THE ASSOCIATION BETWEEN ALCOHOL CONSUMPTION AND THE METABOLIC SYNDROME AND ITS COMPONENT DISEASES IN A RURAL GHANAIAN POPULATION

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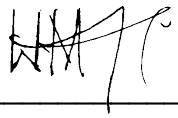
Declaration

I declare that this research report is my own work. It is being submitted in partial fulfilment of the requirements for the degree of Master of Science in Epidemiology in the field of Epidemiology & Biostatistics at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination to any other University.



Dr Violet Wairimu Mathenge

20th day of November 2019 in Johannesburg

Dedication

To my father and mother

You truly are the wind beneath my wings

Abstract

Background: Metabolic syndrome (MS) is a combination of risk factors that increase cardiovascular disease (CVD) risk. Current evidence suggests an association between alcohol intake and MS. Despite the high levels of alcohol consumption in Navrongo, data on its association with MS is non-existent. The aim of this study was to determine the prevalence of MS and its components and determine the association of alcohol consumption patterns with MS and its component diseases among 40-60 year olds in rural Northern Ghana.

Methods: This was a cross-sectional study leveraged on secondary data from the Navrongo, Ghana site of the African-Wits-INDEPTH Partnership for Genomic Studies (AWI–Gen study). The CAGE questionnaire was used to assess harmful alcohol consumption and MS was defined based on the 2009 International Diabetes Federation/ National Heart, Lung, and Blood Institute/ American Heart Association (IDF/AHA/NHLBI) criteria. Multivariable regression analyses were used to determine the association between alcohol intake and MS.

Results: We present results for 1875 participants of which 53.9% were women. The mean age was 51.1±5.78 years. The overall MS prevalence was 7.63%, with a notable female predominance (females: 12.5%; males: 1.97% [p<0.001]). The most prevalent MS components were low HDL (55.2%), elevated blood pressure (34.9%) and high waist circumference (17.7%). Majority (84.9%) of the participants had a history of alcohol intake. Current drinking was more prevalent among men than women (77.9% vs. 54.7%; p<0.001). Among men, the adjusted odds ratios [95% CIs] of MS were 0.03 [0.002-3.26]) for previous drinkers, 1.69 [0.18-16.0] for current non-problematic drinkers and 0.46 [0.04-5.19] for current problematic drinkers. For women, the adjusted odds ratios [95% CIs] of MS were 0.82 [0.42-1.57]) for previous drinkers, 0.66 [0.37-1.18] for current non-problematic drinkers and 0.63 [0.30-1.31] for current problematic drinkers with non-drinkers as the reference group. Alcohol consumption was significantly associated with hyperglycaemia among women (p=0.025) and low HDL among both men (p<0.001) and women (p=0.031).

Conclusion: Despite the overall prevalence of MS being relatively low, the much higher prevalence among women is alarming. Alcohol intake did not influence the occurrence of MS in this population. However significant associations with hyperglycaemia and low HDL levels were noted, highlighting the need for further investigation. The high prevalence of alcohol intake in this population suggests that measures to control alcohol consumption are required. Thus, alcohol intake assessment at the primary care level could be introduced.

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Most importantly, I am grateful to the Lord God Almighty for his grace, his faithfulness and strength. Apart from him, I am nothing.

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List of Abbreviations

AIC: Akaike's information criteria

AHA: American heart association

AWI-Gen: African-Wits-INDEPTH Partnership for Genomic Studies

BIC: Bayesian information criteria

CVD: Cardiovascular disease

HDL-C: High-density lipoprotein cholesterol

IDF: International diabetes federation

FAEE: Fatty Acid Ethyl Esters

JNC7: Seventh report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation and Treatment of High Blood Pressure

LDL: Low-density lipoprotein

LMIC: Low and middle-income countries

MS: Metabolic syndrome

NCD: Non communicable disease

NHDSS: Navrongo Health and Demographic Surveillance Site

NCEP ATP III: National Cholesterol Education Program – Third Adult Treatment Panel

NHLBI: National Heart, Lung and Blood Institute

T2D: Type 2 Diabetes

WC: Waist circumference

WHO: World Health Organization

WHR: Waist to hip ratio

RAAS: Renin-angiotensin-aldosterone system

Rx: Pharmacologic treatment

SCAT: Subcutaneous adipose tissue

VAT: Visceral adipose tissue

VLDL: Very low density lipoprotein

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Chapter 1 : INTRODUCTION

This chapter provides a background to the study detailing non-communicable diseases, with emphasis on the metabolic syndrome. It gives a review of previous literature on alcohol consumption, alcohol metabolism and the metabolic syndrome and its component diseases. It further describes the association between alcohol consumption and metabolic syndrome and its component diseases based on previous studies in Ghana and elsewhere. The chapter ends with the problem statement, justification of the study, research question and study aim.

1.1 Background

Non-communicable diseases (NCDs) such as cardiovascular diseases (CVDs), cancers, chronic respiratory diseases and diabetes are the leading cause of death and disability worldwide(1).The burden of these diseases is on the rise in African countries mainly due to the health transition from infectious diseases to chronic diseases of lifestyle. This is often attributed to improved life expectancies and urbanization, the latter of which has resulted in an increased consumption of high caloric diets at the expense of physical activity (2).

As opposed to most communicable diseases, NCDs tend to have long preclinical disease periods and heavily depend on disease screening for timely diagnosis. The lack of overt symptoms in the initial stages leads to a delay in seeking healthcare among those affected, which in turn results in an underestimation of the true burden of disease. Even after detection, most NCDs have no absolute cure and are therefore longstanding diseases relying on lifelong treatment and monitoring to prevent complications and disabilities (3). This brings about an increase in household costs, impedes poverty reduction and dampens development in low income countries.

According to the WHO 2018 estimates, 43.7% of the mortalities resulting from NCDs are attributable to cardiovascular diseases (CVDs), with 82% of these deaths occurring in low- and middle-income countries (LMIC) (3). Cardiovascular diseases are defined as

disorders of the heart and blood vessels and commonly include: coronary heart disease, cerebrovascular disease, deep vein thrombosis, pulmonary embolism, and congenital heart disease (4). Given the role of CVDs in contributing to NCD mortality, a grasp of CVD risk factors and their association with various exposures is critical.

Metabolic syndrome (MS) is a combination of several cardiovascular risk factors, possibly resulting from insulin resistance, that increases the risk of cardiovascular diseases (5). The 2009 International Diabetes Federation/ National Heart, Lung, and Blood Institute/ American Heart Association (IDF/AHA/NHLBI) harmonized definition of MS includes the presence of three or more of: elevated waist circumference (WC ≥ 80cm and ≥ 94 cm for non-European women and men respectively), elevated triglycerides (TG ≥ 1.7 mmol/L), reduced high-density lipoprotein cholesterol levels (HDL-C < 1mmol/L among men and < 1.3 mmol/L among women), elevated blood pressure (systolic blood pressure ≥ 130 mmHg and diastolic blood pressure ≥ 85 mmHg), and elevated fasting glucose levels (≥ 5.6 mmol/L) (6).

High alcohol consumption has been established to have a casual role in 60 different types of diseases (7). Of particular interest is its contribution to CVDs and other NCDs such as cancers and diabetes. It is therefore a major risk factor that is important in the control of CVDs and NCDs. Current evidence from WHO further suggests that harmful alcohol consumption leads to four key metabolic and physiological changes (raised blood pressure, overweight/obesity, raised blood glucose and raised cholesterol) that define MS (8). Studies in Ghana (9,10) and a previous study the study site (11) have observed high levels of alcohol consumption among adults. However, the associated effect on MS and CVDs has not been previously reported.

1.2 Literature review

1.2.1 Non-communicable diseases

In recent years, there has been growing concern over the dramatic increase in the burden of NCDs, particularly in LMIC. In 2016, there were 56.9 million global deaths, 40.5 million (71.2%) of them attributed to NCDs alone. More than three quarters of these deaths occurred in LMIC, with nearly half (46%) occurring before the age of 70 (3).These premature mortalities deal a major blow to African economies, which rely on their youthful population structures for productivity.

Type 2 diabetes (T2D) and CVDs are chronic diseases that put a strain on already overstretched African health care systems. The prevalence of these diseases continues to steadily increase each year. A 69% increase in the prevalence of diabetes in developing countries between 2010 and 2030 is expected (12). Additionally, mortality from CVDs is expected to double between 2005 and 2030 (13). In this regard, it is imperative to device measures towards primary prevention of these diseases.

1.2.2 Metabolic syndrome

Despite the controversy on the standard definition of MS, it remains a useful predictor of CVDs and T2D risk (14,15). A number of organizations have developed clinical criteria for diagnosing MS. Of these, the most commonly accepted ones are those defined by the World Health organization (WHO) (16), the National Cholesterol Education Program – Third Adult Treatment Panel (NCEP-ATP III) (17) and the harmonized International Diabetes Federation/National Heart, Lung, and Blood Institute/American Heart Association (IDF/AHA/NHLBI) (6) (see Table 1.1). These three definitions share similar core components of MS but differ on the diagnostic criteria for some of the component disorders. The existence of multiple criteria for diagnosis has resulted in many studies using different criteria, making comparison between studies difficult. Nonetheless, MS is an important component of the CVD epidemic and timely identification provides an opportunity for lifestyle interventions and treatment to prevent CVD and type 2 DM.

Table 1.1: Definitions of metabolic syndrome by four accepted criteria

	WHO	NCEP ATP III	IDF	IDF/AHA/NHLBI
No. of abnormalities	≥ 3 of the following, one of which must be insulin resistance	≥ 3 of the following	≥ 3 of the following, one of which must be central obesity	≥ 3 of the following
Abdominal obesity	WHR >0.9 in men; 0.85 in women and/or BMI >30 kg/m^2	≥ 102 cm in men ≥ 88cm in women	>94 cm in men >80cm in women	≥ 94 cm in men ≥ 80cm in women
Triglycerides	≥1.7 mmol/L	≥1.7 mmol/L	≥1.7 mmol/L	≥1.7 mmol/L
	and/or			
HDL Cholesterol	<0.9 mmol/L in men <1.0 mmol/L in women	<1.0 mmol/L in men <1.3 mmol/L in women	<1.0 mmol/L in men <1.3 mmol/L in women	<1.0 mmol/L in men <1.3 mmol/L in women
Blood Pressure				
Systolic	≥140 and/or	≥130 and/or	≥130 and/or	≥130 and/or
Diastolic	≥90 mmHg or anti-hypertensive drug Rx	≥85 mmHg or anti-hypertensive drug Rx	≥85 mmHg or anti-hypertensive drug Rx	≥85 mmHg or anti-hypertensive drug Rx
Fasting Glucose	-	≥5.6mmol/L or Rx for hyperglycaemia	≥5.6mmol/L or Rx for hyperglycaemia	≥5.6mmol/ or Rx for hyperglycaemia
Insulin resistance	Type 2 DM / fasting glucose ≥6.1 mmol/L or 2 hour OGTT ≥7.8 & <11.1 mmol/L or Impaired fasting glucose ≥5.6 &<6.1 mmol/L or *Glucose uptake <25% of background population	-	-	-
Others	Microalbuminuria			

WHO, World Health Organization (16); NCEP-ATPIII, National Cholesterol Education Program Adult Treatment Panel III (17); IDF, International Diabetes Federation (18); IDF/AHA/NHLBI, International Diabetes Federation/ American Heart Association/ National Heart, Lung, and Blood Institute (6). *****Determined by hyperinsulinaemic euglycaemic clamp studies. Rx Pharmacologic treatment.

The International Diabetes Federation estimates that a quarter of the global population has MS (18).This is in keeping with studies conducted in the U.S that found a prevalence of 22.9% (19). This paper also highlighted a variation in trends of the various

components of MS by gender and race; with female Mexican Americans having a higher prevalence than other subgroups. Similarly, studies conducted among adults in Turkey and China reported a prevalence of 26.9% and 23.2% respectively (20,21).

Table 1.2: Prevalence of metabolic syndrome across various global populations

Author/year	Country	Prevalence (%)	Age (years)	Sample (n)	Diagnostic Criteria
Sánchez et al,2013 (19)	United states	22.9	≥20	2,034	IDF/AHA/NHLBI
Erem et al, 2008 (20)	Turkey (urban)	26.9	≥20	4,809	NCEP ATP III
Li et al, 2010 (21)	China (urban)	16.2 23.2	≥18	16,442	NCEP ATP III IDF
Harikrishnan et al, 2007 (22)	India (urban and rural)	24.0 29.1 32.8	20-79	5,063	NCEP ATP III IDF IDF/AHA/NHLBI
Al-Rubeaan et al, 2018 (23)	Saudi Arabia (urban and rural)	39.8	≥18	12,126	NCEP ATP III
Jaipakdee et al, 2013 (24)	Thailand	18.2	35-60	2,804	IDF/AHA/NHLBI
De Carvalho et al, 2013 (25)	Brazil (urban and rural)	29.6	19-64	8,505	NCEP ATP III
Kaduka et al, 2012(26)	Kenya (urban)	34.6	≥18	539	IDF/AHA/NHLBI
Ofori-A et al, 2017 (27)	Ghana (urban and rural)	6.00 12.4 21.2	≥18	1,559	WHO NCEP ATP III IDF
Gyakobo et al, 2012 (28)	Ghana (rural)	15.0 35.9	35-64	206	NCEP ATP III IDF
Sumner et al, 2010 (29)	Nigeria and Ghana (urban)	32.0 38.0	25-64	364	NCEP ATP III IDF

WHO, World Health Organization; NCEP-ATPIII, National Cholesterol Education Program Adult Treatment Panel III; IDF, International Diabetes Federation; IDF/AHA/NHLBI, International Diabetes Federation/ American Heart Association/ National Heart, Lung, and Blood Institute.

In sub-Saharan Africa, reliable data on MS remains scanty. In general, most of the studies performed in African countries indicate a higher prevalence of MS in Africa compared to the rest of the world (26,28,29). African women have been consistently

found to have a higher prevalence than their male counterparts. Thus, a study among an urban population in Kenya reported an MS prevalence of 34.6% (IDF/AHA/NHLBI criteria); with a prevalence of 40.2% among women and 29.0% among men (26). In a similar study among West Africans from Nigeria and Ghana, a prevalence of 42.0% among women and 19.0% among men was reported (NCEP-ATPIII criteria) (29). In both studies, the three variables that most often led to the diagnosis of MS were low HDL cholesterol, central obesity and hypertension.

Ofori-Asenso et al (2017), in a systematic review of apparently healthy adults in Ghana, presented data on the prevalence of MS based on IDF/AHA/NHLBI, and NCEP-ATP classifications. The levels were 21.2% and 12.4% respectively. Consistent with findings from Africa, women had a higher prevalence than men (27).This study however, was conducted in 4 out of 10 regions in Ghana, with 8 out of the 9 studies being in urban centres; and as such may not be representative of the entire population. In contrast, another study conducted in rural southern Ghana reported a much higher prevalence of MS (35.9% using IDF criteria and 15.0% with NCEP-ATP criteria) (28). To date there is no study on the prevalence and associated risk factors of MS in adults from rural northern Ghana.

1.2.3 Alcohol consumption

In addition to being characterized by the shift from infectious to chronic diseases, the health transition encompasses behavioural and lifestyle changes. Alcohol consumption is a prevalent lifestyle habit, cutting across all societies (see Table 1.3). Thus, 40.6% of the global adult population consumes alcohol, with Europe and sub-Saharan Africa consuming the most amounts (30).

