# **RISK FACTOR PROFILE OF FEMALE PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION:** A SOUTH AFRICAN PERSPECTIVE

Submitted by: Dr Jaqueline Cindy Govender

Supervised by: Professor Naresh Ranjith

Submitted as the Dissertation component in partial fulfillment (25%) for the degree of Masters of Medicine in the Department of Internal Medicine, School of Clinical Medicine, College of Health Sciences, University of KwaZulu-Natal, Durban.

Date of submission: _____

Supervisor's name:_____ Student's name: _____

Signature: _____ Signature:_____

Date: _____ Date: _____

# DECLARATION

I……..Dr Jaqueline Cindy Govender.....declare that

(i) The research reported in this dissertation, except where otherwise indicated, is my original work.

(ii) This dissertation has not been submitted for any degree or examination at any other university.

(iii) This dissertation does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.

(iv) This dissertation does not contain other persons' writing, unless specifically acknowledged as being sourced from other researchers. Where other written sources have been quoted, then:

a) their words have been re-written but the general information attributed to them has been referenced;

b) where their exact words have been used, their writing has been placed inside quotation marks, and referenced.

(v) Where I have reproduced a publication of which I am an author, co-author or editor, I have indicated in detail which part of the publication was actually written by myself alone and have fully referenced such publications.

(vi) This dissertation does not contain text, graphics or tables copied and pasted from the Internet, unless specifically acknowledged, and the source being detailed in the dissertation and in the References sections.

Signed:_____ Date:_____

# DEDICATION

This dissertation is dedicated to the following people:

1) All my teachers and mentors, the great minds that have helped shaped my future.
2) My parents who have been by my side through every step of my journey towards becoming a doctor and thereafter a specialist and continue to support me every step of the way as I continue on this journey.

# ACKNOWLEDGEMENTS

Thank you to the following individuals:

1) Professor N Ranjith for his supervision on this project
2) Dr Tarylee Reddy for her assistance with the statistical analysis of the data
3) Tonya Esterhuizen for her assistance in a sub-section of the statistical analysis
4) RK Khan hospital for allowing me to conduct the study at their facility
5) The Department of Health KwaZulu-Natal for granting me the permission to conduct this study

# OVERVIEW OF THE THESIS

The study was a retrospective single center study conducted at RK Khan hospital in Durban. The primary aim was to look at the incidence of acute myocardial infarction (AMI) in the female population in our setting with particular interest in the cardiovascular risk profile of female patients presenting with AMI. Data was extracted from a computerized database for the duration of the study period, which was from 2003 to 2016. Patient anonymity was maintained.

All adult female patients that presented to the study center during the study period, with a diagnosis of AMI, based on the European and American Society of Cardiology guidelines, were included in the study. Females with unstable angina were excluded. The cardiovascular disease (CVD) risk factor profile was based on the Framingham risk profile for CVD and included the following: diabetes mellitus (DM), hypertension (HPT), cigarette smoking, dyslipidemia, obesity, a previous history of coronary artery disease and positive family histories of DM, HPT and coronary artery disease. The study population was broadly categorized into 2 age groups, namely <65 years of age and ≥65 years. Both groups were analyzed identically in terms of their age, clinical presentation, CVD risk factors, initial electrocardiogram, medical therapies and whether or not they were referred for angiogram and/or coronary artery bypass surgery. We also divided the study population into those with ST elevation myocardial infarction (STEMI) versus Non ST elevation myocardial infarction. In the STEMI group we assessed the use of thrombolytic therapy or not. Finally we looked at the presence of major adverse cardiac events (MACE) in each of the age groups. MACE was defined as follows: Arrhythmias, cardiac failure, cardiogenic shock, complete heart block, recurrence of angina or myocardial infarction and death.

In addition to the primary study aim, by categorizing patients into 2 age groups we could determine if there was a difference in CVD risk factor profile and the presence of MACE between the younger and older age groups. Finally, by comparing the outcome of our study to studies done in male counterparts we were able to see if there was a difference in CVD risk profile between male and female patients, which in fact there was not. So basically in the presence of the traditional risk factors for coronary artery disease (CAD), males and females can be considered at equal risk of developing acute myocardial infarction and females are not protected by the cardio-protective effects of oestrogen hormone in the pre-menopausal age group as was previously thought. Females are an understudied population when it comes to coronary artery disease and very few studies have been conducted on females with cardiac disease. We believe that this study offers some very valuable information with regards to cardiac disease in females and that treatment strategies should be targeted to include optimizing risk factor control in at-risk females, so that the burden of disease can be reduced in this population.

# TABLE OF CONTENTS

# LIST OF TABLES/GRAPHS:

# PART ONE

## THE LITERATURE REVIEW

# PART 1: THE REVIEW OF THE LITERATURE

Coronary artery disease is one of the leading causes of death and disability worldwide.[1,2,3] Likewise in South Africa it has become a major cause of morbidity and mortality across all ethnic groups.[12,15] Although coronary artery disease was previously thought to be a disease predominantly affecting males, it is now understood that females with underlying cardiovascular risk factors are equally at risk of developing coronary artery disease and specifically manifesting as acute myocardial infarction.[2,16] The traditional and well-studied risk factors for coronary artery disease in males, namely diabetes mellitus, hypertension, dyslipidemia, obesity, cigarette smoking and a family history of coronary artery disease, appear to play the same role in female counterparts.[17] Due to the cardio-protective effects of oestrogen, coronary artery disease in females generally occurs at an older age than when compared to males.[2,3] Multiple studies have shown that women tend to present with coronary artery disease on average 6-10 years later than their male counterparts.[2,5] Studies have also found that the average age of presentation in females in developing countries tends to be lower than that of westernized countries.[17,18] However, although the disease was thought to predominantly affect post-menopausal females, younger females can also develop coronary artery disease in the presence of significant cardiovascular risk factors. In particular diabetes mellitus has been found to be an independent predictor of acute coronary syndrome in younger women, increasing their risk by 4 to 5 fold.[1] Furthermore smoking is an independent predictor of acute coronary syndrome in women less than 40 years of age.[31] Although, even the presence of a single risk factor can predispose females to

the development of coronary artery disease, in particular acute myocardial infarction, like with males, the presence of multiple cardiovascular risk factors increases that risk significantly.[2]

Several studies have shown that females tend to have a higher risk of developing complications following acute myocardial infarction and have higher mortality rates compared to men.[3,5,19,21,22,24,25]

Cardiovascular disease in females is understudied and there is limited data on the disease in females. According to a 2013 update on coronary artery disease in women,[3] it was stated that coronary artery disease is the leading cause of mortality in females and requires further sex-specific research on the disease.

Whilst some risk factors like age, sex, genetic factors and family history, are non-modifiable, it is the modifiable risk factors (diabetes mellitus, hypertension, obesity, dyslipidemia and cigarette smoking) that will impact on future outcomes in these patients. Risk factor control is imperative and should be the focus of primary health care initiatives in reducing the risk of developing cardiovascular disease in females.

# PART TWO

## THE MANUSCRIPT

# INTRODUCTION

Coronary artery disease [CAD] is a major cause of morbidity and mortality worldwide, and although previously reported to be more common in men, is now identified as a leading cause of death and disability in women in the United States.[1,2,3] Significant differences occur between men and women with respect to the epidemiology, diagnosis, treatment, and prognosis of CAD. This may explain the under-representation of women in many studies on CAD in the past, often leading to misdiagnosis and inappropriate treatment.[1,5] These factors include that women are less likely than men to have typical angina, though the similarities in how men and women present with acute myocardial infarction [AMI] are greater than their differences, and women may not identify their initial symptoms and therefore may not seek prompt medical advice. [4,5] In addition, there is an under-evaluation of both typical and atypical symptoms of ischemia in women by clinicians because of gender bias.[6]

Generally women with myocardial infarction are about 10 years older than men at the time of presentation and carry a greater burden of risk factors.[1,2,3] In contrast, while myocardial infarction is an uncommon entity in young people, the incidence is higher in men less than 45 years of age because women of a similar age group are at lower risk due to of the protective influence of circulating oestrogens on the vascular endothelium.[2] These differences should be taken into account in the care of women with CAD.

Despite the growing evidence on CAD in women from developed countries, there is a paucity of data on the prevalence and mortality outcome of CAD in women from developing countries like South Africa. This study, therefore, was undertaken to

determine the incidence of AMI in women in a regional hospital in Durban, South Africa, with particular reference to risk profiles and major adverse cardiac events [MACE].

# METHODS

This was a single-center retrospective study conducted at the Coronary Care Unit (CCU) at RK Khan Hospital (RKKH) in Chatsworth, Durban, over a 13-year period (2003-2016).

Consecutive female patients with a confirmed diagnosis of acute MI were included in the study while those with unstable angina were excluded. Acute MI was defined on admission based on a characteristic history of chest pain/ discomfort, electrocardiograph (ECG) changes consistent with acute ST or Non ST elevation MI (NSTEMI) and elevated cardiac biomarkers, specifically Troponin T levels, as outlined by the Joint European Society of Cardiology/ American College of Cardiology committee.[7]

Ethics approval was obtained from the local ethics committee at the University of Kwazulu-Natal prior to commencement of the study, and carried out according to the principles of the Declaration of Helsinki. Patient anonymity was maintained at all times.

## Clinical assessment:

Demographic and clinical data stored in an electronic database were obtained from all patients, including the presence of risk factors such as diabetes mellitus (DM), hypertension(HPT), dyslipidemia, smoking, previous angina or MI and a family history of vascular disease. Premature atherosclerosis was defined by a history of myocardial infarction in either parents, or in siblings or first degree relatives at the age of 55 years or younger for males and 65 years or younger for females, whilst a

family history of diabetes, hypertension, and cerebrovascular disease was defined as these conditions occurring at any age.[8]

Current smokers were defined as individuals who had smoked any tobacco within the past 12 months leading up to their MI, and former smokers as those who had not smoked for at least one year prior to their MI.

Anthropometric measurements including body mass index [BMI] and waist circumference were used to define obesity. The BMI was calculated as weight [kilograms] divided by height$^2$ [meters] according to World Health Organisation (WHO) guidelines.[9] A BMI ≥ 30 kg/m2 was used as a cut-off to indicate obesity. Waist circumference was measured midway between the lowest rib and the iliac crest on standing subjects, using a soft tape, and the central obesity threshold limits proposed by the International Diabetes Federation [IDF] [females ≥ 80 cm] were used to define visceral obesity.[10]

Patients with ST elevation MI (STEMI) who were eligible for thrombolysis received Metalyse (Tenecteplase) as a reperfusion therapy. Because coronary revascularization procedures such as percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG), are performed at only 1 tertiary public hospital in Kwa-Zulu Natal, only patients who consented for both coronary angiography and revascularization were referred, due to limited resources. Many patients declined intervention and were therefore treated medically.

The occurrence of MACE was recorded during hospital admission and 6 months post-discharge. This included the first occurrence of any of the following; cardiac failure,

cardiogenic shock, complete heart block, atrial or ventricular arrhythmias, recurrence of angina or MI, and death.

## Biochemical analysis:

Routine biochemistry was performed on admission using standardized techniques. Troponin T measured on the Elecsys 2010 (Roche Diagnostics), was considered positive at a cut-off value greater than 0.03ng/ml. Fasting lipograms were performed after an overnight fast. Low-density lipoprotein (LDL) cholesterol levels were calculated utilising the formula of Friedewald.[33] The cut-points used to stratify patients were based on the updated South African Guidelines.[11,12,13] Levels were considered abnormal if total cholesterol was > 4.5 mmol/L, LDL cholesterol >2.5 mmol/L, triglycerides ≥ 1.7 mmol/L, and high-density lipoprotein (HDL) cholesterol < 1.29 mmol/L in females.

# RESULTS

A total of 1311 females were screened of whom 1160 patients fulfilled the inclusion and exclusion criteria and were available for analyses. Of the 1160 females with AMI, the majority of participants were of Asian Indian origin [92.2%], Black African [4.4%], White [2.6%] and Coloured [0.9%] [Table 1]. The mean (SD) age of the study population was 61.6 ± 10.7 years and were stratified into 2 age groups; < than 65 years [n= 666 (57.4%)] and ≥ 65 years [n= 494 (42.6%)].

The commonest risk factors in this study group included dyslipidaemia [97.4%], hypertension [77%], diabetes[75.6%] and obesity [29.3%], while 59% of patients had a family history of premature atherosclerosis, diabetes [51.5%] and hypertension [46.6%]. When adjusted for age, a statistically greater number of patients < 65 years of age had dyslipidaemia [n=645, p-value=0.038], obesity [n=237, p-value<0.001], a history of smoking [n=196, p-value<0.001], and family histories of premature atherosclerosis [n=423, p-value<0.001], hypertension [n=341, p-value<0.001] and diabetes [n=376, p-value<0.001]. In contrast, patients ≥ 65 years were significantly more likely to present with hypertension[n=408, p-value<0.001] and a previous history of myocardial infarction and angina [n=75, p-value= 0.004 and n=94, p-value= 0.03, respectively] (Table 1).

Major adverse cardiac events were observed in 466 [40.2%] of patients with older patients having a significantly higher prevalence of events [46.8%] compared to their younger counterparts [35.3%, ] Most patients presented with ST elevation MI [74%] of whom only 28% received pharmacological reperfusion with Tenecteplase according to standard guidelines. Patients in general received optimal medical

treatment which included statins, dual anti-platelet, b-blockers and RAS (renin angiotensio system) blockers.

Table 1 illustrates the distribution of MACE seen in the study population, cardiac failure was the adverse event found most commonly [54.4%] followed by death [28.1%], recurrence of infarction[16.5%], cardiogenic shock [15%], recurrence of angina [12.5%], while atrial arrhythmias [ 10.7%], ventricular arrhythmias [8.2%] and cerebrovascular events [6.2%] were detected less commonly.

