL, Montalescot G, Theroux P, et al. Effect of Clopidogrel Pre-treatment Before Percutaneous Coronary Intervention in Patients With ST-Elevation Myocardial Infarction Treated With Fibrinolytics. JAMA: The Journal of the American Medical Association. 2005;294(10):1224-32.

128. Chen M, Jiang LX, Chen YP, Xie JX, Pan HC, Peto R, et al. Addition of Clopidogrel to Aspirin in 45 852 patients with acute myocardial infarction: randomised placebo-controlled trial. The Lancet. 2005;366(9497):1607-21.

129. Scirica BM, Sabatine MS, Morrow DA, Gibson CM, Murphy SA, Wiviott SD, et al. The Role of Clopidogrel in Early and Sustained Arterial Patency After Fibrinolysis for ST-Segment Elevation Myocardial Infarction: The ECG CLARITY-TIMI 28 Study. Journal of American College of Cardiology. 2006;48(1):37-42.

130. Antman EM, Hand M, Armstrong PW, Bates ER, Green LA, Halasyamani LK, et al. 2007 Focused Update of the ACC/AHA2004 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 Developed in Collaboration With the Canadian Cardiovascular Society Endorsed by the American Academy of Family Physicians. Journal of American College of Cardiology. 2008;51(2):210-47.

131. Horne S, Weston C, Quinn T, Hicks A, Walker L, Chen R, et al. The impact of pre-hospital thrombolytic treatment on re-infarction rates: analysis of the Myocardial Infarction National Audit Project (MINAP). Heart. 2009;95(7):559-63.

132. Wallentin L, Goldstein P, Armstrong PW, Granger CB, Adgey AAJ, Arntz HR, et al. Efficacy and Safety of Tenecteplase in Combination With the Low-Molecular-Weight Heparin Enoxaparin or Unfractionated Heparin in the Pre-hospital Setting. Circulation. 2003;108(2):135-42.

133. Antman EM, Morrow DA, McCabe CH, Jiang F, White HD, Fox KAA, et al. Enoxaparin versus unfractionated Heparin as antithrombin therapy in patients receiving fibrinolysis for ST-elevation myocardial infarction: Design and rationale for the Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment-Thrombolysis In Myocardial Infarction study 25 (ExTRACT-TIMI 25). American Heart Journal. 2005;149(2):217-26.

134. Morrow DA, Antman EM, Fox KAA, White HD, Giugliano R, Murphy SA, et al. One-year outcomes after a strategy using Enoxaparin vs unfractionated Heparin in patients undergoing fibrinolysis for ST-segment elevation myocardial infarction: 1-year results of the ExTRACT-TIMI 25 Trial. European Heart Journal. 2010;31(17):2097-102.

135. Murphy SA, Gibson CM, Morrow DA, Van de Werf F, Menown IB, Goodman SG,

et al. Efficacy and safety of the low-molecular weight Heparin Enoxaparin compared with unfractionated Heparin across the acute coronary syndrome spectrum: a meta-analysis. European Heart Journal. 2007;28(17):2077-86.

136. Mensah GA, Hand MM, Antman EM, Ryan TJ, Jr, Schriever R, Smith SC, Jr. Development of Systems of Care for ST-Elevation Myocardial Infarction Patients: The Patient and Public Perspective. Circulation. 2007;116(2):e33-8.

137. Guba EG. The paradigm dialog. California: Sage; 1990.

138. Tashakkori A, Teddlie, C. Handbook of mixed methods in social and behavioural research. California: Sage; 2003.

139. Polit DF, Beck CT. Essentials of Nursing Research: Appraising Evidence for Nursing Practice. 7th ed. Philadelphia Lippincott, Williams & Wilkins; 2010.

140. Johnson RB, Onwuegbuzie, A.J. Mixed Methods Research: A Research Paradigm Whose Time Has Come. Educational Researcher. 2004;33(7):14-26.

