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COLLEGE OF HEALTH SCIENCES

DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS

CARDIOVASCULAR DISEASE RISK FACTORS IN PATIENTS WITH SEVERE MENTAL ILLNESSES ADMITTED AT MATHARI NATIONAL TEACHING AND REFERRAL HOSPITAL.

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A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR AWARD OF THE DEGREE OF MASTER OF MEDICINE IN INTERNAL MEDICINE OF THE UNIVERSITY OF NAIROBI

DECLARATION

I certify that this proposal is my original work. It has not been presented for the award of a degree in any other institution.

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DEDICATION

I lovingly dedicate this work to my husband, Dr. Samuel Muriithi Kagema, and my son Ayden Njeru Muriithi for giving me the reason to soldier on through the challenges and the processes in development and completion of this thesis.

DECLARATION OF ORIGINALITY

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LIST OF ABBREVIATIONS

ANS: Autonomic nervous system

BPD: Bipolar disorder

BMD: Bipolar mood disorder

BMI: Body mass index

CAD: Coronary artery disease

CMS: cardiometabolic syndrome

CNS: Central nervous system

CRP: C-reactive protein

CVRFs: Cardiovascular risk factors

CVA: Cerebral vascular accident

CVD: Cardiovascular disease

DM: Diabetes mellitus

DSM: Diagnostic and Statistical Manual of Mental Disorders

ECG: Electrocardiogram

FBS: Fasting blood sugar

FGA: First-generation antipsychotics

HDL-C: High-density lipoprotein cholesterol

HPA: Hypothalamic-Pituitary-Adrenal axis

HRV: Heart rate variability

HTN: Hypertension

JIS: Joint Interim Statement

LDL-C: Low-density lipoprotein cholesterol

MDD: Major depressive disorder

MetS: Metabolic syndrome

MNTRH: Mathari National Teaching and Referral Hospital

MI: Myocardial infarction

MMSE: Mini-mental state examination

NCEP-ATP: National Cholesterol Education Program-Adult Treatment Panel.

NIMH: National Institute of Mental Health (US)

PAD: Peripheral arterial disease

PTSD: Post-traumatic stress disorder

SGA: Second-generation antipsychotics

SMI: Severe mental illness

SNP: Single nucleotide polymorphism

SUD: Substance use disorder

TC: Total cholesterol

TGs: Triglycerides

US: United States

UK: United Kingdom

WC: Waist circumference

WHO: World Health Organization

WHR: Waist hip ratio

YLD: Years lived with disability

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ABSTRACT

Background

Early cardiovascular mortality has been observed in people with severe mental illness (SMI) when compared to matched counterparts in the general population. A high cardiovascular mortality risk has been found in those with SMI. The risk factors driving this mortality arise from psychotropics related cardiometabolic effects, traditional cardiovascular risk factors (CVRFs) and from direct effects of the mental illness on the autonomic nervous system (ANS), neuroendocrine system and behaviour.

Objectives

To determine the prevalence of various CVRFs, the cardiovascular risk level and describe the correlation between age, behavior and clinical characteristics with metabolic syndrome among patients with SMI admitted at Mathari National Teaching and Referral Hospital (MNTRH).

Methodology

This was a descriptive cross-sectional study done at MNTRH. Consecutive sampling technique was used. The participants were interviewed, examined and blood was drawn for lipid profile and FBS. CVRFs: hypertension (HTN), hyperglycemia, dyslipidemia, smoking, risky alcohol use, increased BMI, abdominal obesity, inadequate physical activity and metabolic syndrome (MetS) were assessed. Data was analysed using SPSS version 23.0. Continuous variables were expressed as means ± Standard deviation and categorical variables as percentages. Univariate analysis was used to determine any relationship between age, behavioral and clinical characteristics of participants with Metabolic syndrome in SMI.

Results

We recruited 209 participants of whom 204 had complete data. The mean age was 37.73 ±8.9 years. Prevalence of CVRFs was as follows: dyslipidemia 60.3%, smoking 52.2%, risky alcohol use 42.6%, increased BMI 38.8%, abdominal obesity 37.3%, metabolic syndrome 27.5%, hyperglycemia 24%, hypertension 16.7% and inadequate physical activity 7.6%. Bipolar mood disorder was significantly associated with presence of MetS compared to schizophrenia with OR 2.17, 95% CI (1.14-4.14) p=0.019.

Conclusion

Prevalence of most CVRF was found to be high in SMI and significant associations were observed between having a diagnosis of BMD and having MetS.

CHAPTER ONE

1.0 INTRODUCTION AND PROBLEM STATEMENT.

1.1 INTRODUCTION

According to the 2016 World Health Organization (WHO) global disease burden estimates, 21% of all years lived with disability (YLDs) are due to mental disorders. Depressive disorders, bipolar mood disorder (BMD) and schizophrenia account for 9% of all YLD(1). The prevalence of the major mental disorders (BMD, major depression, schizophrenia and other psychotic disorders) in Kenya is 4.1% which is thought to be an underestimation due to undiagnosed mental illness(2). High income countries such as the UK record a slightly higher prevalence of 5.8% (3) and USA 4.5%(4).

Morbidity and premature mortality rates are high among patients with SMI with physical illness accounting for up to 67.3% of their mortality (5)(6). Patients with bipolar mood disorder, schizophrenia spectrum of disorders and major depressive disorders are the most affected with mortality rates of up to 2.5 times higher compared to the general populations(7). Physical illnesses include cardiovascular disease (CVD), CVAs, DM, cancer, respiratory and infectious illnesses and CVD is the leading physical cause of death(8)(9).

The increased cardiovascular morbidity and mortality rates are due to complex factors such as lifestyle, the SMI and drugs which directly or indirectly influence the development of the cardiovascular risk factors (CRFs) (10)(11). Some of the postulated mechanisms include activation of the ANS and the HPA system as part of the pathophysiology of SMI(12). Psychotropic medications have been shown to mainly lead to the development of metabolic syndrome. Some of

the effects of these agents include increased or reduced blood pressure and vascular-endothelial dysfunction with increased risk for thrombogenesis. Other effects include altering lipid metabolism and weight with subsequent weight gain and dyslipidemia. The weight gain then leads to increased insulin resistance hence impaired glucose tolerance and diabetes (12).

Social economic deprivation and the attendant impact on access to quality health care has also been implicated as a significant factor driving morbidity and mortality in patients with mental illness(13).

1.2 PROBLEM STATEMENT.

It has been acknowledged across many countries that CVD is a significant cause of morbidity and mortality among patients with SMI. These CVDs and the risk factors vary between populations but an increasing trend is reported across most countries.

Information on ongoing trends in prevalence of CVRFs is needed to determine areas with the highest burden and help in planning preventative public interventions. The information on rates of cardiovascular risks and events are also important in the recalibration of existing CVD risk assessment tools for use in various populations(14). However, patients with SMI are still recorded to have low rates of screening and treatment for most cardiovascular risk factors(15)(16). Currents rates of CVRFs in patients with severe mental illness in Kenya are not known yet Kenya's prevalence of SMI is comparable to global rates and that of developed nations at approximately 4%(2).

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Burden of mental illness globally

The World Health Organization (WHO) in its 2016 global disease burden report, estimates 21% of all years lived with disability (YLDs) are due to mental disorders. Depressive disorders, BMD and schizophrenia account for 9% of all YLD. However according to the Emerald project, when adjustments for various diagnostic overlaps and exclusions were made, this estimate increased to 32.4%(1) (17).

Prevalence of severe mental illness in Kenya is 4.1%, which is comparable to high income countries such as the US with a prevalence of 4.5% but lower than the UK which recorded a higher prevalence at 5.8% (2)(4)(3). Further variability is reported in individual mental illnesses with the 2017 global health estimates of depression and common mental disorders by WHO stating a prevalence of 4.4% for depressive disorder. This varies from 2.6% in the Western Pacific region, 3.3% in the UK, 5.9% in the African region to 7.1% in the US(18). Prevalence of schizophrenia and related psychotic disorders is comparable in US at 0.64% and UK 0.7% with a global prevalence of 0.75%. The global prevalence of bipolar mood disorder is 2.4% with UK at 2%, US 2.1% and 0.1-1.83 in African countries(19)(20)(21). Racial differences in the prevalence of severe mental illnesses have been reported in the USA with the highest prevalence in Whites and American Indians at 5.2% and 5.1% respectively followed by Blacks and African Americans at 3.5% and Asians at 2.4%(22). In the UK, prevalence of psychotic disorders is reported to be higher among the black men in the UK(3)

2.2 Definition of severe mental illnesses.

According to the US center for mental health services (CMHS) and the American psychiatric association (APA), **severe mental illness** is defined as an emotional, mental, or behavioral disorder (that is not a developmental or a substance use disorders) that results in significant functional impairment with interference or limitation in one or more major life activities(23).

The US national institute of mental health (NIMH) found that some mental illnesses "defined according to the Diagnostic and Statistical Manual of Mental Disorders (DSM) definition criteria", cause significant impairment enough to be categorized as SMIs. These include schizophrenia and the schizophrenia spectrum of disorders, major depressive disorder (MDD) and bipolar disorders I and II (BPD I and II). People with these disorders as a cluster make up the majority of those defined to have SMI. Other mental illnesses may at times cause significant functional impairment and hence count as a severe mental illness(23).

Severe mental illnesses associated with increased CVD morbidity and mortality are Schizophrenia and its spectrum of disorders, bipolar mood disorder and major depressive disorder(20).

2.3 Epidemiology of CVD in SMI patients.

Physical illness has been reported to be the main cause of mortality in people with SMIs with CVD as the most prevalent causative illness reported to be 2-3-fold higher in SMI than the general population. A pooled meta-analysis of data various regions (Europe, Asia, Oceania and North America) showed generalized increase CVD prevalence among patients with SMI across the regions with a pooled prevalence of 9.9%. The individual prevalence of CVD was 11.8%, 11.7% and 8.4% for Schizophrenia, MDD and BMD respectively(20). According to the same meta-analysis, Patients with SMI had up to 53% higher risk for having CVD, 78% higher risk for

developing CVD and 85% higher risk of death from CVD when compared to matched counterparts in the general population.

Despite the high prevalence of CVDs and risk factors, patients with SMI have low access to specialized health care and interventions for modifiable risk factors such as screening and treatment. De Hert M et al, in a selective review of data published in the USA, found rates of up to 88% of untreated dyslipidemia and 62.4% untreated hypertension in patients with schizophrenia (15).

A study done at Mathari National Teaching and Referral Hospital (MNTRH) by Mwenda in 2008 that included a sample of 161 of admitted patients showed that none of the patients sampled were screened or on treatment for dyslipidemia. Out of the sampled patients, 38.5% had mood disorders and 32.9% had schizophrenia and other psychotic illnesses while the rest had substance use disorders and physical illness. He found a prevalence of 65.2% for inadequate exercise, 55.7% for smoking, 33% for risky alcohol use, 18.3% for hypertension, 21.7% for overweight and obesity and 25.2% for increased waist circumference (WC) among the patients with the SMI (24).

2.4 Cardiovascular risk factors and their patterns in patients with SMI.

Modifiable Risk factors

Smoking.

Cigarette smoking is a major known risk factor for development and progression of CVD. The toxic and oxidant chemicals in tobacco drive endothelial dysfunction, inflammation, dyslipidemia and hyper-coagulable states which are synergistically responsible for athero-thrombosis and subsequent Coronary artery disease (CAD) and other CVDs seen in smokers (25).

Prevalence of smoking is higher in patients with mental illnesses compared to the general population. A review of data from population surveys of 2007 in Australia and 2001-2003 in the USA looked at the relationship between mental illness and smoking and found a prevalence of 36.2% and 40.1% in Australia and USA respectively for patients with mental illness 12 months prior to the survey. This was about double the prevalence in those without mental illness which was 18.8% and 21.3% respectively(26). Locally a study done at Mathari National Teaching and Referral Hospital by Mwenda in 2008 on prevalence of CVD risk factors, found a total smoking prevalence of 66.5% in admitted patients. Patients with schizophrenia and psychotic illnesses had the highest prevalence at 64%. (24). Other studies have also found prevalence of smoking to be highest in schizophrenia among other mental illnesses. A meta-analysis by de Leon and Diaz in 2005 including 42 individual worldwide studies reported odds of smoking in schizophrenia patients to be 5.9 (95% CI: 4.9-5.7) times higher than the general population. This association between schizophrenia and current smoking remained significant with OR of 1.9 (CI 1.7-2.1) even after using other SMIs as controls(27).