In Ghana, alcohol consumption and abuse is on the rise. Abuse of locally brewed alcohol *akpeteshie,* is a particular problem (9). A cross-sectional study in the Volta region found a 43.4% prevalence of alcohol consumption among the youth (10). More recently, a study at the study site reported a prevalence of 51.3% for current alcohol intake with 85.0% of the population having a history of alcohol intake (11).

Table 1.3: Prevalence of alcohol consumption in populations across the world

Author/year	Country	Prevalence (%)	Age (years)	Sample (n)
Osei-bonsu et al, 2017 (10)	Ghana	43.4	15-39	316
Nonterah et al, 2018 (11)	Ghana	51.3	40-60	2014
Vellios et al, 2018 (31)	South Africa	33.1	≥15	20,000
Luecha et al, 2019 (32)	Thailand	31.0	10-14	9,509
Zhao et al, 2016(33)	China	24.2	≥35	11,269
Rathod et al, 2015 (34)	India	13.3	≥18	3220
Grant et al, 2017 (35)	United States	72.7	≥18	36,309
Macinko et al, 2015 (36)	Brazil	26.5	≥18	62,986

1.2.4 Alcohol consumption and metabolic syndrome

Multiple studies on the association between alcohol consumption and MS have been conducted, however, the findings have been inconsistent. Some report associations that are inversely linear (37,38), J-shaped (39,40) or positively linear (8), while others report no association (41). Yoon et al (2018), reported a dose response relationship between alcohol consumption and MS but an inverse relationship with light alcohol consumption (39). Similarly, Kim 2017, in a study among Korean adults, reported the lowest prevalence of MS in light drinkers and the highest prevalence in heavy drinkers compared to non-drinkers (40).

In contrast, a cross-sectional study in the U.S. demonstrated a lower prevalence of MS among drinkers compared to non-drinkers, with this relationship being more pronounced in people who consume greater than 20 alcoholic beverages per month and more so when the beverage was beer or wine. This study also found a greater association between alcohol consumption and MS in Caucasians compared to other races (37). Fan et al (2008), reported a lower prevalence of MS among drinkers irrespective of the level

of consumption (38). Conversely, Baik and Shin 2008, reported a significant increase in the risk of the MS that is restricted to heavy liquor drinkers in particular (42).

Studies investigating this association on the African continent are few (28). In northern Ghana in particular, no studies have been conducted.

1.3 Alcohol metabolism

Alcohol metabolism is carried out by several tissues including the liver, stomach, pancreas, skeletal muscle and brain. The bulk (90%) of the elimination takes place in the liver, with 2-5% being excreted unchanged in urine, sweat or through the lungs (43). The rate of elimination varies with factors such as age, gender, level of consumption, diet, smoking and genetics (44).

Upon ingestion alcohol undergoes first pass metabolism which occurs in the stomach and the liver. This results in blood alcohol concentrations that are lower than the amounts ingested. The speed of gastric emptying influences ethanol contact with gastric aldehyde dehydrogenase and is therefore a major determinant of first pass metabolism (44). Upon absorption in the gut it is transported via the portal circulation to the liver.

Alcohol metabolism involves both oxidative and non-oxidative pathways. Inhibition of oxidative pathways leads to up-regulation of non-oxidative pathways. Genetic variability of enzymes involved in these pathways influences alcohol consumption, dependence, tissue damage and the rate of alcohol elimination (44).

1.3.1 Oxidative metabolism

The fundamental pathway involves oxidation of ethanol to acetate. Enzymes involved include alcohol dehydrogenase (ADH), cytochrome P450 2E1 (CYP2E1) and catalase located in the hepatocyte cytosol, microsomes and peroxisomes respectively. The main enzyme, ADH, converts alcohol to acetaldehyde thereby reducing oxidized Nicotinamide adenine dinucleotide (NAD^+) to NADH. At high ethanol concentrations, CYP2E1 found in the microsomes metabolizes alcohol to acetaldehyde. In the peroxisomes, catalase oxidizes alcohol in the presence of hydrogen peroxide; this is

however a minor pathway of oxidative metabolism. The last step of the oxidative pathway involves metabolism of acetaldehyde to acetate by acetaldehyde dehydrogenase. This occurs in the mitochondria after which the acetate enters into the circulation. This reaction also generates NADH and reactive oxygen species. Acetate is ultimately metabolized to carbon dioxide in the heart, skeletal muscle and brain (45).

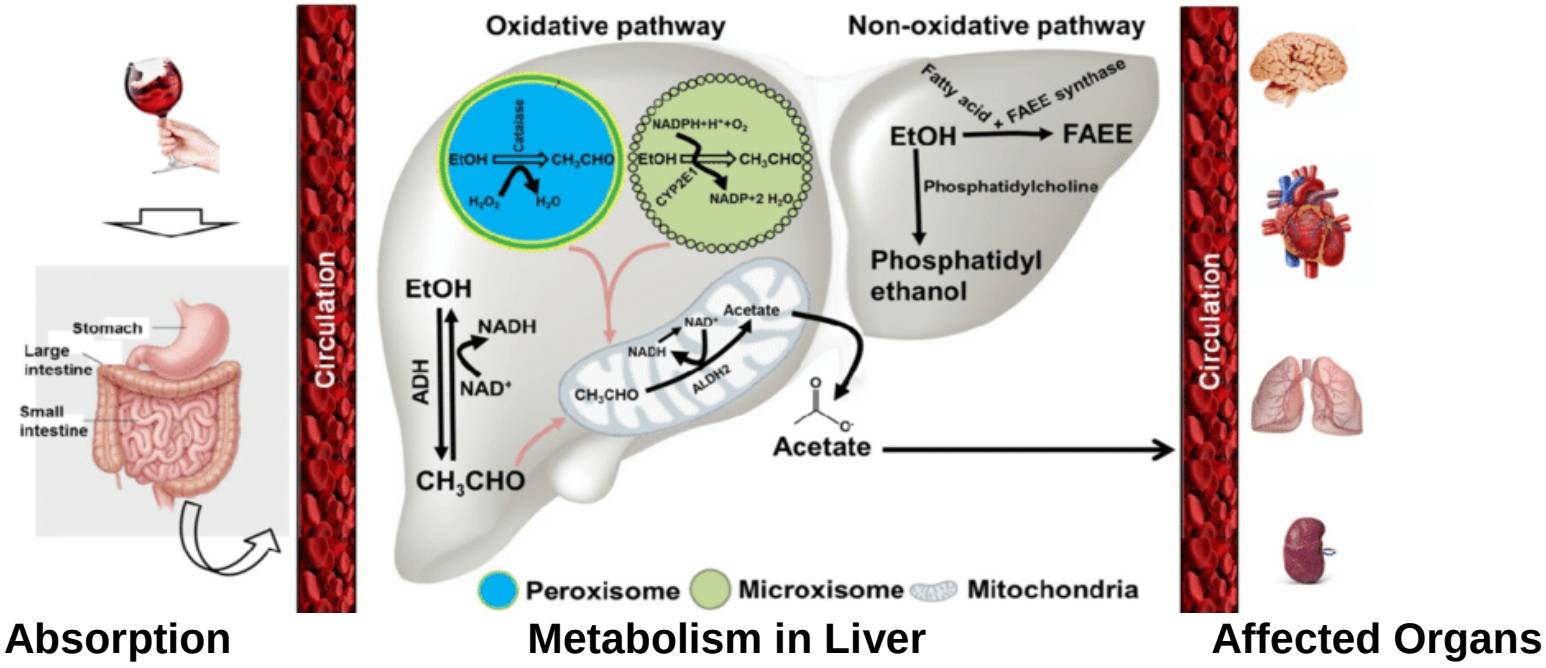


Figure 1.1. Alcohol metabolism in the body (source: Mandal et al, 2017 (45)**.)**

1.3.2 Non-oxidative metabolism

Non oxidative pathways have minimal contribution to overall alcohol metabolism; however non-oxidative metabolites are useful as markers of alcohol consumption. These metabolites are produced in two main pathways; the first involves reaction of alcohol with fatty acids catalysed by fatty acid ethyl ester synthase resulting in the formation of fatty acid ethyl esters (FAEE). These enzymes are mainly located in the hepatocyte cytosol and microsomes. Synthetic activity has also been demonstrated in

other body tissues like the pancreas, heart, liver and brain. The second involves a reaction with phosphatidylcholine catalysed by phospholipase D to generate phosphatidyl ethanol (PEth) (45). The formation of PEth interferes with cellular processes by altering cell membrane structure and membrane transporter function.

These non-oxidative metabolites (FAEEs and PEth) have slow elimination rates and tend to remain in the body tissues long after ethanol is eliminated. Thus they are responsible for a considerable proportion of alcohol's toxic effects and serve as useful biomarkers for alcohol intake.

1.4 Consequences of alcohol metabolism

Acetaldehyde, one of the key products of alcohol metabolism, is a highly reactive toxic metabolite which easily forms adducts with plasma proteins, some of which lead to alcohol dependence, impaired protein secretion and carcinogenesis. Alcohol metabolism also leads to oxygen deficits with resultant hypoxic liver injury. Moreover, reactive oxygen species and immune mediated hepatotoxicity resulting from adduct formation causes additional tissue damage. Altered $NADH/NAD^+$ ratios negatively impact gluconeogenesis and fatty acid oxidation among other metabolic processes. This leads to an increase in the production and deposition of triglyceride in the liver hence the fatty liver syndrome. Liver damage occurs in three stages: fatty liver, alcoholic hepatitis and finally cirrhosis. With the liver being fundamental in nearly all metabolic processes, disturbances in its function have an association with the metabolic syndrome and its component diseases (46).

1.4.1 Alcohol induced hypertension

Multiple studies have demonstrated an association between alcohol and hypertension, with heavy consumption showing a more consistent relationship. Alexandros et al (2012) reported a J shaped association with heavy consumption increasing the risk and mild to moderate consumption having a protective effect among women. Among men,

there was a dose response relationship between the two at all levels of alcohol consumption (47). Nathália et al (2018), reports a positively linear relationship but no beneficial effect at lower levels of alcohol intake (48). Furthermore, a reduction in blood pressure with reduced alcohol intake has been demonstrated especially among previous heavy drinkers (49). Despite this evidence, the threshold for these effects and their underlying mechanisms remains unclear.

Proposed hypotheses for this association include reduced baroreceptor reflex sensitivity with associated increased sympathetic activity, central nervous system imbalance and an increase in intracellular calcium (50). Despite some studies reporting no significant change in activity (51), increased activation of the renin-angiotensin-aldosterone system (RAAS) has also been implicated as a possible mechanism for alcohol-induced hypertension especially among heavy drinkers (52). Endothelial injury, with resultant reduction in vasodilator production has also been suggested as a possible mechanism (53).

1.4.2 Alcohol associated diabetes

At present, it is difficult to simply define the overall effect of alcohol consumption on blood sugar, as the association appears to be complex and inconsistent. Craig et al (2015), in a systematic review, reported a reduced risk for type 2 diabetes (T2D) among female drinkers who consume moderate amounts of alcohol (54). Similarly, in a 20 year cohort study among Finnish twins, moderate alcohol consumption was found to be associated with a decreased risk of diabetes compared to low consumption. In this study, the incidence of diabetes was high among heavy drinkers (55). A study conducted among middle aged Japanese men reported a U shaped association, with moderate drinkers having the lowest diabetes risk (56).

Possible explanations for the reported effects include improved insulin sensitivity among moderate drinkers (57); and insulin resistance accompanied by glucose intolerance among heavy drinkers (58).

1.4.3 Alcohol effect on HDL and triglycerides

Alcohol is known to increase HDL-C concentrations among moderate drinkers (59–61). One postulated mechanism is by increasing the secretion and transport rate of apolipoproteins (59,61). Alcohol is also thought to increase lecithin-cholesterol acyl transferase (LCAT) activity. This is an enzyme that esterifies cholesterol, thereby helping in the conversion of HDL to the spherical form that is transported to the liver (62,63).

In addition, some studies report an increase in lipoprotein lipase levels resulting from alcohol consumption. This enzyme breaks down triglycerides, an action that is accompanied by an increase in HDL cholesterol levels (64). In contrast, hypertriglyceridemia following excessive alcohol intake has been reported, as a result of increased very low density lipoprotein (VLDL) synthesis and reduced lipoprotein lipase activity (65). Current evidence suggests a J shaped association between alcohol and triglyceridemia. Low to moderate alcohol consumption has been shown to be associated with reduced triglyceride levels, with highest levels being reported among heavy drinkers (66).

1.4.4 Alcohol effect on waist circumference

Waist circumference provides a measure of visceral adiposity, and therefore serves as an important predictor of cardiometabolic risk (67).

The majority of research has suggested an association between alcohol intake and waist circumference. Jeanette et al (2017), reported an inverse relationship between body weight, waist circumference and alcohol intake (68). Conversely, in a study among Korean women, waist circumference was observed to increase with increasing frequency of alcohol consumption (69). Other studies report a variation in this association that is dependent on the type of alcoholic beverage consumed. Beer and spirits are said to increase the waist circumference while wines have been associated with a decrease in waist circumference over time (70). In a large scale European cohort

study, lifetime alcohol use was observed to have a positively linear relationship with waist circumference (71).

As with other components of the MS, the mechanisms are not fully understood. One study observed increased lipid accumulation and adipocyte differentiation after ethanol administration and was related to visceral adipose tissue accumulation (58). Other studies propose an imbalance in lipogenesis and lipolysis leading to fat redistribution in the abdomen (72).

1.5 Problem statement

Alcohol consumption is a prevalent lifestyle habit of concern in virtually all societies. Despite the known numerous negative effects on health, it remains a popular habit and Ghana has a high level of alcohol consumption. Thus, a WHO report from 2015 on alcohol consumption ranked Ghana among the top 100 countries globally with a per capita consumption of 5.4 litres (73). The rising trend of alcohol abuse in Ghana saw the launch of a national alcohol policy in 2017 (74). Osei-bonsu et al (2017), reported the prevalence of alcohol consumption among the youth in Ghana to be at 47% (10). Previous studies on this study population have reported a prevalence of current alcohol consumption of more than 50% (22). This study also reported low levels of obesity determined through body mass index (11). However, studies from other parts of Ghana have reported alarmingly high rates of MS (8). Despite the high prevalence of alcohol consumption in the study population, there is no data on the effects of alcohol consumption patterns on MS.

1.6 Justification

Multiple studies have been conducted on the association between alcohol and MS; the findings have however been inconsistent. Some studies demonstrate a positive relationship between alcohol consumption and MS (39), whilst others show a negative relationship (40), and others present a J-shaped association between the two (75).

Further to this, few studies have been conducted in the African context where alcohol consumption is high and MS an increasing health problem. Collectively, these studies outline the critical need for population specific studies to determine related risk factors for formulation of interventions.

1.7 Research Question

What are the effects of alcohol consumption on MS and its component disorders in a population of adults aged 40-60 years from rural Northern Ghana?

1.8 Aims and objectives

The main aims of the study are to determine the prevalence of MS and to analyse the association of alcohol consumption patterns with MS among 40-60 year olds in rural Northern Ghana.

1.8.1 Specific objectives

I. To determine the prevalence of the MS and its component disorders across the following 4 alcohol consumption patterns: abstinence, previous drinkers and current non-problematic and current problematic drinking
II. To determine the association of alcohol consumption patterns with MS and its component disorders and the role of other potential confounding factors in these associations

Chapter 2 : MATERIALS AND METHODS

This chapter gives an overview of the primary study, how the study population was selected and how the variables were measured. It further describes the concept behind this nested sub-study and the data management, statistical analyses and ethical considerations. The statistical analyses described address the main objectives of the study.