141. Wikipedia. Languages of South Africa. 2008 [[01 June 2008]; Available from: http://en.wikipedia.org/wiki/Languages_of_South_Africa.

142. Taylor MH. Planning for Video. London: Kogan Page; 1988.

143. Wikipedia. eThekwini. 2011 [01 August 2011]; Available from: http://en.wikipedia.org/wiki/EThekwini.

144. Republic of South Africa. Emergency Medical Rescue Services: Standing Operational Policies. In: Health Do, editor. Pretoria: Government Printer; 2005.

145. Health professions council of South Africa. Minutes of the Sixteenth Meeting of the Health Professions Council of South Africa. Pretoria; 2006.

146. Thygesen K, Alpert JS, White HD, Jaffe AS, Apple FS, Galvani M, et al. Universal definition of myocardial infarction. European Heart Journal. 2007;28(20):2525-38.

147. Fox K, Garcia MAA, Ardissino D, Buszman P, Camici PG, Crea F, et al. Guidelines on the management of stable angina pectoris: executive summary. European Heart Journal. 2006;27(11):1341-81.

148. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJV, Ponikowski P, Poole-Wilson PA, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008. European Journal of Heart Failure. 2008 October 1, 2008;10(10):933-89.

149. Hamm CW, Ravkilde J, Gerhardt W, Jørgensen P, Peheim E, Ljungdahl L, et al. The Prognostic Value of Serum Troponin T in Unstable Angina. New England Journal of Medicine. 1992;327(3):146-50.

150. Antman EM, Tanasijevic MJ, Thompson B, Schactman M, McCabe CH, Cannon CP, et al. Cardiac-Specific Troponin I Levels to Predict the Risk of Mortality in Patients with Acute Coronary Syndromes. New England Journal of Medicine. 1996;335(18):1342-9.

151. Ohman EM, Armstrong PW, Christenson RH, Granger CB, Katus HA, Hamm CW, et al. Cardiac Troponin T Levels for Risk Stratification in Acute Myocardial Ischemia. New England Journal of Medicine. 1996;335(18):1333-42.

152. Morrow DA, Cannon CP, Jesse RL, Newby LK, Ravkilde J, Storrow AB, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: Clinical Characteristics and Utilization of Biochemical Markers in Acute Coronary Syndromes. Clinical Chemistry. 2007;53(4):552-74.

153. Lincoln YS, Guba, E.G. Naturalistic inquiry. California: Sage; 1985.

154. De Vos AS, Strydom, H, Fouché CB, Delport, CSL. Research at grass roots. Cape Town: Van Schaik Publishers; 2011.

155. Patton MQ. Qualitative research and evaluation methods. 3rd ed. California: Sage; 2002.

156. Brink H. Fundamentals of Research Methodology for Healthcare Professionals.

Cape Town: Juta & Co. (Pty) Ltd; 2009.

157. Kelley K, Clark, B, Brown, V, Sitza, J. Good practice in the conduct and reporting of survey research. International journal for Quality in Health Care 2003;15(3):261-6.

158. Bamgboye EA, Jarallah JS. Long-waiting outpatients: Target audience for health education. Patient Education and Counseling. 1994;23(4):49-54.

159. Ajayi IO. Patients' waiting time at an outpatient clinic in Nigeria—can it be put to better use? Patient Education and Counseling. 2002;47(2):121-6.

160. Caldwell MA, Miaskowski C. Mass media interventions to reduce help-seeking delay in people with symptoms of acute myocardial infarction: time for a new approach? Patient Education and Counseling. 2002;46(1):1-9.

161. Morrow DA, Antman EM, Charlesworth A, Cairns R, Murphy SA, De Lemos JA, et al. TIMI Risk Score for ST-Elevation Myocardial Infarction: A Convenient, Bedside, Clinical Score for Risk Assessment at Presentation. Circulation. 2000 October 24, 2000;102(17):2031-7.

