Profile of coronary artery disease patients at Universitas Academic Hospital: 1994 versus 2014

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MASTERS OF HEALTH SCIENCE IN CLINICAL TECHNOLOGY

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"The more diligent our search, the more accurate our scrutiny, the more we are convinced that our labours can never finish, and that subjects inexhaustible remain behind still unexplored.'

George Adams

(English Instrument Maker)

1750 – 1795

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Declaration of Independent Work

I, Martha Aletta Sophia Elizabeth Bester, do hereby declare that this research project submitted to the Central University of Technology for the degree **MASTERS OF HEALTH SCIENCES IN CLINICAL TECHNOLOGY** is my own independent work that has not been submitted to any institution by me or any other person in fulfilment of the requirements for the attainment of any qualification.

_____   ____25 September 2020__

              Signature   **Date**

Abstract

Introduction

Coronary artery disease (CAD) is a condition that decreases the flow of blood through the coronary arteries around the heart (Merriam-Webster Incorporated, 2019) that can lead to a heart attack (Yayan, 2014). It is the leading cause of death worldwide (Nowbar et al., 2019) and there are several risk factors that contribute to its development (Fuster and Kelly, 2010). Non-modifiable risk factors are age, gender and ethnicity/race and family history, while modifiable risk factors include hypertension, hypercholesterolemia, obesity and sedentary lifestyle, diabetes mellitus and smoking (Jaggi & Kearns, 2012; Winham et al., 2014; Yayan, 2014; Papadakis & McPhee, 2016; Nowbar et al., 2019).

While it is reported that CAD in Sub-Saharan Africa is rare (Forouzanfar et al., 2012) reports from the World Health Organization (WHO) African region suggest that non-communicable diseases in this region are on the rise (World Health Organization African Regional Office, 2018). However, epidemiological data of this region is scanty. The only major studies available for South Africa (SA) are the Heart of Soweto study and the work of Prof. Bongani M Mayosi which report that the prevalence of modifiable risk factors for CAD is high and rising, especially in the black African population (Sliwa et al., 2008; Tibazarwa et al., 2009; Mayosi et al., 2009; Pretorius et al., 2011; Mayosi et al., 2012; Mayosi & Benatar, 2014), emphasizing the need for epidemiological studies into this phenomenon (Stewart et al., 2006; Sliwa & Mocumbi, 2010; Senkubuge & Mayosi, 2013).

No CAD data exists for central SA. The profile of patients of patients presenting with CAD at Universitas Academic Hospital (UAH) have not been documented in the past.

Aim

To document the profile of public sector patients who had confirmed CAD (on coronary angiography) in central SA and determine if there was a change over twenty years.

Methods

This was a retrospective single-centre observational cohort comparing two time periods, twenty years apart, conducted at UAH, Bloemfontein. The main inclusion criterion was confirmed atherosclerotic CAD as reported on coronary angiography. Medical records/data of all public sector patients who underwent coronary angiography during 1994 and 2014 were evaluated. Demographic data, which forms part of the non-modifiable risk factors for CAD, and other relevant clinical information was recorded.

Results

Acute coronary syndrome (ACS) increased over the study period (p<0,0001) and this can be attributed to a notable increase in both Non-ST-Elevation Myocardial Infarction (NSTEMI) (p<0,0001) and ST-Elevation Myocardial Infarction (STEMI) (p<0,0001). Unstable angina decreased significantly over the study period (p<0,0001). There was a significant increase in the number of African patients who experienced STEMI over the study period (p<0,0001) and there was a substantial decrease in Caucasian patients who had ACS (p=0,0015). While NSTEMI increased significantly in Caucasian patients (p<0,0001), unstable angina in this group decreased significantly (p<0,0001).

Females with ACS presented 4 years earlier in 2014 than those in 1994 (1994 median age = 66 years vs. 2014 median age = 62 years) (p=0,0031, 95% CI 1,3941; 6,7202). This trend was predominantly demonstrated in Caucasian females only (1994 median age = 66 years vs. 2014 median age = 62 years; p=0,04811, 95% CI 0,0276; 6,5743). The age of females with STEMI decreased significantly from 1994 (median age 69 years) to 2014 (median age 60 years) (p=0,0119; 95% CI 1,4195; 10,8305). Females with unstable angina were six years younger in 2014 (median age 60 years) than in 1994 (median age 66 years) (p=0,0269, 95% CI 0,5800; 9,1978). Caucasian females with NSTEMI was markedly older in 2014 (median age 66 years) than in 1994 (median age 50 years) (p<0,0001, 95% CI -19,7368; -12,8882), while those with STEMI became younger (1994 median age = 69 years vs. 2014 median age = 60 years, p=0,0269; 95% CI 0,9640; 14,6464).

Conclusions

There was an epidemiological change in public sector patients who had confirmed CAD in central SA with CAD increasing in patients of African and mixed ethnicity. ACS rose significantly over time with females presenting at a significantly younger age. STEMI became the most important presenting condition in patients of African ethnicity whilst NSTEMI increased in Caucasian patients. These findings have important implications for central SA public sector patients presenting with chest pain – the risk of STEMI in patients of African ethnicity is increasing and should not be ignored by clinicians.

Acknowledgements

Firstly, I would like to thank my thesis advisor, Prof. SC Brown (Head: Department of Paediatric Cardiology) for always being available whenever I needed help or had question about my research or writing. He steered me in the right direction, but consistently allowed this study to be my own work. Thank you for sharing your knowledge and expertise with me and for making me see the silver lining on cloudy days.

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Without the persons mentioned above this qualification would have been impossible. Thank you.

Abbreviations and symbols

<	Less than
AASK	African-American Study of Kidney Disease and Hypertension
ACCF	American College of Cardiology Foundation
ACE	Angiotensin-Converting-Enzyme
ACS	Acute Coronary Syndrome
AF	Atrial Fibrillation
AFL	Atrial Flutter
AHA	American Heart Association
A-HeFT	African-American Heart Failure Trial
AIDS	Acquired Immunodeficiency Syndrome
ALLHAT	Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial
ARIC	Atherosclerosis Risk in Communities
aVF	Augmented Vector Foot (ECG lead)
aVL	Augmented Vector Left (ECG lead)
BBC	British Broadcasting Corporation
CABG	Coronary Artery Bypass Graft surgery
CAD	Coronary Artery Disease
Cal	Calorie
CVS	Cardiovascular System
DOH	Department of Health
ECG	Electrocardiogram
EHS-ACS-II	Euro Heart Survey on Acute Coronary Syndromes

ESC	European Society of Cardiology
HAALSI	Health and Ageing in Africa
HDL	High-Density Lipoprotein cholesterol
HDSS	Health and Demographic Surveillance Systems
HIV	Human Immunodeficiency Virus
HSREC	Health Sciences Research Ethics Committee
I.e.	Id Est (In other words)
IHD	Ischemic Heart Disease
LAD	Left Anterior Descending coronary artery
LDL	Low-Density Lipoprotein cholesterol
LMIC	Low- and Middle-Income countries
LVEF	Left Ventricular Ejection Fraction
NCD	Non-Communicable Disease
NHLBI	The National Heart, Lung, and Blood Institute
NSTEMI	Non-ST-Elevation Myocardial Infarction
PCI	Percutaneous Coronary Intervention
PTCA	Percutaneous Transluminal Coronary Angioplasty
PVD	Peripheral Vascular Disease
SA	South Africa
STEMI	ST-Elevation Myocardial Infarction
SYNTAX	The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery trial
UAH	Universitas Academic Hospital
UNFPA	United Nations Population Fund

VLDL	Very Low-Density Lipoprotein cholesterol
WHF	World Heart Federation
WHO	World Health Organization
WISE	Women's Ischemia Syndrome Evaluation
YLL	Years of Life Lost

List of definitions

Term	Definition
Acute coronary syndrome	An acute ischemic insult to the myocardium resulting from sudden reduction in coronary blood flow. ECG findings categorizes patients into two major subdivision of major diagnostic and therapeutic consequences: ST-elevation ACS (generally reflects an acute total coronary occlusion) or non-ST elevation ACS (Patients with acute chest pain but no persistent ST-segment elevation). Non-ST elevation ACS is further classified either unstable angina or NSTEMI (Ahmad & Ali, 2019).
Angina pectoris	Severe constricting pain or sensation of pressure in the chest, often radiating from the precordium to a shoulder (usually left) and down the arm, resulting from ischemia of the heart muscle usually caused by coronary disease (Stedman's Online, 2019).
Artery	A relatively thick-walled, muscular, pulsating blood vessel conveying blood away from the heart. With the exception of the pulmonary and umbilical arteries, the arteries contain red or oxygenated blood (Stedman's Online, 2019).
Atheroma	The lipid deposits in the intima of arteries, producing a yellow swelling on the endothelial surface; a characteristic of atherosclerosis (Stedman's Online, 2019).
Atherosclerosis	Hardening of the arteries characterized by irregularly distributed lipid deposits in the intima of large and medium-sized arteries, causing narrowing of arterial lumens and proceeding eventually to fibrosis and calcification. Lesions are usually focal and progress slowly and intermittently. Limitation of blood flow accounts for most clinical manifestations, which vary with the distribution and severity of lesions (Stedman's Online, 2019).
Cardiac catheterization	Process whereby a thin flexible catheter is introduced into an artery and advanced into the heart for diagnosis or therapy (Stedman's Online, 2019).

Term	Definition
Cardiomyopathy	Any structural or functional disease of heart muscle that is marked especially by enlargement of the heart, by hypertrophy of cardiac muscle, or by rigidity and loss of flexibility of the heart walls and that may be idiopathic or attributable to a specific cause (such as heart valve disease, untreated high blood pressure, or viral infection) (Merriam-Webster Incorporated, 2019).
Cardiovascular system (CVS)	This refers to the whole circulatory system: the heart, the systemic circulation (the arteries and veins of the body) and the pulmonary circulation (the arteries and veins of the lungs). Blood circulates throughout the cardiovascular system, bringing oxygen and nutrients to the tissues and removing carbon dioxide and other waste products (Marcovitch, 2018).
Cholesterol	A lipid that is an important constituent of body cells and is widely distributed throughout the body. It is especially abundant in the brain, nervous tissue, adrenal glands and skin. A high blood-cholesterol level – that is, one over 6 mmol per litre or 238 mg per 100 ml – is undesirable as there appears to be a correlation between a high blood cholesterol and atheroma, the form of arterial degenerative disease associated with coronary thrombosis and high blood pressure. Cholesterol exists in three forms in the blood: high-density lipoproteins (HDL) which are believed to protect against arterial disease; a low-density version (LDL); and a very low-density type (VLDL) – these latter two being risk factors (Marcovitch, 2018).
Coronary	A term applied to any structure in the body encircling an organ in the manner of a crown. Most commonly it is used in reference to the coronary arteries, through which blood is delivered to the muscle of the heart (Marcovitch, 2018).
Coronary angiography	Imaging of the circulation of the myocardium by injection of contrast medium, usually by selective catheterization of each coronary artery (Stedman's Online, 2019).
Coronary artery bypass graft (CABG)	A surgical procedure in which damaged sections of the coronary arteries are replaced with new articular of venous graftings to increase rate of cardiac blood flow (Stedman's Online, 2019).
Electrocardiogram (ECG)	Graphic record of the heart's integrated action currents obtained with the electrocardiograph displayed as voltage changes over time (Stedman's Online, 2019).

Term	Definition
Epidemiology	The study of disease as it affects groups of people. Originating in the study of epidemics of diseases like cholera, plague and smallpox, epidemiology is an important discipline which contributes to the control not only of infectious diseases but also of conditions such as heart disease and cancer. Their distributions in populations can provide important pointers to possible causes (Marcovitch, 2018).
Ethnicity/ethnic group	A social group characterized by a distinctive social and cultural tradition maintained from generation to generation, a common history and origin, and a sense of identification with the group; members have distinctive features in their way of life, shared experiences, and often a common genetic heritage; these features may be reflected in their experience of health and disease (Stedman's Online, 2019).
Heart	A hollow muscular pump with four cavities, each provided at its outlet with a valve, whose function is to maintain the circulation of the blood. The two upper cavities are known as atria, and the two lower ones as ventricles (Marcovitch, 2018).
Heart failure	Inadequacy of the heart so that as a pump it fails to maintain the circulation of blood, with the result that congestion and oedema develop in the tissues (Stedman's Online, 2019).
Ischemia	Local loss of blood supply due to mechanical obstruction (mainly arterial narrowing or disruption) of the blood vessel (Stedman's Online, 2019). Ischaemia develops if myocardial oxygen demand exceeds supply (Swanton & Banerjee, 2008).
Ischemic cardiomyopathy	Ischaemia and infarction with subsequent loss of contractility and remodelling of the heart (Lüscher, 2016).
Myocardial infarction	Infarction of a segment of heart muscle, usually due to occlusion of a coronary artery (Stedman's Online, 2019).
Non-communicable	Not transmissible by direct contact (Merriam-Webster Incorporated, 2019).
Non-Q-wave myocardial infarction	Evidence of infarction in the absence of abnormal Q waves in any combination of leads I, aVL and VI to V6 and leads II and aVF (Montague et al., 1986).

Term	Definition
Non-ST-elevation Myocardial Infarction (NSTEMI)	A type of myocardial infarction causing cardiomyocyte necrosis and death by a rise in serum troponin levels. The ECG may be normal or there may be transient ST-segment elevation, persistent or transient ST-segment depression, T-wave inversion, flat T waves or pseudo-normalization of T waves (Ahmad & Ali, 2019).
Percutaneous coronary intervention (PCI)	An invasive treatment for a stenosed (narrowed) coronary artery. A balloon-tipped catheter is passed through artery of the heart that has developed stenosis. The balloon is aligned with the stenosed section and then inflated to dilate the coronary artery and allow the blood to flow more freely. A stent may be left in place (Marcovitch, 2018).
Percutaneous Transluminal Coronary Angioplasty (PTCA)	A minimally invasive surgical procedure for the treatment of coronary atherosclerosis. A balloon-tipped catheter is inserted percutaneously into the arterial circulation, advanced to the aortic root, and directed with a flexible guide wire to the site of coronary stenosis. Having been positioned within the narrowed arterial segment, the balloon is inflated so as to stretch the lumen, fracture the obstructing plaque, or both (Stedman's Online, 2019).
Retrospective	Relating to or being a study (as of a disease) that starts with the present condition of a population of individuals and collects data about their past history to explain their present condition (Merriam-Webster Incorporated, 2019).
Stable angina	Angina induced by effort and relieved by rest. It does not increase in frequency or severity, and is predictable in nature (Swanton & Banerjee, 2008).
Statin	A lipid-lowering drug used to treat primary hypercholesterolaemia – a condition in which the concentrations of lipoproteins in the blood plasma are raised, increasing the likelihood of affected individuals developing coronary heart disease (Marcovitch, 2018).

Term	Definition
ST-Elevation Myocardial Infarction (STEMI)	Acute myocardial injury (heart attack) detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia and with detection of a rise and/or fall of cardiac Troponin values together with symptoms of myocardial ischemia, new ischemic ECG changes (new ST-segment elevations in 2 contiguous leads or new bundle branch blocks with ischemic repolarization patterns), development of pathological Q waves, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic aetiology (Thygesen et al., 2018).
Stent	A widely used device with metal surfaces that are sometimes coated with a drug to prevent restenosis. It is used to maintain luminal patency (Stedman's Online, 2019).
Unstable angina	Myocardial ischemia at rest or minimal exertion in the absence of cardiomyocyte necrosis (cardiac biomarkers are not increased) (Ahmad & Ali, 2019).

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Chapter 1: Problem statement and rationale

1.1. Introduction

Coronary artery disease (CAD) is a condition that decreases the flow of blood through the coronary arteries around the heart (Merriam-Webster Incorporated, 2019) that can lead to ischemic heart disease (IHD) or a myocardial infarction (heart attack) (Yayan, 2014). It is the leading cause of death worldwide (Nowbar et al., 2019), killing about 3.8 million men and 3.4 million women each year (Clarify Registry Investigators, 2018). Worldwide it is estimated to be prevalent in approximately 153.5 million people (with higher prevalence in males than females) (Benjamin et al., 2019). Put in another way: In adults, CAD causes about one-third of all deaths (Sanchis-Gomar et al., 2016).

There are several, well-known risk factors that contribute to the development of CAD in adults (Fuster and Kelly, 2010). Modifiable risk factors include hypertension, hypercholesterolemia, obesity and sedentary lifestyle, diabetes mellitus and smoking, while non-modifiable risk factors are age, gender and ethnicity/race and family history (Jaggi & Kearns, 2012; Winham et al., 2014; Yayan, 2014; Papadakis & McPhee, 2016; Nowbar et al., 2019).

In developing countries such as India, Egypt and Pakistan, CAD is reported to be on the rise (Sriharibabu, 2016; Prabhakaran et al., 2018). This trend can also be seen in other developing countries. Between 1984 and 1999 Beijing's coronary heart disease mortality rates increased by 27% in women and a staggering 50% in men (ages 35 to 74 years) (Critchley et al., 2004). In North Africa, Tunisia experienced increased CAD mortality rates of 11,8% in men (from 70 to 87 deaths per 100,000) and 23,8% in women (from 28 to 41 deaths per 100,000) from 1997 to 2009 (Saidi et al., 2013).

Forouzanfar et al. (2012) reported that IHD in the southern regions of Africa is quite rare, but reports from the World Health Organization (WHO) African region suggests that non-communicable diseases in Sub-Saharan Africa, as well as the costs related to their treatment, are on the rise (World Health Organization African Regional Office, 2018). CAD is predicted to be one of the leading causes of morbidity and mortality by 2020 for most developing nations (Celermajer et al., 2012). The rise in CAD in African populations is generally ascribed to the increase of modifiable risk factors for CAD (Yusuf et al., 2001a; Gersh et al., 2010; Nowbar et al., 2019; Benjamin et al., 2019). There is, however,

a significant problem: epidemiological data, of any type, is almost totally absent in the southern regions of Africa. Most of this regions' estimates comes from South Africa (SA) alone (Moran et al., 2012).

The only major studies available for SA are the Heart of Soweto study and the work of Prof. Bongani M Mayosi. These studies report that the prevalence of modifiable risk factors for CAD is high and rising, especially in the black African population (Sliwa et al., 2008; Tibazarwa et al., 2009; Mayosi et al., 2009; Stewart et al., 2011; Mayosi et al., 2012; Mayosi & Benatar, 2014). Therefore, emphasizing the need for epidemiological studies into this phenomenon (Stewart et al., 2006; Sliwa & Mocumbi, 2010; Senkubuge & Mayosi, 2013).

While reviewing SA literature it was found that there is a significant lack of data from central SA specifically. The profile of patients who had confirmed CAD at UAH have not been documented in the past. There is a limited number of publications on this subject in central SA, especially in the Free State. By identifying demographic over the past two decades, this study aimed to begin the process of filling this deficit.

1.2. Research question

What is the profile and was there a change in the profile of patients who had confirmed CAD on coronary angiography at UAH in 2014 as compared to 1994?

1.3. Aim

The aim of this study was to determine what the profile was and if there was a change in the profile of patients who had confirmed CAD on coronary angiography at UAH in 2014 as compared to 1994.

1.4. Objectives

- ◈ Establish the total number of patients that underwent coronary angiography in 1994 and 2014 at Universitas Academic Hospital.
- ◈ Analyse the age group, gender, and ethnicity of patients that underwent coronary angiography in 1994 and 2014 at UAH.
- ◈ Determine the number of patients that had healthy coronary arteries among patients that underwent coronary angiography in 1994 and 2014 at UAH.
- ◈ Determine the percentage of patients that had diseased coronary arteries among patients that underwent coronary angiography in 1994 and 2014 at UAH.
- ◈ Compare and contrast the non-modifiable risk factors and the treatment modalities of patients that underwent coronary angiography in 1994 and 2014 at UAH.
- ◈ Quantify the number of patients that underwent CABG after coronary angiography in 1994 and 2014 at UAH.
- ◈ Identify non-modifiable risk factor trends between patients that underwent coronary angiography in 1994 and 2014 at UAH.

Chapter 2: Literature review

2.1. What is coronary artery disease?

Coronary artery disease (CAD) is a condition that decreases the flow of blood through the coronary arteries around the heart, and is mainly caused by atherosclerosis (Merriam-Webster Incorporated, 2019). Atherosclerosis is the chronic inflammation of arteries (Nabel & Braunwald, 2012) that results from damage to the endothelial cells of the blood vessels (Hall, 2011), in this case the coronary arteries around the heart. Adults often develop some coronary atherosclerosis in their early years of life (Gould et al., 2013) but it usually takes decades for the disease to progress to a stage where patients experience any symptoms (Sanchis-Gomar et al., 2016). Cardiovascular ischemic events often do not appear until men are in their fifties and women are in their sixties (Sayols-Baixeras et al., 2014). More recently it was shown to take even longer: the average age for a first heart attack is 65,6 years for males and 72 years for females (Benjamin et al., 2019).

The disease begins when large quantities of cholesterol are deposited underneath the endothelium of an artery (Hall, 2011) thereby causing thickening of the intramural layer of the artery. This cholesterol deposition and intramural thickening results in a fatty streak developing throughout the artery. Plaques, also known as atheromas, start to develop in "patches" at many points throughout the artery. These plaques consist of inflammatory cells, smooth muscle cells, fibrous connective tissue cells and lipids (Aziz & Yadav, 2016). These plaques can be obstructive or non-obstructive. Obstructive plaques lead to impaired blood flow through the artery as seen in Figure 2-1 (Maddox et al., 2014) causing the muscle to suffer damage from lack of oxygen and nutrients.
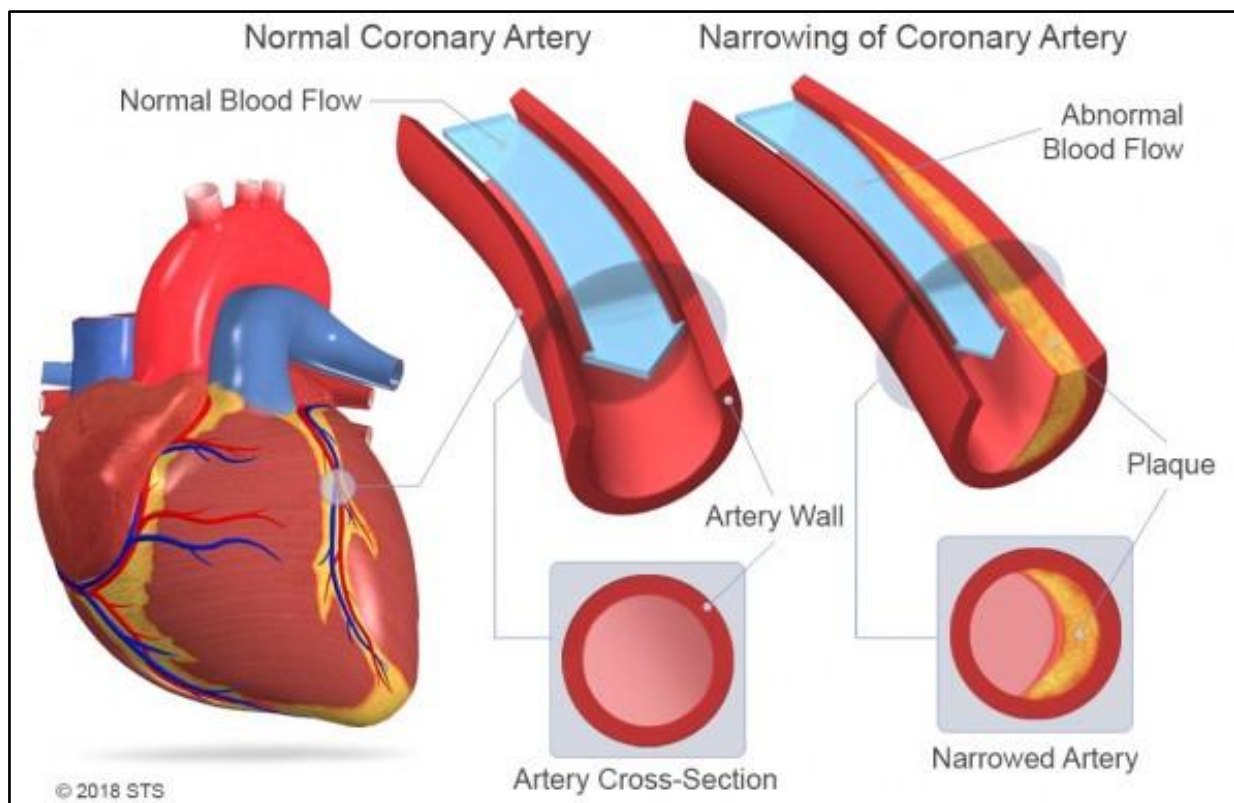
Figure 2-1: Comparison between normal artery and atherosclerotic artery. Adapted from Reddy & Grubb, 2018.

As atherosclerosis progresses over the course of decades, there is an ever-increasing reduction in the diameter of the artery and a resultant impairment of blood flow to the heart muscle. This leads to ischemic cardiomyopathy (heart failure) or, ultimately, a myocardial infarction (heart attack) due to a complete blockage of the blood vessel (Yayan, 2014). At certain points in the artery the atherosclerotic plaque can rupture and come into direct contact with the flowing blood. Platelets adhere to the site of rupture, fibrin is deposited and red blood cells are trapped leading to thrombus formation inside the vessel. The thrombus can occlude the vessel at the site of rupture, or break off and travel to a more distal (farther) part of the artery and occlude it at that point (Hall, 2011). This process is demonstrated in Figure 2-2.

Coronary occlusion causes prolonged ischemia of the myocardial cells, leading to myocardial cell death in as little as twenty minutes (Vojáček et al., 2013). If the blood flow is interrupted on a temporary basis it causes unstable angina (chest pain) and if it is interrupted on a permanent basis it causes a myocardial infarction (heart attack) (Nabel & Braunwald, 2012). Most myocardial infarctions

are caused by rupture of an unstable atherosclerotic plaque that then causes thrombosis and total occlusion of a coronary artery (Khamis et al., 2016). In America it is estimated that there is a myocardial infarction every forty seconds (Benjamin et al., 2019).
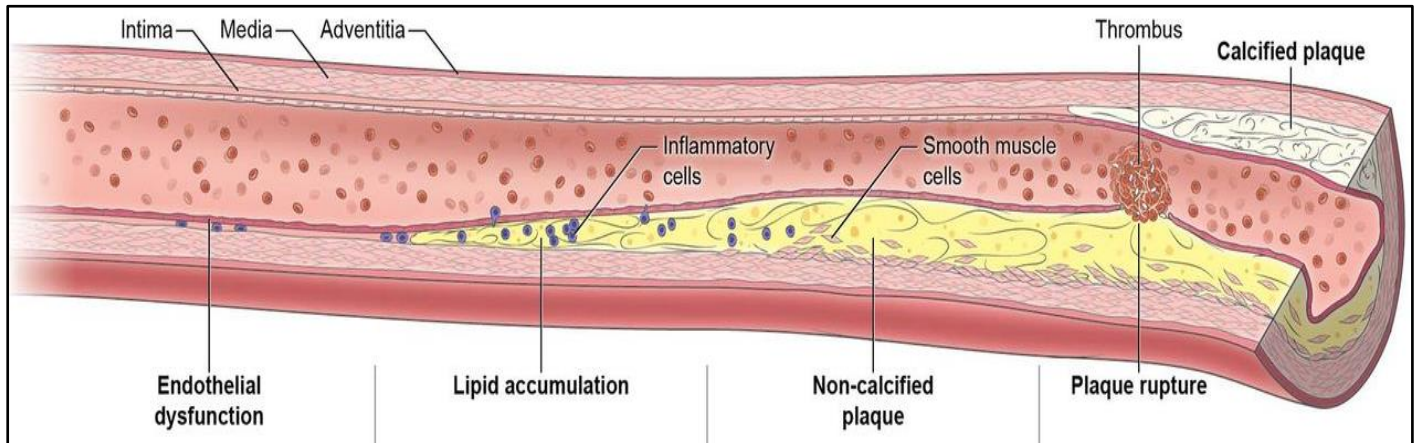
Figure 2-2: Progression of atherosclerosis. Adapted from Groenendyk & Mehta, 2018.

2.2. Symptoms of CAD

As described by Hall (2011), the main functions of the circulatory system i.e. the heart and blood vessels, are:

- Transport of nutrients, waste products and hormones to and from body tissues, and
- The general maintenance of an appropriate environment in all the tissue fluids of the body to ensure optimal survival and functioning of the cells.

If the circulation of blood in the coronary arteries is impaired a mismatch between oxygen demand and supply occurs which leads to chest pain and, possibly, heart failure: This is referred to as ischemic heart disease (IHD) or coronary insufficiency (Merriam-Webster Incorporated, 2019). IHD results from CAD. The symptoms of CAD can be classified into two groups: Stable angina, and acute coronary syndrome (ACS). ACS is a subcategory of CAD (Sanchis-Gomar et al., 2016) and the collective term used to describe unstable angina, Non-ST-segment Elevation Myocardial Infarction (NSTEMI), and ST-segment Elevation Myocardial Infarction (STEMI) (Yayan, 2014).

ST-segment elevation, or T-wave changes, are the earliest manifestations of myocardial ischemia on the electrocardiogram (ECG) (Vojáček et al., 2013). During a myocardial infarction myocyte cell death

occurs and certain biomarker proteins are released from inside the cells. These biomarkers include myoglobin, creatine-kinase MB, C-reactive protein and cardiac troponin (Fathil et al., 2015). Cardiac troponin (Troponin T and I) is a commonly-used marker of cardiac damage because it is highly specific and sensitive to heart cells (Garg et al., 2017). In short, the difference between STEMI and NSTEMI is as follows:

- During a STEMI the ECG shows elevation of the ST-segment, and blood tests are positive for cardiac markers.
- During a NSTEMI the ECG may show signs of ischemia such as ST-depression or T-wave changes, or it may be normal, while blood tests are positive for cardiac biomarkers (Daga et al., 2011).

Angina pectoris is chest pain that is pressure-like in nature (Moran et al., 2012) that occurs as a result of decreased myocardial blood flow, or subsequent myocardial cell death (Shah & Sikkel, 2013). In American adults the overall presence of angina is 3,6% in adults older than the age of 20 (Benjamin et al., 2019). Angina pectoris can be stable, meaning that it is induced by exertion, physical or mental stress; or unstable, meaning that it occurs at rest (Forouzanfar et al., 2012). Angina pectoris and the subsequent classification of ACS are depicted in Figure 2-3.
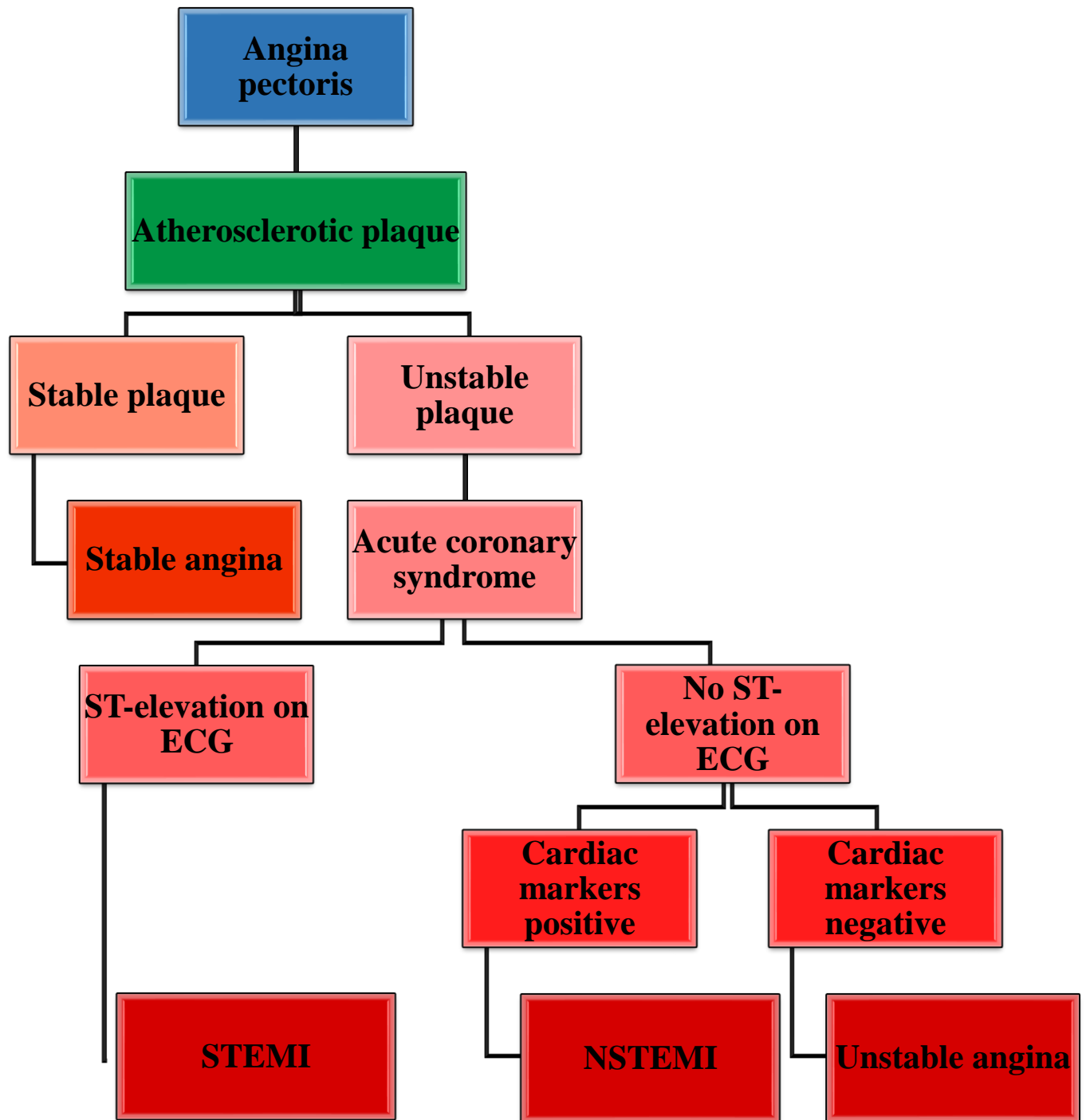
Figure 2-3: Angina pectoris and classification of acute coronary syndrome. Adapted from Pleister et al., 2013 and Ford et al., 2018.

2.3.   Risk factors associated with CAD

There are several, well-known risk factors that contribute to the development of CAD in adults (Nowbar et al., 2019) (Table 2-1). Estimates show that 47% of Americans have at least one key risk factor for CAD (Fryar et al., 2012; Benjamin et al., 2019). In SA these risk factors have been emerging in both rural as well as urban communities for several decades (Mayosi et al., 2009; Pretorius et al., 2011). Modifiable risk factors are those which the individual can change and therefore has control over; non-modifiable risk factors are those over which the individual has no control.

For this study emphasis was placed on the non-modifiable risk factors as outlined in Table 2-1.

Table 2-1: Risk factors for CAD. Adapted from Jaggi & Kearns, 2012; Yayan, 2014; Winham et al., 2014 and Nowbar et al., 2019.

Modifiable	Non-modifiable
Hypertension	Age (Males >45 years and females >55 years)
Hypercholesterolemia	Gender
Obesity (coupled with sedentary lifestyle)	Ethnicity/race
Diabetes Mellitus	Family history of CAD (genetic predisposition)
Smoking	

2.3.1. Non-modifiable risk factors

2.3.1.1.   Age

Merriam-Webster Incorporated (2018) defines age as "*an individual's development measured in terms of years*" A long lifespan is a non-modifiable risk factor that can increase the burden of cardiovascular disease (Nabel and Braunwald, 2012) because it causes loss of function in multiple systems of the body (Papadakis and McPhee, 2016). This is evident in the fact that the incidence of CAD increases with age, in both men and women (Keller and Howlett, 2016). The reason for this is that endothelial function progressively deteriorates the older a person gets and this causes increased stiffness of blood vessels

(Harvey, Montezano and Touyz, 2015). From 2005 to 2015, in both high and low income countries, the mortality rates of CAD increased with age (Nowbar et al., 2019).

Not only is age itself a risk factor for development of CAD, but the traditional risk factors are also independently associated with ageing (Yayan, 2014). This is observed in people over 60 years of age who develop a slight increase in systolic blood pressure (Hall, 2011), and in people who develop markedly increased amounts of epicardial adipose tissue as they age (Silaghi et al., 2008).

In Figure 2-4 one can see that the death rates for non-communicable diseases in SA gradually increases with age. It is predicted that an estimated 14.8% of the SA population will be older than 60 years of age in 2050 (United Nations Population Fund (UNFPA), 2012). This is worrisome because an ageing population might mean a higher burden of CAD and increased healthcare cost.
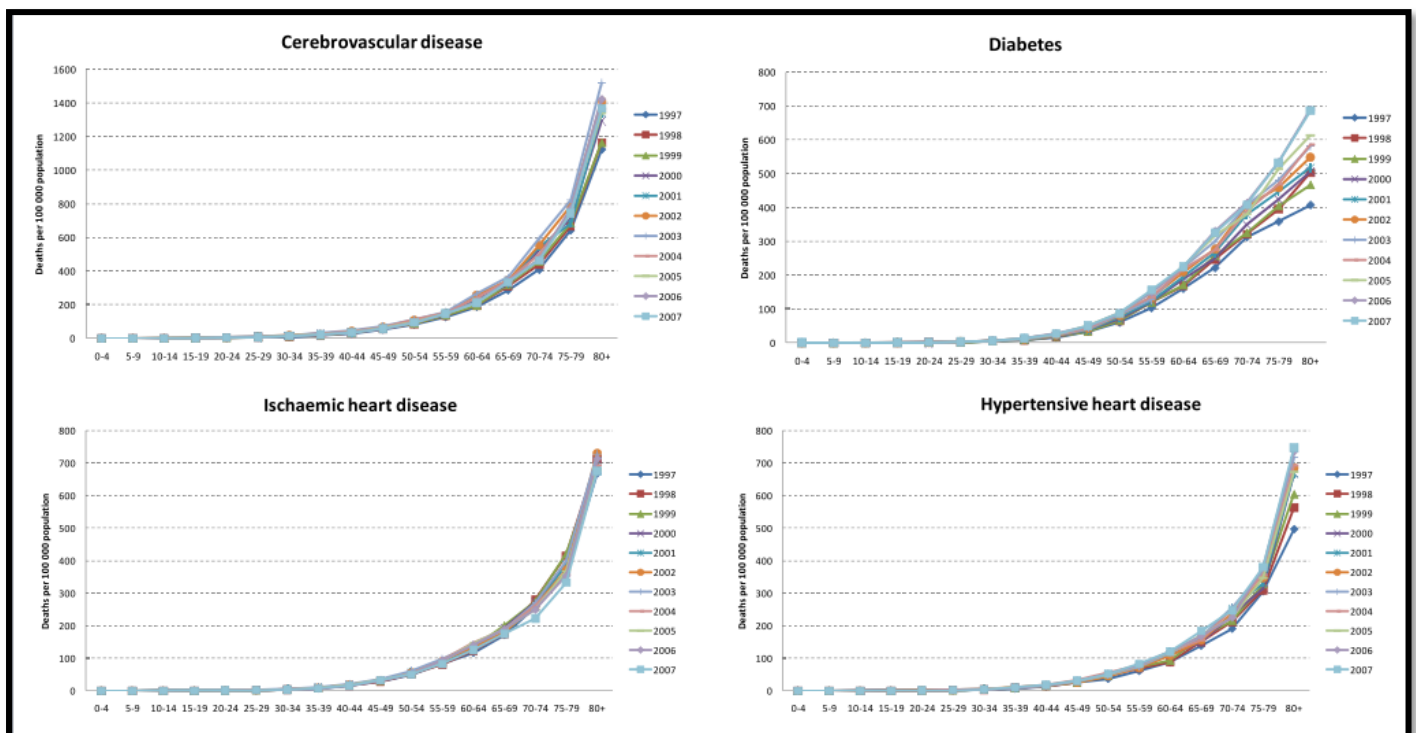

Figure 2-4: Age-specific death rates for non-communicable diseases in South Africa from 1997 to 2007, by age group. Adapted from Bradshaw et al., 2010.

2.3.1.2.   Gender

It has long been debated whether a person's gender predisposes them to higher risk for the development of CAD. It is known that CAD occurs more frequently in men than in women of all ages (Benjamin et al., 2019). Due to a particular combination of sex chromosomes as well as different levels of sex hormones between men and women there is a marked difference between males and females (Winham et al., 2014; Duda-Pyszny et al., 2018). Even the widths of the QRS complex (on the ECG) have been found to be different between men and women (Hnatkova et al., 2016). Therefore, it is only logical to deduce that there are differences in CAD between men and women.

Even though the systemic risk factors for CAD are very similar between men and women, the impact of the various risk factors on men and women are different (Yahagi et al., 2015). For example, it has been suggested that higher levels of testosterone can lead to reduced levels of atherosclerosis in men (Oskui et al., 2013). Men also tend to have a higher risk for obstructive CAD, while it is more likely caused by microvascular disease in women (Gulati et al., 2012). Another example is that women who suffer from diabetes are subject to a 40% greater risk of having a coronary heart disease incident than men with the same condition (Peters et al., 2014); additionally, women also have a much higher risk of losing more years of life after they had a myocardial infarction (Bucholz et al., 2015).

Arshad and Pasha (2013) carried out a study that analysed the variations in risk factor prevalence among men and women. Although they only studied hypertensive patients, they found that obesity was more common among women while smoking was more common among men. When looking at cholesterol, the "bad" low-density lipoprotein (LDL) cholesterol is lower in women than it is in men, until 50 years of age. After this age LDL gradually increases with age and this offers an explanation for the higher CAD incidence in older women (Yahagi et al., 2015). This is in agreement with the finding that women usually have better risk factor profiles when they are younger, but the opposite occurs when they age (Duda-Pyszny et al., 2018).

There are various explanations for differences in CAD between men and women, including different lifestyles and diets, different behaviours and differing attitudes with regards to prevention among men and women (Kautzky-Willer et al., 2016). No matter what the cause of the difference, it is important to keep in mind that there are special gender-related factors, such as pregnancy and menopause in women (Khamis et al., 2016; Benjamin et al., 2019) as well as the presence of oestrogen and other female reproductive hormones (Duda-Pyszny et al., 2018) that cause differences in CAD. Therefore, gender

should be considered as a risk factor on its own in order to develop a targeted approach for the optimal reduction of CAD among males and females.

2.3.1.3.   Ethnicity/Race

Ethnicity/race has been shown to influence the development of CAD (Winham et al., 2014). CAD has been a significant problem among certain SA population groups for a long time (Seedat et al., 1990). It is known that hypercholesterolemia occurs in about one of every 200 white Afrikaners (Steyn et al., 1996) and that the Indians of SA are more prone to IHD because they are more resistant to insulin than other population groups (Mayosi et al., 2009). Among black South Africans the leading risk factors for CAD are hypertension (40%), smoking (40%) and obesity (39%) (Brand et al., 2013).

In spite of these high risk factor percentages among black individuals, Mayosi et al. (2009) report that IHD still only accounts for about 10% of all heart disease, which makes it fairly uncommon. This is evident in the fact that white people in SA have a higher rate of clinically documented myocardial infarction than black people (Zhang et al., 2016). One possible explanation might be that black people metabolize homocysteine more effectively than white people (Ubbink et al., 1995).

In spite of CAD being reported as rare among African patients, the ACCESS (Acute Coronary Events – a Multinational Survey of Current Management Strategies) registry showed that (from January 2007 to January 2008) 10,7% of ACS patients in SA were of mixed ancestry and 5,9% were African (Schamroth, 2012). This seem to indicate that there is an upward trend in African patients with ACS and thus CAD.

Several physicians agree that the race of a patient is a very important factor in understanding disease risk and for the implementation of effective treatment strategies (Snipes et al., 2011). The differences among different population groups, i.e. racial and ethnic differences, should be taken into consideration when undertaking research (Karter, 2003), as this will lead to better understanding of the different pathophysiology mechanisms (in order to target treatment accordingly); it will also help minimise healthcare disparities among different racial groups (Taylor et al., 2005).

2.3.1.4.   Family history of familial hypercholesterolemia or CAD

Familial hypercholesterolemia is an inherited, or genetic, condition that leads to increased levels of LDL cholesterol which then increases the risk of early cardiovascular disease (Kandoria et al., 2017). Kulkarni (2015) found that a family history of early CAD is also a risk factor for developing CAD and actually

lowers the age of diagnosis. This is especially true if one has a first-degree relative who is affected by cardiovascular disease, the risk thereof being increased by 60% to 75%, as compared to the presence of cardiovascular disease in only a sibling, which typically represents a risk of 40% (Kolber & Scrimshaw, 2014). According to the Framingham Heart Study a family history of premature CAD should be considered as an independent risk factor for CAD when there is a diagnosis of CAD of a first degree relative at <65 years in men and <55 years in women (Dai et al., 2016).

Familial hypercholesterolemia among white Afrikaans-speaking communities in the South-Western Cape has been reported at about 1:87 (Jooste et al., 1986). A more recent study estimated the prevalence of familial hypercholesterolemia at the even higher rate of 1:72 (Steyn et al., 1996). In Johannesburg 1:5 patients with hypercholesterolemia had familial hypercholesterolemia (Seftel et al., 1980). A similar prevalence of 1:4 was found a few years later, even though the study only analysed patients undergoing CABG (Seftel et al., 1987). In the same year 1:10 young Afrikaners who had myocardial infarctions were found to have familial hypercholesterolemia (Wyndham et al., 1987). In spite of these findings, Pedoe (1980) argued that genetics should not be blamed for the high prevalence of hypercholesterolemia, but rather the lifestyle of the specific group and the presence of other common modifiable risk factors.

Even though the current statistics on this topic is scanty for SA the literature not only shows that familial hypercholesterolemia is a problem among white South Africans of Afrikaner descent (Delport, 2009), but that they are not the only group with a high prevalence of familial hypercholesterolemia. Due to founder effects in the SA population, Jewish South Africans of Lithuanian descent as well as Indian South Africans of Gujarati descent also have a higher prevalence of familial hypercholesterolemia (Blom, 2011).

The prevalence of a family history of CAD is not known for the public sector of central SA. Due to the fact that patients with a family history of CAD are usually associated with a higher incidence of atherosclerosis than their counterparts (Cohen et al., 2014), the prevalence of a family history of hypercholesterolemia or CAD was also documented for this study. As a first step in generating a body of research, this retrospective data analysis lead to new information about CAD risk factors among the different population groups that underwent coronary angiography in central SA in 2014 as compared to 1994, and demonstrated that there has been a change in the non-modifiable risk profile of these patients.

2.4. Prevention and treatment of CAD

2.4.1. Modifiable risk factor control

As early as 1948, during the Framingham Heart Study, the risk factors for CAD were identified and it was realized that this "lifestyle disease" could be prevented (Nabel & Braunwald, 2012). The most effective way of reducing adverse events due to CAD is by controlling the modifiable risk factors thereof (Gould et al., 2013). This is relatively manageable, and may be achieved by the adoption of a healthy, balanced diet, not smoking, daily physical activity and regular healthcare check-ups (Fuster & Kelly, 2010). In their study of 55 685 participants, Khera et al. (2016) found that by simply following a healthy lifestyle the risk for CAD was substantially reduced.

The prevention of CAD can also be attained by implementing public healthcare policies that has an impact on the population as a whole; examples are bans on smoking (Sayols-Baixeras et al., 2014) or the recent salt reduction policy that was implemented in SA in order to decrease hypertension (Watkins et al., 2016).

2.4.2. Medical therapy

The main medical approach to preventing CAD is statin drugs (Winham et al., 2014). These are lipid-lowering drugs that are safe as well as effective (Blom, 2011). However, it should be noted that the risk of developing CAD is not completely eliminated by statin therapy (Nabel & Braunwald, 2012). The medical treatment of patients with CAD aims to reduce the progression of the disease, stabilize atherosclerotic plaques as well as cardiac function, and to improve patient symptoms (Holmes & Herrmann, 2018). Additional drugs that can be used for the treatment of CAD include Angiotensin-Converting-Enzyme (ACE) inhibitors, beta-blockers and antiplatelet drugs such as aspirin and clopidogrel (Aziz & Yadav, 2016).

2.4.3. Coronary revascularization procedures

2.4.3.1. Cardiac Angiography

Coronary angiography is performed to assess the severity of CAD (Gould et al., 2013) (Figure 2-5) and done according to standard catheterization laboratory procedure (Kosova & Ricciardi, 2017): For left heart catheterizations arterial vascular access is obtained either through the femoral or radial artery

(Figure 2-5A). The brachial artery can also be used but is a less common pathway to access the heart. A catheter is then advanced through the chosen access site, into the heart (Figure 2-5B). Usually the catheter is advanced all the way into the left ventricle, unless there is a contraindication for crossing the aortic valve (such as aortic stenosis).

Once the catheter is in the left ventricle the internal cardiac pressure is recorded and contrast medium is injected under fluoroscopy. This is referred to as a ventriculogram and shows the contraction of the left ventricle. By measuring the chamber size during diastole as well as systole, the ejection fraction can be calculated. Wall motion abnormalities as well as the degree of mitral or aortic incompetence is also assessed during left ventriculography.

Thereafter the catheter is withdrawn, over the aortic valve, back into the aorta. The pressure in the aorta is also recorded and any difference in pressure (pressure gradient) between the left ventricle and the aorta is recorded. Pressure gradients exist when aortic stenosis is present.

Next the cardiologist engages the catheter in the ostium of the right and left coronary arteries, respectively. Although the sequence does not matter, some cardiologists prefer to start with the culprit artery that is causing the patient's symptoms. Contrast medium is then injected into the artery and any flow-limiting lesions is identified under fluoroscopy (Figure 2-5C).
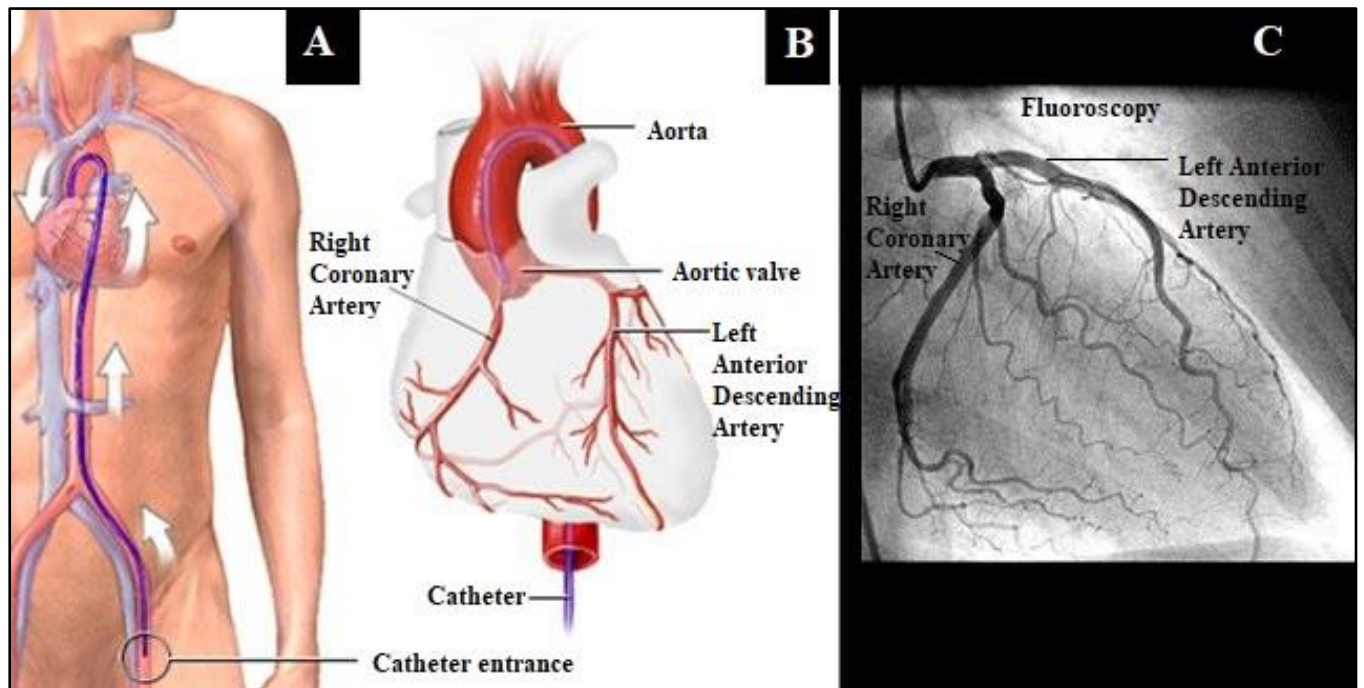
Figure 2-5: Angiogram procedure. Adapted from Kulathilake, 2017.

2.4.3.2. Percutaneous Coronary Intervention (PCI)

If there are obstructions present in the coronary circulation they can be opened in the catheterization laboratory (Nabel & Braunwald, 2012). This can be done by performing Percutaneous Transluminal Coronary Angioplasty (PTCA), or by placement of a stent. During PTCA a balloon-tipped catheter is advanced into the coronary artery, under radiographic guidance. The balloon is pushed through the obstruction until it straddles the partially occluded point. On inflation of the balloon the diseased artery is then stretched and blood flow through that point is increased.

Although effective, PTCA is not always sufficient to open a vessel. In some cases it is necessary to place a stent in the artery. This is a small tube-like mesh structure designed to hold the artery open. Metals used to make stents include stainless steel, cobalt-chromium, gold, and tantalum. Polymers such as silicone and polyurethane can also be used. A stent is deployed in a similar manner as the PTCA balloon. Percutaneous coronary stent placement can be seen in Figure 2-6. The collective term for PTCA and stent placement in a coronary artery is PCI, or Percutaneous Coronary Intervention (Hall, 2011) For patients with one or two diseased coronary arteries that does not involve the proximal left anterior descending (LAD) artery, PCI is usually the preferred option (Holmes & Herrmann, 2018).
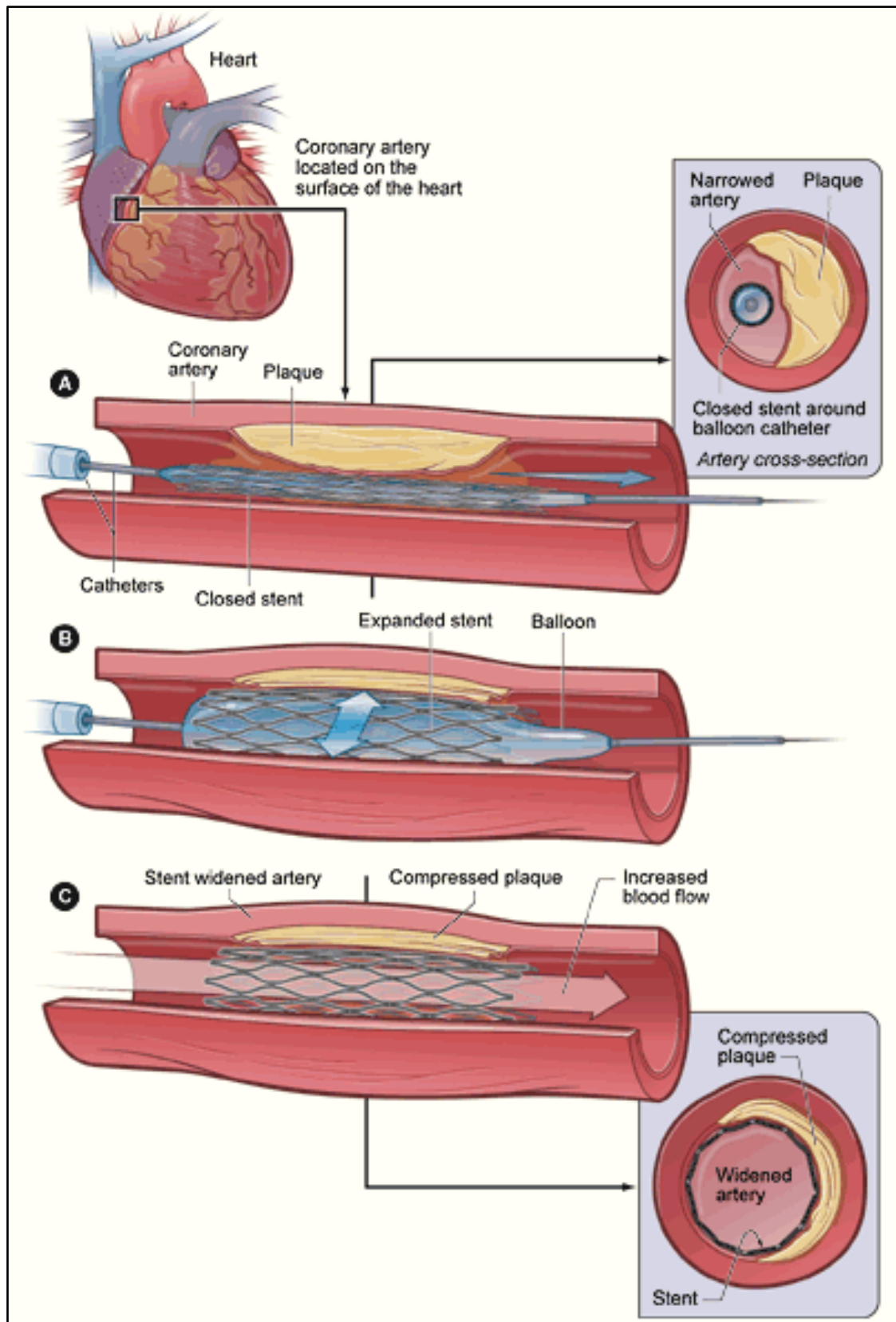
Figure 2-6: Coronary artery stent placement. Adapted from Reddy & Grubb, 2018.

2.4.3.3.   Coronary artery bypass graft (CABG) surgery

Coronary artery bypass graft (CABG) surgery is performed in patients who have severe coronary artery obstruction and who are not eligible for PCI. A graft vessel such as a leg vein is grafted onto the aorta and anastomosed onto the coronary artery distal to the obstruction. This is done to shunt or bypass blood around the obstruction and increase blood flow to the myocardium (Merriam-Webster Incorporated, 2019). According to Rahman et al. (2017), the indications for CABG surgery include:

- Triple vessel disease (with left ventricular ejection fraction <50%
- Left main stem stenosis ≥50%
- At least 70% stenosis in proximal Circumflex and LAD (also known as left main equivalent)
- Where a large area of heart muscle is at risk with only single or double vessel disease
- Debilitating angina despite optimal medical therapy
- Subacute (>12 hours) unstable angina, STEMI or non-Q-wave myocardial infarction when ischemia is ongoing and cardiogenic shock is present despite maximal non-surgical therapy (such as intravenous thrombolytics and primary PCI).

CABG surgery is preferred in patients who have two – or three vessel disease with left main disease and a SYNTAX (The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery trial) score greater than 32 (Mohr et al., 2013). The SYNTAX score is a tool used to determine which patients may benefit from CABG as opposed to PCI, by quantifying the extent of CAD (Yerokun et al., 2016). Patients who have intermediate or high SYNTAX scores (therefore complex CAD) usually benefit more from CABG, while patients with low SYNTAX scores (less complex CAD) can be treated with PCI, although repeat revascularization might be necessary for future treatment (Head et al., 2014). CABG should be combined with medical therapy to achieve better long term patient outcome (Velazquez et al., 2016).

With this retrospective data analysis, the hope was to determine if there were any changes/improvements in the treatment modalities used to treat patients with CAD in 2014 as compared to 1994.

2.5. World figures on CAD

According to the WHO, in 2015 there were a total of 56.4 million deaths worldwide. An astounding 15 million (26.6%) of these deaths were caused by IHD (caused by CAD) and stroke (Figure 2-7) (World Health Organization, 2015). Even though mortality trends show that there might be some variability within broad geographic regions (Moran et al., 2012) and that mortality rates in Western countries have gradually declined over the last few decades, there are still 15.5 million people (20 years and older) who live with CAD in the United States of America alone. To put in it another way, CAD causes about one-third of all deaths in adults (Sanchis-Gomar et al., 2016).
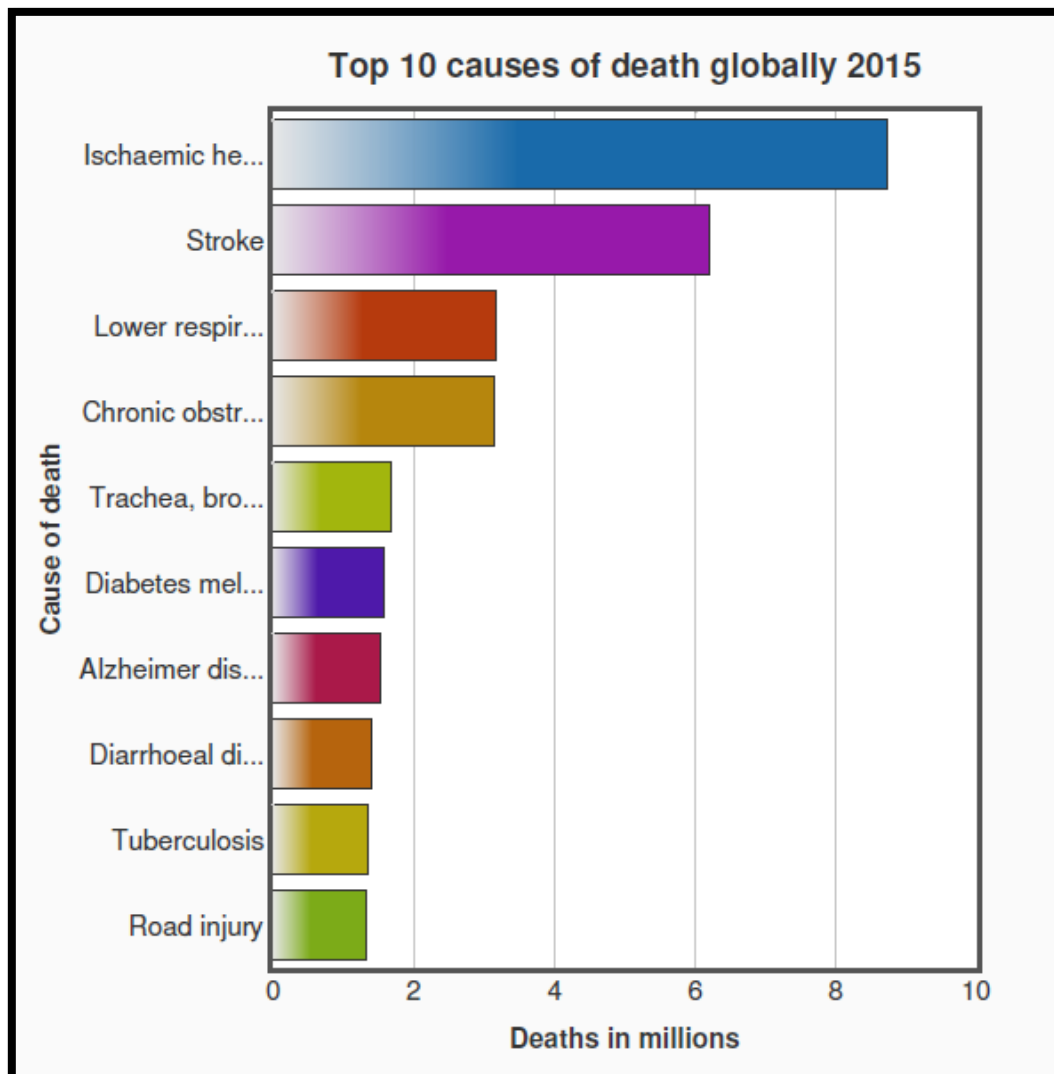
Figure 2-7: Top 10 causes of death globally 2015. Adapted from: http://www.who.int/mediacentre/factsheets/fs310/en/

In metropolitan France acute myocardial infarction (STEMI + NSTEMI) cases rose from 15 per 10^4 (10 000) in 2009 to 19.8 per 10^4 in 2014 for men and 6.3 per 10^4 to 8 per 10^4 for women (Pinaire et al., 2019). Singapore saw in increase in STEMI incidence among Malay patients from 97 per 100,000 population in 2007 to 114 per 100,000 population in 2014 (Zheng et al., 2019). Across Europe CAD accounts for 1.8 million (±45%) of the more than 4 million deaths caused by cardiovascular disease each year (Townsend et al., 2016). The Euro Heart Survey on Acute Coronary Syndromes (EHS-ACS-II) also reported a 5% rise (from 42% in 2000 to 47% in 2004) in STEMI among ACS patients (Mandelzweig et al., 2006).

In India the situation is even more grave, with IHD and stroke together causing 83% of cardiovascular deaths, and with IHD being more predominant than stroke (Prabhakaran et al., 2016). From 2007 to 2009, in Kerala (India), more patients presented with STEMI (37%) than NSTEMI (31%), or unstable angina (32%) (Mohanan et al., 2013).

In other developing countries such as Egypt and Pakistan, CAD is also reported to be on the rise (Sriharibabu, 2016; Prabhakaran et al., 2018). There are also upward trends in other developing countries. Between 1984 and 1999 Beijing's coronary heart disease mortality rates increased by 27% in women and a staggering 50% in men (ages 35 to 74 years) (Critchley et al., 2004).

From these figures one can see that CAD is a major problem worldwide, but what does the situation look like in Africa?

2.6.   African figures of CAD

Figure 2-8 indicates that IHD as a cause of death is by far much higher in North Africa and the Middle East, when compared to other regions of the world (Almahmeed et al., 2012). From 1997 to 2009 Tunisia experienced increased CAD mortality rates of 11,8% in men (from 70 to 87 deaths per 100,000) and 23,8% in women (from 28 to 41 deaths per 100,000) (Saidi et al., 2013).
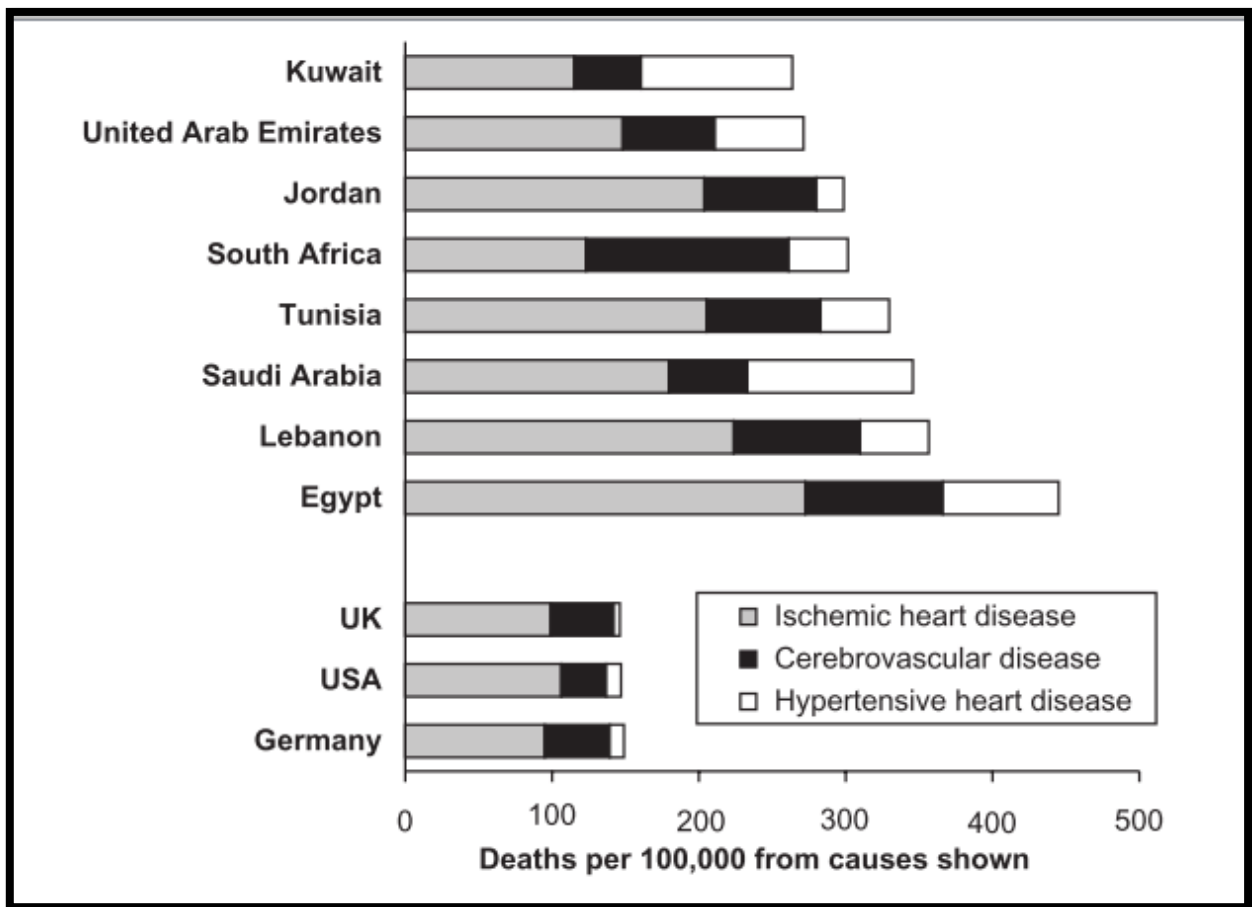
Figure 2-8: Death rates from cardiovascular disease in selected countries in Africa and the Middle East. Adapted from Almahmeed et al., 2012.

When looking at a figure of the proportion of years of life lost (YLL)[1] due to IHD (Figure 2-9) one can see that it was one of the leading causes of premature deaths in North Africa and the Middle East (Roth et al., 2015). Popkin, Adair and Ng (2012) attribute these high figures to a change in dietary habits (from a traditional diet to one of more processed foods which are higher in calories) that leads to an increase in obesity. Another reason for this might be that the prevalence of smoking is widespread in the general population of the Middle East as well as North Africa, as found by Alzaabi et al. (2017), even though their study was not conducted to evaluate the incidence or risks for CAD.

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[1] Years of life lost (YLL) is a measure of premature mortality calculated across countries. using a normative goal for survival computed from the lowest observed death rate

In Figure 2-9, Roth et al. (2015) also demonstrate that the proportion of years of life lost in Sub-Saharan Africa due to IHD is relatively low compared to North Africa and the Middle East. This is supported by Forouzanfar et al. (2012) who also reported that IHD in the southern regions of Africa is quite rare. The difference between the figures in the northern regions of Africa and the southern regions might be because people who live in northern parts of Africa are wealthier and have a higher life-expectancy than those living in other regions of Africa (The World Bank, 2018). Another reason may be that it is not so much IHD that drives cardiovascular disease mortality in sub-Saharan Africa, but rather hypertension that leads to hypertensive heart disease (Fuster & Kelly, 2010). In 2001, Sub-Saharan Africa was one of only two world regions where IHD was not the leading cause of death (Finegold et al., 2013).

There is, however, a significant problem when comparing IHD figures between North – and Southern Africa: Epidemiological data in the southern regions of Africa, is scanty and aged, and the majority of this regions' estimates comes from SA alone (Moran et al., 2012).

Another plausible explanation for the lower IHD figures in Sub-Saharan Africa is that people in this region tend to have a shorter life expectancy and are therefore not at risk for CAD (Steyn et al., 2005). In spite of this, data suggests that the incidence of heart diseases normally thought of as "Western diseases", such as CAD, is on the rise throughout Africa (World Health Organization African Regional Office, 2006). This was seen in Accra, the capital of Ghana, where cardiovascular diseases (including CAD) rose to being the leading cause of death in 1991 and 2001 after being in seventh place in 1953 and tenth place in 1966 (Agyei-Mensah & De-Graft Aikins, 2010). The incidence of CAD is still low in Nigeria, but also on the rise (Essien et al., 2014). CAD incidence will continue to rise with the age-standardised mortality rates[2] increasing with 74% in African men and 70% in African women by the year 2030 (Onen, 2013). In fact, CAD is predicted to be one of the leading causes of morbidity and mortality by 2020 for most developing nations (Celermajer et al., 2012), which includes those on the African continent.

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[2] The age-standardized mortality rate is a weighted average of the age-specific mortality rates per 100,000 persons, where the weights are the proportions of persons in the corresponding age groups of the WHO standard population.
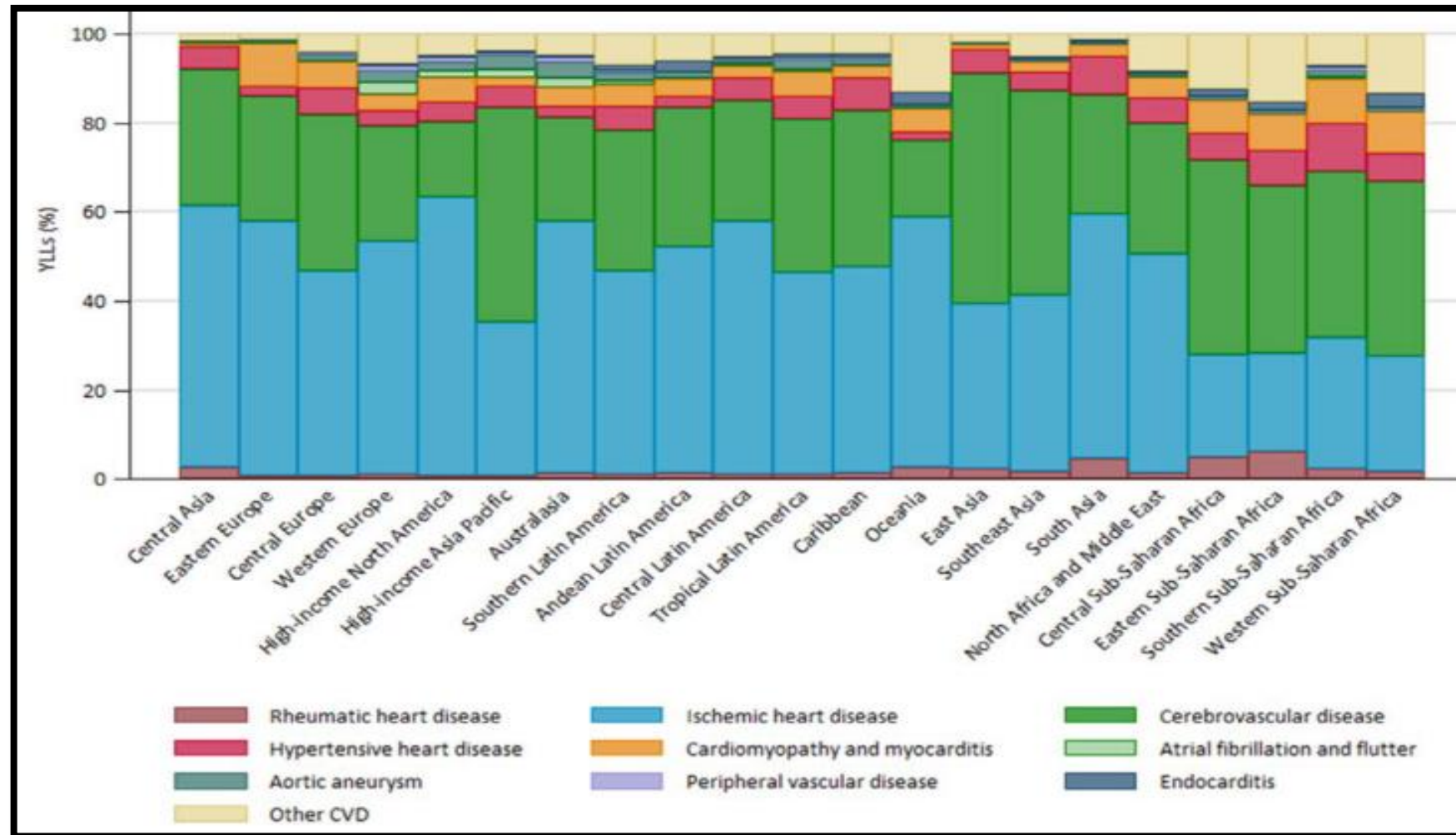
Figure 2-9: Proportion of years of life lost (YLL) due to cardiovascular disease in 2013, stratified by global region. Adapted from Roth et al., 2015.

2.7. Lack of epidemiological data from Southern Africa

Geographically speaking, the Southern region of Africa can be divided into two large countries (Botswana and Namibia), both with small populations, and the two small kingdoms of Swaziland and Lesotho. These are surrounded by SA which is the wealthiest country with the highest population in the entire region (Keates et al., 2017). Since the end of Apartheid in 1994, SA has undergone a relatively peaceful transition to a constitutional democracy (Mayosi & Benatar, 2014). However, social disparity still exists, as many households do not yet have access to basic services such as healthcare and clean water (Kahn et al., 2012; Padayachee & Desai, n.d.).

SA has also seen a very interesting fluctuation in life expectancy[3] over the past six decades. In 1960 the average life expectancy was 52 years of age. This figure increased steadily, to 62 years of age in 1990. Thereafter it plummeted back to 52 years of age in 2005, from where it has climbed steeply back to 62 years of age in 2015, as depicted in Figure 2-10 (The World Bank, 2018). The reason for this sudden drop in life expectancy may be that in 2007, an estimated 5.7 million adults and children in SA were living with Human Immunodeficiency Virus (HIV) (The Joint United Nations Programme on HIV/AIDS & World Health Organization, 2008). The subsequent rise in life expectancy since that time is largely due to the increased availability of antiretroviral medication to HIV positive individuals, according to Statistics SA's statistician general, Pali Lehohla (British Broadcasting Corporation (BBC) News, 2014).

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[3] Life expectancy at birth indicates the number of years a new-born infant would live if prevailing patterns of mortality at the time of its birth were to stay the same throughout its life.
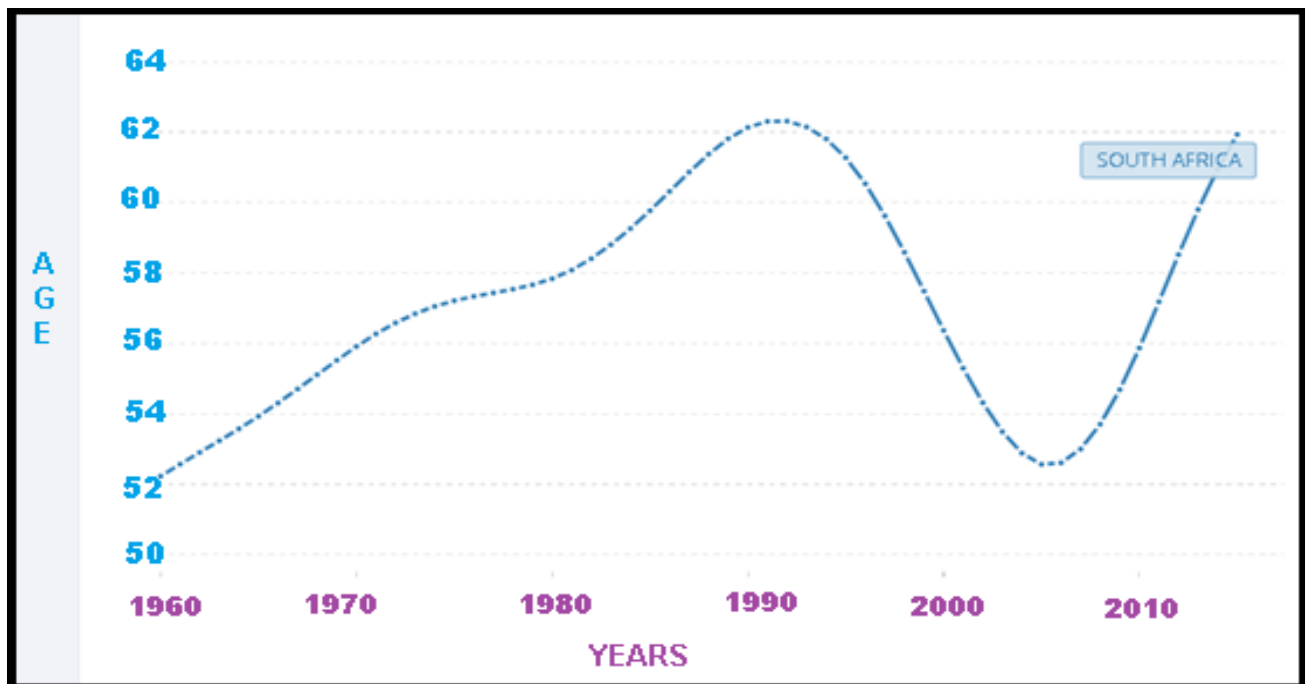
Figure 2-10: Life expectancy trend in South Africa. Adapted from:
https://data.worldbank.org/indicator/SP.DYN.LE00.IN?end=2015&locations=ZA&start=1960&view
=chart

Even though accessibility to anti-retroviral treatment has improved tremendously, SA is overburdened with infectious diseases, while at the same time seeing a rise in non-communicable diseases which are mainly due to an aging population and the increased prevalence of hypertension (Bradshaw et al., 2003; Mayosi et al., 2009).

Ntsekhe and Mayosi (2009) concluded that CAD is not a significant problem for individuals who live with HIV, in Sub-Saharan Africa. The major problem with this is that the weight loss and early mortality associated with HIV (Almahmeed et al., 2012) can ultimately mask the risk factors[4] for CAD (Houle et al., 2014); as a result a chronic disease like this will not be given a very high priority or adequate resources in the healthcare sector (World Health Organization African Regional Office, 2006), making CAD seem like an unimportant problem.

The sad fact is that because atherosclerosis takes a long time to develop and does so silently (Sayols-Baixeras et al., 2014), and because anti-retroviral treatment campaigns are affective in further reducing

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[4] See 2.3.   Risk factors associated with CAD.

HIV mortality rates, SA's non-communicable disease burden will continue to rise (Mayosi & Benatar, 2014) and Mayosi et al. (2012) reports that SA's exposure to modifiable risk factors for cardiovascular disease is indeed rising. It is also clear that the healthcare sector are aware of this health transition that is taking place, but not much is known regarding the consequences thereof (Gómez-Olivé et al., 2018). For this reason empirical research is of vital importance, especially at local, national and regional levels (Houle et al., 2014).

2.7.1. Lack of epidemiological data from central South Africa

Though most of the estimates for IHD in Sub-Saharan Africa come from SA alone (Moran et al., 2012)[5], while reviewing the literature it was found that there is significant lack of data from SA, and especially from central SA. This is evident in the fact that the last data, regarding SA's IHD mortality figures, was submitted to the WHO in 2009! That is ten years ago, and the reason for this is not known (Nowbar et al., 2014). Mayosi et al. (2009) also found that data needed to track the prevalence of different risk factors for non-communicable diseases in SA, such as IHD, is scant indeed.

When searching for publications regarding central SA's IHD situation, the results are disappointing and unsatisfactory. For the last three decades only a limited number of journals have published studies related to the risk factors for IHD in SA could be identified, and three of these were published before 1994, as shown in Table 2-2[6]. One recent study that could be found showed that in Durban, from 2008 to 2012, a staggering 83% of acute myocardial infarctions among black African patients were caused by STEMI and only 17% by NSTEMI (Masina et al., 2016). Another recent study showed risk factor increases of epidemic proportions in the Indian population of Durban, with high prevalence of hypertension (47.5%), diabetes mellitus (20.1 %) and total body obesity (raised body mass index) (32.4%) (Prakaschandra et al., 2016). This emphasises the need for research into similar trends in central SA.

Sliwa et al. (2008) attributes the rise in non-communicable diseases, or epidemiological transitioning, to SA's extreme population diversity that ranges from industrialized cities, where people follow an urban lifestyle, to rural regions where people lead more traditional lives. Persons living in rural areas

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[5] See 2.6.   African figures of CAD

[6] Only publications that came out of SA itself were included. Publications before 1990 were not included.

tend to be more physically active as a part of their daily living (farming, performing their own housework, walking longer distances between destinations etc.) and they tend to eat healthier food (less processed food that does not contain artificial preservative substances, or food that is often grown by the consumers themselves). Those who become urbanised, however, often replace these salutary habits with a diet of sugary, salty and fatty foods, and tend to settle into sedentary jobs (World Health Organization African Regional Office, 2006).

Table 2-2: Summary of publications from South Africa related to this study.

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Seedat et al., 1990	Risk factors for coronary heart disease in the Indians of Durban	1990	In a study of 778 subjects aged 15 - 69 years (408 men), 15,3% (sex and age adjusted 13,4%) had a history of CHD. The important risk factors in men were hypercholesterolaemia, hypertriglyceridemia, diabetes, and smoking, and in women diabetes, hypercholesterolaemia, and hypertriglyceridemia. This study showed that the risk factors leading to coronary heart disease in Indians were similar to the Afrikaans-speaking whites, except that diabetes was common in the Indian population. **A positive history of CHD was obtained from 12% of the men and 18,9% of the women, i.e. 15,3% of respondents in the total sample.**	
Venter et al., 2015	Autopsies performed at Universitas Academic Hospital, South Africa, 1990–2010, and perceptions and opinions of health professionals on the importance of autopsies in modern medicine	1990 - 2010	The percentage of deaths caused by the cardiovascular system decreased from 12% in 1990 to 3% in 2010. **Prevalence of CAD not addressed in this study.**	The nature of the cardiovascular disease is not reported
Steyn et al., 1991	Risk factors for coronary heart disease in the black population of the Cape Peninsula. The BRISK study.	1991	Percentages of deaths from IHD in the Cape Peninsula (15 - 64 years) were as follows: 22,5% for males and 13,3% for females. Among males the bulk of the risk was due to the smoking of cigarettes, while among females the biggest contribution to the risk profile was made by hypertension. **IHD accounted for 22,5% of deaths in males and 13,3% of deaths in females.**	Absolute rates could not be calculated because of considerable uncertainties about the true size of the black population.

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Steyn et al., 1992	The impact of chronic diseases of lifestyle and their major risk factors on mortality in South Africa	1992	**IHD caused 8.7% of all deaths and 9.6% of deaths in individuals between the ages of 35 and 64.** Out of the total of 4.88 million smokers throughout SA, the largest group of was black males (2.6 million). For hypertension, 5.5 million South Africans had blood pressures above 140/90 mmHg and again the largest group was black people (3.0 million). 4.8 Million South Africans had hypercholesterolemia and 3.1 million South Africans had raised LDL cholesterol levels, with black individuals having the lowest levels.	The results were based on the size of the SA population recorded in the 1985 census figures
Mollentze et al., 1995	Coronary heart disease risk factors in a rural and urban Orange Free State black population	1995	The age- and sex-adjusted prevalence of hypertension were 29% in QwaQwa and 30,3% in Mangaung. Diabetes was present in 4,8% of the QwaQwa sample and 6% of the Mangaung sample. The prevalence of heavy smoking in the Mangaung sample was almost double that of the QwaQwa sample and mostly confined to men. **The incidence of CAD was not assessed, only the risk factors for CAD, but according to Walker and Walker (1985) incidence of CAD was estimated at 10 per 100 000 for the population of Soweto.**	Risk factors were only evaluated in individuals of 25 years and older
Ubbink et al., 1995	Effective homocysteine metabolism may protect South African blacks against coronary heart disease	1995	Blacks metabolized homocysteine more effectively than did whites, which may partly explain their relative resistance against coronary heart disease despite a high prevalence of obesity, hypertension, and smoking. **The prevalence of CHD was not assessed, but this study was done on the assumption that CHD in the SA black population is rare, despite widespread westernization.**	The study samples were very small in whites (n = 18) as well as blacks (n = 12).

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Metcalf et al., 1996	Design and baseline characteristics of a hypertension intervention program in a South African village	1996	The age-adjusted prevalence of hypertension in people aged 15 years or more was 13.9% in men and 16.3% in women. **The prevalence of CAD was not assessed in this study.**	This survey only assessed a rural community of Mamre, located in the Western Cape.
Steyn et al., 1996	Estimation of the prevalence of familial hypercholesterolaemia in a rural Afrikaner community by direct screening for three Afrikaner founder low density lipoprotein receptor gene mutations	1996	There are about 112 000 familial hypercholesterolemia patients in the country who are underdiagnosed as a group and therefore not receiving the care that would help to reduce the burden of familial hypercholesterolemia-associated IHD in SA. **This study did not assess the prevalence of CAD.**	This study only assessed white, Afrikaans speaking individuals.
Walker & Sareli, 1997	Coronary heart disease: Outlook for Africa	1997	**In the urban African population CHD is rare (±0.2%of the roughly 20000 deaths occurring annually in Soweto).** However, there is a rising prevalence of virtually all risk factors for the disease.	
Sitas et al., 2004	Tobacco attributable deaths in South Africa	1998	In 1998, about 8% of all adult deaths in SA (more than 20 000 deaths a year) were caused by smoking. About 8% of adult deaths (21 500 deaths per year) in SA could be attributed to smoking. **IHD comprised about a third of all vascular deaths.**	
R Norman, Bradshaw, Schneider, et al., 2007	A Comparative Risk Assessment for South Africa in 2000: Towards Promoting Health and Preventing Disease	2000	**IHD (as a condition) was the cause of 6.6% of all deaths in 2000.** Deaths attributable to risk factors were as follows: Hypertension 9%, Smoking 8.5%, Excess body weight 7.0%, High cholesterol 4.6%, Diabetes 4.3%.	Data reported for the whole of SA, although there might be differences in risk profiles for different sub-populations.

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Bradshaw et al., 2007	Estimating the burden of disease attributable to diabetes in South Africa in 2000	2000	Of South Africans aged >30 years, 5.5% had diabetes which increased with age. Overall, about 14% of IHD, 10% of stroke, 12% of hypertensive disease and 12% of renal disease burden in adult males and females (30+ years) were attributable to diabetes. **This study focused on diabetes and did not assess the prevalence of IHD itself, but found that 14% of IHD was caused by diabetes.**	Study only evaluated persons of 30 years and older.
Norman et al., 2007	Estimating the burden of disease attributable to high blood pressure in South Africa in 2000	2000	42% of IHD in males and females older than 30 years were attributable to high blood pressure (systolic BP >115mmHg). **This study focused on hypertension and did not assess the prevalence of IHD itself, but found that almost half of IHD was caused by high blood pressure.**	
Norman, Bradshaw, Steyn, et al., 2007	Estimating the burden of disease attributable to high cholesterol in South Africa in 2000	2000	Overall; about 59% of IHD and 29% of ischemic stroke burden in adult males and females (30+ years) were attributable to high cholesterol (>3.8 mmol/L) with marked variation by population group. **This study focused on high cholesterol and did not assess the prevalence of IHD itself, but found that high cholesterol contributed significantly to the IHD burden.**	
Joubert et al., 2007	Estimating the burden of disease attributable to physical inactivity in South Africa in 2000	2000	Overall, in adults ≥ 15 years in 2000, 30% of IHD were attributable to physical inactivity. Compared to the global average, SA adults had a particularly high prevalence of physical inactivity. **This study focused on physical inactivity and did not assess the total prevalence of IHD itself, but found that physical inactivity caused one third of the IHD burden.**	

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Joubert et al., 2000	Ischaemic Heart Disease in Black South African Stroke Patients	2000	Coronary vessel stenosis of >50% was observed in >1 of the coronary arteries in over half of all necropsy patients examined, and 17.4% had histological evidence of previous myocardial infarction. **The prevalence of CAD in black African stroke patients was significantly higher than has been documented in the general non-stroke black population as well as in stroke patients.** Black stroke patients may have a risk for CAD similar to that of their white counterparts.	This study only examined CAD in stroke patients.
Bourne et al., 2002	Where does the black population of South Africa stand on the nutrition transition?	2002	31.8% of African women were obese (body mass index (BMI) $\geq$ 30 kg/m²) and a further 26.7% were overweight (BMI $\geq$ 25 to ,30 kg/m²). The obesity prevalence among men was 6.0%, with 19.4% being overweight. The national prevalence of hypertension in blacks was 24.4%, using the cut-off point of 140/90mmHg. **This study did not focus on the prevalence of IHD, but rather on selected risk factors related to the emergence of non- communicable diseases in the black population of SA**	Only black adults over the age of 15 years were examined
Department of Health et al., 2007	South Africa Demographic and Health Survey 2003	2003	12.5% of men and 17.9% of women were hypertensive and more than 70% of hypertensive patients in SA has uncontrolled hypertension. 35% of men and 10% of women smoke cigarettes either daily or occasionally. **IHD self-reported prevalence in men was 6% while the self-reported prevalence among women was 8% (Because the prevalence of IHD is usually higher in men than in woman, this may be indicative of the inaccuracy of self-reported IHD. It is also possible that IHD is interpreted more so by female than male older respondents to mean 'all heart disease'.).** **A family history of IHD was reported by 11 percent of men and 14 percent of women, a slight decrease from the 1998 figures of 13 and 16 percent respectively.**	

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Alberts et al., 2005	Prevalence of cardiovascular diseases and associated risk factors in a rural black population of South Africa	2005	A sample of 1608 women and 498 men aged 30 years and above participated in the study. There was a high prevalence of tobacco use for men (57%) and women (35.4%). 51.7% of women were either overweight or obese. Diabetes was diagnosed in 8.8 and 8.5% of women and men, respectively. Hypertension (blood pressure >140/90mmHg) was found in 25.5% of women and 21.6% of men. **The data presented in this study did not focus on the prevalence of IHD, but have highlighted the finding that even rural black people in SA have a cardiovascular disease risk profile that predisposes them to the emergence of atherosclerosis and related chronic diseases.**	Study done in a rural adult black population from Limpopo Province. This study did not include a dietary survey to determine whether the results were due to eating habits.
Rosana Norman et al., 2007	Estimating the burden of disease attributable to high blood pressure in South Africa in 2000	2007	50% of stroke, 42% of IHD, 72% of hypertensive heart disease and 22% of other cardiovascular diseases in males and females >30 years of age were caused by systolic blood pressure ≥115mmHg. **Although this study did not focus on the prevalence of IHD, it did find that 42% of IHD was caused by a systolic blood pressure of >115mmHg in adults older than 30 years.**	Only adults ≥30 years of age were studied
Prakaschandra et al., 2016	High prevalence of cardiovascular risk factors in Durban South African Indians: The Phoenix Lifestyle Project	2007 – 2008	There was high prevalence of hypertension (47.5%), diabetes mellitus (20.1%) and total body obesity (raised body mass index) (32.4%), as well as increased waist circumference (73.1%). Over half of the males and 14.6% of females were current smokers. **This study did not focus on the prevalence of IHD.**	There were low response rates of male participants.
Bärnighausen et al., 2008	Hiding in the shadows of the HIV epidemic: Obesity and hypertension in a rural population with very high HIV prevalence in South Africa	2008	From 2003 to 2004, in rural uMkhanyakude, KwaZulu-Natal, the crude prevalence of obesity and hypertension was 32% and 33% respectively, despite a very high HIV prevalence. The percentage of overweight people was 58%. **This study did not focus on the prevalence of IHD.**	This study was conducted at a time when antiretroviral treatment was not yet widely available in SA, except to the few people able to afford private care.

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Sliwa et al., 2008	Spectrum of heart disease and risk factors in a black urban population in South Africa (the Heart of Soweto Study): a cohort study.	2008	Prevalence of cardiovascular risk factors was very high, with 56% of patients diagnosed with hypertension (44% of whom were also obese). Only 13% of patients had no identifiable risk factors, whereas 59% had several risk factors. **Out of the total 1593 new cases of cardiovascular disease, 165 patients had CAD (10%) and 28 had CAD without risk factors (17%). Black Africans were far less likely to be diagnosed with CAD than were all other racial groups (77 [6%] vs 88 [38%]). Proportionately fewer women than men were diagnosed CAD (68 [7%] vs 97 [15%]).**	Since not all patients being managed by the cardiology unit were captured by the registry, selection bias might exist
Erasmus et al., 2012	High prevalence of diabetes mellitus and metabolic syndrome in a South African coloured population: Baseline data of a study in Bellville, Cape Town	2008 – 2009	This study showed a crude prevalence of 28.2% of type 2 diabetes in an urban community of Bellville South, Cape Town. **This study did not focus on the prevalence of CAD.**	The nature of this study is cross-sectional, with high female-to-male participation, which is a common trend in SA population studies.
Masina et al., 2016	Risk factor assessment in South African Black patients presenting with acute myocardial infarction at R.K. Khan Hospital, Durban	2008 – 2012	The majority presented with ST-elevation myocardial infarction (STEMI) (83%) whilst 17% had Non-ST-Elevation Myocardial Infarction (NSTEMI). Smoking (48%) and hypertension (46%) were the most commonly observed risk factors.	Only patients with acute myocardial infarction who were of Black SA origin (n=94) were analysed.
Mayosi et al., 2009	The burden of non-communicable diseases in South Africa	2009	Non-communicable diseases are emerging in both rural and urban areas, most prominently in poor people living in urban settings, and are resulting in increasing pressure on acute and chronic health-care services. **IHD accounts for only 10% of patients presenting to hospital with heart disease, in the black population. The favourable total cholesterol profile in association with very high levels of the protective HDL cholesterol in more than 80% of black South Africans is thought to be the reason for the fairly low prevalence of IHD in this population.**	

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Brand et al., 2013	Chronic diseases are not being managed effectively in either high-risk or low-risk populations in South Africa	2013	In a group of randomly selected families of black African descent (Nguni and Sotho chiefdoms) from Johannesburg's South Western Townships (Soweto): 39% were obese, 42% were hypertensive, 40% were current/previous smokers, and 8% had Diabetes Mellitus. **This study did not focus on the prevalence of IHD.**	Cardiovascular risk-factor management was studied with the focus on critical limb ischemia
Roos et al., 2013	Physical Activity Levels and Activity Preferences of a Cohort of South African Individuals Living With HIV	2013	Physical inactivity was present in the majority of study participants (n=195) as they took less than the recommended 10000 steps per day. Intervention programmes addressing this risk factor for IHD at a primary care level could potentially lessen the future burden of disease related to inactivity. **Although this study did not focus on the prevalence of IHD, they did note that 30% of IHD cases in SA are attributed to physical inactivity.**	This study only evaluated the physical activity levels of individuals living with HIV.
Mayosi & Benatar, 2014	Health and Health Care in South Africa — 20 Years after Mandela	2014	**When looking at years of life lost, IHD was ranked 7th (3.2% of total) among the causes of premature death in 1990 and decreased to the 10th rank (1.6% of total) in 2010.** The highest proportion of disability-adjusted life-years lost is attributable to alcohol use, a high body-mass index, and high blood pressure.	
Houle et al., 2014	The unfolding counter-transition in rural South Africa: Mortality and cause of death, 1994-2009	2014	Non-communicable diseases have increased steadily over time. For non-communicable diseases the probability of dying for both females and males has slowly increased over time periods relative to 1994– 1997, particularly since 2002. The probability of dying from non-communicable diseases was higher among males than females. **This study did not focus on the prevalence of IHD itself, but rather non-communicable diseases as a group.**	This data is from a defined geographic region within SA: the Agincourt sub-district of Bushbuckridge, Mpumalanga Province.

Reference	Publication name	Year	Main finding/s pertaining to this study	Comments
Gaziano et al., 2017	Cardiometabolic risk in a population of older adults with multiple co-morbidities in rural South Africa: the HAALSI (Health and Aging in Africa: longitudinal studies of INDEPTH communities) study	2017	70% of women and 44% of men were overweight or obese. Blood pressure was similar for men and women with a combined hypertension prevalence of 58.4% and statistically significant increases were observed with increasing age. High total cholesterol prevalence in women was twice that observed for men (8.5 vs. 4.1%). **The self-reported prevalence of "heart attacks" (therefore CAD) were 0.5% in males and 0.4% in females. Total study cohort consisted of 5059 patients who were interviewed.**	This data has limitations associated with all cross-sectional assessments, limiting the extent to which causal inferences can be made.
Gómez-Olivé et al., 2018	Cohort Profile: Health and Ageing in Africa: a Longitudinal Study of an INDEPTH Community in South Africa (HAALSI)	2018	More than 50% of male and more than 60% of female participants had hypertension. 44% of male and 69.6% of female participants were overweight or obese. 4.2% of male and 8.5% of female participants had high cholesterol. 19.2% of male and 0.4% of female participants use tobacco. **The self-reported prevalence of myocardial infarction (therefore CAD was 0.4% in both males and females. See previous study.**	This was not a nationally representative sample, but HAALSI findings are likely to be mirrored in similar rural communities.

Published information on the demographics and epidemiology of patients with CAD in central SA could not be found, and there is a critical scarcity of publications from this region. By not researching the factors that contribute to CAD, especially the demographics, healthcare disparities might exist in the treatment strategies of a disease such as this (Taylor et al., 2005).

In order to effectively allocate public health resources, governments are in need of accurate statistics on diseases (Moran et al., 2012). Currently a large portion of the SA population receives subsidized healthcare from the government, making the treatment of cardiovascular disease a costly affair (Watkins et al., 2016). The programmers and policymakers of the public healthcare sector also have to work whilst trying to overcome the critical barrier of a lack of data with which to determine the effects of a health transition, especially with regards to cardio-metabolic disease (Gaziano et al., 2017).

The first step that those responsible for the implementation of government programmes need to take in order to address this problem is to determine the nature and extent of the risk factors for CAD (Fuster & Kelly, 2010). This can be done by supporting research (such as this study) that seeks to quantify disease burdens in a particular area so that trends may be determined and effective (and potentially cost-saving) intervention plans implemented (Houle et al., 2014).

2.8.   Universitas Academic Hospital (UAH)

UAH is a part of the Bloemfontein Academic Hospital Complex, and is associated with the University of the Free State. This is a tertiary hospital that acts as a referral hospital for smaller hospitals and clinics in the central SA region. UAH is the only tertiary referral facility for the public sector in the central SA region and mainly serves patients from the Free State, Northern Cape and Lesotho. It is also the sole tertiary care referring public institution for this region. This region consists of roughly 6,23 million people (Free State, Northern Cape and Lesotho) (Stats SA, 2019; World Population Review, 2019).

To date only one study related to cardiovascular disease, which was conducted at UAH, could be found. This study was undertaken in order to assess a perceived decrease in the number of autopsies requested at the UAH in Bloemfontein. Unfortunately the nature of the cardiovascular disease that was discussed in this study was not reported, as outlined in Table 2-2 (Venter et al., 2015).

The CAD profile of patients presenting for coronary angiography at UAH have not been documented in the past. There is a critical scarcity of publications on this subject in central SA, especially the Free State, as seen in Table 2-2. This means that trends of non-modifiable CAD risk factors over the past two decades have not yet been identified.

2.9.   Significance of this study

From Table 2-2 (page 28) one can see that there exists the definite presence of risk factors for CAD in the rest of SA. Coronary angiography was performed on 640 patients during 1994 compared to 631 in 2014. If the profile of these patients can be identified then more focused research can be undertaken in fields such as prevention, diagnosis, treatment and health resource planning; this will in turn lead to improved patient outcome and the reduced cost of healthcare for the public sector. In his maiden State of the Nation Address, even newly-elected President Cyril Ramaphosa stressed the need for confronting lifestyle diseases such as cardiovascular disorders, hypertension and diabetes (Ramaphosa, 2018). This can be achieved by the study of population differences and by subsequently conducting focused studies, which will then lead to enhanced treatment strategies among different population groups (Taylor et al., 2005).

In order to implement effective action against CAD, research is needed into the extent of CAD, as well as its risk factors (Mayosi et al., 2012). This study was undertaken because almost no published information is available on the profile and risk factors of CAD in patients of central SA, specifically those presenting at UAH. To my knowledge this was the first population-based study on this subject in this region. With this Master's degree a contribution can be made to the improvement of CAD prevention planning. This study, which included only public sector patients, was the first step in generating possible hypotheses for more individual-level research, which is important for policy makers at a population level (Forouzanfar et al., 2012).

Chapter 3: Journal article

Profile of coronary artery disease patients in central South Africa: 2014 versus 1994

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Abstract

Studies report that coronary artery disease (CAD) in Sub-Saharan Africa is rare but epidemiological data of this region is scanty. No CAD data exists for central South Africa (SA).

Aim

To document the profile of CAD in public sector patients in central SA and determine if there was a change over twenty years.

Methods

Retrospective observational study comparing patients with confirmed CAD, on coronary angiography, of 2014 to 1994 in central SA.

Results

Acute coronary syndrome (ACS) increased significantly ($p<0,0001$). There was a notable increase in Non-ST-Elevation Myocardial Infarction (NSTEMI) ($p<0,0001$) and ST-Elevation Myocardial Infarction (STEMI) ($p<0,0001$). African patients with STEMI increased significantly [1994: n=8 (8,5%); 2014: n=45 (29,4%); ($p<0,0001$)]. Caucasian patients with ACS decreased [1994: n=240 (92%); 2014: n=192 (56,8%); ($p=0,0015$)], but NSTEMI in this group increased significantly [1994: n=12 (75%); 2014: n=75 (65,8%); ($p<0,0001$)].

Conclusions

ACS rose significantly over time and STEMI is the most important presenting condition in African patients. Chest pain in African patients should not be ignored by clinicians.

Keywords

Coronary artery disease; Acute coronary syndrome; South Africa; African ethnicity

Introduction

Coronary artery disease (CAD) is the leading non-communicable cause of death in developed countries and is responsible for about one third of all deaths in adults (Sanchis-Gomar et al., 2016). Worldwide it is estimated that approximately 153.5 million people are affected, with higher prevalence in males than females (Benjamin et al., 2019). Annually about 3.8 million men and 3.4 million women die due to CAD worldwide (Clarify Registry Investigators, 2018).

In developing countries such as India, Egypt and Pakistan, CAD is reported to be on the rise (Sriharibabu, 2016; Prabhakaran et al., 2018). This trend can be seen in most developing countries. Between 1984 and 1999 Beijing's coronary heart disease mortality rates increased by 27% in women and a staggering 50% in men (1608 more deaths than expected from baseline mortality rates in 1984 among patients aged 35 to 74 years) (Critchley et al., 2004). In North Africa, Tunisia experienced increased CAD mortality rates of 11,8% in men (from 70 to 87 deaths per 100,000) and 23,8% in women (from 28 to 41 deaths per 100,000) from 1997 to 2009 (Saidi et al., 2013).

CAD in the southern regions of Africa is perceived to be rare (Forouzanfar et al., 2012). Reports from the World Health Organization (WHO) African region suggests that non-communicable diseases in Sub-Saharan Africa, as well as the costs related to their treatment, are on the rise (World Health Organization African Regional Office, 2018). Epidemiological data of the southern regions of Africa is scanty and aged; most of this regions' estimates comes from South Africa (SA) alone (Moran et al., 2012). Cardiovascular diseases (including CAD) rose to being the leading cause of death in Ghana's capital, Accra, in 1991 and 2001 after being in seventh place in 1953 and tenth place in 1966 (Agyei-Mensah & De-Graft Aikins, 2010). The incidence of CAD is still low in Nigeria, but is also on the rise (Essien et al., 2014). CAD is predicted to be one of the leading causes of morbidity and mortality by 2020 for most developing nations (Celermajer et al., 2012). The rise in CAD in African populations is generally ascribed to the increase in modifiable risk factors for CAD, which include hypertension, diabetes mellitus, hypercholesterolemia, smoking and obesity (Yusuf et al., 2001a; Gersh et al., 2010; Nowbar et al., 2019; Benjamin et al., 2019).

In SA ischaemic heart disease is the ninth leading cause of death (Statistics South Africa, 2016). However, limited data about this topic is available. The only major studies available for SA are the Heart of Soweto study and the work of Prof. Bongani M Mayosi. These studies report that the prevalence of modifiable risk factors for CAD is high and rising, especially in the black African population (Sliwa et al., 2008; Tibazarwa

et al., 2009; Mayosi et al., 2009; Stewart et al., 2011; Mayosi et al., 2012; Mayosi & Benatar, 2014; Masina et al., 2016). Therefore, emphasizing the need for epidemiological studies into this phenomenon (Stewart et al., 2006; Sliwa & Mocumbi, 2010; Senkubuge & Mayosi, 2013; Masina et al., 2016; Prakaschandra et al., 2016).

No CAD epidemiological data exists for central SA. The primary aim of this study was to document the profile of patients who had confirmed CAD, on coronary angiography, in the public sector of central SA. Since this was a pilot study the main objective was to determine whether there was a change in non-modifiable risk factors over a twenty-year period.

Methods

Study design and location

A retrospective single-centre observational cohort comparing two time periods, twenty years apart, was conducted at Universitas Academic Hospital (UAH), Bloemfontein. UAH is the only tertiary referral facility for the central SA region and mainly serves patients from the Free State, Northern Cape and Lesotho. It is also the sole tertiary care referring public institution for this region. This region consists of roughly 6,23 million people (Free State, Northern Cape and Lesotho) (Stats SA, 2019; World Population Review, 2019).

Study population and data collection

The main inclusion criterion was confirmed atherosclerotic CAD as reported on coronary angiography. Medical records/data of all public sector patients who underwent coronary angiography during 1994 and 2014 were evaluated. Information was collected using physical catheterization laboratory and cardiothoracic theatre registries, clinical patient files as well as a computerized surgical database (cardiothoracic surgical patients only). Patients who had previous Coronary Artery Bypass Graft (CABG) surgery and previous Percutaneous Coronary Intervention (PCI) were included among the patients with confirmed atherosclerotic CAD.

Data was captured using Excel spreadsheets. Demographic data, which forms part of the non-modifiable risk factors for CAD, and other relevant clinical information was recorded. This included age, gender, ethnicity,

region of origin, family history of heart disease, clinical diagnosis (indication for coronary angiography), final angiographic diagnosis (vessels affected) and treatment.

Definitions

CAD was defined as atherosclerotic build-up on the inner lumen of coronary arteries as recorded in clinical records by a cardiologist (Mendis et al., 2011).

The following definitions were used because of the historical nature of 1994 data: non-Q wave infarction (also labelled as "subendocardial infarction" or "limited infarction") was considered similar to Non-ST-Elevation Myocardial Infarction (NSTEMI) and transmural infarctions were defined as modern day ST-Elevation Myocardial Infarction (STEMI) (Gorlin et al., 1986; Montague et al., 1988; Saleh & Ambrose, 2018).

In 2014 the terms STEMI and NSTEMI were used based on changes seen on the ECG and the presence of cardiac biomarkers according to modern day guidelines (Thygesen et al., 2007; Mendis et al., 2011; Thygesen et al., 2012; Saleh & Ambrose, 2018).

Unstable angina included crescendo angina which was defined as " the sudden acceleration and intensification of existing angina" (Braunwald, 2012) and Prinzmetal angina (a variant form of angina associated with cyclical rest pain of long duration and transient ST-segment elevation) (Prinzmetal et al., 1959; Allaire & Schroeder, 1975; Huckell et al., 1981). Angina was classified as unspecified when clinical records did not state whether it was stable, unstable, Prinzmetal or crescendo angina. To ensure the accuracy of data, unspecified angina was not included in the ACS group.

"Other" clinical indications included: Heart muscle disease (Dilated/Hypertrophic/Restrictive Cardiomyopathy), valvular and congenital heart disease, heart rhythm abnormalities, tumours and masses, syncope, peripheral vascular disease, pulmonary hypertension/oedema and aortic aneurysms/dissections.

Ethics

This study was approved by the Health Sciences Research Ethics Committee (HSREC) of the University of the Free State (UFS-HSD2019/0053/2304) as well as the Free State Department of Health (DOH) and was conducted according to the principles of the Declaration of Helsinki (World Medical Association, 2013).

Statistics

Statistical analysis was done in collaboration with a biostatistician affiliated with the Robert Frater Cardiovascular Research Centre. A t-test was used to compare normally distributed data. Comparisons were carried out using a Chi square test or Fisher's exact test. Analysis was done using R-software (R Core Team, 2019). A p-value of <0,05 was considered significant. Subgroup analysis was performed with unpaired t-tests and 95% confidence interval based on ethnicity, gender and age.

Results

Coronary angiography was performed on 640 patients during 1994 and 631 in 2014. Healthy coronary arteries (no atherosclerosis) was observed in 165 (25,8%) of the 1994 cohort and 171 (27,1%) of the 2014 cohort; in 15 (2,3%) of the 1994 cohort angiographic diagnosis was undocumented. Interestingly, an identical number (460) of angiographically-confirmed atherosclerotic CAD was demonstrated in both cohorts [1994: n=460 (71,9%); 2014: n=460 (72,9%)]; this was an incidental finding and groups were not selected to be similar.

Coronary artery disease (1994, n=460; 2014, n=460)

Non-modifiable risk factors

Demographic data of patients with confirmed CAD can be viewed in Table 3-1 and Figure 3-1. Patients of African ethnicity and mixed origins (both males and females) increased more than five-fold from 1994 to 2014, whilst Caucasian patients decreased from a total of 431 in 1994 to 283 in 2014. CAD was present in about two-thirds of males in both cohorts [1994: n=319 (69,3%); 2014: n=308 (67,0%)]. Subgroup analysis (based on age, gender and ethnicity) showed that Caucasian males with CAD were slightly older in 2014 (median age = 63 years) than in 1994 (median age = 61 years) (p=0,0073, 95% CI -4.8602; -0.7624). No significant differences were observed in other demographic groups. Family history of heart disease was not analysed since it was undocumented in a large number of patients of both cohorts [1994: n=304 (66,1%); 2014: n=209 (45,4%)].

Table 3-1: Demographic data of patients with confirmed CAD.

	1994 (n=460)				2014 (n=460)			
	Male		Female		Male		Female	
	n	Age (median)	n	Age (median)	n	Age (median)	n	Age (median)
African ethnicity	10	51 (33-63)	5	61 (51-71)	54	56 (30-75)	27	60
Caucasian	297	61 (29-85)	134	66 (35-84)	200	63 (26-85)	83	64
Mixed race	7	51 (49-69)	2	60 (53-67)	40	57 (36-83)	38	61
Indian	5	55 (44-74)	0	-	14	43 (31-62)	4	60
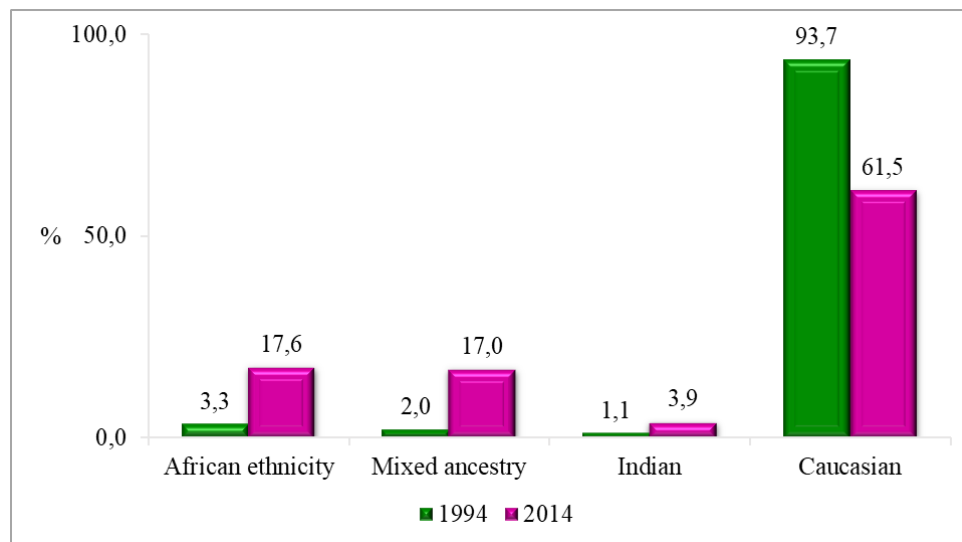
Figure 3-1: Ethnicity of CAD patients.

Referral patterns and clinical indications

In both cohorts the majority of CAD patients were referred from the Free State [1994: n=352 (76,5%); 2014: n=300 (65,2%)]; of these, nearly half were referred from the Mangaung district (Central Free State) [1994: n=159 (45,2%); 2014: n=145 (48,3%)]. There was a substantial increase in the number of patients referred from the Northern Cape from 1994 (n=47; 10,2%) to 2014 (n=132; 28,7%). ACS was the main indication

for angiography in both 1994 and 2014. Clinical indications for performing coronary angiography are presented in Table 3-2.

Table 3-2: Clinical indications for coronary angiography.

	1994 (n=460)	2014 (n=460)
	n (%)	n (%)
Stable angina	20 (4,3)	5 (1,1)
Unstable angina	151 (32,8)	71 (15,4)
NSTEMI	16 (3,5)	114 (24,8)
STEMI	94 (20,4)	153 (33,3)
Unspecified angina	56 (12,2)	19 (4,1)
Atypical chest pain	1 (0,2)	3 (0,7)
Follow-ups and positive stress testing	91 (19,8)	67 (14,6)
Other	31 (6,7)	28 (6,1)

Vessel involvement

Bypass grafts were present in 18,5% (n=85) of the 1994 cohort and 16,5% (n=65) of the 2014 cohort. Patients who had patent vessels after previous PCI were slightly less in 2014 (n=5; 1,1%) than in 1994 (n=12; 2,6%). Of the remaining patients the majority had only one coronary artery affected by atherosclerosis in 1994, while more patients had three vessel disease in 2014 (Table 3-3). Subgroup analysis of vessel involvement (based on age, gender and ethnicity) showed no remarkable differences except that females with three vessel involvement presented at a younger age (median age = 64 years) in 2014 compared to 1994 (median age = 69 years) (p=0,0294, 95% CI 0,4589; 8,4280).

Table 3-3: Vessel involvement of patients with confirmed CAD.

	1994 (n=363)				2014 (n=379)			
	Male		Female		Male		Female	
	n	Age	n	Age	n	Age	n	Age
One vessel								
African ethnicity	6	50	3	54	29	56	5	61
Caucasian	77	60	49	64	38	59	17	63
Mixed race	0	-	3	49	11	58	11	53
Indian	1	48	0	-	4	37	1	66
Two vessels								
African ethnicity	4	53	0	-	12	52	5	60
Caucasian	68	62	24	70	33	59	19	63
Mixed race	0	-	0	-	9	57	8	65
Indian	0	-	0	-	2	40	1	57
Three vessels								
African ethnicity	0	-	2	62	13	57	13	64
Caucasian	82	61	35	70	78	62	28	64
Mixed race	3	53	2	60	18	60	15	64
Indian	0	-	4	56	7	46	2	55

Treatment

In 1994 simple PTCA was performed more frequently than in 2014 (n=65 vs. n=5); in 2014 PTCA with stenting tended to be more frequent (n=9 vs. n=155). CABG almost doubled over the study period (2014 n=104 vs. 1994 n=56). It must be noted that the treatment modality of 50,7% (n=233) of patients in the 1994 cohort and 1,1% (n=5) in the 2014 cohort could not be confirmed (files not found/incomplete clinical records).

Acute coronary syndrome (1994, n=261; 2014, n=338)

ACS 1994 (n=261)

The majority of ACS patients had unstable angina (n=151; 32,8%) and the minority NSTEMI (n=16; 3,5%). There were 94 patients (20,4%) diagnosed with STEMI.

Non-modifiable risk factors

Almost one third of the total 1994 ACS group was female (n=79; 30,3%). Caucasians made up 92% (n=240) while patients of African ethnicity were only 5% (n=13). The median age of Caucasian females was 66 years compared to 60 years in Caucasian males. Females of African ethnicity were 10 years older than males of African ethnicity (61 vs. 51 years). There were 6 patients of mixed ancestry (2,3%), of which 5 were male (median age 53 years), and only 2 Indian patients (0,8%), both males with a median age of 50 years. The demographic data for patients presenting with unstable angina/NSTEMI/STEMI is demonstrated in Table 3-4.

Table 3-4: Demographic data of patients presenting with ACS.

	1994 (n=261)				2014 (n=338)			
	Male		Female		Male		Female	
	n	Age	n	Age	n	Age	n	Age
Unstable angina								
African ethnicity	2	49	0	-	7	60	2	56
Caucasian	94	61	51	66	34	64	19	61
Mixed race	2	58	1	67	3	63	6	63
Indian	1	44	0	-	0	-	0	-
NSTEMI								
African ethnicity	2	58	1	61	7	63	5	65
Caucasian	10	63	2	50	59	63	16	66
Mixed race	1	51	0	-	9	65	12	61
Indian	0	-	0	-	4	48	2	55
STEMI								
African ethnicity	2	63	6	46	30	54	15	60
Caucasian	61	56	22	69	50	60	14	60
Mixed race	2	59	0	-	20	56	14	61
Indian	1	56	0	-	8	38	2	62

ACS 2014 (n=338)

The majority of ACS patients had STEMI (n=153; 33,3%) and NSTEMI was almost a quarter of the group (n=114; 24,8%). Unstable angina was diagnosed in 71 patients (15,4%).

Non-modifiable risk factors

Almost two thirds were male (n=231; 68,3%) and had a slightly younger median age (60 years) than females (62 years). The largest ethnic group were Caucasians (n=192; 56,8%). Patients of African ethnicity (n=66; 19,5%) and mixed ancestry (n=64; 18,9%) were the second largest groups, and Indian patients (n=16; 4,7%) were the smallest group. Both Caucasian males and females had a median age of 62 years. Males of African

ethnicity presented 6 years younger than females of African ethnicity (55 vs. 61 years). Of the mixed ancestry group exactly half (50%) was male (n=32) and their median age was slightly lower (59 years) than those of mixed ancestry females (61 years). The majority of Indian patients were male (n=12; 75%) with a much lower median age of 41 years, as compared to Indian females (60 years). The demographic data for patients presenting with unstable angina/NSTEMI/STEMI is demonstrated in Table 3-4.

ACS comparison 2014 vs. 1994 (1994, n=261; 2014, n=338)

ACS increased significantly over the study period (p<0,0001) and this can be attributed to a notable increase in both NSTEMI (p<0,0001) and STEMI (p<0,0001). Unstable angina decreased significantly over the study period (p<0,0001).

There was a significant increase in the number of African patients who experienced STEMI over the study period (p<0,0001) while unstable angina and NSTEMI remained the same. There was a substantial decrease in Caucasian patients who had ACS (p=0,0015). While NSTEMI increased significantly in Caucasian patients (p<0,0001), unstable angina in this group decreased significantly (p<0,0001).

A significant finding was that ACS females presented 4 years earlier in 2014 than those in 1994 (1994 median age = 66 years vs. 2014 median age = 62 years) (p=0,0031, 95% CI 1,3941; 6,7202). This trend was predominantly demonstrated in Caucasian females only (1994 median age = 66 years vs. 2014 median age = 62 years; p=0,04811, 95% CI 0,0276; 6,5743) while Caucasian males tended to be about two years older (1994 median age = 60 years vs. 2014 median age = 62 years; p=0,0260, 95% CI -5,6230; -3,602).

The age of females with STEMI decreased significantly from 1994 (median age 69 years) to 2014 (median age 60 years) (p=0,0119; 95% CI 1,4195; 10,8305). A similar pattern was observed in females with unstable angina, who were six years younger in 2014 (median age 60 years) compared to 1994 (median age 66 years) (p=0,0269, 95% CI 0,5800; 9,1978).

Caucasian females with NSTEMI was markedly older in 2014 (median age 66 years) than in 1994 (median age 50 years) (p<0,0001, 95% CI -19,7368; -12,8882), while those with STEMI became younger (1994 median age = 69 years vs. 2014 median age = 60 years, p=0,0269; 95% CI 0,9640; 14,6464). Subgroup analysis did not reveal any other significant demographic changes as some sample sizes were too small for statistical analysis.

Discussion

This is the first study in central SA describing the profile of patients with CAD based on cardiac angiographic findings. Results of this study showed significant changes in the profile of patients who presented with CAD at UAH over a twenty-year period. Numbers of patients with CAD increased in African and mixed ethnicity patients. ACS increased significantly over time. STEMI increased significantly in patients of African ethnicity whilst NSTEMI was significantly increased in Caucasian patients.

Patients of African and mixed race with CAD increased more than five-fold over the study period (Figure 3-1). CAD was predominantly seen in males, similar to other studies (Ford & Capewell, 2007; Bhatnagar et al., 2015; The EUGenMed Cardiovascular Clinical Study Group et al., 2016; Masina et al., 2016). Caucasian males with CAD were slightly older in 2014 (median age = 63 years) than in 1994 (median age = 61 years). This study did not assess the reasons for these changes but the authors speculate that it could be due to the fact that more African individuals are exposed to modifiable risk factors during urbanization as predicted by Mayosi and others (Yusuf et al., 2001b; Steyn et al., 2005; Alberts et al., 2005; Department of Health et al., 2007; Sliwa et al., 2008; Tibazarwa et al., 2009; Mayosi et al., 2009; Gersh et al., 2010; Pretorius et al., 2011; Mayosi et al., 2012; Onen, 2013).

In both years most CAD patients came from the Free State and almost half of these came from the Mangaung district, the largest metropolitan area in central SA. The second largest referral district was the Northern Cape. Urbanization presents an increased risk for unhealthy lifestyles and is another plausible explanation for our study findings (Yusuf et al., 2001a; Smith et al., 2012; Sliwa et al., 2016). Due to the fact that CAD often takes years to develop, the steady increase in overall life expectancy of South Africans (up from 52,1 years in 2003 to 59,6 years in 2013) (Stats SA, 2013) is an added factor in more patients presenting with CAD.

Females with CAD who had three vessel involvement presented at a younger age (median age = 64 years) in 2014 as compared to 1994 (median age = 69 years). However, this trend was only demonstrated in Caucasian females (1994 median age = 70 years vs. 2014 median age = 64 years) while Caucasian males were one year older (1994 median age = 61 years vs. 2014 median age = 62 years).

ACS showed a significant increase in 2014 compared to 1994. Our findings are in agreement with the ACCESS (Acute Coronary Events – a Multinational Survey of Current Management Strategies) registry

which showed that (from January 2007 to January 2008) 10,7% of ACS patients in SA were of mixed race and 5,9% were African (Schamroth, 2012). This seem to indicate that there is an upward trend in African patients with ACS.

In 2014 almost a third of ACS patients who presented with STEMI were of African ethnicity. By contrast, NSTEMI increased significantly in Caucasian patients over the same period. Our results compare favourably to the rise in STEMI and NSTEMI as observed in other countries. In metropolitan France acute myocardial infarction (STEMI + NSTEMI) cases rose from 15 per 10^4 (10 000) in 2009 to 19.8 per 10^4 in 2014 for men and 6.3 per 10^4 to 8 per 10^4 for women (Pinaire et al., 2019). Singapore saw an increase in STEMI incidence among Malay patients from 97 per 100,000 population in 2007 to 114 per 100,000 population in 2014 (Zheng et al., 2019). In Europe and the Mediterranean, the Euro Heart Survey on Acute Coronary Syndromes (EHS-ACS-II) reported a 5% rise (from 42% in 2000 to 47% in 2004) in STEMI among ACS patients (Mandelzweig et al., 2006).

In our study STEMI in African patients showed a significant increase of 20,9% compared to 1994. A similar trend has been observed in other developing countries. From 2007 to 2009, in Kerala (India), more patients presented with STEMI (37%) than NSTEMI (31%), or unstable angina (32%, p< 0,001) (Mohanan et al., 2013). The same phenomenon was seen in Nairobi (Kenya) from 2008 to 2010 where 56% of ACS patients had STEMI and 44% NSTEMI/unstable angina (Shavadia et al., 2012) . In Durban, SA, 2008 to 2012, a staggering 83% of acute myocardial infarctions among black African patients were caused by STEMI and only 17% by NSTEMI (Masina et al., 2016).

A possible explanation for the rise in STEMI may be difficulties and delays in referrals from rural areas and late patient presentation with subsequent worsening of symptoms from angina to STEMI. Delayed referrals may be due to the false assumption that STEMI infrequently occurs in the African population and is therefore not expected to be of imminent importance. Patients in some communities may be ignorant of the fact that chest pain can be caused by myocardial ischemia. Patients therefore only present to a medical facility once symptoms worsen. In a multicentre registry study done in India long pre-hospital delays were due to lack of awareness of symptoms of ACS, consulting local practitioners, and long traveling time (Negi et al., 2016). Similar to this, one SA study showed that misinterpretation of symptoms as being non-cardiac in nature was the most common reason for pre-hospital delays, and in some cases it took more than ten hours for the patient

to arrive at the hospital (Meel & Gonçalves, 2016). Other reasons for delays include difficulties in ECG interpretation, problematic referral methods and lack of transport (Maharaj et al., 2012; Stassen, 2018).

The decrease in Caucasian patients who had ACS (p=0,0015) can be attributed to several factors such as access to private medical aid (Department of Health et al., 2007; Mayosi et al., 2012; Statistics South Africa, 2014), dissatisfaction with the public healthcare system (Shisana et al., 2013) and therefore preferring to be treated in a private facility (Lillie-Blanton et al., 2002). It is also known that Caucasian South Africans are sufferers of familial hypercholesterolemia (Steyn et al., 1996; Department of Health et al., 2007; Firth & Marais, 2008; Delport, 2009; Blom, 2011) and it is probable that increasing numbers of Caucasians are on primary prevention therapies like statins and aspirin (Biccard et al., 2006; Bouhairie & Goldberg, 2015; Klug et al., 2015), leading to a decrease in ACS events.

NSTEMI increased significantly in Caucasian patients (p<0,0001) while unstable angina in this group decreased significantly (p<0,0001). This change seems to be reciprocal in nature and the data must be interpreted with caution because the distinction between unstable angina and NSTEMI is complex and involves multiple test results, patient history as well as risk stratification based on clinical presentation (Kleinschmidt, 2006). Due to the more modern use of high-sensitivity biomarkers to diagnose NSTEMI it is plausible that many patients previously diagnosed with unstable angina could have been reclassified as having NSTEMI (Goodman et al., 2006). Several studies reported similar findings where the incidence of NSTEMI and unstable angina changed due to changing myocardial infarction definitions and criteria (Falahati et al., 1999; Alpert et al., 2000; Kontos et al., 2003; Abildstrom et al., 2005; Thygesen et al., 2007; Nielsen et al., 2007; Parikh et al., 2009; Myerson et al., 2009; Yeh et al., 2010; Roger et al., 2010; Reichlin et al., 2012; D'Souza et al., 2015).

A significant finding was that ACS females presented 4 years earlier in 2014 than those in 1994 (1994 median age = 66 years vs. 2014 median age = 62 years) (p=0,0031, 95% CI 1,3941; 6,7202). This was mainly attributed to the age of females with STEMI that decreased significantly from 1994 (median age 69 years) to 2014 (median age 60 years) (p=0,0119; 95% CI 1,4195; 10,8305). From 2002 to 2014, the median age of females with STEMI significantly decreased from 73.7 (57.9–81.8) to 69.6 years (57.0–82.4) in France, even though there was no significant variation in the prevalence of risk factors (Loyeau et al., 2018). It should be noted that the median age of ACS females found in our study is about ten years younger. This is concerning

since it seems to indicate that there is an increase in the prevalence of risk factors for CAD in central SA, especially among females. This strongly supports the need for further research.

Caucasian females with NSTEMI was markedly older in 2014 (median age 66 years) than in 1994 (median age 50 years) whilst those with STEMI became younger (1994 median age = 69 years vs. 2014 median age = 60 years. A similar NSTEMI trend was observed in Taiwan (Yang et al., 2012). Females with unstable angina were six years younger in 2014 (median age 60 years) as compared to 1994 (median age 66 years).

In spite of the important increase in ACS, the pattern of CAD (one, two or three vessels affected) did not change significantly over the study period. Additionally, the difference in treatment modalities between the two eras reflect that there was a shift towards the more modern use of PTCA and stent as opposed to using PTCA alone in the past.

Limitations

Although this is a single-centre retrospective study, UAH is the sole public referral institution for the region as described and therefore the vast majority of public sector patients with CAD will be seen at this institution. Historical data was used and therefore strict definitions for NSTEMI, STEMI and unstable angina were used to ensure accuracy of data in the absence of high-sensitivity cardiac biomarker assays. Although all catheterization data was available, a large number of clinical files of 1994 could not be found and this explains the lack of family history and treatment data. However, catheterization data was verified as described in the methods section. Subgroup analysis was performed (based on age, gender and ethnicity) even though some subgroup sample sizes were small, therefore results should be interpreted accordingly. This study assessed the patient profiles and emphasizes the need for research into modifiable risk factors in central SA. The incidence in the African population may be underestimated by this study, as the most affluent African patients are at the highest risk and have medical insurance: they present to the private healthcare sector. Therefore, this study also highlights the need for research on this subject in the private sector.

By generating local data this study serves as an important first step in demonstrating an epidemiological change in public sector CAD patients in central SA. These findings are crucial to the planning of public health and demonstrates the urgent need for aggressive risk factor control as well as education regarding CAD prevention.

Conclusion

Results of the study showed an epidemiological change in CAD in the public sector of central SA with CAD increasing in patients of African and mixed ethnicity. ACS has risen significantly over time with females presenting at a significantly younger age. STEMI became the most important presenting condition in patients of African ethnicity whilst NSTEMI increased in Caucasian patients. These findings have important implications for central SA public sector patients presenting with chest pain – the risk of STEMI in patients of African ethnicity is increasing and should not be ignored by clinicians.

Abbreviations

ACS: Acute Coronary Syndrome

CABG: Coronary Artery Bypass Graft

CAD: Coronary Artery Disease

DOH: Department of Health

ECG: Electrocardiogram

EHS-ACS-II   Euro Heart Survey on Acute Coronary Syndromes

HSREC: Health Sciences Research Ethics Committee

NSTEMI: Non-ST-Elevation Myocardial Infarction

PCI: Percutaneous Coronary Intervention

PTCA: Percutaneous Transluminal Coronary Angioplasty

SA: South Africa

STEMI: ST-Elevation Myocardial Infarction

UAH: Universitas Academic Hospital

WHO: World Health Organization

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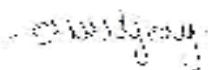
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Chapter 5: Appendices

Appendix A: **Ethical approval**

UNIVERSITY OF THE
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Health Sciences Research Ethics Committee

08-Apr-2019

Dear Marlet Bester

Ethics Clearance: Profile of coronary artery disease patients at Universitas Academic Hospital: 1994 versus 2014
Principal Investigator: Marlet Bester
Department: Clinical Technology – CUT

APPLICATION APPROVED

Please ensure that you read the whole document

With reference to your application for ethical clearance with the Faculty of Health Sciences, I am pleased to inform you on behalf of the Health Sciences Research Ethics Committee that you have been granted ethical clearance for your project.

Your ethical clearance number, to be used in all correspondence is:**UFS-HSD2019/0053/2304**

The ethical clearance number is valid for research conducted for one year from issuance. Should you require more time to complete this research, please apply for an extension.

We request that any changes that may take place during the course of your research project be submitted to the HSREC for approval to ensure we are kept up to date with your progress and any ethical implications that may arise. This includes any serious adverse events and/or termination of the study.

A progress report should be submitted within one year of approval, and annually for long term studies. A final report should be submitted at the completion of the study.

The HSREC functions in compliance with, but not limited to, the following documents and guidelines: The SA National Health Act. No. 61 of 2003; Ethics in Health Research: Principles, Structures and Processes (2015); SA GCP(2006); Declaration of Helsinki; The Belmont Report; The US Office of Human Research Protections 45 CFR 461 (for non-exempt research with human participants conducted or supported by the US Department of Health and Human Services- (HHS), 21 CFR 50, 21 CFR 56; CIOMS; ICH-GCP-E6 Sections 1-4; The International Conference on Harmonization and Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH Tripartite), Guidelines of the SA Medicines Control Council as well as Laws and Regulations with regard to the Control of Medicines, Constitution of the HSREC of the Faculty of Health Sciences.

For any questions or concerns, please feel free to contact HSREC Administration: 051-4017794/5 or email EthicsFHS@ufs.ac.za.

Thank you for submitting this proposal for ethical clearance and we wish you every success with your research.

Yours Sincerely

Dr. SM Le Grange
Chair : Health Sciences Research Ethics Committee

Health Sciences Research Ethics Committee
Office of the Dean: Health Sciences
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Appendix B: **Cardiovascular Journal of Africa (CVJA) submission confirmation letter**

Gmail   Marlet Bester <marlet.bester@gmail.com>

A manuscript number has been assigned to Profile of coronary artery disease patients in central South Africa: 2014 versus 1994

CardioVascular Journal of Africa <em@editorialmanager.com>   22 July 2020 at 11:04
Reply-To: CardioVascular Journal of Africa <info@clinicscardive.com>
To: Martha Aletta Sophia Elizabeth Bester <marlet.bester@gmail.com>

Dear Miss Bester,

Your submission entitled "Profile of coronary artery disease patients in central South Africa: 2014 versus 1994" has been been received online and assigned the following manuscript number: CVJSA-D-20-00071.

You are required to submit the off-line documents which is available on our website www.cvja.co.za or click on the following link :
(http://www.cvja.co.za/downloads/CVJA_Offline_Document.pdf)
Please complete these offline documents which require signatures and e-mail it to info@clinicscardive.com or fax to +2786 664 4202.

You will be able to check on the progress of your paper by logging on to Editorial Manager as an author.
The URL is https://www.editorialmanager.com/cvjsa/.

Thank you for submitting your work to this journal.

Kind regards,

Marcelle Ayres, Admin
Editorial Assistant
CardioVascular Journal of Africa

_____

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. (Use the following URL: https://www.editorialmanager.com/cvjsa/login.asp?a=r). Please contact the publication office if you have any questions.

Appendix C: Glossary

A

Term	Definition
Absent	Not present at a usual or expected place.
Accessible	Capable of being reached.
Acquired Immunodeficiency Syndrome (AIDS)	A chronic, potentially life-threatening condition caused by the Human Immunodeficiency Virus (HIV). By damaging the immune system, HIV interferes with the body's ability to fight the organisms that cause disease.
Acute	Severe but of short duration.
Acute coronary syndrome	An acute ischemic insult to the myocardium resulting from sudden reduction in coronary blood flow. ECG findings categorizes patients into two major subdivision of major diagnostic and therapeutic consequences: ST-elevation ACS (generally reflects an acute total coronary occlusion) or non-ST elevation ACS (Patients with acute chest pain but no persistent ST-segment elevation). Non-ST elevation ACS is further classified either unstable angina or NSTEMI.
Adhesion molecules	Proteins located on the cell surface involved in binding with other cells or with the extracellular matrix (ECM) in the process called cell adhesion. In essence, cell adhesion molecules help cells stick to each other and to their surroundings.
Adipose tissue	An anatomical term for loose connective tissue composed of adipocytes. Its main role is to store energy in the form of fat, although it also cushions and insulates the body. Also called fat.
Adrenergic	Relating to or denoting nerve cells in which adrenaline, noradrenaline, or a similar substance acts as a neurotransmitter.

Term	Definition
Adult	Fully developed and mature.
African-American Heart Failure (a-HeFT)	A clinical trial that was performed to evaluate treatment with a fixed dose of isosorbide dinitrate (a medication used for heart failure, oesophageal spasms, and to treat and prevent chest pain caused by inadequate blood flow to the heart) plus hydralazine (a medication used to treat high blood pressure and heart failure) compared with placebo among black patients with advanced heart failure.
African-American Study of Kidney Disease and Hypertension (AASK)	The African American Study of Kidney Disease and Hypertension study (AASK Trial) was a multi-centre, randomized clinical trial that investigated the effects of blood pressure (BP) control and the use of specific antihypertensive regimens on the progression of chronic kidney disease (CKD). The study was designed to address the high incidence of CKD in African Americans with hypertension.
Afrikaans	A language developed from 17th century Dutch that is one of the official languages of South Africa.
Age	The length of an existence extending from the beginning to any given time.
Age-standardised	In epidemiology and demography, age adjustment, also called age standardization, is a technique used to allow populations to be compared when the age profiles of the populations are quite different.
Aggregation	The formation of a number of things into a cluster.
Alcohol	A colourless volatile flammable liquid which is produced by the natural fermentation of sugars and is the intoxicating constituent of wine, beer, spirits, and other drinks, and is also used as an industrial solvent and as fuel.

Term	Definition
American College of Cardiology Foundation (ACCF)	The American College of Cardiology (ACC), based in Washington, D.C., is a non-profit medical association established in 1949. It bestows credentials upon cardiovascular specialists who meet its qualifications. Education is a core component of the college, which is also active in the formulation of health policy and the support of cardiovascular research.
American Heart Association (AHA)	The American Heart Association is a non-profit organization in the United States that funds cardiovascular medical research, educates consumers on healthy living and fosters appropriate cardiac care in an effort to reduce disability and deaths caused by cardiovascular disease and stroke.
Anastomosis	A connection made surgically between adjacent blood vessels, parts of the intestine, or other channels of the body.
Angina pectoris	Severe constricting pain or sensation of pressure in the chest, often radiating from the precordium to a shoulder (usually left) and down the arm, resulting from ischemia of the heart muscle usually caused by coronary disease.
Angiotensin-Converting-Enzyme (ACE)-inhibitors	Any of a group of antihypertensive drugs (such as captopril) that relax arteries and promote renal excretion of salt and water by inhibiting the activity of angiotensin converting enzyme.
Antiaggregant	See Antiplatelet drug.
Anticoagulant	Having the effect of retarding or inhibiting the coagulation of the blood.
Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack (ALLHAT) Trial	A clinical trial performed to determine if the combined incidence of nonfatal myocardial infarction and coronary heart disease death differs between diuretic-based and each of three alternative antihypertensive pharmacological treatments.

Term	Definition
Antiplatelet drug	A member of a class of pharmaceuticals that decrease platelet aggregation and inhibit thrombus formation. They are effective in the arterial circulation, where anticoagulants have little effect. Also called antiaggregant.
Antiretroviral medication	Medications for the treatment of infection by retroviruses, primarily HIV. Different classes of antiretroviral drugs act at different stages of the HIV life cycle. Combination of several (typically three or four) antiretroviral drugs is known as Highly Active Anti-Retroviral Therapy (HAART).
Aorta	The main artery of the body, supplying oxygenated blood to the circulatory system. In humans it passes over the heart from the left ventricle and runs down in front of the backbone.
Aortic aneurysm	An enlargement (dilation) of the aorta to greater than 1.5 times normal size. They usually cause no symptoms except when ruptured. Occasionally, there may be abdominal, back, or leg pain. They are most commonly located in the abdominal aorta but can also be located in the thoracic aorta.
Aortic incompetence	Also known as aortic regurgitation (AR), is the leaking of the aortic valve of the heart that causes blood to flow in the reverse direction during ventricular diastole, from the aorta into the left ventricle.
Aortic valve	The semilunar valve separating the aorta from the left ventricle that prevents blood from flowing back into the left ventricle.
Apartheid	A policy or system of segregation or discrimination on grounds of race.
Artery	A relatively thick-walled, muscular, pulsating blood vessel conveying blood away from the heart. With the exception of the pulmonary and umbilical arteries, the arteries contain red or oxygenated blood.

Term	Definition
Artificial	Made or produced by human beings rather than occurring naturally, especially as a copy of something natural.
Aspirin	A synthetic compound used medicinally to relieve mild or chronic pain and to reduce fever and inflammation, usually taken in tablet form.
Atheroma	The lipid deposits in the intima of arteries, producing a yellow swelling on the endothelial surface; a characteristic of atherosclerosis.
Atherosclerosis	Hardening of the arteries characterized by irregularly distributed lipid deposits in the intima of large and medium-sized arteries, causing narrowing of arterial lumens and proceeding eventually to fibrosis and calcification. Lesions are usually focal and progress slowly and intermittently. Limitation of blood flow accounts for most clinical manifestations, which vary with the distribution and severity of lesions.
Atherosclerosis Risk in Communities (ARIC) study	A multi-site, prospective, biracial cohort study that was designed to investigate the etiology and clinical outcomes of atherosclerosis. A total of 15,792 middle-aged (45–64 years) men and women were enrolled from four U.S. communities. The study was performed between 1987 and 2013.
Atrial fibrillation (AF)	An abnormal and irregular heart rhythm in which electrical signals are generated chaotically throughout the upper chambers (atria) of the heart. AF can lead to blood clots, stroke, heart failure and other heart-related complications.
Atrial flutter (AFL)	Well-organized but overly rapid contractions of the atrium of the heart (usually at a rate of 250-350 contractions per minute). Flutter refers to a rapid vibration or pulsation. The difference between flutter and fibrillation is that flutter is well organized while fibrillation is not.

Term	Definition
Attenuate	Reduce the force, effect, or value of.
Autopsy	A post-mortem examination to discover the cause of death or the extent of disease.
aVF	A unipolar ECG lead called augmented Vector Foot (aVF) that measures the electrical activity of the heart through a positive electrode placed on the foot of the patient.
aVL	A unipolar ECG lead called augmented Vector Left (aVL) that measures the electrical activity of the heart through a positive electrode placed on the left shoulder of the patient.

B

Term	Definition
Barrier	A circumstance or obstacle that keeps people or things apart or prevents communication or progress.
Beta-blocker	Any of a class of drugs which prevent the stimulation of the adrenergic receptors responsible for increased cardiac action, used to control heart rhythm, treat angina, and reduce high blood pressure.
Biomarker	A naturally occurring molecule, gene, or characteristic by which a particular pathological or physiological process, disease, etc. Can be identified.
Blood pressure (BP)	The pressure of the blood in the circulatory system, often measured for diagnosis since it is closely related to the force and rate of the heartbeat and the diameter and elasticity of the arterial walls.
Body mass index (BMI)	An approximate measure of whether someone is over- or underweight, calculated by dividing their weight in kilograms by the square of their height in metres.
Brachial	Relating to the arm or an arm-like structure.

Term	Definition
British Broadcasting Corporation (BBC)	The British Broadcasting Corporation is a British public service broadcaster. Its headquarters are at Broadcasting House in Westminster, London, and it is the world's oldest national broadcasting organisation and the largest broadcaster in the world by number of employees.
Burden	A load, typically a heavy one.

C

Term	Definition
Calorie (Cal)	A unit of energy: the energy needed to raise the temperature of 1 kilogram of water through 1 °C, equal to one thousand small calories (cal) and often used to measure the energy value of foods.
Carbon monoxide	A colourless, odourless toxic flammable gas formed by incomplete combustion of carbon.
Cardiac catheterization	Process whereby a thin flexible catheter is introduced into an artery and advanced into the heart for diagnosis or therapy.
Cardiogenic shock	A medical emergency resulting from inadequate blood flow due to the dysfunction of the ventricles of the heart.
Cardiomyopathy	Any structural or functional disease of heart muscle that is marked especially by enlargement of the heart, by hypertrophy of cardiac muscle, or by rigidity and loss of flexibility of the heart walls and that may be idiopathic or attributable to a specific cause (such as heart valve disease, untreated high blood pressure, or viral infection).

Term	Definition
Cardiovascular system (CVS)	This refers to the whole circulatory system: the heart, the systemic circulation (the arteries and veins of the body) and the pulmonary circulation (the arteries and veins of the lungs). Blood circulates throughout the cardiovascular system, bringing oxygen and nutrients to the tissues and removing carbon dioxide and other waste products.
Catheter	A flexible tube inserted through a narrow opening into a body cavity.
Cathlab	A catheterization laboratory or cathlab is an examination room in a hospital or clinic with diagnostic imaging equipment used to visualize the arteries of the heart and the chambers of the heart and treat any stenosis or abnormality found.
Cell	The smallest structural and functional unit of an organism, which is typically microscopic and consists of cytoplasm and a nucleus enclosed in a membrane.
Cerebrovascular	Relating to the brain and its blood vessels.
Child	A young human being below the age of puberty or below the legal age of majority.
Cholesterol	A lipid that is an important constituent of body cells and is widely distributed throughout the body. It is especially abundant in the brain, nervous tissue, adrenal glands and skin. A high blood-cholesterol level – that is, one over 6 mmol per litre or 238 mg per 100 ml – is undesirable as there appears to be a correlation between a high blood cholesterol and atheroma, the form of arterial degenerative disease associated with coronary thrombosis and high blood pressure. Cholesterol exists in three forms in the blood: high-density lipoproteins (HDL) which are believed to protect against arterial disease; a low-density version (LDL); and a very low-density type (VLDL) – these latter two being risk factors.

Term	Definition
Chromosome	A thread-like structure of nucleic acids and protein found in the nucleus of most living cells, carrying genetic information in the form of genes.
Chronic	Persisting for a long time or constantly recurring.
Circumflex artery (LCX)	Fully titled as the circumflex branch of the left coronary artery, is an artery that branches off from the left coronary artery to supply portions of the heart with oxygenated blood. The circumflex artery itself divides into smaller arterial systems.
City	A large town.
Clinic	An establishment or hospital department where outpatients are given medical treatment or advice, especially of a specialist nature.
Clopidogrel	An inhibitor of platelet aggregation, used in the form of the bisulphate salt to prevent formation of thrombi and prevent myocardial infarction, stroke, and vascular death in patients with atherosclerosis. Sold as the brand name Plavix, among others.
Cobalt-chromium	A metal alloy of cobalt and chromium used in many surgical implants. The metal has been a preferred material for implant surgeries, and in particular total hip replacement, because it is tolerated well by the body.
Community	A group of people living in the same place or having a particular characteristic in common.
Connective tissue	Tissue that connects, supports, binds, or separates other tissues or organs, typically having relatively few cells embedded in an amorphous matrix, often with collagen or other fibres, and including cartilaginous, fatty, and elastic tissues.
Consequence	A result or effect, typically one that is unwelcome or unpleasant.
Constitutional	Relating to an established set of principles governing a state.

Term	Definition
Constrict	Make narrower, especially by encircling pressure.
Contrast medium	A substance introduced into a part of the body in order to improve the visibility of internal structures during radiography.
Coronary	A term applied to any structure in the body encircling an organ in the manner of a crown. Most commonly it is used in reference to the coronary arteries, through which blood is delivered to the muscle of the heart.
Coronary angiography	Imaging of the circulation of the myocardium by injection of contrast medium, usually by selective catheterization of each coronary artery.
Coronary artery bypass graft (CABG)	A surgical procedure in which damaged sections of the coronary arteries are replaced with new articular of venous graftings to increase rate of cardiac blood flow.
C-reactive protein (CRP)	An annular (ring-shaped), pentameric protein found in blood plasma, whose levels rise in response to inflammation.
Creatine-kinase MB (CK-MB)	A cardiac marker used to assist diagnoses of an acute myocardial infarction. A ck-mb blood test measures the blood level of ck-mb (creatine kinase-muscle/brain), the bound combination of two variants (isoenzymes CKM and CKB) of the enzyme phosphocreatine kinase.
Critical	Crucial, judged, analysed, at a turning point or on the verge of a crisis.
Crude	In a natural or raw state; not yet processed or refined.
Culprit	The cause of a problem or defect.
Cytokine	Any of a number of substances, such as interferon, interleukin, and growth factors, which are secreted by certain cells of the immune system and have an effect on other cells.

D

Term	Definition
Death	The end of the life of a person or organism.
Debilitating	Tending to weaken something.
Decade	A period of ten years.
Democracy	Control of an organization or group by the majority of its members.
Demographics	Statistical data relating to the population and particular groups within it.
Department of Health (DOH)	The executive department of the South African government that is assigned to health matters.
Deteriorate	Become progressively worse.
Diabetes mellitus	A group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both.
Diagnosis	The identification of the nature of an illness or other problem by examination of the symptoms.
Diameter	A straight line passing from side to side through the centre of a body or figure, especially a circle or sphere.
Diastole	The phase of the heartbeat when the heart muscle relaxes and allows the chambers to fill with blood.
Disease	A disorder of structure or function in a human, animal, or plant, especially one that produces specific symptoms or that affects a specific location and is not simply a direct result of physical injury.
Disparity	A great difference.
Distal	Situated away from the centre of the body or from the point of attachment.

Term	Definition
Dose-dependent	Refers to the effects of treatment with a drug. If the effects change when the dose of the drug is changed, the effects are said to be dose-dependent.

E

Term	Definition
Electrocardiogram (ECG)	Graphic record of the heart's integrated action currents obtained with the electrocardiograph displayed as voltage changes over time.
Empirical	Based on, concerned with, or verifiable by observation or experience rather than theory or pure logic.
Endocarditis	Inflammation of the endocardium.
Endocardium	The thin, smooth membrane which lines the inside of the chambers of the heart and forms the surface of the valves.
Endogenous	Having an internal cause or origin.
Endothelium	The tissue which forms a single layer of cells lining various organs and cavities of the body, especially the blood vessels, heart, and lymphatic vessels. It is formed from the embryonic mesoderm.
Epicardium	A serous membrane that forms the innermost layer of the pericardium, attached to the muscles of the wall of the heart.
Epidemic	A widespread occurrence of a disease in a community at a particular time.
Epidemiology	The study of disease as it affects groups of people. Originating in the study of epidemics of diseases like cholera, plague and smallpox, epidemiology is an important discipline which contributes to the control not only of infectious diseases but also of conditions such as heart disease and cancer. Their distributions in populations can provide important pointers to possible causes.

Term	Definition
Estimate	Roughly calculate or judge the value, number, quantity, or extent of.
Ethnicity/ethnic group	A social group characterized by a distinctive social and cultural tradition maintained from generation to generation, a common history and origin, and a sense of identification with the group; members have distinctive features in their way of life, shared experiences, and often a common genetic heritage; these features may be reflected in their experience of health and disease.
Euro Heart Survey on Acute Coronary Syndromes (EHS-ACS-II)	A study performed to examine the management of acute coronary syndromes (ACS) in Europe and the Mediterranean basin, and to compare adherence to guidelines with that reported in the first Euro Heart Survey on ACS (EHS-ACS-I), 4 years earlier.
European Society of Cardiology (ESC)	A non-profit knowledge-based professional association that facilitates the improvement and harmonisation of standards of diagnosis and treatment of cardiovascular diseases.
Exertion	Physical or mental effort.
Extent	The particular degree to which something is or is believed to be the case.

F

Term	Definition
Familial	Relating to or occurring in a family or its members.
Familial hypercholesterolemia	An inherited condition that results in high levels of low-density lipoprotein cholesterol and increased risk of premature cardiovascular disease in men and women.
Family history	Information concerning the disorders suffered by the direct relatives of a patient.

Term	Definition
Farming	The activity or business of growing crops and raising livestock.
Fat	A natural oily substance occurring in animal bodies, especially when deposited as a layer under the skin or around certain organs.
Female	Of or denoting the sex that can bear offspring or produce eggs, distinguished biologically by the production of gametes (ova) which can be fertilized by male gametes.
Femoral	Of or relating to the femur or thigh.
Fibrin	An insoluble protein formed from fibrinogen during the clotting of blood. It forms a fibrous mesh that impedes the flow of blood.
Fibrous	Consisting of or characterized by fibres.
First degree relative	A person's parent.
Fluctuation	An irregular rising and falling in number or amount; a variation.
Fluoroscopy	Fluoroscopy is an imaging technique that uses X-rays to obtain real-time moving images of the interior of an object.
Free radical	An uncharged molecule (typically highly reactive and short-lived) having an unpaired valency electron.

G

Term	Definition
Gender	The state of being male or female.
Genetic	Relating to genes or heredity.
Glycoxidation	The oxidation of sugars, glycoproteins or glycolipids.
Gold	A yellow precious metal.
Graft	A piece of living tissue that is transplanted surgically.

Term	Definition
Gujarati	An Indo-Aryan language native to the Indian state of Gujarat. It is part of the greater Indo-European language family.

H

Term	Definition
Health and Ageing in Africa (HAALSI) study	A highly interdisciplinary study aiming to investigate over time the social, economic and biological risks for chronic health conditions, whether infectious or non-infectious, in a random sample of adults 40 years and older in the Agincourt sub-district. HAALSI focuses on cardio metabolic disease, HIV/AIDS, cognitive functioning and dementias, multi-morbidity and their social and economic correlates, as these are of special interest in South Africa as it undergoes profound social, epidemiological and demographic transitions.
Health and Demographic Surveillance Systems (HDSS)	In the fields of demographics and public health, a health and demographic surveillance system (HDSS), gathers longitudinal health and demographic data for a dynamic cohort of the total population in a specified geographic area. An HDSS is created by first executing a census of households in the area as a baseline, followed by regular visits to each household to gather health and demographic data. The cohort is dynamic in that members are added through birth or immigration and members are subtracted through death or emigration.
Health Sciences Research Ethics Committee (HSREC)	The Health Sciences Research Ethics Committee (HSREC) is responsible for managing and facilitating the ethical and governance review processes for all health research. This involves coordinating scientific and ethical review of research. In addition, the HSREC is responsible for compliance governance, including research

Term	Definition
	monitoring, the provision of researcher support and advice, and risk management.
Heart	A hollow muscular pump with four cavities, each provided at its outlet with a valve, whose function is to maintain the circulation of the blood. The two upper cavities are known as atria, and the two lower ones as ventricles.
Heart failure	Inadequacy of the heart so that as a pump it fails to maintain the circulation of blood, with the result that congestion and oedema develop in the tissues.
High density lipoprotein (HDL)	A class of lipoproteins of relatively high density, the main function of which is to transport cholesterol from the tissues to the liver for excretion.
Homocysteine	An amino acid which occurs in the body as an intermediate in the metabolism of methionine and cysteine.
Hormones	A regulatory substance produced in an organism and transported in tissue fluids such as blood or sap to stimulate specific cells or tissues into action.
Human Immunodeficiency Virus (HIV)	A lentivirus that causes HIV infection and over time Acquired Immunodeficiency Syndrome.
Hypercholesterolemia	An excess of cholesterol in the bloodstream.
Hyperglycaemia	An excess of glucose in the bloodstream, often associated with diabetes mellitus.
Hypertension	Abnormally high blood pressure.
Hypertensive heart disease	The cardiomyopathy that results from the response of the myocardium to the biomechanical stress imposed on the left ventricle by progressively increasing arterial pressure.

Term	Definition
Hypertriglyceridemia	The presence of an excess of triglycerides in the blood.
Hypotheses	A supposition or proposed explanation made on the basis of limited evidence as a starting point for further investigation.

I

Term	Definition
Incidence	The occurrence, rate, or frequency of a disease, crime, or other undesirable thing.
INDEPTH	A global network of health and demographic surveillance systems (HDSS's) that provide a more complete picture of the health status of communities. This network collects data from whole communities over extended time periods, thereby reflecting health and population problems in low- and middle-income countries (LMIC's)
Industrialize	Develop industries (in a country or region) on a wide scale.
Infarction	An area of tissue necrosis caused by impairment of arterial or venous blood supply due to mechanical factors (e.g., emboli, thrombi) or to blood pressure alterations.
Infectious	Liable to be transmitted to people, organisms, etc. Through the environment.
Inflammation	A localized physical condition in which part of the body becomes reddened, swollen, hot, and often painful, especially as a reaction to injury or infection.
Inherit	Derive (a quality, characteristic, or predisposition) genetically from one's parents or ancestors.
Inhibit	Hinder, restrain, or prevent (an action or process).
Insight	An accurate and deep understanding.

Term	Definition
Insulin	A hormone produced in the pancreas by the islets of Langerhans, which regulates the amount of glucose in the blood. The lack of insulin causes a form of diabetes.
Intermediate	Coming between two things in time, place, character, etc.
Intervention	Action taken to improve a medical disorder.
Intima	The innermost coating or membrane of a part or organ, especially of a vein or artery.
Intramural	Situated within the wall of a hollow organ or a cell.
Intravenous (IV)	Existing or taking place within, or administered into, a vein or veins.
Ischemia	Local loss of blood supply due to mechanical obstruction (mainly arterial narrowing or disruption) of the blood vessel (Stedman's Online, 2019). Ischaemia develops if myocardial oxygen demand exceeds supply.
Ischemic cardiomyopathy	Ischaemia and infarction with subsequent loss of contractility and remodelling of the heart.
Ischemic Heart Disease (IHD)	A heart disease that involves the reduction of blood flow to the heart muscle due to build-up of plaque in the arteries of the heart.

K

Term	Definition
Kingdom	A country, state, or territory ruled by a king or queen.

L

Term	Definition
Left anterior descending (LAD) artery	One of two major branches of the left coronary artery. It runs down the anterior interventricular groove, and it supplies blood to the anterior walls of the right and left ventricles and to the interventricular septum. Occlusion of this artery is often called the widow-maker infarction due to a high death risk.
Left Ventricular Ejection Fraction (LVEF)	Left ventricular ejection fraction (LVEF) is the measurement of how much blood is being pumped out of the left ventricle of the heart (the main pumping chamber) with each contraction.
Lentivirus	A genus of retroviruses that cause chronic and deadly diseases characterized by long incubation periods, in the human and other mammalian species. The best-known lentivirus is the Human Immunodeficiency Virus (HIV), which causes Acquired Immunodeficiency Syndrome (AIDS.)
Leukocyte	A colourless cell which circulates in the blood and body fluids and is involved in counteracting foreign substances and disease; a white (blood) cell. There are several types, all amoeboid cells with a nucleus, including lymphocytes, granulocytes, and monocytes.
Life expectancy	The average period that a person may expect to live.
Lifespan	The length of time for which a person or animal lives or a thing functions.
Linear	Progressing from one stage to another in a single series of steps; sequential.
Lipid	Any of a class of organic compounds that are fatty acids or their derivatives and are insoluble in water but soluble in organic solvents. They include many natural oils, waxes, and steroids.

Term	Definition
Lithuanian	Relating to Lithuania (a country and the southernmost of Europe's Baltic states) or its people or language.
Low- and Middle-Income countries (LMIC)	Countries which are defined as low-income economies ($1,005 or less gross national income per capita) or as lower-middle-income economies ($1,006 to $3,955 gross national income per capita), as defined by The World Bank Group.
Low density lipoprotein (LDL)	A class of lipoproteins of relatively low density, the main function of which is to transport cholesterol to the tissues.

M

Term	Definition
Male	Of or denoting the sex that produces gametes, especially spermatozoa, with which a female may be fertilized or inseminated to produce offspring.
Markedly	To an extent which is clearly noticeable; significantly.
Menopause	The period in a woman's life (typically between the ages of 45 and 50) when menstruation ceases.
Mesh	An interlaced structure.
Metabolize	Process (a substance) by metabolism.
Microvascular	Relating to the smallest blood vessels.
Mismatch	A failure to correspond or match; a discrepancy.
Mitral incompetence	A malfunction of the mitral valve that permits the backflow of blood (regurgitation) from the left ventricle into the left atrium.
Modifiable	To change somewhat the form or qualities of; alter partially.
Morbidity	The rate of disease in a population.

Term	Definition
Mortality	The number of deaths in a given area or period, or from a particular cause.
Myocardial cell	The muscle cells (myocytes) that make up the cardiac muscle (heart muscle).
Myocardial infarction	Infarction of a segment of heart muscle, usually due to occlusion of a coronary artery.
Myocarditis	Inflammation of the heart muscle.
Myoglobin	A red protein containing haem, which carries and stores oxygen in muscle cells. It is structurally similar to a subunit of haemoglobin.

N

Term	Definition
National Heart, Lung, and Blood Institute (NHLBI)	The third largest Institute of the National Institutes of Health, located in Bethesda, Maryland, United States. It is tasked with allocating about $3.0 billion in tax revenue per year (fiscal year 2015 estimate) to advancing the understanding of the following issues: development and progression of disease, diagnosis of disease, treatment of disease, disease prevention, reduction of health care disparities within the American population, and advancing the effectiveness of the US medical system.
Necropsy	Another term for autopsy.
Nicotine	A toxic colourless or yellowish oily liquid which is the chief active constituent of tobacco. It acts as a stimulant in small doses, but in larger amounts blocks the action of autonomic nerve and skeletal muscle cells.
Non-communicable	Not transmissible by direct contact.

Term	Definition
Non-modifiable	That cannot be modified.
Non-obstructive	Not causing or characterized by obstruction.
Non-Q-wave myocardial infarction	Evidence of infarction in the absence of abnormal Q waves in any combination of leads I, aVL and VI to V6 and leads II and aVF.
Non-ST-elevation Myocardial Infarction (NSTEMI)	A type of myocardial infarction causing cardiomyocyte necrosis and death by a rise in serum troponin levels. The ECG may be normal or there may be transient ST-segment elevation, persistent or transient ST-segment depression, T-wave inversion, flat T waves or pseudo-normalization of T waves.
Nutrient	A substance that provides nourishment essential for the maintenance of life and for growth.

O

Term	Definition
Obesity	The state of being grossly fat or overweight.
Obstructive	Causing a blockage or obstruction.
Occlusion	The blockage or closing of a blood vessel or hollow organ.
Ostium	An opening into a vessel or cavity of the body.
Overweight	Above a weight considered normal or desirable.
Oxidative	Relating to the process or result of oxidizing or being oxidized.
Oxygen	A colourless, odourless reactive gas, the chemical element of atomic number 8 and the life-supporting component of the air.

P

Term	Definition
Pathophysiology	The disordered physiological processes associated with disease or injury.
Percutaneous coronary intervention (PCI)	An invasive treatment for a stenosed (narrowed) coronary artery. A balloon-tipped catheter is passed through artery of the heart that has developed stenosis. The balloon is aligned with the stenosed section and then inflated to dilate the coronary artery and allow the blood to flow more freely. A stent may be left in place.
Percutaneous Transluminal Coronary Angioplasty (PTCA)	A minimally invasive surgical procedure for the treatment of coronary atherosclerosis. A balloon-tipped catheter is inserted percutaneously into the arterial circulation, advanced to the aortic root, and directed with a flexible guide wire to the site of coronary stenosis. Having been positioned within the narrowed arterial segment, the balloon is inflated so as to stretch the lumen, fracture the obstructing plaque, or both.
Peripheral vascular disease	A disease of blood vessels outside the heart. Peripheral vascular disease (PVD) affects the peripheral circulation, as opposed to the cardiac circulation. PVD comprises diseases of both peripheral arteries and peripheral veins.
Physician	A person qualified to practise medicine, especially one who specializes in diagnosis and medical treatment as distinct from surgery.
Placebo	An inert substance or treatment which is designed to have no therapeutic value.
Plaques	A small, distinct, typically raised patch or region on or within the body resulting from local damage or deposition of material, such as a fatty deposit on an artery wall in atherosclerosis or a site of localized damage of brain tissue in Alzheimer's disease.

Term	Definition
Platelet	A small colourless disc-shaped cell fragment without a nucleus, found in large numbers in blood and involved in clotting.
Plausible	Seeming reasonable or probable.
Plummet	Fall or drop straight down at high speed.
Population	All the inhabitants of a particular place.
Predispose	Make someone liable or inclined to a specified attitude, action, or condition.
Pregnancy	The condition or period of being pregnant.
Preservative	A substance used to preserve foodstuffs, wood, or other materials against decay.
Pressure gradient	The change in pressure measured across a given distance is called a "pressure gradient".
Prevalence	The fact or condition of being prevalent; commonness.
Preventable	Able to be prevented or avoided.
Priority	The fact or condition of being regarded or treated as more important than others.
Processed	Perform a series of mechanical or chemical operations on (something) in order to change or preserve it.
Pro-fibrotic	That promotes fibrosis.
Pro-inflammatory	A proinflammatory cytokine or more simply an inflammatory cytokine is a type of signalling molecule (a cytokine) that is excreted from immune cells like helper T cells (Th) and macrophages, and certain other cell types that promote inflammation.
Prolonged	Continuing for a long time or longer than usual; lengthy.

Term	Definition
Protein	Any of a class of nitrogenous organic compounds which have large molecules composed of one or more long chains of amino acids and are an essential part of all living organisms, especially as structural components of body tissues such as muscle, hair, etc., and as enzymes and antibodies.
Prothrombin	A protein present in blood plasma which is converted into active thrombin during coagulation.
Proximal	Situated nearer to the centre of the body or the point of attachment.
Publication	The preparation and issuing of a book, journal, or piece of music for public sale.

Q

Term	Definition
QRS complex	The QRS complex is a name for the combination of three of the graphical deflections seen on a typical electrocardiogram (EKG or ECG). It is usually the central and most visually obvious part of the tracing. It corresponds to the depolarization of the right and left ventricles of the human heart.
Quantify	Express or measure the quantity of.

R

Term	Definition
Race	A group or set of people or things with a common feature or features.
Radial	Relating to the radius bone in the skeleton.

Term	Definition
Red blood cell (Erythrocyte)	A red blood cell, which (in humans) is typically a biconcave disc without a nucleus. Erythrocytes contain the pigment haemoglobin, which imparts the red colour to blood, and transport oxygen and carbon dioxide to and from the tissues.
Referral	An act of referring someone or something for consultation, review, or further action.
Remodelling	Any process of reshaping or reorganizing.
Research	The systematic investigation into and study of materials and sources in order to establish facts and reach new conclusions.
Resistance	The refusal to accept or comply with something.
Resource	A stock or supply of money, materials, staff, and other assets that can be drawn on by a person or organization in order to function effectively.
Retrospective	Relating to or being a study (as of a disease) that starts with the present condition of a population of individuals and collects data about their past history to explain their present condition.
Revascularization	The restoration of perfusion to a body part or organ that has suffered ischemia.
Rheumatic heart disease	Active or inactive disease of the heart that results from rheumatic fever and that is characterized by reduced functional capacity of the heart caused by inflammatory changes in the myocardium or scarring of the valves.
Rupture	Break or burst suddenly.
Rural	In, relating to, or characteristic of the countryside rather than the town.

S

Term	Definition
Scarcity	The state of being scarce or in short supply; shortage.
Sedentary	Characterized by much sitting and little physical exercise.
Shock	An acute medical condition associated with a fall in blood pressure, caused by such events as loss of blood, severe burns, allergic reaction, or sudden emotional stress, and marked by cold, pallid skin, irregular breathing, rapid pulse, and dilated pupils.
Shunt	An alternative path for the passage of the blood or other body fluid.
Sibling	Each of two or more children or offspring having one or both parents in common: a brother or sister.
Signalling pathway	A set of chemical reactions in a cell that occurs when a molecule, such as a hormone, attaches to a receptor on the cell membrane. The pathway is actually a cascade of biochemical reactions inside the cell that eventually reach the target molecule or reaction.
Slight	Small in degree; inconsiderable.
Smoking	The action or habit of inhaling and exhaling the smoke of tobacco or a drug.
Smooth muscle	Muscle tissue in which the contractile fibrils are not highly ordered, occurring in the gut and other internal organs and not under voluntary control.

Term	Definition
South Africa (SA)	The southernmost country in Africa. It is bounded to the south by 2,798 kilometres (1,739 miles) of coastline of Southern Africa stretching along the South Atlantic and Indian Oceans; to the north by the neighbouring countries of Namibia, Botswana, and Zimbabwe; and to the east and northeast by Mozambique and Eswatini (Swaziland); and it surrounds the enclaved country of Lesotho. South Africa is the largest country in Southern Africa and the 24th-largest country in the world by land area and, with over 58 million people, is also the world's 24th-most populous nation.
Stable angina	Angina induced by effort and relieved by rest. It does not increase in frequency or severity, and is predictable in nature.
Stainless steel	A form of steel containing chromium, resistant to tarnishing and rust.
Statin	A lipid-lowering drug used to treat primary hypercholesterolaemia – a condition in which the concentrations of lipoproteins in the blood plasma are raised, increasing the likelihood of affected individuals developing coronary heart disease.
ST-depression / ST-elevation	The ST segment is the flat, isoelectric section of the ECG between the end of the S wave (the J point) and the beginning of the T wave. It represents the interval between ventricular depolarization and repolarization. The most important cause of ST segment abnormality (elevation or depression) is myocardial ischemia or infarction.

Term	Definition
ST-Elevation Myocardial Infarction (STEMI)	Acute myocardial injury (heart attack) detected by abnormal cardiac biomarkers in the setting of evidence of acute myocardial ischemia and with detection of a rise and/or fall of cardiac Troponin values together with symptoms of myocardial ischemia, new ischemic ECG changes (new ST-segment elevations in 2 contiguous leads or new bundle branch blocks with ischemic repolarization patterns), development of pathological Q waves, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic aetiology.
Stenosis	The abnormal narrowing of a passage in the body.
Stent	A widely used device with metal surfaces that are sometimes coated with a drug to prevent restenosis. It is used to maintain luminal patency.
Stroke	A sudden disabling attack or loss of consciousness caused by an interruption in the flow of blood to the brain, especially through thrombosis.
Subacute	Between acute and chronic.
Subsidize	Support (an organization or activity) financially.
Sympathetic	Relating to or denoting the part of the autonomic nervous system consisting of nerves arising from ganglia near the middle part of the spinal cord, supplying the internal organs, blood vessels, and glands, and balancing the action of the parasympathetic nerves.
Symptom	A physical or mental feature which is regarded as indicating a condition of disease, particularly such a feature that is apparent to the patient.
SYNTAX score	An angiographic grading tool to determine the complexity of coronary artery disease.

Term	Definition
Systemic	Denoting the part of the circulatory system concerned with the transport of oxygen to and carbon dioxide from the body in general, especially as distinct from the pulmonary part concerned with the transport of oxygen from and carbon dioxide to the lungs.
Systole	The phase of the heartbeat when the heart muscle contracts and pumps blood from the chambers into the arteries.

T

Term	Definition
Tantalum	A rare, hard, blue-grey, lustrous transition metal that is highly corrosion-resistant.
Tertiary	Third in order or level.
Testosterone	A steroid hormone that stimulates development of male secondary sexual characteristics, produced mainly in the testes, but also in the ovaries and adrenal cortex.
Thrombolysis	The dissolution of a blood clot, especially as induced artificially by infusion of an enzyme into the blood.
Thrombosis	Local coagulation or clotting of the blood in a part of the circulatory system.
Thrombus	A blood clot formed in situ within the vascular system of the body and impeding blood flow.
Tobacco	A preparation of the nicotine-rich leaves of an American plant, which are cured by a process of drying and fermentation for smoking or chewing.
Total cholesterol	The total amount of cholesterol in the blood, which includes low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol.

Term	Definition
Town	A built-up area with a name, defined boundaries, and local government, that is larger than a village and generally smaller than a city.
Toxic	Poisonous.
Traditional	Existing in or as part of a tradition; long-established.
Treatment	Medical care given to a patient for an illness or injury.
Triglyceride	An ester formed from glycerol and three fatty acid groups. Triglycerides are the main constituents of natural fats and oils.
Triple vessel disease	One or more lesions in each of the three major coronary arteries (left anterior descending, left circumflex, right coronary artery).

U

Term	Definition
United Nations Population Fund (UNFPA)	Formerly known as the United Nations Fund for Population Activities, is a UN organization whose work involves the improvement of reproductive health; including creation of national strategies and protocols, and birth control by providing supplies and services.
Universitas Academic Hospital (UAH)	An academic hospital located in the Free State province of South Africa.
Unstable angina	Myocardial ischemia at rest or minimal exertion in the absence of cardiomyocyte necrosis (cardiac biomarkers are not increased).
Urban	In, relating to, or characteristic of a town or city.

V

Term	Definition
Vasoconstriction	The constriction of blood vessels, which increases blood pressure.
Ventricle	A hollow part or cavity in an organ.
Ventriculogram	A medical imaging test used to determine a patient's cardiac function in the right, or more typically, left ventricle. Cardiac ventriculography involves injecting contrast media into the heart's ventricle(s) to measure the volume of blood pumped.
Village	A group of houses and associated buildings, larger than a hamlet and smaller than a town, situated in a rural area.
Vital	Absolutely necessary; essential.

W

Term	Definition
Wealthy	Having a great deal of money, resources, or assets; rich.
Weight loss	A decrease in body weight.
Western	Living in or originating from the West, in particular Europe or the United States.
Women's Ischemia Syndrome Evaluation (WISE)	A prospective cohort study of 936 clinically stable symptomatic women who underwent coronary angiography to evaluate symptoms and signs of ischemia.
Workload	The amount of work to be done by someone or something.

Term	Definition
World Health Organization (WHO)	A specialized agency of the United Nations that is concerned with international public health. It was established on 7 April 1948, and is headquartered in Geneva, Switzerland. The WHO is a member of the United Nations Development Group. Its predecessor, the Health Organization, was an agency of the League of Nations.
World Heart Federation (WHF)	A nongovernmental organization based in Geneva, Switzerland in 1971. In 1978 the International Society of Cardiology merged with the International Cardiology Federation (which had been founded in 1970) to form the International Society and Federation of Cardiology. This body changed its name in 1998 to the World Heart Federation.

Y

Term	Definition
Years of life lost (YLL)	An estimate of the average years a person would have lived if he or she had not died prematurely. It is, therefore, a measure of premature mortality. As an alternative to death rates, it is a method that gives more weight to deaths that occur among younger people.