2.1 Primary Study

2.1.1 Background

This study is a nested sub-analysis of the parent study: the African-Wits-INDEPTH [International Network for the Demographic Evaluation of Populations and Their Health] Partnership for Genomic Studies (AWI–Gen). The AWI-Gen study is one of the Human Heredity and Health in Africa (H3A) consortium studies that aims at facilitating research that will lead to a greater understanding of the genetic, environmental and behavioural risk factors for obesity and associated cardiometabolic diseases in sub-Saharan Africa (76).

2.1.2 Study setting

The AWI-Gen study was carried out in six centres spread across 4 African countries: Ghana, Burkina Faso, Kenya and South Africa. The study in Ghana was based at the Navrongo Health and Demographic Surveillance Site (NHDSS), which is one of the pioneer INDEPTH member sites. It is hosted by the Navrongo Health Research Centre (NHRC), located in the two Kassena-Nankana districts (Kassena-Nankana East and West).

Established in 1993 (77), the NHDSS routinely monitors health and demographic events and evaluates the impact of health interventions. The NHDSS coverage area includes Kassena-Nankana East Municipality and Kassena-Nankana West district which cover an area of 1675km^2. The study area borders Burkina Faso to the northeast, the Builsa

district to the southwest and the Upper West region to the west. The NHDSS currently monitors approximately 165,000 people in 5 zones (north, east, west, central and south) which include 275 clusters of communities and 32,000 households with an average of 70 households per cluster (78).

2.1.3 Study design

The study was a population based cross-sectional study conducted between 2013 and 2016 (79).

2.1.4 Study population

The primary study involved men and women aged 40-60 years resident in the NHDSS coverage area for the previous 10 years. Recruitments involved mainly the pure Kasem and pure Nankam speaking communities located in the West, North and East zones of the NHDSS.

Closely related individuals, pregnant women, and recent immigrants were excluded from the study. Participants with medical conditions hindering blood pressure and anthropometric measurements were also excluded from the study. Participant selection was not based on prior exposure or outcome information.

2.1.5 Sampling

A two-stage sampling approach was used with the initial stage involving purposeful selection of the West and North zones (Kasem speaking zones) and East zone (Nankam speaking zone) of the NHDSS area based on predominant ethno-linguistic groupings. The second stage was the random sampling of adults aged 40-60 years old from the existing sampling frame of these zones in the NHDSS database and with a roughly equal number of men and women and the two predominant ethno-linguistic groups. A combined sample of 2000 individuals plus 10% for non-response were included in the study.

2.1.6 Data collection

Details of the AWI-Gen study and how data were collected have been published elsewhere (79). Briefly, this data was collected using an AWI-Gen standardized detailed paper based interviewer administered questionnaire. The questionnaire, completed by trained field workers and/or clinicians includes sections on socio-demographics, participant past medical history, physical examination findings and laboratory investigations. Socioeconomic status (SES) was calculated using household data on ownership of assets and dwelling characteristics such as water and sanitation facilities; and household services such as electricity. Principle component analysis was subsequently carried out and based on this information, the SES variable was stratified into quintiles.

2.1.7 Measurement of variables in the AWI-Gen study

Below is a brief summary of how variables relevant to this study were measured. All measurements were taken by experienced or trained research assistants. Equipment used was standardized, well maintained and inspected to ensure proper calibration.

2.1.7.1 Anthropometric and blood pressure measurements

These included height, weight, waist circumference, visceral adipose tissue and subcutaneous adipose tissue.

2.1.7.1.1 Height and weight

Weight and height were measured using a digital weighing scale (Seca GmbH & Co. KG, Hamburg, Germany) and stadiometer (Holtain, Crymych, Wales) respectively. Height was measured to the nearest 0.1milimeters (mm) with participants standing and maintaining a straight posture, either barefoot or wearing thin socks. Weight was measured to the nearest 0.1kilogram (kg) with participants wearing light clothing and without shoes.

2.1.7.1.2 Waist and hip circumference

These measurements were taken in millimetres, using a stretch resistant tape measure. The waist circumference was measured in between the iliac crest and the lowest rib. The hip circumference was measured around the widest part of the buttocks.

2.1.7.2 Visceral and subcutaneous adipose tissue

A LOGIQ e ultrasound system (GE Healthcare, CT, USA) with a 2–5 MHz 3C-RS curved array transducer was used to measure visceral adipose tissue (VAT) and subcutaneous adipose tissue (SCAT). The SCAT was measured as the distance from the skin to the linea alba. The VAT was determined by measuring the distance between the vertebra and the peritoneum at an ultrasound depth of 15cm. Both of these measurements were taken twice and recorded in centimetres.

2.1.7.3 Blood pressure

A digital sphygmomanometer was used to measure blood pressure. Prior to the measurement, the participants were allowed time to relax and be calm. The blood pressure was measured with participants sitting up with their feet on the floor and with the elbow at the level of the heart. Three readings were taken from either arm and an average of the last two was calculated as the final reading.

2.1.7.4 Biochemical markers (Glucose and fasting lipids)

Fasting venous blood samples were collected from each of the participants into labelled collection tubes. The samples were centrifuged to separate serum and plasma after which the supernatant was aliquoted into 1 ml samples. The samples were stored at −80°C and were subsequently shipped to the AWI-Gen Collaborative Centre where they were stored in a freezer at -80°C before analysis.

A Randox Plus clinical chemistry analyser (UK) was used for analysis of glucose and lipid levels. Direct measures of high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides and total cholesterol were obtained.

2.1.7.5 Hypertension status

Participants' hypertension status was defined based on the JNC7 guidelines as the presence of at least one of the following: previous diagnosis by a health professional, antihypertensive medication intake or a systolic blood pressure greater than 140mmHg and/or a diastolic blood pressure greater than 90mmHg (80). Note that the definition of hypertension as a stand-alone disease uses different recommended cut points to those used for defining high blood pressure in MS.

2.1.7.6 Diabetes status

A diagnosis of diabetes was based on the presence of at least one of the following: previous diagnosis by a health professional, diabetes medication intake or a fasting blood glucose greater than ≥ 7.0 mmol/l (81).

2.1.7.7 Dyslipidaemia

Dyslipidaemia was determined based on the presence of measurements above pre-defined cut off points (≥5.0 mmol/l for total cholesterol, ≥3.0mmol/l for LDL and HDL levels of <1.0 mmol/l among men and <1.3 mmol/l among women), previous diagnosis or ongoing treatment (82).

2.2 Secondary Data Analysis

2.2.1 Study design

This sub-study was a cross-sectional study leveraged on secondary data from the Navrongo, Ghana site of the AWI–Gen study.

2.2.2 Data source

The data for this study was obtained from the gate keepers of the AWI-Gen study at the Navrongo Health Research Centre.

2.2.3 Study population

Men and women aged 40-60 years resident in the coverage area of the Navrongo Health and Demographic Surveillance Site for 10 years prior to the study.

2.2.4 Study sample.

All participants in the original study were part of this study. However the analytical data set included participants without missing data. A retrospective power calculation was carried out to establish if the sample size was satisfactory to answer the research question using STATA.

Out of the 1875 participants in the study, 1591 had a history of alcohol intake (exposed) and 284 had never consumed alcohol before (unexposed). The proportion with MS among the exposed was 6.35% and among the unexposed was 14.79%. The study therefore had 99% power to detect as statistically significant (at an alpha level of 5%) an absolute difference of 8% between the proportion of participants with MS in the exposed and unexposed groups. Based on this, the sample size was sufficiently powered to answer the research question.

2.2.5 Study variables

2.2.5.1 Outcome variable

The outcome variable of interest in this study was MS. A diagnosis of MS was made based on the IDF/AHA/NHLBI-2009 criteria, which entailed the presence of three or more of: elevated waist circumference, elevated blood pressure, elevated fasting glucose, low HDL-cholesterol and elevated triglyceride levels (6).

2.2.5.2 Exposure variable

The exposure variable of primary interest was pattern of alcohol consumption assessed using the CAGE questionnaire (83), which was incorporated into the main AWI-Gen questionnaire. Alcohol consumption was categorized into never (abstinence), previous but not current intake, current non-problematic and problematic intake. A participant was said to have a current problematic drinking pattern if they reported yes to currently taking alcohol and answered yes to more than two of the following questions: 1. Have you ever felt that you should cut down on your drinking? 2. Have people annoyed you by criticizing your drinking? 3. Have you ever felt bad or guilty about your drinking? 4. Have you ever had an alcoholic drink first thing in the morning to steady your nerves or get rid of a hangover? If they reported currently taking alcohol and answered yes to less

than two of the four responses above, they were said to have a current non-problematic drinking pattern. Previous drinking was defined as having ever taken an alcoholic beverage more than 12 months prior to the study and not currently taking any alcoholic beverage.

2.2.5.2 Secondary explanatory variables

Secondary explanatory variables included: age, sex, ethnicity, educational status, household socio-economic status (SES), smoking history, smokeless tobacco use, physical activity, fruit & vegetable servings per day, hip circumference, visceral adipose tissue and subcutaneous adipose tissue. These were selected based on prior literature demonstrating their association with MS (84–87).

2.2.6 Conceptual framework

Figure 2.1 presents the conceptual framework adopted in this study.

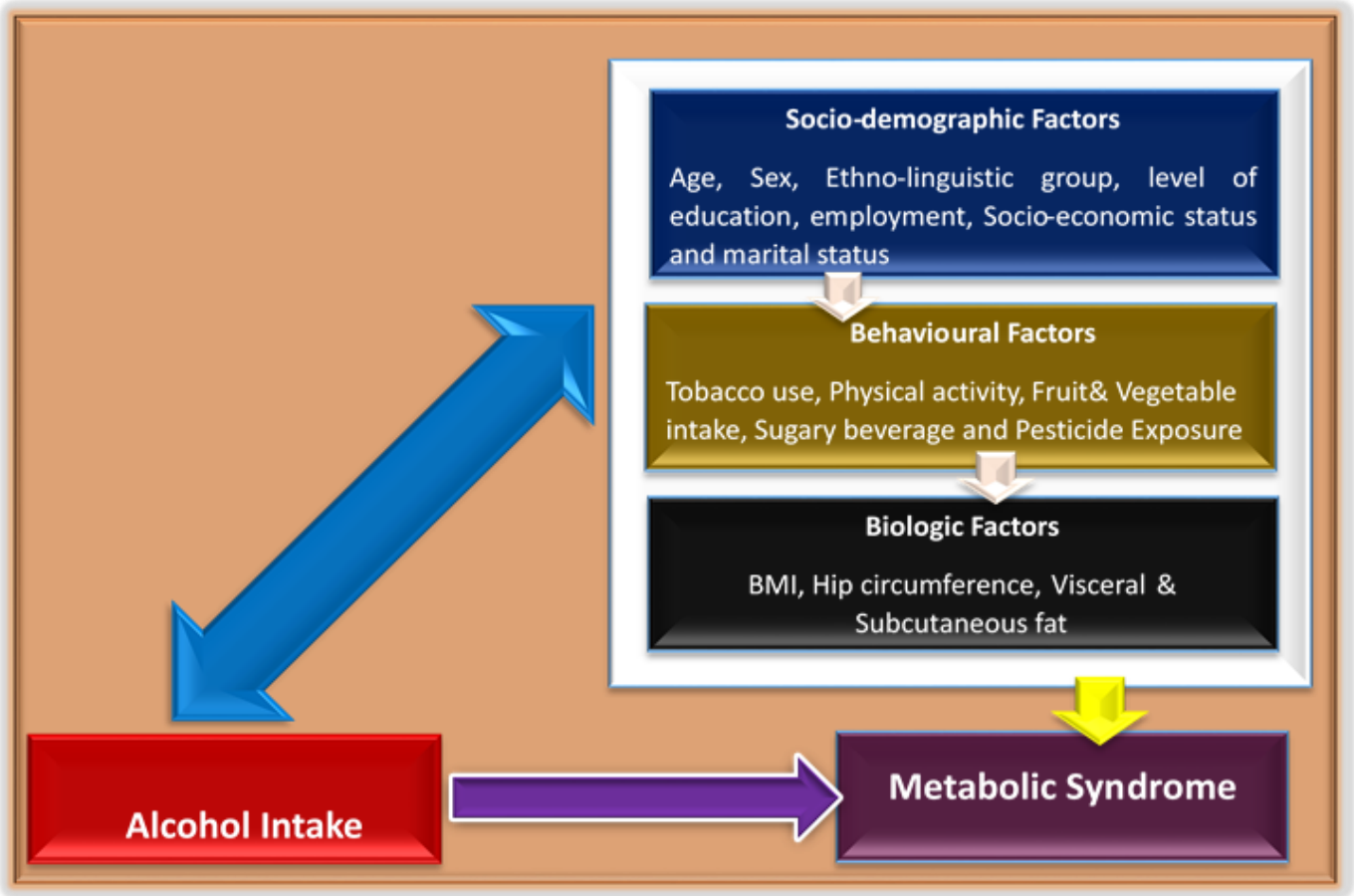


Figure 2.1. Conceptual framework explaining how confounders were controlled

Adjustment for variables that can confound the association between alcohol consumption patterns and MS followed the conceptual framework shown in Figure 2.1. Each of the selected confounding factors does not influence the association at the same level. Instead, a direct and proximate causal relationship exists whereby some factors also known as proximate determinants, affect this relationship directly, others act as intermediates; while some others - distal determinants - act through the intermediate and proximate factors (88). For instance, BMI (proximate determinant) has a direct influence on the occurrence of MS. Age on the other hand, is a distal determinant which influences the association between alcohol intake and MS by acting through behavioural factors like physical activity (intermediate determinant) which then impact on the odds of MS through BMI. Consequently, to effectively control for confounding, there was need to bear in mind these hierarchical relationships. The determinants are grouped into three levels: socio-demographic factors, behavioural factors and biological factors. The most immediate factors being biological, while socio-demographic factors are the most distant. A change in each of these factors may have a possible influence on the association between alcohol intake and MS.

2.2.7 Data management and statistical analyses

2.2.7.1 Data management

Data from the paper based tool was captured onto the REDCap electronic database (89). Data from REDCap was then exported into an Excel spreadsheet for data cleaning**.** This included checks for missing values, inconsistent responses and duplicate observations using participants' study identifiers. Cleaned data were exported to STATA version 15.0 (College Station, Texas 77845 USA) for analyses.

A complete case analysis approach was adopted and hence participants with at least one missing variable were dropped from the analytical dataset. The final analytical data set was thus made up of 1875 participants.

2.2.7.2 Generation of variables relevant to this study

2.2.7.2.1 Exposure: Alcohol consumption

Harmful alcohol consumption as defined by the CAGE questionnaire was categorized as never (abstinence), previous but not current intake, current non-problematic and problematic intake. Problematic intake served as a proxy for harmful alcohol use.

2.2.7.2.2 Outcome: Metabolic syndrome

A composite binary outcome (metabolic syndrome) with two mutually exclusive categories was generated as 1 ("yes metabolic syndrome") defined as having three or more of the MS components (elevated waist circumference, hypertension, hyperglycaemia, elevated triglycerides and low HDL-cholesterol levels) and 0 ("no metabolic syndrome") defined as having less than 3 of the stated components (6).

2.2.7.3 Re-categorization of variables

Ethnicity was categorized into 3 groups: Kassena, Nankana and “other”. The latter entailed all ethnicities with exception of the first two.