Cigarette smoking is reported to transiently normalize an abnormal auditory sensory gating mechanism present in schizophrenic patients. This suggests a shared neurobiological mechanism behind the deficits observed in schizophrenia and drug dependence. Use of some antipsychotics such as Haloperidol has been found to increased rates of smoking in patients with schizophrenia when compared to other antipsychotics such as clozapine, olanzapine and risperidone. The mechanism for this observation is unclear but it is thought to be due to increased cortical dopamine release seen with olanzapine and risperidone which helps reduce cravings buy acting as nicotine substitutes (28).

Heavy alcohol use.

Heavy alcohol use is now linked to various CVDs, risk factors and outcomes such as High TGs, hypertension, atrial fibrillation, MI, dilated cardiomyopathy, congestive heart failure and haemorrhagic stroke(29)(30). Alcohol use disorders among other drug use disorders has been reported to be particularly high in patients with SMI compared to the general population. These rates vary in different populations and seem to be higher in mood disorders especially bipolar mood disorder as reported in a Norwegian patient registry-based study and a New Hampshire USA state hospital study. The two studies looked at prevalence of comorbid mental illness and substance use disorders in patients with mental illness. For alcohol use disorders the prevalence in patients with schizophrenia, BPD and MDD was 9.6% and 47.1% in the Norwegian and New Hampshire study respectively with the highest prevalence seen in BPD at 12.5% and 52.1% respectively. A similar study done in South Africa at Stikland hospital reported a prevalence of 31% for Alcohol use disorder in patients with SMI which was similar to that found by M.R. Mwenda in Kenya at 33%. (31)(32)(33)(15).

Physical Inactivity.

It has been shown that moderate physical activity ranging from 150 to 300 minutes weekly or 75 to 150 minutes for vigorous activity, reduces the risk for coronary heart disease by about 30% (34). This is due to benefits of Physical activity in regulating weight and improving peripheral glucose uptake through improved insulin sensitivity in skeletal muscles, lowering BP, lipid, glucose levels and clotting factors(35). Physical Inactivity is highly prevalent in patients with SMI with a negative relationship being observed between physical activity and depressive symptoms(36)(37). Chwastiak et al in a large health survey of 510,161sampled veterans in the USA found a prevalence of 56.5% of physical inactivity in the veterans. The prevalence was highest in veterans with MDD

and PTSD at rates of 67% and 67.5% respectively. Veterans with MDD and PTSD had higher odds of physical inactivity with OR of 1.14 (95% CI:1.10, 1.17) and 1.09 (95% CI:1.06, 1.12) respectively. This was contrary to findings in those with schizophrenia who were significantly less likely to be inactive (38).

Obesity.

Obesity is a significant independent risk factor for cardiovascular disease. It also indirectly influences development of other risk factors such as glucose intolerance and diabetes (DM), hypertension and dyslipidemia. A correlation between cardiovascular disease and high BMI has been proven and reported in many large scale studies making obesity or high BMI a significant risk factor for CVD related morbidity and mortality (39)(40). Obesity in SMI is associated with lifestyle factors just as in the general population such as Inactivity and poor diet. However, in SMI some of these factors are driven by the illness and therapy given such as disorganized, negative or depressive symptoms causing inactivity and changes in appetite favouring a poor diet and psychotropic induced weight gain and sedation causing inactivity(15)

Dyslipidemia.

Risk factors for dyslipidemia commonly seen in patients with SMI include: sedentary tendencies, excess weight, central obesity, cardiometabolic syndrome, hypertension and dietary factors (high fats, high salt and high dietary sugars) among others found in the general population including hypothyroidism and genetic factors such as familial hypercholesterolemia.(41).

High TGs are associated with excess weight and obesity, sedentary tendencies, alcohol intake, high carbohydrate diet, tobacco use and other diseases such as diabetes and HIV whose prevalence is noted to be high in patients with mental illness, medications such as corticosteroids or oestrogens and use of antipsychotic medications and protease inhibitors(41)(8).

Dyslipidemia is also reported to be higher in patients with mental illness compared to the general population. The prevalence of dyslipidemia in patients with SMI varies from as low as 23% to as high as 69%. The low prevalence reported in some studies is however thought to be an underestimation of the real prevalence as many review studies have reported low screening rates for dyslipidemia in SMI with up to 88% of SMI patients lacking evidence of screening for dyslipidemia (15). In Kenya, Mwenda et al in 2008 found that none of the participants he recruited had been screened for dyslipidemia.

Hypertension.

There is recognized association between hypertension and cardiovascular disease with WHO naming it a major cardiovascular disease risk factor in 2002. The risk of stroke and Myocardial infarction (MI) is reported to be 4 times and 2 times higher respectively among patients with hypertension(42). According to an analysis of Global burden of disease in the 2008 report, hypertension was a causal factor in 45% of deaths in heart disease and 51% of deaths in stoke(43) There is scanty and contradicting data on hypertension as an isolated risk factor in SMI with most studies reporting it as a comorbid finding. A meta-analysis by Osborn in 2008 of data from various databases found no significantly elevated risk of hypertension in SMI with higher risk of DM but not HTN being reported in patients with SMI(44). This is supported by another study in the Danish population which found an association of hypertension with anxiety disorders but not schizophrenia(45). However, contrary findings are reported from a population based study among patients with schizophrenia in China by Chun-Hui Liao et al who found an age specific antipsychotic associated risk for metabolic disorders that was higher in young patients than older patients especially for hypertension(46).

Hyperglycemia.

Uncontrolled diabetes and IGT are cardiometabolic risk factors that are significantly higher in patients with SMI with diabetes reported as the highest medical co-morbidity with varying prevalence in studies done in different countries; US, Japan and Qatar (47)(48). A study done in South Africa however found higher prevalence of hypertension, dyslipidemia, overweight and obesity and lowest prevalence of diabetes which was a sharp contrast from the studies done in the US, Japan and Qatar(49).

Metabolic syndrome.

Metabolic syndrome refers to a cluster of at least 3 of 5 known cardiometabolic risk factors namely: hypertension, abdominal obesity, hyperglycemia, hyper-triglyceridemia and low HDL-C. The clinical significance of metabolic syndrome is that it doubles the risk of developing CVD within the subsequent 5–10 years(50). Prevalence of metabolic syndrome has been noted to be higher in SMI with gender and racial disparities being reported. It is also noted that the patterns of the individual cardiometabolic risk factors vary between populations. The cause of the increased prevalence of metabolic syndrome is complex and multi-factorial with use antipsychotic medication being recognized as a significant contributing factor.

Rates of metabolic syndrome however differ across regions with ranges of 3.9% to 55%(51).

Table 1: Summary of some studies on prevalence of metabolic syndrome in SMI.

Author & Year	MetS criteria	Population	No of patients.	Prevalence of MetS	Prevalence of MetS risk factors
Saloojee.S 2017 (52)	2009 JIS	South Africa	232 Schizo' 195 BPDI 37	Total **19.4%** Women **37.7%** Men 10.3% Schizo' 20**%** BPDI 13.6%	↑WC **53%** HTN(sys) 16.8% Hyperglycemia 13.7% ↑TGs 9.91% ↓HDL 52.15%
Gubbins A 2012 (53)	NCEP-ATP III 2005	Ireland	100 Schizo 50 MDD 31 BPD 9 Others 10	Total **55%** Schizo' 52% MDD **58.1%** BPD 55.6% Others 60%	↑WC **88%** HTN 41%% Hyperglycemia 32% ↑TGs 43% ↓HDL 29%
S. Khatana 2011 (54)	NCEP-ATP III 2005	USA	1401 Schizo'579 BPD 822	Total **48.4%** Schizo' **51.92%** BPD 46.6%	
S.Grover 2009 (55)	NCEP-ATP III 2005	North India	198 Schizo 126 BPD72	Total **45.95%** Schizo' 36.5% BPD **62.5%** Control 6%	

Non-modifiable risk factors

Age

Older age is still recognized as a non-modifiable risk factor. However, in SMI,CVDs are seen at earlier ages with a large UK study by Osborn, Levy et al in 2007 which looked at Relative risk of cardiovascular and cancer mortality, reporting that young SMI patients aged 18-49 had a three

times higher risk of death from heart disease than those without SMI, while in SMI patients aged 50-75yrs, the risk was doubled.(56)

Sex

Traditionally, cardiovascular disease (CVD) has been reported to be more prominent in Men than women but recent data shows that apart from hormonal status, CVD risk factors are equally distributed between men and women(57). Additionally, DM, high HDL-C and high TGs have a greater CHD risk in women than men and risk factors such as smoking, family history and inflammatory factors such as C-reactive protein (CRP) have a more negative influence on CHD in women than in men.

Genetic factors.

Schizophrenia, MDD, BPD and CVD are highly heritable with twin studies and genetic studies revealing possible genetic correlations between metabolic disorders, CVD and mental illness. Most of these studies are done in schizophrenia and depressive disorders suggesting potential pleiotropic effect of shared gene locus of mental disorders and cardiometabolic diseases(12). Jensen K.G et al in 2017 demonstrated higher rates of pretreatment dyslipidemia and increased WC in children and adolescents with first episode psychosis in Denmark compared to matched healthy controls. This supports the suggestion that other mechanisms other than antipsychotic induced metabolic effects play a role in pathogenesis of MetS in schizophrenia (58). Genetic studies done in schizophrenia patients have found many pleiotropic signals associated with lipid levels, suggesting that lipid biology might be involved in schizophrenia pathophysiology. This is additionally in line with evidence for white matter disease and myelin dysfunction in schizophrenia patients(59). About 24 pleiotropic genes also referred to as cardiometabolic mood disorder hub genes have been discovered shared between mood disorders and cardiometabolic diseases risks and are thought to

influence a shared biological pathway in both disorders(60). One extensively examined pathway is the serotonin pathway where two genes, serotonin transporter gene (SLC6A4) and tryptophan hydroxylase-2 (TPH2) can undergo length polymorphism and single nucleotide polymorphism (SNP) with subsequent alteration in synthesis of serotonin transporter hence the effects on the brain being depression. Peripherally serotonin causes proliferation of vascular smooth muscle and promotes platelet aggregation at vascular sites with endothelial damage which explain the CVD risk(61)(62)

Social-economic status/social economic deprivation

Social economic deprivation impacts profoundly on health and mortality with a correlation seen between social economic deprivation and increased mortality especially in individuals with mental illness. Social economic deprivation impacts on the patients access to healthcare due to poor health seeking behavior, inequalities in affordability and quality of health care, increased crime and social isolation(63)

2.5 Pathogenesis of cardiovascular disease in mental illness

The independent contribution of mental illness to CVD have been explained but not fully elucidated. Biological, psychological, genetic mechanisms have been identified besides the effects of altered behavior on modifiable cardiovascular risk factors(12).

Implicated biological mechanisms include dysregulation of the hypothalamic-pituitary-adrenal axis (HPA) seen prominently in patients with mental illness, dysfunction of the ANS with subsequent hypertension, diminished heart rate variability, increased variability in the QT interval and increased dispersion of the QT and P wave, inflammation, dyslipidemia, oxidative stress and increased platelet activation.

Enhanced activity of the HPA is observed to be profound in depressed patients in response to psychological stress. Excessive or prolonged stress results in dysregulation of the HPA axis causing abnormal changes in hormones circulating through both the periphery and the CNS such as cortisol which is persistently elevated. Hypercortisolism is associated with metabolic syndrome as observed in patients with Cushing's syndrome. High cortisol levels have also been observed in patients with SMI especially depressive disorders(64).

Autonomic nervous system dysfunction is high in patients with SMI especially schizophrenia evidenced by reduced heart rate variability (HRV) which is an independent risk factor for cardiac mortality. The mechanisms behind ANS dysfunction have however not been fully elucidated with evidence showing high levels of catecolamines in patients with MDD and anxiety disorders as a marker of sympathetic activation (65).