162. Tang EW, Wong CK, Herbison P. Global Registry of Acute Coronary Events (GRACE) hospital discharge risk score accurately predicts long-term mortality post acute coronary syndrome. American Heart Journal. 2007;153(1):29-35.

163. Morrow DA, Antman EM, Giugliano RP, Cairns R, Charlesworth A, Murphy SA, et al. A simple risk index for rapid initial triage of patients with ST-elevation myocardial infarction: an InTIME II substudy. The Lancet. 2001;358(9293):1571-5.

164. De Lemos JA, Braunwald E. ST segment resolution as a tool for assessing the efficacy of reperfusion therapy. Journal of the American College of Cardiology. 2001;38(5):1283-94.

165. Kardesoglu E, Isilak, Z., Uz, O, Celik, T. Electro-cardiographic evaluation of

successful reperfusion: Time to revisit. Cardiology Journal. 2011;18(1):114-5.

166. Abdel-Salam A, Wafa, S, Kamel, S, Nammas, W. The modified Selvester QRS score: Can we predict succesful ST segment resolution in patients with myocardial infarction receiving fibrinolytic therapy? Cardiology Journal. 2010;17(4):367-73.

167. Wallis LA, Gottschalk, SB, Wood, D, Bruijns, S, de Vries, S, Balfour, C. The Cape Triage Score - a triage system for South Africa. South African Medical Journal. 2006;96(1):53-6.

168. Rosedale K, Smith, ZA, Davies, H, Wood, D. The effectiveness of the South African Triage Score (SATS) in a rural emergency department. South African Medical Journal. 2011;101(8):537-40.

169. Brieger D, Eagle, KA, Goodman, SG, Steg, PG, Budaj, A, White, K, Montalescot, G. Acute Coronary Syndromes Without Chest Pain, An Under-diagnosed and Under-treated High-Risk Group*: Insights From The Global Registry of Acute Coronary Events. Chest. 2004;126(2):461-9.

170. Postma S, Bergmeijer T, Ten Berg J, Van 't Hof A. Pre-hospital diagnosis, triage and treatment in patients with ST elevation myocardial infarction. Heart. November 1, 2012;98(22):1674-8.

171. Huber K, Caterina RD, Kristensen SD, Verheugt FWA, Montalescot G, Maestro LB, et al. Pre-hospital reperfusion therapy: a strategy to improve therapeutic outcome in patients with ST-elevation myocardial infarction. European Heart Journal. October 2005;26(19):2063-74.

172. Ranjith N, Verho NK, Verho M, Winkelmann BR. Acute Myocardial Infarction in a Young South African Indian-based Population: Patient Characteristics on Admission and Gender-specific Risk Factor Prevalence. Current Medical Research and Opinion. 2002;18(4):242-8.

173. Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, Cifkova R, et al. European guidelines on cardiovascular disease prevention in clinical practice: executive summary. European Heart Journal. 2007;28(19):2375-414.

174. Walker L, Birkhead JS, Weston C, Van Leeven R, Quinn T. Myocardial Ischaemia National Audit Project (MINAP); 2008.

175. Birkhead JS, Walker L, Pearson M, Weston C, Cunningham AD, Rickards AF. Improving care for patients with acute coronary syndromes: initial results from the National Audit of Myocardial Infarction Project (MINAP). Heart. 2004;90(9):1004-9.

176. Kalla K, Christ G, Karnik R, Malzer R, Norman G, Prachar H, et al. Implementation of Guidelines Improves the Standard of Care. Circulation. 2006;113(20):2398-405.

177. Saia F, Marrozzini C, Ortolani P, Palmerini T, Guastaroba P, Cortesi P, et al. Optimisation of therapeutic strategies for ST-segment elevation acute myocardial infarction: the impact of a territorial network on reperfusion therapy and mortality. Heart. 2009 March 1, 2009;95(5):370-6.

178. University of Cape Town. South African Medicines Formulary. 8th ed. Cape Town: Health and Medical Publishing Group of the South African Medical Association; 2008.