A sum of fruits and vegetable servings per day was computed from the individual variables. The combined new variable was subsequently categorized into a dichotomous variable; category 0 representing < 5 fruit and vegetable servings per day and category 1, ≥ 5 fruit and vegetable servings per day as per WHO recommendations (90).

2.2.8 Statistical analyses

Descriptive and inferential statistics were used to summarize the data according to the outlined objectives. STATA version 15.0 (College Station, Texas 77845 USA) was used for analyses.

2.2.8.1 Descriptive statistics

Participants’ characteristics were summarized either using frequency measures or using measures of central tendency with corresponding measures of dispersion depending on the distribution of the variables. Means (±standard deviation; SD) if normally distributed

or medians (with interquartile range; IQR) if skewed were used to report continuous data. Frequencies and proportions were used to summarize categorical data.

The differences in the mean or median levels between men and women were examined using a two sample Student t-test or a Mann-Whitney U test respectively. The Pearson's chi squared ($\chi 2$) test was used to examine the sex differences in proportions of participant characteristics. A $p<0.05$ was regarded as statistically significant.

The prevalence of MS components for the four categories of alcohol consumption patterns is reported in proportions with corresponding 95% confidence intervals (CI) and the differences determined by Pearson's chi squared (χ^2) test. In addition, the overall prevalence of each of the five components of MS is presented in percentages, stratified by sex and differences examined by χ^2 test.

2.2.8.2 Regression analysis

To determine association between alcohol consumption patterns and MS, we used logistic regression analysis. We initially assessed the independent association between alcohol consumption patterns and metabolic syndrome. To determine the role of confounding factors in this association, we adjusted for these factors in a sequential manner. These confounding variables included socio-demographic (age, sex, ethnicity, marital status, education, employment, household SES); behavioural (tobacco use, diet, physical activity and pesticide exposure) and biological factors (BMI, hip circumference, VAT and SCAT). On account of the disparity in characteristics between sexes, separate but identical analyses were carried out for men and women.

The steps in sequential model building were as follows: In model 1 we adjusted for socio-demographic variables (age, sex, ethnicity, marital status, education level, employment status and socio-economic status); in model 2, we adjusted for behavioural factors (smoking tobacco, smokeless tobacco use, pesticide exposure, fruit and vegetable servings, sugary drinks intake and physical activity) in addition to variables from model 1; in final model 3, we adjusted for biological factors (BMI, hip circumference, visceral fat and subcutaneous fat) in addition to factors previously fitted in model 2. For each of the fitted models, checks for multicollinearity using variance

inflation factors (*VIF*) were carried out and any variables with a *VIF* > 5 were removed from the model. In addition, variables that predicted failure perfectly (resulting from all/nearly all of the participants having the outcome) were not useful to the models and were therefore excluded. Models were built for the entire sample, in which gender was included and we also built models separately for women and men.

For categorical variables, a single p value to denote the overall significance of the variable was generated using post-estimation Wald tests. Likelihood ratio tests were used to compare the nested models; a p value of <0.05 denoting significant model improvement. In addition, the Akaike's/Bayesian information criteria (AIC/BIC) were used for model comparison. A smaller AIC/BIC indicated model improvement. The Hosmer-Lemeshow test was used to check for the goodness-of-fit of the final model. Associations were reported as odds ratios (OR) with corresponding 95% CI and a two-sided p<0.05 was considered statistically significant.

2.3 Ethical Considerations

The main AWI-Gen study was approved by the Human Research Ethics Committee of the University of the Witwatersrand (Protocol Number: M121029). Further clearance was obtained from the Ghana Health Service Ethics Review Committee (approval number: GHS-ERC: 05/05/14) and the Navrongo Health Research Centre's Institutional Review Board (Approval number: NHRCIRB178). Community engagement processes to introduce the research project into the study site were carried out and each of the participants gave informed consent before participating in the study. Data and specimens were de-identified during processing to preserve confidentiality.

For this secondary analysis, ethical clearance was sought from the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg (Approval number: M181084). Relevant data was obtained from the gatekeepers of the AWI-Gen study. The data was stored on an external hard drive and access was restricted to the researcher and supervisors.

Chapter 3 : RESULTS

This chapter presents our study findings. It details the socio-demographic, behavioural and the metabolic risk profile of study participants as well as the prevalence of alcohol consumption, MS and its component diseases stratified by sex. We also present results on prevalence of MS by alcohol consumption status. Finally, we present findings from the logistic regression analyses that indicate the association between alcohol consumption and MS as well as the role of confounders in this relationship.

3.1 Socio-demographic characteristics

A total of 1875 subjects were included in the final analysis and the baseline socio-demographic characteristics of these participants, stratified by sex, are presented in Table 3.1.

Within the total sample, 1011 (53.9%) were women while 864 (46.1%) were men. The mean age of the women was 51.5 ± 5.76 years while that of men was 50.5 ± 5.77 years. This difference was statistically significant ($p<0.001$). Nearly all of the participants were either from the Kassena (52.2%) or the Nankana (42.8%) community with other communities forming the minority (5.07%).

The larger majority (69.8%) of the participants had no formal education. Of these, women formed the larger percentage (61.0%) while men dominated the other levels of education ($p<0.001$). About 63.1% of the population was employed; women were more likely to be unemployed than men ($p=0.029$).

Overall, more than half (73.6%) of the study subjects were either married or living together. There was a higher proportion of married men (85.2%) than married women (63.7%; $p<0.001$). In addition, there was a significantly higher proportion of widows (32.2%) than there was of widowers (3.82%; $p<0.001$).

Table 3.1: Socio-demographic characteristics of participants stratified by sex

Characteristic	All (N=1875)	Women (n=1011)	Men (n=864)	P-value
Age (years)	51.1±5.78	51.5±5.76	50.5±5.77	<0.001
Ethno-linguistic group				
Kassena	978 (52.2)	528 (52.2)	450 (52.1)	<0.001
Nankana	803 (42.8)	408 (40.4)	395 (45.7)	
Others	94 (5.01)	75 (7.42)	19 (2.20)	
Educational status				
No formal education	1308 (69.8)	781 (77.3)	527 (61.0)	<0.001
Primary	363 (19.4)	166 (16.4)	197 (22.8)	
Secondary	169 (9.01)	55 (5.44)	114 (13.19)	
Tertiary	36 (1.92)	9 (0.89)	26 (3.01)	
Partnership status				
Never married	20 (1.11)	5 (0.50)	15 (1.73)	<0.001
Currently Married/cohabiting	1379 (73.6)	644 (63.7)	735 (85.2)	
Divorced/separated	117 (6.24)	37 (3.66)	80 (9.26)	
Widowed	358 (19.1)	325 (32.2)	33 (3.82)	
Employment status				
Unemployed	692 (40.0)	396 (39.2)	296 (34.3)	0.028
Employed	1181 (63.1)	614 (60.8)	567 (65.7)	
Household SES				
Poorest	337 (18.0)	207 (20.5)	130 (15.1)	<0.001
Poorer	339 (18.1)	197 (19.5)	142 (16.4)	
Poor	356 (19.0)	197 (19.5)	159 (18.4)	
Less poor	437 (23.3)	232 (33.0)	205 (23.7)	
Least poor	406 (21.7)	178 (17.6)	228 (26.4)	

Data given as mean ±SD or n (%)

3.2 Behavioural characteristics of participants

The prevalence of current smoking was 20.9%; 68.5% reported to have never smoked before, while 10.7% previously smoked (see Table 5). Current smoking was noted to be significantly (p<0.001) more prevalent among men (43.1%) compared to women (1.88%). Conversely, smokeless tobacco use, though less prevalent (10.1%), was equally popular among women (10.2%) and men (10.1%).

In general, a majority (84.9%) of the participants had a history of alcohol intake. One fifth of the population (19.5%) were previous drinkers; 33.5% fell under the current non-problematic category while 31.9% were in the current problematic category (harmful use). Significant differences in alcohol consumption across sex were evident (p<0.001). Half (51.2%) of the men were current problematic drinkers while 7.64% of the men had never consumed alcohol before. In contrast, 39.3% of the women were current non-problematic consumers, the minority (15.4%) being current problematic consumers. Over half of the population reported exposure to pesticides with men having slightly more exposure than women (p<0.001).

Table 3.2: Behavioural characteristics of participants

Characteristic	All (N=1875)	Women (n=1011)	Men (n=864)	P-value
Smoking tobacco				
Never	1284 (68.5)	978 (96.7)	306 (35.4)	<0.001
Current	391 (20.9)	19 (1.88)	372 (43.1)	
Previous	200 (10.7)	14 (1.38)	186 (21.5)	
Smokeless tobacco				
No	1685 (89.8)	908 (89.8)	777(89.9)	0.93
Yes	190 (10.1)	103 (10.2)	87 (10.1)	
Physical activity				
MVPA<150	272 (14.5)	189 (18.7)	83 (9.61)	<0.001
MVPA≥150	1603 (85.5)	822 (81.3)	781 (90.4)	
Fruits & vegetables				
<5 serving/day	1087 (58.0)	608 (60.1)	479 (55.4)	0.040
≥5 serving/day	788 (42.0)	403 (39.9)	385 (44.6)	
Alcohol consumption				
Never	284 (15.1)	218 (21.6)	66 (7.64)	<0.001
Previous	365 (19.5)	240 (23.7)	125 (14.5)	
Current non problematic	628 (33.5)	397 (39.3)	231 (26.7)	
Current problematic	598 (31.9)	156 (15.4)	442 (51.2)	
Pesticide exposure				
No	850 (45.3)	504 (49.9)	346 (40.0)	<0.001
Yes	1025 (54.7)	507 (50.1)	518 (60.0)	

Data presented as median (interquartile range) or n (%)

3.3 Anthropometric and metabolic characteristics

Women and men were significantly different in all anthropometric measurements at a significance level of p<0.001. The median BMI for women was 21.5 (IQR 15.1-37.3) and that for men was 20.6 (14.0-33.3). The majority (71.6%) of the subjects had normal weight. A significant proportion (14.9%) of the entire population was underweight while 10.7% were overweight and 2.77% were obese. The proportion of women who were overweight (14.8%) and obese (4.25%) was significantly higher than that of men (5.79% and 1.04% respectively).

Table 3.3: Anthropometric and metabolic characteristics of study participants

Characteristic	All (N=1875)	Women (n=1011)	Men (n=864)	P-value
Waist circumference (cm)	74 (57-112)	75 (59-112)	72 (57-101)	<0.001
Hip Circumference (cm)	86 (67-133)	88 (68-127)	83 (70-108)	<0.001
BMI (kg/m²)	21.0 (13.9-41.2)	21.5 (15.1-37.3)	20.6 (14.0-33.3)	<0.001
BMI category				
Underweight	280 (14.9)	122 (12.1)	158 (18.3)	<0.001
Normal weight	1343 (71.6)	696 (68.8)	647 (74.9)	
Overweight	200 (10.7)	150 (14.8)	50 (5.79)	
Obese	52 (2.77)	43 (4.25)	9 (1.04)	
Visceral adipose tissue (cm)	3.63 (1.48-8.53)	3.32 (1.48-8.49)	4.03 (2.05-8.05)	<0.001
Subcutaneous adipose tissue (cm)	0.83 (0.23-3.47)	1.01 (0.31-3.14)	0.70 (0.27-2.65)	<0.001
Fasting glucose (mmol/L)	4.55±0.81	4.61±0.85	4.48±0.75	<0.001
Total cholesterol (mmol/L)	3.17(0.45 -6.61)	3.21 (0.60 -6.61)	3.13 (0.59 -6.03)	0.047
High density lipoprotein (mmol/L)	1.11 (0.14-2.93)	1.08 (0.23- 2.44)	1.15 (0.17- 2.84)	0.001
Low density lipoprotein (mmol/L)	1.60 (0.40-4.80)	1.61 (0.40-4.39)	1.58 (0.40-4.73)	0.34
Triglycerides (mmol/L)	0.56 (0.19-2.47)	0.55 (0.17-2.45)	0.56 (0.19-2.32)	0.78
Systolic blood pressure (mmHg)	121 (79-216)	120 (79-216)	122 (85-198)	0.007
Diastolic blood pressure (mmHg)	76 (49-126)	76 (50-122)	76 (51-122)	0.69

Data presented as mean ±SD, median (interquartile range) or n (%)

More men (18.3%) were underweight or had normal weight (74.9%) compared to women (12.1% and 68.8% respectively). The median waist circumference was 75 (59-112) cm for women and 72 (57-101) cm for men. The median hip circumference for women was 88 (68-127) cm while that of men was 83 (70-108) cm. The waist-to-hip ratio differed significantly by sex; men had a higher WHR (0.87 [0.74-1.19]) than women (0.86 [0.66-1.18]; p<0.001). Women had more subcutaneous adipose tissue than men (1.01 [0.31-3.14] cm vs 0.70 [0.27-2.65] cm respectively) while men had more visceral adipose tissue than women (4.03 [2.05-8.05] cm vs 3.32 [1.48-8.49] cm respectively).

On average, the fasting glucose, total cholesterol and triglyceride levels were within the normal ranges. The median cholesterol levels of women (3.21 (0.60-6.61) mmol/L) were significantly higher (p=0.047) than those of men (3.13 (0.59-6.03) mmol/L). Similarly, median LDL levels were higher among women (1.61 (0.40-4.39) mmol/L) compared to men (1.58 (0.40-4.73) mmol/L) though not statistically significant. HDL levels were significantly higher in men than women (p=0.001). In addition, women had significantly higher glucose levels (4.61 ± 0.85 mmol/L) than men (4.48 ± 0.75 mmol/L). No significant differences in the median triglyceride levels across sex were noted.

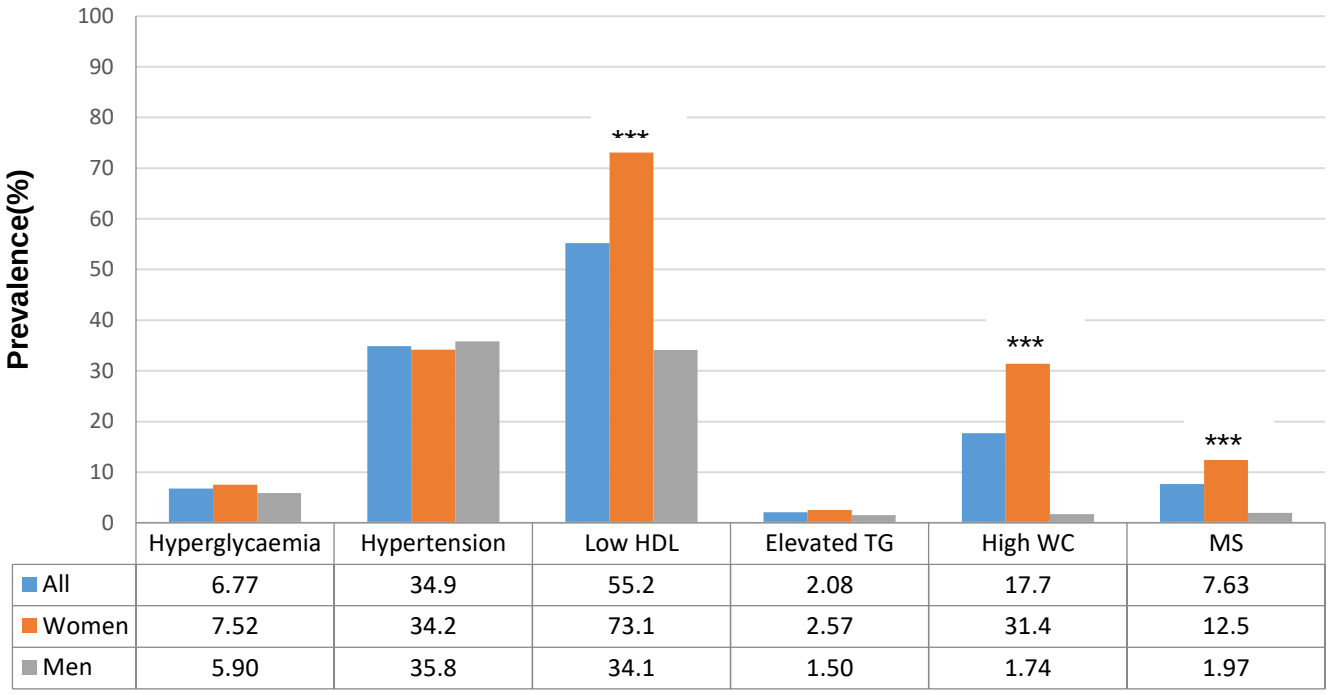
The median systolic and diastolic blood pressure readings were normal for both men and women. The median systolic blood pressure readings were higher among men (p=0.007).