Figure 2 shows the angiographic characteristics of patients that underwent coronary angiography at another referral hospital. Only 337 patients [29%] were subjected to angiographic studies because most patients either declined coronary revascularization, presented too late for percutaneous coronary intervention (PCI) or because of other significant co-morbidities. The majority of patients were found to have triple vessel disease [TVD 48.7%], 22.6 % each had double vessel disease [DVD] and single vessel disease [SVD 22.6%] and 6.2% had normal coronary epicardial vessels. Of those that were subjected to coronary angiography, 50% (n=169) underwent CABG. Of the total study population only 14.6% (n=169) underwent CABG compared to 4.7% (n=55) that received PCI+/-Stent. A majority of those that underwent CABG belonged to the younger (<65year ) age group (n=121) (Table 1).

Following multivariable analysis using logistic regression, our data showed that a few clinical and laboratory parameters were significantly associated with MACE such as hyperglycaemia [p=0.006], hyperuricaemia [p= 0.001] and hypertriglyceridaemia [p= 0.014] [Table 2].

# DISCUSSION

Multiple studies have indicated that females are understudied and undertreated with regards to CAD[1,5] because CAD has always been noted to be one of the leading causes of death and disability in males worldwide. This study shows that CAD is also prevalent in the female population, who also have an increased likelihood of developing MACE post AMI (40% of the total study population).

In this study we looked at the risk factor profile of female patients presenting with AMI, and what we found was that in the presence of the traditional risk factors (diabetes mellitus, hypertension, dyslipidemia, obesity, cigarette smoking and a family history of coronary artery disease) for AMI, female patients were, like their male counterparts, predisposed to developing AMI.[2] The Framingham study[17] has shown that the traditional risk factors for CAD in males, is applicable in females as well, and our study confirms that in the presence of these risk factors, females are at similar risk of developing CAD and more importantly, that they can present at an earlier age than previously thought.[1,17] There were a total of 3698 patients (males and females) admitted to the Coronary Care Unit at RKKH during the study period and females with a diagnosis of AMI comprised 32% (n=1160) of that population. The commonest risk factors for AMI in our study were HPT, DM, Obesity (BMI), and family histories of CAD, DM and HPT. Although these risk factors were prevalent across both age groups of the study population, our study emphasized the fact that age is not a protective factor for females developing AMI, as was previously thought in other studies.[1] We had a greater proportion of our patients in the younger (<65years) age group (57% vs 43%). Furthermore the prevalence of DM, obesity (BMI),

dyslipidemia, smoking and family histories of DM, HPT and CAD were higher in the younger population which emphasizes the fact that these traditional risk factors play a big role in increasing the risk of the development of AMI irrespective of age or gender.

Previous studies have shown that women tend to present with coronary artery disease on average 6-10 years later (around 69-70 years of age) than their male counterparts[2] and this was believed to be in part due to the cardio-protective role of oestrogen.[2] In contrast, the majority of patients in our study presented in the younger age group and this concurs with previous reports which showed that the average age of presentation in females in developing countries tends to be lower than that of westernized countries (62 years versus 69-70 years in western countries).[2,3,23]

Very few studies have been undertaken in the South African setting and the majority of information that we have on CAD in our female population has been obtained from other parts of Africa, with the Interheart study providing some valuable information.[16] One study on CVD in Africa showed that females had a higher prevalence of hypertension, obesity and hyperlipidemia compared to men, with Hypertension being the major risk factor for females.[18] Other studies have shown that the major risk factors for females with CAD are diabetes mellitus and hypertension +/- dyslipidemia.[19,20] These studies however did not compare females of different age groups. Both DM and HPT were prevalent in both age groups in our study, with total values for DM and HPT being 76% and 77% respectively. Furthermore, for DM, the percentages where similar in each age group, with 76% in the <65 year age group and 75% in the ≥ 65 age group (Table1). The large proportion of patients with family

history of vascular disease in our study re-emphasizes the significance of heritable disease in contributing to the risk of CAD.

Furthermore, besides the traditional risk factors (mentioned above) for AMI, we found in our study that hyperglycemia, hypertriglyceridemia and hyperuricemia were independent risk factors for the development of CAD and also negatively contributed to the development of MACE. Hyperuricemia is the end product of purine metabolism and its role as an independent risk factor in cardiovascular disease is still being debated.[34] Several patho-physiological mechanisms on how hyperuricemia contributes as a risk factor for CAD have been postulated including endothelial dysfunction, oxidative metabolism, and platelet adhesiveness and aggregation.

Several studies have shown that females have poorer outcomes following acute myocardial infarction and have higher mortality rates compared to men.[1,3] In our study we found a large proportion of our patients to have developed MACE (n=466, 40%). This was greater than in any of the studies we had reviewed. The commonest adverse events in our study were cardiac failure (55%, n= 255) followed by death (28%, n=131) and this was similar to adverse events in other studies.[23,25] The reasons for poorer outcomes are not well understood but are possibly linked to an array of events, including delayed presentation to hospital, refusal of medical therapies and invasive interventions, as well as the pathophysiological factors such as smaller coronary vessels in females with fewer collaterals. One possibility is that the prevalence of DM is so high in our study population and the cardiovascular disease risk is increased in the presence of diabetes mellitus. Cardiac failure, cardiogenic

shock and death had a slightly higher rate in the older females, whereas recurrence of angina seemed to occur more in the younger population.

Although most studies reported on males and females found that STEMI was less common in females[26] in our study 74% of subjects had STEMI (n=858). In addition, only a small proportion of those with STEMI went on to receive thrombolysis with Metalyse (n=325, 38%). This is in keeping with other studies were only a small proportion of females received thrombolysis.[24,25]

The reasons for this may be multifactorial and could include delayed presentation to hospital, prolonged door to needle times for various reasons, or patients declining therapy. These are some of the reasons that have been found particularly amongst females in international studies[1,5].

A small proportion of our patients were up-referred for invasive intervention in the form of angiogram (n=337, 29%). The reasons for this again could most likely be patients declining further intervention and this would be in keeping with international studies[5].

Of the patients that did agree to Angiogram a majority were found to have triple vessel disease (48.7%) indicating the severity of the disease in this population and the importance of early screening for the disease (Graph 2). Of the patients that underwent Coronary angiogram, 50% underwent CABG.

# LIMITATIONS

A few potential limitations merit consideration. Firstly, this was a single center study of a predominantly Asian Indian population and a racial selection bias may exist because of this. This is important because we could not adequately compare race groups to determine if risk factors for AMI in females differ in different racial groups. Secondly, we had no available data on which of our patients belonged to the pre and post-menopausal age groups and as such were unable to accurately provide results that may have made a confounding difference in view of the believed cardio-protective role of oestrogen in premenopausal women. Thirdly, we had no information on which, if any our patients were receiving Hormone replacement therapy at the time of presentation with their acute MI, and given the assumed protective effects of female hormones on the endothelium, we cannot conclude on this further. Finally, although a majority of our patients had STEMI (n=858) only a small proportion received thrombolysis with Metalyse (n=325), due to late presentation or because of other contraindications to lytic therapy. Similarly, only 29% of patients were subjected to coronary angiographic studies, which are performed at another tertiary center (only one such center is capable of performing these procedures in the public domain in the province of Kwa-Zulu Natal), and therefore results for these smaller sub-groups should be interpreted with caution.

# CONCLUSION

There were 2 major outcomes from our study. Firstly, we found that younger females presented with AMI in the presence of traditional risk factors for CAD. Females in our study comprised 32% of the total population of acute MI admitted to the study center, and of that >50% of patients were younger than the age of 65years. This is younger than the average age of presentation of females with AMI in other studies[2,3,5] and raises the question as to whether female hormones are cardio-protective in the presence of traditional risk factors for CAD. We also found that younger females tend to have multiple risk factors, of which a large proportion had diabetes mellitus and/or hypertension and dyslipidemia. There were also strong positive family histories for DM, HPT and CAD. This emphasizes the fact that heritable conditions contribute significantly to the risk of developing AMI, and is in keeping with other studies.

The second biggest outcome of our study was the large proportion of patients that developed MACE with 466 subjects (40%) having developed some form of MACE, with over a half of this being cardiac failure (54,7%) and over a quarter being death (28%) we and believe that this is quite significant and proves that females are at an increased risk of developing MACE post MI.[1,3,19]

According to a 2013 update on coronary artery disease in women,[5] it was stated that coronary artery disease is the leading cause of mortality in females and requires further sex-specific research on the disease. As such we need to be more vigilant in our screening and treatment of the female population presenting with risk factors that predispose them to CAD.

# TABLE 1: **Baseline characteristics according to age**

| | TOTAL | <65 years | ≥65 years | | P-value |
|---|---|---|---|---|---|
| | n=1160 (100%)* | n=666 (57.4%) | n=494 (42.6%) | | |
| **RACE :** Asian | 1069(92.2%) | 595 (55.7%) | 474 (44.3%) | | |
| Black | 51 (4.4%) | 41(80.4%) | 10(19.6%) | | |
| Coloured | 10 (0.9%) | 9(90%) | 1(10%) | | |
| White | 30 (2.6%) | 21(70%) | 9(30%) | | |
| | | | | | |
| **RISK FACTORS:** Diabetes Mellitus | 877(75.6%) | 507 (76.1%) | 370 (74.9%) | | 0.63 |
| Hypertension | 897 (77%) | 489 (73.4%) | 408 (82.6%) | | **<0.001** |
| Dylipidemia | 1130 (97.4%) | 645 (98.9%) | 465 (97.3%) | | 0.038 |
| Obesity (BMI) | 340 (29.3%) | 237 (35.6%) | 103 (20.9%) | | **<0.001** |
| Smoking | 243 (21%) | 196 (29.4%) | 47 (9.5%) | | **<0.001** |
| Previous Myocardial infarction | 139 (12%) | 64 (9.6%) | 75 (15.2%) | | **0.004** |
| Previous Angina | 189 (16.3%) | 95 (14.3%) | 94 (19%) | | **0.03** |
| | | | | | |
| **FAMILY HISTORY:** Coronary artery disease | 683 (59%) | 423 (63.5%) | 260 (52.6%) | | **<0.001** |
| Cerebrovascular disease | 229 (19.7%) | 145 (21.8%) | 84 (17%) | | 0.044 |
| Hypertension | 540 (46.6%) | 341 (51.2%) | 199 (40.3%) | | **<0.001** |
| Diabetes Mellitus | 597 (51.5%) | 376 (56.5%) | 221 (44.7%) | | **<0.001** |
| | | | | | |
| **MEDICATION AT DISCHARGE:** Nitrates | 1145(98.7%) | 659 (98.9%) | 486 (98.3%) | | 0.397 |
| Disprin | 1154(99.5%) | 664 (99.7%) | 490 (99.2%) | | 0.232 |
| Statins | 1097(94.6%) | 640 (96.1%) | 457 (92.5%) | | 0.008 |
| ACE-I/ARB'S | 964 (83.1%) | 556 (83.5%) | 408 (82.6%) | | 0.688 |
| Beta-Blockers | 753 (64.9%) | 455 (68.3%) | 298 (60.3%) | | 0.005 |
| Calcium channel blockers | 110 (9.5%) | 68 (10.2%) | 42 (8.5%) | | 0.326 |
| | | | | | |
| **MACE** | 466 (40.2%) | 235 (35.3%) | 231 (46.8%) | | **<0.001** |
| **STEMI** | 858 (74%) | 505 (75.8%) | 353 (71.5%) | | 0.094 |
| **NSTEMI** | 300 (25.9%) | 160 (24%) | 140 (28.3%) | | 0.097 |
| **Metalyse** | 325 (28%) | 207 (31.1%) | 118 (23.9%) | | **0.007** |
| **Coronary Angiogram** | 337 (29.1%) | | | | |
| **PCI +/- STENT** | 55 (16.3%) | 45 (13.4%) | 10 (3%) | | **<0.001** |
| **CABG** | 169 (50.1%) | 121 (35.9%) | 48 (14.2%) | | **<0.001** |
| **CONTINUOUS VARIABLES** | **TOTAL** | **<65years** | **≥65years** | **Mean ±SD** | **P-Value** |
| | n=1160 | n=666 (57.4%) | n=494 (42.6%) | | |
| Systolic BP(mmHg) | 1160 | 135.4 (29.2) | 137.6 (29.8) | 136.4± 29,5 | 0.22 |
| Diastolic BP(mmHg) | 1160 | 81.1 (17.9) | 77.0 (16.6) | 79.4 ± 17.6 | **0.0001** |
| Abdominal Girth(cm) | 905 (78.0%) | 100.6 (13.2) | 98.5 (12.7) | 99.8 ± 13.0 | 0.0182 |
| | | | | | |
| **BIOCHEMICAL DATA** | | | | | |
| Total Cholesterol (mmol/L) | 846 (72.9%) | 5.6 (1.4) | 5.3 (1.3) | 4.8 + 0,2 | 0.100 |
| LDL cholesterol (mmol/L) | 1083 (93.4%) | 3.5 (1.2) | 3.4 (1.1) | 2,6 ± 0,1 | 0.3314 |
| HDL cholesterol (mmol/L) | 1113 (95.9%) | 1.1 (0.5) | 1.1 (0.4) | 1.1 + 0.06 | 0.1655 |
| Trigylcerides (mmol/L) | 1126 (97.1%) | 2.3 (1.7) | 1.7 (0.9) | 2.4 + 0.1 | **<0.001** |
| Haemoglobin (g/dL) | 1155 (99.6%) | 12.4 (1.9) | 11.8 (1.9) | 10.9 + 0.6 | **<0.001** |
| Creatinine (mmol/L) | 1156 (99.7%) | 93.9 (58.5) | 111.9 (76.0) | 101.6 ± 67.2 | **<0.001** |
| Uric Acid (mmol/L) | 1083 (93.4%) | 0.4 (0.1) | 0.4 (0.1) | 0.4+ 0.02 | **0.0001** |