Increased levels of inflammatory biomarkers such as interleukin (IL)-1, IL-6, TNF-α and CRP have been demonstrated in MDD, schizophrenia, and BMD and have a predictive value in mortality due to CVD. Treatment of MDD has been seen to reduce levels of inflammatory markers suggesting a the relationship between CVD and depressive diseases(66)

2.6 Effects of Antipsychotics and antidepressants on the CVS

Use of antipsychotics has been associated with increased risk for CVD with 2nd generation antipsychotics (SGA) having more extensive metabolic disorders than 1st generation antipsychotics (FGA). The same metabolic derangements are seen with antidepressants but to a lesser extent when compared to antipsychotics. Atypical antipsychotics such as clozapine and risperidone are also associated with hypotension which increases risk of injury while others are associated with hypertension such as olanzapine(67)(10). The commonest ECG abnormality seen with antipsychotic is QTc interval prolongation with sometime progression to torsade de pointes.

Torsade de pointes has been attributed only in part to ziprasidone. Myocarditis has been reported with clozapine(67)

2.7 JUSTIFICATION OF STUDY

When compared with the general population in various studies, morbidity and early mortality is significantly higher in SMI patients by 2-3 folds and this difference is reportedly increasing. CVD disease has been found to be the leading causal factor for physical causes of morbidity and mortality in these patients. High prevalence of cardiovascular risk factors has been demonstrated in patients with SMI. Besides the mental illness and the traditional risk factors occurring in patients with mental illness, use of Antipsychotic and Antidepressants is postulated to cause adverse metabolic effects that initiate or propagate the development of cardiometabolic syndrome. Cardiometabolic risk factors such as dyslipidaemia, diabetes and obesity and possible raised levels of BP are more common in people with SMI and are reported to be synergistic when they cluster in one individual, making the risk of developing cardiovascular disease higher.

The prevalence of CVRFs though generally increased in SMI varies between different populations, ages, races, by gender and SMI diagnosis. Each population therefore needs to have their own statistics.

Most of the CVRFs are modifiable yet some studies in Kenya have reported that most patients with severe mental illness are neither screened nor treated for these risks, especially dyslipidemia. There are no recent studies in Kenya that have examined CVRFs comprehensively including the burden of cardiometabolic risk factors in patients with severe mental illness. The last study on CVRFs done by Mwenda et al 2008 found some of the CVRF prevalent in SMI but did not evaluate for presence of metabolic syndrome and dyslipidemia which are modifiable risk factors found to significantly affect people with SMI.

2.8 STUDY SIGNIFICANCE

The results from this study will inform us better on the current prevalence of CVRFs in patients with SMI in our population. This will translate into a better understanding of the burden of the various CVRFs and inform policy and protocols on screening for this CVRFs, early treatment and follow-up in patients with SMI.

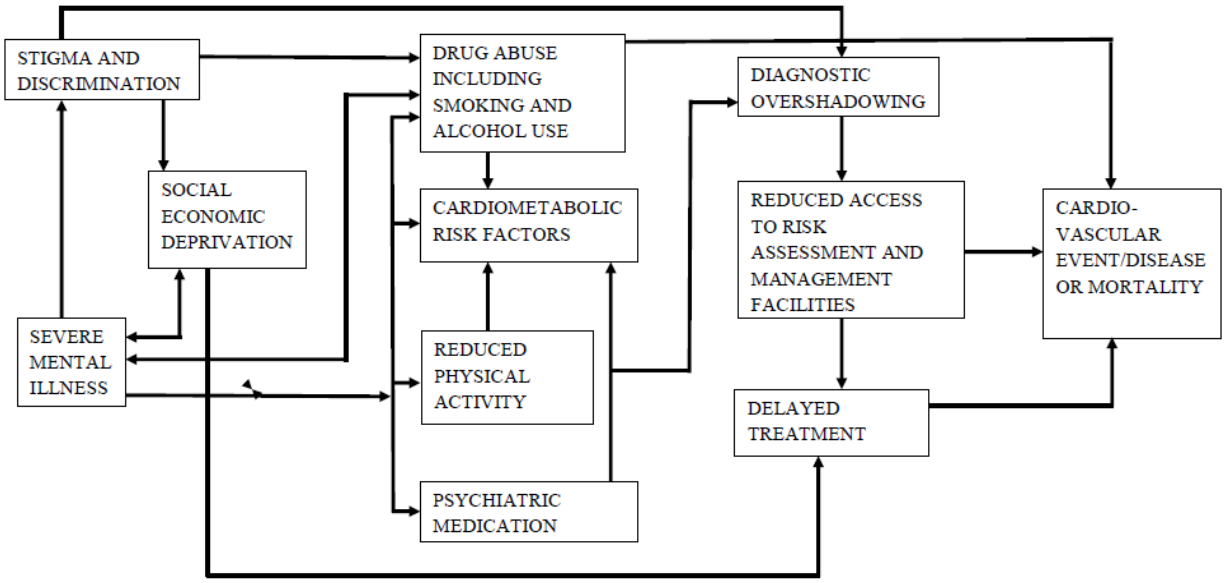
2.9 CONCEPTUAL FRAMEWORK

Severe mental illness directly or indirectly influences development of CVRFs. System failures and socioeconomic factors have also been found to mediate development and worsening of CVRFs in patients with severe mental illness which ultimately lead to the increased rates of CVD in people with SMI.

SMI has been confirmed as an independent risk factor for development of CVD through behavioural, genetic, biological and psychological mechanisms which include: smoking and alcohol use, sedentary tendencies and reduced physical activities, influencing development of cardiometabolic risk factors via direct and indirect mechanisms. SMI directly causes dysregulation HPA and ANS. HPA dysregulation leads to persistently elevated cortisol and subsequent insulin resistance and metabolic syndrome. ANS over-activation leads to adverse cardiovascular responses such as: increased heart rate (HR), reduced HR variability, reduced baroreflex sensitivity with subsequent oxidative stress, cardiovascular remodeling and CVD or event.

Patients with severe mental illness also have higher rates of socioeconomic deprivation due to the effect of SMI on global function. This functional impairment results in social isolation and poor health seeking behavior hence delayed identification and treatment of CVRFs.

Figure 1: Potential causal factors for CVD and inter-relationships between CVRFs and SMI



2.10 RESEARCH QUESTION

What is the cardiovascular risk profile of patients with severe mental illness (SMI) admitted at Mathari National Teaching and Referral Hospital (MNTRH)?

2.11 BROAD OBJECTIVE

To determine the prevalence and some associations of cardiovascular risk factors in the patients with SMIs admitted at MNTRH.

2.12 SPECIFIC OBJECTIVES

2.3.1 Primary objectives

1. Determine prevalence of the following selected cardiovascular risk factors in patients with schizophrenia spectrum of disorders, bipolar mood disorder and major depressive disorder admitted at MNTRH:
    a) Smoking
    b) Risky alcohol use
    c) Inadequate physical activity
    d) Hypertension
    e) Hyperglycemia
    f) Dyslipidemia
    g) Excess weight/obesity
    h) Abdominal obesity
    i) Metabolic syndrome.

2.3.2 Secondary objectives

1. Determine the cardiovascular risk score in patients with SMI admitted at MNTRH according to the WHO/ISH risk score chart.
2. Describe associations between age (≥ 35yrs men and ≥ 45yrs women), behavioral (Smoking, Risky alcohol use, Inadequate physical activity), clinical characteristics and metabolic syndrome. Clinical variables included: SMI diagnosis phenotype, high LDL, Use of antipsychotics and antidepressants.

CHAPTER THREE

3.0 STUDY DESIGN AND METHODOLOGY

3.1 Study design

A descriptive cross-sectional study

3.2 Study site

The study took place at Mathari National Teaching and Referral Hospital (MNTRH). MNTRH is the only public level 6 hospital for patients with mental illness in Kenya. It has a bed capacity of 700 and is divided into 2 main sections: forensic and civil. The civil section is made up of general wards, amenity ward, infirmary ward which admits psychiatric patients with comorbid conditions and a drug rehabilitation unit. The general wards are made up of 3 female wards and 5 male wards. The general wards have approximately 390 patients at any one time. The facility admits approximately 41 patients with severe mental illness per week.

3.3 Study population

They were adult psychiatric patients, 18 years or above with a diagnosis of severe mental illness. They were required to signed informed consent before commencement of the study.

3.3.1 Case definition.

An inpatient psychiatric patient with a diagnosis of severe mental illness as per American Psychiatry Association (APA) and NIMH definition (23). This includes either of the following as defined in DSM 5 criteria (2.2 Definition of severe mental illnesses.):

a. Schizophrenia or its spectrum of disorders.
b. Bipolar mood disorders: bipolar 1 or bipolar 2 mood disorder.
c. Major depressive disorder.

3.3.2 Inclusion criteria

1. A patient above 18 years who fits the case definition.
2. A patient who has had the mental illness for at least 6 months.
3. Patient who has already been stabilized with no active psychotic, manic and/or depressive symptoms.
4. Patient whose insight is intact according to the assessment by the resident psychiatrist.

3.3.3 Exclusion criteria

- Pregnancy

3.4 Sample size determination

The main objective of this study was to determine the prevalence of CVD risk factors in selected patients in an institution. Therefore, the formula for sample size calculation in a prevalence study that was used is the Fisher formula with finite population correction.

$$n = \frac{Nz^2pq}{E^2(N-1) + z^2pq}$$

n = Desired sample size

N = population size (Average number of patients with SMI admitted at Mathari National Teaching and Referral hospital in the 7 general wards are 390).

Z = value from standard normal distribution corresponding to desired confidence level (Z=1.96 for 95% CI)

p = expected true proportion (Prevalence for each cardiovascular risk factor was used to obtain the highest calculated sample size. Prevalence from a study conducted by M.R. Mwenda (2008) looking at prevalence of some Cardiovascular risk factors in patients admitted at Mathari National Teaching and Referral Hospital were used. For metabolic syndrome, hyperglycemia and dyslipidemia, prevalence from a study by Salooje S et al 2017 in South Africa were used.)

$q = 1 - p$

E = desired precision (0.05)

$$n = \frac{390\ x\ 1.96^2\ x\ 0.5215\ x\ 0.4785}{0.05^2(390-1) + \ (1.96^2\ x\ 0.5215\ x\ 0.4785)} = 194$$

The highest calculated sample size (Table 2), was that for dyslipidemia (low HDL) which was 194 patients. Therefore 194 patients were required for this study.

Table 2: Calculated sample sizes

Author & year	Population	No of patients.	Prevalence of cardivascular risk.	Calculated Sample size
Mwenda 2008	Kenya	Total: 115 Schizo 53 Mood disorders 62	Inadequate exercise 65.2%	185
			Risky alcohol use 33%	182
			Smoking 55.7%	193
			↑WC 25.2%	167
			↑BMI 21.7%	157
			Hypertension 18.3%	145
Saloojee.S 2017	South Africa	Total: 232 Schizo' 195 BPDI 37	Hyperglycemia 13.7%	124
			↑TGs 9.91%	102
			↓HDL 52.15%	**194**
			Met S 19.4%	149

3.5 Sampling and recruitment technique.

Consecutive sampling technique was used to recruit participants into the study. The principal investigator and two trained research assistants went to the wards, identified the files of patients who fit the case definition and in collaboration with the psychiatrist or psychiatry registrar in the ward determined patients who meet the inclusion criteria. The first ward was randomly selected through a lottery pick from labels with the ward numbers written on them. The subsequent ward was selected from the remaining 7 wards according to proximity to last visited ward without repetition of wards in each round. The identified patients were then screened using a screening proforma (Appendix 1) to exclude pregnant women. The principal investigator and the research assistants then presented the eligible participant with the opportunity to participate in the study. For those who agreed, information about the study was given in a written consent explanation form (Appendix 3) and also verbally by the principal investigator or the research assistant. Patients who

finally agreed to participate and sign the consent form (Appendix 4) were recruited into the study. This procedure was repeated every day moving from one ward to another in rotatory fashion until the desired sample size of 194 participants is achieved and surpassed. We started with ward 5F which was the ward selected by a random lottery pick followed by 4M, 2F, 9M, 8M, 6F, 5M and 6M consecutively. This order was repeated until the desired sample size was achieved.

3.6 Study procedures

3.6.1 Data collection.

The principal investigator (PI) recruited and trained two research assistants (trained clinical officers) to help with data collection.

Using a study proforma and the Global physical activity questionnaire (GPAQ), the recruited participants were interviewed by the PI or the research assistant to obtain information on social-demographic data, smoking history, alcohol use, physical activity and medical history of cardiometabolic risk factors. The study proforma was then updated using the patients file to include information on primary psychiatric diagnosis, psychiatric co-morbidities, current general medical conditions current psychotropic and other medication. The PI or the research assistant then performed physical examination to obtain patients' blood pressure, pulse rate, weight, height, abdominal and hip circumference. These measurements were then updated on the study proforma. The participant was then given instructions on the 8 hours fast in preparation for phlebotomy the next morning.

Cardiovascular risk factors that were assessed included: smoking, alcohol use, physical inactivity, hypertension, hyperglycemia, dyslipidemia, excess weight/obesity and metabolic syndrome.

The following physical and laboratory examinations were performed and recorded on the study proforma:

- Waist circumference (WC): The abdominal circumference was measured at the level between the 12th rib and the iliac crest using non-stretch tape measure while in expiratory phase and the measurement recorded in centimeters(68).
- Hip circumference measurement was taken at maximum circumference of the buttocks and recorded in centimeters(69).
- Body weight: Was measured using a digital weighing machine and recorded to the nearest 0.1kg. Patients had light clothing and no shoes during the measurement(68).
- Height was determined using a standard stadiometer with the participants not wearing shoes. It was recorded to the nearest 0.5cms(68).
- Systolic BP and diastolic BP: measurements were taken using an OMRON Digital Automatic Blood Pressure Monitor and an appropriate size cuff. Participants were required to rest for at-least 15 minutes before measurements are taken. Two BP readings were taken 1-2 minutes apart on the left arm at the level of the heart with the patient seated (69).
- Blood samples were collected for fasting blood glucose and lipid profile analysis after a minimum eight hours overnight fast.

  Each participant had three millilitres of venous blood sample collected from the median cubital vein under aseptic conditions as per the WHO guidelines on drawing blood. The blood samples were then be transferred to a plain vacutainer, clearly labeled with participant's unique study number and transported to the laboratory by

the noon of each day's collection for analysis(70). Analysis was then done using the Huma Star 600 chemistry analyzer

FBS was done at the point of venipuncture using an approved automatically coded glucometer (ACCU-CHEK smart view) and recorded in the study proforma(71).

3.6.2 Clinical Variables

- Age in years: Was recorded in categories. Cutoff age as a CVRF was considered to be > 45years for male and > 55years for female(41)
- Gender entered as Male or female.
- Duration of mental illness since the first diagnosis was recorded in years.
- Hypertension was defined as a measured elevated blood pressure ≥ 140/90mmHg or as being on antihypertensive treatment.
- Impaired fasting glucose (IFG) was defined as a measured FBS of ≥ 5.6 – 6.9 mmols/l.
- Diabetes (DM) was defined as a measured FBS of ≥ 7 mmols/l or being on hypoglycemic agents.
- Alcohol use was assessed using the Audit-C questionnaire and risky alcohol used determined at a score of 4 for men and 3 for women.
- Smoking status was recorded as current, former or never smoker according to the CDC classification. Former smokers were further categorized into those who quit less than 15years and those who quit more than 15 years prior to recruitment. Former smokers were considered to still have significant cardiovascular risk linked to smoking if they were within 15 years since cessation of smoking at the time of recruitment (72). The definition for smoking status were as follows (73).

Current smoker: An adult who currently smokes and has smoked 100 cigarettes or more in his or her lifetime.

Former smoker: An adult who quit smoking at time of interview and has smoked at least 100 cigarettes in his or her lifetime.

Never: An adult who has never smoked or who has smoked less than 100 cigarettes in his or her lifetime.

- Excess weight or Obesity was assessed using BMI, Waist circumference and WHR with cutoffs and categories as follows according to WHO(74):
    - Waist circumference:

        Women: Normal (≤80cms), Increased (>80 cms), Substantially Increased (>88cms)

        Men: Normal (≤94cms), Increased (>94cms), Substantially Increased (>102cms)
    - WHR: Substantially Increased (≥ 0.85 women), (≥0.9Men)
    - BMI (kg/m2): Underweight (<18.5), Normal (18.5-24.9), Overweight (25-29.9), Obese (≥30)
- Physical activity was assessed and recorded using the WHO recommended Global physical activity questionnaire where:(Appendix 5)
    - Adequate physical activity: At least 150 minutes OR 75 minutes of moderate OR vigorous intensity activity respectively in a week.
    - Inadequate physical activity: Less than 150minutes of moderate OR less than 75 minutes of vigorous intensity activity in a week.

- The GPAQ questionnaire was developed by WHO as a physical activity surveillance instrument and is currently in use in about 50 developing countries (75).It is validated and has shown reproducibility and good reliability. The reliability and validity studies have been done in Bangladesh, Indonesia, China, Ethiopia, India, Brazil, Japan, Portugal and South Africa (76). It is designed to help the interviewer objectively assess physical activity in three levels or domains of work, travel and recreation individually.
- Lipid profile: The four components were measured in mmols/l (TC, LDL-C, HDL-C, TGs) and recorded into the following categories according to NCEP cutoffs(77).

Table 3: Lipid profile reference values

Lipids	**Cut off value (mmols/l)**	
	Acceptable	**Abnormal**
Total Cholesterol (TC)	< 6.2 mmols/l	≥6.2mmols/l (240mg/dL)
Triglycerides (TGs)	<2.3 mmols/l	≥2.3 mmols/l (200mg/dL)
LDL-C	<3.0 mmols/l	≥ 3.0 mmols/l (130mg/dL)
HDL-C		
– Women	≥1.2 mmols/l	<1.2 mmols/l (48mg/dL)
– Men	≥1.0 mmols/l	<1.0 mmols/l (40mg/dL)

– Metabolic syndrome was assessed following the recommendation the 2009 Joint Interim Statement(JIS) of the International Diabetes Federation(IDF) Task Force on Epidemiology and Prevention, The American Heart Association(AHA), The National Heart, Lung and Blood Institute(NHLBI), The International Atherosclerosis Society, The World Heart Federation, and The International Association for the Study of Obesity (78).

Table 4 : 2009 JIS criteria for MetS.

Presence of three or more of these components

Abdominal obesity: Increased waist circumference	Men: ≥94 cms Women: ≥80 cms
Elevated triglycerides	≥ 150 mg/dL (1.7mmol/l) or drug treatment for elevated triglycerides
Reduced HDL-Cholesterol (HDL-C)	Men: < 40 mg/dL (1.03mmols/l) Women: < 50 mg/dL(1.3mmols/l)
Elevated blood pressure	≥ 130/85 mm Hg or drug treatment for elevated blood pressure
Elevated fasting glucose	≥ 100 mg/dL (5.6mmols/l) or drug treatment for elevated glucose

– Cardiovascular Risk level according to WHO/ISH Chart African region E(79), (Appendix 6):

□<10%, □10-<20%, □20-<30%, □30-<40% □≥40%

3.6.3 Specimen processing, analysis and disposal

The blood samples collected were taken to the University of Nairobi clinical chemistry lab and received by a specific technician assigned to process the study samples. Processing of samples by centrifuging was then be done followed by analysis the same day using the Huma Star 600 chemistry analyzer for total cholesterol, triglycerides, HDL-C and calculated LDL-C.

FBS was done at the point of venipuncture by the principal investigator or the research assistant using an approved automatically coded glucometer (ACCU-CHEK smart view) and recorded in the study proforma.

There was no storage of the specimen after analysis. Any remaining sample was discarded through the laboratory's waste management system after analysis.

A copy of the results was then given to the PI who updated the study proforma for data analysis

3.6.4 Data protection, retention and destruction

Standards to protect personal data were followed. Data collection instruments have only the study number. For the lab reference, participant's details (names, age, IP number and contact) were confirmed before the test and a code attributed to every participant to preserve the confidentiality. All information was stored safely in a lockable cabinet by the principal investigator after analysis for any future verification and sub analysis.

The information will be retained for a minimum of 5 years after which the codes together with the data will be destroyed.

3.7 Quality assurance

Clinical:

The principal investigator recruited and trained two research assistants to a competent level to ensure timely, efficient and accurate data collection and recording. All the recorded data was verified against the study proforma by the Principal Investigator to ensure accuracy in the transfer of information. The supervisors offered continued guidance to the principal investigator who also worked in consultation with the statistician through the process of proposal development, data entry and analysis of results

Laboratory:

Standard operating procedures for specimen collection, preparation and storage were followed to minimize pre-analytical errors. The laboratory tests were carried out at the University of Nairobi clinical chemistry lab by a study dedicated technician.

3.8 Ethical consideration

1. Approval was obtained from the Department of Clinical Medicine and Therapeutics of the University of Nairobi and the Kenyatta National Hospital Scientific and Ethical committee before data collection began. Reference number for this study was P676/08/2019.
2. Protection of the participants was ensured with inference to the standard operation procedure for research in the vulnerable population by KEMRI(80).
    - Selection issues were considered in preservation of patient autonomy: In view of the fact that acute psychiatric illness and impaired insight are the major contributors to impaired capacity to consent, we only selected patients who were ready for

discharge (81). Part of the discharge criteria is resolution of acute psychotic and depressive symptoms with regained insight therefore, they were able to give consent. The input of the psychiatrist in the ward was sought to ensure that all the patients approached for recruitment had their insight assessed.

- Only those who gave informed consent were recruited.

- Privacy and confidentiality was ensured: Information gathered from the study participants was kept confidential. Each participant has a study number used as the only identifier on all materials uses in the study.
- There was no coercion and undue influence: Patients participated out of their own free will and there was no victimization or discrimination for those who declined to participate.
- Risk-benefit analysis: Participants were notified about experiencing a small prick pain during phlebotomy procedure and about the volume of blood that would be collected during consent explanation before signing consent. Other sources of discomfort such as exposure during physical exam and personal questions during the interview were mitigated by conducting the interview in a private room so as to help the patient to be comfortable. The principal investigator catered for the expense of the investigations so the participants bore no financial costs.
- Only blood samples intended for study were drawn and thereafter discarded after analysis
- All patients with abnormal BP sugars or cholesterol were informed of the issues and the psychiatrist covering informed of the same so as to treat the patient.

3.9 Data management and analysis

Data entry and analysis was done using SPSS version 23.0. Upon completion of entry and verification of correctness of data, the hard copy forms were stored safely in the lockable cabinet. Data collected with the GPAQ questionnaire was cleaned and analyzed using GPAQ analysis guide and the Epi-info program version 3.2 before entry into SPSS for further analysis.

Descriptive statistics for demographic, behavioural, clinical and laboratory characteristics were expressed as means (± SD) for continuous variables and as percentages for categorical variables which were inclusive of Cardiovascular risk factors.

Univariate analysis was performed to test association between age (≥ 35yrs men and ≥ 45yrs women), behavioral (smoking, risky alcohol use, inadequate physical activity), clinical characteristics and metabolic syndrome. P-values and 95% confidence intervals (CIs) were calculated where a P value <0.05 was considered statistically significant. The significant associations were taken to a multivariate model where odds ratio (OR) and 95% Confidence intervals were calculated. Clinical variables included: SMI diagnosis, high LDL and use of antipsychotics and antidepressants.

CHAPTER 4

RESULTS

Between December 2019 and February 2020, we recruited 209 participants, 204 respondents had complete data while 5 did not give a blood sample; 3 got discharged before samples could be collected while 2 declined phlebotomy. Complete analysis was done for 204 of the recruited participants.

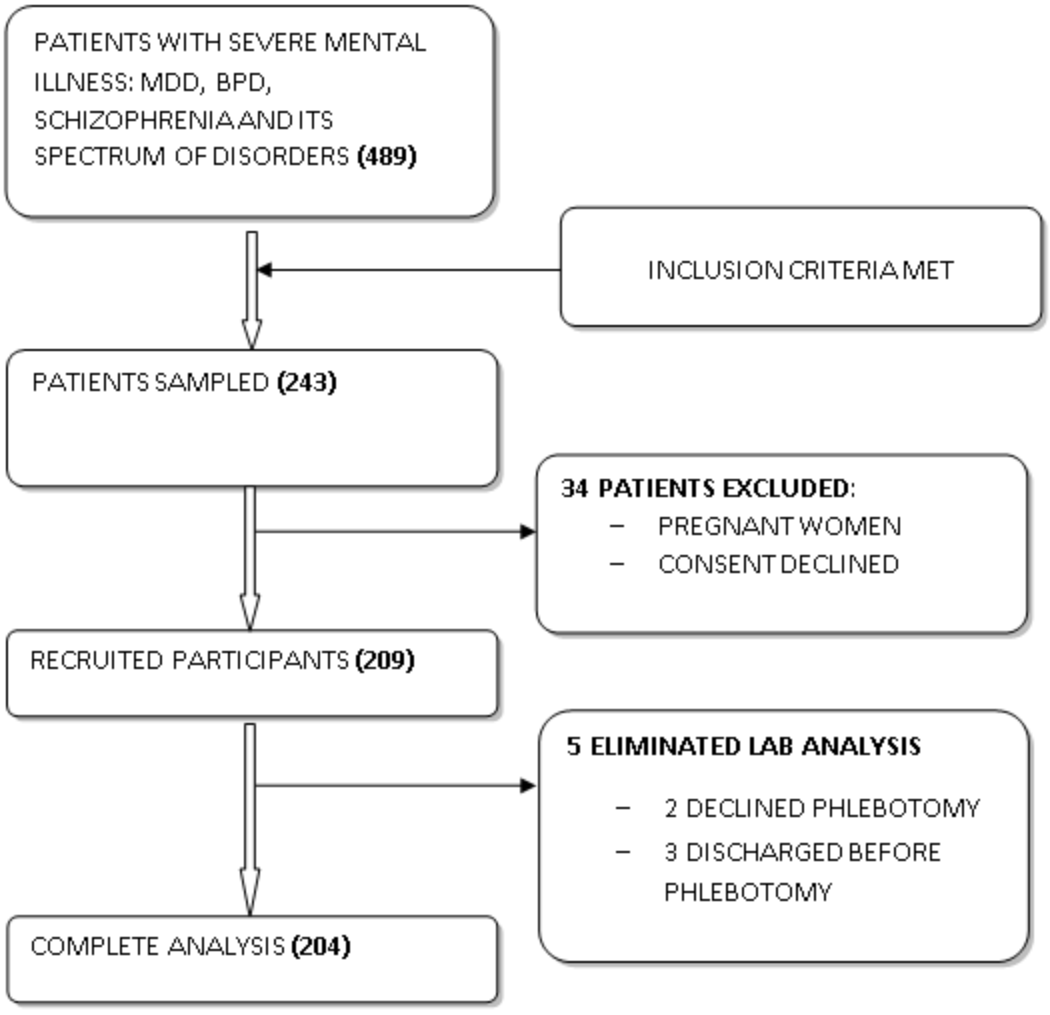


Figure 2: STUDY FLOW CHART DIAGRAM

4.1 SOCIAL-DEMOGRAPHIC CHARACTERISTICS

Majority of the participants were young people with an average age of 37.73 years and median of 37 years ranging from 19-74years. The ratio of male: female was 3:2 with male participants being 127(60.8%) and females 82(39.2%). Most were single 68.4% and 40.7% had attained secondary level of education. 112 (53.6%) of the participants had a form of employment.

Table 5: SOCIAL-DEMOGRAPHIC CHARACTERISTIC OF PARTICIPANTS

	Frequency	**Percentage**
Age in years	**N**	**%**
18-25	32	15.3
26-35	60	28.7
36-45	71	34.0
46-55	29	13.9
>55	17	8.1
Gender		
Male	127	60.8
Female	82	39.2
Marital status		
Single	143	68.4
Married	55	26.3
Widowed	11	5.3
Occupation		
Student	13	6.2
Self-employed	59	28.2
Employed	53	25.4
Unemployed	80	38.3
Retired	4	1.9
Education level		
None	3	1.4
Primary	71	34.0
Secondary	85	40.7
Tertiary	50	23.9

4.2 CLINICAL CHARACTERISTICS OF THE STUDY PARTICIPANTS.

Ninety-five patients (45.5%) had a diagnosis of schizophrenia and formed majority of the participants followed by those with bipolar mood disorder at 74 (35.4%). The mean duration of illness was 10.5(±9.6) years. Preexisting hypertension and DM was noted in 8.6% and 1.9% of the respondents respectively. Most of the participants 183 (87.6%) were on antipsychotics only while 18 (8.6%) were on both an antipsychotic and antidepressant and 2 (1%) were on an antidepressant only.

Table 6: BASELINE CLINICAL CHARACTERISTICS OF STUDY PARTICIPANTS

	Frequency/Mean	**Percentage**
Diagnosis	**N**	**%**
Bipolar mood disorder	74	35.4
Major depressive disorder	12	5.7
Schizoaffective disorder	28	13.4
Schizophrenia	95	45.5
Duration of mental illness (years)	**10.5 ±9.6**	
<1-5	86	41.2
6-10	36	17.2
11-15	37	17.7
16 -20	18	8.6
>20	32	15.3
Medication		
Antidepressant + Antipsychotic	18	8.6
Antidepressant	2	1
Antipsychotics	183	87.6

The most prescribed oral antipsychotic was haloperidol in 49.5% (102) followed by olanzapine 35.4% (73) of the patients.

Table 7: PSYCHOTROPIC AGENTS USED BY PARTICIPANTS

	Frequency	Percent of Patients (%)		Frequency	Percent of Patients (%)
Medication	**N**	**N=206**	**Medication**	**N**	**N=20**
Haloperidol	102	49.50%	Fluoxetine	9	45.00%
Fluphenazine decanoate	97	47.10%	Amitriptyline	6	30.00%
Olanzapine	73	35.40%	Mirtazapine	3	15.00%
Chlorpromazine	66	32.00%	Escitalopram	1	5.00%
Zuclopenthixol acetate/decanoate	48	23.30%	Nortriptyline	1	5.00%
Risperidone	23	11.20%	Venlafaxine	1	5.00%
Quetiapine	19	9.20%	***Anticonvulsants***		
Flupentixol decanoate	6	2.90%	Carbamazepine	155	74.20%
Aripiprazole	3	1.50%	Sodium valproate	21	10%
Amisulpride	1	0.50%	***Others***		
Clozapine	1	0.50%	Benzhexol	58	27.80%

PATTERNS OF ANTIPSYCHOTICS PRESCRIPTION		
	No of patients (**n=209**)	Percentage
None	3	1.4%
Single antipsychotic	46	22.0%
Multiple antipsychotics		
2	96	45.9%
3	64	30.6%

4.3 CARDIOVASCULAR RISK FACTORS

4.3.1 Prevalence of Smoking, Risky alcohol use and Inadequate exercise.

Prevalence of smoking was (109) 52.1%. Current smokers were 41.1% and former smokers with significant smoking cardiovascular risk of less than 15 years since cessation of smoking were 11%. Former smokers with 15 years or more since smoking cessation and never smokers were 2.9% and 45% respectively.

A hundred and five participants 50.2% reported no use of alcoholic drinks. Participants with Risky alcohol use were 42.6% (89) and those with non-risky alcohol use were 7.18%.

Participants who met the WHO recommendation on physical activity for health were 92.3% (193) with prevalence of physical inactivity being 7.7% (16) of the participants.

Table 8: PREVALENCE OF SMOKING RISKY ALCOHOL USE AND INADEQUATE PHYSICAL ACTIVITY

RISK FACTOR	**Frequency**	**Percentage**
Smoking status	**N**	**%**
Current smoker	86	41.1
Former smoker (quit <15 years ago)	23	11.0
Former smoker (quit ≥15 years ago)	6	2.9
Never smoker	94	45.0
Alcohol Use		
Risky alcohol use	89	42.6
Non-risky alcohol use	15	7.18
No alcohol use	105	50.2
Physical Exercise		
Adequate	193	92.3
Inadequate	16	7.7

4.3.2 Prevalence of Hypertension, Hyperglycemia.

Prevalence of hypertension was (35) 16.7%. Among the hypertensive patients 18 where aware (already diagnosed), 12 were on treatment and 7 were controlled.

The prevalence of hyperglycemia was 24% consisting of 50 participants having an FBS of 5.6mmols/l or more.

Table 9: PREVALENCE OF HYPERTENSION AND HYPERGLYCEMIA

	Frequency	Percentage
Hypertension (Known or BP ≥ 140/90) (n=209)	N	%
Yes	35	16.7
No	174	83.2
FBS*(n=204)*	**N**	**%**
Normal (4.0-5.5)	155	76.0
IFG	42	20.6
Diabetes	7	3.4
IFG and DM (n=205)		
Yes	50	24.0
No	155	76.0

4.3.3 Prevalence of Dyslipidemia

A hundred and twenty-three participants 60.3% had dyslipidemia with either one or more lipoproteins elevated. 8.3% of the study participants had high TC, 26.5% had high TGs, 23% had low HDL-C and 29.4% had high LDL-C.

Table 10: PREVALENCE OF DYSLIPIDEMIA

	Frequency	Percentage
Total cholesterol*(n=204)*	**N**	**%**
Acceptable	187	91.7
Abnormal	17	8.3
Triglycerides*(n=204)*		
Acceptable	150	73.5
Abnormal	54	26.5
HDL-C*(n=204)*		
Acceptable	157	77
Abnormal	47	23
LDL-C*(n=204)*		
Acceptable	144	70.6
Abnormal	60	29.4
Dyslipidemia (n=204)		
Any abnormal lipid	123	60.3
All lipids normal	81	39.7

4.3.4 Prevalence of Excess weight, Abdominal Obesity and Metabolic Syndrome

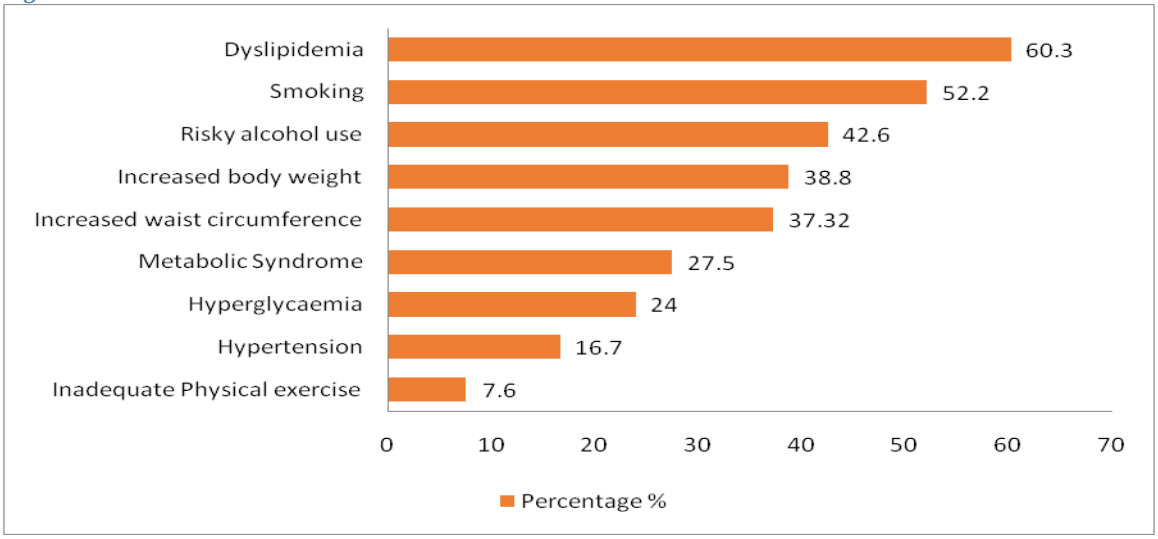
Prevalence of excess weight by calculated BMI was found to be 38.8% with 43 (20.6%) and 38 (18.2%) of the participants being overweight and obese respectively. Increased waist circumference was at 37.3% and increased WHR at 46.4%.

Fifty-six participants satisfied the criteria for MetS with the prevalence of metabolic syndrome at 27.5%.

Table 11: PREVALENCE OF INCRESED BMI, WC AND METABOLIC SYNDROME.

	Frequency	**Percentage**
BMI (Kgs/M^2)	**N**	**%**
Underweight (<18.5)	19	9.1
Normal (18.5-24.9)	109	52.2
Overweight (25-29.9)	43	20.6
Obese (≥30)	38	18.2
Waist Circumference (WC) in Cm.		
Normal	131	62.7
Increased	36	17.2
Substantially increased	42	20.1
Increased WHR (Waist Hip Ratio)		
Yes	97	46.4
No	112	53.6
Presence of Metabolic Syndrome(n=204)		
Yes	56	27.5
No	148	72.5

Figure 3: PREVALENCE OF CVRF IN SMI



4.4 CARDIOVASCULAR RISK LEVELS

Cardiovascular risk level was assessed using to the WHO/ISH risk score chart for the African Region E to determine the 10-year risk of combined MI and

stroke risk (fatal and non-fatal). Most of the patient 91.1% (82) had a low risk of less than 10%, those with moderate risk were 5.6% and high risk were 3.3%.

Cardiovascular risk level (n=90)	**Frequency N**	**Percentage %**
<10% (Low)	82	91.1
10% to <20% (Moderate)	5	5.6
20% to <30% (High)	3	3.3

4.5 ASSOCIATIONS BETWEEN AGE, BEHAVIOURAL, CLINICAL CHARACTERISTICS AND METABOLIC SYNDROME.

Univariate analysis was performed to determine the association between metabolic syndrome and some of the participants' behavioural and clinical characteristics. This included age (≥ 35yrs men and ≥ 45yrs women), smoking, risky alcohol use, inadequate physical activity, SMI phenotype and use of antipsychotics and antidepressants. There was a positive trend for an association between the age and metabolic syndrome. Participants aged 35 or 45 years and above for male and female respectively, had a 1.33 chance of having metabolic syndrome OR 1.33, 95% CI (0.72-2.46) compared to younger ones. Similarly, participants with inadequate physical exercise had a 1.66 chance of having metabolic syndrome with p = 0.352 compared to those with adequate exercise.

A diagnosis of bipolar mood disorder was significantly associated with the presence of MetS compared to Schizophrenia with OR 2.17, 95% CI (1.14-4.14), p=0.019. There was no association seen between Risky alcohol use and metabolic syndrome. Smoking appeared protective with lower risk of MetS syndrome being observed in smokers OR 0.46 (0.24-0.86) p=0.015.

Table 12: ASSOCIATIONS BETWEEN AGE, BEHAVIOURAL, CLINICAL CHARACTERISTICS AND MetS

	With MetS	Without MetS	OR (95% CI)	p-value
Age				
Male (≥35 yrs.)/Female (≥45 yrs.)	27	61	1.33 (0.72-2.46)	0.368
Male (<35 yrs.)/ Female (<45 yrs.)	29	87	Ref	
Cigarette smoking (significant)				
Smoker	21	84	0.46 (0.24-0.86)	**0.015**
Non smoker	35	64	Ref	
Risky alcohol use				
Risky alcohol use	24	63	1.01 (0.54-1.88)	0.970
None or none risk alcohol use	32	85	Ref	
Inadequate physical exercise				
Inadequate	6	10	1.66 (0.57-4.79)	0.352
Adequate	50	138	Ref	

Psychiatric diagnosis				
Bipolar mood disorder	27	45	2.17 (1.14-4.14)	**0.019**
Major depressive disorder	3	9	1.21 (0.30-4.78)	0.791
Schizophrenia spectrum	26	94	Ref	
Psychiatric medication				
Antidepressant + Antipsychotic	6	12	1.45 (0.52-4.08)	0.482
Antidepressant	2	0	-	
Antipsychotics	47	136	Ref	
None	1	0	-	
High LDL				
Acceptable (<3.0 mmols/l)	40	104	Ref	
Abnormal (=>3.0 mmols/l)	16	44	0.95 (0.48-1.86)	0.871

CHAPTER 5

5.1 DISCUSSION

The study population was of patients admitted with a diagnosis of SMI with the distribution of the SMI specific diagnosis being 45.5% for schizophrenia, 13.4% schizoaffective disorder, 35.4% BMD and 5.7% MDD. The male to female ratio was 3:2 with mean age of 37.7±8.9 years. All evaluated CVRFs were found to be prevalent at varying degrees from one risk factor to another.

The highest prevalence was of dyslipidemia at 60.3% which included any participant with an abnormality in any one of the 4 assessed cholesterol components. Prevalence of high total cholesterol was 8.3%, hypertriglyceridemia 26.5%, low HDL-C 23% and high LDL-C 29.4%. Similar and higher prevalences were reported in a South African study by K. Maaroganye et al who found TC dyslipidaemia of 32%, triglyceride dyslipidaemia of 29% and low density lipoprotein LDL) dyslipidaemia of 50%(82). The mean age of the participants in this study was 42yrs with 60% male. The cutoffs for high TC in this study was ≥5.2mmols/l, High LDL-C ≥3.4mmols/l and hypertriglyceridemia ≥1.7mmols/l. Distribution of specific SMI diagnosis was 44% for schizophrenia, 16% other psychotic illnesses, 12% mood disorders and 28% had either cognitive, personality or anxiety disorders.

However, contrary to our findings and that of the south African study, an Italian study by M. Clerici et al showed a relatively lower prevalence of hypertriglyceridemia of 15.1% and LDL dyslipidemia of 11.7% despite having an older population of people with SMI(83). The participants mean age was 47.2 ± 14.8 years with 42.9% male. Participants were 119 with 82 having psychotic disorders, 31 BMD and 6 with MDD. The cutoffs for Hypertriglyceridemia was ≥ 200mg/dl (2.3mmol/l) and that of LDL dyslipidemia was ≥160mg/dl (4.1mmols/l).

Some of the differences observed in prevalence of dyslipidemia may be attributed to the different cutoffs adopted by authors investigating dyslipidemia. Another reason may be heavy use of psychotropic drugs that cause dyslipidemia in some of the studies. Such drugs include chlorpromazine, SGAs such as quetiapine, olanzapine, clozapine and mood stabilizers such as carbamazepine and sodium valproate. In our study 74.2% of the participants were on carbamazepine, 32% on chlorpromazine and 35.4% on olanzapine. In the US study which had similarly high prevalence of dyslipidemia 60.7% of the participants were on a SGAs and 54.9% on mood stabilizers. In the south African study 48 of the 84 participants were on sodium valproate and 25 on clozapine. The Italian study which reported a relatively lower prevalence of dyslipidemia had only 32 of the 119 participants (26.8%) on olanzapine and no use of any other psychotropic agent associated with dyslipidemia. Another contributing factor to dyslipidemia is dietary practices which were not assessed in any of the studies.

A local study looking at cardiometabolic disease markers in an urban population reported a prevalence 18.8% for hypertriglyceridemia(84). This suggests a relatively higher prevalence hypertriglyceridemia in patients with SMI. However, better representative population-based studies are needed on prevalence of all components defining dyslipidemia in the general population for comparative data. Our high prevalence of dyslipidemia occurring in a young population with SMI points to the need for screening people with SMI from an earlier age than the 40 years recommended in most screening and treatment guidelines for dyslipidemia. Despite the high prevalence of dyslipidemia in our study, we only found one patient who was identified and on treatment for dyslipidemia. This points to the need for emphasis on regular screening and early intervention preferably at the point of first contact. Some studies have demonstrated high prevalence of hypertriglyceridemia at the onset of SMI even before initiation of psychotropic

agents. Evaluation of baseline lipid profiles would thus help tailor treatment choices to avoid worsening pre-existing dyslipidemia and initiate modification therapies.

Significant tobacco exposure was also high at 52.2%. This is over 3 time higher than the prevalence in the general population which was 13.3% according to the WHO 2015 Kenya steps survey(85). It is a slight reduction from previously reported prevalence of 65.5% in 2008 by M.Mwenda showing minimal penetration of smoking cessation interventions to people with SMI (24). In other populations, similarly high prevalence of smoking in SMI have been reported with US at 51.8%, Italy 64.7% and South Africa 61% with low rates of smoking cessation being observed (83)(54)(82). Other substance use disorders (SUD) evaluated included risky alcohol use which was 42.6% and like smoking, it was higher than general population prevalence of risky alcohol use at 6.7%(86). M.Mwenda reported a similar prevalence of risky alcohol use at 44.1% in 2008. This reemphasis the observation that SMI is associated with poor drug rehabilitation outcomes. Similarly high prevalence of Alcohol use disorders in SMI have been reported in New Hampshire US at 51% and Stikland South Africa at 31 % among patients with SMI(32)(33). The high prevalence of risky alcohol use and smoking may also be due to overreporting on drug use as a manifestation of overvalued ideas, which are symptoms that may not be obviously apparent in SMI. Comorbid substance use disorder and mental illness is fairly common and known to affect pattern, course and outcomes of mental illness besides the cardiovascular effects.

Comorbid substance use disorder and mental illness is now thought to be driven by overlapping genetic and epigenetic vulnerabilities. Early diagnosis and an integrated approach in management of the disorders has been proven to be effective(87). There is hence need to improve cohesiveness between the drug rehabilitation and psychiatry services at MNTRH to enable early diagnosis and management of existing mental illness in patients presenting with substance use disorders.

The prevalence of physical inactivity at 7.7% was comparable to population prevalence at 7.8% (91). This largely contrasts with the with previously reported prevalence by Mwenda 2008 who found a prevalence of physical inactivity at 64.4%. It may largely be due to the differences in tools used to assess physical activity in the two studies. M.Mwenda in 2008 used a researcher designed questionnaire with questions developed to assess physical activity according to CDC. This may have introduced bias with underestimation of the level of physical activity as it was not a validated questionnaire. Our study on the other hand used GPAQ questionnaire which is validated for assessing physical activity in developing nations. A study by A.Thuy et al in 2010 however reported poorer reliability of GPAQ in assessing physical activity in participants more variable work patterns compared to those with stable work patterns (88). Though not assessed in our study population, most of our participants may have had variable work patterns as most were either unemployed or self-employed hence were not on shift-based jobs which are associated with stable work patterns. Variability in work patterns may have introduced bias with overestimation. Further studies with accelerometers and pedometers may be needed to verify this finding.

Changes in prescriptions of antipsychotics from predominantly FGAs to predominantly SGAs may be another reason that may explain the current low levels of physical inactivity. According to M. Mwenda in 2008, 67% of the participants were on FGAs and 2.4% on SGAs. In our study the patients on FGAs were fewer at 45% and majority were on SGAs at 52.6%. Additionally, among participants on FGAs 87% were on haloperidol which is a low milligram high potency antipsychotic with less sedative effects. chlorpromazine was previously the most prescribed FGA and is high milligram low potency antipsychotic with more sedative effects (91). The current use of more SGAs which have less extrapyramidal effects and FGAs with less sedative effects may have on overall impact on the different levels of physical activity observed in the two studies.

Some studies have shown that the risk of physical inactivity is more in conditions with depressive symptoms and in schizophrenia patients with negative symptoms and reduces as the patients get optimal treatment for the depressive symptoms (92).

Excess weight by BMI was found to be 38.8% with 43 (20.6%) and 38 (18.2%) of the participants being overweight and obese respectively. Increased WC was at 37.3% and increased WHR at 46.4%. Our rates are higher than the rates reported by M. Mwenda in 2008. He found prevalence of excess weight at 18.6%, increased WC at 19.9% and increased WHR of 35%. This may also be attributed to the changes in prescribed psychotropic medication. SGAs, carbamazepine and sodium valproate are associated with weight gain and other cardiometabolic side effects. There was more use of SGAs and mood stabilizers (such as carbamazepine and sodium valproate) in our study with 52.6% of participants being on SGAs and 84.2% on mood stabilizers. M.Mwenda only found 2.4% and 11.8% of the participants in his study on SGAs and mood-stabilizers respectively.

Our rates were also higher than the population prevalence of excess weight which is 27.9% (with 19% being overweight and 8.9% obese), increased WC at 12.3 % and Increased WHR of 27 to 35.9%(89). Other populations report different prevalence from our study but maintain this observed higher prevalence of obesity in SMI patients compared to population controls. A cross-sectional comparative study from Italy found a prevalence of abdominal obesity at 17.6% in SMI group with an increased chance of obesity in the SMI group OR 2.34, 95% CI (1.04–5.25) compared to obesity in Non-SMI control group(83). Another study from South Africa reported a prevalence of 55.1% for increased waist circumference(WC) in SMI group with significant association between increased WC and a diagnosis of SMI with an OR 1.79, 95% CI (1.28–2.52) compared to non SMI group(90).