3.4 Prevalence of metabolic syndrome and components

Figure 3.1 presents the prevalence of the MS and its components stratified by sex. The prevalence of MS in this population was 7.63%, being higher in women (12.5%) than men (1.97%; p<0.001).

Among the five components of the MS, low HDL levels and elevated blood pressure were the most prevalent. Over half (55.2%) of the participants had low HDL levels, 34.9% had elevated blood pressures, 17.7% had an elevated waist circumference, 6.77% had elevated blood sugar levels and 2.08% had elevated triglycerides. Women were more likely to have deranged levels of HDL (73.1% vs 34.1%; p<0.001) and waist

circumference (31.4% vs 1.74%; p<0.001) measurements than men. No variations across sex were found for the rest of the components.



	Hyperglycaemia	Hypertension	Low HDL	Elevated TG	High WC	MS
All	6.77	34.9	55.2	2.08	17.7	7.63
Women	7.52	34.2	73.1	2.57	31.4	12.5
Men	5.90	35.8	34.1	1.50	1.74	1.97

Figure 3.1. Prevalence of MS and its component diseases stratified by sex.

Data expressed in percentages (%); *p<0.05, **p<0.01 and ***p<0.001 women vs men

Table 3.4 shows the prevalence of MS and its components across the four categories of alcohol consumption patterns stratified by sex.

For both women (17.9 [13.3, 23.6] %) and men (4.55 [1.45, 13.2] %), non- drinkers had a higher prevalence of MS compared to the other categories of alcohol consumption. This was followed by previous (12.1 [8.56, 16.9] %) and current problematic drinking (11.5 [7.39, 17.6] %) in women. The opposite was observed in men where 3.03 [1.45, 6.22] % of current non-problematic drinkers had MS compared to 0.80 [0.11, 5.46] % among previous drinkers.

The following were observed regarding components of MS. Women who were non-drinkers had the highest prevalence of hypertension (38.5 [32.3, 45.2] %), low HDL-C

(77.1 [71.0, 82.2] %), elevated TG (4.13 [2.16, 7.75] %) and high WC (37.6 [31.4, 44.2] %) but for hyperglycaemia previous drinkers had the highest prevalence (9.21 [6.14, 13.6] %).

In men, previous drinking was associated with the highest prevalence of hypertension (37.6 [29.6, 46.4] %), hyperglycaemia (8.00 [4.36, 14.2] %), and high WC (3.20 [1.21, 8.22] %) while low HDL-C (53.0 [41.0, 64.7] %) and high TGs (3.03 [0.76, 11.3] %) were highest among non-drinkers. The proportion of participants with elevated triglycerides and high waist circumference was identical among non-drinkers (3.03 [0.76, 11.3] %) and the same case was observed for current non-problematic drinkers (1.30 [0.42, 3.95] %).

Table 3.4: Prevalence of MS and its components according to alcohol consumption status and stratified by sex

Variable	Hypertension	Hyperglycaemia	Low HDL	Elevated TG	High waist circumference	MS
Women						
Never	38.5 (32.3 45.2)	5.96 (3.49 10.0)	77.1 (71.0 82.2)	4.13 (2.16 7.75)	37.6 (31.4 44.2)	17.9 (13.3 23.6)
Previous	32.5 (26.9 38.7)	9.21 (6.14 13.6)	75.0 (69.1 80.1)	3.33 (1.67 6.53)	26.3 (21.1 32.2)	12.1 (8.56 16.9)
Current non-problematic	31.7 (27.3 36.5)	8.82 (6.40 12.0)	73.8 (69.3 77.9)	1.01 (0.38 2.66)	29.7 (25.4 34.4)	10.1 (7.47 13.4)
Current problematic	37.2 (30.0 45.0)	3.85 (1.74 8.30)	62.8 (55.0 70.0)	3.21 (1.34 7.47)	34.6 (27.6 42.4)	11.5 (7.39 17.6)
P value	0.28	0.13	**0.014**	0.079	**0.043**	**0.044**
Men						
Never	28.8 (19.2 40.8)	6.06 (2.29 15.1)	53.0 (41.0 64.7)	3.03 (0.76 11.3)	3.03 (0.76 11.3)	4.55 (1.45 13.2)
Previous	37.6 (29.6 46.4)	8.00 (4.36 14.2)	44.0 (35.6 52.8)	0.80 (0.11 5.46)	3.20 (1.21 8.22)	0.80 (0.11 5.46)
Current non-problematic	35.5 (29.6 41.9)	3.46 (1.74 6.77)	35.9 (30.0 42.3)	1.30 (0.42 3.95)	1.30 (0.42 3.95)	3.03 (1.45 6.22)
Current problematic	36.4 (32.1 41.0)	6.56 (4.60 9.29)	27.6 (23.6 32.0)	1.58 (0.76 3.29)	1.36 (0.61 2.99)	1.36 (0.61 2.99)
P value	0.64	0.28	**<0.001**	0.67	0.42	0.15

Data presented as proportions (%) with 95% confidence intervals.

3.5 Association between alcohol consumption and MS

Presented in Table 3.5 are outputs from logistic regression analyses. In the unadjusted model comprising both men and women, highly significant associations between alcohol consumption status and MS were noted ($p<0.001$). Overall, the odds of having MS were lower among drinkers compared to those who had never consumed alcohol before. Upon stratification by sex, most of these associations were not significant. However, women who were current non-problematic drinkers had the lowest odds of MS compared to other categories (OR 0.51 [0.32, 0.83]).

Compared to the unadjusted model, introduction of the socio-demographic factors (model 1) significantly improved the model, as evidenced by a significant likelihood ratio test ($p=0.001$) for the model inclusive of men and women. In addition, model 1 had a smaller AIC (980) compared to the unadjusted model (988).However, this model lost significance. The odds of MS highest among abstainers compared to other levels of alcohol consumption. Among women, the odds of MS appeared to decrease with progression from previous, to current non-problematic to current problematic. In contrast, for men the current non-problematic drinkers had the highest odds of MS while previous drinkers had the lowest odds compared to abstainers. However these associations were not significant.

In model 2, socio-demographic as well as behavioural factors were included in the model. The AIC for this model (949) in which both men and women were included, showed further improvement from the previous model (980). According to the likelihood ratio test, there was overwhelming evidence that behavioural factors significantly improved the model ($p<0.001$). In this model, alcohol consumption was still not a significant predictor of MS. The odds of MS for current drinkers increased compared to model 1 but were still lower than those of abstainers. Upon stratification by sex, men who were current non-problematic consumers were 38% more likely to have MS compared to non-drinkers (OR 1.38 [0.23, 8.31]). This association however, was not significant. Model 2 for women was also not significant ($p=0.26$).

Table 3.5: Association between MS and patterns of alcohol consumption

Models	All		Women		Men	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Unadjusted						
Never	Ref (1)	<0.001	Ref (1)	0.054	Ref (1)	0.18
Previous	0.52 (0.32 0.85)		0.64 (0.38 1.07)		0.17 (0.017 1.66)	
Current non problematic	0.47 (0.30 0.73)		0.51 (0.32 0.83)		0.66 (0.17 2.61)	
Current problematic	0.24 (0.14 0.41)		0.60 (0.33 1.09)		0.29 (0.070 1.18)	
AIC/BIC	988/1010		760/780		170/189	
Model 1						
Never	Ref (1)	0.12	Ref (1)	0.18	Ref (1)	0.31
Previous	0.63 (0.37 1.10)		0.69 (0.39 1.21)		0.23 (0.019 2.60)	
Current non problematic	0.62 (0.39 1.00)		0.59 (0.36 0.97)		0.94 (0.17 5.13)	
Current problematic	0.53 (0.30 1.00)		0.58 (0.30 1.10)		0.42 (0.077 2.32)	
AIC/BIC	980/1090		750/848		171/248	
LR test		0.001		0.001		0.20
Model 2						
Never	Ref (1)	0.19	Ref (1)	0.26	Ref (1)	0.25
Previous	0.63 (0.37 1.09)		0.69 (0.39 1.23)		0.23 (0.017 3.06)	
Current non problematic	0.63 (0.39 1.02)		0.60 (0.36 1.00)		1.38 (0.23 8.31)	
Current problematic	0.59 (0.33 1.06)		0.62 (0.33 1.24)		0.51 (0.076 3.34)	
AIC/BIC	949/1099		752/880		172/281	
LR test		<0.001		0.62		0.018
Model 3						
Never	Ref (1)	0.34	Ref (1)	0.47	Ref (1)	0.17
Previous	0.72 (0.40 1.33)		0.82 (0.42 1.57)		0.030 (0.002 3.26)	
Current non problematic	0.66 (0.39 1.14)		0.66 (0.37 1.18)		1.69 (0.18 16.0)	
Current problematic	0.56 (0.29 1.10)		0.63 (0.30 1.31)		0.46 (0.041 5.19)	
AIC/BIC	792/975		639/795		156/291	
LR test		<0.001		<0.001		<0.001

In model 3 we incorporated biological factors into the model. These included BMI, hip circumference, visceral fat and subcutaneous fat. This model, when including both men and women, was an improvement from model 2 as shown by a smaller AIC (792) as well as a significant likelihood ratio test ($p<0.001$). This model was well fitted as evidenced by the Hosmer and Lemeshow goodness of fit test ($p=0.24$). None of the variables in this final model displayed any collinearity with the VIF for each predictor variable being < 3.0. The mean VIF for this model was 1.51.

With this addition of biological factors, the odds of MS remained highest among the non-drinkers followed by previous drinkers. The previous drinkers were 28% less likely to have MS, while current problematic drinkers had half the odds of having MS (OR 0.56 [0.29, 1.10]) as those of non-drinkers. However, the overall association of alcohol intake with MS in this model was not significant.

An interaction term was introduced in this model to investigate whether the effect of alcohol consumption on MS varied across sex in this population. The interaction term was not significant ($p=0.37$).

When analysed according to sex, the odds of MS among female previous drinkers were second to those of non-drinkers, with this category having 0.82 times the likelihood of having MS as non-drinkers. This was followed by the current non-problematic consumer category (OR 0.66 [0.37, 1.18]), with the current problematic drinkers having the lowest odds of MS (OR 0.63 [0.30, 1.31]). These findings were in contrast to those of the men, whereby current non-problematic drinkers had the highest odds of MS (OR 1.69 [0.18, 16.0]) followed by non-drinkers. Previous drinkers were least likely to have MS (OR 0.030 [0.002, 3.26]). However, the level of alcohol consumption was insignificant among males ($p=0.17$) and females ($p=0.47$).Table 3.6 shows the association between the various confounders and metabolic syndrome stratified by sex from our final model (model 3). Before stratification, the association between age and MS was not significant. The odds of MS were significantly lower among males (OR 0.26 [0.12, 0.56]) compared to females. Obesity and overweight were associated with significantly higher odds of MS ($p=0.004$). Smoking was not associated with odds for MS.

Table 3.6: Association between MS and socio-demographic, behavioural and biological factors

Variable	All		Females		Males	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.02 (0.99 1.07)	0.117	1.02 (0.98 1.06)	0.31	**1.13 (1.00 1.28)**	**0.044**
Sex						
Women	1 (ref)	**<0.001**	**-**		**-**	
Men	**0.26 (0.12 0.56)**		**-**		**-**	
Ethnicity						
Kassena	1 (ref)	0.70	1 (ref)	0.80	1 (ref)	0.49
Nankana	1.05 (0.64 1.70)		1.02 (0.59 1.75)		2.25 (0.48 10.5)	
Other	0.73 (0.33 1.59)		0.77 (0.34 1.77)		3.15 (0.12 80.7)	
Education						
No formal education	1 (ref)	0.34	1 (ref)	0.39	1 (ref)	.0.36
Primary	0.97 (0.56 1.67)		0.96 (0.53 1.73)		1.94 (0.33 11.0)	
Secondary	1.50 (0.73 3.11)		1.15 (0.47 2.85)		4.03 (0.78 20.8)	
Tertiary	2.59 (0.79 8.54)		4.37 (0.75 25.9)		4.92 (0.44 54.8)	
Employment						
Unemployed	1 (ref)	0.64	1 (ref)	0.95	1 (ref)	0.28
Employed	1.12 (0.70 1.70)		1.02 (0.61 1.68)		2.73 (0.44 17.1)	
SES						
Poorest	1 (ref)	0.84	1 (ref)	0.76	1 (ref)	0.94
Very poor	0.90 (0.42 1.92)		0.99 (0.46 2.17)		1 (empty)	
Poor	1.15 (0.57 2.33)		1.08 (0.51 2.29)		1.81 (0.095 34.4)	
Less poor	1.29 (0.66 2.52)		1.42 (0.70 2.91)		1.33 (0.074 24.0)	
Least poor	1.01 (0.49 2.08)		0.97 (0.44 2.12)		0.96 (0.064 14.3)	
Smoking						
Never	1 (ref)	0.29	1 (ref	0.99	1 (ref)	0.20
Current	0.31 (0.065 1.44)		1 (empty)		0.41 (0.049 3.37)	
Previous	1.06 (0.39 2.87)		0.99 (0.12 8.09)		2.72 (0.52 14.4)	
Smokeless tobacco						
No	1 (ref)	0.96	1 (ref)	0.74	1 (ref)	0.57
Yes	1.02 (0.49 2.11)		0.86 (0.36 2.06)		1.71 (0.27 11.1)	
Sugary beverage	0.86 (0.63 1.15)	0.31	0.78 (0.49 1.25)	0.19	0.87 (0.39 1.95)	0.74
Pesticide exposure						
Yes	1 (ref)	0.62	1 (ref)	0.38	1 (ref)	0.071
No	0.90 (0.58 1.39)		0.81 (0.50 1.30)		4.67 (0.87 25.0)	

Fruit & Vegetable servings						
<5 servings/day	1 (ref)	0.98	1 (ref)	0.39	1 (ref)	0.24
≥5 servings/day	1.00 (0.66 1.54)		0.81 (0.50 1.31)		2.27 (0.58 8.87)	
MVPA						
<150	1 (ref)	0.15	1 (ref)	0.092	1 (ref)	0.36
≥150	1.52 (0.86 2.66)		1.68 (0.92 3.08)		0.43 (0.072 2.60)	
BMI categories						
Underweight	1 (ref)	**0.004**	1 (ref)	**0.011**	1 (ref)	0.67
Normal weight	1.47 (0.55 3.89)		1.51 (0.50 4.53)		0.23 (0.018 2.94)	
Overweight	**3.75 (1.22 11.5)**		**3.99 (1.13 14.0)**		0.28 (0.008 10.3)	
Obese	**6.07 (1.51 24.5)**		**5.28 (1.09 25.4)**		0.65 (0.006 75.0)	
Hip circumference	1.00 (0.99 1.00)	0.147	1.00 (0.99 1.00)	0.40	1.01 (1.00 1.03)	**0.016**
Visceral fat	**1.28 (1.07 1.54)**	**0.006**	1.20 (0.98 1.47)	0.074	1.78 (0.99 3.19)	0.052
Subcutaneous fat	**2.39 (1.53 3.75)**	**<0.001**	**3.13 (1.84 5.31)**	**<0.001**	0.55 (0.098 3.08)	0.49

An increase in both visceral and subcutaneous fat was accompanied by a significant increase in the odds of MS (OR 1.28 [1.07, 1.54] and (OR 2.39 [1.53, 3.75], respectively).