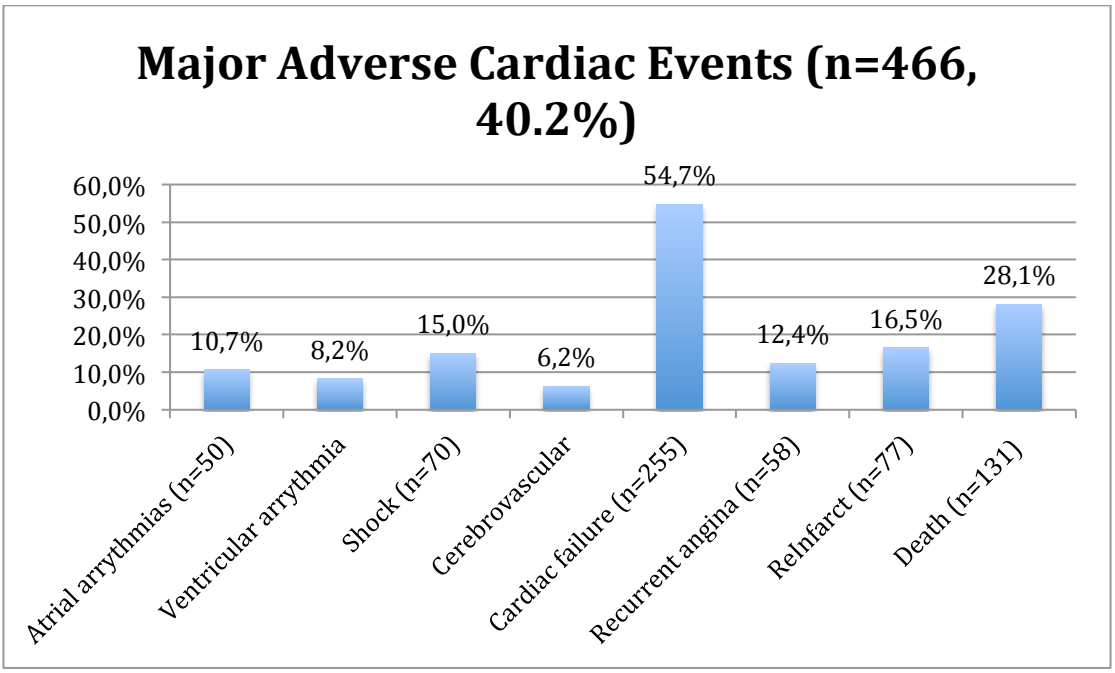
- 1160 patients is our study population, however it made up 88.5% of the total number of females presenting to the study centre with chest pain. The 1160 patients are those with a diagnosis of AMI.
- Significant p-values have been marked in bold.

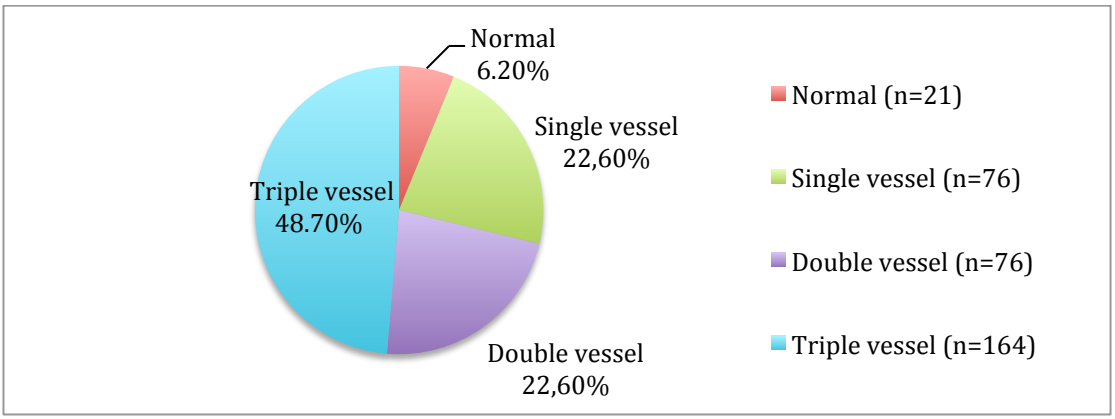
BMI: Body mass index
ACE-I/ARB'S: Angiotensin converting enzyme inhibitor/Angiotensin receptor blockers
MACE: Major adverse cardiac events
STEMI: ST elevation myocardial infarction
NSTEMI: Non ST elevation myocardial infarction
PCI: Percutaneous coronary angriography
CABG: Coronary artery bypass graft

TABLE 2: **Logistic Regression Analysis: Predictors of Mace**

| CHARACTERISTICS | ODDS RATIO (95% CI) | STD ERROR | P-VALUE |
|---|---|---|---|
| Age >=65 | 1.25 (0.91-1.70) | 0.20 | 0.162 |
| Dyslipidemia | 0.87 (0.27-2.82) | 0.52 | 0.817 |
| Central obesity | 1.53 (0.65-3.61) | 0.67 | 0.333 |
| Diabetes | 1.43 (0.95-2.17) | 0.30 | 0.089 |
| Hypertension | 0.93 (0.64-1.35) | 0.18 | 0.698 |
| Smoking | 0.77 (0.52-1.14) | 0.15 | 0.190 |
| Family Hx CAD | 0.77 (0.57-1.03) | 0.12 | 0.082 |
| STEMI | 1.09 (0.78-1.53) | 0.19 | 0.597 |
| Elevated Urea (mmol/l) | 1.05 (0.99-1.11) | 0.31 | 0.112 |
| Elevated Creatinine (mmol/l) | 1.00 (0.99-1.00) | 0.00 | 0.201 |
| Hyperglycaemia (mmol/l) | 1.04 (1.01-1.07) | 0.01 | 0.006 |
| Hypertriglyceridemia (mmol/l) | 0.86 (0.76-0.97) | 0.05 | 0.014 |
| Hyperuricemia (mmol/l) | 11.52 (2.81-47.20) | 8.29 | 0.001 |

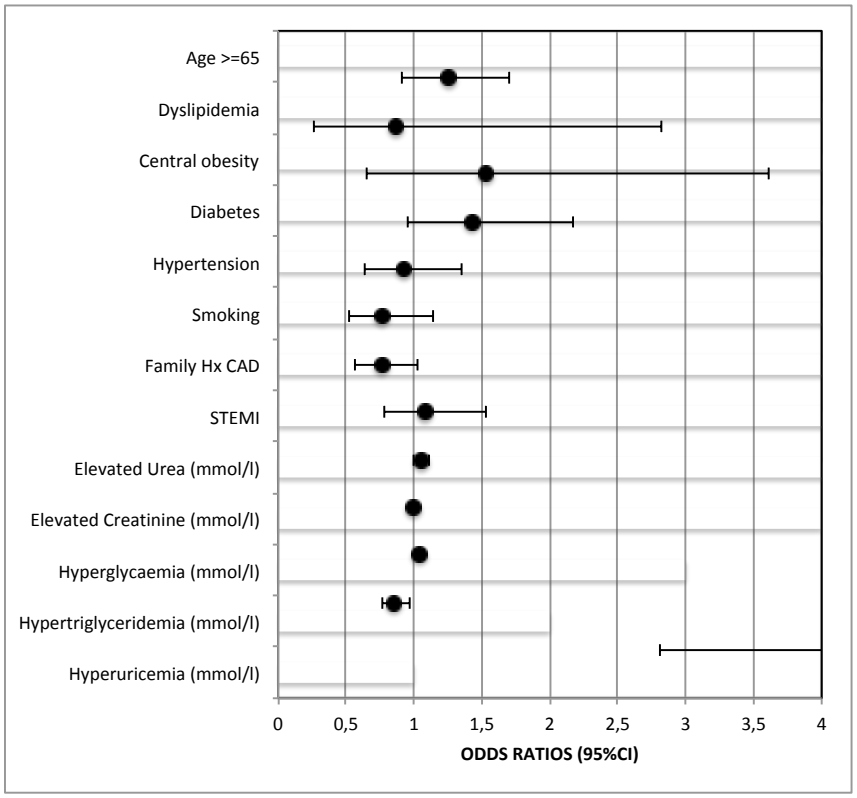
GRAPH 1


Major Adverse Cardiac Events (n=466, 40.2%)
60,0%
50,0%
40,0%
30,0%
20,0%
10,0%
0,0%
10,7%
8,2%
15,0%
6,2%
54,7%
12,4%
16,5%
28,1%
Atrial arrythmias (n=50)
Ventricular arrythmia
Shock (n=70)
Cerebrovascular
Cardiac failure (n=255)
Recurrent angina (n=58)
ReInfarct (n=77)
Death (n=131)




GRAPH 2: **Angiographic characteristics of the study population** (n=337, 29.1% of the total study population only)

GRAPH 3: **Forest Plot: Odds Ratio**




| | OR (95%CI) | P-VALUE |
|---|---|---|
| Age >=65 | 1.25 (0.91-1.70) | 0.162 |
| Dyslipidemia | 0.87 (0.27-2.82) | 0.817 |
| Central obesity | 1.53 (0.65-3.61) | 0.333 |
| Diabetes | 1.43 (0.95-2.17) | 0.089 |
| Hypertension | 0.93 (0.64-1.35) | 0.698 |
| Smoking | 0.77 (0.52-1.14) | 0.190 |
| Family Hx CAD | 0.77 (0.57-1.03) | 0.082 |
| STEMI | 1.09 (0.78-1.53) | 0.597 |
| Elevated Urea (mmol/l) | 1.05 (0.99-1.11) | 0.112 |
| Elevated Creatinine (mmol/l) | 1.00 (1.00-1.00) | 0.201 |
| Hyperglycaemia (mmol/l) | 1.04 (1.01-1.07) | 0.006 |
| Hypertriglyceridemia (mmol/l) | 0.86 (0.76-0.97) | 0.014 |
| Hyperuricemia (mmol/l) | 11.52 (2.81-47.20) | 0.001 |

# REFERENCES


1) Mehta LS, Beckie TM, DeVon HA, et al. Acute Myocardial Infarction in Women: A Scientific Statement from the American Heart Association. American Heart Association Circulation 2016;133(9):916-47.

2) Anand SS, Islam S, Rosengren A, et al. Risk Factors for myocardial infarction in women and men: Insights from the INTERHEART study. European Heart Journal 2008;29(7):932-40.

3) Sharma K, Gulati M. Coronary Artery Disease in Women: A 2013 Update. Global heart Journal 2013;8(2):105-112.

4) Gimenez MR, Reiter M, Twerenbold R, et al. Sex-specific Chest Pain Characteristics in the Early Diagnosis of Acute Myocardial Infarction. JAMA Intern Med 2014;174(2):241-49.

5) Loboz-Grudzien-K, Jaroch J. Women with Acute Coronary syndromes have a worse prognosis-Why? The Need to reduce 'Treatment-seeking delay'. Cardiology Journal 2011;18(3):219-21.

6) Stangl V, Witzel V, Baumann G, et al. Current diagnostic concepts to detect coronary artery disease in women. European Heart Journal 2008;29(6):707-17.

7) Alpert JS, Thygesen K, Antman E, et al. Myocardial infarction redefined--a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. Journal of the American College of Cardiology 2000;36(3):959-69.

8) De Sutter J, De Bacquer D, Kotseva K, et al. Screening of family members of patients with premature coronary heart disease: Results from the EUROASPIRE II family survey. European Heart Journal 2003;24(3):249–57.

9) World Health Organisation (1998) Obesity: Preventing and managing the global epidemic. Report of a WHO Consultation on Obesity, Geneva,3-5 June, 1997.

10) International Diabetes Federation. The IDF Consensus Worldwide Definition of the Metabolic Syndrome. April 14, 2005.

11) Van Schoor J. South African Cholesterol guidelines compared. SA Pharmaceutical Journal 2010;77(9):46-53.

12) Ranjith N, Pegoraro RJ, Zaahl MG. Risk Factors Associated with Acute Coronary Syndromes in South African Asian Indian Patients (The AIR Study). Journal of Clinical and Experimental Cardiology 2011;2(10):163.

13) The Society for Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee. Chapter 3: Screening and diagnosis of type 2 diabetes and intermediate hyperglycemia in 2017 SEMDSA Guideline for the Management of Type 2 Diabetes Guideline Committee. JEMDSA 2017; 21(1): S1-S196.

14) Seedat YK, Rayner BL, Veriava Y. South African hypertension practice guideline 2014. Cardiovascular Journal of Africa 2014;25(6):288-94.

15) Chetty R, Ross A. Chart review of acute myocardial infraction at a district hospital in KwaZulu-Natal, South Africa. African Journal of Primary Health Care & Family Medicine 2016;8(1):1-5.

16) Steyn K, Sliwa K, Hawkin S et al. Risk factors Associated with Myocardial Infarction in Africa: The INTERHEART Africa study. American Heart Association Journal 2005;112(23):3554-61.

17) D'Agostino RB, Vasan RS, Pencina MJ, et al. General Cardiovascular Risk Factor Profile For Use in Primary Care, The Framingham heart study. American Heart Association Journal 2008;117(6):743-53.

18) Keates AK, Mocumbi AO, Ntsekhe M, et al. Cardiovascular disease in Africa: epidemiological profile and challenges. Nature Reviews.Cardiology 2017;14(5):273-93.

19) Hochman JS, Tamis JE, Thompson TD, et al. Sex, Clinical Presentation , And Outcome in Patients with Acute Coronary Syndromes. The New England Journal of Medicine 1999;341(4):226-32.

20) Gonzalez-Pacheco H, Vargas-Barron J, Vallejo M, et al. Prevalence of conventional risk factors and lipid profile in patients with acute coronary syndrome and significant coronary disease. Therapeutics and Clinical Risk Management 2014;10:815-23.

21) Alonso J, Bueno H, Bardaji A, et al. Influence of Sex on Acute coronary syndrome mortality and Treatment in Spain. Rev Esp Cardiol 2008;8(Supl D):8-22.

22) Cabrerizo-Garcia JL, Perez-Calvo JI, Zalba-Etayo B. Influence of Gender on prognosis of Coronary syndromes. Portuguese Journal of Cardiology 2015;34(1):43-50.

23) Sahni M, Kumar R, Thakur S, et al. Clinical Profile, Risk Factors and Short Term Outcome of Acute Myocardial Infarction in Females: A Hospital Based Study. Heart India journal 2013;1(3);73-7.

24) Barakat K, Wilkinson P, Suliman A, et al. Acute myocardial infraction in women: Contribution of treatment variables to adverse outcome. American Heart Journal 2000; 140 (5): 740-46.

25) Pimenta L, Bassan R, Potsch A, et al. Is Female Sex an Independent Predictor of In-Hospital Mortality in Acute Myocardial Infarction? Arq Bras Cardiol 2001;77(1):44-50.

26) Elsaesser A, Hamm CW. Acute Coronary Syndrome: The Risk of Being Female. American Heart Association Journal 2004;109(5):565-67.

27) Ngoungou EB, Aboyans V, Kouna P, et al. Prevalence of cardiovascular disease in Gabon: A population study. Archives of Cardiovascular Disease 2012; 105(2):77-83.

28) Rahman A, Naher N. A Study on Myocardial Infarction in Female-Risk Factor Anaylsis. International Journal of Scientific and Engineering Research 2016;7(8):2051-57.

29) Masina SC, Ranjith N, Sartorius B. Risk factor assessment in South African Black Patients presenting with Acute Myocardial infarction at RK Khan Hospital, Durban. SA Heart Journal 2016;13(1):12-18.

30) Nanjappa V, Aniyathodiyil G, Keshava R. Clinical profile and 30-day outcome of women with acute coronary syndrome as a first manifestation of Ischemic heart disease: A Single center observational study. India heart Journal 2016;68(2):164-68.

31) Dominguez-Rodriguez A, Arroyo-Ucar E, Abreu-Gonzalez P. Smoking and the risk of acute coronary syndrome in young women treated in an emergency department. World Journal of Cardiovascular diseases 2013;3(4A):9-12.

32) Hochman JS, McCabe CH, Stone PH, et al. Outcome and Clinical Profile of Women and Men presenting with Acute Coronary Syndromes: A report from TIMI IIIB. Journal of American College of Cardiology 1997;30(1):141-8.

33) Klug EQ, Raal FJ, Marais AD, et al. South African Dyslipidemia Guideline

Consensus Statement. South African Family Practice 2015;57(2):22-31.

34) Maruhashi T, Hisatome I, Kihara Y, et al. Hyperuricemia and endothelial function: From molecular background to clinical perspectives. Atherosclerosis Journal 2018;278:226-31.

# Appendix 1: The final study protocol as approved by BREC

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

**PROTOCOL NUMBER:**

.....
*For office use only*

**RESEARCH OFFICE CONTACT DETAILS:** Biomedical Research Ethics Administration, Westville Campus, Govan Mbeki Building, Private Bag X 54001, Durban, 4000, KwaZulu-Natal, South Africa; Tel: +27 31 2602486; Email: BREC@ukzn.ac.za ; Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

## SECTION A:

**APPLICANT/PRINCIPAL INVESTIGATOR:** ** For UKZN statistical reporting purposes*

| Title: | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Mr | | Ms | | Mrs | | Dr | ✔ | Prof | | *(Select option)* |

Name : JAQUELINE CINDY GOVENDER

*Gender: FEMALE

*Race: INDIAN

UKZN College: NELSON R MANDELA SCHOOL OF MEDICINE

| | | | |
|---|---|---|---|
| UKZN School/Discipline: | HEALTH SCIENCES | NA | |
| Hospital/Institution where employed: | RK KHAN HOSPITAL | NA | |

Professional status: DOCTOR- SPECIALIST PHYSICIAN

Postal address: P.O.BOX 31347, MEREBANK, 4059, DURBAN

Contact phone Numbers: 031 4596000
Office:

Mobile number:
082 302 5888

Fax number: NONE

Email address: cindygov@hotmail.com

Full/Part time Employment: FULL TIME

Current HPCSA Number (or equivalent): MP 0666734
*if registration is pending, submit proof of application

| Purpose of research: If postgraduate degree *(Please tick)* | Hons | MMedSc | MMed | MSc | MFamMed | MHIV | PhD |
|---|---|---|---|---|---|---|---|
| | | | ✔ | | | | |

Other degree not listed above: N/A

Student Number and year of study: (*if applicable)* 211560810

| | | | |
|---|---|---|---|
| If for postgraduate degree, please confirm whether the application has been reviewed and approved by your school's Academic Leader (Research): | Yes | | No ✔ |

If yes, provide approval date and attach approval letter:
N/A

**Title of the research project: The risk factor profile assessment of female patients presenting with Acute Myocardial Infarction: A South African perspective**

Name and qualifications of Supervisor: PROFESSOR NARESH RANJITH
e-mail address: RANJITH@LANTIC.CO.ZA

Name and qualifications of Co-supervisor: N/A
e-mail address:

If not for degree purposes, state other (example, self-initiated research): N/A

| | | | | | | |
|---|---|---|---|---|---|---|
| Has this study been, or is it likely to be, submitted to any other Research Ethics Committee? | Yes | | No ✔ | | N/A | |

If yes, please name the Committee/s and or institution and give outcome - i.e. approved/rejected/pending/not applicable? *(If approved, attach approval letter)* N/A

**Please state name and number of Co-investigators in project:[1]**
**(if additional space is required for more investigators details please add to the end of application)**

**CO-INVESTIGATOR/S ROLE IN PROJECT : N/A NO-CO-INVESTIGATORS** *For UKZN statistical reporting purposes*

Name:
Faculty:
Department:
*Gender:
*Race:
Role:
e-mail address:
Signature of Co-Investigator:

Name:
Faculty:
Department:
*Gender:
*Race:
Role:
e-mail address:
Signature of Co-Investigator:

Name:
Faculty:

[1] Please note that because of conflict of roles and interests that can arise, academic supervisors and co-investigators should be separate individuals.

| | | | | |
|---|---|---|---|---|
| Department: | | | | |
| *Gender: | | | | |
| *Race: | | | | |
| Role: | | | | |
| e-mail address: | | | | |
| Signature of Co-Investigator: | | | | |
| Has the Principal Investigator or any of the co-investigators been previously/or are presently being investigated for alleged research misconduct? *(If yes, please provide details and dates)* | Yes | | No ✔ | |
| **FUNDING OF THE RESEARCH:** | | | | |
| Has funding been secured? | Yes | | No ✔ | |
| Amount: R N/A | | | | |
| Name of funder: *(full details)* N/A | | | | |
| Is this project funded from a US DHHS funding source? N/A | Yes | | No | |
| If yes, name the federal funagency: N/A | | | | |
| Can this project proceed without funding? It is a retrospective chart review analyzing data that is stored in a computerized database and as such no funding is needed to proceed with the study. *(give a brief explanation)* | Yes ✔ | | No | |
| Has an application for funds been made to other sources to support this project? | Yes | | No ✔ | |
| If yes, state name/s of funding agency and amount requested: N/A | | | | |

**Note:**

For all US Federally funded studies (e.g. NIH, CDC, NIAID, DAIDS, NIMH, etc), one complete copy of the original funding application and approval must accompany the BREC ethics application.

All University contracts need to be uploaded on the Contracts Management online submission form with either the signed **Approval letter** (non-research) **or Form 1**(research related). The website link to the system is http://legalservices.ukzn.ac.za/ContractsManagement.aspx

If you require assistance with the completion of the online submission form, or with any aspect of the new system, please contact Mr Rendra Phalad on Ext 7455 for all contracts (non-research contracts), and Mr Deon Moodley on Ext 8199 (for research contracts).

**FAILURE TO MAKE FULL FINANCIAL DISCLOSURES WILL DELAY ETHICS APPROVAL**

| | | | | |
|---|---|---|---|---|
| Please indicate whether a BREC review fee is applicable for this study? (See Fee Schedule on BREC Website) | Yes | | No | ✔ |
| If Yes, is the study covered by your Centre/Unit's annual levy fee to BREC? N/A | Yes | | No | |

| **TYPE OF RESEARCH** *(please tick)* | | | | |
|---|---|---|---|---|
| Expedited | ✔ | Full review | | |

**Note:**

* Expedited review only applies to minimal risk studies – e.g. retrospective chart reviews, studies on stored samples etc., for details see BREC ToR and SoP at *http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx*

## SECTION B:

**NATURE OF STUDY**

**Quantitative**

| Type of Study: *(please tick)* | Epidemiological | Observational clinical study | Experimental | Clinical Trial | Observational |
|---|---|---|---|---|---|
| | Retrospective Chart Review ✔ | Prospective Chart Review | Laboratory study on stored samples | Other:(Specify) | |

**Qualitative N/A**

### 1. THE PROTOCOL FOR STUDY

1.1 Full title of research project: *(Please DO NOT use abbreviations or acronyms)*

**Risk factor profile assessment of female patients presenting with Acute Myocardial Infarction: A South African Perspective**

1.2 Aims (what you hope to achieve) and Objectives (how you will achieve your aims) of study: *(please list)*

**AIMS**

1) The study will be a retrospective chart review from the year 2002 up to and including 2016. The primary aim of the study will be to determine the cardiovascular risk factor profile of female patients presenting with a diagnosis of Acute Myocardial Infarction to the Coronary Care unit at RK Khan Hospital in Chatsworth, Durban from the year 2002 until December 2016.
2) I would also like to determine if the cardiovascular risk factor profile differs between pre and post-meonapausal age groups.

**OBJECTIVES:**

1) The main objective is to provide a detailed analysis of the cardiovascular disease risk factor profile and clinical presentation of all adult female patients admitted to the Coronary Care unit at RK Khan Hospital between 2002 and 2016 with a diagnosis of Acute myocardial infarction- which will include ST segment elevation Myocardial infarction as well as Non-ST segment elevation myocardial infarction.
2) The study period continues for 6months post hospitalization where available and I will also evaluate for any Major adverse cardiac events that occurred in the study population, from the time of admission up to six months post discharge.
3) The area of infarction as determined by electrocardiogram findings will be stated for each patient and quantified for the study population following analysis of data.
4) For the study population we will determine what proportion of patients received reperfusion therapy or not.
5) Angiographic characteristics and disease severity will be assessed from Angiographic findings for those subjects who underwent an angiogram at the referral centre, Inkosi Albert Luthuli hospital.
6) To determine whether the risk factors, namely Diabetes mellitus, hypertension, obesity, dyslipidemia, obesity , smoking and a family history of coronary artery disease, is a predictor of major adverse cardiac events (MACE) namely Arrythmias, cardiac failure, cardiogenic shock, complete heart block, recurrence of angina or myocardial infarction and death, in our study population (females presenting with acute myocardial infarction).

1.3 Hypothesis to be tested, or Research Question to be answered:

1) Is the cardiovascular disease risk factor profile for females presenting with an acute myocardial

infarction any different to that of their male counterparts? This will be determined from information obtained on studies done in male counterparts presenting with Acute myocardial infarction in the local setting, that being South Africa.

2) What is the most common cardiovascular risk factor amongst females presenting with an acute myocardial infarction?

3) How do the risk factors differ in the pre and post-menopausal groups?

1.4 Summary of the proposed research methodology (restrict to 100 words)

The study to be performed will be a retrospective single center study. Data from a computerized database will be extracted for the study period 2002-2016.
All adult female patients with a diagnosis of acute myocardial infarction based on European and American society of Cardiology guidelines will be selected on consecutive admissions for the above mentioned study period. Patient anonymity will be maintained throughout the study period. The cardiovascular risk factor profile which will include the following: Diabetes Mellitus, Hypertension, cigarette smoking (current or ex-smokers), Dyslipidemia, Obesity, a previous history of coronary artery disease and a positive family history of Coronary artery disease, will be reviewed and stratified to determine which of the risk factors play a more significant role in predisposing female patients to the development of an acute myocardial infarction.
Patients will be divided into 2 groups, namely those with ST segment elevation myocardial infarction and those with Non-ST segment elevation myocardial infarction. Both groups will be analyzed identically in terms of their age, clinical presentation, cardiovascular risk factors, initial electrocardiogram, use of thrombolytic therapy or not and for the development of any major adverse cardiovascular events up to six months post myocardial infarction. The Major adverse cardiovascular events that will be assessed are as follows: Arrythmias, cardiac failure, cardiogenic shock, complete heart block, recurrence of angina or myocardial infarction and death.
Finally we will also be able to sub-categorize study participants into a pre and post-menopausal group and determine whether the cardiovascular risk factor profile differs in these 2 groups.

1.5 Keywords (for database):

- Acute myocardial infarction
- Female gender
- Age
- Major adverse cardiac events
- Cardiovascular risk factors
- Coronary angiogram
- Coronary revascularisation surgery

1.6 Background and Literature Review (maximum 1 page):

Coronary artery disease is one of the leading causes of death and disability worldwide (4). Likewise in South Africa it has become a major cause of morbidity and mortality across all ethnic groups (1,2). Although Coronary artery disease was previously thought to be a disease predominantly affecting males, it is now understood that females with underlying cardiovascular risk factors are equally at risk of developing coronary artery disease and specifically manifesting as acute myocardial infarction(3,4,13).The traditional and well-studied risk factors for coronary artery disease in males, namely Diabetes Mellitus, Hypertension, dyslipidemia, obesity, cigarette smoking and a family history of coronary artery disease, appear to play the same role in female counterparts(3,4,11,12,13). Due to the cardio-protective effects of Oestrogen, coronary artery disease in females generally occurs at an older age than when compared to males(11,12). Multiple studies have shown that women tend to

present with coronary artery disease on average 6-10 years later than their male counterparts (7,8,10, 13, 14). Studies have also found that the average age of presentation in females in developing countries tends to be lower than that of westernized countries (7, 14). However, although the disease was thought to predominantly affect post-menopausal females, younger females can also develop coronary artery disease in the presence of significant cardiovascular risk factors. In particular, smoking and diabetes mellitus has been found to be an independent predictor of acute coronary syndrome in women below the age of 40 years (6). Although, even the presence of a single risk factor can predispose females to the development of coronary artery disease, in particular acute myocardial infarction, like with males, the presence of multiple cardiovascular risk factors increases that risk significantly (3).