Excess weight in SMI has been reported to be an independent risk factor for diffuse brain alterations with cognitive decline and brain ageing. It is thus a risk factor with additional impact on mental health yet simple strategies such as use of metformin, GLP-1 analogues dose reduction of offensive antipsychotic and alternative choice of antipsychotics have been shown to be effective in reducing weight(91,92). The antipsychotics prescription revisions and use of metformin which is easily available locally can therefore be adopted among other behavioral strategies in management of excess weight in SMI.

Further evaluation of the nutritional factors associated with excess weight in our SMI population may be important in determining other risk factors associated with excess weight.

The prevalence of hypertension from our study was 16.7% which is lower than the population prevalence of 24.5% (93). It was also slightly lower than that reported in the Italian study by M. Clerici et al that found a prevalence of 21.8% against a control group prevalence of 32.7%. Regionally the South African study by K. Maaroganye et al found a relatively high prevalence of HTN in patients with SMI at 32% (82). The relative low prevalence of hypertension in our study population may be attributed to their low age. The average age of participant in our study was 37.7±8.9 years making our study population relatively young compared to the Italian and South African study whose average age was 47.2±14.8 years and 42 years respectively.

The overall hyperglycemia prevalence from our study was 24% with IGT at 20.6% and diabetes at 3.4%. Prevalence of IGT is notably higher than the population prevalence of prediabetes of 3.1% but prevalence of diabetes is comparable to population prevalence of 2.4%(94). The Italian study found a prevalence of hyperglycemia relatively lower than ours at 10.9% in SMI group against 13.9% in the non-SMI control group despite having older participants. A South African study found a prevalence comparable to ours at 17.4% in the SMI group against 13.8 in the non-SMI

control group. Though the two studies demonstrated increased adjusted odds (OR 1.14) and (OR 1.32) of hyperglycemia in the SMI group in Italian study and South African study respectively, these associations were not statistically significant(83)(90).

The high prevalence of hyperglycemia in our participants and the south African study may be due the impact of SGAs on glucose metabolism. SGAs have been associated with elevation in blood glucose which occurs early upon introduction of the antipsychotics and before observed weight gain seen with SGAs(95).

The prevalence of metabolic syndrome was 27.5% which is comparable to population studies by G.Omuse et al, 2017 and L.Kaduka et al 2012 which reported prevalence of 25.6 and 34.6% respectively (96)(97). The mean age of participants was 39±20yrs in G. Omuses study and 38± 13 years in L. Kadukas study. In L. Kadukas study, participants were black Africans from different ethnic groups drawn from 30 clusters across five social-economic classes. However, these population studies are only from urban settings and hence may not be a good population representative sample. Our prevalence was in keeping with rates reported in a South African study which found a prevalence of 23.2% with no significant difference from a prevalence of 19.9% from population controls without SMI(90). Similarly, pooled prevalence from a meta-analysis of studies in India and Canada reported rates of 26.3% and 27.4% respectively while other countries reported higher prevalences such as 36.5% and 36.4% in Netherlands and USA respectively. However, according to a pooled relative risk analysis from the same meta-analysis, patients with SMI had an increased risk of MetS (RR = 1.58, 95% CI: 1.35-1.86, $p<0.001$; Q = 62, p = 0.003) compared with the general population(98).

Most of hyperglycemia and MetS has been strongly linked to use of SGA. This prompted release of evaluation guidelines by ADA/APA in 2004 on metabolic evaluation of patients on SGA.

However, none of the participants had been evaluated as per the guidelines. Adoption of such guidelines may go a long way into the objective metabolic screening of patients with SMI.

The 10-year risk of combined MI and stroke risk (fatal and non-fatal) was assessed for ninety participants and 91.1% found to be low risk <10%, 5.6 % had moderate risk and 3.3% high risk. Only 90 participants could be analyzed as WHO/ISH chart can only be used in people who are 40 years and above. Most of our participants were young and with age being a significant driver of CVD risk, this may explain the low risk observed in our assessment by the tool. Other general population risk assessment tools have also been found to underestimate the total CVRF level in patients with SMI(99). We therefore need to expand the current CVRF assessment tools to include people with SMI as a special high-risk group.

A diagnosis of bipolar mood disorder compared with schizophrenia seemed more associated with MetS with OR 2.17, 95% CI (1.14-4.14) p=0.019. This was however on bivariate analysis and therefore we cannot conclude on the observed association with certainty. This association may be due to factors apart from the SMI phenotype but related such as the choice of drugs for patients with BMD. No significant differences have been observed in studies comparing prevalence of MetS within the different psychiatric disorders(100).

We found a high prevalence of metabolic and behavioral risk factors. These are modifiable risk factors yet most of the participants were neither diagnosed nor managed for them. There would be benefit in setting up a multidisciplinary team including mental health, medical and nutritional experts in addressing CVRF in SMI. Secondly, there is need for concerted effort from the medical and psychiatry expert bodies to develop local comprehensive screening and management protocols for CVRFs in SMI with prompts on timely referral of patients to relevant specialist.

5.2 STUDY LIMITATIONS

1. A major limitation of our study was the lack of population references for most of the assessed variables hence we were unable to compare all our prevalence findings of risk factors against populations rates.
2. The study was a descriptive cross-sectional study so confounding variables cannot be controlled and temporal relationships were difficult to establish. Some of the confounders that may have been present but were not addressed included presence of undiagnosed medical conditions such as HIV, inflammatory diseases and hypothyroidism. These are known to be associated with metabolic risk factors hence may have affected some of the clinical variables besides the factors associated with mental illness and psychiatric drugs.
3. It was a single-center based study hence results from our study cannot be generalizable to the rest of the population.
4. Due to ethical reasons, patients with impaired insight and active psychotic or depressive symptoms could not be recruited to the study. This inadvertently excluded patients with chronic, advanced or residual mental illness from our analysis. These patients are therefore not represented in our findings.

CHAPTER 6

CONCLUSION AND RECOMMENDATION

6.1 CONCLUSION

The results from this study show that the patients in this study have a high prevalence of some cardiovascular risk factors namely: dyslipidemia, smoking, risky alcohol use, excess weight, abdominal obesity, impaired glucose tolerance and metabolic syndrome.

Despite the high prevalence of the CVRF in our study population, most had not been diagnosed neither were they on treatment or intervention programs. This may have a major impact on the future burden of CVDs in this group.

Our study provide insight on some of the most prevalent CVRFs. This may help in directing policy, focused interventions and resources in screening and management of CVRF in SMI in a bid to avert CVD and mortality.

6.2 RECOMMENDATION

This study recommends further studies exploring.

- Cohort studies looking into fatal and non-fatal cardiovascular outcomes in patients with SMI.

In view of the high prevalence of the CVRF there is need for emphasis on an integrated cardiovascular risk assessment and preventative program into the mental health care services in the country.

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APPENDIX

Appendix 1: Screening proforma

Study N°……..

Age …….

Date of birth……..

Gender: □ Male □ Female,

If female: When was your last normal menstrual period..../…./….,

If female, are you pregnant? Yes□ No□.

Year of Mental illness diagnosis ……..

Are you willing to participate in the study *Cardiovascular risk factors in mental illness.*

□ YES

□ NO

Appendix 2: Study Proforma

STUDY PROFORMA……Study Number…….

1. Date

2. Patient's contact……LAR's contact……..

SOCIO-DEMOGRAPHICS

3. Date of birth: ……/……/……..

4. Age: ……Yrs: □ (18-24yrs), □ (25-34yrs), □ (35-44yrs), □ (45-54yrs), □ (≥55yrs)

5. Gender: □Male □ Female

6. Marital status: □ Single □ Married □ Widowed □ Divorce □ Separated

7. Occupation: □ Student □ Self-employed □ Employed □ Unemployed □ Retired

8. Education level: □ None □ Primary □ secondary □ Tertiary □ Other

9. Monthly Income (Ksh):……..

PSYCHIATRIC HISTORY

10. Year of Mental illness Diagnosis ……...

11. Duration of Mental illness……..

12. Number of admissions ……..

13. Psychiatric medication from the record (List)……..

……

MEDICAL HISTORY

14. Hypertension □YES □ NO Duration (yrs)……..

15. Diabetes □ YES □NO Duration (yrs)……...

16. Lipid disorder □ YES □NO Duration (yrs)……...

17. History of CVD: MI, PAD, stroke or CAD…….

16. Other chronic illness □ YES □NO Specify…….

17. Any Other medication □ YES □NO Specify…….

FAMILY HISTORY

18. Known premature CAD or Ischaemia stoke in 1st degree relative.

(Father or brother <55years, sister or mother< 65years).

19. Diabetes in 1st degree relative.

SMOKING

18. Smoking status □ Current smoker □ Former smoker □ Non smoker

If a former smoker how long ago did you stop smoking? .....

ALCOHOL USE (AUDIT C QUESTIONNAIRE)

Which type of alcoholic beverages do you take?

In the past year:

19. How often do you have a had a drink containing alcohol?	Never	Monthly or less	2 - 4 times per month	2 - 3 times per week	4+ times per week
20. How many drinks of alcohol do you drink on a typical day when you are drinking?	1 -2	3 - 4	5 - 6	7 – 9	10+
21. How often have you had 6 or more drinks if female, or 8 or more if	Never	Less than monthly	Monthly	Weekly	Daily or

male, on a single occasion in the last year?					almost daily

MEDICATIONS

22. Hypoglycemic agents □ YES □ NO

23. Antihypertensive agents □ YES □ NO

24. Lipid lower agents: □YES □ NO Specify……

25. Antipsychotics: □YES □ NO Specify……

26. Antidepressants: □YES □ NO Specify……

PHYSICAL EXAMINATION

27. Weight (kg)…….

28. Height (m)……

29. Waist circumference (cm)……

Women: □Normal (≤80) □Increased (>80) □Substantially Increased (>88)

Men: □Normal (≤94) □Increased (>94) □Substantially Increased (>102)

30. Hip circumference (cm)……...

31. WHR (cm) ……

□Substantially Increased (≥ 0.85 women) (≥0.9Men)

32. BMI (kg/m2)

□ Underweight (<18.5) □ Normal (18.5-24.9) □ Overweight (25-29.9) □ Obese (≥30)

LAB PARAMETERS

33. FBS ……..

34. TOTAL CHOLESTEROL ……..

35. TRIGLYCERIDES ……..

36. HDL-C ……..

37. LDL-C ……

38. CARDIOVASCULAR RISK LEVEL:

□<10%, □10-<20%, □20-<30%, □30-<40% □≥40%

39. Presence of metabolic syndrome: □YES □NO

Appendix 3: Consent Explanation form

I am Dr. Valentine Kei, a postgraduate student in the department of Clinical Medicine and Therapeutics at the University of Nairobi.

I would like to invite you to participate in a study that I am conducting on *checking for factors that increase your risk for developing heart disease.*

Risk factors for heart disease are Physical, behavioral and laboratory features which have been shown to increase the probability of someone getting a heart disease or complication. These risk factors have been found to be more common in people with mental illness. Identifying some of these risk factors and managing then can help someone prevent the development of heart disease and reduce the severity if the heart disease if they already have It.

The purpose of this study is to examine for the presence of these risk factors in people with mental illness at Mathari national teaching and referral hospital. This will be done through asking a few questions. The questions will be mainly about your lifestyle and behaviour in your day to day living. You will also be requested to give a blood sample to check blood sugar and blood cholesterol/lipids levels. The investigator will also examine your file for more information.

Your participation in this study is voluntary and there is no compensation for participating. Refusal to participate will not affect the medical management you are already receiving.

If you accept to participate in the study, you will be required to answer few questions about yourself and your medical condition. You will also undergo a physical examination and a private comfortable area will be provided for this. You will then be requested to go without food for at least 8hours (This will be done overnight after your evening meal to avoid any discomfort) and a blood sample of 3mls will be taken from your arm in the early morning before you take breakfast.

You may benefit from this study by getting free screening for heart disease. In case you are found to have any abnormality in the tests done, this will be communicated to your doctor and you will receive appropriate management.

All information collected from you will be kept confidential. Any publications arising from this study will not identify you in person.

If you have understood the information, I have given you and you are willing to participate in this study, I will require you to sign a form indicating your willingness to participate.

For further information, you may contact any of the following:

1. Dr. Valentine Kei.

Department of Internal Medicine. University of Nairobi. P.O BOX 19676

Telephone number: 0724-890129.

2. Professor. E.N. Ogola

Department of Internal Medicine. University of Nairobi. P.O BOX 19676.

Telephone number: 0722-737944

3. Dr Marybeth Maritim

Department of Internal Medicine. University of Nairobi. P.O. BOX 19676.

Telephone number: 0733729963

3. The Secretary KNH-UON Ethics and Review Committee.

Telephone number: 2726300 Ext 44102

Email: uonknh_erc@uonbi.ac.ke

Appendix 4: Consent form

I _____ do confirm that I have read/ been explained to the above study, understood the information presented to me and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw from this study at any time without giving reason. I confirm that I have agreed to have a physical examination done on me and blood drawn for analysis. I agree to take part out of my own free will and no coercion or incentive has been offered.

Signature of participant_____ Date: _____

Signature of investigator _____ Date: _____

Appendix 5: Global physical activity questionnaire (GPAQ)

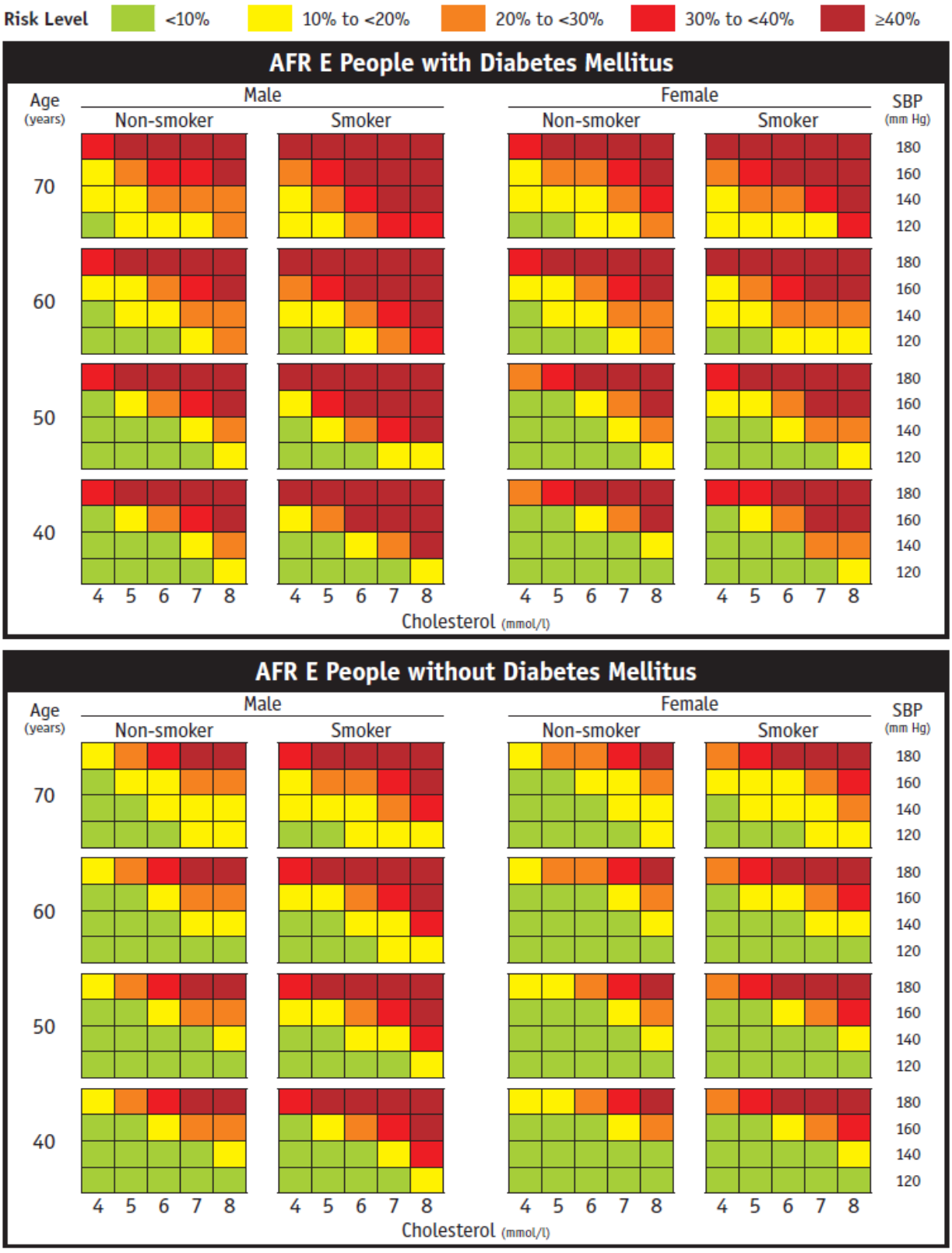
Physical Activity			
Next, I am going to ask you about the time you spend doing different types of physical activity in a typical week. Please answer these questions even if you do not consider yourself to be a physically active person. Think first about the time you spend doing work. Think of work as the things that you have to do such as paid or unpaid work, study/training, household chores, harvesting food/crops, fishing or hunting for food, seeking employment. *[Insert other examples if needed].* In answering the following questions 'vigorous-intensity activities' are activities that require hard physical effort and cause large increases in breathing or heart rate, 'moderate-intensity activities' are activities that require moderate physical effort and cause small increases in breathing or heart rate.			
Questions		**Response**	**Code**
Activity at work			
1	Does your work involve vigorous-intensity activity that causes large increases in breathing or heart rate like *[carrying or lifting heavy loads, digging or construction work*] for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 4*	P1
2	In a typical week, on how many days do you do vigorous-intensity activities as part of your work?	Number of days ⌊__⌋	P2
3	How much time do you spend doing vigorous-intensity activities at work on a typical day?	Hours: minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs. mins	P3 (a-b)
4	Does your work involve moderate-intensity activity that causes small increases in breathing or heart rate such as brisk walking *[or carrying light loads*] for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 7*	P4

5	In a typical week, on how many days do you do moderate-intensity activities as part of your work?	Number of days ⌊__⌋	P5
6	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P6 (a-b)
Travel to and from places			
The next questions exclude the physical activities at work that you have already mentioned. Now I would like to ask you about the usual way you travel to and from places. For example to work, for shopping, to market, to place of worship. [insert other examples if needed]			
7	Do you walk or use a bicycle (*pedal cycle*) for at least 10 minutes continuously to get to and from places?	Yes 1 No 2 *If No, go to P 10*	P7
8	In a typical week, on how many days do you walk or bicycle for at least 10 minutes continuously to get to and from places?	Number of days ⌊__⌋	P8
9	How much time do you spend walking or bicycling for travel on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P9 (a-b)
Recreational activities			
The next questions exclude the work and transport activities that you have already mentioned. Now I would like to ask you about sports, fitness and recreational activities (leisure), [insert relevant terms].			
10	Do you do any vigorous-intensity sports, fitness or recreational (*leisure*) activities that cause large increases in breathing or heart rate like [*running or football,]* for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P 13*	P10
11	In a typical week, on how many days do you do vigorous-intensity sports, fitness or recreational (*leisure*) activities?	Number of days ⌊__⌋	P11

12	How much time do you spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?	Hours : minutes └─┴─┘ : └─┴─┘ hrs mins	P12 (a-b)

Recreational activities cont……..			
13	Do you do any moderate-intensity sports, fitness or recreational *(leisure*) activities that causes a small increase in breathing or heart rate such as brisk walking,(*cycling, swimming, volleyball*)for at least 10 minutes continuously? *[INSERT EXAMPLES] (USE SHOWCARD)*	Yes 1 No 2 *If No, go to P16*	P13
14	In a typical week, on how many days do you do moderate-intensity sports, fitness or recreational (*leisure*) activities?	Number of days ⌊__⌋	P14
15	How much time do you spend doing moderate-intensity sports, fitness or recreational (*leisure*) activities on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs mins	P15 (a-b)
Sedentary behavior			
The following question is about sitting or reclining at work, at home, getting to and from places, or with friends including time spent [sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television], but do not include time spent sleeping. *[INSERT EXAMPLES] (USE SHOWCARD)*			
16	How much time do you usually spend sitting or reclining on a typical day?	Hours : minutes ⌊__⌋⌊__⌋ : ⌊__⌋⌊__⌋ hrs min s	P16 (a-b)

Appendix 6: WHO/ISH CHARTS FOR AFRICAN REGION E



Appendix 7: FOMU YA MAELEZO KUHUSU UTAFITI.

Kitangulizi:

Jina langu ni daktari Valentine Kei-Muriithi, mwanafunzi wa shahada ya uzamili kwenye somo la udaktari wa magonjwa ya undani katika chuo kikuu cha Nairobi.

Ningependa kukualika uhusike katika utafiti ambao naufanya kuhusu ‘Hali tatanishi zinazoambatana na kusababisha ugonjwa wa moyo katika watu waliathirika na matatizo ya akili kwenye Hospitali kuu ya Mathari.

Hali hizi tatanishi huonekana katika tabia na vipimo vya mwili na damu. Hali hizi zinapodumu bila kurekebishwa, hatimaye huweza kusababisha hitilafu za moyo.

Lengo la utafiti huu

Lengo la utafiti huu ni kutathmini kiwango na aina ya hali hizi tatanishi katika watu walioathirika na matatizo ya akili. Utafiti huu unahuzu mahojiano, vipimo vya mwili na vipimo vya damu kubainisha kuwepo kwa hali hizi tatanishi zinazosababisha ugonjwa wa moyo.

Hiari ya Kujiunga na Utafiti

Kuhusika kwako kwa utafiti huu ni kwa hiari yako. Hakuna malipo yoyote ambayo mtafiti atakupea ili uweze kushiriki. Una hiari ya kukataa kushiriki na hilo haliwezi kuathiri zile huduma zako za matibabu za kawaida kwa njia yoyote ile.

Jinsi utafiti utakavyofanywa

Iwapo utakubali kushiriki kwenye utafiti huu, utahitajika kujibu maswali kuhusu mazoea yako ya kila siku na pia maradhi ambayo unatibiwa. Baada ya mahojiano mtafiti atakupimia uzani na kuchunguza hali yako ya kimwili. Pia, mtafiti atakuomba umruhusu kukutoa damu kwa mkono kiwango cha milliliter 3 kwa sababu ya kipimo cha sukari na mafuta(lipids) mwilini.

Iwapo matokeo ya vipimo hivi yataonyesha hali tatanishi mwilini, Utajulishwa kupitia daktari wako ili upate ushauri na matibabu ipasavyo.

1. Dr. Valentine Kei.

Department of Internal Medicine. University of Nairobi. P.O BOX 19676

Telephone number: 0724-890129.

2. Professor. E.N.Ogola

Department of Internal Medicine. University of Nairobi. P.O BOX 19676.

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3. Dr Marybeth Maritim

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Telephone number: 0733729963

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Telephone number: 2726300 Ext 44102

Email: uonknh_erc@uonbi.ac.ke

Appendix 8: FOMU YA RIDHAA

Hali tatanishi ninazoambatana na kusababisha ugonjwa wa moyo katika watu waliathirika na matatizo ya akili:

Mimi _____nathibitisha ya kwamba nimesoma/ nimepewa maelezo kuhusu huu utafiti, nikaelewa na nikapata fursa ya kuuliza maswali. Naelewa kuwa kushiriki ni kwa hiari yangu na kwamba niko na uhuru wa kujiondoa kwenye utafiti wakati wowote bila kutoa sababu yoyote. Nathibitisha kwamba nimekubali nifanyiwe kipimo cha sukari na mafuta ya damu (lipids).

Nimekubali kuhusika kwa hiari yangu mwenyewe na sijalazimishwa wala kuhongwa.

Sahihi ya mhusika_____ Tarehe: _____

Sahihi ya mtafiti _____ Tarehe: _____