The findings among females were that the odds of MS increased with an increase in BMI; those who were obese had five times the odds of MS compared to those were underweight (OR 5.28 [1.09, 25.5]). Overweight women were 4 times as likely to have MS as those who were underweight (OR 3.99 [1.13, 14.0]). Though marginally significant, an increase in visceral fat was associated with higher odds of MS (OR 1.20 [0.98, 1.47]; p=0.074). Every unit increase in subcutaneous fat was associated a significant increase in the odds of MS (OR 3.13 [1.84, 5.31]; p<0.001). There was no difference in the odds of MS across ethnicity. More than five fruit and vegetable servings per day were associated with lower odds of MS though this was not statistically significant.

Among men, every year increase in age was accompanied by a 13% increase in the odds of MS (OR 1.13 [1.00, 1.27]; p=0.033). Every unit increase in hip circumference was accompanied by a 1% increase in the odds of MS (OR 1.01 [1.00, 1.03]; p=0.016). Similarly an increase in visceral fat was accompanied by a marginally significant increase in the odds of MS (OR 1.78 [0.99, 3.18]; p=0.052). The odds of MS increased

with increasing level of education, however this was not significant. Previous smoking was associated with higher odds of MS, while current smoking was associated with lower odds compared to not smoking however, these differences lacked statistical significance. Men who had been exposed to pesticides were four times more likely to have MS compared to those who were not exposed but this association missed significance (p=0.071).

3.6 Association between alcohol consumption and MS components

Tables 3.7-3.11 show the results of the multivariable logistic regression analyses used to investigate the association between alcohol consumption and each of the MS components.

3.6.1 Association between alcohol consumption and hypertension

In the entire population and among women and men, alcohol consumption was not significantly associated with hypertension (Table 3.7). With every year increase in age, the odds of hypertension significantly increased in both men (OR 1.05 [1.02, 1.07]) and women (OR 1.05 [1.02, 1.08]). The odds of hypertension were significantly higher among males (OR 1.46 [1.07, 1.99]) compared to females.

Increasing SES was associated with hypertension in the entire population and among men and women (see Table 3.7). The absence of pesticide exposure was protective in women (p=0.005) but not significant among men. The level of education, smoking and BMI were not significantly associated with hypertension.

A unit increase in visceral fat was accompanied by an 11% significant increase in odds of hypertension (OR 1.11 [1.01, 1.22]) however, significance was lost upon stratification by sex. There was a significant positive relationship between subcutaneous fat and hypertension in the total cohort (OR 1.71 [1.29, 2.27]) and in males (p<0.001) but this relationship only tended toward significance (p=0.083) in females.

Table 3.7: Association between alcohol consumption and hypertension

Variable	All		Females		Males	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Alcohol						
Never	1 (ref)	0.43	1 (ref)	0.33	1 (ref)	0.88
Previous	0.91 (0.64 1.30)		0.79 (0.51 1.20)		1.22 (0.57 2.59)	
Current non problematic	0.86 (0.62 1.18)		0.78 (0.54 1.13)		1.17 (0.58 2.36)	
Current problematic	1.05 (0.74 1.49)		1.06 (0.67 1.69)		1.29 (0.64 2.59)	
Age	**1.05 (1.03 1.07)**	**<0.001**	**1.05 (1.02 1.08)**	**0.001**	**1.05 (1.02 1.07)**	**0.004**
Sex						
Women	1 (ref)	**0.018**	**-**		**-**	
Men	**1.46 (1.07 1.99)**		**-**		**-**	
Education						
No formal education	1 (ref)	0.42	1 (ref)	0.44	1 (ref)	0.45
Primary	1.02 (0.80 1.33)		0.83 (0.56 1.23)		1.24 (0.86 1.78)	
Secondary	0.94 (0.65 1.37)		1.08 (0.56 2.08)		0.90 (0.56 1.46)	
Tertiary	1.83 (0.87 3.87)		2.13 (0.4 9.92)		1.68 (0.68 4.13)	
SES						
Poorest	1 (ref)	**0.024**	1 (ref)	**0.046**	1 (ref)	0.46
Very poor	0.86 (0.61 1.21)		0.947 (0.61 1.48)		0.73 (0.43 1.24)	
Poor	1.04 (0.75 1.45)		1.04 (0.67 1.64)		0.96 (0.57 1.60)	
Less poor	**1.43 (1.05 1.97)**		**1.70 (1.11 2.60)**		1.13 (0.69 1.85)	
Least poor	1.09 (0.77 1.56)		1.28 (0.78 0.09)		0.88 (0.52 1.51)	
Smoking						
Never		0.43	1 (ref)	0.093	1 (ref)	0.78
Current	0.84 (0.60 1.17)		0.24 (0.053 1.12)		0.96 (0.67 1.39)	
Previous	1.05 (0.73 1.52)		0.66 (0.20 2.20)		1.11 (0.74 1.68)	
Pesticide exposure						
Yes	1 (ref)	**0.037**	**1 (ref)**	**0.005**	1 (ref)	0.94
No	**0.79 (0.64 0.98)**		**0.65 (0.48 0.89)**		0.99 (0.71 1.38)	
MVPA						
<150	1 (ref)	0.076		0.15		0.50
≥150	0.77 (0.58 1.03)		0.77 (0.54 1.10)		0.83 (0.49 1.41)	
BMI categories						
Underweight	1 (ref)	0.64	1 (ref)	0.29	1 (ref)	0.45
Normal weight	0.96 (0.71 1.30)		1.41 (0.88 2.27)		0.72 (0.48 1.09)	
Overweight	1.02 (0.61 1.69)		1.68 (0.84 3.38)		0.73 (0.30 1.75)	
Obese	1.49 (0.66 3.27)		2.74 (0.96 7.84)		1.04 (0.23 4.71)	
Visceral fat	**1.11 (1.01 1.22)**	**0.031**	1.08 (0.94 1.25)	0.30	1.13 (0.99 1.29)	0.073
Subcutaneous fat	**1.71 (1.29 2.27)**	**<0.001**	1.38 (0.96 2.00)	0.083	**2.60 (1.53 4.41)**	**<0.001**

3.6.2 Association between alcohol consumption and hyperglycaemia

Alcohol consumption was associated with hyperglycaemia only in women (p=0.025). The odds of hyperglycaemia were highest among current non problematic drinkers (1.21 [0.56, 2.59]) followed by previous drinkers (1.05 [0.45, 2.43]) and lowest among the current problematic drinkers (0.30 [0.095, 0.95]) (Table 3.8).

Ethno-linguistic grouping was significantly associated with hyperglycaemia. Participants from the Nankana community had more than double the odds of hyperglycaemia compared to those from the Kassena community (OR 2.61 [1.61, 4.25]; p<0.001). This pattern was similar among women and men (see Table 3.8) with women having a threefold increased odds of hyperglycaemia. The odds of hyperglycaemia increased with increasing level of education among women (p<0.001) and in the entire population (p<0.001). In contrast, socio-economic status, age and sex were not associated with hyperglycaemia in this study.

Female participants with a previous history of smoking (OR 4.86 [1.18, 20.0]; p=0.049) and who were currently smoking (4.07 [0.84, 19.7]) were more than 4 times as likely to be hyperglycaemic compared to those who had never smoked before. Compared to the exposed participants, those who were unexposed to pesticides had lower odds of hyperglycaemia (OR 0.57 [0.37, 0.86]; p=0.008). This was observed in females (p=0.013) but not males (p=0.22).

Visceral fat was not significantly associated with hyperglycaemia among females and was marginally significant among males (OR 1.30 [0.99, 1.71]; p=0.059). The association between subcutaneous fat and hyperglycaemia did not achieve statistical significance among either men or women.

Table 3.8: Association between alcohol consumption and hyperglycaemia

Variable	All		Females		Males	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Alcohol						
Never	1 (ref)	0.70	1 (ref)	**0.025**	1 (ref)	0.25
Previous	1.32 (0.67 2.60)		1.05 (0.45 2.43)		1.77 (0.42 7.51)	
Current non problematic	1.11 (0.58 2.11)		1.21 (0.56 2.59)		0.74 (0.18 3.12)	
Current problematic	0.96 (0.48 1.93)		**0.30 (0.095 0.95)**		1.60 (0.42 6.08)	
Age	0.97 (0.93 1.00)	0.051	0.97 (0.92 1.01)	0.37	0.97 (0.92 1.03)	0.32
Sex						
Women	1 (ref)	0.30	-		-	
Men	0.74 (0.41 1.32)		-		-	
Ethnicity						
Kassena	1 (ref)	**<0.001**	1 (ref)	**<0.001**	1 (ref)	**0.049**
Nankana	**2.61 (1.61 4.25)**		**3.75 (1.89 7.46)**		**2.21 (1.03 4.75)**	
Other	2.25 (0.99 5.14)		2.45 (0.88 6.77)		2.90 (0.45 18.8)	
Education						
No formal education	1 (ref)	**<0.001**	1 (ref)	**<0.001**	1 (ref)	0.14
Primary	0.79 (0.45 1.41)		0.76 (0.34 1.74)		0.76 (0.32 1.79)	
Secondary	1.64 (0.86 3.11)		2.59 (0.96 6.99)		1.03 (0.40 2.72)	
Tertiary	**9.73 (3.62 26.1)**		**9.20 (1.02 10.2)**		5.88 (1.66 20.7)	
SES						
Poorest	1 (ref)	0.627	1 (ref)	0.076	1 (ref)	0.79
Very poor	1.18 (0.66 2.14)		1.67 (0.79 3.53)		0.54 (0.18 1.62)	
Poor	0.97 (0.52 1.80)		1.00 (0.44 2.27)		0.84 (0.30 2.33)	
Less poor	0.91 (0.49 1.70)		1.06 (0.47 2.39)		0.62 (0.22 1.74)	
Least poor	0.68 (0.34 1.40)		0.37 (0.11 1.19)		0.60 (0.20 1.75)	
Smoking						
Never	1 (ref)	0.15	1 (ref)	**0.049**	1 (ref)	0.146
Current	0.76 (0.38 1.53)		4.07 (0.84 19.7)		0.51 (0.23 1.13)	
Previous	1.56 (0.80 3.04)		**4.86 (1.18 20.0)**		1.10 (0.51 2.39)	
Pesticide exposure						
Yes	1 (ref)	**0.008**	**1 (ref)**	**0.013**	1 (ref)	0.22
No	**0.57 (0.37 0.86)**		**0.48 (0.27 0.87)**		0.66 (0.34 1.29)	
MVPA						
<150	1 (ref	**0.35**	1 (ref	0.15	1 (ref	0.85
≥150	1.34 (0.73 2.46)		1.81 (0.81 4.02)		0.91 (0.32 2.54)	
Visceral fat	1.07 (0.88 1.28)	0.67	0.73 (0.54 1.00)	0.40	1.30 (0.99 1.71)	0.059
Subcutaneous fat	1.17 (0.69 1.97)	0.57	0.57 (0.91 3.58)	0.091	0.98 (0.35 2.75)	0.96

3.6.3 Association between alcohol consumption and low HDL

Table 3.9 shows the association between alcohol consumption and low HDL levels.

Table 3.9: Association between alcohol consumption and low HDL

Variable	All		Females		Males	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Alcohol						
Never	1 (ref)	**<0.001**	1 (ref)	**0.031**	1 (ref)	**<0.001**
Previous	0.88 (0.59 1.27)		0.76 (0.50 1.14)		0.60 (0.30 1.21)	
Current non-problematic	**0.70 (0.50 0.99)**		1.00 (0.98 1.03)		**0.43 (0.22 0.82)**	
Current problematic	**0.43 (0.30 0.62)**		**0.48 (0.29 0.79)**		**0.28 (0.15 0.53)**	
Age	0.99 (0.98 1.01)	0.54	0.81 (0.51 1.03)	0.34	0.99 (0.30 1.02)	0.28
Sex						
Women	1 (ref)	**<0.001**	**-**		**-**	
Men	**0.27 (0.20 0.37)**		**-**		**-**	
Ethnicity						
Kassena	1 (ref)	0.57	1 (ref)	0.44	1 (ref)	0.50
Nankana	1.03 (0.80 1.31)		1.32 (0.93 1.89)		0.79 (0.55 1.13)	
Other	1.32 (0.79 2.22)		1.67 (0.88 3.14)		0.59 (0.20 1.77)	
Education						
No formal education	1 (ref)	0.55	1 (ref)	0.26	1 (ref)	0.094
Primary	0.99 (0.76 1.29)		0.99 (0.66 1.48)		1.03 (0.72 1.49)	
Secondary	1.07 (0.73 1.55)		1.35 (0.67 2.74)		1.07 (0.67 1.71)	
Tertiary	0.57 (0.25 1.28)		1.49 (0.27 8.16)		0.37 (0.12 1.10)	
SES						
Poorest	1 (ref)	0.31	1 (ref)	0.27	1 (ref)	0.88
Very poor	1.07 (0.76 1.52)		1.22 (0.76 1.97)		0.96 (0.57 1.62)	
Poor	0.90 (0.64 1.27)		0.90 (0.57 1.42)		0.92 (0.55 1.53)	
Less poor	0.91 (0.66 1.28)		0.98 (0.62 1.55)		0.86 (0.52 1.41)	
Least poor	0.74 (0.51 1.06)		0.68 (0.41 1.14)		0.77 (0.45 1.31)	
Smoking						
Never	1 (ref)	0.45	1 (ref)	**0.035**	1 (ref)	0.71
Current	0.85 (0.61 1.17)		**0.27 (0.095 0.74)**		0.97 (0.67 1.39)	
Previous	0.80 (0.55 1.17)		0.82 (0.24 2.80)		0.84 (0.56 1.28)	
MVPA						
<150	1 (ref)	0.63	1 (ref)	0.59	1 (ref)	0.11
≥150	0.93 (0.68 1.26)		1.11 (0.76 1.62)		0.66 (0.40 1.10)	
Visceral fat	0.96 (0.87 1.05)	0.36	1.17 (0.99 1.37)	0.057	1.00 (0.88 1.14)	0.99
Subcutaneous fat	1.21 (0.91 1.60)	0.18	0.88 (0.59 1.30)	0.52	1.01 (0.63 1.62)	0.97

Current alcohol consumption was associated with lower odds of low HDL levels. In the entire population, the lowest odds were among current problematic drinkers (OR 0.43 [0.30, 0.62]), followed by current non–problematic drinkers (OR 0.70 [0.50, 0.99]) and previous drinkers (OR 0.88 [0.59, 1.27]). These findings were consistent among males and females.