Several studies have shown that females tend to have a higher risk of developing complications following acute myocardial infarction and have higher mortality rates compared to men(10, 11, 14). Cardiovascular disease in females is understudied and there is limited data on the disease in females. According to a 2013 update on coronary artery disease in women (5), it was stated that coronary artery disease is the leading cause of mortality in females and requires further sex-specific research on the disease.

Whilst some risk factors like age, sex, genetic factors and family history, are non-modifiable, it is the modifiable risk factors (Diabetes Mellitus, hypertension, obesity, dyslipidemia and cigarette smoking),that will impact on future outcomes in these patients as well as be the target of primary health care initiatives in reducing the risk of developing cardiovascular disease in females.

1.7 Key References:

*(Give approximately 5 key references)*


35) S.C. Masina et al, Risk factor assessment in South African Black Patients presenting with Acute Myocardial infarction at RK Khan Hospital, Durban, University of Kwazulu Natal, SA Heart Journal, 2016, Volume 13.

36) Krisela Steyn et al, Risk factors associated with Myocardial infarction in Africa: The Interheart Africa study, Circulation American Heart Association, 2005;112:3554-3561.

37) S.C. Jain et al, Retrospective study of common prevalent risk factors among female patients presented with Acute coronary syndrome, Jhalawar hospital and Medical college society, Jhalawar, NJIRM 2014, Volume 5(3), May-June.

38) R.B.D'Agostino et al, General Cardiovascular risk factor profile for use in Primary Care, The Framingham heart study, Boston University, Circulation American Heart Association, 2008;117:743-753.

39) K. Sharma et al, Coronary Artery disease in women: A 2013 Update, Columbus OH, USA, Global heart Journal 2013, Volume 02.001.

40) A. Dominguez-Rodriguez et al, Smoking and the risk of acute coronary syndrome in young women treated in an emergency department, Department of Cardiology, Hospital Universitario de Canarias, Tenerife, Spain, World Journal of Cardiovascular diseases, 2013, Volume 3.

41) M. Sahni et al, Clinical profile, risk factors and short term outcome of Acute Myocardial infarction in females: A hospital based study, Indira Gandhi Medical college, Shimla, Himachal Pradesh, India, Heart India journal Volume 1, Issue 3, October- December 2013.

42) A. Elsaesser et al, Acute coronary syndrome the risk of being female, Kerckhoff Heart centre, Bad Nauheim, Germany, Circulation American Heart association, 2004: 109.

43) A. Rosengren et al, Cardiovacular risk factor and clinical presentation in Acute coronary syndromes, Heart Journal, Volume 91, 2005.

44) J. Alonso et al, Influence of Sex on Acute coronary syndrome mortality and treatment in Spain, Hospital de Fuenlabrada, Fuenlabrada, Madrid, Spain, Rev Esp Cardiol Supl. 2008; 8:8D-22D.

45) V. Nanjappa et al, Clinical profile and 30-day outcome of women with acute coronary syndrome

as a first manifestation of Ischemic heart disease: A Single centre observational study, Fortis Hospital, Bangalore, India, India heart Journal, 2015.08.006.
46) N. Hamdulay et al, Clinical profile of Acute ST elevation Myocardial infarction in Females, Volume 5, Issue 10, October 2015, ISSN-2249-555X
47) S.S.Anand et al, Risk Factors for myocardial infarction in women and men: Insights from the INTERHEART study, European Heart Journal, 2008, volume 29, 932-940.
48) J. Sial et al, Gender differences in presentation of Acute myocardial infarction, Pakistan Heart Journal, Volume 41, No. 3-4 July – December 2008.

## 2. PLAN OF INVESTIGATION FOR STUDY

* In the case of Higher Degrees, please state name and School of person consulted regarding the design:

| | | | | | |
|---|---|---|---|---|---|
| 2.1 | Is this a retrospective chart review with no human contact? | Yes | ✔ | No | |
| 2.2 | Is this a study of stored tissue? | Yes | | No | ✔ |
| 2.3 | Are host genetic factors being studied? | Yes | | No | ✔ |

2.4 How many hours per week will the PI devote to this project? 6-8 HOURS ON AVERAGE
(Timetable the project in terms of the resources and time available)

2.5 Describe your data collection methods for the research project in detail: Data will be extracted from an electronic database that was used by the Coronary Care unit at RK Khan hospital. Patient anonymity will maintained throughout the study period.

## 3. STATISTICAL PLANNING AND DATA ANALYSIS

| | | | | | |
|---|---|---|---|---|---|
| 3.1 | Has this project been approved by a professional statistician? If No, please justify. | Yes ✔ | | No | |

3.2 If answered "yes" to (3.1), provide the name of the statistician: TARYLEE REDDY from Medical Research
Council- DURBAN

3.4 Please provide a brief overview of statistical and data analytic considerations, including: Please refer to the attached document from the above statistician
*How was the number of participants determined? Please include assumptions made in any power analysis (e.g. control incidence or mean and standard deviation of primary outcome variable, desired or anticipated effect of treatment or intervention, level of statistical significance and desired power), and list all planned statistical methods to be used. For descriptive studies list statistical operations to be performed.*

***SAMPLE SIZE CALCULATION:***

The study is powered on estimating the prevalence of key risk factors in the population of females with Acute myocardial infarction with a high degree of precision. Based on previous research, we estimate that the prevalence of diabetes, hypertension etc in this group is greater than 60%. The most conservation approach would be to determine sample size based on a 50% prevalence. To detect a risk factor prevalence of 50% within a 5% margin of error, at a type 1 error rate of 5%, a minimum of 385 participants are required. The aforementioned sample size is also sufficient to estimate prevalence rates greater than or less than 50% with greater precision. We estimate that there will be approximately 1000 participants available which exceeds the minimum sample size of 385.

***ANALYSIS PLAN:***

The prevalence of factors (eg. Diabetes mellitus, hypertension etc) will be reported as proportions with 95% binomial confidence intervals. To determine whether the prevalence of risks factors differs between subgroups of women, the Chi-Square test and Fishers exact test, where appropriate, will be

used. Continuous variables will be summarized as means with standard deviations, or medians with interquartile ranges depending on the distribution. Univariate and multivariate logistic regression will be used too determine factors associated with MACE. All analysis will be conducted using Stata 14.

3.5 For *qualitative* studies: What is the analytic paradigm to be used for analysis of the data? **N/A as this is a retrospective chart review.**

## 4. PARTICIPANTS IN THE STUDY

| | | | | | | |
|---|---|---|---|---|---|---|
| 4.1 Is this a multi-national study? (*If yes, state collaborating countries)* | Yes | | | No | ✔ | |

4.2 List all sites in South Africa in which the project will be carried i.e. geographic location (e.g. KwaZulu-Natal) and type of place (e.g. hospital, clinic, schools, community etc). **CORONARY CARE UNIT at RK KHAN HOSPITAL in CHATSOWRTH, DURBAN, KWAZULU NATAL.**

| 4.3 Source: *(Please indicate number per group)* | Inpatients | Outpatients | Volunteers | Animals |
|---|---|---|---|---|
| | ✔ | | | |

| 4.4 Age (human studies) *(Please indicate number per group)* | Neonates (<28 days) | Infants (1-11 month) | Children (1-12 years) | Adolescent (13-17 years) | Adults |
|---|---|---|---|---|---|
| | | | | | ✔ |

| 4.5 Is there a control group(s)? | Yes | | No | ✔ | |
|---|---|---|---|---|---|

4.6 Demographic profile of participants *(please tick ALL appropriate boxes below.)*

4.6.1 Gender: Female ✓ Male

4.6.2 Population Group: Black ✓ Coloured ✓ Indian ✓ White ✓

4.6.3 Language Group/s: Specify……ENGLISH ……

4.7 Describe the recruitment process in detail for all groups. **The study is a retrospective chart review and all details will be obtained from an electronic database used by the Coronary care unit at RK Khan hospital.**

| | | | | | |
|---|---|---|---|---|---|
| 4.8 Will incentives be offered to facilitate recruitment? (*If yes, describe in detail*) | Yes | | No | ✔ | |
| 4.9 Will participants be reimbursed in some way for participation? (*If yes, describe in detail*) *See SA DoH Guidelines on BREC Website* | Yes | | No | ✔ | |
| 4.10 Will reimbursement for participants and investigators be in accordance with: *(If no, please explain)* **The study is a retrospective chart review and as such will not incur any expense for the participants**.<br>• Guidelines for Good Practice in the Conduct of Clinical Trials in Human Participants in South Africa: Department of Health (2006) and;<br>• Ethics in Health Research: Principles, Structures and Processes: (2015)? | Yes | | No | ✔ | |

| | | | | | | |
|---|---|---|---|---|---|---|
| • Current SA DoH Guidance on reimbursement (*See BREC website*) | | | | | | |
| 4.11 Will participants be insured against research related injury**? N/A as this is a retrospective chart review and an anaysis of computerised data so there are no interventions.**<br>*(If yes, please provide details; If no, please provide rationale)*<br>*Mandatory for Clinical Trials* | Yes | | No | ✔ | | |

4.12 List in detail the inclusion and exclusion criteria.

**INCLUSION CRITERIA:**

- All adult females (≥18years of age) admitted to the Coronary Care unit at RK Khan hospital with a diagnosis Acute myocardial infarction(MI) between the years 2002 and 2016.
- Acute myocardial infarction, both ST elevation MI and Non-ST elevation MI
- All races- Asian, Black, Coloured and White
- Risk factors: Diabetes Mellitus, Hypertension, Dyslipidemia, Cigarette smoking, Obesity and family history of Coronary artery disease

**EXCLUSION CRITERIA:**

- All male patients admitted to the coronary care unit during the aforementioned study period .
- All patients admitted to the coronary care unit at RK Khan hospital with a diagnosis of Unstable Angina
- All patients below the age of 18years.

## 5. CLINICAL TRIALS

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 5.1 Has Medicines Control Council (MCC) approval been applied for? | Yes | | No | | N/A | ✔ | | |
| 5.2 Indicate current status of MCC approval application**: N/A** | | | | | | | | |
| 5.3 Has this clinical trial been registered with the SA National Clinical Trials Register? | Yes | | No | | N/A | ✔ | | |
| 5.4 If "yes" to (5.3), please provide SANCTR registration number: **N/A** | | | | | | | | |
| 5.5 If "no" to (5.3), PI hereby undertakes to register the trial with SANCTR after final ethics and MCC approval<br>Yes No N/A | | | | | | | | |
| 5.6 Please provide the names of all members of the Data Safety and Monitoring Board (DSMB) (CLINICAL TRIALS ONLY) N/A | | | | | | | | |
| 5.7 The PI hereby undertakes to ensure that all DSMB reports are forwarded to BREC for comment as soon as possible.<br>Yes No N/A | | | | | | | | |
| 5.8 Are any of the intended research participants in other research studies and/ or trials? (*If yes, describe in detail*) | Yes | | No | ✔ | | | | |
| 5.9 Is the PI presently involved in other research and/or clinical trial activities? (*If yes, please provide details and % time allocated to each)* | Yes | | No | ✔ | | | | |
| 5.10 Has the funder imposed any restrictions on PI regarding | Yes | | No | ✔ | | | | |

| | | | | | |
|---|---|---|---|---|---|
| publication of study results? **N/A**<br>If **Yes**, give details: | | | | | |

## 6. POTENTIAL RISKS OR DISCOMFORT

| | | | | | |
|---|---|---|---|---|---|
| 6.1 Can the project have any potential risks or discomfort on participants, members of the public, researchers, field staff or the physical environment? | Yes | | No | ✔ | |

6.2 If "yes" to (6.1) indicate, for each study group/arm, the potential additional risks as follows: **N/A**

6.2.1 Biological risks
6.2.2 Psychological risks
6.2.3 Social Risks
6.2.4 Legal risks
6.2.5 Financial risks
6.2.6 Other risks

6.3 Please detail steps that will be taken to minimise the risks indicated above: **N/A**

6.3.1 Biological risks
6.3.2 Psychological risks
6.3.3 Social Risks
6.3.4 Legal risks
6.3.5 Financial risks
6.3.6 Other risks

## 7. BIOLOGICAL SAMPLES

| | | | | | | |
|---|---|---|---|---|---|---|
| 7.1 | Will human tissues (blood, blood products, gamete, gonads, oocyte, organs, flesh, bone, gland, skin, bone marrow or body fluids, waste materials such as urine and stools), microbial isolates and human genetic materials (DNA, RNA) be stored? | Yes | | No | ✔ | |

7.2 If "yes" to (6.1), give details of storage facilities (name, location, conditions and duration of storage). **N/A**

| | | | | | | |
|---|---|---|---|---|---|---|
| 7.2 | Will human tissues, genetic materials and or microbial isolates be exported? | Yes | | No | ✔ | |

7.3 If "yes" to (7.2), please attach current copies of export and import permits and International Aviation Clearance Certificates and a Materials Transfer Agreement (*see template on BREC website).* It is illegal to export human tissues and biological materials without an export permit (National Health Act, 2003). **N/A**

7.4 Please provide a rationale for export of biological materials (i.e. why the work cannot be done locally why local capacity cannot be upgraded) **N/A**

7.5 Conflict of Interest:

Investigators should have no undisclosed conflict of interest with their study collaborators, sponsors or participants. Conflicts can arise, for example, when a commercial or other sponsor may not wish research results detrimental to their corporate image/interest to be disclosed, especially when the investigator is being remunerated by the sponsor for the research in question; or when an investigator has a vested interest in, or is an employee/shareholder/director in the sponsor's corporate entity. Conflicts of interest can also arise when an academic supervisor is also a co-investigator on a study with a student. Investigators should note that the duty to disclose a conflict of interest to BREC begins during application for ethical approval and continues until the research in question is complete and the research results are submitted to the sponsor/published (if applicable).

If the investigator(s) has/have/foresees any such conflict of interest, please provide details here: **NONE**

## 8. GENERAL

8.1 Indicate, for each study group, the likely additional, i.e., over and above standard of care:

8.1.1 Duration of hospital stay (days): **N/A**

8.1.2 Outpatient attendances (number): **N/A**

8.1.3 Laboratory services used, including those appointed by the sponsor (name and location): **N/A**

8.1.4 Type of samples and volumes to be drawn: **N/A**

8.1.5 Which laboratory services will be used? **N/A**

8.1.5.1 Has a preliminary agreement been reached with laboratory service providers? **N/A**

| Yes | | No | ✔ |
|---|---|---|---|

If Yes, attach letter of confirmation. **N/A**

| | | | | | | |
|---|---|---|---|---|---|---|
| 8.2 | Has the nursing team who will be involved in the study been informed of the study and the nursing involvement which will be required? **Nursing staff was not engaged in the study.** *(If no, please explain; other, please specify)* | Yes | | No | ✔ | |

8.3 In the case of participants drawn from patient populations, indicate, in respect of each sub-group, how management differs from that usually offered to patients with similar conditions. **N/A**

8.4 In the case of community based studies, explain what consultation is planned within the community at the following stages: **N/A**

8.4.1 Preparation

8.4.2 Implementation of the study and

8.4.3 Dissemination of the results thereafter

8.5 State the expected benefits arising from this study under the following headings:

8.5.1 Possible direct benefits to study participants

8.5.1.1 Clinical care: **There is a gender bias in terms of publication and females have been a poorly studied group with regards to coronary artery disease, so we hope that the data derived from this study will help narrow that gap and improve outcomes for coronary care in female patients.**

8.5.1.2 Public health: **We will be able to determine if female patients with coronary artery disease behave differently to their male counterparts**

8.5.1.3 Financial: **The results of the study will be of benefit to all centres admitting female patients with acute myocardial infarction and by improving the management of this patient population there will be reduced hospitalization and reduced financial costs.**

8.5.1.4 Prospects of tested intervention being available to the study population if proven effective
**NONE as there is no interventional work being done in this study**

8.5.1.5 Other (Specify): **NIL**

8.5.2 Specify the Indirect benefits arising from this study: **This study will assist in drawing up guidelines for cardiovascular disease in the female population and will impact on future management and outcomes in this population group.**

8.6 Describe the intended strategy for dissemination of study results

8.6.1 To the scientific community: **By publication in a scientific journal**

8.6.2 To research participants: **They can be informed of the scientific journal that the article has been published in**.

8.6.3 To the general public (if applicable): **If the results of this study are profound then It would be possible to get a newspaper publication.**

8.6.4 Other: Specify: **NIL**

## 9. RESEARCH DATA/SAMPLES

9.1 Please explain where the data/samples will be stored and how long they will be stored for? **Data is currently stored on a computerized database where it will remain for the timeframe of the study and thereafter.**

| | | | | | |
|---|---|---|---|---|---|
| 9.2 Will data/samples be destroyed after analyses? Data will be stored for at least 15years in the Database. *(If no, please explain)* | Yes | | No | ✔ | |

## 10. INFORMED CONSENT: GIVEN TO PARTICIPANTS: Not applicable as the study is a Retrospective chart review in which data will be extracted from an existing database. Patient anonymity will be maintained.

See SAMPLE INFORMATION SHEET AND CONSENT FORM ON UKZN BREC WEBSITE at *http://research.ukzn.ac.za/Libraries/Notices2011/BREC_Informed_consent_form_sflb.sflb.ashx*

Other consent forms are acceptable provided that they contain at least the essential elements outlined in the current UKZN BREC Terms of Reference (ToR) and Standard Operating Procedures (SoP) available a15*http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx*

If necessary, information sheets and consent forms, after ethics approval of the English version, must be translated into appropriate local languages and submitted to BREC for further approval prior to implementation, with a copy of the translator's certificate, and back translations if applicable.

The correct and complete contact details for the UKZN Biomedical Research Ethics Committee should be in the information sheets and consent forms as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION
Research Office, Westville Campus
Govan Mbeki Building
University of KwaZulu-Natal
Private Bag X 54001, Durban, 4000
KwaZulu-Natal, SOUTH AFRICA
Tel: 27 31 2602486 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

## 11. QUESTIONNAIRES: GIVEN TO PARTICIPANTS

**Not applicable as the study is a Retrospective chart review in which data will be extracted from an existing database. Patient anonymity will be maintained.**

Provide 25 copies of all questionnaires, interview guides**, data collection sheets** etc.

List all such attachments here:
DATA COLLECTION TOOL

12. DECLARATION OF PRINCIPAL INVESTIGATOR

Conflict of Interest:

I declare that all potential conflicts of interest regarding my application for ethics approval to conduct this study have been declared in accordance with UKZN and BREC Terms of Reference and Standard Operating Procedures.

Oversight of study: Will this study be overseen by a professional Clinical Research Organisation or study sponsor?

| Yes | | No | ✔ |
|---|---|---|---|

If Yes, please give details:

Undertaking:

I understand and accept that I will be required to submit a yearly recertification application, failing which authorisation to continue the study lapses. Progress reports may be required more frequently depending on level of risk and other factors – this will be detailed in the BREC approval letter. Where applicable, all reports from the Data Safety Monitoring Boards (or similar committees) will be provided to the Biomedical Research Ethics Committee within 7 days.

I undertake to request permission for any changes/amendments to the study from BREC in advance of implementing any such changes, unless they are emergencies required to prevent harm or save life. In such cases BREC must be notified urgently.

I agree to provide monitoring data if and when required.

I expect the project to be completed by Date……

I agree to abide by the guidance contained in the SA Department of Health (2015) Ethics in Health Research: Principles, structures and processes and the (2006) South African Good Clinical Practice Guidelines and the current UKZN Biomedical Research Ethics Committee Terms of Reference and Standard Operating Procedures. These are available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

I understand and accept that all information pertaining to this application is a true reflection of the project proposed and I take full responsibility should there be any transgression.

SIGNATURE OF PRINCIPAL INVESTIGATOR……

FULL NAME OF PRINCIPAL INVESTIGATOR……

DATE……..

**13. DECLARATION AND APPROVAL FROM SUPERVISOR AND CO-SUPERVISOR (if applicable)**
*(I HAVE READ AND CHECKED THE PROPOSAL AND IT IS READY FOR SUBMISSION;*

Remarks:

**SIGNATURE OF SUPERVISOR** ……..……

**FULL NAME OF SUPERVISOR…..**……

**DATE**……..

**SIGNATURE OF CO-SUPERVISOR** ……..……

**FULL NAME OF CO-SUPERVISOR…..**……

**DATE**……..

If applicable, attach a signed copy of the Supervision Agreement between the student, supervisor and any co-supervisor.

14. DECLARATION AND APPROVAL OF LINE MANAGER/HOD/ACADEMIC LEADER
(Must include verification of interdepartmental agreements and co-operation)

Remarks:

SIGNATURE OF ACADEMIC LEADER/HOD OR LINE MANAGER ……

FULL NAME OF ACADEMIC LEADER/HOD OR LINE MANAGER……

DATE……..

NB: If applicant is ACADEMIC LEADER/DEAN/HOS, the ACADEMIC LEADER'S/DEAN'S/HOS's Line Manager (DVC) must sign.

SIGNATURE OF ACADEMIC LEADER's/ HOS's/DEAN's Line Manager……

FULL NAME OF ACADEMIC LEADER's, HOS's/DEAN's Line Manager……

DATE……..

Tel: 27 31 2602486 - Fax: 27 31 2604609
Email: BREC@ukzn.ac.za

**11. QUESTIONNAIRES: GIVEN TO PARTICIPANTS**

**Not applicable as the study is a Retrospective chart review in which data will be extracted from an existing database. Patient anonymity will be maintained.**

Provide 25 copies of all questionnaires, interview guides, **data collection sheets** etc.
List all such attachments here:
DATA COLLECTION TOOL

12. DECLARATION OF PRINCIPAL INVESTIGATOR

Conflict of Interest:

I declare that all potential conflicts of interest regarding my application for ethics approval to conduct this study have been declared in accordance with UKZN and BREC Terms of Reference and Standard Operating Procedures.

Oversight of study: Will this study be overseen by a professional Clinical Research Organisation or study sponsor?

| Yes | | No | ✔ |
|---|---|---|---|

If Yes, please give details:

Undertaking:

I understand and accept that I will be required to submit a yearly recertification application, failing which authorisation to continue the study lapses. Progress reports may be required more frequently depending on level of risk and other factors – this will be detailed in the BREC approval letter. Where applicable, all reports from the Data Safety Monitoring Boards (or similar committees) will be provided to the Biomedical Research Ethics Committee within 7 days.

I undertake to request permission for any changes/amendments to the study from BREC in advance of implementing any such changes, unless they are emergencies required to prevent harm or save life. In such cases BREC must be notified urgently.

I agree to provide monitoring data if and when required.

I expect the project to be completed by Date.....

I agree to abide by the guidance contained in the SA Department of Health (2015) Ethics in Health Research: Principles, structures and processes and the (2006) South African Good Clinical Practice Guidelines and the current UKZN Biomedical Research Ethics Committee Terms of Reference and Standard Operating Procedures. These are available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

I understand and accept that all information pertaining to this application is a true reflection of the project proposed and I take full responsibility should there be any transgression.

SIGNATURE OF PRINCIPAL INVESTIGATOR.....

FULL NAME OF PRINCIPAL INVESTIGATOR..... JAQUELINE CINDY GOVENDER

DATE..... 7/03/2017

**13. DECLARATION AND APPROVAL FROM SUPERVISOR AND CO-SUPERVISOR (if applicable)**
*(I HAVE READ AND CHECKED THE PROPOSAL AND IT IS READY FOR SUBMISSION;*

Remarks:

**SIGNATURE OF SUPERVISOR** .....

**FULL NAME OF SUPERVISOR**.....PROF. N. RANJITH

**DATE**.....7/3/2017.....

**SIGNATURE OF CO-SUPERVISOR** .....N/A.....

**FULL NAME OF CO-SUPERVISOR**.....

**DATE**.....

If applicable, attach a signed copy of the Supervision Agreement between the student, supervisor and any co-supervisor.

**14. DECLARATION AND APPROVAL OF LINE MANAGER/HOD/ACADEMIC LEADER**
*(Must include verification of interdepartmental agreements and co-operation)*

Remarks:

HOSPITAL MANAGER
R.K. KHAN HOSPITAL
PRIVATE BAG X004
CHATSWORTH 4030

SIGNATURE OF ACADEMIC LEADER/HOD OR LINE MANAGER.....

FULL NAME OF ACADEMIC LEADER/HOD OR LINE MANAGER 9-03-2017 S SUBRUN

DATE.....9/3/2017.....

NB: If applicant is ACADEMIC LEADER/DEAN/HOS, the ACADEMIC LEADER's/DEAN's/HOS's Line Manager (DVC) must sign.

SIGNATURE OF ACADEMIC LEADER's/ HOS's/DEAN's Line Manager.....

FULL NAME OF ACADEMIC LEADER's, HOS's/DEAN's Line Manager.....

DATE.....

## SUGGESTED CURRICULUM VITAE FORMAT

## (3 COPIES AND MAXIMUM 4 PAGES)

**CURRICULUM VITAE (of Principal Investigator and all Co-Investigators)**
***(CVs to be completed and signed for each member of the research team)***

Full name:
Date of birth:
Male/Female:
Telephone (Home):
Telephone (Business):
Cell:
Fax No:
E-mail Address:
Current HPCSA No: **(or equivalent statutory health council registration No. as appropriate)**
Present position:
Institution:
Department/Section:
Nationality/Permanent residency:
Previous positions held (last 10 years):
Qualifications:
University where obtained/year:
Area of study:
Number of Postgraduate theses supervised (Masters and Doctoral):
Publication list over the past 3 years:
Details of all other research studies presently being conducted:
Certificate of recent (past 3 years) research ethics and/or GCP training (GCP required for clinical trials):

**Signature of PI/Co-PI:** _____

**CHECKLIST FOR BIOMEDICAL RESEARCH ETHICS APPLICATIONS**

**NB: DO NOT BIND SUBMISSIONS (STAPLE ONLY)**

**Applications to be addressed to: The Administrator, Biomedical Research Ethics Committee, Govan Mbeki Building, University Road, Westville Campus, Tel: 031-260 4769 / 2486 Email: BREC@ukzn.ac.za**

## Note to Students:

**PLEASE NOTE THAT ONLY ONE COPY OF APPLICATION AND SUPPORTING DOCUMENTS NEED BE SUBMITTED IF STUDY IS FOR DEGREE PURPOSES. ALL APPLICATIONS FOR DEGREE PURPOSES MUST BE SUBMITTED VIA THE COLLEGE POST-GRADUATE OFFICE WITH AN APPROVAL LETTER ATTACHED.**

**INCOMPLETE SUBMISSIONS MAY RESULT IN DELAYED REVIEW OF THE APPLICATION**

## For all non-degree, non-expedited (full) review applications:

- **25** TYPEWRITTEN COPIES OF APPLICATION **(Back-to-back (double-sided) copies preferred)**
- **5 COPIES** OF THE PROTOCOL
- **5 COPIES** OF CURRENT CV/s **(abbreviated 2 PAGES)**
- **5 COPIES** OF **EVIDENCE OF CURRENT GCP / RESEARCH ETHICS TRAINING**
- **25 COPIES** OF ALL QUESTIONNAIRES TO BE USED IN THE STUDY
- **25 COPIES** OF THE INFORMED CONSENT FORMS (See BREC templates)
- **25 COPIES** OF THE PATIENT INFORMATION LEAFLET (See BREC templates)
- HAVE YOU FAMILIARISED YOURSELF WITH THE BREC TERMS OF REFERENCE? (See http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx )
- DETAILS OF ALL FUNDING SUPPORT?
- ALL PERSONAL INFORMATION?
- ANSWERED ALL QUESTIONS?
- GIVEN DETAILS OF ALL RESEARCH PRESENTLY BEING UNDERTAKEN?
- DELETED UNNECESSARY BLANK SPACES IN THE DOCUMENT?
- **IS DECLARATION PAGE SIGNED BY PI AND HOS/DEAN OR SUPERVISOR?**

**In addition: FOR CLINICAL TRIALS – SUBMIT:**

- **5 COPIES** OF THE INVESTIGATOR'S MANUAL
- **5 COPIES** OF MCC APPROVAL
- **5 COPIES** OF THE FINANCIAL AGREEMENT

**FINAL CHECKLIST FOR FULL (Non-expedited) APPLICATIONS:**

| | | | | |
|---|---|---|---|---|
| 1 | Proof of PI and Co–PI current HPCSA registration | **YES** | **NO** | **N/A** |
| 2 | Permission from hospital manager/clinics submitted | **YES** | **NO** | **N/A** |
| 3 | For degree purposes, please attach copy of postgraduate approval letter | **YES** | **NO** | **N/A** |
| 4 | Roles of PI & co-investigators given | **YES** | **NO** | **N/A** |
| 5 | CV of PI submitted | **YES** | **NO** | **N/A** |
| 6 | CV's of co-investigators submitted | **YES** | **NO** | **N/A** |
| 7 | GCP/ethics training certificate of PI | **YES** | **NO** | **N/A** |
| 8 | GCP/ethics training certificates of co-investigators | **YES** | **NO** | **N/A** |
| 9 | Have other REC approval letters been submitted? | **YES** | **NO** | **N/A** |
| 10 | Is applicant affiliated to BREC – e.g. BREC member? If yes, please specify | **YES** | **NO** | **N/A** |
| 11 | Clinical protocol submitted | **YES** | **NO** | **N/A** |
| 12 | BREC details on Information Sheet updated/checked | **YES** | **NO** | **N/A** |
| 13 | Statistics addressed | **YES** | **NO** | **N/A** |
| 14 | Information to participants submitted | **YES** | **NO** | **N/A** |
| 15 | Informed consent documents submitted | **YES** | **NO** | **N/A** |
| 16 | Signature of PI | **YES** | **NO** | **N/A** |
| 17 | Signed supervision agreement (if applicable) | **YES** | **NO** | **N/A** |
| 18 | Signature of ACADEMIC LEADER/HOS/DEAN or Line Manager | **YES** | **NO** | **N/A** |
| 19 | Signatures of co-investigators | **YES** | **NO** | **N/A** |
| 20 | Questionnaires submitted | **YES** | **NO** | **N/A** |
| 21 | Translation of documents certified | **YES** | **NO** | **N/A** |
| 22 | Materials Transfer Agreement (MTA) | **YES** | **NO** | **N/A** |
| 23 | Will genetic studies be performed? If yes, provide consent form | **YES** | **NO** | **N/A** |
| 24 | Export certificate for tissue storage/transportation | **YES** | **NO** | **N/A** |
| 25 | Permission from Department of Health/Province | **YES** | **NO** | **N/A** |
| 26 | One copy of grant funding proposal and Award notice if funded by any US DHHS source, e.g., NIH, CDC, DAIDS | **YES** | **NO** | **N/A** |
| 27 | Copy of MCC approval or application | **YES** | **NO** | **N/A** |

# Appendix 2: Ethical Approval

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

10 July 2017

**Dr JC Govender (211560810)**
**Discipline of Medicine**
**School of Clinical Medicine**
cindygov@hotmail.com

Dear Dr Govender

**Protocol: Risk factor profile assessment of female patients presenting with acute myocardial infarction: A South African perspective. Degree: MMed BREC ref: BE225/17**

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application received on 28 March 2017.

The study was provisionally approved pending appropriate responses to queries raised. Your response dated 27 June 2017 to BREC letter dated 23 May 2017 have been noted by a sub-committee of the Biomedical Research Ethics Committee. The conditions have now been met and the study is given **full ethics approval** and may begin as from 10 July 2017.

This approval is valid for one year from **10 July 2017.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be RATIFIED by a full Committee at its next meeting taking place on 08 August 2017.

We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

Professor V Rambiritch
Deputy Chair: Biomedical Research Ethics Committee

cc supervisor: ranjith@lantic.co.za cc postgraduate administrator: scmpg@ukzn.ac.za

**Biomedical Research Ethics Committee**
**Professor J Tsoka-Gwegweni (Chair)**
**Westville Campus, Govan Mbeki Building**
**Postal Address:** Private Bag X54001, Durban 4000
**Telephone:** +27 (0) 31 260 2486 **Facsimile:** +27 (0) 31 260 4609 **Email:** brec@ukzn.ac.za

# Appendix 3: Permission To Conduct Study At RK Khan Hospital

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

R.K KHAN HOSPITAL

Postal Address: Private Bag X004, Chatsworth, 4030
Physical Address: 336 R. K. Khan Circle, Croftdene, Chatsworth, 4030
Tel.: 031-459 6001
Fax: 031-401 1247
Email: siphephelo.mabatha@kznhealth.gov.za

OFFICE OF THE CEO

**ENQUIRIES: DR P.S. SUBBAN**

**14 FEBRUARY 2017**

Dr JC Govender

Dear Madam

**RE: PERMISSION TO CONDUCT RESEARCH: THE RISK FACTOR PROFILE OF FEMALE PATIENTS PRESENTING WITH ACUTE MYOCARDIAL INFARCTION: A SOUTH AFRICAN PERSPECTIVE**

Permission is granted to conduct the study at this institution.

Please note the following:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Institution with regards to this research.
2. Please ensure this office is informed before you commence your research.
3. You will be expected to provide feedback on your findings to this institution.
4. You will be liaising with : Dr Mayise
   Tel.: 031 459 6410

Yours faithfully

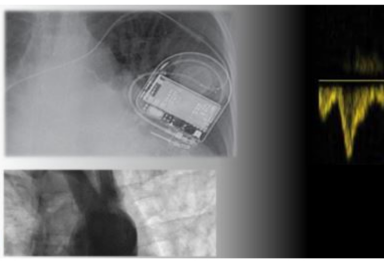
DR P.S. SUBBAN
HOSPITAL CEO

HOSPITAL C.E.O.
R.K. KHAN HOSPITAL
14 -02- 2017
PRIVATE BAG X004
CHATSWORTH 4030

Fighting Disease, Fighting Poverty, Giving Hope

# Appendix 4: The Guidelines for Authorship for the Journal selected for submission of the manuscript





Journal of the South African Heart Association





## Submissions



### Online Submissions

Already have a Username/Password for SA Heart Journal?
**GO TO LOGIN**

Need a Username/Password?
**GO TO REGISTRATION**

Registration and login are required to submit items online and to check the status of current submissions.

### Author Guidelines

Authors need to **register** with the journal as an Author prior to submitting or, if already registered, can simply **log in** and begin the five-step process.

For any technical problems, please contact – **scholar@sun.ac.za** / 021 808 9046

Download the **Author Manual** with regards to the Submission of articles, Reviewers Recommendations, Re-submission, etc.

**Instructions for authors**

SA Heart publishes peer reviewed articles dealing with cardiovascular disease, including original research, topical reviews, state-of-the-art papers and viewpoints. Regular features include an ECG quiz, image in cardiology and local guidelines. Case reports are considered for publication only if the case or cases are truly unique, incorporates a relevant review of the literature and makes a contribution to improved future patient management.

**Publication policy**

Articles must be the original, unpublished work of the stated authors. Written permission from the author or copyright holder must be submitted with previously published material including text, figures or tables. Articles under consideration elsewhere or previously published (except as abstracts not exceeding 400 words) may not be submitted for publication in SA Heart. On acceptance transfer of copyright to the South African Heart Association will be required. No material published in SA Heart may be reproduced without written permission. Permission may be sought from the Chief Editor (Email: **afd@sun.ac.za**).

**Disclosures**

Authors must declare all financial disclosures and conflicts of interest in the cover letter and on the title page of the manuscript.

**Ethics**

All studies must be in compliance with institutional and international regulations for human and animal studies such as the Helsinki declaration (2008) (http://www.wma.net/
en/30publications/10policies/b3/17c.pdf) and the South African MRC ethics guidelines (http://www.sahealthinfo.org/ethics/index.htm). Human studies require ethics committee
approval and informed consent which must be documented in your manuscript. Animal studies require ethics committee approval and must conform to international guidelines for
animal research, as well as the South African National Standard for the care and use of animals for scientific purposes. Compliance with these requirements must be documented in your manuscript.

**Content**

1. Title page: It should contain the title of the manuscript, the names of all authors in the correct sequence, their academic status and affiliations. If there are more than 4 authors, the contribution of each must be substantiated in the cover sheet. The main author should include his/her name, address, phone, fax and email address.
2. Authors are solely responsible for the factual accuracy of their work.
3. Articles should be between 3 000 and 5 000 words in length.
4. A 200-word abstract should state the main conclusions and clinical relevance of the article.
5. All articles are to be in English.
6. Abbreviations and acronyms should be defined on first use and kept to a minimum.
7. Tables should carry Roman numeral, I, II etc., and figures Arabic numbers 1, 2 etc.

8. References should be numbered consecutively in the order that they are first mentioned in the text and listed at the end in numerical order of appearance. Identify references in the text by Arabic numerals in superscript after punctuation, e.g. …trial.

9. Articles are to be submitted directly via the journal. The text should be in MS Word. Pages should be numbered consecutively in the following order wherever possible: Title page, abstract, introduction, materials and methods, results, discussion, acknowledgements, tables and illustrations, references.

10. Where possible all figures, tables and photographs must also be submitted electronically. The illustrations, tables and graphs should not be imbedded in the text file, but should be provided as separate individual graphic files, and clearly identified. The figures should be saved as a 300 dpi jpeg file. Tables should be saved in a MS Word or PowerPoint document. If photographs are submitted, two sets of unmounted high quality black and white glossy prints should accompany the paper. Figures and photographs should be of high quality with all symbols, letters or numbers clear enough and large enough to remain legible after reduction to fit in a text column. Each figure and table must have a separate self-explanatory legend.

11. Remove all markings such as patient identification from images and radiographs before photographing.

**The following format should be used for references:**

**Articles**

Kaplan FS, August CS, Dalinka MK. Bone densitometry observation of osteoporosis in response to bone marrow transplantation. Clin Orthop 1993;294:73-8. (If there are more than six authors, list only the first three followed by et al.)

**Chapter in a book**

Young W. Neurophysiology of spinal cord injury. In: Errico TJ, Bauer RD, Waugh T (eds). Spinal Trauma. Philadelphia: JB Lippincott; 1991:377-94.

**Online media**

Norback JS, Lwellyn DC and Hardin JR (2001). Shoptalk 101. Integrating workplace communication into undergraduate engineering curricula [online]. Retrieved February 15, 2012: http://www.lionhrtpub.com/orms/orms-8-01/norback.html.

## Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. The submission has not been previously published, nor is it before another journal for consideration (or an explanation has been provided in Comments to the Editor).
2. The submission file is in OpenOffice, Microsoft Word, RTF, or WordPerfect document file format.
3. For online resources and where possible URLs for the references have been provided.
4. The text is single-spaced; uses a 12-point font; employs italics, rather than underlining (except with URL addresses); and all illustrations, figures, and tables are placed within the text at the appropriate points, rather than at the end.
5. The text adheres to the stylistic and bibliographic requirements outlined in the **Author Guidelines**, which is found in About the Journal.
6. If submitting to a peer-reviewed section of the journal, the instructions in **Ensuring a Blind Review** have been followed.

## Copyright Notice



## Privacy Statement

The names and email addresses entered in this journal site will be used exclusively for the stated purposes of this journal and will not be made available for any other purpose or to any other party.

ISSN: 2071-4602 (online) ISSN: 1996-6741 (print)

# Appendix 5: Data collections tool (sample)

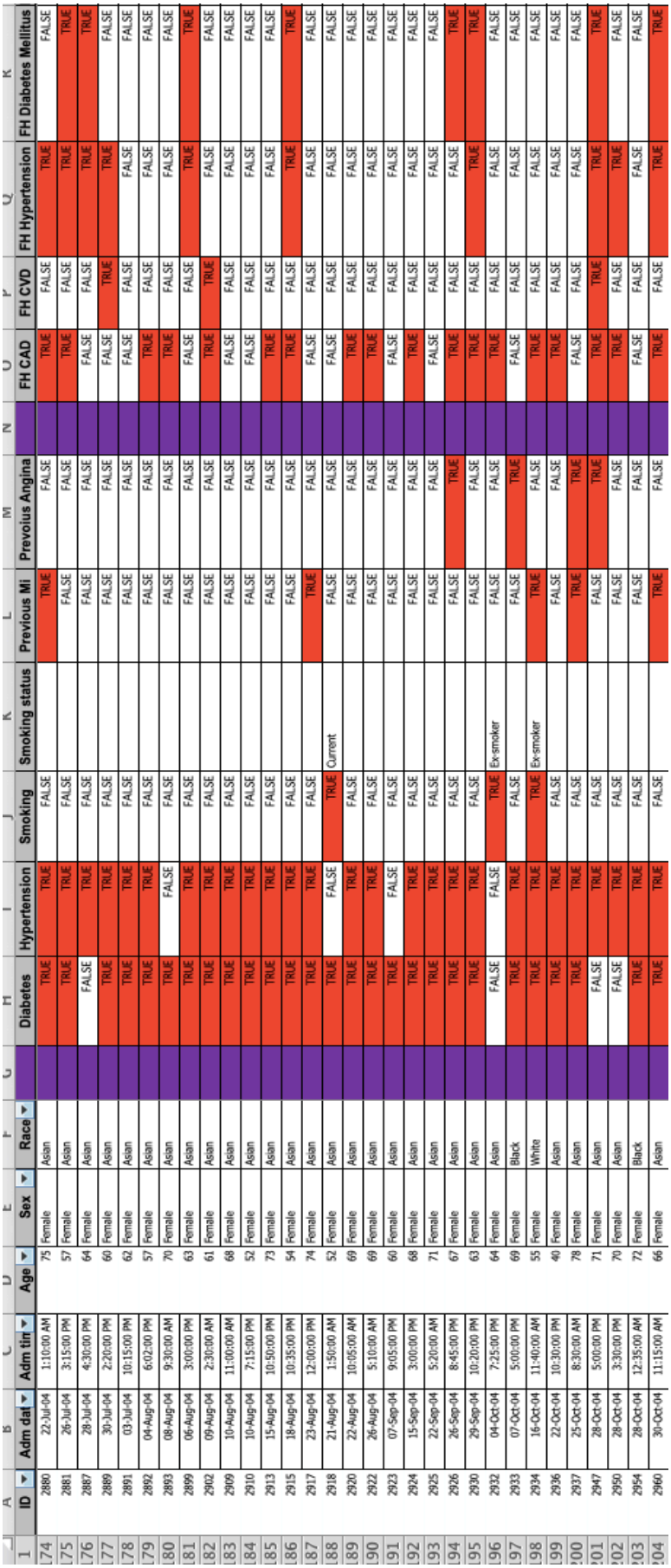
| DATA COLLECTION TOOL BY DR JC GOVENDER- RK KHAN CORONARY CARE UNIT | | | | |
|---|---|---|---|---|
| RISK FACTOR PROFILE OF FEMALE PATIENTS PRESENTING WITH AMI | | | | |
| **PERSONAL DETAILS** | | | | |
| | PATIENT NUMBER | | | |
| | AGE | | | |
| | SEX | | | |
| | RACE | | | |
| | | | | |
| **ONSET OF PAIN** | | | | |
| | DATE | | | |
| | TIME | | | |
| | | | | |
| **ADMISSION CRITERIA** | | | | |
| | DATE | | | |
| | | | | |
| **ADMISSION DIAGNOSIS** | | | | |
| | STEMI | | | |
| | NSTEMI | | | |
| | | | | |
| **SITE OF INFARCTION** | | | | |
| | ANTERIOR | | | |
| | ANTEROLATERAL | | | |
| | ANTEROSPTAL | | | |
| | INFERIOR | | | |

| | | | | |
|---|---|---|---|---|
| | HIGH LATERAL | | | |
| | POSTERIOR | | | |
| | RIGHT VENTRICLE | | | |
| | | | | |
| **EXAMINATION** | | | | |
| | ABDOMINAL GIRTH | | | |
| | SYSTOLIC BLOOD PRESSURE | | | |
| | DIASTOLIC BLOOD PRESSURE | | | |
| | | | | |
| | | | | |
| **RISK FACTOR PROFILE** | | | | |
| | DIABETES MELLITUS | Y/N | | |
| | | Duration | | |
| | | | | |
| | HYPERTENSION | Y/N | | |
| | | Duration | | |
| | | | | |
| | BMI | Normal | | |
| | | Pre-obese | | |
| | | Obesse | | |
| | | | | |
| | DYSLIPIDEMIA | Y/N | | |
| | | Duration | | |
| | | | | |
| | SMOKING | Y/N | | |
| | | Current | | |

| | | | | |
|---|---|---|---|---|
| | | Ex-smoker | | |
| | | | | |
| | PREVIOUS MYOCARDIAL INFARCTION | Y/N | | |
| | | Date | | |
| | | | | |
| | PREVIOUS ANGINA | Y/N | | |
| | | | | |
| | FAMILY HISTORY | | | |
| | Coronary artery disease | Y/N | | |
| | Cerebrovascualr disease | Y/N | | |
| | Diabetes Mellitus | Y/N | | |
| | Hypertension | Y/N | | |
| | | | | |
| **INVESTIGATIONS** | | | | |
| | TOTAL CHOLESTEROL | | | |
| | LDL CHOLESTEROL | | | |
| | HDL CHOLESTEROL | | | |
| | TRIGLYCERIDES | | | |
| | HAEMOGLOBIN | | | |
| | CREATINIE | | | |
| | URIC ACID | | | |
| | | | | |
| **MAJOR ADVERSE CARDIAC EVENTS** | | | | |
| **(Up to 6months post discharge)** | VENTRICULAR ARRYTHMIA | | | |
| | SUPRAVENTRICULAR TACHYCARDIA | | | |
| | HEART BLOCK | | | |

| | | | | |
|---|---|---|---|---|
| | CARDIAC FAILURE | | | |
| | CARDIOGENIC SHOCK | | | |
| | CEREBROVASCULAR ACCIDENT | | | |
| | REHOSPITALISATION | | | |
| | DEATH | | | |
| | | | | |
| **MEDICAL THERAPY** | | | | |
| | METALYSE | Y/N | | |
| | NITRATES | | | |
| | DISPRIN/ASPIRIN | | | |
| | STATIN | | | |
| | ACE-I/ARB'S | | | |
| | B-BLOCKER | | | |
| | CALCIUM CHANNEL BLOCKER | | | |
| | | | | |
| **SURGICAL PROCEDURES** | | | | |
| | CORONARY ANGIOGRAM | Y/N | | |
| | Normal | | | |
| | Single vessel disease | | | |
| | Double vessel disease | | | |
| | Triple vessel disease | | | |
| | | | | |
| | PCI/STENT | Y/N | | |
| | | | | |
| | CORONARY ARTERY BYPASS GRAFT | Y/N | | |
| | Type | | | |

# Appendix 6: Raw data (sample)



| ID | Adm dat | Adm tim | Age | Sex | Race | Diabetes | Hypertension | Smoking | Smoking status | Previous Mi | Prevoius Angina | FH CAD | FH CVD | FH Hypertension | FH Diabetes Mellitus |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2880 | 22-Jul-04 | 1:10:00 AM | 75 | Female | Asian | TRUE | TRUE | FALSE | | TRUE | FALSE | TRUE | FALSE | TRUE | FALSE |
| 2881 | 26-Jul-04 | 3:15:00 PM | 57 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | TRUE | TRUE |
| 2887 | 28-Jul-04 | 4:30:00 PM | 64 | Female | Asian | FALSE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE |
| 2889 | 30-Jul-04 | 2:20:00 PM | 60 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | TRUE | TRUE | FALSE |
| 2891 | 03-Jul-04 | 10:15:00 PM | 62 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2892 | 04-Aug-04 | 6:02:00 PM | 57 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2893 | 08-Aug-04 | 9:30:00 AM | 70 | Female | Asian | TRUE | FALSE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2899 | 06-Aug-04 | 3:00:00 PM | 63 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE |
| 2902 | 09-Aug-04 | 2:30:00 AM | 61 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | TRUE | FALSE | FALSE |
| 2909 | 10-Aug-04 | 11:00:00 AM | 68 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2910 | 10-Aug-04 | 7:15:00 PM | 52 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2913 | 15-Aug-04 | 10:50:00 PM | 73 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2915 | 18-Aug-04 | 10:35:00 PM | 54 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | TRUE | TRUE |
| 2917 | 23-Aug-04 | 12:00:00 PM | 74 | Female | Asian | TRUE | TRUE | FALSE | | TRUE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2918 | 21-Aug-04 | 1:50:00 AM | 52 | Female | Asian | TRUE | FALSE | TRUE | Current | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2920 | 22-Aug-04 | 10:05:00 AM | 69 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2922 | 26-Aug-04 | 5:10:00 AM | 69 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2923 | 07-Sep-04 | 9:05:00 PM | 60 | Female | Asian | TRUE | FALSE | FALSE | | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2924 | 15-Sep-04 | 3:00:00 PM | 68 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2925 | 22-Sep-04 | 5:20:00 AM | 71 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2926 | 26-Sep-04 | 8:45:00 PM | 67 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | TRUE | TRUE | FALSE | FALSE | TRUE |
| 2930 | 29-Sep-04 | 10:20:00 PM | 63 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | TRUE | TRUE |
| 2932 | 04-Oct-04 | 7:25:00 PM | 64 | Female | Asian | FALSE | FALSE | TRUE | Ex-smoker | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2933 | 07-Oct-04 | 5:00:00 PM | 69 | Female | Black | TRUE | TRUE | FALSE | | FALSE | TRUE | FALSE | FALSE | FALSE | FALSE |
| 2934 | 16-Oct-04 | 11:40:00 AM | 55 | Female | White | TRUE | TRUE | TRUE | Ex-smoker | TRUE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2936 | 22-Oct-04 | 10:30:00 PM | 40 | Female | Asian | TRUE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE |
| 2937 | 25-Oct-04 | 8:30:00 AM | 78 | Female | Asian | TRUE | TRUE | FALSE | | TRUE | TRUE | FALSE | FALSE | FALSE | FALSE |
| 2947 | 28-Oct-04 | 5:00:00 PM | 71 | Female | Asian | FALSE | TRUE | FALSE | | FALSE | TRUE | TRUE | TRUE | TRUE | TRUE |
| 2950 | 28-Oct-04 | 3:30:00 PM | 70 | Female | Asian | FALSE | TRUE | FALSE | | FALSE | FALSE | TRUE | FALSE | TRUE | FALSE |
| 2954 | 28-Oct-04 | 12:35:00 AM | 72 | Female | Black | TRUE | TRUE | FALSE | | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE |
| 2960 | 30-Oct-04 | 11:15:00 AM | 66 | Female | Asian | TRUE | TRUE | FALSE | | TRUE | FALSE | TRUE | FALSE | TRUE | TRUE |

| | A | B | C | D | E | F | AF | AG | AH | AI | AJ | AK | AL | AM | AN | AO | AP | AQ | AR | AS | AT | AU | AV | AW | AX | AY | AZ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | ID | Adm dat | Adm tim | Age | Sex | Race | SVT | H.Block | Paced | Shock | CVA | VT | VF | C.FAIL | Roa | ROI | Death | MACE | | Inferior | pmbo2 | Posterior | pmbo4 | Anteroseptal | pmbo2 | Anterolateral | pmbo2 |
| 42 | 4590 | 20-Mar-10 | 10:25:00 AM | 53 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | FALSE | TRUE | | TRUE | Q | FALSE | | FALSE | | FALSE | |
| 43 | 4597 | 21-Mar-10 | 9:40:00 AM | 73 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE | | FALSE | | FALSE | | TRUE | Non Q | FALSE | |
| 44 | 4602 | 25-Mar-10 | 4:40:00 PM | 65 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | FALSE | | FALSE | | FALSE | |
| 45 | 4607 | 05-Apr-10 | 12:25:00 PM | 69 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | TRUE | FALSE | FALSE | FALSE | TRUE | | TRUE | Non Q | FALSE | | FALSE | | TRUE | Non Q |
| 46 | 4609 | 02-Apr-10 | 10:40:00 AM | 65 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Non Q | FALSE | | FALSE | | TRUE | Non Q |
| 47 | 4615 | 03-May-10 | 6:35:00 PM | 63 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Non Q | FALSE | | FALSE | | TRUE | Non Q |
| 48 | 4616 | 09-May-10 | 12:22:00 AM | 56 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE | TRUE | | FALSE | | FALSE | | TRUE | Q | TRUE | Q |
| 49 | 4618 | 26-Apr-10 | 5:40:00 AM | 64 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | FALSE | | FALSE | | TRUE | Q | FALSE | |
| 50 | 4623 | 23-Apr-10 | 5:20:00 AM | 61 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | | TRUE | Non Q | FALSE | | FALSE | | FALSE | |
| 51 | 4626 | 11-May-10 | 9:20:00 PM | 47 | Female | Black | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | FALSE | | FALSE | | TRUE | Q | FALSE | |
| 52 | 4627 | 12-May-10 | 11:00:00 PM | 69 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | TRUE | Q | FALSE | | TRUE | Q |
| 53 | 4630 | 15-May-10 | 10:00:00 PM | 57 | Female | Asian | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | | TRUE | Q | FALSE | | FALSE | | TRUE | Q |
| 54 | 4632 | 21-May-10 | 3:35:00 AM | 62 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | FALSE | | TRUE | Q | FALSE | | FALSE | |
| 55 | 4634 | 22-May-10 | 11:05:00 AM | 76 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE | | FALSE | | FALSE | | TRUE | Q | FALSE | |
| 56 | 4636 | 15-Apr-10 | 3:30:00 AM | 58 | Female | Coloured | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | FALSE | | TRUE | Q | FALSE | |
| 57 | 4641 | 26-May-10 | 6:30:00 PM | 62 | Female | Black | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE | | FALSE | | FALSE | | TRUE | Non Q | FALSE | |
| 58 | 4647 | 26-May-10 | 5:50:00 AM | 53 | Female | Asian | FALSE | TRUE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE | | TRUE | Non Q | FALSE | | FALSE | | TRUE | Non Q |
| 59 | 4655 | 29-May-10 | 1:40:00 PM | 67 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | FALSE | | TRUE | Q | FALSE | |
| 60 | 4656 | 06-Jun-10 | 11:20:00 PM | 51 | Female | Black | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE | TRUE | | FALSE | | FALSE | | TRUE | Q | TRUE | Q |
| 61 | 4657 | 08-Jun-10 | 7:50:00 PM | 79 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | TRUE | Q | FALSE | | FALSE | |
| 62 | 4660 | 17-Jun-10 | 12:40:00 PM | 78 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | FALSE | | FALSE | | FALSE | |
| 63 | 4662 | 16-Jun-10 | 3:20:00 AM | 55 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | FALSE | | FALSE | | TRUE | Non Q | FALSE | |
| 64 | 4665 | 04-Jun-10 | 1:50:00 PM | 41 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | FALSE | | FALSE | | FALSE | |
| 65 | 4670 | 25-Jun-10 | 8:50:00 AM | 34 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | FALSE | | FALSE | | TRUE | Q | FALSE | |
| 66 | 4671 | 01-Jul-10 | 3:05:00 PM | 44 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | FALSE | | FALSE | | FALSE | |
| 67 | 4676 | 04-Jul-10 | 8:50:00 PM | 77 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE | TRUE | | TRUE | Q | FALSE | | FALSE | | FALSE | |
| 68 | 4678 | 08-Jul-10 | 8:00:00 AM | 54 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | | TRUE | Q | TRUE | Q | FALSE | | FALSE | |
| 69 | 4681 | 09-Jul-10 | 10:19:00 AM | 68 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | TRUE | TRUE | | TRUE | Non Q | FALSE | | FALSE | | FALSE | |
| 70 | 4685 | 11-Jul-10 | 5:53:00 PM | 75 | Female | Asian | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | FALSE | FALSE | FALSE | FALSE | FALSE | TRUE | | FALSE | | FALSE | | TRUE | Q | FALSE | |