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# The prevalence of the metabolic syndrome in men presenting with erectile dysfunction at a South African tertiary care centre

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# THE PREVALENCE OF THE METABOLIC SYNDROME IN MEN PRESENTING WITH ERECTILE DYSFUNCTION AT A SOUTH AFRICAN TERTIARY CARE CENTRE.

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in partial fulfilment of the requirements for the degree

of

Master of Medicine in the branch of Urology

Johannesburg, 2009

**DECLARATION**

I, Bradley Ryan Wood declare that this research report is my own work. It is being submitted for the degree of Master of Medicine in the branch of Urology, in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

……day of……., 2009

Wendy-Ann you are my nirvana.

Indigo you make all the other colours look like shades of grey.

Thank you Kurt, Eddie, Ant and Dave for keeping me alive.

## PRESENTATIONS AND PUBLICATIONS

The work contained in this research report was presented as a poster presentation at the Joint Congress of the European and International Societies of Sexual Medicine in Brussels, Belgium from 7-11 December 2008.

The abstract is published in the Journal of Sexual Medicine, Abstracts of the Joint Meeting of the European and International Societies for Sexual Medicine Brussels, Belgium, 7-11 December 2008, page 137-138.

The work was also presented at the Bert Myburgh Research Forum in the Department of Surgery, University of the Witwatersrand, 26 November 2008.

**ABSTRACT**

The metabolic syndrome has recently become one of the major public health challenges and results from the increasing prevalence of obesity. Erectile dysfunction (ED) affects up to half of men over the age of forty. Men with co-morbid disease and risk factors including cardiovascular disease, hypertension, dyslipidaemia and depression all report a higher prevalence of ED. The current study investigated the prevalence of the metabolic syndrome in one hundred men with (ED) presenting to the Male Sexual Dysfunction Clinic at the Johannesburg Hospital.

Participants underwent a thorough history taking and examination session which included the International Index of Erectile Function Score. Several fasting biochemistry and hormonal tests were performed. Participants were divided by race into three groups. Data was recorded in EXCEL and reported as mean±std or as a number (frequency). Where applicable, correlation between variables was determined.

The prevalence of the metabolic syndrome was 39%, with the highest prevalence (54%) in the group comprising Asian, Coloured and Chinese participants. Eighty percent of participants had moderate-severe (ED), with a mean duration of 3,8 years. Glucose and HbA1c were strong predictors of ED duration. Severity of ED was not influenced by the presence of the metabolic syndrome. Men presenting with ED may represent an ideal patient group to screen for the metabolic syndrome, and therefore for cardiovascular disease, especially for those men within the asymptomatic period.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| ANOVA | Analysis of variants |
| BMI | Body mass index |
| cm | centimeter |
| ED | erectile dysfunction |
| FSH | Follicle Stimulating Hormone |
| HbA1c | Glycated Haemoglobin |
| HDL | High density lipoprotein |
| HOMA-IR | Homeostasis Model Assessment-Insulin Resistance |
| IDF | International Diabetes Federation |
| IIEF | International Index of Erectile Function |
| kg | kilogram |
| LDL | Low density lipoprotein |
| LH | Luteinising Hormone |
| MALES | Men’s Attitudes to Life Events and Sexuality |
| MMAS | Massachusetts Male Aging Study |
| mmHg | millimetres Mercury |
| mmol/l | millimol per litre |
| MS | metabolic syndrome |
| MSDC | Male Sexual Dysfunction Clinic |
| NHLS | National Health Laboratory System |
| SD | standard deviation |
| WHO | World Health Organisation |

# CHAPTER ONE

# INTRODUCTION, REVIEW OF THE LITERATURE AND AIMS OF THE CURRENT STUDY

## 1.1 Introduction and literature review

"The penis does not obey the order of its master, who tries to erect it or shrink it at will. Instead, the penis erects freely while its master is asleep. The penis must be said to have its own mind, by any stretch of the imagination."

Leonardo da Vinci

### 1.1.1 Introduction

Erectile dysfunction (ED) is defined as the persistent inability to attain and maintain an erection adequate for satisfactory sexual performance (Feldman et al 1994).ED affects up to 52% of men between 40 and 70 years, and is an important cause of a decreased quality of life in men (Laumann et al 1999, Litwin et al 1998). Of the 52% of men with ED in a community prevalence study of 1709 men (Massachusetts Male Aging Study), 17,2% had minimal ED, 25,2% moderate and 9,6% complete ED (Feldman et al 1994).

It is estimated that by the year 2025, 322 million males will be affected by erectile dysfunction, the largest increase will be in the developing world: Africa , Asia and South America (Ayta et al 1995). The overall prevalence of ED in the MALES study involving 2912 men between the ages of 20-75 years was 16% (Rosen et

al 2004). The prevalence of self-reported ED increased with age. Men with co-morbid disease and risk factors including cardiovascular disease, hypertension, dyslipidaemia and depression all reported higher prevalence of ED. Men with ED also reported increased prevalence rates of these co-morbid conditions. The prevalence of diagnosed hypertension, hyperlipidaemia, diabetes mellitus and depression in men with ED has been further quantified (Seftel et al 2004). In 272 325 men with ED the prevalence rates for hypertension were 42,4%, for hyperlipidaemia 20,2%, for diabetes mellitus 11,1% and for depression 23,9%. Only 32% had none of the above co-morbid illnesses.

One of the most significant advances in research into ED is the awareness of the high prevalence of ED in men with cardiovascular disease. In the Framingham Heart Study, a long-term cardiovascular study, the life-time risk of coronary artery disease in men at age 40 was 50% (Lloyd-Jones et al 1999). It is therefore possible that in this group half of the men could develop coronary heart disease and half could develop ED. The incidence of ED appears to be significantly higher in patients suffering from coronary artery disease (CAD), therefore some authors have proposed screening CAD patients for ED or vice versa (Levine et al 2000). Patients with established CAD experienced ED symptoms on average two to three years before the onset of coronary symptoms, suggesting that ED may be a warning sign or an opportunity for early intervention (Montorsi et al 2006).

### 1.1.2 Pathophysiology of erectile dysfunction

Endothelial pathology often leads to erectile dysfunction and the degree of ED varies directly with the number of atherosclerotic risk factors including hypertension, dyslipidaemia, diabetes mellitus and smoking (Virag et al 1985). These authors found that lesions in the pudendal arteries were more common in men with ED compared with controls of similar age. Atherosclerotic arterial occlusive disease of the hypogastric-cavernous-helicine tree can decrease the perfusion pressure and arterial flow to the sinusoidal spaces thus increasing the time to maximal erection and decreasing the rigidity of the erect penis (Lue 2007).

Hypertension is an independent risk factor for ED, and its consequent cardiovascular complications such as coronary heart disease and renal failure further worsen ED (Feldman et al 1994). It is the stenotic lesions found in the arterial tree that cause ED in hypertensive patients rather than the blood pressure itself (Hsieh et al 1989). A narrowed lumen or increased wall-to-lumen ratio in the arteries contributes to the increased peripheral vascular resistance in hypertensive subjects. This increased resistance has been documented in the penile vasculature of hypertensive rats, an alteration ascribed to structural changes in the arterial and erectile tissues (Hale et al 2001). In arteriogenic ED, oxygen tension in cavernosal blood is decreased thereby impairing the production of prostaglandin $E_1$ and $E_2$ and enhancing TGF-$\beta_1$ (transforming growth factor) induced collagen synthesis (Nehra et al 1999). It is well known that enhanced sympathetic activity forms part of the pathophysiology of

hypertension leading to increased basal tone in the vascular smooth muscle and even smooth muscle hypertrophy.

Diabetes mellitus is a common, chronic medical disease affecting up to 2% of people worldwide. The prevalence of ED is three times higher in diabetic men, occurs at an earlier age and increases with disease duration (Feldman et al 1994). Diabetes causes ED by affecting one or more of the following: nervous system function, androgen secretion, endothelial dysfunction and smooth muscle contractility (Dunsmuir et al 1996). Important components of diabetes induced ED include a reduced nitric oxide synthetase, decreased efficacy of released nitric oxide and the presence of oxidative free radicals such as advanced glycosylation end-products (Saenz de Tejada et al 2004).

### 1.1.3 The metabolic syndrome

The metabolic syndrome (MS, syndrome X) is characterised by lipid storage abnormalities, insulin resistance, hypertension, glucose intolerance, central obesity is characteristic and overt diabetes (type 2) or atherosclerosis develop over time (Ford et al 2002). MS is therefore a major cause of cardiovascular disease that increases the risk of myocardial infarcts and cerebrovascular events. The concept of MS has existed for at least 80 years. The syndrome of metabolic disturbances, all risk factors for cardiovascular disease, was first described by a Swedish physician Kylin in 1922 as a clustering of hypertension, hyperglycaemia and gout (Kylin 1922). Over the past 20 years the syndrome has

become one of the major public health challenges worldwide as the global epidemic of diabetes and obesity has occurred.

MS brings with it an elevated risk of diabetes mellitus and cardiovascular disease, and may in fact predict future diabetes, and therefore strategies to prevent this global epidemic are needed urgently (Zimmet et al2001). MS is a master of disguise as it presents in multiple ways according to the various components that make up the syndrome. These components exist together in an individual more often than would be expected by chance (Eckel et al 2005).

Several research groups have attempted to define criteria for diagnosing MS. The first attempt came in 1999 when a WHO diabetes group proposed a definition that could be modified as more information becomes available (Alberti et al 1998). The criteria had insulin resistance, impaired glucose tolerance or diabetes as essential components, together with at least two of: hypertension, raised triglycerides and/or low HDL cholesterol, obesity and microalbuminuria. A revised definition came from the US National Cholesterol Education Programme: Adult Treatment Panel III in 2001 (Adult Treatment Panel III 2001). It was designed to facilitate the diagnosis of high cardiovascular risk individuals, requiring the presence of three of the following criteria: central obesity, hypertension, raised triglycerides, low HDL-cholesterol and fasting hyperglycaemia. The different definitions inevitably led to confusion and lack of consistency between studies.

One problem has been the difficulty in explaining the underlying mechanisms of MS (IDF Epidemiology Task Force Consensus Group 2005). It is not known whether to define MS according to insulin resistance, the metabolic consequences of obesity, risk for cardiovascular disease or a collection of related factors. A further problem with the above definitions was their lack of applicability to different ethnic groups particularly as relates to obesity or waist circumference cutoffs. One example is in the Asian population where the risk of diabetes is apparent at lower levels of obesity than in the European population (Tan et al 2004). The above two definitions would underestimate the prevalence of MS in the Asian population.

The International Diabetes Federation (IDF) realised the need for one practical definition that could be applied to any country to assess the risk of diabetes and cardiovascular disease (2005). This definition would allow comparative studies between two different population groups. The IDF Consensus Group met in 2004 and their new worldwide definition of MS is used in the current study. They agreed that diabetes and insulin resistance had been overemphasised in previous definitions and measurement of insulin resistance was deemed impractical. It was stated that certain components such as waist circumference and triglycerides are highly correlated with insulin sensitivity. Central obesity as assessed by waist circumference is regarded as essential due to its strong link to cardiovascular disease.

Ethnic-specific waist circumference was incorporated into the definition and the values for males are given below:

| **Ethnic group** | **Waist circumference (cm)** |
|---|---|
| Europeans | ≥94cm |
| South Asians | ≥90cm |
| Chinese | ≥90cm |
| Japanese | ≥85cm |
| South and central Americans | As for Asians |
| Sub-Saharan Africans | As for Europeans |
| Mediterranean, Middle East | As for Europeans |

Ethnicity is based on classification, not country of residence. If body mass index is above 30 kg/m², central obesity can be assumed, and waist circumference does not need to be measured.

The other variables in the definition are included below, the presence of any two along with central obesity are required for a diagnosis of MS to be made:

**Raised triglycerides**

>1,7 mmo/l

Specific treatment for this abnormality

**Reduced HDL-cholesterol**

<1,03 mmol/l in men

Specific treatment for this abnormality

**Raised blood pressure**

Systolic ≥130 mmHg

Diastolic ≥85 mmHg

Treatment of previously diagnosed hypertension

**Raised fasting plasma glucose**

Fasting plasma glucose ≥5,6 mmol/l

Previously diagnosed type two diabetes

Oral glucose tolerance test is not necessary to diagnose MS

(IDF Consensus Group 2005)

Recently the American Diabetes Association and the European Association for the Study of Diabetes have published an article on the syndrome (Kahn et al 2005). They raise three questions regarding MS:

1. Is it indeed a syndrome, particularly as the cause of MS is yet to be defined?
2. Does it serve a useful purpose?
3. Is it labelling a person unnecessarily?

The IDF, however feel strongly that the clustering of closely related risk factors for cardiovascular disease and diabetes is a good basis for calling this a syndrome. Many conditions have been given a name without the underlying cause being known, for example type two diabetes. The epidemic of cardiovascular disease and diabetes worldwide seems enough reason to identify people with the syndrome as an opportunity exists to manage the components of MS if recognised early (IDF Epidemiology Task Force Consensus Group 2005).

The prevalence of MS is highly age dependent. In a US study the prevalence of MS increased from 7% in participants aged 20-29 years to 44% for those aged 60-69years (Ford et al 2002). Several studies have shown that MS predicts future development of diabetes and cardiovascular disease as well as mortality from these conditions. In the DECODE study in Europe involving non-diabetic participants, those with MS had an increased risk of all-cause and cardiovascular mortality compared to those without it . All-cause mortality was 1,44 times higher (95% confidence interval 1,17-1,84), while cardiovascular disease was 2,26 higher (95% confidence interval 1,61-3,17) in men with MS (Hu et al 2004).

### 1.1.4 Erectile dysfunction and the metabolic syndrome

It is postulated that an association between ED and MS exists as four of the five components of MS are risk factors for ED (Calermayer et al 1994). In a European study ED prevalence increased linearly as the number of components of MS increased (Esposito et al 2005). The ED scores were significantly worse in

men with MS compared to those without in another recent study (Demir et al 2006).

The underlying causes of MS (and ED) include physical inactivity, obesity and genetic predisposition and several risk factors are common to both disorders (Roth et al 2003). Obesity is associated with insulin resistance and MS, abdominal obesity in particular is more highly correlated with insulin resistance and may reflect a strong genetic component to MS. The most accepted and unifying hypothesis to incorporate the pathophysiology of MS is insulin resistance (Eckel et al 2005). Insulin resistance has been defined as a defect in insulin action resulting in fasting or postprandial hyperinsulinaemia to maintain normal glucose concentrations. A major contributor to the development of insulin resistance is an excess of circulating fatty acids (Eckel et al 2005). Obesity is associated with hypogonadism in males due to an increased aromatase activity causing low libido, depression and less frequent intercourse (Roth et al 2003).

Insulin resistance reduces the concentration of lipoprotein lipase in peripheral tissue, particularly adipose tissue. This along with an overproduction of very low-density lipoproteins contributes to hypertriglyceridaemia (Eckel et al 2005). In the Massachusetts Male Aging Study baseline obesity predicted a higher risk for ED regardless of follow-up weight loss. Physical activity was also associated with ED, with the highest risk among men who remained sedentary and the lowest among those who initiated activity or stayed active (Feldman et al 1994). In a study by Derby et al 2000, the prevalence of complete ED amongst cigarette

smokers was not significantly different to that amongst non-smokers, however cigarette smoking increased impotence associated with cardiovascular disease, hypertension and medication use.

The other major lipoprotein disturbances in MS include an increased clearance of high-density lipoproteins and a predominance of small dense low-density lipoprotein (Eckel et al 2005). In MS and dyslipidaemia, low density lipoprotein (LDL) production destroys endogenous nitric oxide synthetase, leading to a decreased bioavailability of nitric oxide on the endothelial surface which results in vasoconstriction (or inhibition of vasodilation) and damaged endothelium (early atherosclerosis) (Kim 2000, Wheatcroft et al 2003). Nitric oxide inhibits atherogenesis, thrombogenesis, platelet adhesion, lipid peroxidation and monocyte adhesion. A good arterial inflow of blood along with efficient venous trapping of blood is required for normal erections to occur. This vascular function relies heavily on nitric oxide bioavailability. Endothelial dysfunction, defined as a reduced biovailability of nitric oxide is associated with many of the common risk factors for ED and cardiovascular disease (Ker 2006), see figure 1.1. Endothelial dysfunction leads to early atherogenesis and insulin resistance (Chaula 2004). Superimposed and contributory to the insulin resistance produced by the lipoprotein abnormalities, is the effect of a pro-inflammatory state. The increased secretion of interleukins and tumour necrosis factor from adipose tissue results in more insulin resistance and lipolysis of triglycerides (Eckel et al 2005). The cytokines and lipoproteins increase the production of pro-thrombotic markers from the liver, for example fibrinogen and plasminogen

activator inhibitor-1. ED and vascular disease are clearly linked at the level of the endothelium and the presence of ED in asymptomatic men may be a marker of silent cardiovascular disease.

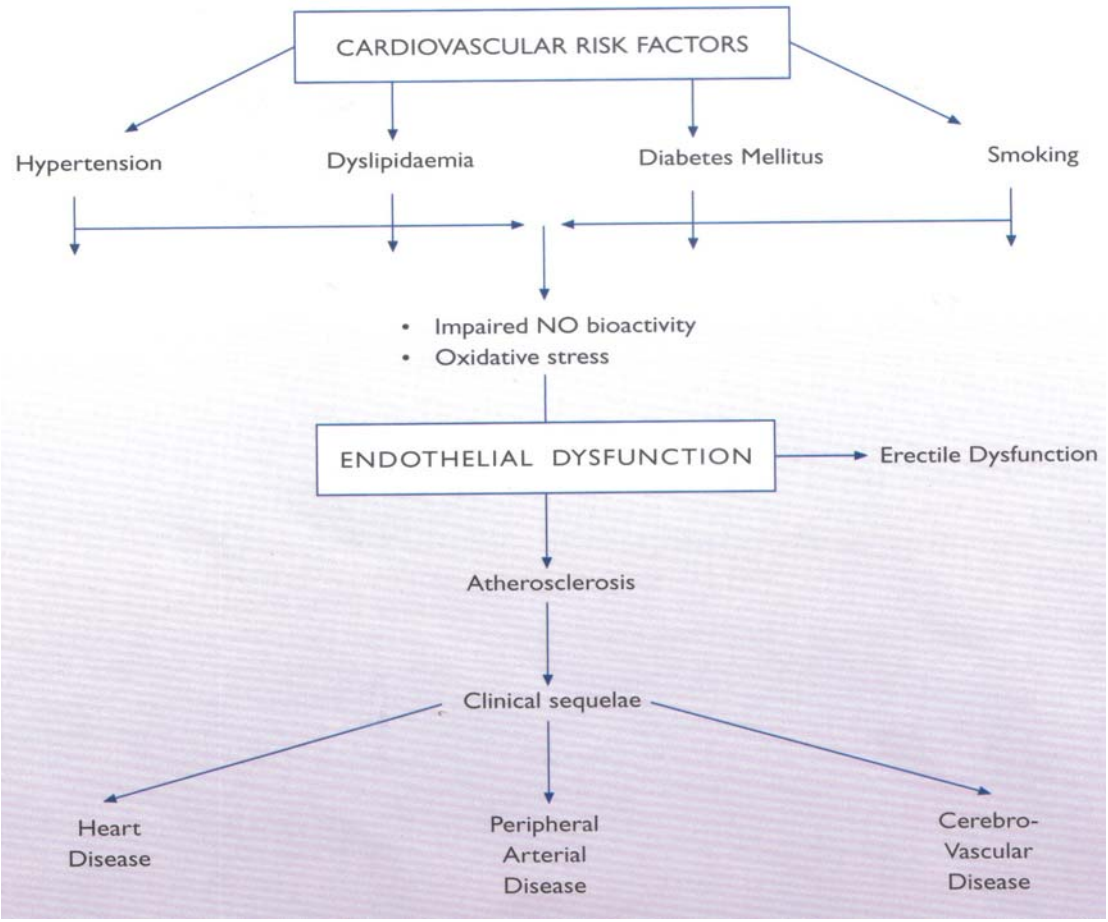



Figure 1.1 Endothelial dysfunction

### 1.1.5 Erectile dysfunction score

Assessing the severity of ED has been made more accurate by the development of standardised questionnaires, most of which are self-administered. The International Index of Erectile Function (IIEF) is a brief, reliable, self administered measure of erectile function. It is a cross-cultural, psychometrically sound, reliable assessment with proven validity (Rosen et al 1997). It has been validated in many languages and is the most widely used self-administered questionnaire for sexual function. It measures five domains of sexual function in males namely erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction in fifteen questions (Appendix 7).

An abridged five item version of the original fifteen item version has been specifically validated for use in ED (Rosen et al 1999) and is used in the current study. ED is classified into five categories based on IIEF-5 scores: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (7-21) and no ED (22-25). The most important difference between IIEF-15 and IIEF-5 is that the latter assesses ED over the last six months as opposed to the last four weeks, a more clinically relevant and practical time frame (Appendix 3).

The metabolic syndrome has recently become one of the major public health challenges and results from the increasing prevalence of obesity. Men with co-morbid disease and risk factors including cardiovascular disease, hypertension, dyslipidaemia all report a higher prevalence of ED.

### 1.2 Problem statement

There is no research from tertiary care hospitals in South Africa evaluating the prevalence of MS in men presenting with ED. International studies may not be applicable in our setting. The total impact that MS has on men's health in South Africa is still unknown and needs to be more clearly defined. ED is probably the most sensitive barometer of men's health worldwide, and several new insights will allow us to see ED as part of a broader health risk and not as an isolated dysfunction.

### 1.3 Significance of the study

This study will provide an overview of the prevalence of MS in males presenting with ED to a South African tertiary hospital. The impact that these disorders have on the health budget is significant, particularly in the developing world, and early detection via screening will help introduce preventative strategies to curtail the consequences that impact so heavily on quality of life.

### 1.4 Research questions

- What is the prevalence of MS in males presenting with ED to a South African tertiary hospital?
- Do males with MS and ED present with more severe ED, and which other factors contribute to ED duration and severity?

### 1.5 Aims of the current study

- The primary aim of this study is to determine the prevalence of MS in males presenting with ED to a South African tertiary hospital.
- A secondary aim of this study is to determine whether MS affects the severity of ED, and which other parameters affect the severity and duration of ED.

### 1.6 Objectives of the current study

1. To establish the proportion of males presenting with ED to the Men's Sexual Dysfunction Clinic (MSDC) who also fit the criteria for the diagnosis of MS.
2. To establish the proportion of males presenting with ED to the MSDC who do not fit the criteria for MS.
3. Evaluate and compare the severity of ED in males with and without MS at the MSDC, by standardised questionnaire format.
4. To determine which racial groups in South Africa are more at risk for ED and MS, and any ethnic-specific risk factors for ED duration and severity.
5. To analyse the factors contributing to the duration and severity of ED in the South African male population

## CHAPTER TWO

## MATERIALS AND METHODS

The following chapter includes a description of the research design used in the current study. The choice of subjects, including inclusion and exclusion criteria is discussed, a well as sample size and ethical considerations such as informed consent. All procedures followed during the history taking, physical examination, blood sampling and administration of the questionnaire are included. A brief summary of the statistical tests performed on the data is given at the end of the chapter.

### 2.1 Research design

Permission to conduct research on human participants was obtained from the Human Research Ethics Committee (Medical). Clearance certificate protocol number: M070737 (Appendix 5). Permission was also obtained from the Superintendent of the Johannesburg Hospital (Appendix 6).

A clinic survey amongst males suffering from ED who presented to a tertiary hospital MSDC (Male Sexual Dysfunction Clinic) was conducted. The study was conducted at the Johannesburg Hospital MSDC, situated in the Out-patient Department, Area 456. Men may only attend this clinic once they have been referred from the Urology Out-patient Clinics at Johannesburg or Helen Joseph Hospitals. Men were invited to participate and were able to decline without being disadvantaged in anyway. They were provided with information about the study

and their questions were addressed. An interpreter was always available on site should the participant not be fluent in English. After reading the information leaflet (Appendix 1) and signing informed consent (Appendix 2), anonymity was maintained by allocating study numbers to the questionnaires and data collection sheets (see below). Names and hospital numbers did not appear on the questionnaires and data collection sheets. Participants did not receive any financial remuneration for participating in the study.

### 2.2 Subjects

The first one hundred men presenting to the Johannesburg Hospital MSDC who met the study criteria and who agreed to participate were recruited. All racial groups were included and the final proportions of racial groups enrolled more or less resembles the population statistics of South Africa. The following criteria were used to determine whether the potential participant was eligible for the study.

**Inclusion criteria**

- Males above 30 years of age presenting with spontaneous-onset ED, defined as an inability to achieve and sustain erections adequate for sexual intercourse.

**Exclusion criteria**

- Prior pelvic surgery leading to onset of ED
- Prior pelvic irradiation therapy leading to onset of ED
- Prior major pelvic trauma leading to onset of ED
- Spinal cord injuries

The above criteria were used to exclude men with ED due to non-spontaneous causes, as even if these men had MS it would not be known whether the MS or another cause was responsible for their ED.

**2.3 Procedure**

The following is a list of procedures followed during the first clinic visit at the Johannesburg Hospital MSDC.

- Men who met the inclusion criteria were invited to participate.
- The study was explained to them and any questions they had were addressed. They were given the opportunity to read through the information sheet (Appendix 1). If necessary they were allowed to take this document home while considering their potential participation. If they agreed to participate, informed consent was signed (Appendix 2).
- A thorough history and examination was performed by the principal investigator. This was the routine history and examination done at the MSDC for all patients during their first visit.
- General demographic data such as age, race, sex and occupation was collected. A smoking history, medical and surgical history, drug history and ED duration was obtained. The above data was entered onto an anonymous data collection sheet (Appendix 4).
- A general medical examination was performed on all participants. Parameters that were measured and recorded specifically for the study by the principal investigator were as follows :

Waist circumference, measured with a horizontal tape measure halfway between the lowest rib and the iliac crest in the standing position, greater than 85-94 cm (depending on race) being a criterion for MS.

Systolic and diastolic blood pressure measured in the seated position with a manual sphygmomanometer cuff over the brachial artery, greater than 130/85 mmHg being a criterion for MS.

Weight and height as measured with a calibrated electronic scale and tape measure respectively, with subsequent calculation of body-mass index (BMI kg/m²):

BMI ranges: low < 18,5 ; normal 18,5-24,9 ; high 25-29,9 ; obese >30

- The IIEF-5 was explained and completed by the participants (see tools section below).
- Blood specimens were collected by the clinic staff. These specimens are routinely collected for all clinic attendees. The specimens were analysed by The National Health Laboratory Service, which is the routine biochemistry laboratory at the Johannesburg Hospital. The following serum tests were analysed, significant reference values are included :

Fasting lipogram :

Total cholesterol

Triglycerides, greater than 1,7 mmol/l being a criterion for MS

HDL, less than 1,03 mmol/l being a criterion for MS

LDL

Fasting glucose, greater than 5,6 mmol/l being a criterion for MS

Fasting serum insulin levels as a measure of insulin resistance

Glycated haemoglobin

Hormone profile:

Testosterone (morning specimen): less than 12 nmol/l indicates hypogonadism

Luteinising Hormone

Follicle Stimulating Hormone

Should results be available for non-fasting specimens only, participants were called back for fasting specimens to be drawn.

Participants were counselled at their next clinic visit regarding any abnormal results or alternatively they were contacted. Contact details are kept among clinic records.

- All of the above data was recorded on a separate collection form (Appendix 4).
- Participants with significant, newly diagnosed abnormalities were referred to the relevant clinics at the Johannesburg Hospital for example Diabetes, Hypertension and Lipid Clinic. Further assessment of their cardiovascular status, for example an electrocardiogram would be performed at the relevant clinics and was not done for the present study.
- A diagnosis of type 2 diabetes, hypertension or lipid abnormality is accommodated within the definition of the metabolic syndrome. The IDF criteria (2005) for the diagnosis of MS, as included in the literature review, were used to diagnose MS.

## 2.4 Tools

The International Index of Erectile Function (IIEF) is a brief, reliable, self-administered measure of erectile function that is cross-cultural, psychometrically sound and has been validated (Rosen et al 1997, Appendix 7). An abridged five item version has been developed (IIEF-5) to assess ED more specifically as opposed to overall sexual function (Rosen et al 1999, Appendix 3). ED is classified into five categories based on IIEF-5 scores: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (7-21) and no ED (22-25).

A data sheet was used to record participant demographics, relevant history and examination, measurements taken and blood results (Appendix 4).

In each participant, the degree of insulin resistance was estimated by HOMA (homeostasis model assessment) insulin resistance score (Matthews et al 1985). The HOMA-IR score was computed with the following formula:

fasting plasma glucose (mmol/l) x fasting plasma insulin (mU/l) / 22,5. Higher values indicate insulin resistance and the present cut-off for the diagnosis of insulin resistance is 2,5. Normal subjects with normal weight should have a score of 1.

## 2.5 Analysis of data

Data was recorded in EXCEL and analysed using SAS Version 9.1. Data is reported as mean±std or as number (frequency). Where applicable, correlation between variables was determined (e.g. degree of IIEF (rank variable) and continuous variable) and plotted graphically.

### 2.6 Time frame

The MSDC runs on a weekly basis with an average of ten men seen weekly. Every  week on average three to five first time attendees are seen, who were invited to participate. Data collection was completed within a period six months. The data collection began as soon as permission had been granted by the relevant committees.

### 2.7 Costing and resources

All participants were regular clinic attendees and incurred no extra cost in participating in the study. Clinic equipment was used to perform the measurements (tape measure, scale, sphygmomanometer). No additional laboratory tests were performed over and above the routine tests performed at MSDC, therefore no additional costs were incurred. Printing and stationery costs were covered by the principal investigator. No grants or sponsorships were obtained, and there was no conflict of interest.

# CHAPTER THREE

# RESULTS

The following chapter presents the results for the current study. Participants are divided into three large population groups, namely Black, White and a third group containing participants of Asian, Chinese and Coloured people of South African descent. The numbers in the three groups are approximate reflections of official population statistics in South Africa, although this was unintentional. The first 100 completed assessments are included in the data, and this includes 61 black, 15 white and 24 participants in the third group which is referred to as the Other group henceforth for ease of reference. A total of 107 participants were assessed but 7 were excluded due to incomplete data sets. The reasons for these exclusions included laboratory errors and lost specimens.

## 3.1 Demographic data

The demographics of the study sample are shown in Table 3.1.

The average age of participants in the White group was significantly higher than in the other groups (p=0,02) as shown by ANOVA. Of the 100 participants, 32 were retired, 14 were unemployed and the remaining 54 were employed.

Table 3.1 Demographic data

| BLACK | WHITE | OTHER |
|---|---|---|
| n=61 | n=15 | n=24 |
| AVERAGE AGE IN YEARS (SD) | | |
| 56,7 (13,6) | 69,6 (9,1) | 59,8 (11,2) |
| AGE RANGE IN YEARS | | |
| 30-83 | 56-81 | 44-77 |

SD Standard deviation

### 3.2 Past medical history

The number of participants presenting with a co-morbid medical illness associated with ED risk is presented in Table 3.2. Medication use amongst participants included diuretics, alpha and beta blockers, calcium-channel blockers, ACE inhibitors, nitrates, statins and oral hypoglycaemic agents.

In the Black group, 27(44%) participants were smokers with a mean15 pack-year history, while 7(47%) White participants had a mean smoking history of 27 pack years and 12(50%) participants in the Other group had an average of 22 pack-years. In addition, 3 Black men had a past or current history of marijuana use and 1 smoked a tobacco pipe. One Asian man had a significant pipe-smoking history.

Table 3.2 Past medical history

| | BLACK | WHITE | OTHER |
|---|---|---|---|
| | n=61(%) | n=15(%) | n=24(%) |
| Co-morbid illnesses | 28(46) | 12(80) | 18(75) |
| Hypertension | 26(43) | 9(60) | 14(58) |
| Diabetes (type 2) | 9(15) | 2(13) | 8(33) |
| Hypercholesterolaemia | 1 | 5(33) | 2(1) |
| Epilepsy | 1 | 0 | 0 |
| BPH | 15(25) | 3(20) | 0 |
| IHD | 0 | 3(20) | 5(21) |
| CRF | 0 | 1 | 1 |

BPH Benign prostatic hyperplasia IHD Ischaemic heart disease

CRF Chronic renal failure

### 3.3 Physical characteristics

The measurements performed during the physical examination are summarised in Table 3.3. Among the Black participants, 12(20) had a body mass index above 30kg/m², as did 2(13) White participants and 6(25) participants in the Other group making them by definition obese. The overall BMI values did not differ significantly between groups (p=0,91). Those participants with central obesity as defined by IDF criteria according to their race, included 30(50) Black, 11(73) White and 15(63) Other participants.

Table 3.3 Physical characteristics

| BLACK | WHITE | OTHER |
|---|---|---|
| n=61 | n=15 | n=24 |
| AVERAGE WEIGHT (Kg) (SD) | | |
| 78,2 (22,0) | 81,9 (12,6) | 78,1 (19,6) |
| AVERAGE HEIGHT (cm) (SD) | | |
| 169,4 (7,8) | 176,1 (5,2) | 171,3 (9,3) |
| AVERAGE BMI (Kg/m²) (SD) | | |
| 27,1 (6,4) | 26,4 (4,0) | 27,0 (6,2) |
| AVERAGE WAIST CIRCUMFERENCE (cm) (SD) | | |
| 93,0 (15,0) | 100,2 (12,2) | 98,6 (16,7) |
| WAIST CIRCUMFERENCE RANGE (cm) | | |
| 64-150 | 80-131 | 76-129 |
| AVERAGE HIP CIRCUMFERENCE (cm) (SD) | | |
| 101,1 (11,8) | 105,0 (7,5) | 102,3 (13,6) |
| AVERAGE WAIST/HIP RATIO (SD) | | |
| 0,91 (0,07) | 0,95 (0,06) | 0,96 (0,07) |
| AVERAGE BLOOD PRESSURE (mmHg) | | |
| 133/84 | 130/86 | 134/83 |

| | | | |
|---|---|---|---|
| SD | Standard deviation | m | metre |
| Kg | Kilogram | BMI | body mass index |
| cm | centimetre | mmHg | millimetres mercury |

Overall waist-to-hip ratios were significantly different between groups as shown by ANOVA (p=0,008). Blood pressures were recorded for those participants who were not taking an antihypertensive or had no prior diagnosis of hypertension. Those taking antihypertensives or with a previous diagnosis of hypertension automatically qualify as a component of MS diagnosis. Neither the systolic nor diastolic values differed between the groups as shown by ANOVA (p=0,95 and 0,91 respectively).

### 3.4 Erectile function

Figure 3.1 shows the average IIEF score as well as the average duration of ED amongst the three groups. The average ED duration in years does not differ statistically between groups as shown by ANOVA (p=0,12), with the total sample having an average ED duration of 3,8 years (4,0) and individual group means (SD) of 3,2(3,7), 4,7(3,8) and 5(4,7) respectively. Pearson correlation co-efficients of univariate relationships between ED duration and other measured parameters were performed. ED duration correlated with a number of parameters dependent on ethnic origin.

In the Black group, ED duration correlated inversely with systolic blood pressure (r=-0,383; p=0,02), triglyceride level (r=0,240; p=0,06) and HDL (r=-0,279; p=0,03). In the White group ED duration correlated significantly with glucose (r=0,557; p=0,03), HbA1c (r=0,583; p=0,02) and cholesterol (r=0,572; p=0,03). In the Other group no statistically significant correlations were found with ED duration.

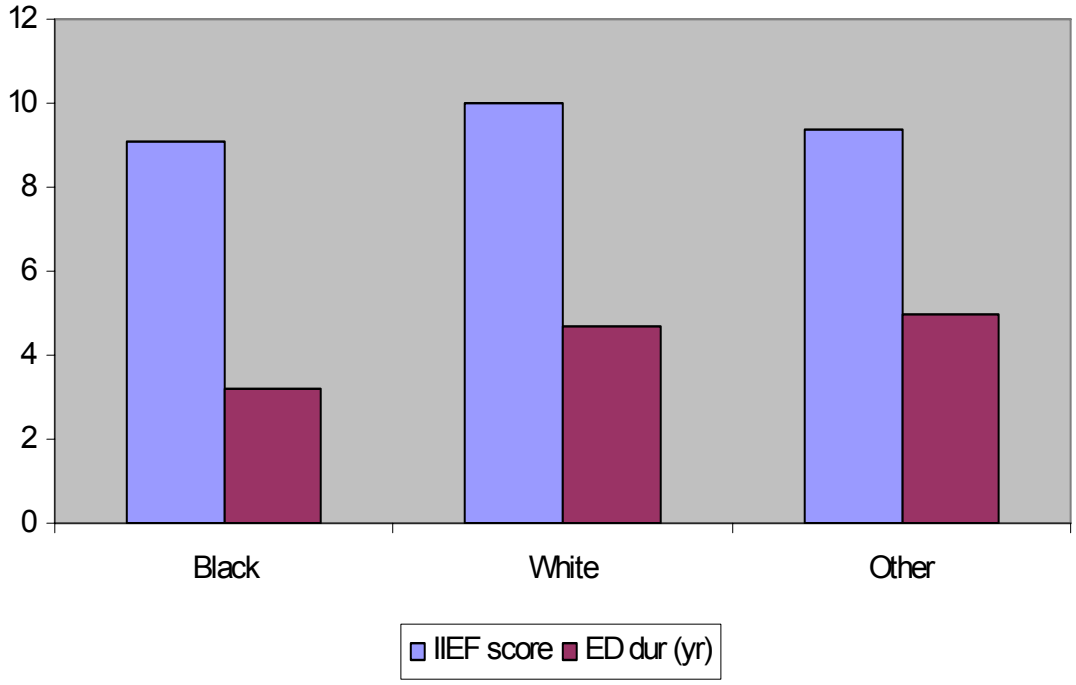



Figure 3.1 Erectile function

When all participants were included ED duration correlated significantly with triglycerides only (r=0,188; p=0,06) and not with blood pressure. However, once adjusted for HDL, triglycerides, glucose, HbA1c, HOMA and waist to hip ratio, ED duration correlated inversely with systolic blood pressure (r=-0,337; p=<0,02) but the inverse relationship with diastolic blood pressure was not statistically significant (r=-0,21; p=0,16). For all participants multivariate analysis showed after adjusting for co-variates, glucose (p=0,013) and HbA1c (p=,0001) to be significant predictors of ED duration. Figure 3.2 shows the proportion of participants in each group presenting with mild (17-21), mild to moderate (12-16), moderate (8-11) and severe (5-7) ED according to their IIEF scores.

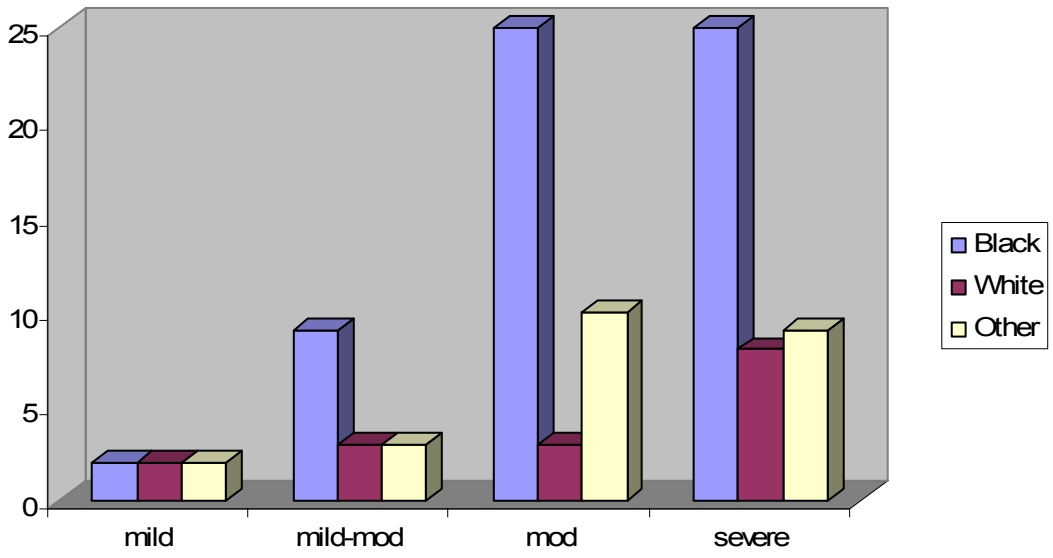



Figure 3.2 Severity of ED in each group

Average IIEF scores (SD) per group were 9,1(3,4); 10,0 (6,1) and 9,4 (3,6) respectively. These scores were not statistically different between the groups as shown by ANOVA (p=0,74). All three groups had a predominance of participants with moderate or severe ED. All the groups had participants with the most severe ED (IIEF score of 5), while the highest scores in each of the three groups were 18, 22 and 17 respectively. Pearson correlation co-efficients of univariate relationships between IIEF score and other measured parameters were performed within ethnic groups. Although no correlations reached statistical significance (p<0,05) LH, testosterone, age, smoking history, ED duration, HDL and waist to hip ratio showed a strong correlation with IIEF score. When participants were divided into three groups (mild, moderate, severe) according to IIEF scores, there was no correlation between ED duration and ED severity (p=0,43). Age was a strong but not significant predictor of ED severity within

these groups (p=0,07). No other parameters within the lipogram or hormone profile were significant predictors of ED severity.

### 3.5 Fasting lipogram

The results from the fasting lipogram are depicted in Table 3.4. All values are given in mmol/l (standard deviations).

Table 3.4 Fasting lipogram

| | ALL | BLACK | WHITE | OTHER |
|---|---|---|---|---|
| | n=100 | n=61 | n=15 | n=24 |
| Cholesterol | 4,5(1,2) | 4,4(1,2) | 4,3(07) | 4,9(1,3) |
| Triglycerides | 1,5(1,0) | 1,4(1,0) | 1,3(0,6) | 1,8(1,1) |
| HDL | 1,2(0,3) | 1,2(0,3) | 1,3(0,3) | 1,2(0,3) |
| LDL | 2,6(1,1) | 2,5(2,0) | 2,5(0,6) | 3,1(1,3) |

The higher cholesterol value in the Other group did not reach statistical significance as shown by ANOVA (p=0,18). The higher triglyceride value in the Other group was not significantly higher as shown by ANOVA (p=0,15). There was clearly no significant difference in group HDL (p=0,57) as shown by ANOVA. The higher LDL value in the Other group tended towards but never reached statistical significance (p=0,07) as shown by ANOVA.

### 3.6 Indices of glucose metabolism

Figure 3.3 presents the results from the fasting blood samples taken for glucose (mmol/l), insulin (IU/l), HbA1c (%) and the calculated HOMA scores from these samples. Mean values per group are depicted graphically.

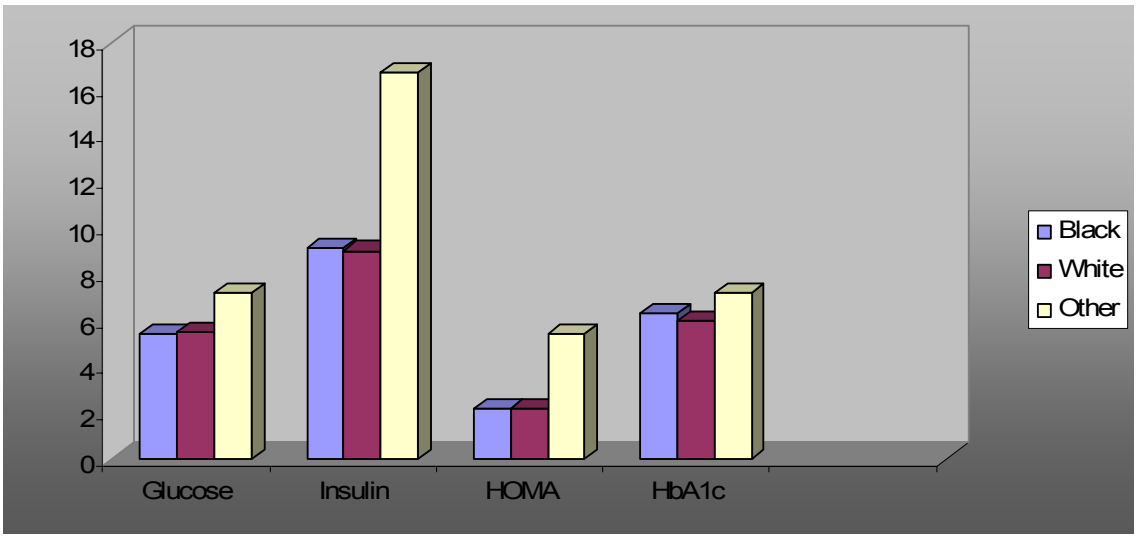



Figure 3.3 Indices of fasting glucose metabolism per group

The mean (SD) values for the total population were as follows: glucose 5,9 mmol/l (3,1); insulin 10,9 IU/l (13,4); HOMA 3,0 (4,0) and HbA1c 6,5 % (2,1). Insulin levels were significantly higher amongst participants in the Other group as shown by ANOVA (16,7 compared to 9,5 and 9,0; p=0,049). HOMA scores were significantly higher in the Other group as compared to the first two groups as shown by ANOVA (mean of 5,5 compared to2,2 in the first two groups, p=0,002). Glucose concentration differences between groups were of borderline

significance (p=0,05). HbA1c levels did not differ between groups as shown by ANOVA (p=0,17).

### 3.7 Endocrine parameters

The endocrine parameters testosterone, FSH and LH are presented in Table 3.5. The four values in each group represent the mean (standard deviation), minimum and maximum.

Table 3.5 Endocrine parameters

| | TOTAL<br>n=100 | BLACK<br>n=61 | WHITE<br>n=15 | OTHER<br>n=24 |
|---|---|---|---|---|
| **TESTOSTERONE** | **15,4 (6,6)** | **14,9 (6,2)** | **17,2 (7,7)** | **15,6 (6,9)** |
| **(µmol/l)** | **4,0 / 35,9** | **4,0 / 28,4** | **5,2 / 29,1** | **7,3 / 35,9** |
| **FSH** | **6,5 (7,7)** | **4,9 (3,1)** | **11,0 (17,5)** | **7,9 (5,1)** |
| **(IU/l)** | **0,8 / 69,7** | **0,8 / 18,6** | **2,0 / 69,7** | **2,9 / 20,9** |
| **LH** | **5,5 (5,1)** | **4,5 (2,2)** | **8,3 (11,7)** | **6,5 (2,9)** |
| **(IU/l)** | **1,6 / 44,2** | **1,6 / 15,2** | **2,0 / 44,2** | **2,3 / 12,2** |

FSH Follicle Stimulating Hormone (1,4-18,1 IU/l)

LH Luteinising Hormone (<70y: 1,5-9,3 IU/l; >70y: 3,1-34,6 IU/l)

Testosterone levels did not differ significantly between groups (p=0,46). Hypogonadism (defined as a serum testosterone less than 12 μmol/l) was present in 23 Black (38%), 6 White (40%) and 8 Other (33%) participants. The mean (SD) LH concentration for all groups was 5,5 (5,1), with individual group means being significantly different between groups as shown by ANOVA (p=0,021).

### 3.8 The metabolic syndrome

As discussed in the methods section, the International Diabetes Federation (2005) criteria were used to determine the prevalence of MS in the study population. The ethnic specific criteria were applied to all three groups. As mentioned in an earlier section, those individuals already on medication for hypertension and lipid abnormalities as well as a prior diagnosis of type two diabetes mellitus were considered to have one or more positive criteria for the diagnosis of MS. Two or more of these criteria along with central obesity is required for the diagnosis of MS.

In the study population, 20 of 61 (33%) Black participants were diagnosed with MS. Five(8%) of these participants had no prior medial history and were not on any chronic medications. Seven(11) of these participants were known to suffer from type two diabetes, while 13(21) had a prior diagnosis of hypertension. Of these 20, 8 were hypogonadal (40%). Amongst the White participants, 6 of 15 (40%) participants had MS. Two of these 6 had no medical history or chronic medications. There were 2 type two diabetics amongst the remaining 4, all of

which also suffered from hypertension. Of the 6 with MS, 3 were hypognadal (50%). Amongst the Other group 6(25) participants had no prior medical history, while 5(21) had a prior diagnosis of diabetes and 10(42) were already on treatment for hypertension. This group had the highest prevalence of MS with 13 of 24 (54%) participants. Of these 13, 6 were hypogonadal (46%). The prevalence of MS in the total study sample was therefore 39 of 100 participants (39%). Table 3.6 shows some differences in parameters between participants with and without MS. No significant correlation was found between ED duration, severity and presence of MS when adjusted for cholesterol, HDL, triglycerides, glucose, HOMA and $HbA_1c$.

Table 3.6 Comparison between participants with and without MS (mean and SD).

| | MS | No MS |
|---|---|---|
| | n=39 | n=61 |
| AGE | 62,7(11,7) | 57,1(13,7) |
| TESTSTERONE (µmol/l) | 14,1(5,8) | 16,3(7,0) |
| LH (IU/l) | 4,8(2,0) | 6,0(6,5) |
| FSH (IU/l) | 6,5(4,0) | 6,6(9,6) |
| IIEF score | 9,2(4,1) | 9,4(3,9) |
| ED duraton | 4,3(4,1) | 3,5(3,9) |

# CHAPTER FOUR

# DISCUSSION

This chapter discusses the results outlined in the previous chapter. Results are discussed in the same order as they were presented and not necessarily in the order of importance, however a more detailed discussion on the important aspects of the study is given in order to fulfil the objectives and aims of the study. Emphasis is placed on the statistically significant findings from the study and other parameters that did not reach significance but are particularly interesting or contradictory are discussed. Included in the discussion are some limitations of the study and recommendations for future research.

A prevalence study conducted in a South African tertiary care centre has been outlined. The study enrolled one hundred participants, all men over the age of thirty with varying degrees of erectile dysfunction. A thorough history, physical examination, questionnaire administration and serum tests were performed in order to identify risk factors for ED, severity of ED and the prevalence of the metabolic syndrome. The data was collected over a period of six months at the Johannesburg Hospital Male Sexual Dysfunction Clinic.

## 4.1 Demographic data

The 100 participants were divided into three population groups according to ethnicity. The numbers in the groups are approximate reflections of the population statistics in South Africa, although this was unintentional. The varying

numbers of participants per group, 61,15 and 24 makes analysis of results between groups more complex and sample sizes smaller if the data sets are considered separately. The emphasis is placed on the total sample, being 100 South African men of different ethnicity.

The average age of the sample is 59 years which is in keeping with the population presumed to be at risk for primary ED. The significantly higher age among White participants may alter the results somewhat, if it is assumed that older men are predisposed to more degenerative diseases and may have more cardiovascular and hence ED risk factors. Maximum ages across the groups are similar, although the youngest Black participant (30 years) is well below the youngest participant in the other two groups. Age did not significantly affect the severity of ED when separate age cohorts and IIEF-5 scores were compared, although it was a strong predictor (p=0,07).

**4.2 Past medical history**

There is a very high prevalence of co-morbid diseases amongst the participants. As discussed in the literature review cardiovascular risk factors such as hypertension, diabetes mellitus and hypercholesterolaemia are also risk factors for ED (Levine et al 2000; Rosen et al 2004; Seftel et al 2004). The prevalence of these co-morbid diseases in the three groups is 46%, 80% and 75%. As a comparison in Rosen's study of almost 300 000 men with ED, only 32% did not have one of the above co-morbid diseases. Perhaps surprisingly, the lower prevalence of co-morbid illnesses among Black participants is not associated

with a less severe ED (IIEF 9,1; p=0,74) compared to the other two groups. Smoking habits and number of pack years among participants are similar between groups. The higher pack year history amongst White participants is likely related to the higher mean age in this group. According to the latest Demographic and Health Survey in South Africa, the percentage of South African males currently smoking was 31,1% (Department of Health 2003). The prevalence of smoking in the current sample is therefore higher than the national prevalence, which could be a contributing factor to the ED in almost half of the participants.

### 4.3 Physical characteristics

During the physical examination, weight and height measurements were performed in order to calculate the body mass index. The average weight for the total sample is 78,4 kg with no differences in height, weight and BMI between groups. The average BMI for all the groups falls within the high range (25,0-29,9 kg/m²). Overall 20 participants were classified as obese just by their BMI alone. One Black participant weighed 200kg with a calculated BMI of 61 kg/m², this outlying measurement may have skewed the results for the Black group. The lightest participant weighed just 50 kg, with the lowest BMI for the sample being 17,1 kg/m². These results appear to confirm that no body morphology is excluded from developing ED.

Those participants with central obesity as defined by IDF criteria according to their race, included 30(50%) Black, 11(73) White and 15(63) Other participants.

As mentioned during the discussion of the IDF criteria for MS, a large ethnic-specific waist circumference is a prerequisite for the diagnosis of MS. Of the 56 participants with a large ethnic-specific waist circumference, 39 were found to have MS. Hip circumference is included in the assessment as a control measure for waist circumference. Waist circumference and waist-to-hip ratios are lowest in the Black group (p=0,008) and it is not surprising therefore that this is the only group in which ethnic-specific waist circumference falls below the IDF cut-off for central obesity (93 cm vs 94 cm). The other two groups have average waist circumferences well above central obesity levels (100,2 cm vs 94cm and 98,6 cm vs 90 cm respectively). The new IDF criteria introduced the lowest waist circumference measurements for people of Asian descent (<90 cm), yet in the current sample, the Other group has a much higher average waist circumference than the Black group. It is not surprising therefore that the Other group has the highest prevalence of MS (54%).

Blood pressure measurements are less useful in the current study as a significant proportion (49%) of the participants were taking an antihypertensive at the time of assessment. Blood pressures were recorded in the remaining 51 participants but showed no differences between groups. The average systolic (133 mmHg) and diastolic (84 mmHg) values are not that raised considering the population being assessed. Blood pressure does form an important component of MS diagnosis with levels above 130/85 mmHg being diagnostic. The fact that 49 participants were taking treatment for hypertension qualifies as a component for MS diagnosis regardless of measurements.

### 4.4 Erectile function

The average duration of ED is highest among the Other group (5 years) although not significantly longer than the total average of 3,8 years. ED duration correlates with several parameters of the fasting lipogram and indices of glucose metabolism, although these are mostly ethnic specific correlations. Glucose and HbA1c appear to correlate strongly with ED duration and these parameters would be part of the initial diagnostic workup for men presenting with ED worldwide. The lack of correlation (and in fact an inverse correlation) between blood pressure and ED duration or severity should be interpreted with caution as blood pressure was measured as a once off reading in only half of the participants. What is surprising is the length of time from disease onset to first presentation at the clinic (average 3,8 years) which may reflect the lack of access that some individuals have to medical care in South Africa or a reluctance on their part to seek help for a private matter such as ED.

Late presentation of illness may also be assumed when one considers that 80% of participants had moderate to severe ED based on IIEF scores (between 5-11). Of these 80 participants, 42% had severe ED (IIEF 5-7), making this the largest group at presentation. This is in contrast to the findings of the Massachusetts Male Aging Study where only 9,6% of the 52% of men who had ED presented with complete ED, while 25,2% had moderate ED and 17,2% had minimal ED (Feldman et al 1994). LH, testosterone, age, smoking history, ED duration, HDL and waist to hip ratio showed strong correlation with IIEF score although none reached significance. The average IIEF score among the 39 participants with MS

is 9,2 and this is not worse than the score of 9,4 among those without MS. In the current study, it can be concluded that participants with MS do not have more severe ED than those without MS. This is contrary to the findings of Demir et al 2006.

**4.5 The fasting lipogram**

Hypercholesterolaemia is a well known risk factor for cardiovascular events and men with ED may well have dyslipidaemias (Seftel et al 2004).The mean total fasting cholesterol is 4,5 mmol/l. The recommended cholesterol limits vary between institutions and generally depend on other risk factors. Category one risk or high risk individuals should keep their fasting cholesterol below 4,5 mmol/l. This includes people with established atherosclerosis, coronary artery disease, cerebrovascular disease, peripheral vascular disease and type two diabetes mellitus. The average fasting cholesterol in the Other group is well above this level and since 18 of the 24(75%) participants in this group had a co-morbid disease increasing their cardiac risk profile, the target cholesterol for them would be <4,5 mmol/l.

The mean total fasting triglyceride of 1,5 mmol/l falls within the recommended range of <1,7 mmol/ l (IDF criteria). However once again the Other group had a mean triglyceride level above the recommended range with a value of 1,8 mmol/l. Eleven participants(46%) in this group had raised triglycerides which is a much higher percentage than in the Black (n=13;21%) and White (n=2;13%) group. Since triglyceride levels fluctuate with food intake, it is important to

consider only fasting levels, for these one has to rely on participants being truthful regarding their recent intake.

Fasting HDL forms an important component in the diagnosis of MS, less than 1,03 mmol/l being a criterion. All group means and the total mean HDL are above this level in the current study. Only 14(23%) Black and 3(20%) White participants had HDL below the critical level, but once again the Other group had the highest percentage of participants with low HDL, totalling 12(50%).

Although LDL is not included in the definition of MS, it has clearly been shown to be a risk factor for cardiovascular disease (Eckel 2005, Kim 2000). Individuals at high risk (category one) should aim for fasting LDL levels <2,5 mmol/l. The sample mean for LDL is above this level at 2,6 mmol/l. Once again the Other group had the worst results with a mean of 3,1 mmol/l with only 7(29%) participants having LDL levels < 2,5 mmol/l.

**4.6 Indices of glucose metabolism**

Disorders of glucose metabolism carry significant risk for cardiovascular disease and ED, the main one in the elderly being type two diabetes mellitus (Seftel et al 2004). Nineteen participants had been diagnosed with type two diabetes mellitus prior to participation in the study which is on its own a positive criterion for MS diagnosis.

The other criterion is a fasting plasma glucose ≥5,6 mmol/l. Mean fasting plasma glucose levels are 5,9 with the Other group having a significantly higher level, 7,2 mmol/l (p=0,05). Accurate indices of glucose metabolism are highly dependent on a state of fasting and once again study participants were requested to fast and be truthful about their intake.

Glycated haemoglobin levels can be used as an indicator of glucose control over the preceding three month period. Non-diabetic participants are expected to have levels < 6% while diabetic sufferers can aim for a target value < 7%. The mean total HbA1c is 6,5% with the Other group having a value of 7,2%. However this result is to be expected as this group does have highest prevalence of diabetes mellitus.

Serum insulin levels can vary markedly with oral intake and the presence of insulin resistance or diabetes mellitus. The reference range for insulin given by National Health Laboratory Services is 8,9-28,4 mU/l. Higher levels would appear to suggest insulin resistance, however considered on their own insulin levels are notoriously inaccurate. The highest levels are found in the Other group (16,7 mU/l; p=0,049) which would appear to correlate with the higher prevalence of diabetes. To improve the predictive capabilities of insulin, the HOMA-IR score was computed with the following formula: fasting plasma glucose (mmol/l) x fasting plasma insulin (mU/l) / 22,5 (Matthews et al 1985). Higher values indicate insulin resistance and the present cut-off for the diagnosis of insulin resistance is 2,5. Normal subjects with normal weight should have a score of 1. Once again

the significant differences between the groups as shown by ANOVA was due to the Other group having a score of 5,5 (p=0,02).

### 4.7 Endocrine parameters

A male hormone profile is usually performed as part of a diagnostic work-up of a man with ED. It stands to reason that men with hypogonadism may experience weak or absent erections. There is no standard value for low testosterone, and laboratory reference ranges are usually provided. The NHLS range is 8,4-28,7 nmol/l. Follicle Stimulating or Luteinising Hormone levels accompany testosterone and give an indication of testicular function. Reference ranges are given in section 3.7. Hypogonadism was present in 37 participants, while 17(44%) men with MS were also hypogonadal. The significantly raised LH in the White group is likely due to an outlying value of 44 IU/l in one participant, and all groups had normal mean LH and testosterone levels.

### 4.8 The metabolic syndrome

The real prevalence of MS worldwide is difficult to ascertain due to the various definitions which have been used in the past. Data from developed countries would be difficult to extrapolate to South Africa. Prevalence studies from South Africa have been infrequent and rarely focused on Men's Health issues such as ED. Prevalence of MS is certainly showing an upward trend due to obesity, inactivity and urbanisation. It is estimated that half of South Africans may be overweight or obese and that as many as 1 in 4 South African adults may have MS. Worldwide prevalence statistics for MS appear to be in the region of 25% of

adults. It may be assumed that certain populations or groups of patients would have a higher prevalence of MS, for example diabetics or patients with coronary heart disease. Since these are well known risk factors for ED as well, it may be extrapolated that men with ED would have a higher prevalence of MS. The 39% prevalence of MS in the current study may be explained by the multitude of co-morbid illnesses the participants presented with, as hypertension, dyslipidaemias and diabetes are all associated with MS. The Black participants showed the lowest prevalence of MS at 33%. Historically, South African Black people had a lower incidence of cardiac events due to less sedentary liestyles and lower fat diets than their white countrymen. With urbanisation and exposure to 'Westernised' diets this seems to be changing as more Black people are presenting with lifestyle diseases. The 40% prevalence of MS among White participants is also higher than would be expected from the general public, but this figure is more understandable considering the more sedentary lifestyles and high fat diets that are more prevalent in this population group. Cardiovascular disease is usually cited as the most common cause of death in Caucasian males in South Africa. The highest prevalence of MS is found in the group composed of males of Asian, Chinese and Coloured descent where 54% of participants were diagnosed with MS. Although the group numbers are small, the results show that if men from these population groups present with ED, they are more likely to have MS than not.

Of interest, 8(21%) participants with MS had no prior history of chronic illnesses or chronic medications suggesting that MS can be completely asymptomatic.

Men presenting with ED may represent an ideal patient group to screen for MS, and therefore for cardiovascular disease, especially for those men within the asymptomatic period.

### 4.9 Limitations and recommendations

Modern day prevalence studies in developed countries usually involve thousands of participants. The three largest and most relevant studies conducted in Men's Health recently, namely Framingham, MALES and MMAS referenced in the literature review, enrolled thousands of men. It is difficult making comparisons with the current study due to the much smaller sample size, particularly when the 100 participants are further subdivided into three groups. The smaller the sample is, the more likely it is that results may be influenced by chance. The tertiary care Centre is not the ideal place to do epidemiological or prevalence studies of such large magnitude, and future studies could perhaps be community-based where a significantly larger population may have access to the study.

Limiting participants to those with ED does not allow assessment of the prevalence of ED in a South African setting. This could be done by screening men in the community for ED symptoms. The IIEF proved to be a valuable, standardised, cross-cultural tool which was easily administered in the current study. Reliance on participant honesty when filling out the questionnaire is always a consideration when administering a functional score tool.

A comprehensive cardiovascular assessment was not performed in the current study, for example an electrocardiogram or angiogram, to detect symptomatic or asymptomatic coronary artery disease. It would be interesting to know the prevalence of cardiovascular disease in the current sample as some participants had been suffering from ED for several years, this was however beyond the scope of the current study.

## CHAPTER FIVE

## CONCLUSIONS

The metabolic syndrome is a combination of medical disorders that increase the risks of cardiovascular disease and diabetes mellitus. It affects a great number of people, with prevalence increasing with age. The pathophysiology is complex and only partially understood. Controversy exists as to whether MS is a real syndrome as the aetiology has not been well defined. The fact remains that the clustering of components of MS are very prominent among those people at risk for ischaemic heart disease or frank diabetes. These components are also the risk factors for erectile dysfunction, therefore it has been suggested that screening ED patients for asymptomatic coronary artery disease may be cost effective. Patients with established CAD experienced ED symptoms on average two to three years before the onset of coronary symptoms, suggesting that ED may be a warning sign or an opportunity for early intervention. Considering the impact that cardiovascular disease has on morbidity, mortality and the health budget, screening for asymptomatic disease and primary prevention should be a priority. Aggressive lifestyle changes and possibly medications could be implemented to prevent the progression from asymptomatic MS to life-threatening cardiovascular and cerebrovascular disease.

The prevalence of MS in South Africa has not been well studied, particularly not in a subset of males with ED. The current study was designed to determine this prevalence as well as the severity of ED and other risk factors contributing to this

common disorder with a significant impact on quality of life. The prevalence of MS in one hundred men with ED was 39%, with the highest percentages in a mixed group of Asian, Coloured and Chinese origin. The average duration of ED was 3,8 years with an average IIEF-5 score of 9 (moderate ED). MS did not affect ED severity as per IIEF-5 score. Of interest, 8 participants with MS had no prior history of chronic illnesses, other than ED, or chronic medications suggesting that MS can be completely asymptomatic. Men presenting with ED may represent an ideal patient group to screen for MS, and therefore for cardiovascular disease, especially for those men within the asymptomatic period. ED is probably the most sensitive barometer of men's health worldwide, and several new insights will allow us to see ED as part of a broader health risk and not as an isolated dysfunction.

## CHAPTER SIX

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# APPENDIX 1

# PARTICIPANT INFORMATION SHEET

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

# DEPARTMENT OF SURGERY

**UNIVERSITY OF THE WITWATERSRAND**

***DIVISION OF UROLOGY***

**JOHANNESBURG HOSPITAL**

---

## *Study title: The prevalence of the metabolic syndrome in men presenting with erectile dysfunction in South Africa*

PARTICIPANT INFORMATION SHEET

Hello. My name is Dr BR Wood; I am a Urology Registrar in the Department of Urology at the Johannesburg Hospital. I will be conducting a study on men suffering from erectile dysfunction and the risk factors involved, in particular the metabolic syndrome. The metabolic syndrome consists of several irregularities in cholesterol, blood glucose, blood pressure and body weight. The study will take place at the Johannesburg Hospital as part of a post-graduate degree (MMed).

I would like to invite you to consider participation in the study. Participation is entirely voluntary and refusal to participate will involve no penalty or loss of benefits. You may discontinue participation at any time without giving a reason.

Should you agree to participate, you will be asked to sign the accompanying consent form, and you will be given a copy to take home.

Before you agree to participate, I would like you to read through this information leaflet about the study. This leaflet will help you decide whether you would like to participate in the study. It may contain words that you do not understand. Please ask me to explain any information. You may take home an unsigned copy of this leaflet and consent form to think about it or to discuss with your family before making your decision.

The study will take place at the Johannesburg Hospital Men's Sexual Dysfunction Clinic. Approximately one hundred participants who meet the study criteria will be enrolled in the study. The total assessment will be completed in the first clinic visit and will take roughly thirty minutes. A medical history including medications, illnesses and smoking habits will be taken. A brief questionnaire consisting of five questions regarding your sexual health will be filled in. Should you participate, it is very important that you be truthful during the history and questionnaire so as not to jeopardise the results.

An examination, which is the routine examination done at the clinic, will then be performed whether or not you are involved in the study. The following additional measurements will be recorded: height, weight, blood pressure and waist circumference.

Certain blood tests will be performed as part of the study. Once again, these blood tests are done routinely for all clinic attendees as part of standard clinical care, regardless of whether you are enrolled in the study or not. Approximately fifteen millilitres (three teaspoons) of blood will be drawn by experienced clinic staff using a sterile technique. You may experience slight discomfort during the procedure as well as bleeding from the puncture site, bruising and a feeling of faintness. The following tests will be done on your blood samples: fasting lipogram (cholesterol and fats), fasting blood glucose and hormone profiles (testosterone and insulin).

Your participation in this study will contribute to medical knowledge that may help other patients, however, you may not benefit directly from this study. If you do not give an accurate history or do not follow the study guidelines, you may be withdrawn at any time. You will not be paid money to participate in the study as no extra cost will be incurred by you.

All your details will be treated with complete confidentiality, and your identity will not be made known. Data from the study will be pooled, analysed and may be presented at scientific meetings and in scientific journals. At no stage will it be possible to identify you as a participant. You will be informed of any finding of importance to your health at your next clinic visit, alternatively we will contact you with the details provided by you to the hospital. Should you be newly diagnosed with any abnormality we will refer you to the relevant clinics at the Johannesburg

Hospital for example diabetic, hypertension or lipid clinic. This clinical study protocol has been submitted to The University of Witwatersrand Human Research Ethics Committee and written approval has been granted by that Committee, approval has also been sought from the Hospital Superintendent. If you would like more information, please contact me at the clinic on (011) 488 4463.

Dr BR Wood

Department of Urology

University of the Witwatersrand and Johannesburg Hospital

# APPENDIX 2

# PARTICIPANT CONSENT FORM

# DEPARTMENT OF SURGERY

**UNIVERSITY OF THE WITWATERSRAND**

DIVISION OF UROLOGY

**JOHANNESBURG HOSPITAL**

---

***Study title: The prevalence of the metabolic syndrome in men presenting with erectile dysfunction in South Africa***

PARTICIPANT CONSENT FORM

I hereby confirm that I have been informed by the study doctor, Dr BR Wood about the nature, conduct, benefits and risks of the abovementioned study.

I have also received, read and understood the participant information sheet regarding the study.

I am aware that the results of the study including personal details regarding sex, age, date of birth and diagnosis will be anonymously processed into a report.

I may at any stage, without prejudice, withdraw my consent and participation in the study.

I have had sufficient opportunity to ask questions and of my own free will declare myself prepared to participate in the study.

PARTICIPANT

| | | |
|---|---|---|
| _____ | _____ | _____ |
| Print name | Signature | Date and time |

I Dr BR Wood, herewith confirm that the above participant has been fully informed about the nature, conduct and risks of he above study.

STUDY DOCTOR

| | | |
|---|---|---|
| _____ | _____ | _____ |
| Print Name | Signature | Date and time |

WITNESS/TRANSLATOR

| | | |
|---|---|---|
| _____ | _____ | _____ |
| Print name | Signature | Date and time |

# APPENDIX 3

# IIEF-5 QUESTIONNAIRE

**The IIEF-5 Questionnaire**

Please tick appropriate box

Over the past 6 months:

| | | | | | |
|---|---|---|---|---|---|
| 1. How do you rate your confidence that you could get and keep an erection? | Very low 1 | Low 2 | Moderate 3 | High 4 | Very High 5 |

| | | | | | |
|---|---|---|---|---|---|
| 2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration? | Almost never / never 1 | A few times (much less than half the time) 2 | Sometimes (about half the time) 3 | Most times (much more than half the time) 4 | Almost always / always 5 |

| | | | | | |
|---|---|---|---|---|---|
| 3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner? | Almost never / never 1 | A few times (much less than half the time) 2 | Sometimes (about half the time) 3 | Most times (much more than half the time) 4 | Almost always / always 5 |

| | | | | | |
|---|---|---|---|---|---|
| 4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse? | Extremely difficult 1 | Very difficult 2 | Difficult 3 | Slightly difficult 4 | Not difficult 5 |

| | | | | | |
|---|---|---|---|---|---|
| 5. When you attempted sexual intercourse, how often was it satisfactory for you? | Almost never / never 1 | A few times (much less than half the time) 2 | Sometimes (about half the time) 3 | Most times (much more than half the time) 4 | Almost always / always 5 |

IIEF, International Index of Erectile Function, Adapted from Rosen RC et al(1999)

International Journal of Impotence Research 11(6). Study number:

# APPENDIX 4

# DATA COLLECTION SHEET

# DEPARTMENT OF SURGERY

**UNIVERSITY OF THE WITWATERSRAND**

***DIVISION OF UROLOGY***

**JOHANNESBURG HOSPITAL**

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***Study title: The prevalence of the metabolic syndrome in men presenting with erectile dysfunction in South Africa***

DATA COLLECTION SHEET

- Study number:
- Age:
- Race:
- Occupation:
- Smoking History:
- Medical illnesses:
- Current medications:
- Duration of ED:
- IIEF-5 score:
- Waist circumference(cm):
- Hip circumference(cm):
- Weight(kg):
- Height(cm):

- BMI:
- Blood pressure(mmHg):
- Total fasting cholesterol(mmol/l):
- Fasting triglycerides(mmol/l):
- Fasting HDL(mmol/l):
- Fasting LDL(mmol/l):
- Fasting glucose(mmol/l):
- Fasting serum insulin(mU/l):
- HbA1c(%):
- Testosterone(nmol/l):
- LH(IU/l):
- FSH(IU/l):

# APPENDIX 5

# ETHICAL CLEARANCE CERTIFICATE

**UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG**

Division of the Deputy Registrar (Research)

**HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)**
R14/49 Wood

| | |
|---|---|
| **CLEARANCE CERTIFICATE** | **PROTOCOL NUMBER M070737** |
| **PROJECT** | The prevalence of the metabolic syndrome in men presenting with erectile dysfunction in South Africa |
| **INVESTIGATORS** | Dr BR Wood |
| **DEPARTMENT** | Urology/Surgery |
| **DATE CONSIDERED** | 07.07.27 |
| **DECISION OF THE COMMITTEE*** | APPROVED UNCONDITIONALLY |

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

**DATE** 07.08.20 **CHAIRPERSON** .....
(Professors PE Cleaton-Jones, A Dhai, M Vorster, C Feldman, A Woodiwiss)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Prof M Haffajee

---

**DECLARATION OF INVESTIGATOR(S)**

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

# APPENDIX 6

# HOSPITAL SUPERINTENDENT PERMISSION

Gauteng Department of Health

## PERMISSION FOR RESEARCH

DATE: JULY 2007

NAME OF RESEARCH WORKER: DR BR WOOD

TITLE OF RESEARCH PROJECT PREVALENCE OF METABOLIC SYNDROME IN MEN PRESENTING WITH ERECTILE DYSFUNCTION IN S.A.

OBJECTIVES OF STUDY (Briefly or include a protocol): SEE ATTACHED PROTOCOL

METHODOLOGY (Briefly or include a protocol): SEE ATTACHED PROTOCOL

CONFIDENTIALITY OF PATIENTS MAINTAINED: YES

COSTS TO THE HOSPITAL: NO ADDITIONAL COSTS

APPROVAL OF HEAD OF DEPARTMENT: YES

APPROVAL OF CRHS OF WITS UNIVERSITY: PENDING

SUPERINTENDENT PERMISSION:

Signature: [signature] Date: 16/07/2007

Subject to any restrictions: Subject to Ethic Committee approval.

# APPENDIX 7

# IIEF QUESTIONNAIRE

**The IIEF Questionnaire**

Please tick appropriate box

Over the past 4 weeks:

1. How often were you able to get an erection during sexual activity?
   0 = No sexual activity
   1 = Almost never/never
   2 = A few times (much less than half the time)
   3 = Sometimes (about half the time)
   4 = Most times (much more than half the time)
   5 = Almost always/always

2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?
   0 = No sexual activity
   1 = Almost never/never
   2 = A few times (much less than half the time)
   3 = Sometimes (about half the time)
   4 = Most times (much more than half the time)
   5 = Almost always/always

3. When you attempted sexual intercourse, how often were you able to penetrate (enter)?
   0 = Did not attempt intercourse
   1 = Almost never/never
   2 = A few times (much less than half the time)
   3 = Sometimes (about half the time)
   4 = Most times (much more than half the time)
   5 = Almost always/always

4. During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) you partner?
   0 = Did not attempt intercourse
   1 = Almost never/never
   2 = A few times (much less than half the time)
   3 = Sometimes (about half the time)
   4 = Most times (much more than half the time)
   5 = Almost always/always

5. During sexual intercourse, how difficult was it to maintain your erection to complete intercourse?
   0 = Did not attempt intercourse
   1 = Extremely difficult
   2 = Very difficult
   3 = Difficult
   4 = Slightly difficult
   5 = Not difficult

6. How many times have you attempted sexual intercourse?
   0 = No attempts
   1 = One to two attempts
   2 = Three to four attempts
   3 = Five to six attempts
   4 = Seven to ten attempts
   5 = Eleven or more attempts

7. When you attempted sexual intercourse, how often was it satisfactory to you?
   0 = Did not attempt intercourse
   1 = Almost never/never
   2 = A few times (much less than half the time)
   3 = Sometimes (about half the time)
   4 = Most times (much more than half the time)
   5 = Almost always/always

8. How much have you enjoyed sexual intercourse?
   0 = No intercourse
   1 = No enjoyment
   2 = Not very enjoyable
   3 = Fairly enjoyable
   4 = Highly enjoyable
   5 = Very highly enjoyable

9. When you had sexual stimulation or intercourse, how often did you ejaculate?
   0 = No sexual stimulation/intercourse
   1 = Almost never/never
   2 = A few times (much less than half the time)
   3 = Sometimes (about half the time)
   4 = Most times (much more than half the time)
   5 = Almost always/always

10. When you had sexual stimulation or intercourse, how often did you have the feeling of orgasm or climax?
    0 = No sexual stimulation/intercourse
    1 = Almost never/never
    2 = A few times (much less than half the time)
    3 = Sometimes (about half the time)
    4 = Most times (much more than half the time)
    5 = Almost always/always

11. How often have you felt sexual desire?
    1 = Almost never/never
    2 = A few times (much less than half the time)
    3 = Sometimes (about half the time)
    4 = Most times (much more than half the time)
    5 = Almost always/always

12. How would you rate your level of sexual desire?
    1 = Very low/none at all
    2 = Low
    3 = Moderate
    4 = High
    5 = Very high

13. How satisfied have you been with your overall sex life?
    1 = Very dissatisfied
    2 = Moderately dissatisfied
    3 = About equally satisfied and dissatisfied
    4 = Moderately satisfied
    5 = Very satisfied

14. How satisfied have you been with your sexual relationship with your partner?
    1 = Very dissatisfied
    2 = Moderately dissatisfied
    3 = About equally satisfied and dissatisfied
    4 = Moderately satisfied
    5 = Very satisfied

15. How do you rate your confidence that you could get and keep an erection?
    1 = Very low
    2 = Low
    3 = Moderate
    4 = High
    5 = Very high

IIEF, International Index of Erectile Function, Adapted from Rosen RC et al(1997)

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