The odds of low HDL were higher among men (OR 0.27 [0.20, 0.37]) compared to women. Age and ethnicity were not significantly associated with low HDL levels. There was no significant association between smoking and low HDL in the total population. However upon stratification, this association was only significant among female smokers (p=0.035). Visceral and subcutaneous fat were not significant predictors of low HDL.

3.6.4 Association between alcohol consumption and triglycerides

Alcohol consumption in this population was not a significant predictor of triglyceride levels (see Table 3.10).

The odds of elevated triglycerides were lower among men compared to women and this association was marginally significant (p=0.075). Being a member of the Nankana community was associated with lower odds of elevated triglycerides compared to the Kassena community (OR 0.19 [0.054, 0.65]). After stratification by sex, this association remained significant among women (p=0.027) but missed significance among men (p=0.062).

A unit increase in visceral adipose tissue was associated with an increase in the odds of elevated triglycerides in the total cohort (OR 1.30 [1.05, 1.69]; p=0.046). No other variables showed a significant association with triglycerides.

Table 3.10: Association between alcohol consumption and triglycerides

Variable	All		Females		Males	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Alcohol						
Never	1 (ref)	0.26	1 (ref)	0.099	1 (ref)	0.84
Previous	1.33 (0.47 3.70)		1.75 (0.55 5.52)		0.35 (0.020 6.12)	
Current non-problematic	0.49 (0.17 1.41)		0.38 (0.10 1.38)		0.70 (0.68 7.19)	
Current problematic	1.16 (0.42 3.19)		1.31 (0.37 4.60)		0.77 (0.084 6.98)	
Age	1.00 (0.94 1.06)	0.92	0.99 (0.92 1.07)	0.85	1.01 (0.91 1.12)	0.83
Sex						
Women	1 (ref)	0.075	-		-	
Men	0.35 (0.11 1.11)		-		-	
Ethnicity						
Kassena	1 (ref)	**0.022**	1 (ref)	**0.027**	1 (ref)	0.062
Nankana	**0.19 (0.054 0.65)**		**0.17 (0.035 0.82)**		0.20 (0.023 1.77)	
Other	1.38 (0.47 4.12)		1.46 (0.43 4.93)		1.71 (0.090 32.5)	
Education						
No formal education	1 (ref)	0.57	1 (ref)	0.12	1 (ref)	0.99
Primary	1.73 (0.76 3.91)		2.44 (0.81 6.58)		1.03 (0.23 4.71)	
Secondary	1.44 (0.51 4.08)		1.44 (0.32 6.37)		1.31 (0.28 6.25)	
Tertiary	0.76 (0.071 8.07)		1 (empty)		3.13 (0.24 40.5)	
SES						
Poorest	1 (ref)	0.53	1 (ref)	0.85	1 (ref)	0.19
Very poor	0.68 (0.16 2.97)		0.62 (0.10 3.69)		0.98 (0.057 16.9)	
Poor	0.71 (0.18 2.81)		0.75 (0.15 3.75)		0.62 (0.036 10.5)	
Less poor	0.94 (0.27 3.23)		1.25 (0.30 5.15)		0.51 (0.029 9.00)	
Least poor	1.90 (0.61 5.97)		1.38 (0.34 5.70)		3.80 (0.38 37.7)	
Smoking						
Never	1 (ref)	0.64	1 (ref)	(empty)	1 (ref)	0.22
Current	1.79 (0.53 6.08)		1 (empty)		4.00 (0.76 21.0)	
Previous	1.25 (0.27 5.69)		1(empty)		2.55 (0.38 37.7)	
Pesticide exposure						
Yes	1 (ref)	0.09	1 (ref)	0.156	1 (ref)	0.26
No	2.04 (0.89 4.66)		2.01 (0.75 5.40)		2.40 (0.41 15.8)	

BMI categories						
Underweight	1 (ref)	0.13	1 (ref)	0.115	1 (ref)	0.93
Normal weight	1.22 (0.27 5.58)		1.23 (0.14 10.7)		1.00 (0.11 9.27)	
Overweight	0.58 (0.084 4.04)		0.62 (0.050 7.79)		0.42 (0.010 16.8)	
Obese	2.98 (0.56 31.2)		4.13 (0.26 65.1)		1.00 (0.021 47.2)	
Visceral fat	**1.30 (1.05 1.69)**	**0.046**	1.25 (0.88 1.79)	0.22	1.57 (0.99 2.47)	0.059
Subcutaneous fat	1.48 (0.77 2.85)	0.25	1.61 (0.65 4.03)	0.31	0.960 (0.170 5.42)	0.96

3.6.5 Association between alcohol consumption and waist circumference

The association between alcohol consumption and waist circumference is presented in Table 3.11. There was no association between alcohol intake and waist circumference among either men or women.

Nankana ethnicity was associated with significantly lower odds of elevated waist circumference particularly among women (OR 0.50 [0.36, 0.70]) but not in men. Among men (p=0.025) and women (p<0.001), the odds of having an elevated waist circumference significantly increased with increasing level of education.

In the general population, smokers had lower odds of elevated waist circumference measurements compared to non–smokers (p=0.009). After stratification by sex this association remained significant among women (p=0.046) but lost significance among men (p=0.30). Pesticide exposure and physical activity were not significant predictors of elevated waist circumference measurements.

Table 3.11: Association between alcohol consumption and waist circumference

Variable	All		Females		Males	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Alcohol						
Never	1 (ref)	0.50	1 (ref)	0.32	1 (ref)	0.37
Previous	0.86 (0.57 1.31)		0.81 (0.53 1.24)		4.32 (0.44 42.2)	
Current non problematic	0.95 (0.66 1.36)		0.95 (0.66 1.38)		1.05 (0.12 8.87)	
Current problematic	1.21 (0.78 1.89)		1.27 (0.79 2.02)		1.40 (0.18 10.8)	
Age	0.98 (0.96 1.01)	0.19	0.98 (0.96 1.01)	0.16	1.00 (0.90 1.11)	0.98
Sex						
Women	1 (ref)	**<0.001**	**-**		**-**	
Men	**0.039 (0.021 0.076)**		**-**		**-**	
Ethnicity						
Kassena	1 (ref)	**<0.001**	1 (ref)	**<0.001**	1 (ref)	0.15
Nankana	**0.47 (0.34 0.65)**		**0.50 (0.36 0.70)**		0.30 (0.057 1.55)	
Other	0.95 (0.57 1.59)		1.03 (0.62 1.74)		1 (empty)	
Education						
No formal education	1 (ref)	**<0.001**	1 (ref)	**<0.001**	1 (ref)	**0.025**
Primary	**1.68 (1.18 2.40)**		**1.59 (1.10 2.29)**		4.93 (0.87 28.1)	
Secondary	**2.65 (1.55 4.52)**		**2.22 (1.23 4.01)**		**13.0 (2.29 34.6)**	
Tertiary	**7.62 (2.64 22.0)**		**16.7 (2.04 36.9)**		**17.4 (1.74 47.2)**	
Smoking						
Never	1 (ref)	**0.009**	1 (ref)	**0.046**	1 (ref)	0.30
Current	**0.15(0.044 0.51)**		**0.094 (0.012 0.73)**		0.26 (0.049 1.42)	
Previous	0.70 (0.28 1.77)		0.44 (0.096 2.00)		0.76 (0.17 3.37)	
Pesticide exposure						
Yes	1 (ref)	0.29	1 (ref)	0.48	1 (ref)	0.09
No	1.17 (0.88 1.55)		1.11 (0.83 1.50)		8.14 (0.90 17.4)	
MVPA						
<150	1 (ref)	0.30	1 (ref)	0.44	1 (ref)	0.10
≥150	0.83 (0.58 1.17)		0.87 (0.61 1.24)		0.26 (0.054 1.23)	

Chapter 4 : DISCUSSION

This chapter provides an overview of the study findings with possible explanations for the results and makes comparisons with similar studies conducted previously. We describe the prevalence of MS and its component diseases and the prevalence of the various levels of alcohol consumption. We also discuss determinants of MS in the general population and among men and women. In closing, we discuss the association between alcohol consumption and MS among the study subjects.

4.1 Main study findings

Alcohol intake was highly prevalent in both genders in this population. The prevalence of MS was 7.63%, with a notably higher prevalence in women than men. The prevalence of MS was highest among current non-problematic drinkers for both men and women. The most prevalent MS components were low HDL levels, elevated blood pressure and elevated waist circumference.

From the regression analysis, we ascertained that the level of alcohol intake did not influence the occurrence of MS. However, alcohol consumption decreased the risk of low HDL levels among men and women. Among women, problematic drinking reduced the risk of hyperglycaemia. Other factors that increased the likelihood of having MS were age (men only) and anthropometry (BMI and subcutaneous fat in women, hip circumference in men).

4.2 Socio-demographic characteristics of participants

The study included 1875 participants of middle age (51.1±5.8) with nearly equal numbers of males (46%) and females (54%). This age range was ideal for the study given the long latency periods associated with lifestyle diseases (91).

The participants were predominantly from the Kassena and Nankana communities, which dominate the coverage area of the Navrongo Demographic Surveillance Site.

The majority of the participants had no formal education. This in itself puts them at a disadvantage owing to the known impact of education on population health (92). Education influences populations' awareness and understanding of health needs, access to resources, living environment and propensity to risky behaviour (93). Moreover, there was a larger proportion of educated men than women. This, along with cultural gender roles could explain the higher unemployment rate among women compared to men.

Most of the participants were either married or cohabiting, with the minority being single. There were more widows than widowers, which could be a demonstration of sex differences in longevity and is in keeping with other studies which show that females tend to live longer than males (94). The proposed hypotheses for this disparity include biological (hormonal and chromosomal) variation and differences in behavioural tendencies and exposures (95).

4.3 Behavioural characteristics of participants

Smoking and drinking were more prevalent among men than women. This is a common finding and is ascribable to societal and cultural norms in this region (96).The prevalence of current alcohol consumption of 65.4% was higher than that of studies previously conducted in Ghana. One study among 50-70 year old Ghanaians reported a prevalence of 42.2% (97). Another study in Northern Ghana reported a prevalence of 51.3% (11). In a comparative study, Juliet et al. (2018) found a higher prevalence of alcohol consumption in rural Ghana (58.2%) compared to urban Ghana (41.9%) (98). In the same study, the prevalence of alcohol consumption was found to be higher among Ghanaians living in Europe (71.0%) compared to those resident in Ghana (41.4%) (98).

The vast majority of the population comprised either previous or current alcohol consumers. This is attributable to the easy accessibility and availability of alcoholic beverages in Ghana. Until recently, there was no clear cut policy regulating the production, distribution, advertisement and consumption of alcohol in the country (74). In addition heavy drinking has been a problem particularly in rural Northern Ghana (97).

A fifth of the population were previous drinkers, while a quarter were lifetime abstainers. The former may be as a result of the recent legislation geared at increasing awareness of the harmful effects of alcohol abuse (74).

The prevalence of current smoking of 21% was much higher than that of studies previously conducted in Ghana by Yawson et al. (2013) and Owusu-Dabo et al. (2009) that placed current smoking at 7.65% and 3.8% respectively (99,100). This may signify an upward trend in smoking despite tobacco control activities in the country (101). However, the study by Owusu-Dabo (2009) was conducted in central Ghana and entailed a wider age range (14 years and above) than our present study (100).

In terms of physical activity 81% of females and 90% of males met the current WHO recommended guidelines of at least 150 minutes of moderate intensity physical activity per week (102). This is beneficial as it has a protective effect on NCDs(103). In contrast, the fruit and vegetable intake of most of the participants in the study was inadequate, as it was below the WHO recommended cut off of at least five fruit and vegetable servings per day(90).

4.4 Metabolic risk profile of participants

The majority of the study subjects were of normal weight. Most of the overweight or obese participants were women; while the majority of the underweight participants were men. This observation has been previously reported in this population (11) and seems to represent the epidemiology of obesity in most SSA countries (104,105). In Ghana in particular, weight gain is culturally seen as a symbol of beauty, affluence and high social standing (106). This may therefore contribute to the desire by most women to gain weight eventually resulting in overweight and obesity. The high prevalence of underweight among men may be traceable to the high prevalence of smoking in this group compared to women. Multiple studies have linked smoking to weight loss and smoking cessation to weight gain (107,108). Nicotine has been shown to alter metabolism by increasing sympathetic nervous system activation and lipolysis which result in increased energy expenditure and decreased appetite (109). Moreover, larger

proportions of males than females were physically active and ate at least five fruit and vegetable servings per day in this population.

4.5 Metabolic syndrome

The prevalence of MS in this population was 7.63%. These findings are comparable to those from other studies from rural South-east Nigeria (110), Cameroon (111), Benin (112) and India (113) that report MS prevalence rates between 4 and 10%. This low prevalence can be explained by the location of our study site. The dietary and lifestyle changes associated with the epidemiologic transition are brought about by urbanization and westernization. For this reason, they tend to manifest in urban areas faster than they do in remote rural areas. In addition, subsistence level agriculture is the main economic activity in the study site (78), thus the majority of participants are likely to be subjected to a substantial amount of physical labour and tend to rely on home cooked meals, both of which are beneficial. That being said, some studies have reported much higher prevalence rates of MS in rural areas. Gyakobo et al. (2012), reported a prevalence of 35.9% and 15.0% based on the IDF and ATPIII criteria respectively in rural Ghana (28). However this study was conducted among participants affiliated to a particular company and thus may not be entirely representative of the general population. In another study in rural Nigeria, the prevalence of MS was 12% and 14% using the IDF and NCEP ATP III definitions respectively (114).

There was a dramatic difference in the MS prevalence across genders in this population. The prevalence of MS among women was six times as high as that of men and is similar to findings from other studies though not in the same magnitude (28,115,116). This variation was due to the high prevalence of elevated waist circumference and low HDL levels among women. In addition, there was a higher proportion of overweight and obese women than men.

The most common components of MS in this population were low HDL levels, elevated blood pressure and elevated waist circumference. This is a frequent finding among studies from Africa (28,117) and a recent study from this population also demonstrated

very high levels of low HDL (118). Elevated blood pressure and low HDL were the most prevalent components among males and females respectively.

A quarter of the population had at least two components of MS. This is a matter of concern because despite the current low prevalence, these figures signify a looming problem. The MS risk factors tend to occur together therefore this population is at high future risk of MS.

4.6 Metabolic syndrome prevalence across alcohol consumption patterns

In this study, differences in the prevalence of MS and its component diseases across alcohol consumption patterns were noted. For both men and women, the highest prevalence of MS was among non-drinkers. These findings are consistent with previous findings from studies among African (119) and non- African populations (120,121) that reported a higher prevalence of MS among drinkers compared to non-drinkers. Among women, this finding is attributable to the MS components; with female non-drinkers having the highest prevalence of all MS components except hyperglycaemia.

For women, the second highest prevalence of MS was among previous drinkers followed by current problematic drinkers. Current non-problematic drinkers had the lowest prevalence. Elevated waist circumference was most prevalent among non-drinkers and lowest among previous drinkers. The prevalence of low HDL was highest among non-drinkers and lowest for current problematic drinkers. Previous studies on the association between HDL and alcohol intake have reported a dose response relationship, with frequent drinking being linked to high HDL levels (122).

Among men, there was no significant difference in prevalence of MS and most of its components for the various alcohol consumption levels. However, the prevalence of low HDL was highest among non-drinkers and lowest among current problematic drinkers. These variations in the associations between the levels of alcohol intake and MS across genders may be explained by the differences in metabolism, drinking patterns, types of drinks consumed and in perceptions on alcohol intake between men and women.

4.7 Role of confounders in the association between alcohol intake and MS

Despite the obvious effect of westernization on the occurrence of NCDs (2), alcohol consumption patterns and indeed, the occurrence of MS are influenced by socio-demographic, behavioural and biological factors which are geography and population specific (30,123). There is need therefore to investigate the role of these factors on the association between alcohol intake and MS both independently and cumulatively. In order to achieve this, we adjusted for the confounders in a hierarchical manner.

In the unadjusted model inclusive of men and women, alcohol consumption was protective from MS. Of the three levels, current problematic drinking was most beneficial followed by current non-problematic drinking. Inclusion of socio-demographic factors in the model (model 1) resulted in an increase in the odds of MS among alcohol consumers and was accompanied by a loss in the significance of the association between alcohol and MS. Socio-demographic factors were therefore negative confounders.

In model 2, inclusion of behavioural factors was accompanied by a slight reduction in the significance of alcohol consumption and a small increase in the odds of MS among drinkers. In model 3, a larger effect on the association between alcohol intake and MS was noted. Inclusion of biological factors in the model resulted in a slight change in the odds of MS for alcohol consumers and a bigger reduction in the significance of alcohol consumption.

In the final model (model 3), the significance of the individual variables was in keeping with the findings discussed above. The socio-economic factors included in this study were age, sex, ethnicity, level of education, employment and socio-economic status. Of these, only sex was significant, hence it was the most important socio-demographic factor and was accountable for the loss of significance observed. The behavioural factors were smoking, smokeless tobacco use, sugary beverage consumption, fruit and vegetable intake, pesticide exposure and moderate to vigorous physical activity. None of these factors were significant. Three of the four biological factors (BMI, visceral and subcutaneous fat) were highly significant.

This therefore means that biological factors play a key role in the relationship between alcohol and MS. These findings are in keeping with previous studies that have demonstrated an association between alcohol intake, MS and these factors (124,125).

These biological factors were considered as the direct/proximate determinants through which the behavioural (intermediate determinants) and socio-demographic factors (distal determinants) influenced the occurrence of MS. The link between the distal and the proximate determinants may be influenced by multiple factors, leading to complexity in the relationship. In addition, the latency period associated with NCDs further complicates this association as the impact of the direct and intermediate determinants may manifest faster than that of the distal determinants. As such, the dominance of biological factors in this study may be explained by the reduction in causal conclusiveness and consistency with progression from direct to distal determinants (126).

Sex was considered as an important factor and was analysed by stratifying the models by gender. Stratification resulted in weaker associations between alcohol consumption and MS. This was particularly evident in the unadjusted model, where it was accompanied by loss of significant associations for each gender. This finding may be attributable to loss of statistical power as a result of a reduction in the sample size of each model upon stratification,

4.8 Association between alcohol intake and MS

After adjusting for confounders, a history of either previous or current alcohol intake reduced the odds of MS in the total cohort. Current problematic drinking was most protective followed by current non-problematic drinking. A similar pattern was observed among women and is in keeping with a cross-sectional study in the US that reported an inverse relationship between alcohol intake and MS (37). Among men, current non-problematic drinking was associated with the highest likelihood of MS, followed by abstinence. In contrast, problematic drinking and previous drinking were protective. This is in consonance with a study by Valmore et al. (2015), which found an increased

risk of MS among male moderate drinkers. These findings may be attributable to the protective effect of alcohol on HDL levels that was evident in this study and has been previously reported in the literature (37,127). However in our study, the association between alcohol intake and MS did not achieve statistical significance.

In contrast to the above studies, multiple studies have documented divergent findings. A study among Korean adults reported a lower prevalence of MS among light drinkers compared to abstainers. This study found no association between MS and heavy drinking (40). In a study among Japanese men, a dose response relationship was reported (128). Another study in the U.S reported increased risk of MS among heavy drinkers (122).

These inconsistent findings may be as a result of disparities in type of beverage consumed, frequency of consumption, irregular drinking habits like binge drinking and genetic variation among study populations. Moreover, some of the variables are difficult to measure accurately and may therefore produce unreliable results when included in the multivariable models. For instance non-drinkers could include: lifetime abstainers, previous drinkers and irregular abstainers. Each of these groups has different levels of exposure thus their risks may not be of the same magnitude; previous drinkers in themselves may have quit drinking at different times hence variability exists within the group.

Further to this, inferences made based on these studies should be made with caution. Reverse causality makes it difficult to establish whether previous drinkers quit alcohol consumption because they developed MS or whether quitting in itself contributed to the development of MS. Similarly for abstainers, inferences made by previous studies on the protective effect of alcohol compared to non-drinking may be inaccurate as the presence of MS beforehand may have been the reason for abstinence (129). In addition some of the factors considered as confounders in this study, for instance biological factors, may have mediatory effects.

4.8.1 Factors associated with MS

An increase in age was associated with a small increase in the odds of MS among men but not among women. For the majority of chronic diseases, age is a critical determinant of health and the prevalence of disease is expected to increase with increasing age. This can be explained by degenerative cell changes coupled with a reduction in the ability to withstand stressors that occur with increasing age (130). In this study however, this feature was not clearly seen; possibly due to the narrow age range of the study participants (40-60yrs). It may also be attributable to a survival effect whereby healthy participants tend to live longer resulting in a lower disease prevalence among older participants (131).

Women in this population were at a greater risk of MS than men; with men having less than half the odds of MS compared to women. These findings were consistent with several other studies conducted across African countries (28,114,132). This variation was present despite adjusting for BMI. It may be explained by inherent differences in hormonal function and in adipocyte size and function (133). However, our study findings are not universal; some studies from Asia and some parts of Europe reported a higher risk among men (134–136). This variability may be a consequence of geographic differences and may be linked to cultural and environmental disparities between regions.

Contrary to reports from other studies, education had no influence on the occurrence of MS in this population. This could be because the bulk of the population had not received any formal education, thus the other levels of education were underrepresented. Similarly the majority (97%) of female participants had never smoked before, thus there were insufficient numbers of female smokers for comparison. Among males, current smoking reduced the risk of MS while previous smoking doubled the odds of MS. These findings were however not significant.

Among men pesticide exposure markedly increased the likelihood of MS. This is in keeping with studies which have linked persistent organic pollutants (POPs) which include most commonly used pesticides, with MS (137–139). These chemicals tend to

persist in the environment and exposure through various routes has been associated with insulin resistance (138).

Among women, the odds of MS increased with increasing BMI. It was lowest for underweight participants and highest for overweight participants. This could be explained by the correlation between waist circumference and BMI. Though BMI is not a reliable measure of adiposity, a positively linear relationship between BMI and body fat exists, thus an increase in BMI would be coupled with an increase in waist circumference (140).

There was a dose response relationship between visceral fat and MS. Similar findings have been reported by other studies (141,142). Visceral adiposity is known to be associated with altered free fatty acid (FFA) metabolism and reduced adiponectin production, which in turn leads to reduced insulin signalling and increased risk of atherosclerosis. This then results in the dyslipidaemic, insulin resistant and inflammatory state that characterises MS (143).

An increase in subcutaneous fat increased the risk of MS among females, while no significant difference was seen among males. This finding is consistent with previous studies that report a positive relationship between subcutaneous fat and MS (144,145). However, evidence from existing literature is inconsistent. Some studies have reported no relationship (142,146), while others have reported an inverse correlation between the two (141,147). Variation in the association between subcutaneous fat and MS exists across populations and may be attributable to genetic and physiological differences. In addition, differing methods of subcutaneous fat measurement between studies may explain the varied findings.

4.9 Association between alcohol intake and MS components

4.9.1 Association between alcohol consumption and hypertension

After controlling for other covariates, there was no difference in the odds of hypertension across the various levels of alcohol consumption. These findings were

consistent with previous reports by Halanych et al. (2010) and Li et al. (2016) who reported no association between alcohol consumption and hypertension in African – American and Chinese populations respectively (33,148).

Multiple studies have reported varied findings; some studies report an increased risk of hypertension among drinkers compared to non-drinkers (149), others report an increased risk that is confined to heavy drinkers (150), while others have found a protective effect among light to moderate drinkers (47,151).

In this population, the odds of hypertension increased with increasing age. This feature is attributable to the progressive loss of vascular elasticity and the higher predisposition to secondary causes of hypertension that is associated with aging (152). Similarly there was a positive relationship between subcutaneous and visceral fat with hypertension. This may be explained by the association of central obesity, which contains metabolically active fat depots with insulin resistance and atherosclerosis. Hyperinsulinaemia leads to enhanced renal sodium retention resulting in an increase in intravascular volume. It has also been shown to contribute to increased vascular stiffness resulting in increased peripheral vascular resistance (153). In addition, inflammation of visceral adipose tissue results in increased cardiac output by activating the renin-angiotensin-aldosterone system (RAAS) (153).

4.9.2 Association between alcohol consumption and hyperglycaemia

Among men, there was no association between alcohol consumption and hyperglycaemia. However, among women current problematic drinking was associated with lower odds of elevated blood sugar levels. This finding among women may be explained by alcohol's inhibitory effect on hepatic gluconeogenesis (154) and is in keeping with a study conducted in South Africa, which reported a negative correlation between both occasional and regular alcohol consumption and diabetes (155).

Evidence from literature is inconsistent; some studies report a decreased risk of diabetes among moderate drinkers (55,56), others report an inverse dose response relationship, whereby an increase in the frequency of alcohol consumption was coupled

with a reduction in the risk of diabetes (156) while others have reported no association between heavy drinking and diabetes risk (157). These differences may be related to variations in length and patterns of alcohol consumption across populations as well as differences in the markers of alcohol intake used across studies.

4.9.3 Association between alcohol consumption and HDL

Alcohol consumption was significantly associated with low HDL levels in this study, being protective among both men and women. Thus, the odds of low HDL levels decreased with progression from current non–problematic to problematic drinking. These results are in keeping with studies from Africa (127), Asia (158), Australia (159), and the U.S (37). The proposed mechanisms include increased cholesterol esterification and an increased transport rate of apoliproteins A-I and A-II with alcohol consumption (59).

Men were less likely to have low HDL levels compared to women. Current smoking was associated with decreased odds of low HDL levels. This finding was particularly present among female current smokers, but should be interpreted with caution because a very small proportion of women (1.88%) were current smokers in this population.

4.9.4 Association between alcohol consumption and triglycerides

Results of the present study indicate no association between alcohol consumption and triglycerides among men. However among women, this association was marginally significant. Compared to abstinence, non-problematic drinking among women was protective whilst problematic drinking was associated with increased odds of elevated triglycerides. These findings were similar to another African study that reported no association between self-reported drinking and triglycerides among men but an increased risk among female drinkers (160). In keeping with these findings, a J shaped association has been reported in which moderate drinking has been found to be protective while heavy drinking poses greater risk than abstinence (65,66). The reason for the discrepancy between men and women is unclear, however findings among male

heavy drinkers are attributable to increased lipoprotein lipase levels among moderate drinkers and increased VLDL synthesis among heavy drinkers (65,66).

4.9.5 Association between alcohol consumption and waist circumference

Alcohol consumption was not associated with waist circumference in this study. As with other components of MS, there is no consistent conclusion on the association between the two within the literature. Positively linear (69,71) and inverse (72) relationships have been reported. Some evidence suggests varied associations with different types of alcoholic beverages (70,150). This may partially explain the results in this study; stratification by type of drink may have yielded different findings. In addition, the effect of local brews that are popular in the study site may be different from alcoholic drinks previously studied.

Waist circumference increased with increasing level of education among both men and women. Current smoking had protective effects compared to non-smoking, particularly among women. This is in keeping with studies previously discussed linking smoking with weight loss (107), but as previously stated, should be interpreted with caution. Previous smoking was not significant; this may be related to varying times of smoking cessation among participants and bias associated with self-reporting.

4.10 Limitations

The study being cross-sectional in nature, lacks temporality, therefore causal inferences could not be made. Participants' alcohol consumption status was based on self-reporting and was therefore at risk of misclassification. It was also prone to recall and social desirability biases, as participants' responses may have been influenced by presence of disease and societal expectations. In addition, alcohol consumption was based on a categorical classification derived from questions asked as opposed to measuring blood alcohol content and this may reduce its sensitivity. Thirdly, the study was conducted in rural Ghana and therefore the findings may not be generalizable to

the rest of the country. In addition, important variables like the type of beverage consumed were unavailable and therefore not put into consideration during the analyses. Some categories like smoking among females had very few participants thus making it difficult to generate a true picture of the associations.

4.11 Strengths

This study is to our knowledge, the first of its kind at the study site; therefore its findings are useful in assessing the burden of disease in this population and informing health policy and planning. In addition, it highlights the prevalence of alcohol intake in this community and thus may serve as a useful reference point to assess the effect of current interventions that are geared towards reducing alcohol consumption. The study was adequately powered to detect a significant difference in MS prevalence for the various alcohol consumption categories.

4.12 Implications of the study

NCDs were previously a preserve of high income countries but not anymore. Low and middle income countries are in desperate need of solutions to curb the rising trend of these chronic diseases and Ghana is no exception (161).

The presence and value of the MS as a discrete entity has been subject to debate over the years. Several critical appraisals coupled with multiple definitions from various organizations have further fuelled this ongoing debate (162,163). Nonetheless, the tendency of these risk factors to cluster and serve as a precursor to NCDs is undeniable and makes MS pertinent in the fight against NCDs.

Over and above being a common social habit, alcohol consumption is a modifiable risk factor, therefore an understanding of its association with the MS in this population is useful and actionable.

In this study the findings between men and women were consistently different. This finding highlights the importance of sex specific guidelines on alcohol consumption. The

high prevalence of alcohol intake points towards the need for regulation of availability of alcohol in this population, given the known harmful effects of alcohol intake.

Alcohol intake did not influence the occurrence of MS in this study. However, among women non-problematic drinking was associated with increased risk of hyperglycaemia while problematic drinking appeared to be beneficial. Moreover, alcohol consumption decreased the risk of low HDL levels among men and women. Despite these beneficial effects, the multiple known negative effects of heavy alcohol consumption negate any possible advantages.

This study further underpins the need for routine screening for MS in the population and alcohol intake assessment at the primary care level particularly among patients with the MS.

Finally there is need to educate the community on the negative effects of alcohol intake, the risks associated with MS and the importance of healthy habits using methods that put the high level of illiteracy in this population into account. The female predominance among MS cases draws attention to the need for interventions that target women in this population.

4.13 Conclusion

In summary, our analysis of middle aged adults from rural Northern Ghana suggests that the prevalence of MS is relatively low. However, a quarter of the population had at least two components of MS, pointing towards an impending problem. Alcohol intake was a popular habit in this population. The risk of MS was higher among women compared to men. Alcohol intake did not influence the occurrence of MS. However significant associations with hyperglycaemia and low HDL levels were noted, highlighting the need for further investigation.

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UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Violet Mathenge

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M181084

NAME: (Principal Investigator)	Dr Violet Mathenge
DEPARTMENT:	School of Public Health
PROJECT TITLE:	The association between alcohol consumption and the metabolic syndrome and its component diseases in a rural Ghanaian population
DATE CONSIDERED:	26/10/2018
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Engelbert A Nonterah and Prof Nigel J Crowther
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	29/10/2018

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **October** and will therefore be due in the month of **October** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES