The Association of Alcohol Consumption with Diet and Cardiometabolic Risk in Two Independent UK Populations

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Abstract

The association between alcohol consumption and cardiometabolic disease risk has been described as a J or U-shaped curve attributed to a combination of harmful and beneficial effects varying with volume of intake. Diet is an established risk factor for cardiometabolic disease and related traits However, few studies examining this association adequately control for residual confounding by dietary intake. Therefore, the aim of this thesis was to investigate the relationship between alcohol consumption and markers of cardiometabolic health independent of dietary intake.

Cross sectional analyses were conducted using data from the Airwave Health Monitoring Study – a British occupational cohort (n = 9,581). Alcohol consumption behaviour was determined from questionnaire and 7-day diet record data. Diet quality was determined by measuring adherence to the Dietary Approaches to Stop Hypertension (DASH) diet using data from the 7-day diet records. Markers of cardiometabolic health included: adiposity (body mass index and waist circumference), blood pressure, cholesterol, HbA1c and C-reactive protein. All analyses were replicated in an independent UK cohort using UK Biobank data (n =146,888). As part of this thesis, genetic analyses were conducted to investigate whether genes implicated in the regulation of HDL-c may facilitate some of the cardioprotective effects attributed to alcohol intake.

Heavy alcohol consumption is associated with a deterioration in cardiometabolic health. The risk of cardiometabolic disease as indicated by a cardiometabolic risk score was lowest amongst moderate drinkers and highest amongst never, and heavy drinkers. Increasing alcohol intake was associated with a deterioration in diet quality and had an additive effect of total energy intake. Diet quality did not modify the relationship between moderate alcohol intake and cardiometabolic risk. Alcohol intake did not alter the effect of genes implicated in the regulation of HDL-c. These findings were validated in a sub-sample of the UK Biobank cohort.

To conclude, the findings from this thesis show that alcohol consumption plays a key role in determining diet quality and cardiometabolic risk. Specifically, risk of developing obesity.

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Statement of Personal Contribution

The author performed all the work described in this thesis. Collaborations and assistance are detailed below. The work of others is fully cited, referenced and/or acknowledged. The author was responsible for the processing and handling of the Airwave Health Monitoring Study nutritional data presented in this thesis. All critical appraisal and interpretation presented in this thesis are the opinion of the author. The Airwave Health Monitoring Study team at Imperial College London undertook participant recruitment and primary data collection.

Chapter 3. Dietary Intake in the Airwave Health Monitoring Study and the UK Biobank Cohort, Section 3.3 Airwave Health Monitoring Study – Dietary Data Generation

The author, trained the dietary coders, audited the coding process, and cleaned the dietary data with Anwar Al Baloul (PhD Student) and Aleksandra Kopytek (Research Technician). The author contributed to the coding of the food diaries included in this thesis as part of the Airwave Health Monitoring Study nutritional assessment team.

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Acknowledgments

Copyright of Declaration

Glossary of Abbreviations

AHMS   Airwave Health Monitoring Study

AHA   American Heart Association

ANOVA   Analysis of variance

BMR   Basal Metabolic Rate

BSQF   Beverage Specific Quantity Frequency

BMI   Body Mass Index

BHF   British Heart Foundation

BRC   British Research Council

CMR   Cardiometabolic risk

CVD   Cardiovascular Disease

CNS   Central Nervous System

COPD   Chronic Obstructive Pulmonary Disease

CHIAG   Community Health Index Advisory Group

CI   Confidence Interval

CHD   Coronary Heart Disease

CRP   C-reactive protein

DD   Daily Diet Diaries

DNA   Deoxyribonucleic acid

DBP   Diastolic Blood Pressure

DQI   Diet Quality Index

DASH   Dietary Approaches to Stop Hypertension

DALYS   Disability Adjusted Life-Years

EDTA   Ethylenediaminetetraacetic acid

EGIR   European Group for the Study of Insulin Resistance

EPIC   European Prospective Investigation into Cancer

FG   Fasting Glucose

FFQ   Food Frequency Questionnaire

GP   General Practitioner

GWAS   Genome Wide Association Study

GF   Gradient Frequency

HR   Hazard Ratio

HSE   Health Survey for England

HEI	Healthy Eating Index
HDL	High Density Lipoprotein
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
IDF	International Diabetes Federation
IPAQ-SF	International Physical Activity Questionnaire Short Form
IQR	Inter-quartile Range
IHD	Ischemic Heart Disease
LD	Linkage Disequilibrium
LDL	Low-Density Lipoprotein
MetS	Metabolic Syndrome
MAF	Minor Allele Frequency
MI	Myocardial Infarction
NCEP	National Cholesterol Education Program Adult
APT	Treatment Panel III
NDNS	National Dietary and Nutrient Survey
NHS	National Health Service
NIGB	National Information Governance Board for Health & Social Care
NICE	National Institute for Health and Care Excellence
NSP	Non-starch polysaccharide
OR	Odds Risk
ONS	Office of National Statistics
PIAG	Patient Information Advisory Group
PAL	Physical Activity Level
QF	Quantity Frequency
RR	Relative Risk
SD	Standard Deviation
SAT	Subcutaneous Adipose Tissue
SBP	Systolic Blood Pressure
TEI	Total Energy Intake
TIA	Transient Ischemic Attack
TG	Triglycerides

T2DM	Type 2 Diabetes
UKN	UK Nutrient Database
UK	United Kingdom
US	United States
VIF	Variance Inflation Factor
VLDL	Very Low-Density Lipoprotein
VAT	Visceral Adipose Tissue
WC	Waist circumference
WGRS	Weight Genetic Risk Score
WHO	World Health Organisation

1.0 Background

1.1 Chapter Overview

1.1.2 UK Burden of Cardiovascular Disease and Type 2 Diabetes.

Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in the UK, affecting more than 7.6 million people[1]. Type 2 diabetes (T2DM) is a substantial risk factor for CVD. In the UK, more than 4.9 million people have T2DM[2]. A further 13.6 million people are at increased risk, while a further 850,000 people are currently living with this condition but are yet to be diagnosed[2]. Each year, CVD and T2DM place a considerable financial burden on the National Health Service (NHS). In England alone, CVD-related healthcare costs are estimated at £7.4 billion per year[3], while the annual spend on T2DM-related healthcare is projected to increase from an estimated £9.3 billion per year to £16.9 billion per year over the next 25 years[3].

1.1.3 Alcohol Consumption and Cardiometabolic Disease

Alcohol consumption is a prominent risk factor for global disease burden, accounting for more than 2.8 million annual deaths per year worldwide[4]. While it is widely accepted that increasing alcohol consumption poses a serious risk to health, there is accumulating evidence of a cardioprotective effect from low to moderate alcohol intake[5–7]. However, some argue that methodological weaknesses and poor control for the influence of confounding variables hinder the significance of these associations. As a result, the relationship between alcohol and cardiometabolic health remains a matter of public debate.

1.1.4 Alcohol and Diet

Alcohol is both a psychoactive drug and a metabolic fuel. Although not considered an essential nutrient, alcohol provides the body with 7 kilocalories of energy per its weight in grams. Findings from appetite studies suggest that alcohol consumption increases appetite and has an additive effect on total energy intake[8,9]. There is also evidence of a deterioration in diet quality with heavy alcohol intake[10]. However, evidence for an influential effect of low and moderate alcohol intakes on diet is limited and inconsistent. Furthermore, the effect of alcoholic beverage preference and or pattern of consumption on dietary pattern also remains relatively unexplored. Clarifying the effect of alcohol

intake on diet is a key step in understanding the extent to which diet confounds the association between alcohol and cardiometabolic disease risk.

This chapter provides an overview of cardiometabolic disease, its aetiology, and the burden it places on public health. More importantly, it explores the relevant literature relating to alcohol consumption, dietary intake, and cardiometabolic health. In doing so, the chapter provides a summary of the association between alcohol consumption behaviours, dietary patterns, and markers of cardiometabolic disease.

1.2 Cardiometabolic Disease and Risk Markers

1.2.1 Definition of Cardiometabolic Disease

The term cardiometabolic disease is often used to describe the risk of developing cardiovascular disease and type 2 diabetes[11]. Cardiovascular diseases (CVD) are a group of disorders that affect the heart and vascular systems. They include coronary heart disease, cerebrovascular disease, and peripheral artery disease. Myocardial infarctions (MI) and transient and ischemic strokes are acute events that occur in undiagnosed or poorly managed cardiovascular disease[12]. Type 2 Diabetes (T2DM) is a metabolic condition that is characterised by chronic hyperglycaemia secondary to insulin insensitivity and resistance, and in some cases defective insulin production[13]. The term cardiometabolic is assumed to reflect the metabolic abnormalities (e.g., dyslipidaemia, impaired glucose tolerance) at the pathological core of these conditions [14].

1.2.2 The UK Burden of Cardiometabolic Disease

The latest statistics from the British Heart Foundation (BHF) suggest that more than 7.6 million people in the UK are living with cardiovascular disease[15]. These statistics also suggest that cardiovascular disease accounts for more than a quarter of all deaths. The high prevalence of cardiovascular disease in the UK places a significant financial burden on the National Health Service (NHS) with CVD-related healthcare costs amounting to more than £7 billion in England alone[15].

Currently, 4.6 million people are living with a diabetes diagnosis in the UK. Type 2 diabetes accounts for more than 90% of all diabetes diagnoses, meaning type 2 diabetes affects more than 4 million people in this country[2]. The exponential growth in the prevalence of type 2 diabetes is a significant cause for concern. It is estimated that by 2030 more than 5.5 million people in the UK will have type 2 diabetes [2]. Concerning cost, a sizeable proportion of the NHS budget is spent on treating diabetes

related illnesses. In fact, recent estimates suggest that T2DM cost the NHS £10 billion pounds per year[2]. This figure is more than 10% of the entire budget dedicated to healthcare[2].

Risk markers of cardiometabolic disease are biological markers that have been quantitatively associated with the risk of developing this condition[16]. Unlike risk factors of disease, risk markers are not indicators of causality, and the direct alteration of a risk marker may not alter the risk of disease. The most widely studied risk markers of cardiometabolic disease include anthropometric markers of obesity, biochemical markers of blood lipid profile, blood pressure, biochemical markers of inflammation, and biochemical markers of impaired glucose tolerance.

Obesity and Cardiometabolic Disease Risk

The World Health Organisation (WHO) defines obesity as an abnormal accumulation of body weight or fat that poses a risk to health[17]. The global prevalence of obesity is growing exponentially[18]. In the UK alone, the prevalence of adults who are overweight or obese increased from 53% to 64% between 1993 and 2019. Today, the issue of obesity is a concern of epidemic proportions.

Body mass index (BMI) is a commonly used proxy measure of adiposity (obesity). BMI is defined as a person's weight in kilograms divided by their height in metres squared (kg/m^2). WHO-classified BMI ranges are commonly used to screen for overweight and obesity in epidemiological and clinical settings (Table 1.1)[19]. The WHO BMI ranges are based on the association between excessive body fat, disease risk, and morality, and have been strongly correlated to adiposity. There is convincing evidence to show a positive correlation between an elevated BMI and risk of CVD in the general population [20,21]. Findings from a recent meta-analysis report a positive association between a unit increase in BMI and increased odds of developing CVD[21]. Similarly, the evidence points to a positive association between BMI and type 2 diabetes risk. A meta-analysis of 31 studies showed an 18% increase in the risk of developing type 2 diabetes per unit increase in BMI[22].

The association between obesity and cardiometabolic disease risk is undisputed. However, there is debate as to whether BMI is a suitable marker of obesity given its inability to discriminate between fat and fat free mass[23,24]. For example, a person with a high free fat mass and low body fat percentage would be misclassified as overweight or obese using this index. The opposite could also occur in individuals presenting with abdominal obesity in the absence of overall obesity. There is a

growing concern that using the BMI index underestimates cardiometabolic disease risk in those with 'normal weight obesity'[23].

The distribution of body fat is an important indicator of cardiometabolic disease risk [25]. Findings from large epidemiological studies have shown a positive association between waist-circumference, T2DM and CVD independent of BMI [22,25–30]. In a prospective cohort of more than 25,000 men, the relative risk of developing T2DM increased tenfold, from the lowest to the highest quintile of waist circumference, after adjusting for BMI and other confounding variables [30]. Concerning CVD, findings from a case-control study report a 70% higher risk of a myocardial infarction in individuals in the highest versus the lowest quintile of waist-circumference independent of BMI and other confounding variables [26]. Waist circumference is strongly correlated with visceral adipose tissue (VAT) [26]. Compared to subcutaneous adipose tissue (SAT), VAT is a dynamic and metabolically active organ, producing and secreting biologically active compounds, including pro-inflammatory cytokines [31]. VAT is considered to play a significant role in the pathophysiology of cardiometabolic disease [31].

Waist-circumference cut-off points are used in practice to define abdominal obesity and a level of cardiometabolic disease risk. These cut-off points differ according to ethnic background. In Caucasian men and women, the waist circumference cut-off points for abdominal obesity and substantial risk of cardiometabolic disease are set at 94 cm and 80 cm for men and women, respectively[18].

Table 1.1 BMI Cut-Off Points and Nutritional Status

World Health Organisation BMI Cut-off Points and Nutritional Status	
BMI Range	*Category*
< 18.0 kg/m2	Underweight
18.0 – 24.9 kg/m^2	Normal Weight
25.0 – 29.9 kg/m^2	Overweight (Pre-obesity)
30.0 – 34.9kg/m^2	Obesity I
35.0 – 39.9kg/m^2	Obesity II
> 40 kg/m^2	Obesity III

Blood Lipids and Cardiometabolic Disease Risk

Lipoproteins are complex particles with a hydrophobic core and a hydrophilic outer shell. They play an integral role in the absorption and transport of cholesterol and triglycerides around the body.

There are several different classes of lipoprotein, chylomicron and chylomicron remnants, intermediate density lipoprotein, very low-density lipoprotein (VLDL-c), low density lipoprotein (LDL-c), high density lipoprotein (HDL-c), and lipoprotein (a).

VLDL-c, LDL-c, and HDL-c are distinguishable from each another by their density and atherogenic role. While VDL-c is produced by the liver and triglyceride rich, LDL-c is the main carrier of cholesterol in the blood. Both VLDL and LDL easily infiltrate the arterial wall and are pro-atherogenic. Consequently, elevated levels of LDL and VDL are negative indicators of cardiometabolic health[32]. These lipoproteins are found in abundance in states of hypertriglyceridemia and are positively associated with both T2DM and CVD disease risk[33,34]. By comparison, HDL (High Density Lipoprotein) is anti-atherogenic and plays a key role in reverse cholesterol transport from the body's peripheries to the liver for reuse and excretion. HLD-c has antioxidant and anti-thrombotic properties and has also been shown to inhibit vascular inflammation[32]. Findings from observational studies show a strong positive association between HDL concentration and cardiometabolic risk[35–38]. However, the results of recent genetic and pharmacological intervention studies cast doubt on this association. To date, clinical studies have failed to show a cardioprotective benefit of raising HDL levels by pharmacological means[39]. Similarly, findings from mendelian randomisation studies suggest a non-significant association between polymorphisms associated with elevated HDL levels and cardiovascular disease risk[40,41]. Although the evidence is contradicting, HDL concentration is still widely accepted as a risk marker of cardiometabolic disease[42].

Blood Pressure and Cardiometabolic Disease Risk

High blood pressure (hypertension) is characterised by a persistent elevation of blood pressure in the blood vessels. In the UK, the diagnostic threshold for hypertension is a clinic systolic blood pressure ≥140 mmHg and/or a clinic diastolic blood pressure of >90 mmHg[43]. Hypertension is a leading cause of cardiometabolic diseases[44]. Hypertension places excess physical strain on the walls of the blood vessels, increasing propensity to vascular dysfunction and atherosclerotic plague formation[45].

Findings from meta-analyses report an increase in the likelihood of a cardiovascular event with increasing blood pressure[46]. Studies examining the effects of blood pressure lowering suggest that the reduction in the risk of a cardiovascular event is proportional to the reduction in blood pressure achieved[47]. Evidence from observational studies also points to an association between T2DM and

hypertension[48–51]. For instance, a large prospective cohort study in the US (United States) suggest a 2.5 higher risk of T2DM in hypertensives than normotensive individuals[49]. In many cases, these two conditions exist together. In the UK, more than 50% of people with type 2 diabetes are also diagnosed with hypertension[2]. While the co-existence of T2DM and hypertension is well recognised, the causality between the two conditions is still unclear.

The association between blood pressure and cardiometabolic disease risk is not limited to hypertension. Prehypertension is when blood pressure falls between the optimal and hypertensive thresholds. It is defined as a systolic-diastolic blood pressure reading greater than 120/80 mmHg and less than 139/89 mmHg[52]. Pre-hypertension is associated with an elevated risk of cardiovascular disease. For example, evidence from observational studies suggest a higher adjusted risk of coronary heart disease, myocardial infarction, and stroke in prehypertensive versus normotensive individuals[53,54]. The risk of CVD related morality has also shown to be higher in prehypertensive than normotensive individuals[55].

Inflammation and Cardiometabolic Disease Risk

Inflammation is an immunovascular response to an inflammatory stimulus. It is thought to play a significant role in the development and progression of CVD, notably atherosclerosis[56]. The infiltration of the arterial wall by lipoprotein particles during the atherosclerotic process sparks a cascade of inflammatory markers which leads to an increase in acute phase reactants, including c-reactive protein (CRP). CRP is the most sensitive acute phase reactant and is produced by the liver in response to elevated levels of pro-inflammatory interleukin 6[56]. CRP levels rise in states of inflammatory diseases, infections, trauma, cancer or following surgery. Beyond, the role of inflammation marker, CRP levels have been shown to predict the long-term risk of MI, stroke, and other CVDs (cardiovascular disease) in otherwise healthy individuals[57,58]. Elevated CRP levels have also been associated with the development of insulin resistance and T2DM. Findings from a meta-analysis involving 22 cohorts report a higher relative risk (RR) of T2DM with each 1 log increment in CRP levels (RR 1.26 95% CI 1.16-1.37)[59]. Another study showed a positive correlation between CPR and markers of insulin resistance, including fasting insulin, and proinsulin (correlation coefficient (r^2) > 0.30 p <0.001)[59]. A CRP level greater than 10mg/L has been correlated with a 4% increased risk of developing fatal CVD[60]. Consequently, this threshold is often used in epidemiological studies to define elevated CRP and risk in relation to cardiometabolic health.

Impaired Glucose Metabolism and Cardiometabolic Risk

Prediabetes is a term that is used to describe a transitional stage between normal glucose metabolism and overt T2DM. The pathogenesis of prediabetes can be divided into two aetiologies: impaired glucose tolerance (IGT) and impaired fasting glucose (IFG). Insulin resistance and impaired secretion are at the pathological core of these metabolic abnormalities. Whereas isolated IFG is associated with impaired insulin resistance in the liver, impaired first phase stage insulin secretion, and near normal insulin resistance in the muscle, IGT is associated with moderate to severe insulin resistance in the muscle, and impaired first and second phase insulin secretion[61]. The National Institute for Health and Care Excellence (NICE) guidelines define IFG as having a fasting plasma glucose between 6.1 mmol/L and 6.9 mmol/L. Conversely, IGT is defined as having a fasting plasma glucose less than 7.0 mmol/L and a 2-hour venous plasma glucose (after ingestion of 75g oral glucose load) between 7.8 mmol/L and 11.1 mol/L[62]. Chronically elevated blood plasma glucose causes considerable damage to the macro and micro vascular systems[63]. Consequently, pre-diabetes is strongly associated with elevated risk of the T2DM and CVD. For instance, a meta-analysis involving 53 population cohorts show that compared with normoglycemia, prediabetes is associated a higher risk of composite CVD (RR 1.13 IFG, RR 1.30 IGT, *p* <0.001), coronary heart disease (RR 1.10 IFG, RR 1.20 IGT, *p* <0.001), and stroke (RR 1.06, RR 1.20, *p* <0.001)[64]. Concerning diabetes, 70% of prediabetics will eventually develop T2DM[61]. In a meta-analysis of prospective studies, the absolute annual incidence of T2DM in individual with IFG or IGT varied from 5% to 10%[65]. Furthermore, compared with normoglycemic people, the risk of developing T2DM was 5 times higher in people with IGT (RR 6.35 95% CI 4.87,7.82), 3 times higher in people with IFG (RR 4.66 95% CI 2.47, 6.85), and 11 times higher (RR 12.13, 95% CI 4.27, 20.00) in people with both IFG and IGT[65].

Cardiometabolic Syndrome

Cardiometabolic syndrome, commonly referred to as metabolic syndrome (MetS), is the clustering of metabolic abnormalities associated with an amplified risk of CVD and T2DM[66]. The components of the MetS include abdominal obesity, hypertension, atherogenic dyslipidaemia, insulin resistance with or without impaired glucose tolerance, and a prothrombotic and proinflammatory state. Several health bodies have devised definitions of MetS, including the World Health Organisation (WHO)[67], the European Group for the Study of Insulin Resistance (EGIR)[68], the International Diabetes Federation

(IDF)[69], and the National Cholesterol Education Program Adult Treatment Panel III (NCEP APT III)[69,70]. From this group, the NCEP APT III 2005 definition is the most widely used criteria of MetS (Table 1.2). Findings from several meta-analyses of prospective studies show a strong association between MetS and elevated CVD risk[71,72]. In a meta-analysis involving 87 prospective cohorts and more than 900,000 individuals, MetS was associated with an elevated risk of CVD (RR 2.35 95% CI 2.02, 2.73), CVD morality (RR 2.40 95% CI 1.87, 3.08), myocardial infarction (RR 1.99 95% CI 1.61, 2.46), and stroke (RR 2.27 95% CI 1.80, 2.85)[72]. Equally, there is a large body of compelling evidence to show that MetS significantly increases the risk of developing T2DM. In a meta-analysis involving 13 cohorts, MetS (diagnosed using the NCEP ATP III 2001 definition) increased the risk of developing T2DM 4-fold (RR 5.12 95% CI 3.26, 8.05)[72]. Globally, the incidence of MetS parallels the incidence of obesity as well as the incidence type 2 diabetes[73]. In the UK, MetS is thought to affect an estimated 1 in 3 adults over the age of 50[74].

Table 1.2 NCEP ATP III 2005 Criteria for the Diagnosis of Metabolic Syndrome

NCEP ATP III 2005 Criteria for Diagnosis of Metabolic Syndrome	
Clinical Measure	**NCEP ATP III 2005┼**
	Any 3 of the following 5 features
Body weight	WC ≥ 102cm in men or ≥ 88cm in women
Lipid	TG ≥ 150mg/dL
	HDL-c < 40mg/dL in men or < 50mg/dL in women
Blood Pressure	≥ 135/85mmHg
Glucose	FG ≥ 100mg/dL (includes diabetes)
Abbreviations: WC waist circumference, TG triglycerides, HDL-c high density cholesterol, FG fasting glucose.	
Keys: ┼ criteria for glucose cut-offs were updated in 2005. The glucose cut-offs in the earlier 2001 criteria were FG ≥ 110mg/dL	

1.2.4 Determinants of Cardiometabolic Diseases

Cardiometabolic disease has a long incubation period and an intrinsically complex aetiology owing to the joint influence of genetic, environmental, and behavioural factors potentiating risk. The determinants of cardiometabolic disease have been widely studied and can be divided into two groups: modifiable and non-modifiable factors of risk. Figure 1.1 illustrates the known modifiable and non-modifiable factors associated with cardiometabolic risk. This thesis will focus only on the effect of alcohol consumption on cardiometabolic disease risk, as well as its association with dietary intakes. Consequently, the role of other risk factors in the development of cardiometabolic disease risk will not be discussed.

Figure 1.1 *Determinants of Cardiometabolic Disease*

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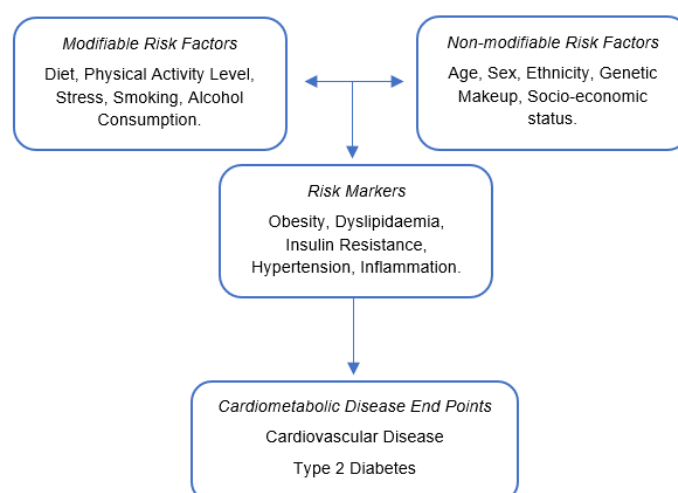
1.3 Alcohol Consumption and Cardiometabolic Disease Risk

1.3.1 Introduction

Alcohol is a toxic substance, a psychoactive drug, a source of caloric energy, and notably, a leading contributor to the global burden of disease. A 2016 study led by the Global Burden of Disease Alcohol Collaborators show that alcohol is the seventh leading risk factor for deaths and disability-adjusted life years (DALYS)[4]. Findings from this study show that in 2016, 2.2% of age-adjusted female deaths, 6.8% of age-adjusted male deaths, 1.6% of female attributable DALYS, and 6.0% of male attributable DALYS, were attributed to alcohol use[4]. Alcohol use is a causal factor in more than 60 conditions, including cancer of the gastrointestinal tract, breast cancer, acute and chronic hepatitis, cardiovascular disease (CVD), as well as a myriad of psychological disorders[75,76]. Within the UK, alcohol misuse is the leading risk factor for death, ill health, and disability among 15–49-year-olds[77]. In England, the rate of persons 65 years and older admitted to hospital for alcohol-related conditions has risen by 15% since 2008[77]. Currently, the treatment of alcohol-related conditions costs the NHS 3.5 billion pounds per year[77]. The latest government statistics suggest that 49% of adults in England consume alcohol at least once a week[77]. In the UK, the guideline for low-risk alcohol intake is less than 14 units of alcohol per week for both men and women. One unit of alcohol (8g of pure alcohol) refers to a small glass (200ml) of 4.5% alcohol beverage volume (abv) beer or cider, 75ml of standard 13% abv wine, or 25ml of 40% abv standard spirit[78]. This section presents an up-to-date summary of the evidence examining the association(s) between alcohol consumption and cardiometabolic disease.

Alcohol Use and Coronary Heart Disease

Coronary heart disease (CHD) is a major form of CVD that affects the structure and function of the heart. The pathogenesis of CHD involves a build-up of atherosclerotic plaque in the arteries supplying oxygenated blood to the heart. This blockage reduces the blood flow to the heart leading to structural and functional damage. Myocardial infarction (MI), angina, and heart failure are common clinical presentations of CHD. The relationship between alcohol use and CHD is inconsistent across the literature[71–81]. Findings from earlier prospective studies suggest a J/U shaped relationship between alcohol intake and aggregated forms of CHD risk, with moderate drinking[1] associated with a lower risk of CHD than heavy drinking or absenteeism[5–7]. In recent years, there is evidence that the relationship between alcohol use and CHD risk differs for fatal and non-fatal forms of the condition, contesting the claim of a J/U shaped relationship[87]. In a large-scale UK cohort study of 1.93 million people, non-drinking was associated with an increased risk of unstable angina (hazard ratio (HR) 1.33 95% CI 1.21, 1.45), MI (HR 1.32 95% CI 1.24, 1.41) and heart failure (HR 1.24 95% CI 1.11, 1.38), when compared with moderate drinking (within UK low risk threshold guidelines)[88]. Whereas heavy drinking (exceeding UK guidelines) was associated with an increased risk of heart failure (HR 1.22 95% CI 1.08, 1.37), cardiac arrest (HR 1.50 95% CI 1.26, 1.77), and unheralded coronary death (HR 1.21 95% CI 1.08, 1.35). A lower association was observed for heavy drinking and risk of MI (HR 0.88 95% CI 0.79, 1.00), as well as risk of stable angina (HR 0.93 95% CI 0.86, 1.00)[88]. These differential associations between alcohol and forms of CHD were confirmed in a combined meta-analysis involving 83 cohorts, as well as a large prospective study involving more than 30,000 participants from the European Prospective Investigation into Cancer (EPIC-COVID) Nutrition cohort[84,86]. Currently the evidence controversially suggests that for some forms of CHD, alcohol use may offer greater cardio-protection than absenteeism.

Alcohol Use and Stroke

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[1] The definition of moderate drinking varies across the literature. In this section moderate drinking refers to adherence to the UK low risk drinking guidelines, unless specified otherwise.

A stroke is a clinical condition that can be physiologically typified as a neurological deficit attributed to an acute focal injury to the central nervous system (CNS), with no apparent cause apart from that of a vascular origin[89]. There are three main types of stroke: ischemic stroke, haemorrhagic stroke, and transient ischemic attack (TIA). The American Heart Association (AHA) defines an ischemic stroke as an episode of neurological dysfunction secondary to focal cerebral, spinal, or retinal infarction (tissue necrosis secondary to inadequate blood supply)[89]. By comparison, haemorrhagic stroke is defined as rapidly developing signs of neurological dysfunction attributed to a focal collection of blood within the brain parenchyma (intracerebral haemorrhagic stroke), or within the subarachnoid space (subarachnoid haemorrhagic stroke) not caused by trauma[89]. A TIA, commonly referred to as a 'mini-stroke' is a short episode of neurological dysfunction caused by a transient blockage without acute infarction[89].

It is well-established that heavy alcohol use confers a significantly elevated risk of stroke. Findings from a large UK cohort study showed that in comparison to moderate drinking (within UK guidelines), the risk of ischaemic stroke (HR 1.33, 95% CI 1.09,1.63), intracerebral haemorrhage (HR 1.37, 95% CI 1.16-1.62) and TIA (HR 1.11, 95% CI 1.02-1.21) is higher with heavy alcohol use (exceeding UK guidelines)[82]. These results are concordant with findings from other prospective cohort studies and combined meta-analyses[82,84,86,90–92]. In a recent meta-analysis involving 599,912 current drinkers across 83 cohorts, the risk of stroke (all types) also increased with increasing alcohol intake (HR per 100g per week higher consumption 1.14 95% CI 1.10-1.17)[86]. Conversely, the relationship between moderate alcohol use and stroke appears to differ for different stroke subtypes. Findings from a meta-analysis involving 27 cohorts showed that low alcohol use (< 1 drink per day) and moderate alcohol use (1-2 drinks per day) was associated with a lower risk of ischemic stroke (low alcohol use relative risk (RR) 0.90 95% CI 0.85 – 0.95; moderate alcohol use (RR) 0.92 95% CI 0.87 – 0.97) than absenteeism[93]. However, a non-significant association was observed between light alcohol use, moderate alcohol use, and risk of haemorrhagic stroke[93]. These results align with findings from a recent large UK cohort study where absenteeism from alcohol was associated with a 33% higher risk of ischemic stroke[82]. Yet the significant difference in the risk of haemorrhagic stroke was non-significant between those who consume alcohol moderately (within UK guidelines) and those who report lifetime alcohol absenteeism[82].

Concerning mortality, findings from a case-cohort study within the EPIC-CVD cohort show a higher risk of fatal stroke in non-drinkers than those who consume low amounts (1-4g alcohol per day)[84]. The results of a meta-regression also show a lower risk of mortality from stroke in moderate drinkers compared with non-drinkers (alcohol use of 2.5-14.5 g/day RR 0.86 95% 0.75 – 0.99)[92]. Amongst those who drink alcohol, evidence suggests a linear association between alcohol intake and mortality from stroke. For instance, the findings of a meta-analysis suggests that amongst drinkers the risk of experiencing a fatal stroke increases by 13% per 100g increase in alcohol intake per week (HR 1.13 95% CI 1.07-1.19)[86]. These findings suggest that the risk of experiencing a fatal stroke is higher in heavier drinkers than those who consume alcohol in low to moderate amounts. The evidence comparing the risk of fatal stroke in those who drink heavily and those who abstain is more divisive. In a pooled analysis of 10 cohorts, a non-significant difference in risk of mortality from stroke was seen between heavy alcohol intake and alcohol absenteeism[92]. Comparable results were also reported in a recent EPIC-cohort case-cohort study and another large meta-analysis involving 27 prospective cohort studies[93,94]. As such, these findings do not propose an added protection from alcohol abstinence and experiencing a fatal stroke.

1.3.2 Alcohol Consumption and Type 2 Diabetes

As defined above, T2DM is a chronic condition characterised by insulin resistance and chronic hyperglycaemia. There is a growing consensus that alcohol consumption may influence the risk of developing T2DM. However, the nature of this relationship is still unclear. Findings from several observational studies propose a protective role of moderate alcohol use against risk of developing T2DM[95–98]. In a 2016 meta-analysis, the risk of T2DM for low (0-12 g/day), moderate (>12-24 g/day), and heavy (≥24 g/day) levels of alcohol intake was evaluated in reference to minimal alcohol use (occasional/ non-drinker). Compared with the minimal category of alcohol intake, the pooled relative risk of developing T2DM was lower in the low-alcohol use category and the moderate alcohol use category (RR low alcohol use 0.83 CI 95% 0.73 – 0.95; RR moderate alcohol use 0.74 95% CI 0.67 to 0.82)[97]. Conversely, the relationship between heavy alcohol use and incidence of T2DM is more conflicting. Several large meta-analyses have shown a non-significant difference in pooled T2DM risk between heavy drinkers and non-consumers[96,97]. However, these results differ from the findings of a recently (2020) published meta-analysis, which reported a positive association between heavy alcohol use (> 52g per day) and risk of T2DM in Asian men (RR 1.16 95% CI 1.04-1.29)[99]. To

summarise, while observational evidence points to a protective effect of moderate drinking against T2DM, the evidence for an effect of heavy alcohol use is conflicting and calls for further investigation.

1.3.3 Alcohol Consumption and Risk Markers of Cardiometabolic Health

Alcohol Use, Dyslipidaemia and Markers of Inflammation

Observational and experimental studies have demonstrated an effect of alcohol consumption on blood lipid markers, specifically HDL-c, LDL-c, and triglycerides. In epidemiological studies, an increase in alcohol consumption has been linked to an improved lipid profile. Findings from these studies suggest a positive association between alcohol consumption, HDL-c levels, HDL-c particle concentration, and HDL-c subfractions[100–103]. These findings are supported by evidence from experimental studies[104,105]. In a meta-analysis involving 63 experimental studies, alcohol consumption was positively associated with circulating HDL-c concentration after adjusting for confounding influences[105]. The proposed cardio-protective effect of moderate alcohol consumption is thought to occur through the effect of alcohol on effect on HDL-c[106]. Nevertheless, the mechanisms and evidence behind this causal link remains unclear.

Alcohol consumption has also been shown to influence LDL-c and triglyceride levels. A lowering effect of alcohol consumption on LDL-c has been reported in a recent meta-analysis of experimental studies[107]. However, findings from other experimental and observational studies do not corroborate this association[108–110]. The evidence for an effect of alcohol consumption on triglycerides levels is equally inconsistent. In an earlier meta-analysis of interventional studies, alcohol use was positively associated with an increase in triglyceride levels[104]. However, more recent evidence suggests that alcohol use does not affect triglyceride levels unless consumed in high quantities (suggest dose of >60g alcohol per day)[107,109,110].

As noted above, CRP is an acute phase reactant and an important inflammatory marker indicative of cardiometabolic disease risk. The association between alcohol use and CRP levels has been assessed in several studies. Findings from meta-analyses of experimental studies suggest a non-significant effect of alcohol use on circulating CRP following ingestion of alcohol[105,107]. However, the results of observational studies contradict these findings and suggest a lowering effect of moderate alcohol consumption on circulating CRP[111–115]. From these observational findings, an anti-inflammatory effect of moderate alcohol use has been proposed. Additionally, this anti-

inflammatory effect has been suggested as a potential mechanism by which moderate alcohol consumption lowers risk of CHD.

Alcohol Use and Obesity

The relationship between alcohol use and obesity has been widely studied. However, the results of these studies are inconsistent. For instance, several studies have reported a negative association or no association between alcohol use and markers obesity or adiposity[116–119]. Other studies have shown that alcohol use, especially heavy alcohol use, is positively associated with obesity[120,121]. In 2021, the first meta-analysis to examine the relationship between alcohol use, abdominal, and general obesity in adults was published[122]. In this study, a pooled analysis of cohort studies did not show an association between alcohol use, overweight, obesity, or abdominal obesity. In contrast, a pooled analysis of cross-sectional evidence showed that alcohol use was associated with a higher risk of being overweight (odds risk (OR) 1.11 95% CI 1.05-1.18), and of having abdominal obesity (OR 1.19 95% CI 1.09-1.29). Additionally, findings from a dose-response analysis suggest that heavy alcohol use (>28 g/day) is positively associated with a higher risk of overweight/obesity (OR 1.32 95% CI 1.16-1.51) and a higher risk of abdominal obesity (OR 1.25 95% CI 1.12-1.38) compared with absenteeism or light drinking. Few experimental studies have examined the effect of alcohol use on markers of obesity. However, for ethical reasons, only the effects of moderate alcohol use have been examined. In a 4-week intervention study, the addition of alcohol (amount equal to 620kcal) to the daily diets of 12 men did not lead to significant mean changes in the body weight[123]. However, following this intervention more than 50% of participants with obesity at baseline gained weight. Similarly, in another study of 14 men, the addition of 2 glasses of wine with dinner over a 6-week did not lead to a change in weight or body fat[123]. However, the researchers of this study could not conclude whether energy taken in from alcohol was compensated by a change in dietary intakes.

The aetiology of obesity involves a chronic disruption of energy balance, whereby energy intake is greater than energy expenditure[124]. Alcohol is a metabolic fuel with a high energy density (7kcal per gram), second only to fat. Findings from appetite studies suggest that ingestion of alcohol stimulates appetite and leads to an increase of food intake[8,125,126]. Based on this evidence, it is biologically plausible that alcohol consumption could lead to an energy imbalance and play a key role in obesity.

Alcohol Use and Impaired Glucose Metabolism

Moderate alcohol consumption has been positively associated with a reduced risk of T2DM, compared with absenteeism and heavy alcohol use[95–98]. This claim is supported by evidence from interventional studies that have demonstrated a favourable association between glycaemic control and moderate alcohol intake. In a systematic review and pooled analysis of interventional studies, moderate alcohol consumption had a significant lowering effect on mean fasting glucose and fasting insulin levels compared to absenteeism[127]. Findings from observational studies are less consistent. Some studies show an inverse association between moderate alcohol use and markers of glycaemic control[91,128]. Ohers have demonstrated a positive effect or no effect at all[127,129–133]. From a biological standpoint, experimental studies have shown that moderate alcohol consumption reduces hyperglycaemia by inhibiting hepatic gluconeogenesis[106]. Experimental studies have also shown a positive effect of acute moderate alcohol consumption on insulin sensitivity. This effect is thought to occur through pathways involving serum adiponectin, as well as free fatty and adipose tissue metabolism[106].

In contrast to the effects of moderate alcohol use, heavy alcohol use (excluding alcoholism) is associated with impaired glucose tolerance. Most observational studies have shown that the odds of a higher fasting blood glucose are higher in heavy drinkers than those who abstain or consume alcohol in low or moderate amounts[127,130–132,134].

Alcohol Use and Blood Pressure

Alcohol consumption has a biphasic effect on blood pressure[135]. While ingestion of alcohol is followed by an acute drop in blood pressure, chronic alcohol consumption is a recognised risk factor of hypertension (blood pressure ≥ 140/90 mmHg)[136]. The association between chronic alcohol consumption and hypertension is widely supported by evidence from observational, interventional, and mendelian randomisation studies. Intervention studies have provided convincing evidence of a causal relationship between alcohol and elevated blood pressure. In a recent systematic review and meta-analysis, a reduction in alcohol consumption was associated with a significant reduction in blood pressure in persons who consume more than 2 standard drinks per day (1 drink contains 12g/1.5 units alcohol)[137] Observational studies have also demonstrated a positive correlation between habitual alcohol consumption and elevated blood pressure[138–143]. The findings of a large meta-analysis in 22 cohort studies, suggests that a 10g increment in daily alcohol consumption corresponds

to a 6% rise in blood pressure in Caucasians (RR 1.06 95% CI 1.01-1.10)[140]. Some epidemiological evidence also suggests a sex-specific effect of alcohol consumption on elevated blood pressure[144–146]. However, these findings are inconclusive.

Alcohol consumption has been strongly linked to mutations of genetic variants that encode enzymes involved in alcohol catabolism, including alcohol dehydrogenase 1 (ADH1) and dehydrogenase 2 (ADH2)[147]. The G to A allele mutation of ADH1 on chromosome 4 (rs1229984) and the G to A allele mutation of AHD2 on chromosome 12 (rs671) are 2 major variants associated with alcohol consumption[147]. The causal link between alcohol consumption and hypertension has been confirmed by findings from mendelian randomisation studies. Findings from a mendelian randomisation meta-analysis of 56 epidemiological studies, showed that carriers of the ADH1 A allele consumed less alcohol than non-carriers, had significantly lower systolic blood pressure, and a lower risk of hypertension[148]. Other mendelian randomisation studies in Asian populations have also consistently supported the causal relationship between alcohol consumption and blood pressure[149,150].

1.3.5 Differential Effects of Beverage Consumption and Drinking Patterns.

The effects of alcohol consumption on cardiometabolic disease and markers of cardiometabolic disease risk are not limited to the amount of alcohol ingested. Studies have suggested that the effects of alcohol on cardiometabolic risk differ with both the type of alcoholic beverage and the pattern of alcohol consumption.

The French paradox is the observation of low coronary heart disease in southern France despite high intakes of saturated fat. This phenomenon was accredited to the high consumption of red wine in the area[151]. This occurrence was first noticed in the early 1990s and led to extensive research into the cardioprotective properties of red wine. Since then, the differential effects of alcoholic beverages on cardiometabolic risk have been widely studied. Some studies have suggested that the cardioprotective effects of wine are superior to beer and spirits[131,151–158]. However, this claim is speculative and there is growing evidence to suggest the amount of alcohol ingested has a greater impact on cardiometabolic disease risk than the type of alcoholic beverage consumed. In a study investigating the differential effects of alcoholic beverages on the risk of CHD, all significant associations between beverage type and risk disappeared after controlling for total alcohol consumption[159]. Findings from a more recent meta-analysis involving 13 cohorts suggest that the

relationship between wine and risk of a vascular event is comparable to the relationship between beer and risk of a vascular event[160]. Wine and beer share similar biochemical properties with both beverages having a high polyphenol content[161]. Polyphenols have antioxidant and anti-inflammatory properties, and the intake of these biomolecules has been strongly associated with a reduced risk of chronic disease[162]. Furthermore, a review of several large observational studies examining the differential effect of wine, beer, and spirits on the risk of ischemic heart disease (IHD) also found no evidence to confirm that the cardioprotective effect of one alcoholic beverage is superior to another[163]. The differential effects of alcoholic beverages on cardiometabolic risk remains inconclusive and calls for further investigation.

According to the UK guidelines, low risk alcohol intake refers to an intake ≤ 14 units per week, spread out over a 7-day period [78]. Binge drinking refers to an excessive intake of alcohol in a singular drinking occasion. In the UK, it is defined as an intake of ≥ 8 units or ≥ 6 units of alcohol in a singular drinking occasion, for men and women, respectively [78]. It is widely acknowledged that binge drinking has deleterious effects on cardiometabolic health. The hangover from a binge occasion to is thought to elevate cardiometabolic risk through its dysregulation of inflammatory cytokines and influence on atherosclerosis[162]. Several prospective studies have demonstrated that binge drinking, even within in light to moderate drinkers, elevated the risk of CHD[164,165]. Notably, the associations between pattern of consumption and risk persisted after controlling for average volume of intake. More recent findings from a pooled analysis also highlighted a differential effect for pattern of consumption irrespective of total alcohol consumed. In this pooled-analysis, the risk of CHD was higher in heavy-binge drinkers than heavy non-binge drinkers, compared to those who abstain (pooled RR heavy binge drinker 1.10 95% CI 1.03 to 1.17, pooled RR heavy non-binge drinker 0.75 95% CI 0.64 to 0.89)[166].

The number of studies investigating the effect of binge drinking on cardiometabolic health is scarce. For ethical and practical reasons, the independent effect of binge drinking on health cannot be examined in a clinical setting. The findings of a social behaviour study also show that light and moderate drinkers do not drink daily[167]. While those that do drink daily, tend to drink heavily[167]. Furthermore, the definition of binge drinking differs with geographic location and is often conflated with patterns of heavy drinking[168]. Regardless, drinking pattern is an important consideration when unpicking the relationship between alcohol intake and cardiometabolic disease risk.

1.4 Alcohol Consumption and Diet

1.4.1 Introduction

While the relationship between alcohol use, disease risk, and health has been extensively studied, less attention has been given to its influence on other lifestyle behaviours, notably dietary habits. Understanding the association between alcohol use and diet could help clarify the link between alcohol use and health. This section will summarise the limited evidence that has examined the effect of alcohol use on diet.

1.4.2 Alcohol Use and Total Energy Intake

The ingestion of alcohol has been shown to stimulate appetite and increase food intake by bypassing the satiety mechanisms that govern short term food intake[8,9]. There is strong experimental evidence to suggest that alcohol consumption has an additive effect on total energy intake[8,126]. Findings from a recent pooled analysis involving cross-over and randomised control trials suggest that drinkers do not make dietary changes to compensate for energy provided by alcohol intake. Compared to a non-alcoholic comparator, the consumption of an alcoholic beverage increased both food energy intake (weighted mean difference 343 95% CI 161-525 kilojoules) and total energy intake (weighted mean difference 1072 95% CI 820-1323 kilojoules)[126]. While the experimental evidence is clear-cut, the findings from observational studies are less consistent. In a large prospective study of Australian participants, researchers observed a higher mean total energy intake in participants who reported alcohol intake compared to those who abstained[169]. By comparison, observational studies in some European populations have also demonstrated an additive effect of alcohol on total energy intake. The findings of a cross-sectional analysis in a French cohort showed a positive correlation between alcohol consumption and energy intake independent of energy derived from alcohol[170]. Comparable results were reported by the Heidelberg EPIC (European Prospective Investigation into Cancer) examining the association between alcohol, diet, and anthropometric markers in a German population[171]. In contrast to these studies, a cross-sectional analysis of nutrient intake data in in the US showed that heavy drinkers (≥ 3 drinks per day) consumed less non-alcoholic energy compared to moderate drinkers (≤ 2 drinks per day)[172]. These findings from the US suggest that heavy drinkers compensate for energy derived from alcohol by reducing energy intake from non-alcohol containing sources. An independent cross-sectional study in women of child-bearing age in New Zealand observed similar findings. In this study, the consumption of alcohol was shown to substitute energy

derived from non-alcohol containing sources[173]. Alcohol use is strongly influenced by societal and cultural factors[1]. For instance, in Mediterranean European countries, alcohol consumption tends to be more frequent and coincide with the meal environment[174]. By comparison, in other countries (the UK, Ireland, Northern Europe) alcohol consumers are less likelihood to drink every day, but when drinking does occur there is a higher likelihood that it leads to intoxication[174]. Cultural and societal influences could explain why the relationship between alcohol use and energy intake appears to differ with geographic location.

1.4.3 Alcohol Use and Macronutrient Intake

Several studies have examined the effect of alcohol use on dietary macronutrient composition e.g., contribution of energy derived from carbohydrate, protein, and dietary fat. However, the evidence is conflicting. In a recent systematic review involving 11 observational studies, 36% of studies reported an inverse association between frequent heavy drinking and energy derived from fat. Another 36% observed higher intakes of fat with heavier alcohol use, and 28% reported no association. Similar findings were observed for heavy alcohol use and protein intake[175]. In contrast, 90% of studies reviewed observed a dose-dependent inverse association between heavy alcohol use and energy intake derived from refined carbohydrates. Similarly, 91% of the studies observed an inverse association between heavy alcohol use and the intake of unrefined carbohydrates. By comparison, the relationship between moderate alcohol use and carbohydrate intake is less consistent. Some studies suggest that moderate drinkers have higher intakes of refined and unrefined carbohydrate than never or former drinkers[175]. However, an equal proportion of studies also report either an inverse association or no association at all. Concerning dietary fat, most studies observed a non-significant difference in intake between moderate drinkers and non-drinkers[175]. Equally, most studies found no association between moderate alcohol use and energy intake derived from protein[175].

Several experimental studies have examined the relationship between a single drinking occasion and macronutrient intake, with similar differing results. The findings of a systematic review assessing the experimental evidence concluded that a single occasion of light to moderate alcohol use is more likely to lead to greater intakes of energy from fat and carbohydrate relative to experiments testing the effect of heavy alcohol use[175]. In contrast, most of the experimental evidence reports a non-significant effect of a single drinking occasion on intakes of unrefined carbohydrates. Importantly,

these findings suggest that the effect of alcohol use on dietary macronutrient composition does not appear to differ for men and women[175].

Other studies have examined the difference in the dietary macronutrient intakes of current drinkers on drinking versus non-drinking days. In a cross-sectional analysis of 1864 current drinkers, moderate male drinkers reported a higher mean non-alcoholic energy intake as well as a higher intake of energy derived from carbohydrate, protein, and fat on drinking days compared to non-drinking days[176]. By comparison, moderate female drinkers did not consume excess non-alcoholic energy on drinking days but did report a higher intake of energy from dietary fat[176].

1.4.4 Alcohol Use and Dietary Pattern

Dietary pattern analysis is an important approach to examining the relationship between diet and health. Instead of looking at the relationship between a single nutrient or food and a disease, dietary pattern analysis examines the whole diet and is better representative of a person's food and nutrient consumption. Approaches to dietary pattern analysis include factor analysis, cluster analysis, and dietary indices[177]. Factor analysis is comprised of multivariate statistical techniques that are used to identify common patterns of food consumption. Using this approach, a summary score is derived from the correlation of food or specific food items in a dataset. This score is then used to examine the correlation between diet and health. Cluster analysis is another multi-variate statistical technique that involves aggregating individuals with similar dietary patterns. By comparison, dietary indices are constructed against dietary recommendations and used to score an individual's adherence to a guideline. Commonly used dietary indices included the dietary approaches to stop hypertension (DASH) index, the healthy eating index (HEI), and the diet quality index (DQI). Additionally, there are several indices that measure adherence to the Mediterranean dietary pattern, for which the moderate intake of red wine is an integral component[178].

Several studies have examined the effect of alcohol use on diet quality, with most reporting a deterioration in diet quality with heavy alcohol use. In a longitudinal study of 4956 young adults, non-drinkers, and moderate drinkers reported higher intakes of fruit, vegetables, and wholegrains, and fewer intakes of red meat and sugary drinks than heavy drinkers[179]. Similarly, in a cross-sectional analysis of dietary intake in a US population, quantity of alcohol consumed was inversely associated with a HEI score, suggesting a worsening of diet quality with increasing alcohol intake[180]. These findings are supported by the results of a smaller study in a French population. In this study, a dietary

pattern identified using factor analysis and characterised as prudish (healthy) was inversely associated with increasing levels of alcohol intake[181].

The effect of alcohol use on diet quality is also thought to differ with alcoholic beverage preference and pattern of consumption. Findings from a cross-sectional analysis of dietary intakes in the US, showed that infrequent heavy drinkers had the lowest HEI score compared to frequent light drinkers[180]. The results of a longitudinal study also suggest that binge drinkers less likely to follow a healthy dietary pattern than non-binge drinkers[179]. The relationship between alcoholic beverage preference and diet quality is less consistent. The findings of recently published systematic review suggest that wine drinkers have healthier dietary patterns than those who primarily drink beer or spirits[182]. However, this finding was limited to non-Mediterranean study populations, suggesting that the effect of beverage preference on diet quality is dependent on geographic location.

1.5 Alcohol, Genetics, and Cardiometabolic Health

The genome wide association study (GWAS) is an experimental design to identify genetic variants that are associated with a specific disease or trait by examining the difference between the frequency of alleles in a population of a shared ancestry that differ phenotypically. To date more than 5700 GWAS studies have been conducted for more than 3300 traits [183]. Results from GWAS have a myriad of applications. Firstly, these findings can offer greater insight into the biology of complex traits which can lead to more targeted therapy and treatment of disease. In the field of epidemiology, trait-associated genetic variants can be used as control variables to account for the confounding group differences, replicating the conditions of a randomized control trial. This application allows researchers to explore the relationships between behaviours and health wherein an experimental trial would be deemed unethical. For example, studies investigating the relationship between alcohol intake or drug use and health outcomes. Genome wide association studies have unequivocally shown that most complex traits are governed by several causal variants that individually confer very little effect. However, combining these variants into a polygenic risk score allows researchers to capture an individual's susceptibility to a disease or trait. Polygenic risk scores are calculated as weighted sum scores of risk alleles, with the weights based on the effect sizes from GWAS[184]. Polygenic risk scores (PRS) are widely applied in research and are laying the groundwork for an era of personalised medicine. For example, PRS can be used alongside traditional screening tools to identify individuals at high risk of disease. However, although the development of GWAS has

significantly advanced scientific research and knowledge for a wide range of diseases and traits some argue that that GWAS will eventually implicate the entire genome in disease predisposition and that most association signals reflect variants and genes with no direct biological relevance to disease[184].

Candidate gene studies and genome wide association studies have identified a considerable number of SNPS related to cardiometabolic disease and disease traits[185–189]. For example, a recent genetic analysis of over 1 million people identified near 535 loci associated with blood pressure traits[190]. Genome wide association studies have also identified and confirmed a number of genetic variants associated with incidence of Type 2 Diabetes and to date more than 400 genetic variants have been linked to this condition[184]. To extend on this, there is good evidence that the effect of genetic variants on cardiometabolic traits can be modified by lifestyle factors. Evidence from a prospective cohort study showed that an increase in diet quality significantly attenuates the genetic association with change in body mass index[191]. Other studies have demonstrated similar findings when examining the inter-play dietary intake and genetic predisposition to poor glycaemic control[192]. Similarly, there is some evidence that alcohol intake can modify the genetic predisposition to cardiometabolic diseases and traits[193–196]. A study in a Chinese cohort demonstrated that alcohol drinkers with a high predisposition to T2DM were at greater risk of developing T2DM compared to non-drinkers within the same genetic risk strata. However, despite the growing body of evidence, there are still gaps in the literature. For example, GWAS studies have identified many genetic variants associated with varying HDL-c levels across large populations of different ethnic backgrounds. These genetic variants include those implicated in the biogenesis (APOA1, APOA2, APOA33, APOA4, ABC A-1), functionality (LCAT) and regulation (CEPT, LPL, LIPC, LIPG, SCARB1, PLTP, ANGPLT3 ANGPLT4) of HDL-c [197]. For example, the expression of APOA1 and APOA2 genes result in the biogenesis of apolipoprotein A-1 and apolipoprotein A-2 which are the protein constituents of HDL-c[198,199]. Other genes associated with HDL-c include the CEPT gene and ABC gene family. The CEPT gene and ABC gene family play important roles in the reverse cholesterol transport system by expressing proteins that ensure the efflux of cholesterol to and from the HDL-c particle[199,200].

Given the important role these genes play in HDL-c metabolism, its plausible that an interplay between variants on these genes and lifestyle behaviours e.g., alcohol intake, could explain the

increasing effect of alcohol on circulating HDL-c levels. However, to date only a small number of studies have examined this association with inconsistent findings[193,201–203]. For instance, lipoprotein lipase (LPL) is an enzyme implicated in the regulation of HDL-C. This enzyme takes part in the initiation of the HDL-C maturation process where this enzyme hydrolyses triglyceride rich lipoproteins releasing apo[197,199]. A recent study investigating the interactive effects between a common LPL polymorphism and lifestyle factors on HDL-c observed an interaction for alcohol intake[203]. Findings from this study suggest that alcohol intake may influence HDL-c levels by modulating LPL gene expression. However, these results are not consistent across the literature. For example, a cross sectional study failed to observe an alcohol-gene interaction for common LPL variants. Furthermore, this study failed observe an alcohol-gene interaction for common variants in more than 19 other candidate genes implicated in the biogenesis and regulation of HDL-C, including ABCA1, CETP, GALNT2, LIPC, MVK+MMAB APOA1, APOA2, APOA4, APOA5, APOC1, APOC2, APOC4, APOD, APOE, and PON1, PON2, PON3.

1.6 Limitations and Gaps to the Research

The cardioprotective benefits of alcohol consumption is a topic of debate in public health. An accumulative body of observational evidence demonstrates a U/J shaped relationship between alcohol use and cardiometabolic disease risk. However, these studies share several limitations that may reduce the strength of the evidence, including inconsistent definitions of moderate alcohol intake, weak and heterogeneous methodologies for measuring alcohol use, and inadequate controlling for the influential effect of confounding variables.

A universal definition on what constitutes moderate alcohol intake is not in use. Across the literature moderate alcohol intake can range from >0.1 g/day to ≤ 30g/day. While some studies have attempted to define thresholds of alcohol use associated with the lowest risk of CVD morbidity and mortality[86], an agreed definition of moderate alcohol intake has not been confirmed. This inconsistency makes extrapolating the data problematic. Furthermore, many studies do not distinguish between lifetime abstainers and former drinkers. Former drinkers may have given up drinking alcohol for health reasons, and therefore combining these groups could introduce bias. Additionally, many studies examine the effect of alcohol use on health using a single measure of alcohol intake and fail to take into consideration the cumulative variation in alcohol drinking behaviours. A consensus guideline on how to measure alcohol intake in large populations advises that assessments of alcohol intake

measure pattern of consumption in conjunction with average intakes. A single-axis approach to alcohol intake assessment may result in highly significant but misleading associations.

Another major limitation of previous research is the inadequate control for confounding influences, most notably the confounding effect of dietary intake. Diet is a well-established risk factor for cardiometabolic disease with a plethora of studies demonstrating an inverse association between diet quality and cardiometabolic disease risk[204–211]. There is evidence to suggest that alcohol consumption influences dietary habits and as such it, is reasonable to question whether diet is in part responsible for the U/J shaped relationship between alcohol use and cardiometabolic risk. Regardless, most studies either have not controlled or have inadequately controlled for the confounding effect of diet. To clarify, while some studies used total energy intake as an indicator of dietary health[127,130], other studies used poorly correlated proxy measures such as receipt of GP (General Practice) provided dietary advice[88]. Moreover, in studies examining the differential effects of consumption pattern or alcoholic beverage preference on cardiometabolic risk, few controlled for the confounding influence of total alcohol intake. This failing could potentially exaggerate the beneficial effects of one alcoholic beverage over another.

Although the relationship between alcohol and cardiometabolic health has been extensively studied, there are several gaps in the literature. Alcohol consumption behaviour is influenced by cultural and societal factors, leading to international differences in how alcohol is consumed. Consequently, alcohol-cardiometabolic associations derived outside the UK, protective or otherwise, may not be applicable to a British cohort. To the author's knowledge, no study has yet examined the multi-dimensional effect of alcohol use on cardiometabolic disease risk in conjunction with its effect on diet in a British study population. Additionally, more studies are needed to understand the complex interplay between genetic and lifestyle factors in determining cardiometabolic disease risk. Moderate alcohol intake is thought to lower cardiometabolic risk through its effect on HDL-c. More studies are needed to understand whether alcohol consumption increases HDL-c levels through modulation of HDL-related genes.

1.7 Chapter Summary

Cardiometabolic disease is a leading cause of morbidity and mortality and places a significant burden on the UK's national health service. Research has associated moderate alcohol consumption with a reduced cardiometabolic risk. However, inherent methodological weaknesses, inconsistent definitions

of moderate alcohol intake, and poor control of influencing variables, notably dietary behaviour, reduces the strength of the evidence. Dietary behaviour is a well-established risk factor for cardiometabolic disease. Additionally, dietary patterns often vary with different alcohol consumption behaviours. However, methodological limitations have prevented a thorough assessment that captures the multi-dimensional effect of alcohol use on diet. Clarifying the multi-dimensional effect of alcohol use on dietary behaviour is a crucial step in understanding to what extent the association between alcohol and cardiometabolic disease is attributable to alcohol-related changes in dietary behaviour. Furthermore, developments in the field of genomics suggest a genetic contribution to cardiometabolic disease and its traits, equivalent to that of environmental factors. More studies are needed to understand how the genetic predisposition to cardiometabolic disease is modified by alcohol use. This thesis aims to

i.) Comprehensively assess the effect of alcohol on dietary behaviour.

ii.) Examine the dimensional effects of alcohol use on cardiometabolic risk independent of dietary influences.

iii.) Investigate whether the association between alcohol use and HDL-c is attributable to an alcohol-induced effect on HDL-related genes.

1.8 Hypotheses, Research Objectives and Thesis Structure

1.8.1 Research Hypotheses

This thesis tested three hypotheses.

H1 Alcohol consumption behaviour influences dietary intake.

H2 The association between alcohol intake and parameters of cardiometabolic risk is attributable to the effect of alcohol use on dietary intake.

H3 Alcohol use increases circulating HDL-c by modifying the effect of HDL-related genes.

1.8.2 Research Objectives

This thesis uses baseline data from the Airwave Health Monitoring Study and UK Biobank cohort. Using this data, the research objectives were to:

i.) Conduct a comprehensive assessment of alcohol-intake behaviour in two independent UK study populations by:

> a. Measuring average alcohol intake, pattern of consumption, and alcoholic beverage preference using robust methodologies.
>
> b. Investigating the agreement between instruments commonly used to measure alcohol consumption in large populations.

ii.) Describe differences in alcohol consumption behaviours of Airwave Health Monitoring Study and UK Biobank participants across sex categories.

iii.) Conduct a comprehensive assessment of dietary-intake behaviour in two independent UK study populations by:

> a. Generating nutritional and food intake data in the Airwave Health Monitoring Study by analysing 7-day food records and contributing to its growing nutrient data bank.
>
> b. Measuring adherence to the DASH diet as a proxy measure of diet quality, food intakes, and dietary macronutrient composition.

iv.) Describe the dietary profile of UK Biobank and Airwave Health Monitoring participants across sex categories,

v.) Describe the dietary intakes across varying levels of alcohol intake.

vi.) Examine the multi-dimensional effect of alcohol use on dietary behaviours.

vii.) Describe cardiometabolic risk (as evidence by anthropometric and biochemical risk markers) across varying alcohol consumption behaviours.

viii.) Examine the association between alcohol use and cardiometabolic risk independent of diet.

ix.) Investigate the modifying effect of alcohol use on genetic predisposition to cardiometabolic risk by:

> a. Determining the influence of combined genetic risk of circulating HDL-c.
>
> b. Using statistical techniques, examine whether alcohol use modifies the effect of HD-c-related genes on HLD-c levels.

1.8.3 Thesis Structure

As noted above, baseline data from the Airwave Health Monitoring Study and UK Biobank cohort is used in this thesis. The data collection methodologies for both study cohorts are described in Chapter 2. Chapter 3 describes the methodologies used to conduct a comprehensive assessment of alcohol intake and describes the alcohol consumption profiles of AHMS and UK Biobank participants across sex categories. This chapter also investigates the agreement between two instruments commonly

used to assess alcohol intake in large study populations. Chapter 4 outlines the methodologies used to (i) generate dietary data in the AHMS (ii) measure dietary intakes across both cohorts. This chapter also describes the dietary profile of AHMS and UK Biobank participants across categories of sex. Chapter 5 uses the findings from Chapter 3 and Chapter 4 to examine the effect of alcohol use on dietary behaviour. Chapter 6 describes the cardiometabolic profile of AHMS and UK Biobank participants across varying alcohol intake behaviours. This chapter draws on the findings from Chapter 4 and Chapter 3 to understand the extent in which the alcohol-cardiometabolic relation is attributable to its effect on dietary behaviours. Chapter 7 measures the effect of a combined genetic risk score on circulating HDL-c and whether its effect is modified by alcohol use. Finally, Chapter 8 contains an integrated discussion of the main findings from each chapter and based on the interpretation of these findings, recommendations for future research are made.

2.0 Background

This chapter provides a summary background of the recruitment and data collection procedures for the Airwave Health Monitoring and UK Biobank study. Data wrangling and management was performed using R Studio Software version 1.4.11032.2. This chapter outlines data collection and wrangling procedures only for those covariates specific to this thesis.

2.1 Airwave Health Monitoring Study

2.1.1 Study Design

The Airwave Health Monitoring Study (AHMS) is a longitudinal study in an occupational cohort of men and women employed by the British police force. Launched in 2003, the primary aim of the AHMS was to initially evaluate the possible health risks associated with the use of Terrestrial Trunked Radio (TETRA)[212]. Since this time, the study's aim has broadened to also investigate the general impact of occupation on health in the police force.

2.2.2 Recruitment

The AHMS was open to all police forces in the UK. Recruitment procedures have already been described in detail by Elliot et al[212]. As of 2013, 28 police forces (of the 54 that existed at the time) in the UK have agreed to participate in this study (Figure 2.1). From the time of study launch, 53,000 participants have been recruited to this study, of whom c. 46,000 have undergone a health screening. The follow-up of participants living in England began in 2015 and is currently ongoing. This study aims to follow up a minimum of 50% of the baseline cohort. The Airwave Health Monitoring Study is conducted according to the guidelines laid down in the Declaration of Helsinki. The National Health Service Multi-Site Research Ethics Committee (Multi-centre Research Ethics Committee (MREC)/13/NW/0588) approved all procedures involving human subjects. Written informed consent was obtained from all participants.

2.2.3 Data Collection

Participants recruited for this study were invited to attend a baseline health screen appointment. During this appointment, various clinical measurements and biological samples were collected.

Participants completed a self-administered touchscreen questionnaire providing extensive information detailing lifestyle and behaviour. Cognitive tests were also performed to understand cognitive health in the population. A full list of the measurements collected has already been described by Elliot *et al.*[212]. This chapter will delineate the data collection procedures and wrangling measures relevant to the work of this thesis.

Figure 2.1 Enrolment to the Airwave Health Monitoring Study per region by 2012
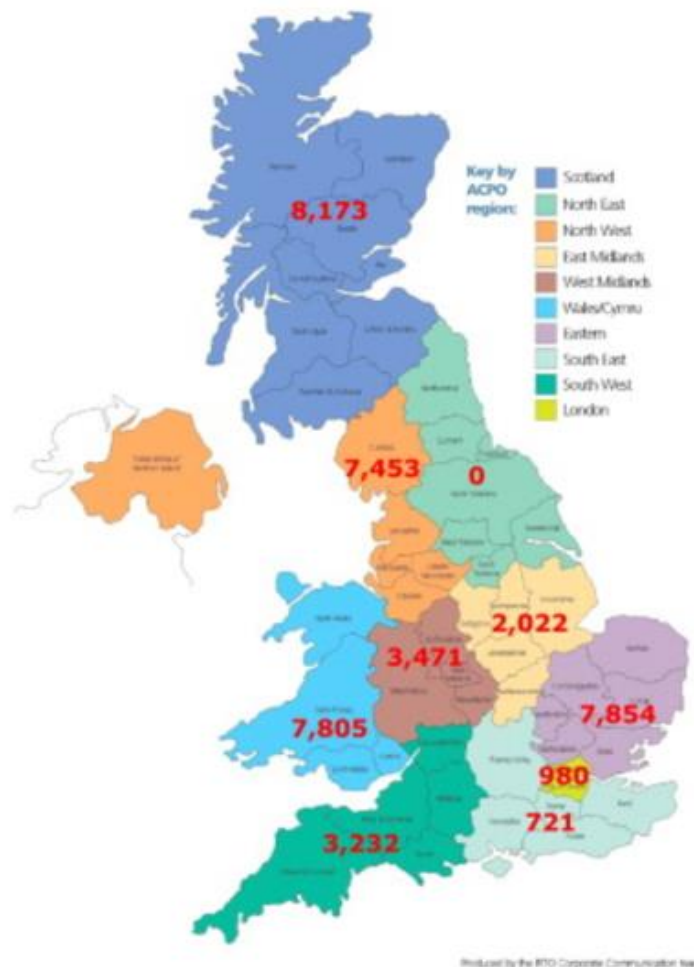
ACPO: Association of Police Chief Officers

Reprinted from *Environ Res*, Elliot *et al.*, The Airwave Health Monitoring Study of police officers and staff in the in Great Britain: Rationale, design, and methods page 280.

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<u>Anthropometric Measures</u>

Trained research nurses took the following anthropometric measurements whilst following a study-specific standard operating protocol[213]. For all anthropometric measures, participants were shoeless and in light clothing. Measurements were taken twice, and the average was recorded.

Bodyweight was measured using a *Marsden Digital Weigh Scale* to the nearest 0.05kg. Standing height was measured using a SECA Leicester Stadiometer. Participants were asked to stand straight, arms relaxed by side and head in the 'Frankfort' plane position. Height was taken to the nearest 0.1cm. Waist circumference was measured at the level of the umbilicus using a Wessex non-stretchable sprung tape measure, to the nearest 0.1cm. Body mass index (BMI) was calculated from measures of weight in height by dividing the weight (kg) by the square of the height (m).

Clinical and Biochemical Measures

Clinical and biochemical measures were collected by a trained research nurse following a study-specific standard protocol[213].

Blood pressure was measured using an Omron 705-IT blood pressure monitor. Three consecutive blood pressure measurements are taken, and the average recorded. Blood samples were taken from the participant in a non-fasted state by a trained phlebotomist. During this procedure 50ml of blood was drawn using the 'vacutainer system'. Blood Samples were spun on-site, (standing for 40 minutes, and then centrifuged at 4300 rpm for 10 minutes), separated into 2ml aliquots and transported overnight (held at 0-4ºC) for further processing at an assigned study laboratory. Biochemical assays using blood plasma were performed to measure blood lipid components (high-density lipoprotein (HDL)(mmol/L), total cholesterol (mmol/L)), and high sensitivity c-reactive protein (HS-CRP) (mg/L). Glycated haemoglobin (HbA1c) was measured using whole blood collect in ethylenediaminetetraacetic acid (EDTA) and reported as a percentage. Blood samples were also used to genotype participants. Genotyping of samples was performed using either an Illumina HumanExome chip, an Illumina HumanCoreExome chip or an Affymetrix chip, dependent on the time of analysis.

Medical and Pharmacological Information

Participant baseline medical history (past and present diagnoses, treatments, therapies) was collected by a trained research nurse at the health screening appointment[213]. The diagnoses and dates of diagnosis of the following conditions were collected: cancer, migraine, diabetes, chronic obstructive pulmonary disease (COPD), asthma, allergy, cataract, glaucoma, epilepsy, arthritis, Parkinson's, hypertension, stroke/transient ischemic attack (TIA), angina, heart attack, thyroid disease, chronic liver disease, and depression. For this thesis, medications prescribed for the

management of cardiometabolic risk were grouped into the following drug categories: blood lipid management, blood glucose control, and blood pressure management.

Socio-economic and Demographic Measures

Participants self-reported for the following characteristics: age (years), sex, ethnicity, highest level of education attained, and household income. Ethnicity was reduced to two categories ('White' and 'Other') as > 95% of participants self-reported as Caucasian. Household income and highest education level were used as proxy measures of socioeconomic status[214].

Lifestyle Behaviours

Information detailing lifestyle behaviours including physical activity, smoking, and alcohol consumption were collected at baseline using the touchscreen health questionnaire. The International Physical Activity Questionnaire Short Form (IPAQ-SF) was used to estimate participant level of physical activity[214]. This questionnaire calculates metabolic equivalents per week across three parameters of exercise (walking, a moderate activity, and a vigorous activity). In line with the IPAQ-SF protocol, participants were classified as low, moderate, or highly active[214]. Regarding cigarette smoking behaviour, participants self-reported their current smoking status as 'Yes' or 'No'. Current smokers provided further information detailing the number of cigarettes smoked per day. Participants were grouped as 'Current', 'Former', or 'Never' alcohol consumers according to self-reported alcohol consumption status. Chapter 4 of this thesis delineates alcohol consumption in terms of average intake, the pattern of consumption, and beverage preference.

Dietary Intake

Dietary intake was collected using a 7-day diet record. Chapter 3 of this thesis describes the dietary data collection and nutritional analysis procedure and protocol. This thesis uses dietary data collected between 2004 and 2012. By the end of 2012, 42,112 participants completed the health screen. Of this total population, 15,404 participants had both a complete health screen and a returned food diary. From this sample cohort, 10,000 participants with baseline health screen and dietary data were randomly selected for further nutritional analysis (A1.1 Figure 1). Before randomisation 312, 7-day diet records not included in the 10,000 diaries randomised sample had already undergone nutritional analysis. To optimise the study sample size these 312 diet records were added to the 10,000 diaries random sample. This sample selection is illustrated in Figure 2.2.

Figure 2.2 *Sample selection of AHMS participants with a 7-day diet record for nutritional analysis.*


```
┌──────────────────────────────────────────────────────────┐
│   n = 42,112 participants with complete health screen 2004-2012 │
└──────────────────────────────────────────────────────────┘
                                    │
                                    ├──────►┌──────────────────────────────┐
                                    │       │ Exclude n= 26,709 participants without │
                                    │       │        7-day diet record        │
                                    ▼       └──────────────────────────────┘
┌──────────────────────────────────────────────────────────┐
│  n =15,404 participants with  baseline health screen and 7-day diet record │
└──────────────────────────────────────────────────────────┘
                                    │
                                    ├──────►┌──────────────────────────────┐
                                    │       │ Exclude n= 5024 participants not in │
                                    │       │       random selection¹          │
                                    ▼       └──────────────────────────────┘
┌──────────────────────────────────────────────────────────┐
│  n =10,000 participants with 7-day diet records included for nutritional analysis │
└──────────────────────────────────────────────────────────┘
                                    │
                                    ◄──────┤┌──────────────────────────────┐
                                    │       │ 312 participants with 7-diet records │
                                    │       │ analysed prior to randomisation and │
                                    ▼       │  not in randomised sample¹      │
┌──────────────────────────────────────────────────────────┐
│        n = 10,312 diaries for nutritional analysis        │
└──────────────────────────────────────────────────────────┘
```

1. Full schematic of random selection can be found in Appendix 2.0 Figure 2.1

2.3 UK Biobank

2.3.1 Study Design

The UK Biobank is a large population-based prospective study established in 2006 to investigate the genetic and non-genetic determinants of disease in middle and older age UK participants[215].

2.3.2 Recruitment

Persons aged 40-69 years and living within 25 miles of an assessment centre were identified through the National Health Service (NHS) were considered eligible for participation. Between 2006 and 2010, more than half a million participants were recruited for this study. The UK Biobank study is conducted according to the guidelines laid down in the Declaration of Helsinki. UK Biobank has approval from the Northwest MREC and from the Patient Information Advisory Group (PIAG) for gaining access to information that would allow it to invite people to participate. PIAG has since been replaced by the National Information Governance Board for Health & Social Care (NIGB). In Scotland, UK Biobank has approval from the Community Health Index Advisory Group (CHIAG).

2.3.3 Data Collection

Following recruitment, UK Biobank participants attended 1 of 22 assessment centres across England, Wales, and Scotland to complete a baseline assessment. During this baseline assessment,

participants underwent a health screen as well as completing a touchscreen questionnaire to collect information detailing lifestyle behaviours and socio-demographic characteristics. Full recruitment and data collection procedures have already been outlined by Sudlow *et al.*[215]. This chapter will delineate the data collection procedures and wrangling of measures relevant to the work of this thesis.

Anthropometric Measures

Anthropometric measures were collected during the Physical Measures section of the assessment centre visit by a trained researcher. During the Physical Measure section, participants were instructed to be barefoot and in light clothing. Waist circumference was measured in centimetres (cm) at the umbilicus level using a Seca 200cm tape measure. Standing height was measured in centimetres sing a Seca 240cm height measure. To collect accurate measure participants were instructed to stand with their back against a vertical scale, shoulders relaxed, feet parallel to each other, soles flat on the floor and head in the Frankfort plane position. Weight was measured in kilograms (kg) using a Tanita BC418MA body composition analyser[216]. Body mass index (BMI) was calculated from measures of weight in height by dividing the weight (kg) by the square of the height (m).

Clinical and Biochemical Measures

Clinical and biochemical measures were collected by a trained researcher following a study-specific standard protocol.

Blood pressure was measured in the sitting position using an Omron 705 IT electronic blood pressure monitor[217]. Blood samples were taken in the fasted state by a trained clinical researcher, nurse, or phlebotomist using the 'vacutainer system'. Following this system, 50ml of blood was drawn from each participant. Blood samples collected in Serum Separator vacutainers are left to stand for 30 minutes and then centrifuged at 2000 RCF for 10 minutes. Blood samples are held in the Assessment Centre Environment holding fridge (temperature controlled 4ºC) until time of transportation to the dedicated laboratory for further biochemical analysis. Transportation was conducted at the same time every evening by a temperature-controlled study-specific courier service. Samples for transportation were packed in line with the study protocol[218]. Standard haematological tests were performed on fresh whole blood within 24 hours of blood collection from participants. Serum biomarker analysis was performed to quantify measures of HDL (mmol/L), total cholesterol

(mmol/L), and HS-CRP (mg/L) amongst others. Serum analysis of the aforementioned biomarkers was conducted using the Beckman Coulter AU5800 analytical platform [219]. An HbA1c assay using five Bio-Rad Variant II Analysers was performed to measure participant glycated haemoglobin (mmol/mol) [220]. This measure was then multiplied by 0.14 to convert HbA1c from mmol/mol to percentage to align with the AHMS. For most UK Biobank participants, blood samples for genotyping were genotyped at the Affymetrix Research Services Laboratory in Santa Clara, California, USA, with the rest of the cohort samples genotyped using the Affymetrix UK BiLEVE Axiom array. Quality control, phasing, and imputation of genotyping procedures have already been described in detail elsewhere [221].

Medical and Pharmacological Information

Information detailing past medical history was collected at the assessment centre visit using a touchscreen questionnaire[222]. Participants were asked to self-report diagnoses for the following conditions: cancer, heart attack, angina, stroke, hypertension, deep vein thrombosis (lung or leg), emphysema, diabetes, allergies, and or fracture (within the previous 12 months). Participants also used the touchscreen questionnaire to provide information concerning current medications. For this thesis, only information detailing the medication for the management of blood lipids, glucose, and pressure is considered.

Socio-economic and Demographic Measures

During the initial assessment centre visit, participants were asked to self-report sociodemographic characteristics using the touchscreen questionnaire. The characteristics relevant to this thesis include age (years), sex, ethnicity (White, Black or Black British, Asian or Asian British, Mixed), and the Townsend index as an indicator of socioeconomic status[223]. In this thesis, ethnicity was collapsed into two categories 'white' and 'other' as > 94% of the cohort self-reported as 'White Background'.

Lifestyle Behaviours

Data concerning lifestyle behaviours including, physical activity, smoking, alcohol consumption, and dietary intake were collected using the touchscreen questionnaire. Physical activity was assessed using adapted questions from the IPAQ-SF and report in MET min/week. This unit of measure was converted to physical activity level (PAL) factors following the IPAQ-SF protocol. In line with this protocol, participants were classified as low, moderate, or highly active according to self-reported

physical activity. Participants self-reported current/past cigarette smoking status as 'current', 'previous', or 'never' Smokers. Participants also self-reported alcohol consumption status as 'current', 'previous', or 'never'. The collection and wrangling of data concerning alcohol consumption behaviour in the UK Biobank is outlined in detail in Chapter 4 of this thesis.

<u>Dietary Intake</u>

In the UK Biobank, dietary intake was collected using two independent tools: the touchscreen food frequency questionnaire (FFQ) and the Oxford WebQ 24hr recall. This thesis includes only the dietary intake collected from the Oxford WebQ 24hr recall. Dietary data collection and wrangling procedures are described in detail in Chapter 3 of this thesis.

2.4 Missing Data and Multicollinearity

2.4.1 Missing Data

Missing data can be defined as a value not stored for the observation of interest [224]. Missing data is common in almost all types of research, and if poorly handled can significantly impact study findings and conclusions. It is recommended that the level and pattern of missing data is reported in observational studies[225]. Amongst 41,082 AHMS participants (total n of participants with health screen and survey data), missing data was at a low level for the following cardiometabolic risk variables: systolic blood pressure (0.2%), BMI (0.2%), waist circumference (0.3%), total cholesterol (0.9%), and HDL (0.9%). The extent of missing data was higher for biochemical markers HbA1c (13% missing observations) and HS-CRP (15% missing observations). Observations were complete for physical activity factor and were missing at a low level for measures of household income (0.6%), education status (0.6%), smoking (0.7%), current alcohol intake status (0.7%), country of enrolment (1.8%), and ethnicity (0.7%). Amongst 10,179 AHMS participants with dietary data, outcome variables relevant to cardiometabolic risk were complete for BMI, systolic blood pressure, and waist circumference. Biochemical markers of risk (blood lipids, HS-CRP) and HbA1c were missing for one participant. Observations for sociodemographic measures were complete for physical activity level, current smoking status, and alcohol consumption behaviour. Information detailing household income and education status was missing for one participant whilst the level of missing observations for ethnicity and country of enrolment was low at 0.2 and 1.7% respectively.

Amongst 502,504 UK Biobank participants with touchscreen survey and health screen data, observations were complete for country of enrolment and were missing at a low level for Townsend

Index (0.1%), current smoking status (0.2%), current alcohol consumption behaviour (0.2%), and ethnic background (0.2%). Missing observations were higher for the indicators of cardiometabolic risk: waist circumference 0.4%, BMI 0.6%, total cholesterol 6.5%, HDL 14.5%, HbA1c 7.2%, HS-CRP 6.7%, and systolic blood pressure 6.8%. Amongst 209,806 participants with dietary intake data, the observations were complete for body mass index, missing at low levels for waist circumference (< 0.001%), systolic blood pressure (4.3%), total cholesterol (5.6%), HS-CRP (5.8%), and HbA1c (5.8%), and higher levels for HDL (13.7%). Observations were missing at low levels for the Townsend deprivation index (3.9%), current smoking status (4.2%), alcohol consumption behaviour (4.3%), and ethnicity (4.3%).

Further analysis was conducted to understand whether there was a pattern to the missing data for the biochemical variables HbA1c and HS-CRP in the AHMS cohort and HDL in the UK Biobank cohort. Within each cohort, a dummy code was created (missing = 0, non-missing = 1) and statistical analysis tests were performed to determine whether there were significant differences in key characteristics participant groups. In the UK Biobank cohort, the difference between participants with and without missing observations for HDL was non-significant for sex, ethnicity, BMI, and country of enrolment. Participants with missing HDL observations were younger than those with complete HLD observations (p <0.001) (A1.2 Table 1.1). The extent and reasoning for missing HDL observations in the UK Biobank study have already been reported elsewhere [226].

In the AHMS, participants with missing observations for HbA1c were significantly older than those with complete observations. A bias in the country of enrolment was also observed. Greater than 95% of participants with missing HbA1c measures were enrolled in England compared to 65.9% of participants with complete HbA1c measures (A1.2 Table 1.1). AHMS participants with missing HS-CRP values were significantly younger and have a higher BMI compared to the participants with complete data for this measure (p<0.001) (A1.2 Table 1.1).

In this thesis, the handling of missing data is dependent on the aim of the study chapter, the nature of the covariates needed for analysis, as well as the study sample size. Therefore, the approach to the treatment of missing data varies from the complete removal of participants with incomplete observations to the imputation of missing values using regression methods.

Multicollinearity can be described as a high degree of correlation between explanatory variables which consequently can inflate and mislead findings from linear regression analyses[227]. In this thesis, multicollinearity is tested by measuring the variance inflation factor (VIF), using the *vif* function in the R studio package *car*. Multicollinearity is said to be present when the VIF was higher than 10 [227]. In the presence of multicollinearity, models were adjusted by removing one or more multicollinear explanatory variable and this adjustment was depending on the degree of multicollinearity that exists between the independent explanatory variables of interest.

3.0 Background

There is growing evidence to suggest that the curvilinear alcohol cardiometabolic risk (CMR) association, discussed in Chapter 1, may be attributed to poorly measured and controlled confounding factors [228–230]. Dietary intake is an example of a confounding factor that is often inadequately assessed in the field of alcohol health association research. For example, there is marked inconsistency across the literature in how diet as a confounding factor is addressed when addressed at all. While some studies adjust for diet by taking measures of total energy/macronutrient intakes [231,232], others take a more simplified approach by classing participants as previous recipients/non-recipients of general practitioner provided dietary advice [82]. While these traditional analyses may be of some value, people do not eat nutrients in isolation. They consume a diet made up of foods with complex combinations of nutrients that interact and work synergistically to influence health and disease risk. It is becoming more evident that a comprehensive assessment of dietary intake is crucial when navigating the relationship between alcohol consumption and cardiometabolic health, specifically when understanding the potential cardioprotective effect of low to moderate intake.

3.1 Aims and Objectives

The overall aim of this study is to comprehensively assess and delineate dietary intakes and patterns in the AHMS and UK Biobank study populations. Dietary misreporting is a recognised limitation to subjective dietary assessment and is an integral component of a comprehensive evaluation of dietary intake. Therefore, this study also sets out to measure and understand the prevalence of dietary misreporting in both study populations. The following objectives were set out to achieve these aims:

Objectives:

i.   To describe nutrient and energy intakes across sex categories in the AHMS and UK Biobank study populations.

ii.   Evaluate diet quality in the AHMS and UK Biobank study cohorts by measuring adherence to the DASH diet using a DASH specific index of diet quality. Explore intake of core food groups associated with health in the AHMS cohort.

iii.   Estimate the prevalence of misreporting using the Goldberg Equation for under-reporting and identify characteristics within and across populations associated with under-reporting.

3.2 Methodology

Participants

This study includes participants from the AHMS and UK Biobank with readily available dietary data as of the end of December 2020. Participants recording pregnancy at the time of dietary collection and or health screen were excluded from all analyses within this thesis.

AHMS – Dietary Data Collection

In the AHMS, baseline dietary has been collected from 2009 using 7-day estimated weight food diaries. These diaries follow the design of the European Prospective Investigation into Cancer and Nutrition (EPIC) dietary measurement tool and have been previously validated against urinary and blood biomarkers in the UK Biobank cohort.[233] Participants were asked to prospectively record dietary for 7 consecutive days across predefined eating occasions, breakfast, mid-morning snack, lunch, tea, dinner, evening snack and other eating occasions. To facilitate accurate assessment each participant received clear written instructions for recording dietary intake. Participants were asked to provide details relating to product, brand, and cooking methods. A food atlas of different meals and different portion sizes was included at the beginning of each diary to help participants accurately estimate the size of the portion of food/beverage consumed (A2.1 diary page 9-15). Each diary also contained an illustrated example of an accurate account of dietary intake across one diary day (A2.1 page diary page 16).

AHMS – Dietary Data Generation

AHMS participants with baseline dietary data were chosen at random for baseline nutritional analysis. Dietary records with <1 complete day or detailing a meal replacement diet were excluded from the nutritional analysis. Nutritional intake was calculated using the nutritional analysis software Dietplan7.0 (Forest field Software Ltd, Horsham, UK) which is based on McCance and Widdowson's 7th Edition Composition of Foods UK Nutritional Dataset (UKN)[234]. To inform nutritional intakes, each diet diary was 'coded' by a trained Dietitian/Nutritionist. This process involves matching the dietary intakes recorded in the diet diary to a UKN database code and a portion size. Each coder followed the 'Airwave Health Monitoring Study Standard Protocol for Dietary Coding' to optimise consistency and standard of coding and minimise intra and intercoder error (A.2.2). This protocol contains a series of decision trees that facilitate the translation of food and beverage records to UKN database codes and portion sizes. A study-specific 'codebook' and 'food portion database' was also used in conjunction with the standard protocol when coding a diet diary (A3.1 Figure 3.1 and Figure

3.2). These supporting materials were designed to assist decision making when the exact code/match or portion size of a food or drink is not present. The codebook provides 'default codes' for common food and drink items and are based (where possible) on published UK retail sales survey information that detail the bestselling food items within specific food categories (e.g., Mintel & Keynote market reports). The 'Food Portion Size Database' was developed to aid standardisation in estimating portion sizes where the exact portion consumed is not recorded. This database was based on national publications 'Food Portion Sizes' (FSA), 3rd Edition[235], as well as information from food and beverage manufactures. These supporting materials are continuously updated in line with changes to UKN databases and nutritional analysis software updates. To standardise and maintain high-quality coding, an audit cycle was used to monitor inter-coder reliability to continuously improve coding consistency. Following this audit process, 5% of all coded diaries were selected at random every two to three months. The selected electronic Dietplan record was checked against the written diet diary and errors were classified as 'code selection error' (code selected does not match written record), 'portion error' (over +/- 10% difference of the protocol weight), 'meal code error' (item entered at the incorrect meal occasion),' missing code error' (item not coded that is in the written record), and 'extra code error' (item code that is not in the written record). An error rate >10% resulted in coder feedback and subsequent training. Only days detailing complete dietary intake were analysed. Participants with a body mass index (BMI)(kg/m^2) of < 16 kg/m^2, pregnant at the time of recording dietary intake, reporting an energy intake of < 500kcal or > 6000 kcal per day were excluded from this study chapter. Figure 2.1 in Chapter 2 of this thesis outlines the sample selection of AHMS participants with dietary intake data.

The AHMS dietary data presented in this thesis was coded by the Imperial College Airwave Nutrition Section research team between 2013 and 2020. During this research period, the author of this thesis contributed to both the dietary analysis, quality assurance, and data cleaning of this dataset. The author also led the training of other staff and student coders contributing to this data.

UK Biobank Dietary Data collection

The UK Biobank study uses two different tools to collect dietary information. The first is a food frequency questionnaire (FFQ) and the second is a web-based 24-hour recall. This thesis and chapter will focus only on the dietary intakes collected using the web-based 24-hour recall.

The Oxford WebQ is a web-based 24-hour recall dietary collection tool that was used to collect and measure dietary intake within the UK Biobank study. This measurement tool asks participants about their consumption of up to 206 types of foods and thirty-two types of drinks over the previous 24-hour period and has shown to have a good correlation with interviewer-administered 24-hour dietary recalls[236]. UK Biobank participants recruited between April 2009 and September 2010 were asked to complete this web-based 24-hour recall at the assessment centre. Following this period, participants who provided an email address at recruitment were emailed every 3-4 months a total of four times between February 2011 and June 2012 (online cycle 1, February 2011 to April 2011; online cycle 2, June 2011 to September 2011; online cycle 3, October 2011 to December 2011; online cycle 4, April 2012 to June 2012) to complete the Oxford WebQ online using their personal computer. These invitations were sent on varying days of the week and participants were given a defined period to complete the recall. Participants asked to provide exact details of dietary intake consumed 'yesterday' and given clear written instructions to accurately recall intake[237].

UK Biobank Dietary Data generation

The energy and nutrient values of the reported dietary intakes are automatically generated on completion of the Oxford WebQ 24-hour recall. For this study, pregnant participants (at time of recall), those with a missing BMI or BMI < 16kg/m^2, or an energy intake of < 500kcal/ day or > 6000kcal were excluded for further dietary analysis in this study chapter. Figure 3.1 illustrates the sample selection of UK Biobank participants with dietary intake data used in this study.

3.3.2 Dietary Intake Measurements

Energy and Nutrient Intake

In both cohorts, mean daily energy and nutrient intakes were estimated for each participant by summing intake across the recording period and dividing by the number of days recorded. To account for variation across individual energy intakes, dietary variables were adjusted for energy using the nutrient density method [238]. In line with this method, for each of the following macronutrients, carbohydrate, total fat, saturated fat, and protein, mean daily intake (g/day) was multiplied by the corresponding Atwater factor (carbohydrate = 3.75, protein = 4, fat = 9) and divided by the mean daily energy intake (kcal/day). This dividend was then expressed as a percentage of total energy intake. In this study, the value for dietary fibre is based on the Englyst analyses method

for non-starch polysaccharide (NSP) determination and is expressed as intake in grams per 1000kcal of energy intake. Dietary energy density was calculated as energy (kcals) per weight (g) of food intake, excluding energy intake from beverages. The classification of beverages was based on previous research and includes all calorie-containing and non-caloric beverages[239].

Food Group Intake

In the AHMS study, the intake of foods from several major food groups featured in the Dietary Approaches to Stop Hypertension (DASH) diet [240] was estimated and presented as intake in weight (g) per day and adjusted for energy intake. The nutritional software program Dietplan 7.0 does not yet report dietary intake at a food group level and while individual food items can be easily grouped, difficulty arises grouping composite dishes that are made up of several ingredients which fall into different food group categories. To accurately estimate dietary from a food level, > 6000 unique food codes used to describe dietary intake were manually disaggregated into the following major food groups: 'Fruit', 'Pure Juice', 'Vegetable', Legumes', 'Total Cereal', 'Proportion Wholegrain', 'Red Meat', 'Total Dairy', 'Proportion Low Fat'. This approach has been previously shown to improve the estimation of fruit, vegetable, and meat intakes from food diaries used in UK surveys [241,242]. To standardise the procedure and minimise error, each code was disaggregated following a standard operating procedure. This protocol was developed in line with the methodology developed by *Bowman* et al. and modified for use in a UK dietary dataset [243]. Table 3.1 illustrates an example of how composite dishes are disaggregated into individual food groups. Each disaggregation was checked by a second researcher and differences were resolved through a group consensus.

Table 3.1. *An Example of AHMS Composite Dish Disaggregation.*

Source	Ref	Item description	Fruit	Pure Juice	Vegetable	Legumes	Tot Cereals	% Wholegrain	Tot Red Meat
UKN	15-531	Lasagne, vegetable	0.0	0.0	0.6	0.0	0.3	0.0	0.0
UKN	19-189	Chicken curry, chilled/frozen, reheated, with rice	0.0	0.0	0.0	0.0	0.4	0.0	0.0

Each number represents the proportion (percentage as a decimal) of the food code within each individual food group. The basis of the proportion estimates is code dependent. For example, information from leading supermarkets was used to disaggregate branded composite dishes and food codes. Whilst information from McCance Widdowson's standard recipes was used to disaggregate homemade composite dishes. For the former method, at least three products are checked, and the mean proportion was then used.

Diet Quality

Diet quality indexes are widely used to demonstrate the relationship between diet quality and health. The Healthy Eating Index (HEI), the Dietary Approaches to Stop Hypertension (DASH), and the Alternate Healthy Eating Index (AHEI) are examples of dietary indexes used to measure diet quality.

While there are some differences to these indexes, there is strong evidence that diet's that score highly on the AHEI, HEI or DASH are associated with a reduction in disease risk[244].

In this thesis, diet quality was calculated by measuring adherence to the Dietary Approaches to Stop Hypertension (DASH) diet. A higher adherence to the DASH diet has been associated with reduced cardiometabolic risk[245]. The use of the DASH index in this study also extends on the work of previous investigations between dietary intake and health within the Airwaves Dietary Analysis team, notably the disaggregation of composite foods into individual food groups.

In this present study, a modified version of the DASH index developed by *Mellen et al* was used to measure adherence.[246] The Mellen et al. DASH index (unmodified) is a nutrient-based 9 point index. In this index, 9 nutrient target goals and intermediate goals are identified. These targets are derived from the nutrient composition of a 2100kcal energy diet used in the DASH clinical trials. The targets set are equal for both men and women. Participants are allocated 1 point if the nutrient intake meets the target goal and 0.5 points if intake meets the nutrient intermediate goal. Participants with a nutrient intake between the target and the intermediate goal are scored 0.5 points for that nutrient. The total score is derived from the sum of all nutrient components for a minimum of 0 and a maximum of 9 points. In this present study, the DASH index is modified to adapt it for use in the UK Biobank study which does not report for sodium and cholesterol intakes using the 24-hour recall method. Firstly, in the UK Biobank cohort, sodium intake (mg/day) was calculated from spot urine samples using previously validated equations.[247] As the UK Biobank does not report daily cholesterol intake, this score was modified for use in both the UK Biobank and AHMS populations to exclude cholesterol. Therefore, in this present study, the modified DASH index is scored out of 8 points with a minimum of 0 points. Previous research suggests that a score of 50% of the total suggests adherence to the DASH diet.[246] As a result, AHMS and UK Biobank participants with a score of ≥ 4 points were classed as DASH adherent. Table 3.2 outlines the standard scoring criteria for the Modified Mellen *et al.* score used in this study.

Table 3.2 Scoring Standards for the Modified Mellen et al. DASH Index Score

Nutrient Targets for the Modified DASH Index Score			
Nutrient	**DASH Diet Nutrient Composition¥**	**DASH Target**	**Intermediate Target**
% TEI Total Fat	27%	27 %	32 %
% TEI Saturated Fat	6%	6 %	11 %
% TEI Protein	18%	18 %	16.5 %
Fibre	31g	14.8g/1000kcal	9.5g/1000kcal
Sodium	2400 mg	1143mg/1000kcal	1286mg/1000kcal
Magnesium	500 mg	238mg/1000kcal	158mg/1000kcal
Calcium	1240 mg	590mg/1000kcal	402mg/1000kcal
Potassium	4700 mg	2238mg/1000kcal	1534mg/1000kcal
Abbreviations: TEI= total energy intake Key: ¥ Based on a 2100kcal diet			

Dietary Misreporting

Dietary misreporting was measured at an individual level using the Goldberg equation.[248] This validated method takes into consideration, physical activity level (PAL), basal metabolic rate (BMR), dietary intake (kcal/day), and the total number of recorded dietary days. Following the Goldberg equation, upper and lower confidence intervals for each participant were calculated as illustrated in Figure 3.1. Participants reporting an EIrep: BMR outside the lower confidence interval were classed as probable under-reporters.

Figure 3.1 Energy Intake: Basal Metabolic Rate Ratio Cut Off Calculations

$$Lower = EIrep{:}BMR > PAL\,x\,exp\left[s.d.min\,x\,\frac{\left(\frac{S}{100}\right)}{\sqrt{n}}\right]$$

$$Upper = EIrep{:}BMR < PAL\,x\,exp\left[s.d.max\,x\,\frac{\left(\frac{S}{100}\right)}{\sqrt{n}}\right]$$

$$\sqrt{\frac{CV^2(wEI)}{d} + CV^2(wBMR) + CV^2(tP)}$$

CV coefficient of variation; EIrep = reported energy Intake; BMR = Basal Metabolic Rate; PAL = Physical Activity Level; n = number (individual); d = days of record; w = within subject coefficient; tP total variation in PAL. Basal metabolic rate was calculated for each participant using Schofield equation. Baseline demographic information, including age (years), sex, weight (kg) and height (cm) informed this calculation.

Non-Dietary covariates

The following non-dietary covariates were included in this study and presented as categorical variables: age (18-24, 25-54, 55-64, 65+), sex, body mass index (BMI) kg/m² (underweight, healthy, overweight, obese), current smoker (yes, no), ethnicity (white, other), country enrolled (England, Wales, Scotland, and Northern Ireland).

3.3 Statistical Analysis

Statistical analysis was performed using R Studio Software version 1.4.1103. Analyses were stratified by cohort and sex and Chi-square ($\chi 2$) tests were used to test whether distribution for each categorical variable differed across cohort sex categories. For continuous variables, the normality of distribution was evaluated using the Anderson-Darling Test. Normal distributed continuous variables were presented as the mean ± standard deviation (SD) and the difference between measures was tested using the analysis of variance (ANOVA) test. Non-parametric distributed continuous variables were presented as median (Interquartile range (IQR)) and the difference between measures was tested using the unpaired Wilcoxon-signed rank test. The Spearman correlation test was conducted to determine the pairwise agreement between the DASH score and food group intake. A correlation matrix was plotted using R package *ggcorrplot.* An insignificant correlation between two variables is indicated by an ✕. The size of Spearman's correlation was evaluated as follows; $0.3 \leq r < 0.5$ low, $0.6 \leq r < 0.8$ moderate, and $r \geq 0.8$ high [249]. For all analyses, statistical significance was accepted as *p*< 0.05.

3.4 Results
3.4.1 Study population

This current study is based upon a cross-sectional analysis of 10,179 AHMS participants and 209,806 UK Biobank participants. The sample selection of AHMS and UK Biobank participants with dietary data for analysis in this study is illustrated in Figure 3.2 and Figure 3.3, respectively.

In the AHMS, men make up a greater proportion of the total population compared to women (men 6210 (61.0%) vs women 3969 (39.0%), *p* <0.05). In the UK Biobank cohort, the opposite is observed (men 94,219 (44.9%) vs women 115,587 (55.1%), *p* > 0.05). Participants in both cohorts were predominantly Caucasian (97.3% AHMS vs 93.0% UK Biobank), residing in England (72.1% AHMS vs 88.4% UK Biobank), and were non-smokers (AHMS 90.9% vs UK Biobank 92.2%). Compared with UK Biobank participants, the AHMS cohort is a younger population (25-54 age category: AHMS 89% vs 40.3% UK Biobank, *p* <0.05), (Table 3.3).

A high proportion (88.8%) of AHMS participants recorded dietary intake for the full 7-day period, and this was equally observed across sex categories. The median number of 24-hour recalls completed by UK Biobank participants was 2 (IQR 2) out of a maximum of 5. A non-significant difference was

observed in the median number of 24-hour recalls between the male and female sex categories (Table 3.4).

Figure 3.2. Participant Flowchart of AHMS Participants with Dietary Intake Included in Present Study
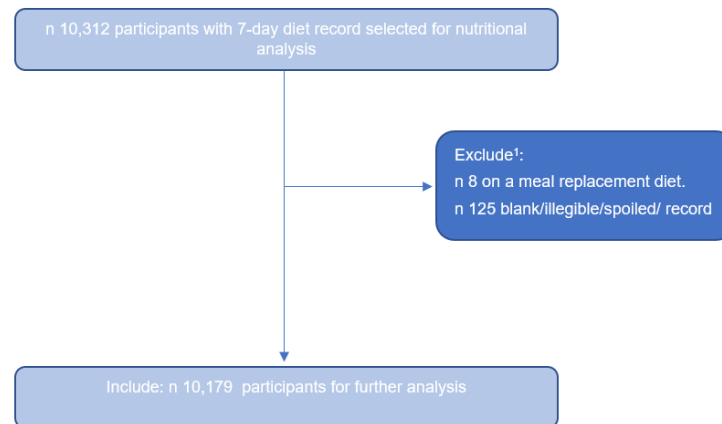
1. $n = 0$ Participants with missing BMI, BMI < 16kg/m^2, energy intake < 500 or > 6000kcal/day, or pregnant.

Figure 3.3 Participant Flow Chart of UK Biobank Participants with Dietary Intake Data
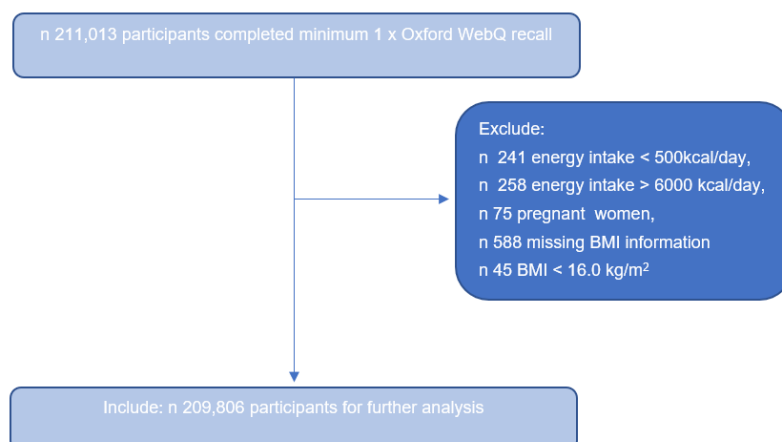
Table 3.3 *Descriptive characteristics Airwave Health Monitoring Study (AHMS) and UK Biobank Participants*

Airwave Health Monitoring Study (AHMS) and UK Biobank Participant Characteristics							
		AHMS			**UK Biobank**		
Sex	**n (%)**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**	***p-value**§*
		6210 (60.0)	3969 (40.0)	10179	94219 (44.9)	115587 (55.1)	209806	-
Age								
18-24	**n (%)**	134 (2.1)	210 (5.3)	344 (3.4)	0 (0.0)	0 (0.0)	0 (0.0)	*ns*
25-54		5631 (90.7)	3516 (88.6)	9147 (89.9)	35307 (37.5)	49148 (42.5)	84455 (40.3)	<0.001
54-65		426 (6.8)	239 (6.0)	665 (6.5)	41168 (43.7)	50234 (43.4)	91402 (43.6)	<0.001
65+		19 (0.4)	4 (0.1)	23 (0.2)	17744 (18.5)	16205 (14.1)	33949 (16.1)	<0.001
BMI Category†								
Underweight	**n (%)**	6 (1.0)	35 (0.9)	41 (0.4)	175 (0.2)	851 (0.7)	1026 (0.5)	*ns*
Healthy		1241 (20.0)	1932	3173 (31.2)	26067 (27.7)	50072 (43.3)	76139 (36.3)	*ns*
Overweight		3465 (55.8)	1374	4839 (47.5)	46724 (49.6)	41059 (35.5)	87783 (41.8)	*ns*
Obese		1498 (23.1)	628	2126 (20.9)	21253 (22.5)	23605 (20.5)	44858 (21.4)	*ns*
Current Smoker								
Yes	**n (%)**	506 (8.1)	420 (10.6)	926 (9.1)	8708 (9.2)	7731 (6.7)	16439 (7.8)	*ns*
Ethnicity								
White	**n (%)**	6026 (97.0)	3880 (97.7)	9906 (97.3)	87611 (93.0)	107456 (93.0)	195157 (93.0)	*ns*
Other		184 (3.0)	89 (2.3)	273 (2.7)	6579 (7.0)	7999 (7.0)	14578 (7.0)	*ns*
Country								
England	**n (%)**	4395 (70.8)	2941 (74.1)	7336 (72.1)	83600 (88.7)	101818 (88.1)	185418 (88.4)	*Ns*
Wales		732 (11.8)	499 (12.6)	1231 (12.1)	2410 (2.5)	3001 (2.6)	5141 (2.4)	<0.05
Scotland		1083 (17.4)	529 (13.3)	1612 (15.8)	8479 (8.8)	10768 (9.3)	19247 (9.2)	*ns*
N Ireland		0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	*ns*

Abbreviations: BMI – body mass index (kg/m^2), *ns* – non-significant *p*-value > 0.05, N Ireland – Northern Ireland.

Keys: † - BMI Categories; Underweight: <18.5 kg/m^2, Healthy: 18.5 – 24.9 kg/m^2, Overweight: 25.0 0- 29.9 kg/m^2, Obese > 30.0 kg/m^2. § - significant difference between study 'Totals'.

Tests: Categorical variables: χ2, significance *p*-value < 0.05.

Energy and Nutrient Intake

Macronutrient intake was described across sex categories in both cohorts. Within the AHMS, the mean energy intake reported was 2098 SD 489 and 1686 SD 390 kcal for men and women, respectively. Men reported a significantly greater mean energy intake compared to women ($p <$ 0.001). Compared to women, men also reported a diet higher in energy density, 0.72 SD 0.19 kcal/g of food vs 0.67 SD 0.19 kcal/g of food, ($p <$0.001). Women derived more energy from carbohydrates compared to men, 45.1 SD 6.6 vs 43.6 SD 6.5 % and greater intakes of fibre, 7.5 SD 2.2 vs 6.8 SD 2.0 g/1000kcal. A non-significant difference was observed in the energy derived from total fat and saturated fat between AHMS men and women (Table 3.4).

In the UK Biobank cohort, the mean daily energy intake report was 2288 SD 655 and 1966 SD 558 kcal for men and women, respectively. Men reported both higher overall energy intake and dietary energy density, men 0.71 SD 0.18 versus women 0.64 SD 0.17 kcal/g of food ($p <$0.001). Women derived more energy from carbohydrate, total fat, and saturated fat compared to men in this study cohort ($p < 0.001$). Women also had higher intakes of fibre than men, 8.4 SD 3.0 versus 7.4 SD 2.7 g/1000kcal ($p<$0.001).

Diet Quality

In the AHMS, the DASH score for participants ranged from 0.0 to 8.0 points. Women scored higher on the DASH index compared to men, 2.6 SD 1.4 versus 2.4 SD 1.3 points, ($p < 0.001$). Less than 20% of the total AHMS population demonstrated adherence to the DASH diet (Table 3.6). A greater proportion of women in the AHMS demonstrated adherence to this diet compared to men ($p =$0.05). The Mellen DASH score was calculated for 201,274 UK Biobank participants. 8532 participants (4.1%) of the original 209,806 sub cohort did not have available spot urine data for sodium calculation and were excluded from the DASH scoring analysis. Within this cohort, the DASH score ranged from 0.0 to 8.0 points. Women had a higher mean DASH score compared to men ($p < 0.001$). The proportion of UK Biobank participants demonstrating adherence was 33.6% and a non-significant difference in adherence was observed across sex categories. The UK Biobank population mean DASH score was significantly higher than the mean DASH score for the AHMS cohort ($p < 0.001$). A significantly greater proportion of UK Biobank participants demonstrated adherence to the DASH diet compared to participants in the AHMS ($p < 0.05$) (Table 3.6).

Table 3.4 *Nutrient Intakes in the Airwave Health Monitoring Study (AHMS) and UK Biobank cohort*

Nutrient Intake of Airwave Health Monitoring Study (AHMS) and UK Biobank Participants									
AHMS					**UKB**				
	Male	**Female**	**All**	**_p_-value**		**Male**	**Female**	**All**	**_p_-value**
Participants **n (%)**	6210 (57.3)	3959 (42.7)	10179	-	**Participants** **n (%)**	94219 (44.9)	115587 (55.1)	209806	-
Complete 7Day Record	5545 (89.3)	3500 (88.4)	9045 (88.8)	*ns*	**Complete 24HR** **Median (IQR)**	2 (2)	2 (2)	2 (2)	*ns*
Energy Intake					*Energy Intake*				
TEI (kcal) **Mean (SD)**	2098 (489.5)	1686 (390.0)	1938 (495.8)	<0.001	*TEI (kcal)* **Mean (SD)**	2288 (654.7)	1966 (557.8)	2100 (624.1)	<0.001
Energy Density (g/kcal)	0.72 (0.19)	0.67 (0.19)	0.70 (0.19)	<0.001	*Energy Density (g/kcal)*	0.71 (0.18)	0.64 (0.17)	0.67 (0.18)	<0.001
Nutrient Intake					*Nutrient Intake*				
%TEI Carbohydrate	43.6 (6.5)	45.1 (6.6)	44.2 (6.6)	<0.001	*%TEI Carbohydrate*	44.8 (8.0)	45.8 (7.8)	45.4 (7.9)	<0.001
% TEI Total Fat **Mean (SD)**	33.3 (5.5)	33.4 (5.6)	33.3 (5.5)	*ns*	*% TEI Total Fat* **Mean (SD)**	32.5 (6.8)	33.1 (6.9)	32.8 (6.8)	<0.001
% TEI Saturated Fat	12.2 (2.8)	12.2 (2.9)	12.2 (2.9)	*ns*	*% TEI Saturated Fat*	12.5 (3.4)	12.6 (3.4)	12.6 (3.4)	<0.001
% TEI Protein	17.2 (3.4)	17.1 (3.4)	17.2 (3.4)	<0.01	*% TEI Protein*	15.5 (3.5)	16.3 (3.7)	15.9 (3.6)	<0.001
Fibre (g/1000kcal) [†]	6.8 (2.0)	7.5 (2.2)	7.1 (2.1)	<0.001	*Fibre (g/1000kcal)* [†]	7.4 (2.7)	8.4 (3.0)	8.0 (2.9)	<0.001

Abbreviations: *ns* = non-significant. TEI = total energy intake.
Keys: † Fibre: Non-Starch Polysaccharides Englyst Method.
Tests: Categorical variables – χ2 -test; Continuous variables – ANOVA test; Significance - p-value < 0.05.

Diet Quality of Airwave Health Monitoring Study (AHMS) and UK Biobank Participants										
		AHMS				**UK Biobank**				
Sex		**Male**	**Female**	**All**	*p*-value°	**Male**	**Female**	**All**	*p*-value°	*p*-value§
Participants	**n**	6210	3969	10179	-	90706	110556	201,274	-	-
	(%)	(60.0)	(40.0)			(45.1)	(54.9)			
DASH Score	**Mean**	2.4	2.6	2.5 (1.3)	<0.001	3.1	3.2	3.1	<0.001	<0.001
	(SD)	(1.3)	(1.4)			(1.4)	(1.4)	(1.4)		
Adherent*	**n**	836	1021	1857	0.05	30208	37385	67593	*ns*	<0.05
	(%)	(13.5)	(25.7)	(18.2)		(33.3)	(33.8)	(33.6)		

Abbreviations: *ns* – nonsignificant p > 0.05.
Keys: ¤ difference between studies, § difference between studies, total population, * DASH Score ≥ 4.0 = adherent.
Tests: Continuous variables - Student T.test, Categorical variables – χ2-Test.

Food Group Intake

Energy adjusted food group intake across sex categories within the AHMS cohort are outlined in Table 3.6. Intake differed significantly across sex categories for all food groups except for intakes of low-fat dairy. Women consumed higher intakes of fruit, vegetables, legumes, total dairy, and wholegrain cereals per 1000kcal of energy intake compared to men ($p < 0.001$). Whilst men consumed higher intakes of red meat (g/1000kcal) compared to women ($p < 0.001$).

The combined median intake of fruit and vegetables was 144.8 (IQR 118.2). The median wholegrain intake for the population was 20.1 IQR 30.3 % of total cereal intake (Table 3.5). Spearman pairwise correlations between DASH score and energy-adjusted food group
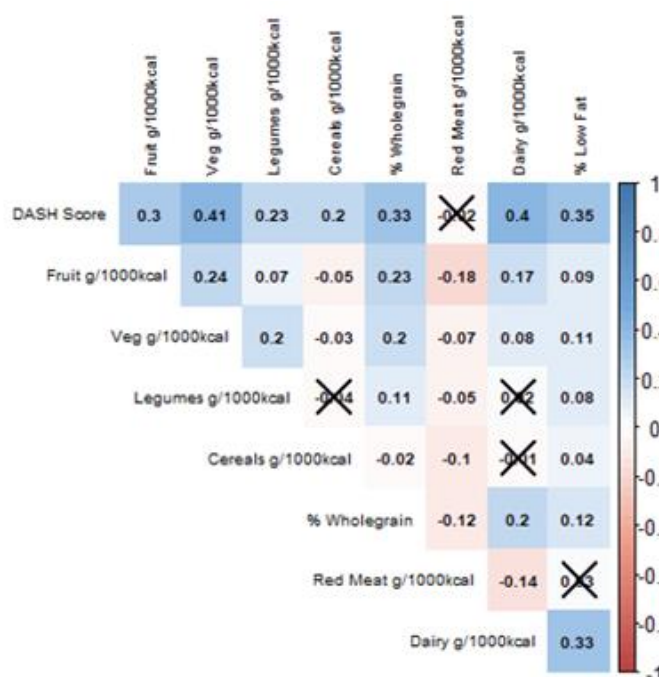
intakes amongst AHMS participants are presented in Figure 3.3. There is a significant and positive correlation between DASH Score, fruit, vegetable, legume, cereal, wholegrain, total dairy, and energy-adjusted low-fat dairy intake. A non-significant inverse correlation was observed between DASH score and intake of red meat.

Table 3.6 *Food Group Intake in the Airwave Health Monitoring Study (AHMS) cohort*

Food Group Intake in Airwave Health Monitoring Study Participants				
Sex		**Male**	**Female**	**All**	**p-value**
Participants **n (%)**		6210 (57.3)	3969 (42.7)	10179	*ns*
Food Group Intake (g/1000kcal/day)	*Median (IQR)*			
Fruit¥		64.7 (87.6)	79.1 (97.8)	70.1 (92.0)	<0.001
Vegetables		59.8 (45.6)	81.0 (60.9)	66.9 (52.9)	<0.001
Legumes		9.7 (13.1)	10.3 (15.1)	9.9 (13.7)	0.02
Total Cereals		104.5 (42.9)	100.8 (43.9)	103.1 (43.3)	<0.001
% Total Cereals – Wholegrain		19.3 (30.3)	21.3 (30.0)	20.1 (30.3)	<0.001
Red Meat		39.8 (28.0)	32.0 (29.3)	37.0 (28.8)	<0.001
Total Dairy		123.7 (84.0)	132.6 (101.1)	126.9 (91.0)	<0.001
% Total Dairy – Low Fat		82.8 (24.6)	83.3 (24.2)	83.0 (24.4)	*ns*
Abbreviations: IQR = interquartile range. *ns* = not significant, p > 0.05. Key: ¥ including pure juice, truncated at 1 small glass (150ml). Tests: Categorical variables – χ2- Test; Continuous variables – Kruskal Wallis test; Significance - *p*-value < 0.05.				

3.4.3 Misreporting

The prevalence of under-reporting in the AHMS and the UK Biobank cohort, stratified by sex is presented in Table 3.7. Greater than one-third of the AHMS cohort were classified as likely under-reporting for energy intake. A significant association between sex and under-reporting was also observed, with 65.2% of women versus 19.9% of AHMS men grouped within the 'underreported' category (p < 0.001). The prevalence of under-reporting in the UK Biobank was 17.1% and differed significantly from the overall under-reporting prevalence in the AHMS (p <0.01). The prevalence of under-reporting was also higher amongst women compared to men in the UK Biobank, 26.2% women versus 6.0% of men (p< 0.001). No significant association was observed between BMI categories and the prevalence of under-reporting.

Table 3.7 *Prevalence of Dietary Misreporting in the Airwave Health Monitoring Study (AHMS) and UK Biobank Study*

Dietary Misreporting in the Airwave Health Monitoring Study (AHMS) and UK Biobank Study Cohorts					
		Male	**Female**	**All**	**p-value**
AHMS	**n (%)**	6210 (60.0)	3969 (40.0)	10179	-
% Under-reporting		1238 (19.9)	2588 (65.2)	3826 (37.6)	<0.001
UK Biobank	**n (%)**	94219 (44.9)	115587 (55.1)	209806	-
% Under-reporting		5618 (6.0)	30281 (26.2)	35899 (17.1)	<0.001
Tests: Categorical variables – χ2- Test *p*-value < 0.05.					

3.5 Discussion

Diet is a well-established risk factor for poor cardiometabolic health and is an important confounder to consider in any model exploring the impact of lifestyle behaviours on cardiometabolic risk (CMR). This study aimed to describe the dietary intakes and quality of participants within the AHMS and UK Biobank cohorts as well as the prevalence of dietary misreporting.

3.5.1 Summary of Main Findings

❖ Macronutrient intakes in the AHMS and UK Biobank are comparable. The mean intake of saturated fat exceeds UK guidance whilst fibre intakes are substantially lower than recommended.

❖ In both cohorts, the macronutrient intake differs between men and women. Women report a lower energy density diet, and higher intakes of fibre and energy from carbohydrate when compared to men.

❖ Diet quality as measured using the DASH index score differed across sex categories in both study cohorts where men had poorer diet quality compared to women.

❖ Adherence to the DASH diet was low in both study populations and disproportionately lower in the AHMS compared to the UK Biobank population.

❖ DASH score was positively correlated with fruit, vegetable, wholegrain, and legume intake. The intakes of these food groups were higher in women compared to men in the AHMS.

❖ There is an association between sex and the likelihood of dietary under-reporting. The prevalence of under-reporting was higher amongst women compared to men in both the AHMS and UK Biobank cohorts.

Objective i. To describe nutrient and energy intakes across sex categories in the AHMS and UK Biobank study populations.

This study explored nutrient and energy intakes within the AHMS and UK Biobank study cohorts. Two frequently used subjective measures were used to collect dietary information. In both cohorts, nutrient intakes were described across sex categories. Findings from this study suggest low adherence to the UK nutrient intake guidelines for optimum health amongst AHMS and UK Biobank participants. Within both cohorts, intakes of saturated fat exceed UK guidelines whilst intakes of fibre are substantially lower than what is recommended for optimum health. Furthermore, an association between nutrient composition and sex was also observed. UK Biobank and AHMS female participants report higher intakes of fibre and energy from carbohydrates as well as lower energy density diets compared to their male counterparts.

The dietary intakes of a smaller AHMS cohort (n = 4412) have previously been described[250]. This present study corroborates earlier findings, including higher intakes of energy derived from carbohydrate and lower mean energy intakes amongst women compared to men. The AHMS is a young occupational cohort of policemen and women of whom most are classed within the 25-54 age category. Albeit an occupational cohort, the macronutrient intakes observed in this AHMS are comparable to those reported by 19-64-year-olds surveyed by the National Dietary and Nutrient Survey (NDNS).[251] NDNS data suggest also reports low intakes of fibre and intakes of saturated fat exceeding guidelines in this age group. However, in contrast with this study, energy derived from carbohydrate is equal amongst NDNS surveyed men and women, whilst reported intakes of fibre intakes are higher amongst men than women.

The macronutrient intake of UK Biobank participants stratified by sex has also been outlined in previous theses and scientific papers [252]. The dietary intakes reported are consistent across these publications with women reporting greater intakes of macronutrients as a percentage of energy, and men reporting a greater absolute mean energy intake. These findings suggest that the energy intake amongst men in the UK Biobank is supplemented by energy derived from alcohol consumption. The relationship between alcohol consumption and dietary intake will be discussed in detail in Chapter 5 of this thesis. Whilst macronutrient intake for this cohort has previously been described [252], to the author's knowledge, this is the first study to measure energy density (kcal/g food) in this population.

These findings are comparable to those reported in the AHMS, with men consuming a more energy-dense diet compared to women.

Objective ii Evaluate diet quality in the AHMS and UK Biobank study cohorts by measuring adherence to the DASH diet using a DASH specific index of diet quality. Explore intake of core food groups associated with health in the AHMS cohort.

In this study adherence to the DASH diet was taken as a proxy measure of diet quality. The low adherence to the DASH dietary pattern observed in the AHMS and UK Biobank cohorts suggest a dietary pattern of poor quality amongst participants in both cohorts. The suitability of this score as a proxy measure of diet quality was highlighted by findings from a correlation analysis within the AHMS which illustrated a dose-response relationship between DASH score and intake of fruit, vegetables, legumes, and whole grains. The diet quality of a smaller AHMS cohort has previously been described in earlier theses and scientific publications. While the dietary indexes may differ, findings of predominantly poor diet quality across the AHMS cohort are consistent throughout the literature [250,253–257]. In the UK Biobank, there is a paucity of published literature delineating population dietary patterns and quality. However, recently published findings also indicate a poor diet quality across a cohort (n= 77,004) of UK Biobank participants [258]. The observation of poor dietary patterns within the AHMS and UK Biobank cohorts is unsurprising. Dietary pattern analyses within the NDNS, a British cohort independent of the AHMS and UK Biobank, have also illustrated a high volume of poor quality dietary patterns, with intakes low in fibre and high in saturated fat [251,259,260]. Findings from this study also suggest an association between sex and the quality of the dietary pattern. In both the AHMS and UK Biobank cohorts, women reported a dietary pattern of higher quality compared to men. The relationship between sex and diet quality has been previously reported both within and outside the UK. Indeed, within the NDNS cohort, a positive association between being male and a dietary pattern of 'Snacks, fast food, fizzy drinks' (SFFD) has been reported [251].

Aside from the sex difference, this present study also observed a significant difference in mean DASH score between cohorts, with the UK Biobank participants reporting a higher mean DASH score compared to participants in the AHMS. There are inherent differences between the two cohorts that could account for this variation. The most notable difference is that, unlike the UK Biobank population, the AHMS cohort is an occupational cohort of British policemen and women. The poorer diet quality observed in the AHMS population could be secondary to the complexities of the

environment within these participants work. For example, several studies report an association between poor quality diet and shift work and that this association is in part owed to lower availability and accessibility to healthy food choices [261–263]. Studies also report the negative effect of work-related stress and pressurised work environments on dietary behaviours. Research shows an association between self-control demands at work and consumption of energy-dense, nutritiously poor-quality foods.

Findings from food group intake analysis illustrate clear dietary differences between AHMS male and female participants with male participants reporting lower intake of fruit, vegetables, legumes, and wholegrains, and greater intakes of red meat. This observation corroborates earlier research which suggests that women are more likely to follow a healthier dietary pattern compared to men [264]. Within both the male and female AHMS populations, the mean combined intake of fruit and vegetables was lower than the recommended 400g per 2000kcal diet/ 5 portions a day [265]. Similarly, the reported mean wholegrain intakes did not meet the recommendation guidance of 50% total cereal intake [266]. These findings coincide with the UK general population's poor adherence to healthy dietary recommendations highlighted by the most recent NDNS report [251]. While this study does not estimate food intake within the UK Biobank cohort, a recently published study of low carbon behaviours in this cohort suggests poor adherence to the 5-a-day recommendations with less than one-third meeting this standard of intake.

Objective iii. Estimate the prevalence of misreporting using the Goldberg Equation for under-reporting. Identify characteristics within and across populations associated with under-reporting.

Dietary under-reporting is one of the fundamental obstacles to collecting accurate dietary intake and can range in prevalence from 18% to 70% in some subgroups. This study reports a variation in the prevalence of under-reporting between cohorts with a higher prevalence of likely under-reporting recorded in the AHMS. This variation in the prevalence of under-reporting is likely owed partially to the inherent differences between the assessment tools. Dietary data in the AHMS and UK Biobank study was collected using two distinct assessment tools. In the AHMS a 7-day diet record is used to collect dietary data which relies on respondents to accurately estimate and record dietary intake prospectively. This approach is especially prone to social-desirability bias and respondent fatigue. In contrast, the UK Biobank uses a web tool to collect dietary information over a 24-hour period. Respondent fatigue is less likely given the shorter record period. However, this approach is still

susceptible to social-desirability bias. Previous surveys suggest higher energy intakes across the weekend compared to the weekdays. As the UK Biobank covers only a 24-hour period, it does not capture this variation in energy intake across a week. Additionally, the UK Biobank requires respondents to report intake retrospectively which places reliance on memory and can introduce recall bias. Whilst both studies have robust procedures to minimise the influence of these biases, without an objective measure of intake, such biases can never truly be avoided. This study also demonstrates a difference in the prevalence of under-reporting with women more likely to under-report energy intake compared to men. This is an observation that is consistent across the literature and not unique to these study cohorts. Whilst a significant difference in under-reporting prevalence across BMI categories was not observed in this study, there is established evidence to suggest a higher tendency to under-report energy intake amongst obese and overweight individuals. [267]

3.5.3 Strengths and Limitations

There are several strengths to this study, the most notable strength being the large-scale collection and assessment of dietary data. To the author's knowledge, this is the first-time dietary intake, collected using 7-day dietary records is described for a UK population of this size. The size of the respective cohorts and the methodologies employed to minimise bias infers confidence in the study's findings. Additionally, diet quality was determined using a validated diet quality index. This approach is thought to be most advantageous in comparison to posterior approaches which generate dietary patterns based on available data without a priori hypothesis and these patterns may not represent the optimum intake for health.[177] Assessing dietary behaviours across two independent UK cohorts also provided an opportunity to compare findings, and to verify trends and observations. Finally, to the author's knowledge, this is the first study to describe the prevalence of under-reporting in the UK Biobank data derived from algorithmic methods.

 As well as the notable strengths, there are certain limitations to this study that should be noted. First, this study is a cross-sectional analysis of dietary intake and temporal changes cannot be examined. Secondly, as with any subjective measure of behaviour, there are known biases that can weaken the confidence in our findings. The dietary intake collection methods in this study are prone to responder bias, specifically recall, and social-desirability biases. Under-reporting in subjective dietary intake is a well-established problem, and without an objective measure, there is residual uncertainty in how accurate these results describe true behaviour and intake. Finally, the estimation of sodium intake

from urinary sodium in the UK Biobank cohort can also be taken as a limitation. Whilst this method is validated, it introduces a systematic difference in how the DASH score was calculated between the two cohorts and could explain the higher DASH score in the UK Biobank population.

3.5.4 Conclusion

To conclude this study delineates dietary intakes in the AHMS and UK Biobank participants. On average, the dietary intakes of AHMS and UK Biobank participants do not fully coincide with that of a healthy dietary pattern. However, they are comparable to what is reported by the NDNS for the general British public. This study also concludes that women are more likely to report 'healthier' dietary patterns compared to men, a finding which corroborates previous evidence of gender differences in dietary intake. Lastly, the prevalence of under-reporting is an established issue in both cohorts. However, in the absence of an objective measure, using large-scale robustly collected dietary data is currently the best approach to capturing the dietary intakes and patterns of large populations. By providing a comprehensive insight into the dietary intakes of these two cohorts, findings from this study will help establish the true effect of alcohol consumption on CMR.

4.0 Background

Alcohol consumption is one of the leading global causes of disease, and yet at low to moderate levels of consumption is thought to infer cardioprotective benefits [4,84,268]. However, our confidence in the presumed risk and benefits of alcohol consumption relies upon the accuracy in which intake is measured. In epidemiological studies, a variety of self-reported measurement tools are used to measure alcohol intake. Of these measurement tools, the quantity frequency (QF), gradient frequency (GF), and daily diet diaries (DD) are three of the most commonly used [269–271]. Yet there is evidence to suggest that these tools largely underestimate actual alcohol intake and account for only 40-60% of total alcohol sales [272,273]. This underestimation is in part due to known psychosocial factors affecting self-reporting accuracy, as well as methodological issues concerning the structure of the reporting tool, e.g., what aspects of intake are measured and how questions used to measure intake are posed [274–276]. As a result, research bodies in this field have released guidelines outlining standard criteria to improve consistency and optimise estimate yields from self-reported measures [270]. Across these guidelines, there is a consensus that self-reported tools should collect information relating to current alcohol consumption status, the volume of average alcohol consumption, and the frequency and volume of excessive (binge) drinking[270].

While there are known advantages and disadvantages to self-reported measures of alcohol intake[269,272,274,277–282], in the absence of an objective marker, these measures currently serve as a method to estimate alcohol intake in large populations.. The Airwave Health Monitoring Study (AHMS) and the UK Biobank studies utilise several self-reported alcohol intake measurement tools to measure alcohol consumption. In both studies, an adapted version of the beverage-specific quantity frequency (BSQF) tool is used to capture a 7-day retrospective alcohol intake. Additionally, within the AHMS, a 7-day diet record is also used to prospectively measure alcohol intake.

4.1 Aims and Objectives

 This study aimed to measure alcohol consumption in line with measurement guidelines in the AHMS and UK Biobank study cohorts, and to measure inter-method reliability between two self-reported alcohol intake measurement tools. To achieve these aims, the objectives of this study were to:

<ol type="I">
Estimate alcohol intake concerning current drinking status, and the average volume of intake, beverage preference, and consumption pattern using survey and diary measures of intake.
Measure the agreement between diary and survey measures estimates of alcohol intake within the AHMS cohort.

4.2 Methodology

4.2.1 Alcohol Intake Data Collection

<u>Participants</u>

Participants with complete data concerning alcohol intake behaviour on alcohol intake were included for analysis in this present study. Recruitment procedures for both cohorts have already been outlined in Chapter 2, section 2.2, and section 2.3 of this thesis.

<u>Instrument - Touchscreen Survey</u>

At the baseline health screen appointment, AHMS and UK Biobanks participants completed a beverage specific -quantity frequency touchscreen. The answers to the survey questions were used to distinguish drinker types, intakes, and consumption patterns. To calculate alcohol intake, the quantity of each beverage type (red wine, white wine, beer/cider, fortified wine, or spirits) was multiplied by its standard drink size and reference alcohol content. Information relating to beverage-specific standard measure and alcohol content is outlined in A4.1. Beverage-specific intake during the reported period was summed and converted to alcohol g/day for all current drinkers. Alcohol intake <1g/day was imputed by bootstrap resampling methods using the R software MICE package and stratified by self-reported drinking frequency (occasional or frequent) and sex. Participants with alcohol intake > 500 g/day were considered outliers and excluded from further analysis. Only participants with complete responses to questions detailing alcohol intake were included in this analysis.

<u>Instrument – Daily Diet Record</u>

A 7-day diet record was used alongside the touchscreen survey to measure alcohol intake amongst current drinkers in the AHMS cohort. Full dietary collection and coding procedures are outlined in Chapter 3, Section 3.3 of this thesis. Dietary analysis software Dietplan 7.0 (Forest field Software Ltd, Horsham, UK) was used to calculate alcohol intake (g/day) from self-reported intakes of alcoholic beverages recorded in the 7-day diet records. Alcohol intake <1g/day was imputed by bootstrap

resampling methods using the R software MICE package, stratified by self-reported drinking frequency and sex. Participants with alcohol intake > 500 g/day were considered outliers and excluded from further analysis.

Current Drinking Status

In this present study, participants were classified as "Current Drinkers", "Former Drinkers", or "Never Drinkers" according to self-reported lifetime alcohol intake. AHMS participants who reported "Yes" to the health survey question "Q.72 Do you currently drink alcohol?" were classified as "Current Drinkers". Those who reported "No" to currently drinking alcohol but "Yes" to question "Q.78 Did you ever drink alcohol?" were classified as "Former Drinkers". Those participants who answered "No" to both questions relating to current and lifetime alcohol consumption were classified as "Never Drinkers". UK Biobank participants were classified as above from direct answers given to the touchscreen survey question "Alcohol drinker status?" for which the options of response include "Current", "Previous", and "Never".

Current drinkers were grouped into drinking levels according to weekly alcohol intake. Alcohol intake in g/day was converted to units per week by multiplying intake by 7 and dividing by 8, under the assumption that 1 unit of alcohol contains 8g of alcohol. At present, there is no agreed definition for drinking levels. For example, the definition of moderate alcohol intake varies across the literature depending on the geographic location of the population studied. In this study, drinking levels were defined by adapting information from the Chief Medical Officer's (2016) low risk drinking guidelines, alongside those definitions of moderate drinking published in the literature. Study-specific drinking levels according to weekly unit alcohol intake are outlined in Table 4.1.

Table 4.1 Drinker Categories and Alcohol Intake Thresholds

Drinker Categories and Alcohol Intake Thresholds	
Units/ Week	Level
1 – 7	Moderate 1
7 – 14	Moderate 2
14 – 21	Moderate 3
>21	Heavy

Adherence to UK Alcohol Intake Guidelines

The UK government recommends an alcohol intake of ≤ 14 units per week for both men and women[78]. Estimated alcohol intake data from the touchscreen survey was used to compare the alcohol intake of AHMS and UK Biobank current drinkers against UK government guidelines. As described above, alcohol intake was calculated from self-reported beverage-specific intake and converted from alcohol (g/day) to units per week by multiplying daily intake (g) by 7 and dividing by 8, under the assumption that 1 unit of alcohol contains 8g its weight.

<u>Beverage Preference</u>

Beverage specific alcohol data from the AHMS and UK Biobank touchscreen surveys were used to group "Current Drinkers" according to preferred alcoholic beverage. Participants were grouped as either dominant "Beer"," Wine", or "Spirit" drinkers based on which beverage had the greatest contribution to weekly alcohol intake (units). Table 4.2 outlines the type of alcoholic beverages belonging to each group.

Table 4.2 *Alcoholic Beverages Main Group & Subgroup Categories*

Alcoholic Beverages Main Group & Subgroup Categories	
Alcoholic Beverage	**Group**
White wine	Wine
Red Wine	Wine
Sparkling Wine/Champagne	Wine
Fortified Wine (Port, Sherry, Sweet Vermouth)	Wine
Spirits and Liqueurs (Gin, Vodka, Rum, Whiskey, Alcopops, Brandy etc.)	Spirits
Bitter/Lager/Stout/Ale/Cider	Beer

<u>Drinking Patterns</u>

Binge drinking is a drinking pattern of excessive alcohol intake. The Office of National Statistics (ONS) defines binge drinking as having over 8 units of alcohol in a single session for men and over 6 units for women[283].In the AHMS cohort, self-reported alcohol intake from 7-day diet records was used to identify binge drinking patterns amongst current drinkers. Using the ONS guidelines for binge drinking, participants reporting one or more binge drinking events throughout the dietary record period were classified as Binge Drinkers and those who do report this pattern of consumption were grouped as Non-Binge Drinkers.

<u>Non-Alcohol Covariates</u>

The following non-dietary covariates were included in this study and presented as categorical variables: age (18-24, 25-54, 55-64, 65+), sex, body mass index (BMI) kg/m^2 (underweight, healthy, overweight, obese), current smoker (yes, no), ethnicity (white, other), country enrolled (England, Wales, Scotland, and Northern Ireland).

4.3 Statistical Analysis

Statistical analysis was performed using R Studio Software version 1.4.1103. Participants from both cohorts with underlying health conditions including pregnancy were excluded. Analyses were stratified by cohort and alcohol-specific variables. Chi-square (χ2) tests were used to test differences in distribution between each categorical variable. For continuous variables, the normality of distribution was evaluated using the Anderson-Darling Test. Normal distributed continuous variables were presented as the mean ± standard deviation (SD) and the difference between measures was tested using the analysis of variance (ANOVA) test. Non-parametric distributed continuous variables were presented as median (Interquartile range (IQR)) and the difference between measures was tested using the unpaired Wilcoxon-signed rank test. The agreement between dietary and touchscreen survey measures of alcohol intake (units/week) was compared using the non-parametric Spearman's correlation coefficient and Bland-Altman plots with limits of agreement[284]. The size of Spearman's correlation was evaluated as follows; $0.3 \leq r < 0.5$ low, $0.6 \leq r < 0.8$ moderate, and $r \geq 0.8$ high[285]. For all tests, statistical significance was accepted as $p < 0.05$.

4.4 Results

4.4.1 Study Population

In the AHMS cohort, 41,082 participants completed both the health screen and touchscreen survey. From this cohort, 306 pregnant women, and 287 non-responders to the qualitative alcohol behaviour question 'Do you currently drinker alcohol?' were excluded, resulting in 40,489 participants included for further analysis.

In the UK Biobank cohort, 502,505 participants completed the baseline assessment centre health screen and touchscreen questionnaire. From this cohort, 150 pregnant women, and 1654 non-

responders to the questions concerning current alcohol intake were removed from further analysis. (Figure 4.2).

Figure 4.1 *Airwave Health Monitoring Study Participant Flow Chart – Alcohol Intake Study*
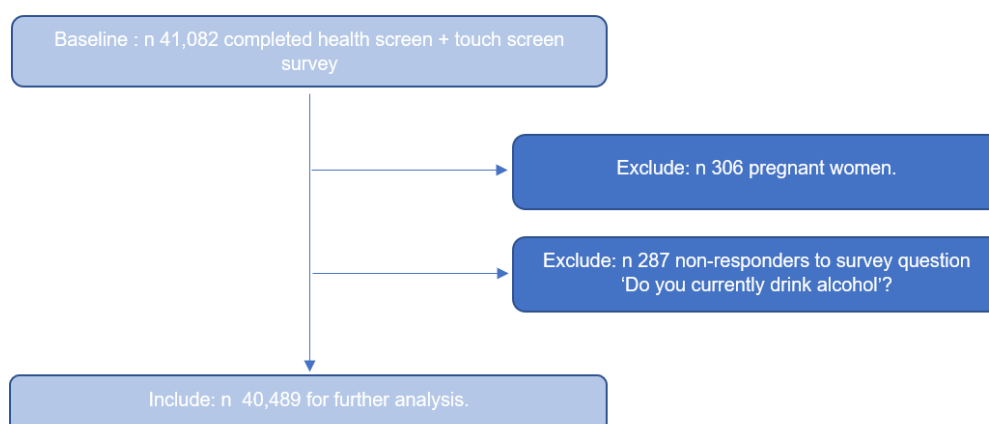
Figure 4.2 *UK Biobank Participant Flow Chart – Alcohol Intake Study*
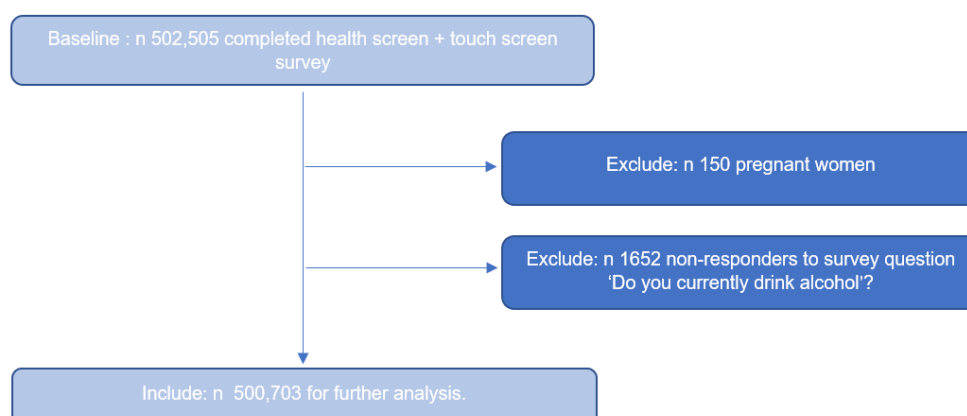
4.4.2 Alcohol Intake Profile

<u>Descriptive Characteristics and Current Alcohol Intake Status</u>

40,489 AHMS and 500,703 UKB participants with complete alcohol intake data at baseline were grouped according to self-reported current intake status (Table 4.3). In both cohorts, current drinkers made up a greater proportion of the total population compared to never and former drinkers ($p <$ 0.001). No significant difference in sex distribution was found between drinking categories across both cohorts. In the AHMS, former drinkers were younger than both current and never drinkers. Whilst, in the UK Biobank cohort, current drinkers were younger than never and former drinkers ($p <$

0.001). No significant difference was observed across drinking categories for ethnicity, smoking prevalence, and country of enrolment.

Alcohol Intakes Amongst Current Drinkers

Current drinkers with alcohol intake data recorded using the touchscreen survey were grouped into study-specific drinking levels (Table 4.3). In the UK Biobank cohort, 24.7% (n 113,815) of current drinkers did not respond to quantitative alcohol questions concerning intake over the previous week and were subsequently removed from further analysis. The final number of current drinkers with alcohol intake data in the AHMS and UK Biobank study was 36,939 and 346,427 participants, respectively. From the touchscreen survey, the median (IQR) alcohol intake of AHMS and UK Biobank current drinkers was 9.7 (15.1) and 14.3 (16.5) units per week, respectively. More than one-third of AHMS current drinkers were grouped within the moderate 1 drinking category. In the UK Biobank cohort, a greater proportion of current drinkers were grouped as heavy drinkers than moderate 1, 2, or 3 drinkers. Age increased with increasing alcohol intake within the AHMS study cohort and decreased with increasing intake in the UK Biobank study. Amongst current drinkers in the UK Biobank study, the proportion of men increased across levels of increasing alcohol intake (p<0.001). The number of current drinkers reporting a weekly alcohol intake within the UK low risk drinking guidelines was 62.1% (22,940) of AHMS current drinkers and 50.3% (174,274) of UK Biobank current drinkers.

A subgroup of AHMS current drinkers (n 9389) with complementary dietary data was grouped a second time using alcohol intake estimates from the 7-day diet record (Table 4.4). Using the estimates from this measurement, 3128 participants (33.3% of the total population) were grouped within the moderate 1 drinker category and the median (IQR) alcohol intake for the total drinking cohort current was 11.7 (16.4) units per week. A difference in the sex distribution across drinking levels was not observed. The mean age of participants increased with increasing levels of alcohol consumption (p<0.001).

Table 4.3 *Descriptive Characteristics*

		Airwave Health Monitoring Study					UK Biobank				
Descriptive Characteristics and Current Alcohol Intake Status											
		Current	**Former**	**Never**	**All**	***p*-value**	**Current**	**Former**	**Never**	**All**	***p*-value**
Total	**n (%)**	36,939 (90.8)	2446 (6.5)	1104 (2.7)	40,489	<0.001	460,242 (91.9)	18,085 (3.6)	22,376 (4.5)	500,703	< 0.001
Age (y)	**Mean (SD)**	40.4 (8.9)	40.4 (9.1)	41.0 (9.6)	40.4 (8.9)	ns	56.5 (8.1)	57.2 (7.9)	56.9 (8.6)	56.5 (8.1)	< 0.001
Sex: Male	**n (%)**	23,682 (64.1)	1354 (55.3)	582 (52.7)	25,618 (63.3)	ns	213,769 (46.4)	8123 (44.9)	6406 (28.6)	228,298 (45.6)	ns
Current Smoker	**n (%)**	3635 (9.8)	287 (11.7)	81 (7.3)	4003 (9.9)	ns	48,540 (10.5)	2842 (15.7)	1443 (6.4)	52,825 (10.5)	ns
Ethnicity: White	**n (%)**	35,218 (95.3)	2,179 (89.1)	767 (69.5)	38,164 (94.2)	ns	428,166 (93.0)	15,880 (87.8)	14,904 (66.6)	458,950 (91.7)	ns
Country Enrolled[+]											
England	**n (%)**	25,496 (69.0)	1789 (73.1)	860 (77.9)	28,145 (69.5)	ns	418,325 (90.9)	16,339 (90.3)	19,601 (85.6)	454,265 (90.7)	ns
Scotland		5949 (16.1)	309 (12.6)	130 (11.8)	6388 (15.8)	ns	28,782 (6.2)	1310(7.2)	2335 (10.4)	32,427 (6.5)	ns
Wales		4810 (13.0)	300 (12.3)	99 (9.0)	5209 (12.9)	ns	13,135 (2.9)	436 (2.5)	440 (4.0)	14,011 (2.8)	ns
N. Ireland		2 (<0.1)	0 (0.0)	0 (0.0)	2 (<0.1)	ns	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	ns

Abbreviations: y = years; N. Ireland = Northern Ireland; ns = non-significant

Keys: + - AHMS n 39,744 complete response to question concerning country of enrolment.

χ^2 Test – categorical, ANOVA – continuous, $p < 0.05$

Table 4.4 *Alcohol Intakes Amongst Current Drinkers*

Alcohol Intakes Amongst Current Drinkers						
Airwave Health Monitoring Study – Survey						
Levels		**Mod 1**	**Mod 2**	**Mod 3**	**Heavy**	**All**	**p-value**
Range (units/wk)		*1-7*	*7-14*	*14-21*	*> 21*	-	-
	n (%)	15,400 (41.7)	8430 (22.8)	5566 (15.1)	7543 (20.4)	36,939	*ns*
Sex: Male		8587 (55.7)	5092 (60.4)	3903 (70.1)	6100 (80.9)	23,682 (64.1)	*ns*
Age (y)	Mean (SD)	39.4 (9.2)	40.4 (9.0)	41.0 (8.6)	42.1 (8.4)	40.4 (8.9)	<0.001
Alcohol Intake (units/wk)		3.4 (1.8)	10.7 (2.0)	17.6 (2.1)	34.2 (12.0)	*9.7 (15.1)	<0.001
Airwave Health Monitoring Study – Diary						
Category		**Mod 1**	**Mod 2**	**Mod 3**	**Heavy**	**All**	**p-value**
	n (%	3128 (33.3)	2324 (24.8)	1483 (15.8)	2454 (26.1)	9389	*ns*
Sex: Male		1607 (51.3)	1346 (57.9)	960 (64.7)	1906 (77.7)	5819 (62.0)	*ns*
Age (y)	Mean (SD)	39.8 (9.6)	41.0 (9.2)	41.3 (8.8)	41.9 (8.6)	40.9 (9.2)	< 0.001
Alcohol Intake (units/wk)		3.9 (1.9)	10.7 (2.0)	17.8 (2.0)	35.4 (14.3)	*11.7 (16.4)	< 0.001
UK Biobank – Survey						
Category		**Mod 1**	**Mod 2**	**Mod 3**	**Heavy**	**All**	**p-value**
	n (%)	71,957 (20.8)	102,256 (29.5)	62,247(18.0)	109,967 (31.7)	346,427	*ns*
Sex: Male		21,460 (29.8)	41,520 (40.6)	32,900 (52.8)	80,685 (73.4)	176,565 (51.0)	<0.001
Age (y)	Mean (SD)	57.0 (8.0)	56.6 (8.0)	56.4 (8.0)	56.4 (7.9)	56.6 (8.0)	<0.001
Alcohol Intake (units/wk)		4.8 (1.6)	10.7 (2.0)	17.7 (2.0)	38.0 (18.8)	*14.3 (16.5)	<0.001

*χ2 Test – categorical, ANOVA – continuous, p < 0.05, * Median (IQR).

Abbreviations: Mod 1 – Moderate 1, Mod 2 – Moderate 2, Mod 3 – Moderate 3, y – years, wk – week.

4.4.3 Alcohol Consumption – Beverage Preference

36,939 AHMS and 346,427 UK Biobank current drinkers were grouped according to their alcoholic beverage preference (Table 4.5). Across both studies, a greater proportion of current drinkers report a preference for wine compared to beer or spirits. Men were more likely to report a preference for beer compared to women. In the AHMS, current drinkers reporting a preference for spirits were younger than current drinkers reporting a preference for wine or beer ($p<0.001$). In the UK Biobank population, current drinkers preferring beer were younger than participants reporting a preference for wine or spirits. There was a non-significant difference in the distribution of drinker category across beverage preference groups in the AHMS. In the UK Biobank cohort, a significantly larger proportion of heavy drinkers report a preference for beer than spirits, or wine. While in the spirit preference group, there is a larger proportion of moderate 1 drinker than moderate 2, 3, or heavy drinkers ($p <0.05$).

Table 4.5 Alcohol Consumption – Alcoholic Beverage Preference

Alcohol Consumption – Beverage Preference					
Airwave Health Monitoring Study					
Preference		**Wine**	**Beer**	**Spirits**	**All**	***p***
	n (%)	18,112 (49.0)	14,552 (39.4)	4275 (11.6)	36,939	< 0.001
Sex: Male		8739 (48.2)	12,981 (89.2)	1962 (45.9)	-	<0.001
Age (y)	**Mean (SD)**	41.3 (8.7)	39.8 (8.7)	38.8 (9.7)	-	<0.001
Drinker Category						
Moderate 1		7219 (39.8)	5946 (40.9)	2235 (52.3)	-	*ns*
Moderate 2		4383 (24.2)	3040 (20.9)	1007 (23.5)	-	*ns*
Moderate 3		2841 (15.7)	2158 (14.8)	567 (13.3)	-	*ns*
Heavy		3669 (20.2)	3408(23.4)	466 (10.9)	-	*ns*
UK Biobank						
Category		**Wine**	**Beer**	**Spirits**	**All**	***p***
	n (%)	228,561 (66.0)	95,808 (27.6)	22,058 (6.4)	346,427	< 0.001
Sex: Male		85,837 (37.5)	81,906 (85.5)	8822 (40.0)	-	< 0.001
Age (y)	**Mean (SD)**	56.8 (7.9)	55.8 (8.2)	58.0 (7.8)	-	< 0.001
Drinker Category						
Moderate 1		50,566 (22.2)	13,996 (14.6)	7395 (33.5)		<0.05
Moderate 2		73,978 (32.4)	22,768 (23.8)	5510 (25.0)		*ns*
Moderate 3		42,646 (18.6)	16,396 (17.1)	3205 (14.5)		*ns*
Heavy		61,371 (26.8)	42,648 (44.5)	5948 (27.0)		<0.05
Abbreviations: ns – non-significant.						
*χ2 Test – categorical, ANOVA – continuous, p < 0.05						

9389 AHMS current drinkers with alcohol intake estimates from 7-day diet record data were grouped as 'binge drinkers' or 'non-binge drinkers following the ONS sex-specific binge drinking guidelines. Within this AHMS sub cohort, 34.7% (3262) of participants report at least one binge-drinking occasion throughout the diet record period. Heavy drinkers make up the largest proportion of binge drinkers (61.3%). Amongst non-binge drinkers, moderate 1 drinker make up the largest proportion (50.4%), whilst heavy drinkers make up the least (7.3%). A greater proportion of men than women report binge drinking, with men making up 67.9% (2215) of the total binge drinking population. Binge drinkers are also younger than non-binge drinkers, mean (SD) age 40.4 (8.8) versus 41.1 (9.3) years, (p< 0.001).

During a single binge drinking occasion, male binge drinkers consume a larger volume of alcohol than female binge drinkers, mean 13.0 SD 5.4 units versus 9.5 SD 4.2 units. The mean alcohol intake of binge drinkers during a single binge occasion is also greater than the ONS sex-specific binge drinking thresholds (Figure 4.3).

Figure 4.3 *Mean Alcohol Intake During Binge Occasion versus UK Binge Thresholds*
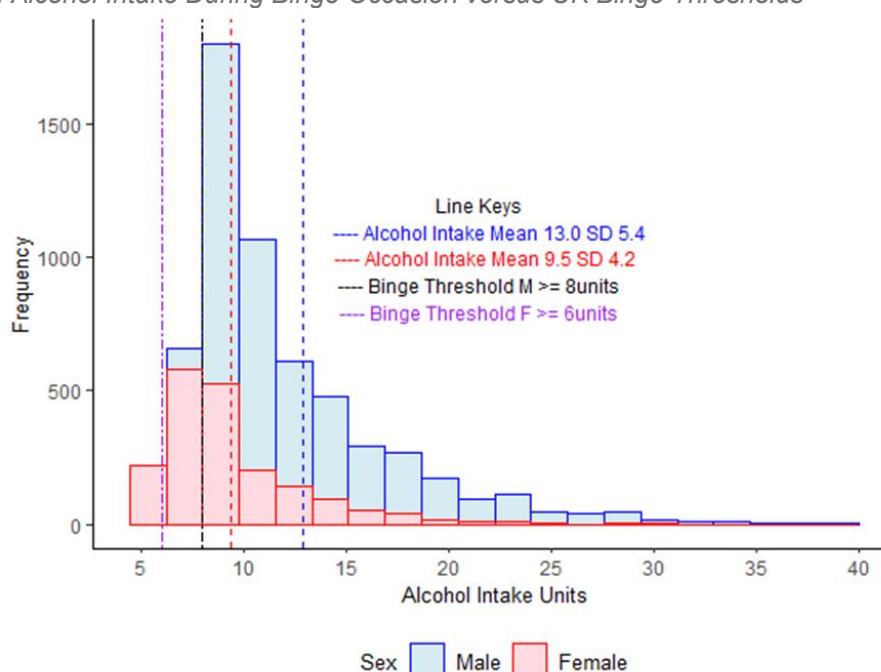
4.4.5 Inter-method Agreement - Correlation Results

A Spearman correlation analysis was conducted for pair-wise alcohol intakes from the survey and dietary measures in 9389 AHMS participants. Findings from this analysis show a positive correlation between the two measures of alcohol intake for the entire cohort (r = 0.78 p-value < 0.001) and within sex groups Figure 4.4.

Figure 4.4 *Correlation Plot Dietary vs Survey Measures of Alcohol Intake (units/wk)*
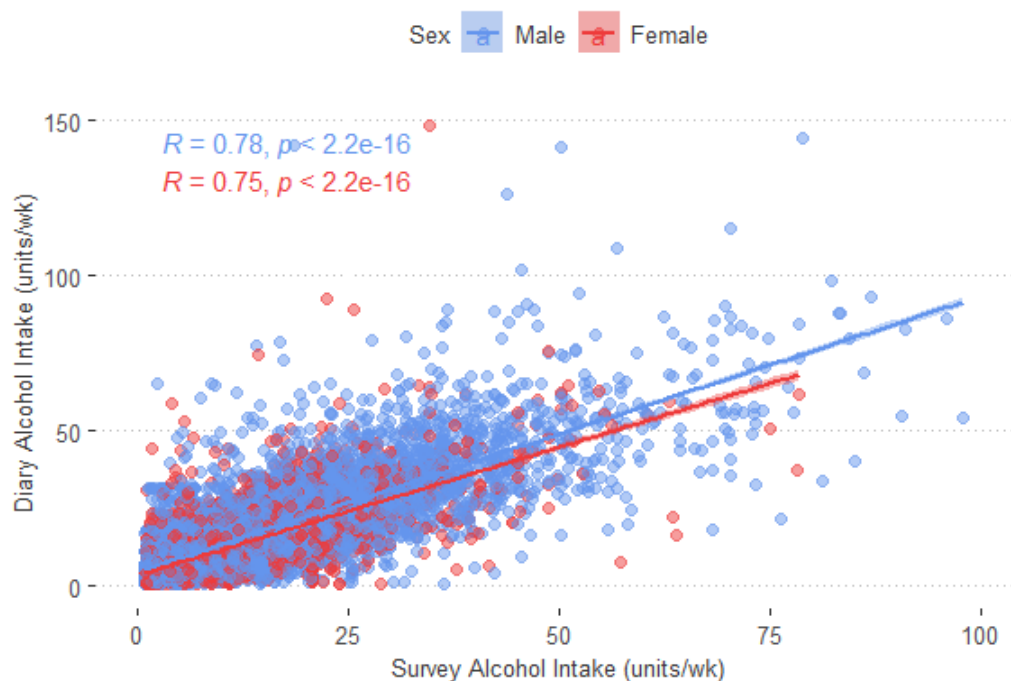
Figure 4.3: Scatterplot to demonstrate correlation between survey and diary measures of alcohol intake (unit/week). R = correlation coefficient.

4.4.6 Inter-method Agreement – Bland Altman Results

A paired Wilcoxon ranked signed test showed a significant difference in measures of alcohol intake between the touchscreen survey and dietary method ($p < 0.001$). The median (IQR) alcohol intake from touchscreen survey data was 9.7 (15.0) compared to 11.7 (16.4) units/week obtained from 7-day dietary records. Bland-Altman analysis for alcohol intake from touchscreen survey versus dietary records shows a mean difference of 2.5 units/week with upper and lower limits of 15.4 and -20.4 units/week (Figure 4.5).

Figure 4.5 *Bland-Altman Plot Dietary vs Survey Measures of Alcohol Intake*
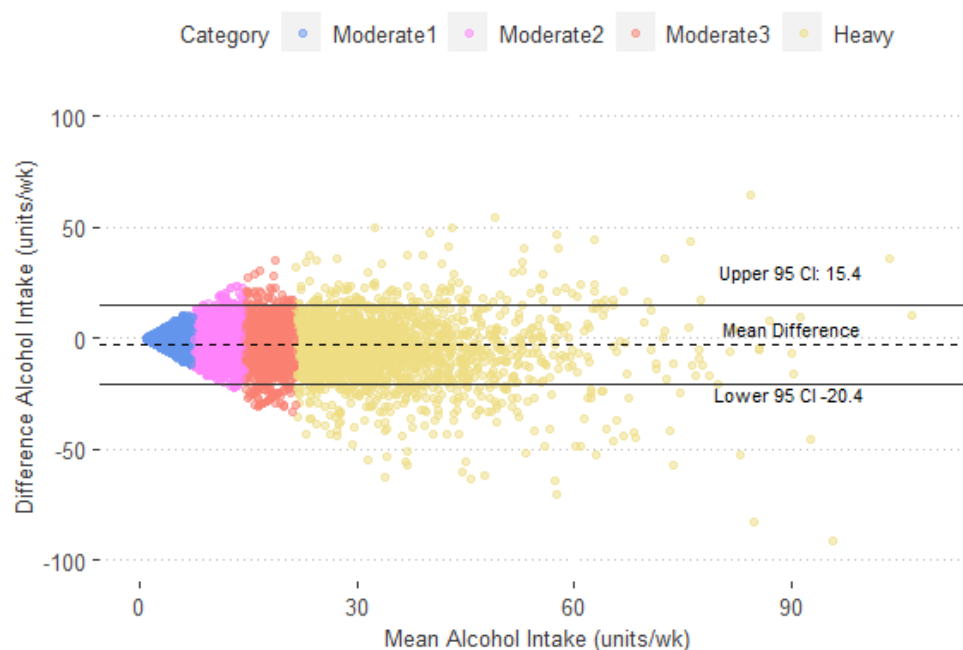
Figure 4.2: Bland-Altman Plot illustrating agreement between survey and dietary measures of alcohol intake. CI = confidence interval.

4.5 Discussion

Alcohol consumption is a causal factor in a large number of medical conditions [286]. These findings are often used to inform alcohol intake policy and guidelines. Therefore, the accuracy of alcohol intake measurements is crucial. Currently, alcohol research relies on self-reported measures of intake to understand alcohol consumption in large populations. A variety of self-reported tools are used to assess intake and can vary from retrospective to prospective measures. This study aimed to:

(i)   Measure alcohol consumption in AHMS and UK Biobank cohorts

(ii)   Measure inter-method reliability between retrospective survey and prospective dietary
        measurement tools.

4.5.1 Summary of Main Findings

❖ In both cohorts, > 90% of participants identify as current drinkers.

❖ The proportion of male participants is greater in categories of higher alcohol intakes.

❖ Male participants are more likely to be dominant beer consumers compared to female participants.

❖ In the AHMS, more than one-third of current drinker's report binge drinking.

❖ Older drinkers are likely to consume higher absolute intakes of alcohol compared to younger drinkers.

- ❖ Younger drinkers were more likely to engage in binge drinking patterns than older drinkers.

- ❖ There is a good correlation between touch screen survey and dietary measures of alcohol intake.

- ❖ Dietary measures of alcohol intake yield higher results compared to survey measures.

4.5.2 Discussion of Main Findings

Objective (i) Estimate alcohol intake concerning current drinking status, and the average volume of intake, beverage preference, and consumption pattern using survey and diary measures of intake.

In both the AHMS and UK Biobank cohorts, a high proportion (> 90%) of participants reported status as 'Current Drinkers' (Table 4.3). This proportion is higher than estimates for the general UK population. For example, in a recent Health Survey for England (HSE) study, 82% of respondent reported having drunk alcohol in the previous 12 months [287]. Furthermore, in an ONS study on adult drinking behaviours, 20% of the surveyed respondents identified as teetotallers, suggesting a current drinking population of 80% of the total surveyed (56,238 participants) [283]. One explanation for the higher prevalence of current drinkers in the AHMS and UK Biobank cohorts compared to national surveys is the difference in age between national survey respondents and respective study cohort participants. The AHMS and UK Biobank participants are older than the age demographic surveyed by the ONS and HSE whose participants equally range in age from 16 to 65 years and over, and there is evidence to suggest that young people between the ages of 16-24 are less likely to drink alcohol than any other age group[283].

In the UK Biobank cohort, a lower proportion of men than women identified as former or never drinkers. However, this finding was not observed in the AHMS, where the ratio of men to women was similar across current, never, and former drinking categories. Traditionally, men are more likely than women to consume alcohol and in greater amounts. The gender difference in alcohol consumption is thought to be in part due to the differences in alcohol pharmacokinetics, as well as the influence of society and its norms[288,289]. Indeed, research into the gender differences in alcohol consumption has consistently shown that men are less likely to be lifetime abstainers compared to women [288]. Findings from a 2017 ONS survey on adult drinking behaviour also supports this trend. In this survey, 23% of women identified as teetotal at baseline compared to 18% of men[283]. Whilst, studies have shown that the size of the gender difference in alcohol consumption can vary according to geographical location[288], there is no clear explanation as to why a similar gender difference is not also observed in the AHMS cohort. One could postulate that the gender convergence (narrowing of differences between genders) observed in the AHMS is a consequence of occupation. The

AHMS is an occupational cohort of policemen and women. It is known that law enforcement is a high pressure, stressful, and complex working environment. In studies of psychological stress and alcohol consumption, there is an association between increased stress and alcohol consumption [290]. Therefore, this convergence could be a result of a difference in drinking behaviour in policewomen compared to the norm. More simply put, because of work-related stressors policewomen are less likely to abstain from alcohol.

The average volume of weekly alcohol intake was estimated in both the AHMS and UK Biobank cohorts. UK Biobank current drinkers recorded a higher median alcohol intake compared to AHMS current drinkers (estimates from both survey and dietary measures) (Table 4.4). The higher alcohol intake in the UK Biobank cohort could be explained by the difference in the age demographic between the two studies. Compared with the AHMS, the UK Biobank cohort is an older demographic with participants ranging in age from 40 to 69 years. As previously discussed, within the UK, there is a known association between age and alcohol intake with older drinkers typically consuming higher intakes compared to younger drinkers[283,287].

The median alcohol intakes (units/week) reported for the AHMS, and UK Biobanks cohorts are less than half that estimated for the UK by the World Health Organisation's (WHO) World Status Report on Alcohol and Health. This report estimates alcohol intake in the UK as 11.4 per capita (alcohol litres per person 15 years and over, per year) which is equivalent to 22 units of alcohol per week. Alcohol intake in this report is derived from both recorded (data recorded in official statistics, i.e., taxation and sales) and unrecorded measures (alcohol that is not accounted for in official statistics on alcohol taxation or sales in the country where it is consumed). The disparity in intake between self-reported measures and sales data is well acknowledged. There is evidence to suggest that alcohol consumption reported in population studies accounts for only 40-60% of sales[272,291,292]. However, without an objective measure of alcohol consumption, it is difficult to ascertain what method better reflects actual intake.

Current drinkers in the AHMS and UK Biobank were grouped into defined drinking levels according to weekly alcohol intake. In the AHMS, a greater proportion of participants were grouped within the lowest level of moderate drinking compared to other levels. In contrast, within the UK Biobank study, a greater share of participants was grouped as heavy drinking compared to other drinking levels. The difference in participant distribution across drinking levels between cohorts can be explained by the association between age and heavy drinking. This relationship is well demonstrated in AHMS current drinkers where the mean age of participants increases with increasing drinking levels (Table 4.4). In both cohorts, men make up a greater proportion of heavier drinking categories compared to women, a finding that is consistent with previous

research in the area of gender and alcohol intake[288,289]. Concerning adherence to UK alcohol drinking guidelines, a little more than half of the current drinkers report consuming alcohol within low risk drinking of ≤ 14 units per week. Adherence to these guidelines was higher amongst AHMS than UK Biobank participants. As these low-risk drinking guidelines are relatively new, it was not possible to find other data on their adherence to benchmark these findings.

Amongst AHMS and UK Biobank current drinkers, wine is the preferred alcoholic beverage, followed by beer and spirits (Table 4.5). This finding coincides with an earlier reported shift in preference amongst UK consumers from wine to beer [293]. In this study, a pronounced gender preference for beer was observed in both cohorts with men making up most of the total beer preferring population. This gender disparity in beverage preference has also been observed in countries across Europe[294]. Within the UK, findings from an ONS also report a greater preference for beer amongst men compared to women who report a higher preference for wine [283].

In this study, more than one-third of AHMS current drinkers reported binge drinking at least once over the 7-day dietary record period. This proportion is higher than that recorded by a 2017 survey of adult drinking behaviours in Great Britain, where 27% of current drinkers were classed as binge drinkers according to their alcohol intake on their heaviest drinking day [283]. A difference in age and gender was also observed between binge and non-binge drinkers. In this study, binge drinkers were younger and more likely to be male compared to non-binge drinkers. This finding is consistent with that reported in previous studies exploring alcohol consumption patterns in large populations [283,295]. For both men and women, the mean alcohol intake during a single binge-drinking occasion was higher than the volumes used in the ONS sex-specific definitions of binge drinking. This finding suggests that during a binge drinking occasion, AHMS binge drinkers consume alcohol well above the volumes known to have a serious and negative impact on health.

Objective (ii) Measure the agreement between diary and survey measures estimates of alcohol intake within the AHMS cohort.

Currently, there is not an operating objective marker of alcohol intake to measure the prevalence of subjective misreporting. In the absence of an objective marker, the agreement between independent subjective alcohol intake estimates can be used as an indicator of misreporting error. This present study observed a good agreement between survey and diary estimates of alcohol intake. Findings from several studies in this area have also reported similar correlations between survey and dietary measurement tools[276,280,296]. The knowledge of how well measurement tools agree with one another is essential to the interpretation of alcohol

health association studies, specifically when underpinning low risk drinking thresholds. In this study, the median alcohol intake estimated from the diary data was higher than the estimated median intake reported for the touchscreen survey. Without an objective measure of intake, it is difficult to establish whether alcohol intake in the touchscreen survey was under-reported or whether intake from the 7-day diet record was over-reported. Previous research in this area has also demonstrated higher alcohol intake estimates from the diary compared to survey measurement[274,280,297–299], as well as the inverse[282]. However, there is evidence to suggest that despite differences in absolute estimates, the general ranking of individuals according to intake by independent measurement tools is quite robust [300,301].

Findings from a Bland-Altman analysis indicate less inter-method reliability between measures with increasing alcohol intakes. As illustrated in Figure 4.2, the difference in absolute intake estimates from diary and survey measures increases from low to higher ranks of alcohol intake. These results align with previous findings from a mixed-method study that demonstrated a greater difference in intake between measures amongst heavier drinkers [302]. Although not observed in this study, other factors, including sex and beverage preference have also been associated with differences in intake estimates yielded between alcohol measurement tools. These findings reinforce the importance of including socio-demographic factors when developing measurement tools, measuring inter-method reliability, and examining the prevalence of misreporting.

4.5.3 Study Strengths and Limitations

One of the weaknesses of this study is that the findings are based on self-reported alcohol consumption, which cannot be relied on as an accurate estimate of intake. Self-reported measures are generally known to be fraught with bias because of several internal and external factors which influence the truthfulness of how the behaviour is reported. Social desirability is a type of response bias where the participant will answer in a manner that they imagine the researcher will find favourable. This bias is very common in the field of alcohol research, and it is a key reason for the large differences observed between self-reported alcohol intakes and intakes calculated from alcohol sales. The survey tool used to estimate alcohol intake relies on a participant's memory to accurately recall intake over the previous 7-day period. Consequently, this study is also prone to recall bias. An objective measure of alcohol intake would eliminate the influence of these biases and offer a reliable and valid estimate of actual intake. Another notable weakness of this study lies in its cross-sectional design. Alcohol intake guidelines note that life changes in consumption and reasons for change are important aspects to measure. This study could only capture baseline alcohol intake and was unable to explore

temporal changes in alcohol consumption behaviour. Furthermore, in the UK Biobank cohort alcohol intake could only be estimated with data from a retrospective tool. As a result, this study was unable to capture the alcohol consumption patterns, an increasingly important aspect of consumption associated with disease risk.

Despite its' weaknesses, this study also has many notable strengths. There is strength in the holistic approach taken when estimating alcohol intake across the independent cohorts. Alcohol consumption was measured using a wide breadth of data from both retrospective and prospective measurement tools. This study followed recommended alcohol intake measurement guidelines and examined several different aspects of alcohol consumption including status, the average volume of intake, the pattern of consumption, and beverage preference. Furthermore, this study contributed to the literature by identifying important differentiating socio-demographic features between groups of participants with varying alcohol intake. Notably, there is lesser inter-method reliability when estimating alcohol intakes in heavier drinkers. This information is important for future research when understanding how self-reported measurement tools can be improved. Another noteworthy strength includes the size of the independent population cohorts. This study captured and compared intake in two large UK populations. The size of these cohorts asserts confidence in the precision of this study's findings. There is also strength in the robust methodology used to 'code' dietary data and translated reported intake of alcoholic beverages to intake per day. Finally, to our knowledge, this is the first study to estimate adherence to UK alcohol intake guidelines and therefore findings may be used to inform government policies and benchmark changes in population intake.

4.5.4 Study Conclusion and Relevance to Further Studies

To conclude, this study successfully delineates alcohol consumption behaviour across the UK Biobank and AHMS cohorts. In both cohorts, there is a significantly higher prevalence of people who currently drink alcohol than those who abstain. Volumes and patterns of alcohol intake seem to vary across demographic factors, most notably sex and age. There are recognised strengths and limitations to measuring alcohol consumption in large populations using self-reported measurement tools. These strengths and limitations are tool-specific, and a holistic estimate of alcohol intake can be captured when these tools are used together. The agreement between retrospective survey and prospective dietary measures of alcohol intake varies with the volume of intake and show to be more reliable for measures of low to moderate drinking. Dietary measures of alcohol intake appear to yield higher estimates of intake compared to survey measures. However, without comparison from an objective marker that can accurately estimate intake without bias, it is not possible to assert which measure, dietary or survey, is more accurate. Measuring urinary metabolites of

ethanol is a promising development in alcohol research that can offer an objective indication of alcohol consumption. Future research should focus on the development of developing objective measures that will capture all aspects of alcohol consumption to understand the actual risk thresholds associated with intake and disease risk.

5.0 Background

Alcohol is a nutrient of high energy density, second only to fat, and unlike other nutrients, it is also a psychoactive drug[303]. In the context of diet, there is some evidence to suggest an association between alcohol intake and dietary behaviour. The ingestion of alcohol has shown to have a stimulating effect on food consumption and is known to contribute to a positive energy balance[8,9,303]. The relationship between alcohol and dietary patterns is less consistent. Whilst there is clear evidence to show that heavy drinking is associated with poorer diet quality[170,180,181], the evidence is inconsistent concerning differences in the dietary patterns for other drinker types. For example, there is inconclusive evidence to determine whether moderate drinkers have more favourable dietary patterns than non-drinkers[172,175]. Similarly, further studies are required to understand whether there is an association between diet and other important aspects of alcohol intake behaviour, including the pattern of consumption and alcoholic beverage preference. At present, the volume of research examining alcohol consumption in the context of dietary intake is very low. Given the confounding role of diet in the relationship between alcohol and cardiometabolic health[228], it is clear that high quality and exhaustive research in this area is warranted.

5.1 Aims & Objectives

The overall aim of this cross-sectional study is to delineate the dietary profile of AHMS and UK Biobank participants across measures of alcohol intake behaviour. The following objectives were set to achieve this aim:

Objectives

i. To describe the dietary profile of participants across alcohol intake category.

ii. To measure the association between alcohol intake and dietary intake measures.

iii. To describe the dietary profile of drinkers according to patterns of alcohol consumption.

iv. To measure the association between patterns of alcohol consumption and intake measures.

v. To measure the differences in the dietary profile of drinkers according to beverage preference.

5.2 Methodology

5.2.1 Study Population

In this present study, AHMS and UK Biobank participants with complete alcohol intake and dietary data were included. Participant recruitment procedures for the AHMS and the UK Biobank cohort have already been described in Chapter 2 of this thesis. Concerning this study chapter, the sampling procedure for each cohort is illustrated in A5.1 Figure 1 and A5.2 Figure 2, respectively.

5.2.2 Dietary Intake Measures

The dietary intake measures used in this study include total energy intake (TEI), total energy intake excluding energy derived from alcohol (TEI-EA), macronutrient intake, the intake of food groups associated with the Dietary Approaches to Stop Hypertension (DASH) diet, and adherence to the DASH diet as a proxy measure of diet quality. The methods used to collect and generate dietary data have already been described in detail in Chapter 3 of this thesis. Energy intake is presented as kilocalories per day (kcal/day) for both energy intake variables excluding and including energy from alcohol whilst dietary energy density is presented as kilocalorie per gram of food intake (kcal/gram). Macronutrient intake was expressed as the proportion of energy from TEI and the proportion of energy from TEI-EA. A modified version of the Mellen et al. DASH score was used to measure diet quality. The scoring procedure for the Modified Mellen et al DASH Score is illustrated in Chapter 3, Table 3.2. A higher DASH score indicates greater adherence to the DASH diet and a diet of higher quality. The DASH score was calculated using total energy intake inclusive of energy from alcoholic beverages. The intake of food groups associated with the DASH diet is estimated in the AHMS study cohort and presented as energy-adjusted intake g/1000kcal/day.

5.2.3 Alcohol Intake Measures

The methods used to collect and generate alcohol intake data have already been outlined in detail in Chapter 4 of this thesis. In this study chapter, alcohol intake estimates from the dietary collection methods (AHMS: 7-day diet record; UK Biobank: OxfordWeb 24-hour Recall) are presented as units/week (AHMS), units/day (UK Biobank) and proportion of TEI from alcohol. Alcohol intake as a proportion of TEI was calculated by multiplying alcohol (g/day) by its corresponding Atwater Factor (alcohol = 7) and presented as a percentage of TEI.

5.2.4 Grouping Variables

The dietary profile of AHMS and UK Biobank participants according to alcohol intake behaviour was explored by comparing dietary intake across i) drinker category (never/former/moderate1/moderate 2/moderate 3/heavy drinker) and ii) alcoholic beverage preference (wine/beer/spirits). In the AHMS cohort, the dietary intakes of drinkers were also compared across patterns of alcohol consumption (binge drinker/non-binge drinker). The methods used to group participants across these measures of alcohol intake are outlined in full in Chapter 4.

5.3.5 Covariate Measures

The following measures were included as covariates: age (years), sex, socioeconomic status (AHMS: highest education and household come; UK Biobank: Townsend index score), current smoking status (yes, no), physical activity level (high, moderate, low), energy density (kcal/g) and plausibility of dietary reporting (under-reporter/plausible reporter). Refer to Chapter 2 and Chapter 3 for full details regarding data collection procedures and measurements of the specified covariate variables

5.3 Statistical Analysis

Statistical analysis was performed using R Studio Software version 1.4.1103. Analyses were stratified by grouping variables and the Chi-square (χ2) test was used to describe differences in the distribution of participants between groups. The normality of the distribution of continuous variables was tested using the Anderson-Darling Test. Normal distributed continuous variables were presented as the mean ± standard deviation (SD) and the difference between measures was tested using the analysis of variance (ANOVA) test, adjusted for participant age and sex. Non-parametric distributed continuous variables were presented as median (Interquartile range (IQR)) and the difference between measures were tested using the Kruskal-Wallis test, adjusted for participant age and sex. Pearson correlation tests were conducted to determine the pairwise agreement between the $\log_{10}$ transformed alcohol intake (AHMS: units/week; UK Biobank units/day), TEI-EA (kcal), macronutrient intake (% TEI-EA), and DASH score. Correlation matrices were plotted using the R package *ggcorrplot.* An insignificant correlation between two variables was indicated by an ✕. The size of Pearson's correlation was evaluated as follows; $0.3 \leq r < 0.5$ low, $0.6 \leq r < 0.8$ moderate, and $r \geq 0.8$ high[249]. Multivariable linear regression was used to examine the association between alcohol intake behaviours and dietary intake measures, controlling for the covariate measures outlined above. In these regression models, measures of absolute alcohol intake (AHMS: units/week; UK Biobank:

units/day) and food group intake (g/1000kcal) were $\log_{10}$ transformed before analysis. For all analyses, statistical significance was accepted as $p< 0.05$.

5.4 Results

5.4.1 Study Population

In this present study, 10,179 AHMS and 165,753 UK Biobank participants with complete alcohol and dietary intake data were included for analysis. In the AHMS, 92.2% (n 9389) of the total sample are current drinkers, and 7.8% (n 790) are non-drinkers. Moderate 1 drinker made up the greatest proportion (30.5%) of the sample studied, whilst never and former drinkers made up the smallest proportion (2.5 and 5.3% respectively) (Table 5.1). In the UK Biobank sample, 92.1% (n 152,595) of participants are current drinkers and 7.9% (n 13,158) are non-drinkers. Most participants in the UK Biobank sample are heavy drinkers (27.6%) whilst the minority are former or never drinkers (4.1 and 3.8%, respectively) (Table 5.2).

5.4.2 Dietary Profile Across Drinker and Non-Drinker Types.

Macronutrient Intake and Diet Quality I

The dietary differences across ranked drinker categories in the AHMS and UK Biobank cohort are presented in (Table 5.1 and Table 5.2, respectively). Heavy drinkers report a higher TEI (kcal), a higher proportion of energy intake derived from alcohol (% TEI) and a lower intake of fibre (g/1000kcal) than moderate (all ranks), never, and former drinkers ($p<0.001$). Compared with never and former drinkers, moderate drinkers (all ranks) and heavy drinkers report a smaller proportion of TEI derived from macronutrients (carbohydrate, protein, fat, and saturated fat) ($p<0.001$). Amongst drinkers, DASH score and fibre intake (g/1000kcal) decreases across higher-ranked drinker categories ($p<0.001$). In the AHMS, former drinkers report a higher fibre intake (g/1000kcal), a higher DASH score and a lower proportion of TEI derived from fat and saturated fat compared with never drinkers (Table 5.1). In the UK Biobank cohort, former drinkers report a lower intake of fibre (g/1000kcal), a lower DASH score, and a higher proportion of TEI derived from fat compared to never drinkers (Table 5.2). Moderate 1 AHMS drinkers have a higher fibre intake than never drinkers, mean 7.6 SD 2.2 versus mean 7.2 SD 2.4 g/1000kcal.

Results from linear regression modelling performed to compare the diet quality of moderate 1 drinkers with never, former moderate 2, moderate 3, and heavy drinkers are illustrated in Table 5.3. These

results indicate a non-significant difference in the diet quality (DASH score) between AHMS moderate 1 and never drinkers, as well as AHMS moderate 1 and former drinkers (Model 1 and Model 2). Relative to AHMS moderate 1 drinkers, AHMS moderate 2, moderate 3 and heavy drinkers have a lower DASH score (p <0.001). UK Biobank former and never drinkers have a higher DASH score than moderate 1 drinkers and this observation is significant in both the crude (Model 1) and the adjusted model (Model 2) (Table 5.3). Relative to UK Biobank moderate 1 drinkers, there is a deterioration in diet quality (DASH score) across higher-ranked drinker categories and the significance of this observation is also retained after adjustment for explanatory covariate variables (Model 2).

Table 5.1 Dietary Profile Across Ranked Drinker Categories in the Airwave Health Monitoring *Study*

Dietary Profile Across Ranked Drinker Categories in the Airwave Health Monitoring Study								
		Never	**Former**	**Moderate1**	**Moderate2**	**Moderate3**	**Heavy**	***p***
Range (Units Alcohol)		-	-	1-7	7-14	14-21	>21	-
Total (10,179)	**n (%)**	253 (2.5)	537 (5.3)	3103 (30.5)	2361 (23.2)	1480 (14.5)	2445 (24.0)	<0.001
Energy Intake								
TEI (kcal)	**Mean (SD)**	1794 (536)	1792 (475)	1813 (476)	1901 (460)	1975 (452)	2156 (503)	<0.001
Energy Density (g/kcal)		0.73 (0.24)	0.71 (0.23)	0.71 (0.20)	0.71 (0.20)	0.70 (0.18)	0.67 (0.17)	<0.001
Nutrient Intake[1]								
%TEI Carbohydrate	**Mean (SD)**	47.8 (6.5)	48.2 (6.4)	47.0 (5.8)	44.8 (5.6)	43.1 (5.3)	39.3 (6.0)	<0.001
% TEI Total Fat		34.7 (6.5)	33.8 (6.0)	34.3 (5.6)	33.9 (5.3)	33.2 (5.1)	31.6 (5.2)	<0.001
% TEI Saturated Fat		12.7 (3.2)	12.4 (3.2)	12.6 (2.9)	12.4 (2.8)	12.0 (2.7)	11.4 (2.7)	<0.001
% TEI Protein		17.4 (4.1)	17.9 (4.4)	17.5 (3.5)	17.4 (3.5)	17.0 (3.1)	16.6 (3.0)	<0.001
Fibre (g/1000kcal)[2]		7.2 (2.4)	7.7 (2.6)	7.6 (2.2)	7.2 (2.1)	7.0 (1.9)	6.2 (1.8)	<0.001
% TEI Alcohol[3]		-	-	1.8 (1.0)	4.8 (1.5)	7.5 (1.9)	13.5 (5.0)	<0.001
DASH Score	**Mean (SD)**	2.6 (1.5)	2.7 (1.5)	2.6 (1.4)	2.5 (1.3)	2.5 (1.3)	2.4 (1.2)	<0.001

Abbreviations: TEI – Total Energy Intake; DASH Dietary Approaches to Stop Hypertension.

Keys: 1 TEI including energy from alcohol 2 - Non-Starch Polysaccharide Fibre; 3 – % TEI from alcohol-containing beverages.

Tests: ANOVA adjusted for age and sex. p < 0.05 – significant

Table 5.2 *Dietary Profile Across Ranked Drinker Categories in the UK Biobank Cohort*

Dietary Profile Across Ranked Drinker Categories in the UK Biobank Cohort								
		Never	**Former**	**Moderate1**	**Moderate2**	**Moderate3**	**Heavy**	**p**
Range (Units Alcohol)		-	-	1-7	7-14	14-21	>21	-
Total (165,753)	**n (%)**	6780 (4.1)	6378 (3.8)	31,876 (19.2)	46,576 (28.1)	28,452 (17.2)	45,691 (27.6)	<0.001
Energy Intake								
TEI (kcal)	**Mean (SD)**	1998 (692)	2072 (717)	2031 (579)	2081 (579)	2141 (600)	2264 (642)	<0.001
Energy Density (g/kcal)		0.68 (0.21)	0.68 (0.22)	0.67 (0.18)	0.67 (0.17)	0.67 (0.17)	0.66 (0.17)	<0.001
Nutrient Intake								
%TEI Carbohydrate	**Mean (SD)**	50.3 (7.8)	49.2 (8.0)	47.1 (7.0)	45.5 (6.6)	44.0 (7.3)	40.9 (7.7)	<0.001
% TEI Total Fat		32.8 (7.3)	33.6 (7.3)	33.4 (6.6)	33.0 (6.6)	32.5 (6.6)	31.4 (6.9)	<0.001
% TEI Saturated Fat		12.6 (3.7)	13.0 (3.7)	12.8 (3.3)	12.7 (3.3)	12.5 (3.3)	12.0 (3.4)	<0.001
% TEI Protein		16.1 (4.0)	16.1 (4.0)	16.2 (3.5)	16.0 (3.5)	15.8 (3.4)	15.3 (3.5)	<0.001
Fibre (g/1000kcal) [†]		8.8 (3.5)	8.7 (3.6)	8.4 (2.9)	8.1 (2.8)	7.8 (2.7)	7.0 (2.6)	<0.001
% TEI Alcohol	**Median (IQR)**	-	-	3.8 (4.9)	5.5 (5.6)	7.6 (6.6)	11.8 (9.5)	<0.001
DASH Score*	**Mean (SD)**	3.30 (1.42)	3.27 (1.41)	3.14 (1.41)	3.08 (1.40)	3.05 (1.39)	3.03 (1.38)	<0.001
Abbreviations: TEI – Total Energy Intake; DASH Dietary Approaches to Stop Hypertension								
Keys: † - Non-starch polysaccharide; * - DASH score calculated for n = 159,140 participants.								
Test: ANOVA – normal continuous variables; Kruskal-Wallis Test – non-parametric continuous variables. Tests adjusted for age and sex. p < 0.05 significant								

Table 5.3 *Linear Regression Modelling, Diet Quality and Drinker Type*

	Model 1			**Model 2**		
Linear Regression Modelling, Diet Quality and Drinker Type						
	DASH Score	Std Error	*p*	DASH Score	Std Error	*p* *
AHMS						
Moderate 1	*Ref*	-	-	*Ref*	-	-
Never	- 0.12	0.09	*ns*	-0.03	0.08	*ns*
Former	0.06	0.06	*ns*	0.06	0.05	*ns*
Moderate2	-0.10	0.04	<0.001	-0.09	0.03	<0.01
Moderate3	-0.17	0.04	<0.001	-0.16	0.04	<0.001
Heavy	-0.25	0.04	<0.001	-0.30	0.04	<0.001
UK Biobank						
Moderate 1	*Ref*	-	-	*Ref*	-	-
Never	0.16	0.02	<0.001	0.14	0.02	<0.001
Former	0.13	0.02	<0.001	0.09	0.02	<0.001
Moderate2	-0.07	0.01	<0.001	-0.09	0.01	<0.001
Moderate3	-0.10	0.01	<0.001	-0.14	0.01	<0.001
Heavy	-0.12	0.01	<0.001	-0.23	0.01	<0.001

Abbreviations: Ref – Reference; ns – nonsignificant

Keys: * p < 0.05 – significant

Model 1: Crude + Age + Sex

Model 2: Model 1 + Socioeconomic Status (AHMS: Education + Income, UKB: Townsend Index) + Smoking Status+ Energy Density + Misreporting Status + Physical Activity Level (PAL)

Food Group Intake AHMS

The dietary differences in the intake of food groups across ranked drinker categories in the AHMS are outlined in Table 5.4. Compared with never, former, and moderate ranked drinkers, heavy drinkers report a lower intake of fruit, vegetables, and legumes, and a higher intake of red meat (g/1000kcal). Amongst drinkers, the intake of fruit (g/1000kcal/day) and proportion intake of wholegrain from total cereals decreases across higher ranked categories of drinker, whilst the intake of red meat increases (g/1000kcal) (*p*<0.001). Compared with former drinkers, never drinkers report a lower intake of fruit, median 90.8 IQR 108 vs median 98.7 IQR 112 g/1000kcal, a lower intake of vegetables median 72.8 IQR 52.2 vs median 79.1 IQR 57.9 g/1000kcal, and a lower intake wholegrain cereal median 22.8 IQR 29.6 vs median 24.7 IQR 30.0 % total cereals. Moderate 1 drinkers report a higher intake of vegetables (g/1000kcal) and wholegrain (% total cereals) than former or never drinkers and a higher intake of fruit (g/1000kcal) than never drinkers. The intake of low-fat dairy (% total dairy) was non-significant across drinker categories.

Table 5.4 *Food Group Intake Across Drinker Type Airwave Health Monitoring Study*

Food Group Intake Across Drinker Type Airwave Health Monitoring Study							
	Never	**Former**	**Moderate 1**	**Moderate 2**	**Moderate 3**	**Heavy**	*p*
Range (Alcohol Units)	-	-	1-7	7-14	14-21	>21	-
Food Intake (g/1000kcal/d)							
Fruit[†] **Median (IQR)**	90.8 (108.0)	98.7 (112.0)	95.6 (96.4)	87.4 (95.9)	81.7 (84.0)	68.1 (80.3)	<0.001
Vegetables	72.8 (52.2)	79.1 (57.9)	81.1 (57.4)	77.1 (54.2)	77.1 (49.9)	69.9 (45.8)	<0.001
Legumes	14.2 (17.1)	13.6 (14.4)	13.6 (15.2)	12.7 (12.8)	12.9 (14.0)	11.6 (12.3)	<0.001
Total Cereals	108.0 (55.6)	111.0 (51.5)	109.0 (43.8)	108.0 (43.5)	105.0 (40.9)	97.2 (39.5)	<0.001
% Wholegrain	22.8 (29.6)	24.7 (30.0)	25.9 (31.7)	25.0 (30.3)	24.7 (29.4)	22.4 (28.2)	<0.001
Red Meat	33.0 (31.5)	36.1 (33.8)	36.5 (30.2)	38.8 (27.9)	40.1 (27.2)	42.6 (27.8)	<0.001
Total Dairy	163.0 (119.0)	161.0 (108.0)	153.0 (96.5)	142.0 (91.6)	127.0 (78.2)	113.0 (75.1)	<0.001
% Low Fat	70.9 (35.5)	75.7 (25.2)	75.9 (24.6)	75.1 (24.5)	76.4 (22.7)	75.1 (25.0)	*ns*
Abbreviations: d – day; ns non-significant; IQR interquartile range.							
Keys: ┼: including pure juice, truncated at 1 small glass (150ml).							
Statistical Test: Kruskal-Wallis Test. p < 0.05 significant							

Macronutrient Intake and Diet Quality II

Findings from Pearson correlation tests conducted to estimate the pairwise correlation between absolute alcohol intake (AHMS: units/week; UK Biobank units/day), TEI-EA, macronutrient intake (% of TEI-EA), and DASH score are presented in Figure 5.1. Results indicate a positive pairwise correlation between alcohol intake (AHMS: units/week; UK Biobank: units/day) and the proportion of TEI-EA derived from fat and saturated fat (*p* <0.05). A negative pairwise correlation was observed for alcohol intake (AHMS: units/week, UK Biobank: units/day), the proportion of TEI-EA from carbohydrate, intake of fibre (g/1000kcal), and diet quality (DASH score) (*p*<0.05). In the AHMS, there was a positive correlation between alcohol intake and TEI-EA (*p*<0.05). The same pairwise correlation was not observed as significant in the UK Biobank cohort. The pairwise correlation coefficients are represented as numeric values within correlation matrices (AHMS: Correlation Matrix A; UK Biobank: Correlation Matrix B) as illustrated in Figure 5.1.
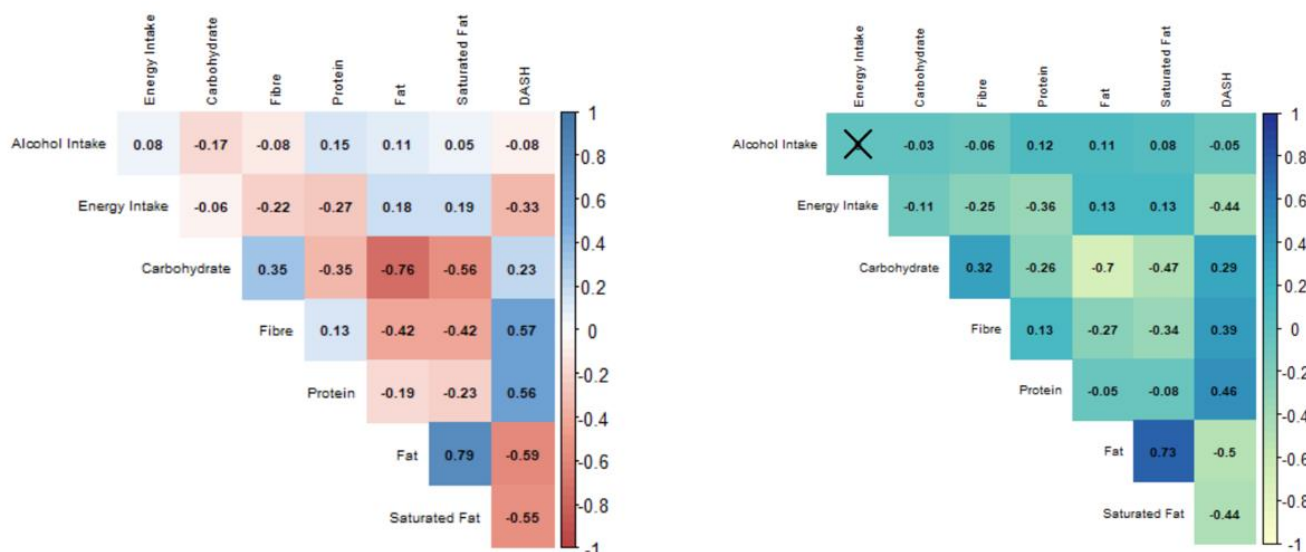
Figure 5.1: A: Correlation Matrix for the Airwave Health Monitoring Study, B: Correlation Matrix for the UK Biobank cohort. The numeric values represent the correlation coefficient r for each pairwise correlation. p < 0.05 is significant. ✕ indicates a non-significant correlation.

The results of linear modelling analyses (crude and adjusted) to estimate the association between absolute alcohol intake and diet quality are presented in Table 5.6. In both the crude and adjusted models there is a deterioration in diet quality (DASH Score) with increasing alcohol intake (AHMS: units/week, UK Biobank: units/day) ($p < 0.001$).

Table 5.5 Linear Modelling Results: Association Between Alcohol Intake (units) and Diet Quality

Linear Modelling Results: Association Between Alcohol Intake (units) and Diet Quality						
	Model 1			Model 2		
	DASH Score	Std Error	p	DASH Score	Std Error	p
AHMS						
Alcohol Intake	- 0.210	0.032	<0.001	-0.254	0.030	<0.001
UK Biobank						
Alcohol Intake	-0.174	0.009	<0.001	-0.243	0.008	<0.001
Model 1: Crude + Age + Sex						
Model 2: Model 1 + Socioeconomic Status (AHMS: Education + Income, UKB: Townsend Index) Smoking Status + Energy Density + Misreporting Status + PAL						

5.4.3 Dietary Profile of AHMS Drinkers Across Patterns of Consumption

In the AHMS, 9389 drinkers were grouped as binge or non-binge drinkers according to their pattern of alcohol consumption (A5.3 Table 5.1). More than a third (34.7%) of drinkers were grouped as binge drinkers, of

whom more than half (61.3%) are in the heavy drinker category. In the non-binge drinker group, half are moderate 1 drinkers, a third are moderate 2 drinkers, while less than 10% are heavy drinkers.

The dietary differences between binge and non-binge drinkers are outlined in A5.3 Table 5.1. Compared with non-binge drinkers, binge drinkers report a higher TEI, a higher proportion of TEI from alcohol, a lower intake of fibre (g/1000kcal), and a lower DASH score. The proportion of TEI derived from macronutrients (carbohydrate, protein, fat, and saturated fat) is lower in binge drinkers than non-binge drinkers.

The dietary differences between binge and non-binge drinkers within drinker categories are presented in Table 5.7. Within the moderate ranked drinker categories, non-binge drinkers report a higher TEI compared to binge drinkers. However, this difference is only significant between non-binge and binge drinkers in the moderate 2 drinker category. In the moderate ranked drinker categories, binge drinkers also have a higher DASH score relative to non-binge drinkers. Though, this difference is significant ($p < 0.05$) only between non-binge and binge drinkers in the moderate 1 drinker category. Within the heavy drinker category, binge drinkers report a higher TEI than non-binge drinkers (mean 2185 SD 501 vs mean 2026 SD 495 kcal/day) ($p < 0.05$) and a lower intake of fibre (mean 6.1 SD 1.7 versus mean 6.9 SD 2.0 g/1000kcal) ($p < 0.05$). Across all drinker categories, binge drinkers report a smaller proportion of TEI derived from fat and saturated fat than non-binge drinkers, but also a higher proportion of TEI derived from alcohol ($p < 0.001$)

Linear modelling analyses were conducted to explore the relationship between binge drinking and diet quality. In unadjusted and adjusted models, the DASH score of binge drinkers is lower than non-binge drinkers in analyses for the total population and drinkers within the heavy drinker category. However, these differences were non-significant after adjustment for covariates including the mean alcohol intake (units/week) (Table 5.8). Among the moderate ranked drinkers, binge drinkers have a higher DASH score than non-binge drinkers. This finding was non-significant in crude and adjusted analyses for moderate 2 and moderate 3 drinkers, and significant only in the crude analysis for moderate 1 drinkers (Table 5.8).

Table 5.6 *Dietary Differences between Binge and Non-Binge Drinkers within Ranked Drinker Category*.

Dietary Differences between Binge and Non-Binge Drinkers within Ranked Drinker Category.										
		Moderate1		Moderate 2		Moderate 3		Heavy		*p*
		Binge	*Non-Binge*	*Binge*	*Non-Binge*	*Binge*	*Non-Binge*	*Binge*	*Non-Binge*	-
Energy Intake	**Mean (SD)**									
TEI (kcal)		1622 (198)	1814 (477)	1847 (443)	1916 (463)	1972 (433)	1978 (470)	2185 (501)	2026 (495)	<0.05 [b, d]
Energy Density (g/kcal)		0.65 (0.17)	0.71 (0.20)	0.68 (0.20)	0.72 (0.20)	0.70 (0.18)	0.71 (0.18)	0.66 (0.16)	0.71 (0.20)	<0.05[b, c, d]
Nutrient Intake										
%TEI Carbohydrate	**Mean (SD)**	48.1 (6.7)	47.0 (5.8)	44.8 (5.4)	44.8 (5.7)	43.0 (5.3)	43.2 (5.4)	38.6 (5.7)	42.4 (6.1)	<0.05[d]
% TEI Total Fat		31.0 (7.1)	34.3 (5.6)	32.8 (5.4)	34.2 (5.3)	32.6 (5.0)	33.8 (5.1)	31.2 (5.2)	33.1 (5.1)	<0.05 [a, b, c, d]
% TEI Saturated Fat		10.7 (3.0)	12.6 (3.0)	11.8 (2.8)	12.6 (2.8)	11.6 (2.6)	12.3 (2.7)	11.3 (2.6)	12.1 (2.9)	<0.05 [a, b, c, d]
% TEI Protein		17.6 (2.2)	17.5 (3.5)	17.2 (3.2)	17.4 (3.6)	16.9 (3.0)	17.1 (3.1)	16.4 (2.8)	17.1 (3.5)	<0.05[d]
Fibre (g/1000kcal)[1]		8.3 (2.5)	7.6 (2.2)	7.2 (2.2)	7.2 (2.0)	7.0 (1.9)	7.1 (1.9)	6.1 (1.7)	6.9 (2.0)	<0.05[d]
% TEI Alcohol[2]	**Median (IQR)**	3.4 (0.8)	1.6 (1.5)	5.0 (2.2)	4.4 (2.0)	7.4 (2.3)	7.1 (2.5)	12.9 (6.2)	12.1 (4.3)	<0.05 [a, b, c, d]
DASH Score		3.3 (1.4)	2.6 (1.4)	2.6 (1.4)	2.5 (1.3)	2.5 (1.2)	2.4 (1.3)	2.4 (1.2)	2.4 (1.3)	<0.05 [a]
Abbreviations: TEI – Total Energy Intake; DASH Dietary Approaches to Stop Hypertension; SD – Standard Deviation, IQR – Interquartile Range.										
Keys: 1 - Non-Starch Polysaccharide Fibre; 2 – TEI from alcoholic beverages: * p < 0.05 – significant; a - Moderate 1; b - Moderate 2; c - Moderate 3; d - Heavy.										
Statistical Test: ANOVA adjusted for age and sex – normally distributed variables, Kruskal-Wallis Test for non-parametric variables.										

Table 5.7 Linear Modelling Results: The Association Between Binge Drinking Behaviour and Diet Quality

Linear Modelling Results: The Association Between Binge Drinking Behaviour and Diet Quality									
	Model 1			Model 2			Model 3		
	DASH Score	Std Error	*p*	DASH Score	Std Error	*p*	DASH Score	Std Error	*p*
All Drinkers									
Non-Binge Drinker	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Binge Drinker	-0.09	0.02	<0.001	-0.16	0.02	<0.001	-0.04	0.03	*ns*
Moderate 1									
Non-Binge Drinker	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Binge Drinker	0.61	0.33	*ns*	0.48	0.29	*ns*	0.49	0.30	*ns*
Moderate 2									
Non-Binge Drinker	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Binge Drinker	0.16	0.07	<0.05	0.07	0.06	*ns*	0.07	0.06	*ns*
Moderate 3									
Non-Binge Drinker	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Binge Drinker	0.07	0.07	*ns*	0.01	0.06	*ns*	0.01	0.06	*ns*
Heavy									
Non-Binge Drinker	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Binge Drinker	-0.01	0.06	*ns*	-0.10	0.06	*ns*	-0.04	0.06	*ns*
Abbreviations: Ref – Reference; ns – non-significant									
Model 1: Crude + Age + Sex									
Model 2: Model 1 + Socioeconomic Status (AHMS: Education + Income, UKB: Townsend Index) + Smoker Status +Energy Density + Misreporting Status+ PAL									
Model 3: Model 2 + Alcohol Intake (Log Units/Week)									

5.4.4 Dietary Profile of AHMS and UK Biobank Drinkers Across Alcoholic Beverage Preference

 Macronutrient Intake and Diet Quality

In this study, 9389 AHMS and 152,595 UK Biobank drinkers were grouped according to alcoholic beverage preference. In both cohorts, there is a significantly greater proportion of drinkers reporting a preference for wine compared to beer or spirits (A5.4 Table 5.2). In the AHMS sample, moderate 1 drinkers make up the largest proportion (41.3%) of drinkers grouped as preferring spirits (*p* <0.001). In the UK Biobank sample, 41.1% of beer preferring drinkers are heavy drinkers. In both cohorts, the difference in the distribution of drinkers across the wine preference category is non-significant.

The differences in the macronutrient intake and diet quality between drinkers of differing alcoholic beverage preference were measured using linear regression analyses. The results of these analyses are presented in Table 5.9. Compared with wine drinkers, beer and spirit drinkers have a lower DASH score. This difference was significant only in beer drinkers after adjustment for covariates including alcohol intake (AHMS: units/week, UK Biobank units: units/day). Beer and spirit drinkers also report a lower intake of fibre g/1000kcal than wine drinkers. This difference was also independent of absolute alcohol intake (Model 3). In

the UK Biobank cohort, the proportion of TEI derived from fat and saturated fat is higher in beer and spirit drinkers than wine drinkers (*p*<0.001). A significant difference in the dietary fat intake between wine, beer and spirit drinkers was not observed in this study.

Table 5.8 *Linear Modelling: Beverage Preference and Dietary Intake*

Linear Modelling: Beverage Preference and Dietary Intake								
Model 1			*Model 2*			*Model 3*		
DASH	**Std Error**	***p*** *	**DASH**	**Std Error**	***p*** *	**DASH**	**Std Error**	***p*** *
AHMS								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	- 0.04	0.03	*ns*	-0.11	0.03	<0.001	-0.12	0.03	<0.001
Spirits	-0.08	0.04	*ns*	-0.04	0.04	*ns*	-0.07	0.04	*ns*
UK Biobank								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	0.06	0.01	<0.001	-0.01	0.01	*ns*	-0.02	0.01	<0.05
Spirits	0.02	0.02	*ns*	0.04	0.02	<0.05	0.01	0.02	*ns*
Fibre	**Std Error**	***p*** *	**Fibre**	**Std Error**	***p*** *	**Fibre**	**Std Error**	***p*** *
AHMS								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	-0.27	0.05	<0.001	-0.32	0.05	<0.001	-0.36	0.05	<0.001
Spirits	-0.18	0.07	<0.001	-0.11	0.06	*ns*	-0.23	0.06	<0.001
UK Biobank								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	-0.23	0.02	<0.001	-0.29	0.02	<0.001	-0.33	0.02	<0.001
Spirits	-0.19	0.03	<0.001	-0.06	0.03	<0.05	-0.21	0.03	<0.001
Fat	**Std Error**	**p** *	**Fat**	**Std Error**	**p** *	**Fat**	**Std Error**	**p** *
AHMS								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	-0.20	0.13	*ns*	0.06	0.12	*ns*	-0.02	0.12	*ns*
Spirits	0.20	0.18	*ns*	0.05	0.17	*ns*	-0.20	0.17	*ns*
UK Biobank								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	-0.02	0.04	*ns*	0.27	0.04	<0.001	0.20	0.04	<0.001
Spirits	0.76	0.08	<0.001	0.57	0.08	<0.001	0.32	0.07	<0.001
SFA	**Std Error**	***p*** *	**SFA**	**Std Error**	**p** *	**SFA**	**Std Error**	***p*** *
AHMS								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	-0.03	0.07	*ns*	0.08	0.06	*ns*	0.04	0.06	*ns*
Spirits	0.07	0.09	*ns*	-0.01	0.09	*ns*	-0.12	0.09	*ns*
UK Biobank								
Wine	*Ref*	-	-	*Ref*	-	-	*Ref*	-	-
Beer	0.02	0.02	*ns*	0.15	0.02	<0.001	0.13	0.02	<0.001
Spirits	0.38	0.04	<0.001	0.27	0.04	<0.001	0.17	0.04	<0.001

Abbreviations: Ref – Reference, ns – non-significant, SFA – saturated fatty acid. Model 1: Crude + age + sex
Model 2: Model 1 + Socioeconomic Status (AHMS: Education + Income, UKB: Townsend Index) + Smoker + Misreporting Status + Energy Density +PAL
Model 3: Model 2 + Log10(Alcohol Intake).

The differences in food group intake between AHMS wine drinkers, beer, and spirit drinkers are outlined in Table 5.10. Relative to wine drinkers, beer drinkers have a lower intake of fruit, vegetables, legumes, fish (g/1000kcal), wholegrain cereals (% of total cereals) and a higher intake of red meat (g/1000kcal) ($p<0.001$). These differences in food group intake between beer and wine drinkers are significant and independent of absolute alcohol intake (Model 3). Spirit drinkers also report a lower intake of fruit, fish (g/1000kcal), wholegrain cereal (% total cereal), and a higher intake of red meat than wine drinkers ($p<0.001$). There was a non-significant difference in the intake of fruit (g/1000kcal) between wine and spirit drinkers and a non-significant difference in low-fat dairy intake between wine, beer, and spirit drinkers.

Table 5.9 *Linear Regression Modelling: Beverage Preference and Food Group Intake*

Linear Regression Modelling: Beverage Preference and Food Group Intake									
	Model 1			**Model 2**			**Model 3**		
Preference	**Fruit**	**Std. Error**	**p**	**Fruit**	**Std. Error**	**p**	**Fruit**	**Std. Error**	**p**
Wine	Ref	-	-	Ref	-	-	Ref	-	-
Beer	-0.03	0.01	0.01	-0.04	0.01	<0.001	-0.04	0.01	<0.001
Spirits	-0.03	0.01	*ns*	-0.01	0.01	*ns*	-0.02	0.01	*ns*
	Vegetable	**Std. Error**	**p**	**Vegetables**	**Std. Error**	**p**	**Vegetables**	**Std. Error**	**p**
Wine	Ref	-	-	Ref	-	-	Ref	-	-
Beer	-0.05	0.01	<0.001	-0.06	0.01	<0.001	-0.06	0.01	<0.001
Spirits	-0.04	0.01	<0.001	-0.03	0.01	<0.001	-0.03	0.01	<0.001
	Legumes	**Std. Error**	**p**	**Legumes**	**Std. Error**	**p**	**Legumes**	**Std. Error**	**p**
Wine	Ref	-	-	Ref	-	-	Ref	-	-
Beer	0.011	0.01	*ns*	0.005	0.01	*ns*	0.004	0.01	*ns*
Spirits	-0.002	0.01	*ns*	-0.003	0.01	*ns*	-0.007	0.01	*ns*
	Red Meat	**Std. Error**	**p**	**Red Meat**	**Std. Error**	**p**	**Red Meat**	**Std. Error**	**p**
Wine	Ref	-	-	Ref	-	-	Ref	-	-
Beer	0.017	0.01	0.016	0.015	0.01	0.020	0.017	0.01	0.012
Spirits	0.002	0.01	*ns*	-0.002	0.01	*ns*	0.003	0.01	*ns*
	Fish	**Std. Error**	**p**	**Fish**	**Std. Error**	**p**	**Fish**	**Std. Error**	**p**
Wine	**Ref**	**-**	**-**	**Ref**	**-**	**-**	**Ref**	**-**	**-**
Beer	-0.03	0.01	0.009	-0.03	0.01	0.003	-0.03	0.01	0.002
Spirits	-0.03	0.01	0.031	-0.02	0.01	*ns*	-0.03	0.01	0.049
	Wholegrain[1]	**Std. Error**	**p**	**Wholegrain[1]**	**Std. Error**	**p**	**Wholegrain[1]**	**Std. Error**	**p**
Wine	Ref	-	-	Ref	-	-	Ref	-	-
Beer	-0.01	0.01	*ns*	-0.02	0.01	*ns*	-0.02	0.01	0.038
Spirits	-0.05	0.01	<0.001	-0.05	0.01	<0.001	-0.05	0.01	<0.001
	LF Dairy[2]	**Std. Error**	**p**	**LF Dairy[2]**	**Std. Error**	**p**	**LF Dairy[2]**	**Std. Error**	**p**
Wine	Ref	-	-	Ref	-	-	Ref	-	-
Beer	-0.005	0.005	*ns*	0.002	0.005	*ns*	0.002	0.005	*ns*
Spirits	-0.004	0.006	*ns*	0.0001	0.006	*ns*	0.0004	0.006	*ns*

Abbreviations: Ref – Reference; ns – non-significant
Keys:1 – Wholegrain intake as a % of total cereal intake; 2- Low-fat dairy intake as a % of total dairy intake.
Model 1: Crude +age +sex
Model 2: Model 1 + Socioeconomic Status (AHMS: Education + Income, UKB: Townsend Index) + Smoker + Misreporting Status + Energy Density
Model 3: Model 2 + Log10(Alcohol Intake (units/week).

5.5 Discussion

The relationship between alcohol consumption and cardiometabolic health is confounded by lifestyle behaviours most notably dietary intake and quality. To fully understand the role of diet in the relationship between alcohol and cardiometabolic risk, it is important to first examine the association between diet and alcohol consumption. This study aimed to delineate dietary intake and quality across alcoholic consumption behaviours.

5.5.1 Summary of Main Findings

❖ Increases in alcohol intake are concurrent with increases in total energy intake.

❖ Heavier drinkers have the poorest quality of diet compared to never, former, or moderate drinkers.

❖ The diet quality of drinkers decreases across higher ranked categories of drinker.

❖ Whether non-drinkers have a better diet quality than those in the lowest category of drinker is inconclusive.

❖ Alcohol intake is positively associated with total dietary fat and saturated fat and negatively associated with intake of fibre and diet quality.

❖ Heavy drinkers who binge drink have a higher total energy intake and lower fibre intake than heavy drinkers who do not binge drink.

❖ Amongst drinkers in the lowest-ranked moderate category (moderate 1), diet quality is higher in binge drinkers than non-binge drinkers.

❖ Compared with wine drinkers, beer drinkers have a poorer diet quality independent of alcohol intake.

5.5.2 Discussion Main Findings

Objectives i) To describe the dietary profile of participants across alcohol intake category ii) To measure the association between alcohol intake and dietary intake measures.

This study reports a concurrent increase in energy intake with alcohol consumption. In both cohorts, total energy intake increased across low to higher-ranked drinker categories. A positive linear association between alcohol and energy intake independent of energy from alcohol was also observed. These findings suggest that in both the AHMS and UK Biobank cohort drinkers do not compensate for the added energy provided by alcohol. This is an observation that has been consistently reported in previous studies including a recently published systematic review and meta-

analysis[8,126,169,304–307]. The additive effect of alcohol on total energy intake could be explained by its effect on appetite and satiety. Although unclear, it has been postulated that ingestion of alcohol bypasses the satiety mechanisms that regulate energy intake [9]. Alcohol is also relatively energy-dense (7kcal per gram) and regular consumption can contribute to a positive energy balance.

Findings from this study indicate a deterioration in diet quality with increasing alcohol intake. Relative to the lowest rank of moderate drinker, higher-ranked moderate drinkers and heavy drinkers had a significantly lower DASH score and intake of fibre. Similarly, whilst the intake of red meat was higher in higher-ranked drinker categories, the consumption of high fibre food groups (fruit, vegetables, legumes, and wholegrains) was lower. Moreover, after adjusting for energy from alcohol, this study observed an increase in energy from fat and saturated fat, and a decrease in energy from carbohydrate with increasing alcohol intake. The observation that diet quality decreases with increasing alcohol consumption corroborates evidence from previous studies, including a longitudinal study in the Framingham Heart Offspring cohort that reported a better diet quality amongst moderate drinkers compared with heavy drinkers[169,170,179–181]. However, whilst the evidence for alcohol-diet quality relation is consistent, there is discordance in the relationship between alcohol and macronutrient intake, with some studies showing higher intakes of fat and saturated fat in moderate drinkers compared to heavier drinkers[308,309].

At present, there is no clear explanation for the relationship between alcohol intake and diet quality. Nevertheless, the involvement of neurochemical systems governing appetite, satiety, restraint and reward have been suggested [8,9].

There is some evidence to suggest that moderate alcohol consumption is associated with healthier dietary patterns compared to abstention [310–313]. In this study, UK Biobank never and former drinkers had a significantly higher DASH score relative to individuals in the lowest rank of moderate drinker. While in the AHMS this difference was non-significant, the intake of fibre rich food groups (fruit, vegetables, and wholegrain cereals) was higher in individuals that drink low amounts of alcohol (moderate 1 drinkers) compared to those who abstain. So far, there is little clarification for moderate drinkers having a better quality diet than abstainers as prior studies have presented evidence both to support and refute this claim [179].

Objective iii) To describe the dietary profile of drinkers according to patterns of alcohol consumption
iv) To measure the association between patterns of alcohol consumption and intake measures.

This study identified differences in dietary intake according to alcohol consumption pattern. Within the full sample, binge drinkers reported a higher total energy intake and a lower intake of fibre compared to non-binge drinkers. Similarly, binge drinkers also had a lower adherence to the DASH diet. However, this finding was non-significant after adjustment for total alcohol intake. The difference in dietary pattern between binge and non-binge drinkers can be explained by poor diet quality associated with heavy drinking. In this study, more than half of binge-drinkers were in the heavy drinking category for average weekly alcohol intake. Findings from within drinker category analysis of differences in diet quality between binge and non-binge drinkers did not show significant differences in DASH score between consumption patterns of alcohol. These findings suggest that within the AHMS cohort, the pattern of alcohol consumption is not a predictor of diet quality independent of the volume of alcohol ingested. There is earlier evidence to also suggest that binge drinkers have unhealthier dietary patterns compared to non-binge drinkers[179,307,314,315]. This evidence indicates that compared to non-binge drinkers, binge drinkers have a lower intake of fruit, vegetables, and wholegrain, a higher intake of dietary fat and poorer adherence to healthy eating guidelines[179,307,314,315]. Notably, only one of these studies reported adjusting for alcohol consumption, after which the main effect (unhealthier dietary patterns in binge drinkers) was retained[315].

Objective v) To measure the differences in the dietary profile of drinkers according to beverage preference.

Findings from this study suggest individuals with a preference for wine have healthier dietary patterns compared with spirit and beer preferring drinkers, independent of the volume of alcohol ingested. In both the AHMS and UK Biobank cohorts, a preference for beer and spirits was associated with a lower intake of fibre and a high intake of total dietary fat and saturated fat compared with a preference for wine. Relative to wine, a preference for beer was associated with a lower DASH score independent of the volume of alcohol ingested. In the AHMS cohort, a preference for beer was also associated with a lower intake of fruit, vegetables, and wholegrain cereals and a higher intake of red meat. By comparison, a preference for spirits was associated with a lower intake of vegetables and wholegrain cereals. The observation that wine drinkers have healthier dietary patterns compared with beer or spirit drinkers corroborates evidence from earlier studies[182,311,316,317]. These differences in socio-demographic factors (sex, age, socioeconomic status) between individuals of differing

alcoholic beverage preference have been used to explain the differences in dietary intake[182]. However, in this study the dietary differences in diet between wine, beer, and spirit drinkers were preserved after adjustment for such factors and were notably independent of the volume of alcohol ingested.

5.5.3 Strengths and Limitations

There are several strengths to this study that should be highlighted. Firstly, this study explores the relationship between diet and alcohol across three important dimensions of consumption including the volume of alcohol ingested, the pattern of consumption and alcoholic beverage preference. To the author's knowledge, this is the first study to examine alcohol consumption in the context of diet across these three dimensions. It is thought that the relationship between alcohol and health is not limited to the volume of intake but differentiates also between beverage preference and pattern of consumption. Understanding the relationship between different aspects of alcohol intake and diet is crucial when examining the role of diet in the relationship between alcohol and cardiometabolic health. Furthermore, this study distinguishes between former drinkers and those individuals who have never drunk alcohol. A reason for quitting drinking may be to improve health and therefore the grouping of former and never-drinkers together could misrepresent the actual diet quality of non-drinkers. The breath of the dietary data used in this study is another notable strength. This study employs dietary data from the AHMS, which to the author's knowledge is the largest set of 7-day dietary data from a UK cohort. The size of cohorts used in this study also asserts confidences in the precision of its findings. There are however several limitations to this study. The cross-sectional design of this study cannot reveal changes in alcohol consumption or dietary patterns over time. Furthermore, response bias and misclassification cannot be ruled out when using self-reported data on dietary or alcohol consumption behaviours. Although dietary reporting plausibility was estimated and integrated into this study's analyses, without an objective measure it is difficult to ascertain a non-bias estimate of dietary and alcohol intake. Finally, most participants included in this study are from a middle class, Caucasian background, which limits the extrapolation of our findings across different ethnicities.

5.5.4 Conclusion

In conclusion, this study reports an association between alcohol consumption and dietary pattern that differentiates across the average volume of intake and alcoholic beverage preference. Whilst the evidence for better diet quality in moderate drinkers compared with abstainers is inconclusive, diet

quality deteriorates with increasing alcohol consumption amongst drinkers. Alcohol intake was also shown to have an additive effect on energy intake and contributes to higher habitual energy intake in AHMS and UK Biobank drinkers. Finally, a preference for wine compared with beer or spirits was associated with a healthier dietary pattern independent of explanatory covariates, most notably the volume of alcohol ingested. There are a limited number of studies that examine alcohol intake behaviour in conjunction with dietary intake and therefore this study is a warranted contribution to the literature.

6.0 Background

Alcohol is a leading risk factor for the global burden of disease [4]. In the UK, alcohol-related illnesses are thought to cost NHS-England more than £3.5 billion per year [108]. Despite the harmful effects associated with alcohol intake, its relationship with health remains complex owing to the suggested cardioprotective effects of moderate alcohol consumption. Findings from a large number of observational studies have identified a U/J-shaped relationship between alcohol consumption and cardiovascular risk, suggesting a lower risk in moderate drinkers than those who abstain or drink in heavier amounts [82,85,92,96,318–323]. However, these studies are hindered by weak methodologies, inconsistent definitions of alcohol consumption, and residual confounding by factors that co-vary with alcohol consumption, making it difficult to interpret their findings [230,324,325]. For instance, the role of diet in the prevention, development, and treatment of cardiometabolic illnesses is well established [245,326–328]. Furthermore, studies have also found a positive correlation between alcohol intake and a deterioration in diet quality [126,179,182,315]. Despite this, few studies examining alcohol-cardiometabolic health relations adequately control for residual confounding by dietary intake. It is plausible to question the role of diet in the relationship between alcohol consumption and cardiometabolic health, specifically the inverse association observed with moderate levels of intake.

6.1 Aims and Objectives

The overall aim of this study was to investigate the relationship between alcohol consumption and cardiometabolic risk independent of diet quality, specifically the inverse association between moderate consumption and risk. The following objectives were taken to achieve this aim:

Objectives:

i.   Describe the cardiometabolic profile of AHMS and UK Biobank participants across non-drinker and drinker categories.

ii.   To measure the association between alcohol consumption and markers of cardiometabolic risk, adjusting for measures of diet quality.

iii.   To investigate the relationship between markers of cardiometabolic risk and pattern of alcohol consumption in the AHMS current drinker population.

    iv.   To investigate the relationship between alcoholic beverage preference and markers of cardiometabolic risk.

6.2 Methodology

6.2.1 Study population

This study includes AHMS and UK Biobank participants with readily available dietary data and complete quantitative and qualitative alcohol intake data. The recruitment procedures for the AHMS and UK Biobank cohorts are outlined in Chapter 2 of this thesis. Participants with a medical history of one or more of the following chronic diseases were excluded from this study: disease of the thyroid, angina, stroke/trans ischemic attack, heart attack, other diseases of the heart and cardiovascular system, chronic liver disease, chronic obstructive pulmonary disease, or cancer. Women who were pregnant at baseline were also excluded.

6.2.2 Measures of Cardiometabolic Health

Anthropometric markers (body weight, BMI, and waist circumference) and biomarkers (HDL, non-HDL, HbA1c, systolic and diastolic blood pressure) of cardiometabolic disease were included in this study as indicators of cardiometabolic disease risk and were treated as continuous variables. In the AHMS, blood samples were taken in the non-fasted state and as a result, it was not possible to measure the risk of Metabolic Syndrome against standard diagnostic criteria due to fasting glucose and blood triglycerides not being collected. To circumvent this issue, a cardiometabolic risk (CMR) score was generated for each participant in both cohorts as an indicator of aggregated cardiometabolic disease risk. This score has been used in earlier research using AHMS data and is comprised of five components that are indicative of cardiometabolic health [255]. Each component is worth one point. Scoring standards for each component are detailed below. The maximum score is 5 and the minimum 0. A person with a score ≥ 3 is considered at high cardiometabolic risk.

    1. Central obesity: waist circumference ≥ 94 cm – men, waist circumference ≥ 80 cm – women.

    2. Dyslipidaemia: HDL <1.0 mmol/L – men and <1.3 mmol/L – women, and/or non-HDL ≥4.0 mmol/L, and/or prescribed cholesterol lowering medication.

    3. High blood pressure: systolic ≥ 130 mmHg, and/or diastolic ≥ 85 mmHg, and/or prescribed hypotensive medication.

4. Inflammation: Hs-CRP ≥3 mg/L <10 mg/L.

5. Impaired blood glucose control: HbA1c ≥ 5.7% and/or prescribed medication for glucose control.

The data collection methods for the anthropometric and biochemical measures used in this study are outlined in Chapter 2.

6.2.3 Alcohol Intake Measures

Alcohol intake estimates from the dietary collection method (AHMS) and touchscreen survey tool (UK Biobank) are presented as intake of alcohol in units per week (units/wk) and are treated as continuous variables. The procedures used to collect and estimate alcohol intake in each cohort are described in Chapter 4.

6.2.4 Grouping variables

The cardiometabolic health profile of AHMS and UK Biobank participants according to alcohol intake behaviour was explored by comparing cardiometabolic health across i) drinker category (never / former / moderate1 / moderate 2 / moderate 3 / heavy drinker) and ii) alcoholic beverage preference (wine / beer / spirits). In the AHMS cohort, the cardiometabolic health of drinkers was also compared across patterns of alcohol consumption (binge drinker / non-binge drinker). The classification methodologies used to define these grouping variables are outlined in Chapter 4.

6.2.5 Covariates

The following variables were considered as covariates: age (years), sex, socioeconomic status (AHMS: highest education and household come; UK Biobank: Townsend index score), current smoking status (yes, no), physical activity level (high, moderate, low), DASH score and energy density (kcal/g). In specific regression models the following factors were also included as covariates: BMI (kg/m2), height (cm), and medication (cholesterol-lowering / blood glucose lowering / blood pressure lowering) for the treatment of cardiometabolic risk. Refer to Chapter 2 and Chapter 3 for full details regarding data collection procedures and measurements of these covariate variables

6.3 Statistical Analyses

Statistical analysis was performed using R Studio Software version 1.4.1103. Analyses were stratified by grouping variables and the Chi-square (χ2) test was used to describe differences in the distribution of participants between groups. The normality of the distribution of continuous variables

was tested using the Anderson-Darling Test. Normal distributed continuous variables were presented as the mean ± standard deviation (SD) and the difference between measures was tested using the analysis of variance (ANCOVA) test, adjusted for participant age and sex. Non-parametric distributed continuous variables were presented as median (Interquartile range (IQR)) and the difference between measures were tested using the Kruskal-Wallis's test, adjusted for participant age and sex. Pearson correlation tests were conducted to determine the pairwise agreement between the $\log_{10}$ transformed alcohol intake (units/wk) and risk markers of cardiometabolic health (weight, BMI, waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP), HDL and non-HDL concentration, HbA1c % and CMR score). Correlation matrices were plotted using the R package *ggcorrplot.* An insignificant correlation between two variables was indicated by an ✕. The magnitude of the Pearson's correlation was evaluated as follows: $0.3 \leq r < 0.5$ low; $0.6 \leq r < 0.8$ moderate; $r \geq 0.8$ high[249]. Multivariable linear regression was used to examine the association between alcohol intake behaviours and markers of cardiometabolic disease risk, controlling for the covariate measures outlined above. In these regression models, measures of absolute alcohol intake (units/wk) were $\log_{10}$ transformed before analysis. For all analyses, statistical significance was accepted as $p < 0.05$.

6.4 Results

6.4.1 Study Population

This study includes 9581 AHMS and 146,888 UK Biobank healthy participants with complete alcohol and dietary intake data. Participants with a history of cardiometabolic disease or cancer were excluded from the analysis. Figure 6.1 illustrates the sample selection procedures used in this study for both AHMS and UK Biobank cohorts.

6.4.2 Cardiometabolic Profile Across of All Participants Stratified by Alcohol Intake Status

The cardiometabolic profile of AHMS and UK Biobank participants was compared across the following drinker and non-drinker categories: never, former, moderate 1, moderate 2, moderate 3, and heavy drinkers (Table 6.1 and Table 6.2, respectively). Compared with never, former, and moderate ranked drinkers, heavy drinkers had a poorer cardiometabolic health profile as demonstrated by a higher weight, waist circumference, BMI, systolic and diastolic blood pressure, and CMR score (p <0.001). This observation was noted across both study cohorts and significant after adjustment for explanatory covariate variables age and sex. Amongst drinkers, a linear deterioration in cardiometabolic health was observed across low to higher-ranked drinker categories. From low-ranked moderate drinkers

through to heavy drinkers an increase in obesity markers, weight, waist circumference, and BMI was observed (p<0.001). Similarly, a stepwise increase in systolic and diastolic blood pressure, CMR score, and proportion of participants in the 'at cardiometabolic risk' category was also noted.

Concerning blood markers of cardiometabolic health, HDL concentration was lower across non-drinker than drinker categories, whilst the HbA1c percentage was higher. Amongst drinkers, HDL concentration increased across low-ranked moderate drinkers through to heavy drinkers, whilst HbA1c% decreased with increasing alcohol consumption. In both cohorts, a u-shaped curve was indicated for CMR score with never, former, and heavy drinkers reporting a higher mean CMR score than moderate-ranked drinkers. Also, compared with other drinker and non-drinker categories the mean CMR score was lowest for moderate 1 drinker, (AHMS mean 2.62 SD 1.46, UK Biobank mean 2.78 SD). The proportion of AHMS and UK Biobanks participants in the 'at cardiometabolic risk' category is 55.6% (n 5331) and 64.0% (n 94,064), respectively. In both cohorts, the difference between the proportion of participants on prescribed cardiometabolic medication across drinker and non-drinker categories was non-significant.

Figure 6.1 *Schematic diagram of the sample selection procedure in AHMS and UK Biobank cohorts.*

A.   Airwave Health Monitoring Study

Baseline n 10,179 sub-cohort

Exclude: n 598 + chronic disease†

Include: n 9581 for final analysis

B.   UK Biobank Cohort

Baseline n 165,753 sub cohort

Exclude: n 18,865 + chronic disease†

Include: n 146,888 for final analysis
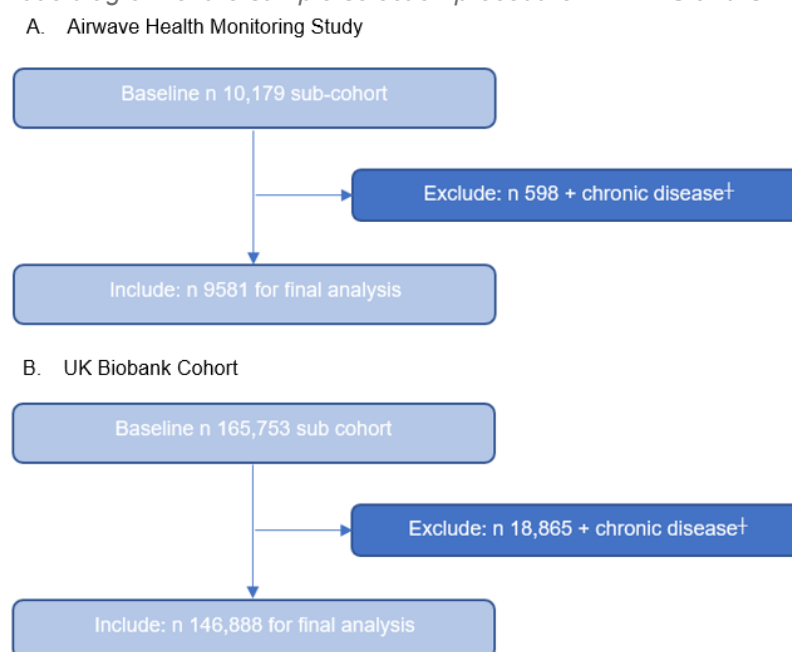
Figure 6.1 schematic diagram for the sample selection procedure in the AHMS cohort. Keys: ┼ - chronic disease diagnosis of at least one of the following: angina, disease of the thyroid, stroke/trans ischemic attack, heart attack, other cardiovascular disease, cancer, chronic obstructive pulmonary disease, and or chronic liver disease

Table 6.1 Cardiometabolic Profile Across Drinker and Non-Drinker Categories in the Airwave Health Monitoring Study Cohort

Cardiometabolic Profile Across Drinker and Non-Drinker Categories in the Airwave Health Monitoring Study Cohort								
Total (n 9581)		**Never**	**Former**	**Moderate 1**	**Moderate 2**	**Moderate 3**	**Heavy**	**p**
	n (%)	235 (2.5)	491 (5.1)	2907 (30.3)	2226 (23.2)	1403 (14.6)	2319 (24.2)	-
Sex: Male		113 (48.1)	256 (52.1)	1454 (50.0)	1382 (62.1)	904 (64.4)	1815 (78.3)	<0.05
Age (y)		41.7 (10.1)	40.2 (9.1)	39.6 (9.5)	40.8 (9.1)	41.0 (8.9)	41.7 (8.5)	<0.001
Weight (kg)	**Mean (SD)**	79.1 (17.8)	80.4 (16.5)	79.9 (16.4)	82.3 (15.5)	82.4 (15.3)	87.0 (14.8)	<0.001
Waist (cm)		87.3 (13.2)	88.2 (12.9)	87.3 (12.3)	89.1 (11.6)	89.3 (11.3)	92.5 (10.9)	<0.001
BMI (kg/m^2)		26.0 (4.7)	27.0 (4.7)	26.7 (4.4)	26.9 (4.0)	27.0 (4.0)	27.7 (3.8)	<0.001
BMI Category (kg/m2)	**n (%)**							
Underweight		1 (0.4)	0 (0.0)	4 (0.1)	4 (0.2)	2 (0.1)	4 (0.2)	ns
Healthy		83 (35.3)	175 (35.6)	1067 (36.7)	715 (32.1)	429 (30.6)	544 (23.4)	ns
Overweight		94 (40.0)	213 (43.4)	1285 (44.2)	1075 (48.3)	703 (50.1)	1220 (52.6)	ns
Obese		57 (24.3)	103 (21.0)	536 (19.0)	411 (19.4)	258 (18.4)	531 (23.8)	ns
SBP (mmHg)	**Mean (SD)**	129.0 (16.4)	128.0 (16.2)	129.0 (14.9)	130.0 (15.4)	131.0 (14.5)	135.0 (14.6)	<0.001
DBP (mmHg)		78.9 (10.4)	77.9 (10.6)	78.2 (9.7)	79.1 (10.0)	80.0 (9.8)	82.1 (9.9)	<0.001
HDL (mmol/L)	**Mean (SD)**	1.40 (0.36)	1.39 (0.33)	1.47 (0.37)	1.49 (0.38)	1.54 (0.39)	1.54 (0.40)	<0.001
Non-HDL (mmol/L)		3.73 (0.97)	3.79 (1.03)	3.65 (1.01)	3.73 (1.02)	3.73 (1.00)	3.93 (1.06)	<0.001
HbA1c (%)		5.85 (0.87)	5.75 (0.61)	5.66 (0.49)	5.63 (0.51)	5.61 (0.49)	5.60 (0.54)	<0.001
CMR Score	**Mean (SD)**	2.89 (1.35)	2.77 (1.37)	2.62 (1.36)	2.66 (1.37)	2.69 (1.36)	2.91 (1.38)	<0.001
CMR Score ≥ 3	**n (%)**	138 (58.7)	281 (57.2)	1525 (52.4)	1199 (53.9)	774 (55.2)	1414 (61.0)	ns
Medication Px								
Glucose Lowering		1 (0.4)	1 (0.2)	6 (0.2)	2 (0.9)	2 (0.1)	4 (0.2)	ns
Statin		7 (3.0)	11 (2.2)	50 (1.7)	40 (1.8)	31 (2.2)	68 (2.9)	ns
Blood Pressure Lowering		13 (5.5)	28 (5.7)	104 (3.6)	102 (4.6)	61 (4.3)	122 (5.3)	ns

Abbreviations: BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; HDL – high-density lipoprotein; CMR – cardiometabolic risk; px – prescription; ns – non-significant.
Tests: Continuous variables – ANOVA adjusted for age and sex; Categorical variables – chi-square test. p < 0.05 accepted as significant.

Table 6.2 *Cardiometabolic Profile Across Drinker and Non-Drinker Categories in the UK Biobank Cohort*

Cardiometabolic Profile Across Drinker and Non-Drinker Categories in the UK Biobank Cohort								
Total 146,888		Never	Former	Moderate 1	Moderate 2	Moderate 3	Heavy	p
		5962 (4.1)	5401 (3.7)	28,264 (19.2)	41,434 (28.2)	25,225 (17.2)	40,602 (27.6)	-
Sex: Male	n (%)	1658 (27.8)	2323 (43.0)	8452 (29.9)	16,345 (39.4)	12,858 (60.0)	28,765 (70.8)	<0.001
Age (y)	Mean (SD)	55.8 (8.4)	55.6 (7.8)	55.8 (7.9)	55.7 (7.9)	55.7 (7.9)	55.9 (7.7)	<0.001
Weight (kg)	Mean (SD)	74.6 (16.7)	78.2 (17.5)	73.5 (14.5)	75.0 (14.8)	77.3 (14.8)	81.9 (15.0)	<0.001
Waist (cm)		87.9 (14.2)	90.3 (14.7)	85.6 (12.6)	86.7 (12.6)	88.6 (12.5)	92.9 (12.3)	<0.001
BMI (kg/m^2)		27.3 (5.5)	27.6 (5.5)	26.2 (4.4)	26.2 (4.3)	26.5 (4.1)	27.3 (4.1)	<0.001
BMI Category (kg/m2)	n (%)							
Underweight		44 (0.7)	37 (0.7)	91 (0.3)	102 (0.2)	43 (0.2)	53 (0.1)	ns
Healthy		2210 (37.1)	1898 (35.1)	12487 (44.2)	17,677 (42.7)	9755 (38.7)	12,085 (29.8)	ns
Overweight		2133 (35.8)	2001 (37.0)	10,816 (38.3)	16,842 (40.6)	11,174 (44.3)	19,542 (48.1)	ns
Obese		1575 (26.4)	1465 (27.2)	4870 (17.2)	6813 (16.4)	4253 (16.8)	8922 (22.0)	ns
SBP (mmHg)	Mean (SD)	138.0 (20.1)	136.0 (19.4)	137.0 (19.6)	137.0 (19.1)	139.0 (18.9)	143.0 (18.9)	<0.001
DBP (mmHg)		81.0 (10.8)	80.6 (10.6)	80.6 (10.5)	81.2 (10.4)	82.2 (10.3)	84.5 (10.5)	<0.001
HDL (mmol/L)	Mean (SD)	1.40 (0.35)	1.34 (0.35)	1.50 (0.37)	1.52 (0.39)	1.52 (0.40)	1.52 (0.40)	<0.001
Non-HDL (mmol/L)		4.22 (1.05)	4.20 (1.08)	4.27 (1.04)	4.25 (1.03)	4.26 (1.03)	4.30 (1.04)	<0.001
HbA1c (%)		5.53 (0.67)	5.50 (0.73)	5.38 (0.48)	5.36 (0.47)	5.35 (0.50)	5.36 (0.51)	<0.001
CMR Score	Mean (SD)	3.04 (1.29)	3.02 (1.28)	2.78 (1.26)	2.79 (1.27)	2.83 (1.26)	3.06 (1.19)	<0.001
CMR Score ≥ 3	n (%)	4067 (68.2)	3643 (67.4)	17,152 (60.7)	25,076 (60.5)	15,718 (62.3)	28,408 (70.0)	ns
Medication Px								
Glucose Lowering	n (%)	389 (6.5)	364 (6.7)	830 (2.9)	1078 (2.6)	704 (2.8)	1422 (3.5)	ns
Statin		292 (4.9)	458 (8.5)	1266 (4.5)	2425 (5.8)	2143 (8.5)	5217 (12.8)	ns
Blood Pressure Lowering		169 (2.8)	236 (4.4)	768 (2.7)	1423 (3.4)	1145 (4.5)	2798 (6.9)	ns

Abbreviations: BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; HDL – high-density lipoprotein; CMR – cardiometabolic risk; px – prescription; ns – non-significant.
Tests: Continuous variables – ANOVA adjusted for age and sex; Categorical variables – chi-square test. p < 0.05 accepted as significant.

Linear regression modelling was performed in 9581 AHMS and 146,888 UK Biobank participants to investigate the difference in CMR score between never drinkers and former, moderate 1, moderate 2, moderate 3, and heavy drinkers, respectively. The results from this analysis are presented in Table 6.3. In the AHMS cohort the differences in CMR scores between never drinkers and former drinkers, and never drinkers and heavy drinkers were non-significant. In this cohort moderate drinkers of all ranks scored significantly lower on the CMR index than never drinkers. In the UK Biobank cohort, former drinkers, all ranks of moderate drinkers, as well as heavy drinkers scored lower on the CMR index than never drinkers. This magnitude of difference was greatest between never drinkers and moderate 2 drinkers.

Table 6.3 *Linear Regression Modelling: Cardiometabolic Risk ~ Moderate 1 Drinkers*

Linear Regression Modelling: Cardiometabolic Risk of Moderate 1 Drinkers Relative to Participants in Other Drinker and Non-Drinker Categories								
Cardiometabolic Risk Score AHMS								
Model 1			**Model 2**			**Model 3**		
Effect	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
Never Ref			Ref			Ref		
Former -0.05	0.11	*ns*	-0.04	0.11	*ns*	-0.08	0.09	*ns*
Moderate 1 -0.17	0.09	*ns*	-0.17	0.09	*ns*	-0.17	0.08	<0.05
Moderate 2 -0.23	0.09	<0.05	-0.23	0.09	<0.05	-0.22	0.08	<0.01
Moderate 3 -0.23	0.10	<0.05	-0.23	0.09	<0.05	-0.22	0.08	<0.01
Heavy -0.08	0.09	*ns*	-0.08	0.09	*ns*	-0.14	0.08	*ns*
Cardiometabolic Risk Score UK Biobank								
Model 1			**Model 2**			**Model 3**		
Effect	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
Never Ref			Ref			Ref		
Former -0.05	0.02	<0.05	-0.05	0.02	<0.05	-0.08	0.02	<0.001
Moderate 1 -0.25	0.02	<0.001	-0.24	0.02	<0.001	-0.09	0.02	<0.001
Moderate 2 -0.29	0.02	<0.001	-0.28	0.02	<0.001	-0.12	0.02	<0.001
Moderate 3 -0.27	0.02	<0.001	-0.25	0.02	<0.001	-0.11	0.02	<0.001
Heavy -0.11	0.02	<0.001	-0.09	0.02	<0.001	-0.05	0.01	<0.001
Abbreviations: BMI body mass index, , , NS non-significant, SE standard error.								
Model 1 – Age + Sex. Model 2 – Model 1 + DASH Score + Energy Density. Model 3 – Model 2 + BMI + Townsend Index (UKB) + Education Status (AHMS) + Household income (AHMS) + Physically Activity Level +Smoking Status								

Findings from the Pearson pairwise correlation tests between alcohol intake and risk markers of

cardiometabolic health in 8855 AHMS and 135,525 UK Biobank current drinkers are illustrated in

Figure 6.2 Matrix A and Matrix B. In both cohorts, alcohol intake was positively correlated with

weight, waist girth, BMI, systolic and diastolic blood pressure, HDL blood concentration, and CMR

score, and negatively correlated with HbA1c % (p <0.05). The pairwise correlation between non-HDL

blood concentration, and alcohol intake was non-significant in the UK Biobank cohort but significant in

the AHMS cohort. In both matrices, the pairwise correlation coefficients are presented as numeric

values

Figure 6.2 Correlation Matrices: Alcohol Intake and Risk markers of Cardiometabolic Health

A.

B.
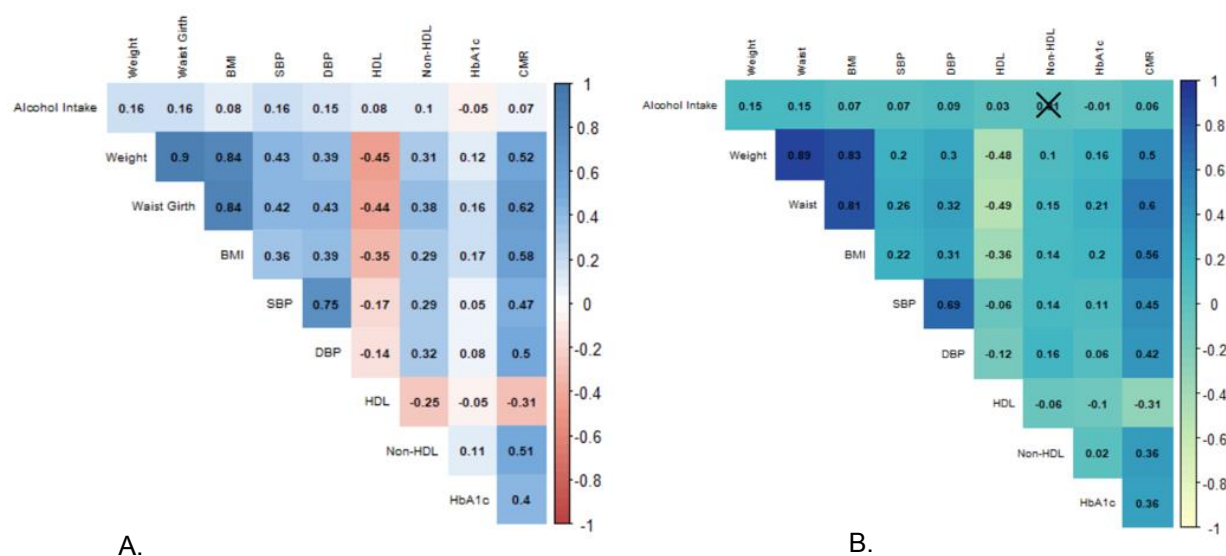
Figure 6.2 A: Correlation Matrix for the Airwave Health Monitoring Study, B: Correlation Matrix for the UK Biobank cohort. The numeric values represent the correlation coefficient r for each pairwise correlation. p < 0.05 is significant. ✕ indicates a non-significant correlation.

Linear Regression modelling was conducted to measure the association between alcohol intake and

risk markers of cardiometabolic health independent of explanatory covariates across both cohorts.

The findings presented in Table 6.4 show a positive association between alcohol intake and BMI,

waist girth, systolic and diastolic blood pressure, and HDL blood concentration (p <0.001). An inverse

association was observed between alcohol intake and glycated haemoglobin blood concentration

(HbA1c %) (p <0.001). In the UK Biobank cohort, alcohol intake was positively associated with an

increase in the CMR score in both the unadjusted and adjusted analyses. Although this association is

likely explained by residual confounding. Alcohol consumption was not significantly associated with a

CMR score in the AHMS cohort.

Alcohol Intake and Risk Markers of Cardiometabolic Health in Current Drinkers								
AHMS Alcohol Intake	**Model 1**			**Model 2**			**Model 3**		
	Effect	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
CMR Score	-0.01	0.03	*ns*	-0.02	0.03	*ns*	-0.03	0.02	*NS*
BMI (kg/m²)	0.03	0.09	*ns*	0.06	0.09	*ns*	0.08	0.09	*NS*
Waist (cm)	0.68	0.22	<0.01	0.71	0.23	<0.01	0.75	0.23	<0.001
SBP (mmHg)	1.92	0.30	<0.001	1.84	0.31	<0.001	1.79	0.30	<0.001
DBP (mmHg)	1.59	0.21	<0.001	1.56	0.21	<0.001	1.48	0.20	<0.001
HDL (mmol/L)	0.17	0.01	<0.001	0.16	0.01	<0.001	0.17	0.01	<0.001
Non-HDL (mmol/L)	0.01	0.02	*ns*	0.01	0.02	*NS*	0.01	0.02	*ns*
HbA1c (%)	-0.07	0.01	<0.001	-0.07	0.01	<0.001	-0.08	0.01	<0.001
UKB Alcohol Intake	**Model 1**			**Model 2**			**Model 3**		
	Effect	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
CMR Score	0.21	0.01	<0.001	0.21	0.01	<0.001	0.06	0.01	<0.001
BMI (kg/m²)	0.81	0.04	<0.001	0.86	0.04	<0.001	0.76	0.04	<0.001
Waist (cm)	2.82	0.09	<0.001	2.94	0.09	<0.001	2.54	0.09	<0.001
SBP (mmHg)	4.72	0.15	<0.001	4.83	0.16	<0.001	4.59	0.16	<0.001
DBP (mmHg)	3.17	0.09	<0.001	3.20	0.09	<0.001	2.90	0.09	<0.001
HDL (mmol/L)	0.21	0.003	<0.001	0.21	0.003	<0.001	0.24	0.003	<0.001
Non-HDL (mmol/L)	0.04	0.009	<0.001	0.04	0.01	<0.001	0.04	0.01	<0.001
HbA1c (%)	-0.04	0.004	<0.001	-0.04	0.004	<0.001	-0.06	0.004	<0.001

Abbreviations: CMR cardiometabolic risk, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL high density lipoprotein, NS non-significant, SE standard error.

Model 1 – Age + Sex. Model 2 – Model 1 + DASH Score + Energy Density. Model 3 – Model 2 + BMI (except BMI and Waist models) + Townsend Index (UKB) + Education (AHMS) + Household Income (AHMS) + Physically Activity Level +Smoking Status+ Statin Prescription (HDL and Non-HDL models) + Blood Pressure medication (SBP and DBP models) + Diabetes Medication (HbA1c model).

The cardiometabolic profile of 8855 AHMS current drinkers was compared across alcoholic beverage consumption patterns. Current drinkers were grouped as binge or non-binge drinkers. The difference in risk markers of cardiometabolic health between the two groups were measured using linear regression analyses. As presented in Table 6.5, the difference in the CMR score between binge and non-binge drinkers was non-significant after adjustment for covariables. Compared with non-binge drinkers, binge drinkers had higher BMI, and a larger waist girth. Results suggest that binge patterns are associated with higher diastolic blood pressure. However, it is likely that this association is attributed to residual confounding given the large drop in the magnitude of effect between the unadjusted and adjusted models. Similarly, binge patterns were associated with higher HDL and HbA1c after adjusting for covariate measures. However, residual confounding cannot be ruled out as an explanation for this association. Findings from within drinker category analysis show a positive association between binge drinking and BMI in the heavy drinker and moderate 3 drinker categories. In the heavy drinker category, binge drinkers also had a higher HDL blood concentration than heavy non-binge drinkers.

Table 6.5 *Alcohol Consumption Pattern and Markers of Cardiometabolic Health*

Alcohol Consumption Pattern and Markers of Cardiometabolic Health								
	Model 1			**Model 2**			**Model 3**		
	Effect	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
Non-Binge Drinker	Ref	-	-	Ref	-	-	Ref	-	-
CMR Score	0.08	0.03	<0.01	0.04	0.03	*ns*	0.02	0.03	*ns*
BMI (kg/m²)	0.41	0.09	<0.001	0.32	0.10	<0.01	0.33	0.10	<0.001[a,c,e]
Waist (cm)	1.29	0.22	<0.001	0.86	0.25	<0.001	0.95	0.25	<0.001[a]
SBP (mmHg)	1.77	0.29	<0.001	0.66	0.34	*ns*	0.29	0.33	*ns*
DBP (mmHg)	1.60	0.20	<0.001	0.74	0.24	<0.01	0.45	0.23	<0.05[a,e]
HDL (mmol/L)	0.10	0.01	<0.001	0.03	0.01	<0.001	0.04	0.01	<0.001[a,e]
Non-HDL (mmol/L)	0.06	0.02	<0.01	0.04	0.02	*ns*	0.02	0.02	*ns*
HbA1c (%)	-0.04	0.01	<0.001	-0.02	<0.01	<0.05	-0.02	0.01	<0.05[a]

Abbreviations: CMR cardiometabolic risk, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL high density lipoprotein, NS non-significant, SE standard error.
Model 1 – Age + Sex. Model 2 – Model 1 + Alcohol intake. Model 3 – Model 2 + BMI (except BMI and Waist models) + DASH Score + Energy Density + Education Status + Household Income + Physically Activity Level +Smoking Status+ Statin Prescription (HDL and Non-HDL models) + Blood Pressure medication (SBP and DBP models) + Diabetes Medication (HbA1c model).

Keys: a – all current drinkers; b- moderate1 drinkers; c- moderate 2 drinkers; d – moderate 3 drinkers; e – heavy drinkers.

6.4.6 Alcoholic Beverage Preference and Risk Markers of Cardiometabolic Health

8855 AHMS and 135,525 UK Biobank current drinkers were grouped according to their alcoholic beverage preference as wine, beer, or spirit drinkers. The cardiometabolic profile of beer, spirit and wine drinkers was compared to the cardiometabolic profiles of never drinkers (reference). The final cohort sample sizes were 9090 AHMS participants and 141,487 UK Biobank participants. The findings of these analyses are outlined in Table 6.6 (AHMS cohort) and Table 6.7 (UK Biobank) respectively. In the AHMS cohort, there was a non-significant in difference in CMR between never drinkers and beer drinkers, and never drinkers and spirit drinkers. The CMR of wine drinkers was significantly lower than never drinkers in both the unadjusted and adjusted models. There was a non-significant difference in BMI, waist circumference, blood pressure, and non-HDL between wine, or beer, or spirit drinkers, and never drinkers. Relative to never drinkers, dominant beer drinkers, spirit

drinkers, and wine drinkers had higher HDL-c and lower HbA1c. For both measures, the magnitude of difference was greatest between wine drinkers and never drinkers. In the UK Biobank cohort, beer drinkers, spirit drinkers, and wine drinkers scored lower on the CMR index than never drinker ($p<0.01$ – $p< 0.001$). Relative to never drinkers, drinkers in all alcoholic beverage preference groups ha a lower BMI, waist circumference, and HbA1c . The HDL-c and non-HDL-c levels in all alcohol beverage preference groups were significantly higher than levels in never drinkers. There was a non-significant difference in diastolic blood pressure between never drinkers and drinkers in respective alcoholic beverage groups. The difference in systolic blood pressure was non-significant between never drinkers, beer drinkers, and spirit drinkers, respectively. In this cohort the systolic blood pressure of wine drinkers was significantly lower than never drinkers after adjusting for covariates ($p<0.001$).

Table 6.6 *Linear Modelling Alcoholic Beverage Preference and Cardiometabolic Risk AHMS*

Linear Modelling: Alcoholic Beverage Preference and Cardiometabolic Risk AHMS								
Model 1			**Model 2**			**Model 3**		
Effect	*S. E*	*p*	*Effect*	*S. E*	*p*	*Effect*	*S. E*	*p*
CMR Score								
Never Drinker **Ref**			**Ref**			**Ref**		
Beer −0.11	0.09	*ns*	−0.17	0.09	*ns*	−0.16	0.08	*ns*
Spirits −0.05	0.10	*ns*	−0.10	0.10	*ns*	−0.16	0.08	*ns*
Wine −0.24	0.09	<0.01	−0.30	0.09	<0.01	−0.24	0.08	<0.01
BMI (kg/m²)								
Beer 0.12	0.29	*ns*	−0.04	0.29	*ns*	−0.05	0.29	*ns*
Spirits 0.42	0.30	*ns*	0.28	0.30	*ns*	0.25	0.30	*ns*
Wine −0.16	0.28	*ns*	−0.34	0.29	*ns*	−0.34	0.28	*ns*
Waist (cm)								
Beer 1.17	0.72	*ns*	0.53	0.72	*ns*	0.48	0.72	*ns*
Spirits 1.98	0.75	<0.01	1.43	0.76	*ns*	1.28	0.75	*ns*
Wine 0.65	0.71	*ns*	−0.05	0.71	*ns*	−0.10	0.71	*ns*
SBP (mmHg)								
Beer 0.42	0.98	*ns*	−0.77	0.99	*ns*	−0.78	0.95	*ns*
Spirits 0.43	1.03	*ns*	−0.59	1.03	*ns*	−0.95	1.00	*ns*
Wine −0.01	0.96	*ns*	−1.30	0.98	*ns*	−0.91	0.95	*ns*
DBP (mmHg)								
Beer 0.55	0.68	*ns*	−0.40	0.69	*ns*	−0.04	0.07	*ns*
Spirits 1.0	0.72	*ns*	0.26	0.72	*ns*	−0.05	0.07	*ns*
Wine 0.45	0.67	*ns*	−0.60	0.68	*ns*	−0.03	0.06	*ns*
HDL (mmol/L)								
Beer 0.15	0.03	<0.001	0.08	0.03	<0.001	0.07	0.02	<0.001
Spirits 0.11	0.03	<0.001	0.05	0.03	<0.001	0.06	0.03	<0.001
Wine 0.18	0.03	<0.001	0.11	0.03	<0.001	0.10	0.02	<0.001
Non-HDL (mmol/L)								
Beer −0.03	0.07	*ns*	−0.06	0.07	*ns*	−0.05	0.07	*ns*
Spirits −0.10	0.07	*ns*	−0.13	0.07	*ns*	−0.15	0.07	*ns*
Wine −0.05	0.07	*ns*	−0.05	0.07	*ns*	−0.06	0.07	*ns*
HbA1c (%)								
Beer −0.11	0.03	<0.01	−0.08	0.03	<0.05	−0.08	0.03	<0.05
Spirits −0.10	0.03	<0.01	−0.08	0.04	<0.05	−0.08	0.03	<0.05
Wine −0.14	0.03	<0.001	−0.11	0.03	<0.001	−0.11	0.03	<0.01

Abbreviations: CMR cardiometabolic risk, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL high density lipoprotein, NS non-significant, SE standard error.

Model 1 – Age + Sex. Model 2 – Model 1 + Alcohol Intake (continuous). Model 3 – Model 2 + BMI (not in BMI or waist models) + DASH Score + Energy Density + Household Income + Education Status + Physically Activity Level +Smoking Status+ Statin Prescription (HDL and Non-HDL models) + Blood Pressure medication (SBP and DBP models) + Diabetes Medication (HbA1c model).

Table 6.7 *Linear Modelling Alcoholic Beverage Preference and Cardiometabolic Risk UK Biobank*

Linear Modelling: Alcoholic Beverage Preference and Cardiometabolic Risk UK Biobank									
	Model 1			Model 2			Model 3		
	Effect	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
CMR Score									
Never-Drinker	**Ref**			**Ref**			**Ref**		
Beer	-0.09	0.02	<0.001	-0.20	0.02	<0.001	-0.19	0.01	<0.001
Spirits	-0.04	0.02	*ns*	-0.13	0.02	<0.001	-0.15	0.02	<0.001
Wine	-0.28	0.02	<0.001	-0.37	0.02	<0.001	-0.36	0.01	<0.001
BMI (kg/m^2)									
Beer	-0.47	0.06	<0.001	-0.85	0.06	<0.001	-0.76	0.05	<0.001
Spirits	0.10	0.08	*ns*	-0.24	0.07	<0.01	-0.23	0.07	<0.01
Wine	-1.20	0.06	<0.001	-1.55	0.06	<0.001	-1.46	0.05	<0.001
Waist (cm)									
Beer	-0.58	0.16	<0.001	-1.87	0.16	<0.001	-1.67	0.16	<0.001
Spirits	0.74	0.20	<0.001	-0.42	0.20	*ns*	-0.59	0.20	<0.01
Wine	-2.43	0.15	<0.001	-3.63	0.15	<0.001	-3.44	0.15	<0.001
SBP (mmHg)									
Beer	1.68	0.27	<0.001	-0.46	0.27	*ns*	0.21	0.27	*ns*
Spirits	1.32	0.33	<0.001	-0.62	0.33	*ns*	-0.31	0.29	*ns*
Wine	-0.04	0.24	*ns*	-2.05	0.25	<0.001	-0.99	0.25	<0.001
DBP (mmHg)									
Beer	0.95	0.15	<0.001	-0.41	0.16	<0.001	0.30	0.15	*ns*
Spirits	1.21	0.19	<0.001	-0.03	0.19	*ns*	0.29	0.19	*ns*
Wine	0.30	0.14	<0.05	-0.98	0.14	<0.001	0.14	0.14	*ns*
HDL (mmol/L)									
Beer	0.17	0.004	<0.001	0.09	0.005	<0.001	0.06	0.005	<0.001
Spirits	0.13	0.006	<0.001	0.06	0.007	<0.001	0.06	0.006	<0.001
Wine	0.21	0.005	<0.001	0.13	0.005	<0.001	0.09	0.005	<0.001
Non-HDL (mmol/L)									
Beer	0.07	0.02	<0.001	0.05	0.02	<0.001	0.07	0.02	<0.001
Spirits	0.05	0.02	<0.001	0.03	0.02	<0.001	0.04	0.02	<0.001
Wine	0.04	0.01	<0.001	0.02	0.02	<0.001	0.06	0.01	<0.001
HbA1c (%)									
Beer	-0.13	0.01	<0.001	-0.13	0.01	<0.001	-0.06	0.01	<0.001
Spirits	-0.13	0.01	<0.001	-0.12	0.01	<0.001	-0.09	0.01	<0.001
Wine	-0.19	0.01	<0.001	-0.18	0.01	<0.001	-0.09	0.01	<0.001

Abbreviations: CMR cardiometabolic risk, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL high density lipoprotein, NS non-significant, SE standard error.

Model 1 – Age + Sex. Model 2 – Model 1 + Alcohol Intake (continuous). Model 3 – Model 2 + BMI + DASH Score + Energy Density + Townsend Index + Physically Activity Level +Smoking Status+ Statin Prescription (HDL and Non-HDL models) + Blood Pressure medication (SBP and DBP models) + Diabetes Medication (HbA1c model).

6.4.7 Post Hoc Analyses: Moderate Alcohol Consumption and Risk Markers of Cardiometabolic Health

Post hoc analyses were conducted in 94,923 UK Biobank moderate drinkers grouped from ranked moderate drinker categories to examine in greater detail the relationship between moderate alcohol consumption and markers of cardiometabolic health. As outlined in Table 6.7, the findings suggest that in the UK Biobank cohort, the inverse association between moderate alcohol consumption and CMR is not significant after adjusting for the confounding effect of alcoholic beverage preference (Model 2). Within the thresholds of moderate alcohol consumption, an increase in intake was positively associated with BMI, waist, systolic and diastolic blood pressure, and HDL blood concentration, whilst simultaneously inversely associated with HbA1c %. The relationship between alcohol intake and BMI was impacted by negative confounding. In the unadjusted models the effect of alcohol intake on BMI is overestimated and doubles in magnitude after controlling for known confounders.

Table 6.8 *Post Hoc Analyses: Moderate Alcohol Intake and Risk Markers of Cardiometabolic Health*

Post Hoc Analyses: Moderate Alcohol Intake and Risk Markers of Cardiometabolic Health									
	Model 1			**Model 2**			**Model 3**		
Alcohol Intake	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*	*Effect*	*S.E*	*p*
CMR Score	-0.01	0.01	*ns*	0.02	0.10	*ns*	-0.02	0.01	*ns*
BMI (kg/m^2)	0.13	0.06	<0.5	0.28	0.06	<0.001	0.25	0.05	<0.001
Waist (cm)	0.69	0.14	<0.001	1.07	0.14	<0.001	0.90	0.14	<0.001
SBP (mmHg)	1.85	0.24	<0.001	1.54	0.24	<0.001	1.85	0.24	<0.001
DBP (mmHg)	1.29	0.14	<0.001	1.40	0.14	<0.001	1.45	0.14	<0.001
HDL (mmol/L)	0.17	0.005	<0.001	0.17	0.005	<0.001	0.17	0.004	<0.001
Non-HDL (mmol/L)	0.003	0.01	*ns*	0.008	0.01	*ns*	0.01	0.01	*ns*
HbA1c (%)	-0.07	0.01	<0.001	-0.07	0.01	<0.001	-0.06	0.01	<0.001

Abbreviations: CMR cardiometabolic risk, BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, HDL high density lipoprotein, NS non-significant, SE standard error.

Model 1 – Age + Sex. Model 2 – Model 1 + Beverage Preference Model 3 – Model 2 + BMI + DASH Score + Energy Density + Townsend Index + Physically Activity Level +Smoking Status+ Statin Prescription (HDL and Non-HDL models) + Blood Pressure medication (SBP and DBP models) + Diabetes Medication (HbA1c model).

6.5 Discussion

There is a plethora of evidence to indicate a J/U-shaped relationship between alcohol intake and cardiometabolic disease risk, suggesting a cardioprotective benefit to alcohol consumption at moderate intakes [85,88,92,318]. The evidence to support this hypothesis is often flawed in its methodological design, specifically due to inadequate control of diet quality, a known confounder in behaviour cardiometabolic health relations. This study aimed to examine the association between alcohol intake and cardiometabolic disease risk in the Airwave Health Monitoring Study and the UK Biobank cohorts, following a robust methodology for the inclusion of diet as a confounding factor.

6.5.1 Summary of Main Findings

- ❖ Increasing alcohol intake is associated with a deterioration in cardiometabolic health. Alcohol intake is significantly associated with an increase in both blood pressure and anthropometric markers of obesity (weight, BMI, and waist circumference).

- ❖ Alcohol consumption is positively associated with HDL concentration and inversely associated with glycated haemoglobin concentration.

- ❖ Across non-drinker and drinker categories, the risk of cardiometabolic disease as indicated by a cardiometabolic risk score is lowest amongst moderate drinkers and highest amongst never and heavy drinkers, suggesting a J-shape relationship between alcohol intake and cardiometabolic disease risk.

- ❖ Wine drinkers have a healthier cardiometabolic profile compared with beer drinkers, spirit drinkers, or non-drinkers independent of alcohol intake and dietary habits.

- ❖ Alcoholic beverage preference negatively confounds the relationship between moderate alcohol intake and BMI.

- ❖ There is a non-significant difference in the cardiometabolic disease risk of binge versus non-binge drinkers.

- ❖ Binge patterns are associated with anthropometric markers of obesity independent to volume of alcohol intake.

6.5.2 Discussion of Main Findings

Objectives: i) Describe the cardiometabolic profile of AHMS and UK Biobank participants across non-drinker and drinker categories. ii) To measure the association between alcohol consumption and markers of cardiometabolic risk, adjusting for measures of diet quality.

A large proportion of AHMS and UK Biobank participants are at high risk of cardiometabolic disease, > 50% of the former and > 60% of the latter. These rates of cardiometabolic risk are substantially higher compared to the general UK population where Metabolic Syndrome (MetS) is thought to affect 1 in 3 adults over the age of 50 [90]. Although the criteria for high cardiometabolic risk in this study differs slightly from the diagnostic criteria of MetS, its components capture some of the key characteristics of MetS, including abdominal obesity, dyslipidaemia, and hypertension [329]. The high rates of high cardiometabolic risk observed in this study could be explained by the age-illness relation in the UK Biobank cohort and by the relationship between occupational stress and health in the AHMS [330,331].

This study describes a J/U-shaped relationship between cardiometabolic risk and alcohol intake behaviour. This observation was described across both cohorts, but significant only across all categories in the UK Biobank after adjustment for key explanatory variables, including measures of diet quality and dietary energy density. A large body of observational evidence has reported this J/U-shaped relationship between alcohol intake and cardiometabolic risk [109,318]. In the UK alone, a previous study in more than 1 million participants observed a J-shaped relationship between alcohol intake and several cardiovascular outcomes. However, this study was inadequately controlled for the residual confounding effects of diet [82]. To the author's knowledge, this is the first study to report a J/U-shape association between alcohol intake and cardiometabolic risk in a large UK cohort, independent of well-assessed indicators of dietary pattern. However, it is important to note that the addition of covariates accounted for a large proportion of variance in the model and residual confounding cannot be ruled out in its interpretation.

This study describes higher HDL blood concentration and lower HbA1c % in participants who currently consume alcohol than those who abstain. This finding supports the body of literature that indicates a favourable relationship between alcohol intake, dyslipidaemia, and blood glucose handling [95–97,109]. In fact, there is a current discussion that these specific alcohol blood biomarker relationships may attribute to the proposed cardioprotective effect of moderate drinking. Studies into the possible pathogenic pathways of alcohol and cardiovascular disease risk suggest alcohol intake causes a reduction in circulating lipase and hepatic gluconeogenesis, resulting in an upregulation of HDL and lowering of plasma glucose levels [106]. Paradoxically, in both cohorts, heavy drinkers are more likely to be affected by abdominal obesity than abstainers or participants who consume alcohol

in moderate amounts. It appears that in the UK Biobank and AHMS cohorts, alcohol intake counteracts the otherwise strong and negative impact of abdominal obesity on blood glucose handling and lipidemic profile [332].

Obesity is a multi-faceted chronic condition with serious health implications [332]. In the UK, the prevalence of obesity has increased over recent decades. In 2018, 63% of adults in England were either overweight or obese, an estimate that is 29% higher than previous years [333]. This study describes a linear increase in anthropometric markers of obesity, weight, BMI, and waist circumference with an increase in alcohol consumption. This increase in obesity risk was observed across both cohorts, and independent of diet quality, dietary energy density, physical activity levels, and other socio-demographic confounding factors. Several studies have reported on the relationship between obesity and alcohol. However, the results are widely inconsistent [122]. This study supports the findings of a more recent meta-analysis that indicated a dose-response relationship between alcohol intake and likelihood of obesity, with heavy drinking positively associated with the odds of being overweight (OR: 1.12, 95% CI: 1.01 to 1.24), overweight/obesity (OR: 1.32, 95% CI: 1.16 to 1.51), and abdominal obesity (OR: 1.25, 95% CI: 1.12 to 1.38) compared to no or light alcohol intake [122]. A positive energy balance is considered a leading cause of obesity [334]. As demonstrated in Chapter 5 of this thesis, alcohol intake has an additive effect on total energy intake and contributes to a positive energy balance in AHMS and UK Biobank participants. Alcohol consumption likely adds to the development of obesity in these cohorts by disrupting energy balance.

Habitual alcohol consumption is a recognised risk factor for hypertension [334] and there strong is evidence to suggest that a reduction in alcohol consumption can lower the risk of hypertension, especially amongst individuals who drink higher levels of alcohol (> 2 standard drinks per day) [335]. In this study, a positive association was observed across both cohorts between alcohol intake and systolic and diastolic blood pressure, with blood pressure highest amongst heavy drinkers compared with moderate drinkers and abstainers. Adjusted analyses within the drinker o show this relation is independent of known risk factors for hypertension, including sex, DASH score, blood pressure lowering pharmacological intervention, BMI, and tobacco use. These findings corroborate the hypothesis that alcohol consumption has a marked effect on blood pressure and the risk of hypertension [335–338].

Objective iii) To investigate the relationship between markers of cardiometabolic risk and pattern of alcohol consumption in the AHMS current drinker population.

This study reports a non-significant difference in the cardiometabolic risk score between binge and non-binge drinkers in the AHMS. However, the lack of significance may be secondary to the small sample size of the AHMS cohort. The deleterious effects of binge drinking on cardiovascular health are well recognised [90,91,108,339], and although not observed in this study, the harmful effects of binge drinking should not be underestimated. Although a difference in cardiometabolic risk was not observed, this study reports a positive association between binge drinking pattern, and anthropometric markers of obesity independent of alcohol intake. Furthermore, findings from within category analysis show that in the heavy and moderate 3 drinker categories, binge drinkers report a higher BMI than non-binge drinkers. These results suggest an association between drinking pattern and obesity risk, especially at heavier levels of intake. This observation supports findings from previous research that recorded a higher risk of obesity in individuals with ≥ 75% of total energy from alcohol compared to ≤ 24% on their heaviest drinking day[340]. Other findings from large observational studies also report a positive association between binge drinking obesity and abdominal obesity risk[340].

Objective iv) To investigate the relationship between absenteeism, alcoholic beverage preference, and markers of cardiometabolic risk.

The results of this study suggest that a preference for wine infers greater cardiometabolic protection than a preference for spirits, or beer, relative to complete absenteeism. Across both cohorts wine drinkers scored lower on the CMR index than never drinkers after consideration for the influential effect of alcohol intake volume. In the UK Biobank cohort, results suggest that a preference for wine is associated with a lower risk of obesity, hypertension, and poor glucose handling, relative to absenteeism. Beer dominant and spirit dominant drinkers were also at lower risk of poor glucose handling and obesity compared to never drinkers. However, the magnitude of difference was greatest between never drinkers and dominant wine drinkers. The findings from this study indicate a cardioprotective role of wine separate from its alcohol content. This hypothesis is supported by findings from earlier experimental studies that suggest the cardioprotective role of wine is attributed to its non-alcoholic components [341]. Wine, particularly red wine, is rich in polyphenols that have antioxidant and anti-inflammatory properties shown to attenuate cardiometabolic risk [342,343]. The

relation between polyphenol intake and cardiometabolic health could offer one explanation as to why in this study a preference for wine appears to offer greater cardiometabolic protection than a preference for other alcoholic beverages. While several prospective studies report greater cardio-protection from wine consumption [131,157,158,160], the observational evidence on this matter is remains unclear. To this date, there is little consensus as to whether specific alcohol beverages modulate cardiometabolic risk [344].

Findings from post hoc analyses indicate that an increase in alcohol intake, at already existing low levels, negatively impacts anthropometric and biochemical markers of cardiometabolic risk. Even within the thresholds of moderate consumption, an increase in alcohol intake was positively associated with markers of obesity (BMI, and waist) and hypertension (increase in systolic and diastolic blood pressure). The findings from this study do not support those of recently published meta-analysis that reported a non-significant association between obesity risk and alcohol intake at moderate amounts (OR: 1.01, 95% CI: 0.92 to 1.10, p= 0.88). Despite the results of this recent meta-analysis, the evidence for moderate alcohol intake and obesity risk is relatively inconsistent [122]. However, given its high energy density and effect on mechanisms governing satiety, it is plausible that an increase in alcohol intake can increase the risk of obesity, even at existing low levels. The literature is equally unclear in its findings for the harmful or beneficial effects of moderate alcohol intake and hypertension. Still, the results of this study are in support of public health guidance that an increase in alcohol consumption at any level increases the risk of hypertension. Interestingly, alcoholic beverage preference was a negative confounder in the positive associations between moderate alcohol intake, body weight, and BMI. As illustrated in the results, the magnitude of these associations increased following adjustment for alcoholic beverage preference. The harmful effects of alcohol consumption on health are well recognised and so identifying negative confounders in alcohol-health relations are imperative to interpreting health risk-benefit ratios.

In this study, an increase in moderate alcohol consumption was positively associated with HDL concentration. The dose-response relationship between alcohol intake and HDL concentration is widely acknowledged [105]. This study also showed a negative association between moderate alcohol intake and HbA1c %, independent of body composition and dietary energy density. This finding signifies a positive effect of moderate alcohol intake on glycaemic control and corroborates the evidence of a negative association between light to moderate alcohol intake and type 2 diabetes risk.

For instance, a large meta-analysis based on more than 700,000 individuals observed a lower risk of Type 2 Diabetes in light and moderate drinkers relative to abstainers; light (RR: 0.83; 95% CI: 0.73, 0.95; P = 0.005) and moderate (RR: 0.74; 95% CI: 0.67, 0.82; P < 0.001) [97]. Findings from experimental evidence also support this observation. In these studies, low doses of alcohol are shown to improve insulin sensitivity by inhibiting gluconeogenesis, facilitating the peripheral uptake of glucose and promoting insulin production in the pancreas [106].

6.5.3 Strengths and Limitations

There are several strengths to this study that warrant further discussion. First, the study's large sample size infers greater power, precision, and confidence when interpreting and generalising significant findings. Second, this study controls for diet and the methodologies employed to measure dietary intake were robust, capturing both quality of diet and dietary energy density. A large body of observational studies examining the alcohol-cardiometabolic health relation inadequately measure and control for the confounding influence of diet [345,346]. Third, the robust methodologies used classify individuals according to alcohol consumption, notably making the distinction between true teetotallers and former drinkers. The mixture of former and never drinkers can introduce bias in alcohol-health relations since many former drinkers may stop drinking in pursuit of a healthier lifestyle. Finally, this study examines the effect of alcohol intake on cardiometabolic health across three important dimensions: i) absolute alcohol intake ii) alcoholic beverage preference iii) pattern of alcohol consumption. This holistic approach allows a comprehensive examination of the relationship between alcohol consumption and cardiometabolic health. This study is also subject to limitations. Firstly, given the cross-sectional nature of this study, it is not possible to draw any causal inferences between alcohol consumption and cardiometabolic risk. Furthermore, dietary and alcohol intakes were self-reported by participants meaning it was not possible to rule out response bias. Finally, due to the limitations of 24-hour dietary recall data, it was not possible to examine the relationship between binge drinking and cardiometabolic risk in the UK Biobank cohort.

6.5.4 Conclusions

In conclusion, this study highlights that in a British adult, the relationship between alcohol intake and cardiometabolic health is complex. While alcohol intake is associated with a higher HDL blood concentration and a better glucose handling, increasing intake at even low levels was associated with hypertension and anthropometric markers of obesity. Furthermore, this study suggests the

relationship between alcohol drinking behaviours and cardiometabolic health are also influenced by alcoholic beverage preference and drinking pattern. This study is thus a valuable addition to the literature and provides an important insight into the relationship between cardiometabolic health and alcohol consumption in a population of British adults.

7.0 Background

Findings from epidemiological studies have long suggested an inverse association between high-density lipoprotein cholesterol (HDL-c) and coronary artery disease[347]. HDL-c plays a key role in the reverse transport of cholesterol from the peripheries to the liver for excretion and reuse which can explain its anti-atherogenic properties[348]. HDL-c is strongly influenced by genetic and environmental factors. For example, several genome-wide association studies have identified a number of loci that account for the variance observed in this trait amongst individuals in large populations[193]. HDL-c is also strongly influenced by lifestyle factors, most notably alcohol consumption[109]. In fact, the positive association between alcohol and HDL-c has been postulated as one explanation for the cardioprotective benefits of moderate alcohol consumption[106]. It is widely accepted that genetic and environmental factors interact with one another to modulate a person's propensity to a trait or disease[349]. At present, only a handful of studies have examined the modulating effect of a gene-alcohol interaction on HDL-c, of which the majority use a single marker analysis approach to investigate the effect of a gene-alcohol interaction[193,201,203,350]. Therefore, it can be said that the interplay between a person's alcohol intake and combined genetic risk on HDL-c has not yet been fully explored

7.1 Aims and Objectives

This study investigates the association between HDL-c and the combined effect of genetic variants on HDL-c blood levels and whether HDL-c is modified by an interplay between combined genetic risk and alcohol consumption. This study was conducted in a large sample of UK Biobank participants. The objectives to achieve these aims are:

(i)   To describe the clinical characteristics of UK Biobank participants across tertiles of combined genetic risk.

(ii)   To investigate the association between combined genetic risk and HDL-c

(iii)   To investigate the interaction between combined genetic risk and weekly alcohol intake on HDL-c.

7.2 Methodology

7.2.1 Study Design and Participants

This is a cross-sectional design study on participants recruited to the UK Biobank cohort with complete and readily available genotype, clinical, and quantitative alcohol consumption data. Participants abstaining from alcohol, women who were pregnant at the time of baseline, and or participants with incomplete data for variables under investigation were excluded from further analysis.

7.2.2 Anthropometric and Biochemical Data Collection

The methodologies used to collect anthropometric and biochemical measures used in this study are described in detail in Chapter 2 of this thesis. A cardiometabolic risk score was calculated for each participant using anthropometric and biochemical markers of cardiometabolic health. The methodology for this score is described in Chapter 6.

7.2.3 Alcohol Consumption Data Collection

Weekly alcohol intake estimates were calculated for UK Biobank participants from touchscreen survey data and presented as units of alcohol per week (alcohol/wk). Refer to Chapter 4 for the methodologies used to estimate alcohol intake in the AHMS and UK Biobank cohorts.

7.2.5 SNP Selection and Genetic Risk Score

A weighted HDL-c polygenic risk score was calculated using the standardized effect sizes (in units of SD) for the association between HDL-c 223 SNPS described by Klarin et al [351]. These effect sizes outlined in Appendix 6.1 represent the association between each SNP with measured levels of HDL-C after adjustment for age, age squared, and study-specific covariates, including principal components to account for population structure before transformation using the inverse normal distribution. A weighted genetic risk score was calculated for each UK Biobank participant by applying the formula illustrated in Figure 7.1. In this formula SNP refers to the number of lipid trait increasing alleles (0,1 or 2) and β is the positive effect size (β-coefficient) for HDL-c. The WGRS was calculated using PLINK software version 1.9.

Figure 7.1 Formula to calculate the Weighted Genetic Risk Score

$$WGRS = \sum SNPi * \beta i + SNPj * \beta j \ldots$$

WGRS Weight Genetic Risk Score, ∑ summation, β Beta-coefficient of the effective allele

Participants were grouped into quintiles of WGRS representing low, medium, and high genetic risk.

7.3 Statistical Analysis

Statistical analysis was performed using R Studio Software version 1.4.1103. Analyses were stratified by grouping variables and the Chi-square (χ2) test was used to describe differences in the distribution of participants between groups. The normality of the distribution of continuous variables was tested using the Anderson-Darling Test. Normal distributed continuous variables were presented as the mean ± standard deviation (SD) and the difference between measures was tested using the analysis of variance (ANCOVA) test, adjusted for participant age and sex. Non-parametric distributed continuous variables were presented as median (Interquartile range (IQR)) and the difference between measures were tested using the Kruskal-Wallis test, adjusted for participant age and sex. A Pearson Correlation Test was conducted to examine the agreement between HDL-c and the HDL-c WGRS. Linear regression modelling was used to examine the association between WGRS, alcohol intake, and HDL-c controlling for the primary characteristics of age and sex. An interaction term was introduced to the model in the format of alcohol x WGRS to investigate the interplay between alcohol and WGRS on HDL-cholesterol level. Before linear regression analyses, alcohol intake (units/wk) was log_{10} transformed to stabilize the variance of the normally distributed data. The proportion of HDL-c variance explained by the WGRS, and alcohol intake respectively was calculated by dividing the sum of squares between groups by the sum of squares total. For all analyses, statistical significance was accepted as $p < 0.05$.

7.4 Results

7.4.1 Study Population

This study includes 135,525 UK Biobank participants with complete genotype, clinical and quantitative alcohol consumption data, and free of pregnancy at the time of baseline screen.

7.4.2 Descriptive Clinical Characteristics Across Tertiles of WGRS

The descriptive and clinical characteristics of participants across quintiles of WGRS are illustrated in Table 7.1. Participant age and the proportion of males per quintile group were evenly distributed across quintiles of WGRS. Cardiometabolic risk score increased with increasing ranks of weighted genetic risk (p <0.001). The difference in BMI and waist circumference between participants of differing WGRS rank was non-significant. Similarly, alcohol use did not differ significantly between

groups. Systolic blood pressure increased across increasing quintiles of WGRS, and this trend was significant. HDL-c also increased across increasing ranks of WGRS ($p < 0.001$). While Non-HDL-c decreased across low to higher ranks of genetic risk ($p < 0.001$). There was also a strong and significant trend for statin use, which decreased from low to high rankings of WGRS.

Table 7.1 *Descriptive Characteristics of Participants in the UK Biobank Cohort Across Quintiles of Weighted Genetic Risk for HDL-c*

Descriptive Characteristics Across Quintiles of Weighted Genetic Risk for HDL-c							
		Q1	Q2	Q3	Q4	Q5	*p*
Age (y)		55.7	55.7	55.7	55.8	55.9	*ns*
Sex: Male	(%)	48.8	48.7	49.6	49.3	49.3	*ns*
CMR Score		2.92	2.90	2.87	2.86	2.81	<0.001
BMI (kg/m2)		26.55	26.61	26.64	26.54	26.58	*ns*
Waist (cm)		88.67	88.68	88.81	88.63	88.60	*ns*
SBP (mmHg)	Mean (SD)	139.21	139.28	139.40	139.40	139.79	<0.05
DBP (mmHg)		82.20	82.30	82.32	82.31	82.03	<0.05
HDL (mmol/L)		1.39	1.46	1.51	1.57	1.66	<0.001
Non-HDL (mmol/L)		4.35	4.30	4.26	4.25	4.19	<0.001
Alcohol (Units/Wk)		18.44	18.55	18.69	18.66	18.67	*ns*
Statin Use (%)	(%)	8.8	8.5	8.3	7.9	7.2	<0.001
Abbreviations: BMI – body mass index; ns – non-significant							
Tests: Continuous data ~ ANCOVA adjusted for age and sex (clinical data only); Categorical data ~χ^2-test.							

7.4.3 Gene-Alcohol Interactions and HDL-cholesterol

The HDL-c polygenic risk score was normally distributed. Measure levels of HDL-c were positively correlated with the polygenic risk R^2 0.24 ($p < 0.001$). Table 7.2 outlines results from the linear and interaction analyses. A positive association was observed for alcohol intake and HDL-c in the UK Biobank cohort. HDL-c was also positively associated with WGRS ($p < 0.001$). In this study, genetic

propensity to HDL-c had a greater effect on HDL-c concentration than weekly alcohol intake. This study failed to observe an interaction effect between alcohol intake and WGRS on HDL-c.

Table 7.2 *Gene – Alcohol Interactions on HDL-c in the UK Biobank Cohorts*

Gene-Alcohol Interactions on HDL-c				
Model				
HDL-c	*Effect*	*S. E*	*p*	*% Of variance explained*
Alcohol Intake	0.133	1.02	<0.05	0.02%
WGRS	27.11	0.06	<0.001	6.10%
*Alcohol Intake * WGRS*	1.03	0.82	*ns*	0.001%
Model adjusted for age + sex. Alcohol intake is expressed as units alcohol per week log transformed.				

7.4 Discussion

Several prospective studies suggest an inverse association between HDL-c and cardiovascular disease risk[347]. It is well recognised that a person's level of HDL-c is influenced by genetic factors and lifestyle behaviours[352]. This study set out to examine the combined effect of genetic variants on HDL-c in the UK Biobank cohort and to understand the potential modification of genetic effects on HDL-c levels by alcohol consumption.

7.4.1 Summary of Main Findings

❖ This study demonstrates a positive association between an HDL-c polygenic risk score and HDL-c in a sub-population of the UK Biobank cohort.

❖ Genetic propensity to HDL-c had a greater influence on HDL-c concentration than alcohol intake.

❖ HDL-c is not modified by an interplay between HDL-c and alcohol intake.

7.4.2 Discussion of Main Findings

Objective i) To describe the clinical characteristics of UK Biobank participants across quintiles of polygenic risk.

This study observed a clear trend for increasing genetic propensity to higher HDL-c and lower cardiometabolic risk. These findings support early epidemiological research that suggests an inverse association between HDL-c and cardiovascular disease risk [353]. As described in earlier chapters HDL-c plays a key role in the reverse cholesterol transport (RCT) system and has properties consistent with athero-protection. Nevertheless, the causal relation between HDL-c and cardiovascular disease risk remains uncertain as failed clinical trials add to the growing scepticism of

the HDL-c hypothesis[354]. Equally the results presented are crosse-sectional and do not indicate causality which could be explained by other influencing factors.

This study observed a relationship between increasing HDL-c genetic risk score and high systolic blood pressure. This finding is supported by two studies that both show a positive association between HDL-c and incidence of hypertension[355,356]. However, it is important to note that this evidence is also limited by a cross-sectional design and does not support a causal relation between HDL-c and high systolic blood pressure. Whether there is a causal relationship between HDL-c and hypertension independent of other factors remains uncertain.

Findings from this analysis suggest an inverse association between genetic propensity to high HDL-c and non-HDL cholesterol. Although causality cannot be determined here, these findings suggest that propensity to higher HDL-c is associated with a more favourable lipid profile. However, this association can likely be explained by the key role of HDL-c in the RCT system. Finally, this study observed lower statin use across increasing ranks of HDL-c genetic propensity. Again, this is likely to be explained by the prominent role of HDL-c in the RCT system lessening the requirement for a pharmacologically controlled lipid profile.

Objectives: (ii) To investigate the association between combined genetic risk and HDL blood level concentration in the AHMS and UK Biobank cohorts with complete genotyped and clinical data.

(iii) To investigate the interaction between combined genetic risk and weekly alcohol intake on HDL blood levels.

This study observed a positive association between an HDL-c polygenic risk score and HDL-c. Findings from this study suggest that within the UK Biobank cohort, the polygenic determinants of HDL-c accounts for 6% of the variance observed. These findings are slightly lower than what has been previously reported in the literature on the heritability of HDL-c. According to the literature, the mean-variance in HDL-c explained by lipid loci is considered to be between 9% and 10%[193].

The positive relationship between alcohol intake and HDL-c functionality is well established and has been proposed as one possible explanation for the cardioprotective effects of moderate drinking[357]. As observed in earlier chapters alcohol consumption was positively associated with HDL-c. However, in comparison to polygenic risk, alcohol intake account for a significantly lower proportion of HDL-c

variance in this population. These findings suggest that in the UK Biobank alcohol use have a lesser impact on HDL-c than predefined polygenic determinants.

While alcohol and polygenic determinants of HDL-c were positively associated with HDL-c, an interactive effect from an interplay between these factors was not observed. These findings suggest that the polygenic effect on HDL-c is not modified by alcohol consumption. A small number of studies have examined the effect of a gene-alcohol interactions on HDL-c[193,201,203,350,358]. So far, only one study has observed a gene-alcohol interaction effect on HDL-c. However, this study was a single-marker analysis of lipoprotein lipase gene polymorphisms, making the results difficult to extrapolate [203]. In general, there is not enough strong evidence to currently suggest a gene-alcohol interaction effect on HDL-c.

7.4.3 Strengths and Limitations

A strength of this study is the calculation of a polygenic risk score from established single markers. Polygenic risk scores offer an overall estimate of a person's genetic susceptibility to a trait. This is advantageous over single marker analysis as it has the potential to offer a predicator with better discrimination properties than one based on single markers only [359].

This study is also subject to several limitations. Firstly, alcohol consumption was reported subjectively and therefore it was not possible to exclude confounding by response bias. Second, this study is based on a largely Caucasian population of European ancestry and therefore the results may not apply to other populations of varying backgrounds and ethnicities. Finally, there is a chance of overfitting given the GRS and analysis were both conducted in the UK Biobank datasets. This reduces the generalisability of the model in unseen data and may bias the significance of the results reported in this study.

7.4.4 Conclusions

To conclude, alcohol consumption and an HDL-c polygenic risk score were shown to have a positive effect on HDL-c in a UK Biobank cohort. However, an interaction effect between these influential parameters on HDL-c was not observed. More studies are required to verify whether these findings can be extrapolated from populations of different backgrounds and ethnicities.

8.0 Synthesis of Results

This thesis characterised the alcohol behaviours and dietary profile of two independent UK populations, spanning young to late adulthood. Notably, it has examined the relationship between alcohol consumption behaviour and cardiometabolic risk independent of diet. Finally, this thesis examined whether an interaction between alcohol intake and genes associated with elevated HDL-c explains the positive effect alcohol intake has on HDL-c concentration. This chapter summarises the main findings from each study presented in this thesis and provides an overall interpretation of the results. This chapter will discuss the key strengths and limitations of the studies conducted and recommend directions for future research.

8.1 Summary of Main Findings.

- ❖ A large proportion of UK adults regularly consume alcohol and alcohol absenteeism rates are relatively low (< 10%). Men are more likely to exceed low risk drinking guidelines than women. Binge drinking behaviour is more common than suggested by national drinking surveys, and younger drinkers are more likely to binge drink than older drinkers.

- ❖ The intake of alcohol has an additive effect on total energy intake. Heavy drinkers have a poorer diet quality than moderate drinkers and those who abstain. It remains inconclusive whether alcohol intake in low amounts has a significant impact on diet quality. Alcoholic beverage preference is an independent indicator of diet quality amongst drinkers. Compared with beer drinkers, wine drinkers are more likely have a diet of higher quality.

- ❖ Heavy alcohol consumption is associated with a deterioration in cardiometabolic health. The risk of cardiometabolic disease as indicated by a cardiometabolic risk score is lowest amongst moderate drinkers consuming an intake of 7-14 units per week and highest amongst never and heavy drinkers, suggesting a J-shape relationship between alcohol intake and cardiometabolic disease risk.

- ❖ Even at existing low levels an increase in alcohol intake increases the risk of obesity and hypertension.

- ❖ There is some suggestion that a preference for wine has more favourable cardiometabolic effects over a preference for beer or spirts relative to complete absenteeism.

- ❖ This thesis did not observe a difference in cardiometabolic risk between binge and non-binge drinkers. However, binge heavy drinkers and high ranked moderates are at a higher risk of obesity than their respective non-binge comparable.

- ❖ The effect of alcohol consumption on HDL-c does is not through an interaction between alcohol and HDL-c related genes.

8.2 Overall Interpretation and Implication of Findings

The findings from this thesis are of value to public health researchers, practitioners, and alcohol governing bodies both within the UK and abroad. Findings from this thesis highlight that alcohol consumption is a public health concern in the UK and intakes recorded by national surveys are likely to underestimate probable alcohol consumption behaviours[283]. For instance, the findings from Chapter 4 suggest alcohol consumed during a binge event is significantly higher than sex-specific binge drinking cut-off definitions, posing a significant threat to public health.

The findings in presented in this thesis corroborates evidence of a J/U shape relationship between alcohol consumption and cardiometabolic risk [82,85,92,96,318–323]. While increasing alcohol intake was generally associated with a deterioration in diet quality, the difference in CMR score between ranks of moderate drinker did not differ significantly after adjustment for dietary variables. However, as demonstrated in Chapter 5 and 6, alcohol consumption was shown to have an additive effect on total energy intake and was strongly associated with increased risk of obesity. This finding is supported by several studies including a recently publish systematic review and meta-analysis [8,126,169,304–307]. Obesity is a key risk factor for cardiometabolic diseases and recognising the role of alcohol consumption in the development of obesity is an important consideration when designing interventions to attenuate cardiometabolic disease risk. The results of this chapter also suggest that a preference for wine is associated with better cardiometabolic health than a preference for beer or spirits or total absenteeism. This finding corroborates a body of literature that proposes that the high polyphenol content of certain alcoholic beverages mediate any health benefit associated with alcohol consumption.[360,361]. Wine, especially red wine is rich in polyphenols which have antioxidant and cardioprotective properties[343]. The results of Chapter 6 also highlight that the effect of alcohol on cardiometabolic health does not solely depend on the amount of alcohol consumed but also varies with corresponding alcohol consumption behaviours such as alcoholic beverage choice. This finding reinforces the importance of measuring all aspects of alcohol consumption behaviour

when examining the relationship between alcohol and health, as highlighted by a recent review of the guidelines when measuring alcohol consumption in the population [270]. On this matter, the findings from this thesis demonstrate a good agreement between diary and survey measures of habitual alcohol consumption. This finding is of special value when examining the evidence and comparing the results studies using these different measures to capture alcohol consumption.

Finally, the findings presented in this thesis confirm a positive association between alcohol consumption and HDL-c blood concentration, corroborating earlier evidence. However, this thesis dismisses an interaction between alcohol intake and HDL-c related genes, suggesting that the effect of alcohol use on HDL-c is unlikely through a gene-alcohol interplay.

8.3 Overall Strengths and Limitations

There are considerable strengths and limitations to this study. A major limitation is the study's cross-sectional design. Cardiometabolic diseases have long incubation period. Consequently, examining the relationship between alcohol and cardiometabolic risk cross-sectionally fails to capture the temporal relationship between the alcohol consumption behaviour and incidence of disease. Response bias is an inherent bias to any study where data is self-reported, and this study is of no exception. The limitations to using self-reported alcohol consumption and dietary intake data are discussed at length in Chapter 3 and Chapter 4, respectively.

The large sample size used in this thesis is a major strength to the studies presented. Using the data from the Airwave Health Monitoring Study alongside data from the UK Biobank cohort offered an opportunity to examine the relationship between alcohol, diet, and health at different points throughout adulthood. Furthermore, repeating analyses within two independent cohorts validated observed associations between alcohol risk behaviour, diet, and cardiometabolic health. A novel aspect of this study was examining whether a gene-environment interaction explains the effect of alcohol intake on HDL-c. The identification of genetic polymorphisms as risk factors for disease is an exciting and emerging development in epidemiology and identifying interaction between more traditional and novel risk factors is crucial step in optimising public health.

Although there are inherent limitations in using self-reported measures of dietary and alcohol intake, a major strength of this study is the robust methodologies employed to minimise the impact of these biases, notably the employment of strict protocol when coding Airwave Health Monitoring Study dietary data. Finally, this study provides valuable insight into the alcohol drinking behaviours of the

British population and their respective associations with dietary pattern and cardiometabolic health, which until now have not been examined at great depth.

8.4 Future Work
Considering the findings presented in this thesis, recommendations for future research are as follows:

- ❖ Explore the association between subjective and objective measures of alcohol intake by measuring metabolites such as ethyl glucuronide in the urine with the aim of utilising metabolomics to capture alcohol consumption in large populations. This work would improve on accuracy of alcohol consumption measures in large cohorts.

- ❖ Within the Airwave Health Monitoring Study and UK Biobank Cohort, respectively, examine the relationship between baseline alcohol consumption and longitudinal risk of cardiometabolic disease e.g., diagnosis of cardiovascular disease and or type 2 diabetes, independent of diet quality, to understand the associations observed in this thesis are subject to change over time.

- ❖ Using data on polyphenol intake to investigate whether higher polyphenol intakes in wine drinkers contributed by wine consumption explains the association between wine consumption and cardiometabolic health.

- ❖ Examine the association and interaction between alcohol related single-nucleotide polymorphisms, reported alcohol intake, and polymorphisms associated with a cardiometabolic disease either cardiovascular disease or type 2 diabetes. This would resolve confidence in the inter-play between alcohol consumption and genetic predisposition to cardiometabolic disease.

8.5 Overall Conclusion
To conclude, the findings from this thesis indicate that a large proportion of the British population currently consume alcohol and that within this population heavy alcohol consumption is negatively associated with both dietary and cardiometabolic health. This thesis also provided evidence to suggest that alcohol consumption behaviours influence dietary pattern and cardiometabolic risk. Notably, this thesis showed that dietary pattern does not modify the relationship between moderate alcohol consumption and cardiometabolic risk. However, alcohol consumption was shown to have a significant effect on total energy consumption and markers of obesity, key risk factors for both cardiometabolic disease and other chronic non-communicable conditions. The findings from this

thesis highlight the role of alcohol consumption behaviours on the dietary and cardiometabolic health (particularly risk of obesity) of the British population. These findings contribute to public health knowledge and will aid future interventions aimed at reducing population alcohol intake.

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Appendices

A1.1 Figure 1.0 Randomization Procedure of Airwave Health Monitoring Study Participants for Dietary Analysis

	Sample size	Number of participant excluded	% of participant excluded	% of total sample
Total participants traced (end 2012)	42112			100
↓		3755	9	
From forces with clinics rolled out + with CDR linkage	38357			91
↓		5947	16	
With health screening	32410			77
↓		3870	12	
With auto questionnaire	28540			68
↓		918	3	
With complete auto questionnaire	27622			66
↓		2725	10	
With "complete" clinical and biological data	24897			59
↓		554	2	
With EDTA white cell sample	24343			58
↓		94	0	
With LHEP plasma sample	24249			58
↓		35	0	
With urine sample	24214			57
↓		11617	48	
With food diary	12597			30
↓		2597	21	
Random selection of participant for food diary coding	10000*			24

Randomisation procedure conducted by Dr Claire-Anne Vaughan, Imperial College London 2014. *1329 participant food diaries werecoded between 2012 – 2014 (before this randomisation process) of these 312 were not included in the 10,000 random sample. In thisthesis, these 312 diet diaries are included in the final sample size to optimise the study sample size.

Table 2.1 Pattern of Missing Data in UK Biobank and Airwave Health Monitoring Study (AHMS)				
		UK Biobank – HDL Observation		
		Missing (0)	*Non-Missing (1)*	*p-value**
Total	**n (%)**	72,633 (14.5)	429,871 (85.5)	-
Sex: *Male*		30,635 (42.2)	198,487	
Age (y)	**Mean (SD)**	56.4 (8.1)	56.6 (8.1)	< 0.001
BMI (kg/m²)	**Mean (SD)**	27.4 (4.9)	27.4 (4.8)	*ns*
Ethnicity: *White*	**n (%)**	65,603 (90.3)	393,885 (91.6)	*ns*
Country Enrolled	**n (%)**			
England		62,668 (86.3)	393,111 (91.4)	*ns*
Scotland		8048 (11.1)	24,583 (5.7)	*ns*
Wales		1181 (1.6)	12,117 (2.8)	*ns*
		AHMS – HbA1c Observation		
		Missing (0)	*Non-Missing (1)*	*p-value**
Total	**n (%)**	5261 (13.7)	35,821 (87.3)	-
Sex: *Male*		3261 (62.0)	22,526 (62.9)	*ns*
Age (y)	**Mean (SD)**	40.7 (8.6)	40.3 (9.0)	<0.01
BMI (kg/m²)	**Mean (SD)**	27.1 (4.4)	27.2 (4.2)	*ns*
Ethnicity: White	**n (%)**	4591 (87.3)	34,054 (95.1)	*ns*
Country Enrolled	**n (%)**			
England		4999 (95.0)	23,621 (65.9)	<0.05
Scotland		108 (2.0)	6331 (17.8)	<0.001
Wales		42 (1.0)	5227 (14.6)	<0.001
N. Ireland		0 (0.0)	2 (<0.1)	*ns*
		AHMS – HS-CRP Observation		
		Missing (0)	*Non-Missing (1)*	*p-value**
Total	**n (%)**	2705 (6.6)	38,377 (93.4)	-
Sex: *Male*		1724 (63.7)	24,063 (62.7)	*ns*
Age (y)	**Mean (SD)**	39.6 (8.7)	40.4 (9.0)	<0.001
BMI (kg/m²)	**Mean (SD)**	27.7 (4.5)	27.2 (4.2)	<0.001
Ethnicity: *White*	**n (%)**	2549 (94.2)	36,096 (94.0)	*ns*
Country Enrolled	**n (%)**			
England		1565 (57.8)	27,055 (70.5)	*ns*
Scotland		94 (3.5)	6345 (16.5)	*ns*
Wales		976 (36.1)	4293 (11.2)	<0.001
N. Ireland		0 (0.0)	2 (<0.1)	*ns*
Abbreviations: BMI = body mass index, ns = non-significant p> 0.05. *χ²-test categorical variables, Student's T.test continuous variables.				

A2.1 Airwave Health Monitoring Study Food Diary Version 1.0

Study No.

Imperial College London

Airwave Health Monitoring Study

FOOD DIARY

Please complete:

Date of birth: ___ ___ / ___ ___ /

Please enter '**M**' if you are Male or '**F**' if you are Female: ___

We would like you to keep this diary of everything you eat and drink over the next seven days.

As we all know, diet is a very important determinant of our day-to-day health and knowing about your dietary habits will help us in looking at health problems related to it.

This is a very important part of the study and will add greatly to the information you have already given us and help us make an accurate assessment of your health.

It is very important that you do not adjust what you eat and drink just because you are keeping a record. Pleasecontinue to eat whatever you would normally eat.

Please provide us with as much detail as you possibly can.

If you have any queries, please telephone:

0207 5943249

Thank you

1. As you will see, each day is marked in sections, beginning with first thing in the morning and ending with bedtime. For each part of the day:

   - Write down all food and drink consumed, the amounts and a description.

   - If nothing is eaten or drunk, draw a line through that section.

   - At the end of each day there is a list of snacks and drinks that can easily be forgotten. Please write any extra items in here if you have not already recorded them in some other part of the day.

   - If you prepare a recipe, please write it in the recipe box provided at the end of each day.

2. Please try to record everything at the time of eating, not from memory at the end of the day.

3. Please read pages 3-8 for help in describing the foods and drinks you have eaten. Pages 9-15 include a range of photographs and page 16 shows an example of part of a completed diary.

4. Give **brand and full name** of products from packaging. Many commercial foods have **weights**printed on them, so please use these to show howmuch you ate.

5. Please answer the questions at the back of the diary (pages 45-48), **after** you have completed the seven days.

2

DETAILED INSTRUCTIONS

The following section is a list of popular foods and drinks. Next to each item is the sort of thing we need to know so that we can tell what it is made of and how much you had. This list cannot cover all foods and drinks, so if anything, that you have eaten is missing try to relate it to a similar item. Please give as much detail as you can. For an example of how you might describe foods you have eaten see page 16.

Please try to state what sort of oil or fat was used for baking, frying etc.

State clearly whether spread was used on crackers and biscuits as well as on bread, rolls, toast and in sandwiches.

Food/Drink	Description & Preparation	Amount
Homemade dishes	Describe as fully as possible, include name of dish; give recipe or ingredients, including amounts if known	Tablespoons One of the suitable photos
Ready-made meals	Give name of dish as described on pack with brand, describe main ingredients and enclose label e.g.,beef lasagna, deep pan pizza, fishpie etc.	Weight from packet including proportion of pack eaten (all or half?) Tablespoons; one of the suitable photos
Meals eaten away from home or take-away meals	Please describe all dishes and give main ingredients e.g., lamb tikka masala and pilau rice, other Indian and oriental dishes, fish and chips, burgers, pizza etc.	Proportion of takeaway or restaurant carton Describe meal size and dimensions where appropriate Tablespoons; one of the suitable photos
BEVERAGES		
Alcoholic drinks e.g.,beer, lager, cider, sherry, wine, spirits,and liqueurs	Describe type and give alcohol content especially for beers, lagers,and wines	Number of pints Number and size of cans, bottles, or glassesNumber of measures Volume (fl. oz. or ml.)
Fruit juice Fruit drinks soft drinks	Without added sugar with added sugar Brand name, regular or diet or low calorie	Glasses, cartons, cans,or bottles with volume

| Coffee | Instant or ground; decaffeinated or caffeinated; with milk or sugar | Cups or mugs
Volume if available |

3

Tea	Tea leaves or tea bag, with milk or sugar. If instant: black or white, sweetened or not	Cups or mugs Volume if available
Milk based or hot chocolate type drinks	Name or type of drink; regular, reduced fat or low sugar Type of milk used	Cups or mugs Volume if available
Water	%Ap, bottled or filtered	Glass, tumbler; volume
BISCUITS / CRACKERS		
Sweet biscuits	Brand and full product name plus description e.g., sandwich, wafer,chocolate half-coated, full-coated, cream-filled Ingredients if homemade	Number of biscuits and size
Crackers, crisp bread, savory biscuits	Brand and full product name plus description e.g., Car's water biscuits, Original Ryvita, Jacob's Choice grain	Number of crackers and size
BREAD		
Bread	White, brown, granary, wholemeal, containing seeds, ciabatta, focaccia, French type, baguette. Was the loaf pre-sliced or hand-cut?	Size of loaf: large or small Thickness of slice Number of slices
Rolls or buns	Describe rolls: crusty, soft, baps, petit pain, finger	Size of rolls and number
Sandwiches	Remember to describe type and amount of spread and filling	Number of rolls or slices of bread
BREAKFAST CEREALS		
Breakfast cereal	Brand and full name e.g., Jordan'sNatural Muesli, Sainsbury's Maltese*Remember to describe milk and sugar added separately*	Photo 1 Tablespoons Milk on cereal: large, medium, or small amount
Porridge or Ready Brik	Porridge oats or Ready break Type of milk used to make it or was water used? *Remember to describe milk and sugar added separately*	Photo 1 Amounts of ingredients

Bran: *wheat* *bran* *wheatgerm* *oatgerm and bran*	Added separately to breakfast cereal or mixed with other foods such as porridge. Please describe type and brand	Dessertspoons or tablespoons

4

BUTTER, MARGARINES, FATS & OILS		
Butter, spreads, ormargarines	Please gi*e specific brand, full name as described on packaging plus the percentage (%) fat if known	Photo 18 for spread on bread or rolls For crackers and biscuits describe thickness of spread
Oils	Describe type of oil used in cooking or dressings e.g., corn, olive, sunflower	Tablespoons
CAKES		
Cakes, scones and sweet buns, pies, and pastries	*Homemade* – describe ingredients and recipe *Commercia*l – give brand and product name with description 0oes cake contain filling e.g., whipped cream, butter icing or have a coating or covering? Are pies made with pastry top and bottom?	Proportion of whole cake or pie Size of slice or individual cake Photos 15 and 16 for cake Photo 7 for pies or flans
	Are scones or cakes spread with butter, margarine and/or jam?	How many whole scones or halves?
CHEESE		
Hard cheese (includes Brie, Danish Blue etc.)	Specify type e.g., Cheddar,Wensleydale, Brie	Photo 2 (amount eaten is equal to the slice OR the chunk OR the grated cheese) Number and size of slices or chunks
Philadelphia type soft cheese or cheese spread	Regular or reduced fat cheese Specify brand and fat content	Thick or thin spread Teaspoons
DESSERT/PUDDINGS		
Puddings	Describe type and ingredients e.g., apple crumble, raspberry cheesecake with biscuit base, dairy cream trifle with banana *Served with custard, ice cream, cream, or yogurt? (See milk)*	Photo 17; tablespoons Size of slice; weight of carton for commercial items Photo 7 for pies or flans
EGGS		

Eggs and egg dishes	Boiled, poached, fried, scrambled, omelette plus topping or other ingredients Was fat or oil used in cooking? Give type of fat or oil used	Size of eggs Number of eggs consumed

5

FISH		
Fish and fish dishes	%Ype of fish; fresh, frozen, or canned, cooking method; from fish and chipshop, homemade or commercial; battered or breadcrumbed	Weight (with or without bones/skin?); size of whole or piece of fish Photo 6

FRUIT		
Fruit	Type of fruit; fresh (was skin eaten or not?), frozen, dried; stewed with or without sugar Canned in syrup or juice	Number of whole fruits Tablespoons; weight (with or without skin) Weight of can

MEAT		
Ham, salami Cold meats Roast meats	Type Cut from joint or pre-sliced	Weight; number and size or thickness of slices Photo 4
Bacon	Back, middle, streaky; unsmoked or smoked Rashers or chops	Number of rashers or chops Weight (raw or cooked)
Gammon	Steaks, rashers or cut from joint	Weight (raw or cooked) Number and size
Sausages	Type, cooking method	Number and size
Chops and steaks	Type and cut, cooking method Were the fat eaten?	Number and size Weight (raw or cooked)
Meat dishes	Recipe or brand and product name with ingredients	Photo 5, 19, or 20 Tablespoons; pack weight

MILK/DAIRY		
Milk	Whole, semi-skimmed or skimmed; percentage (%) fat if known Pasteurised, UHT, or sterilised	Tablespoons Volume in fl.oz. or ml.
Powdered milk	Dried skimmed milk or with added vegetable fat	Teaspoons: volume of made-up milk
Coffee or tea creamer or whitener	Brand and product name e.g., Coffeemate Please state if powder or liquid	Teaspoons Individual cartons or sachets
Cream	Single, whipping, or double; dairy or non-dairy; regular or reduced fat Liquid, whipped or aerosol	Tablespoons Volume
Yogurt and fromage frais	Brand and specific product name or description, fat content as on carton	Tablespoons; size of carton (g. or ml.)
Ice cream	Brand and product name; regular, reduced fat or made with cream	Scoops Tablespoons

Non-dairy milk	Soya, oat, or rice milk; brand; product description; fortified with calcium; sweetened?	Tablespoons Volume

PASTA		
Pasta and spaghetti incl. filled pasta	Dried or fresh pasta; white or wholemeal; describe type e.g., fusillior tagliatelle Filled pasta e.g., Tortelloni withspinach and ricotta	Weight (raw or cooked) Photo 9 Proportion of packet weight
Pasta dishes	Lasagne, cannelloni, or pasta bakes;give recipe and ingredients for homemade; brand, product name and description for commercial	Photo 20 Packet weight
Pasta sauce	Describe sauce type and ingredients	Tablespoons Volume or weight of commercial product
RICE		
Rice	White or brown, long grain or basmati	Photo 8 Weight (raw or cooked)
Rice dishes	Give recipe and ingredients for homemade; brand, product name and description for commercial	Photo 8; tablespoons Packet weight and proportion eaten
SAUCES & SOUPS		
Sauces and ketchups including dips	Describe brand and product name or recipe and ingredients	Tablespoon or teaspoons Volume or weight of commercial product
Soups	Describe type and ingredients Is soup homemade, canned, condensed, dried packet, instant, fresh/carton or low calorie?	Bowls, cups, or mugs Volume in fl.oz. or ml. Weight of can and proportion eaten
Gravy	Describe brand and product name or recipe and ingredients Eade with cornflour, bisto powder, granules; with or without added meat juices, stock, or vegetable juice	Tablespoons Volume in ml. or fl.oz.
Dressings	Type and ingredients; brand and product name; regular, reduced fat or fat free	Tablespoons or teaspoons
Mayonnaise	Regular or reduced fat	Tablespoons etc.
SAVOURY DISHES		

Pies, flans, andquiches *Pizza* *Pancakes* *Sausage rolls* *Filled tortillas or burritos*	Describe dish and ingredients, brand, and product name	Product weight and proportion eaten Number of slices or individual items eaten

7

SAVOURY SNACKS		
Crisps and snacks *Nuts*	Brand name and description Type; fresh or roasted; salted or unsalted	Weight of packet Number of items eaten
SPREADS & CONDIMENTS		
Jams, other preserves, andspreads	Brand name and type of spread Jam, honey, marmalade Peanut butter, other nut butters Chocolate spread Marmite and savoury spread	Thin, medium, or thickspread
Salt, pepper, mustard	Describe type	Sprinkle; teaspoons
SUGARS & CONFECTIONERY		
Sweets and chocolate	Describe type and brand	Weight; number of pieces, whole bars, orindividual sweets
Sugars and sweeteners	Type of sugar Brand and type of sweetener	Teaspoons Tablets or spoons
VEGETABLES (including herbs)		
Vegetables and salad including lentils, beans, and baked beans	Type of vegetables; fresh, frozen, orcanned; cooking method or raw If roasted was fat added? Was butter, sauce or dressing added?	Photos 12,13 or 14 Number of whole vegetables Tablespoons
Vegetable dishes including dishes with potato, beans, lentils,or pulses	Recipe or brand and product name with ingredients	Photo 5 or 20 Weight of commercial dish
Potatoes	Boiled; roasted with or without fat; fried; sautéed; mashed with or without added fat or milk	Photo 10 or 11
Chips	Homemade; commercial e.g., ovenchips; takeaway Size and cut of chip	Photo 7
Herbs and spices	Fresh or dried	Teaspoons or other spoons; leaves; sprigs
VEGETARIAN		

Vegetarian products and dishes with Quorn, soya or TVP or tofu	Describe dish or product and ingredients, brand, and productname e.g., Quorn sausages, Vegetable stir-fry with tofu	Weight from packaging Number of items Number of slices of meat substitute Photo 5 Tablespoons

8

Please choose an appropriate photo to indicate the portion size you have eaten. To help you make this choice, there are some notes below the photos. Write down the picture number and size nearest to your own helping e.g., 2a, 3b or 1c.

The large white circle in the background shows the actual size of the 10" dinner plates used in the photos. Items such as the cake are photographed on a 7" tea plate.

Refer to the detailed instructions on pages 3 - 8 where * is indicated.
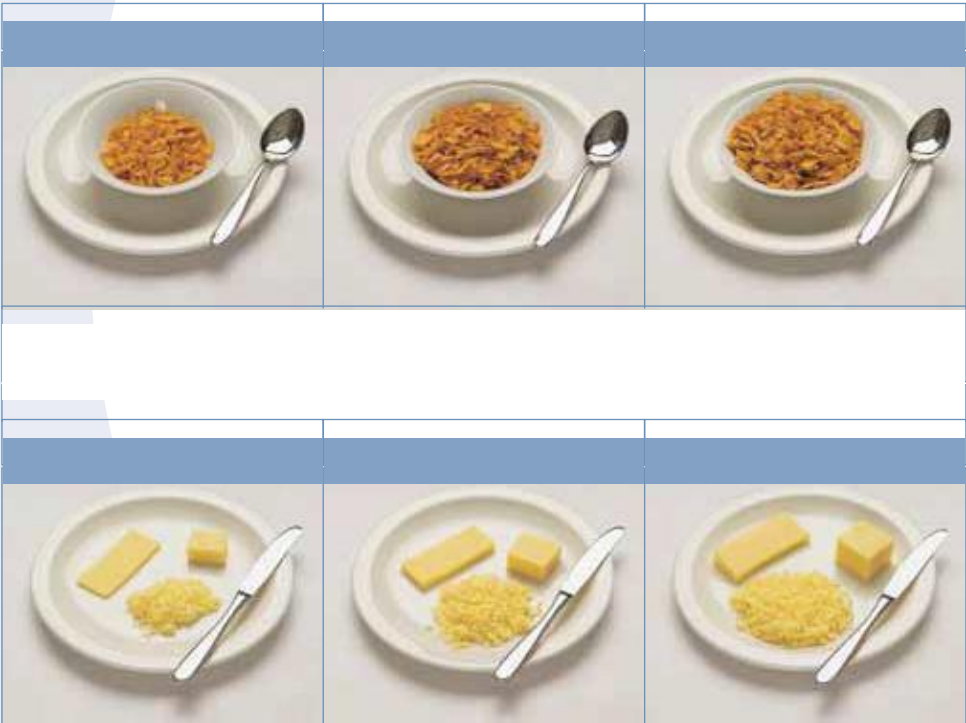
3a   3b   3c

Suitable for - Quiches, flans, sa*oury or sweet pies and pizza
Not for - Cakes (see photos 15 and 16)

4a   4b   4c
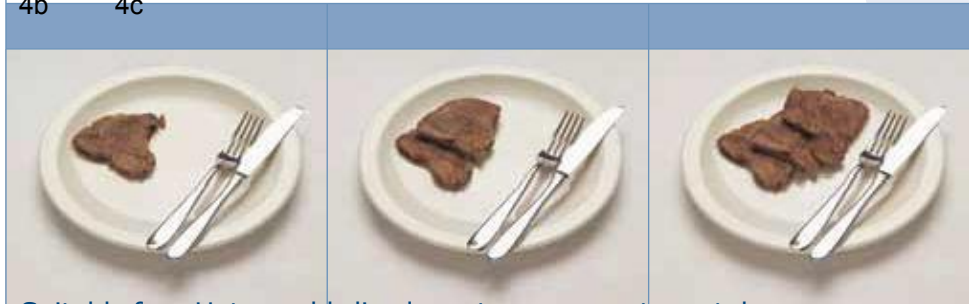
Suitable for - Hot or cold sliced meats, e.g., roast meat, ham, or gammon
Not for - Chops, steaks, or bacon rashers *

5a   5b   5c

Suitable for - Vegetable stews or meat stews and casseroles WITH vegetables, also bolognaise sauce

Not for - Meat stews WITHOUT vegetables (see photo 19)

10

6a	6b	6c

Suitable for - Fish including fish in breadcrumbs or batter
Not for - Chops or steaks *

7a	7b	7c

Suitable for - Chips only

8a	8b	8c

Suitable for - Boiled rice and rice dishes

10" P

9a   9b   9c

Suitable for - Boiled spaghetti, other boiled pastas and noodles plus pasta and noodle dishes

10a   10b   10c

Suitable for – Boiled or roast potato

11a   11b   11c

Suitable for – Mashed potato

LATE

12a

Suitable for – Baked beans and peas

13a

Suitable for – Carrots and other similar vegetables

14a

Suitable for – Cabbage, other leafy vegetables, and
saladsNot for – Peas (see photo 12)

10" P

15a
15b
15c
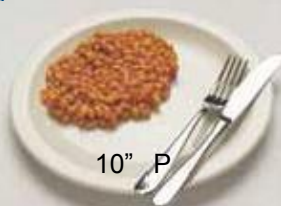
Suitable for – Sponge cake and other similar cakes

Not for - Quiches, flans and sweet or sa*oury pies (see photo 7)

16a
16b
16c

Suitable for - Fruit cake and other cake types with same shape

Not for - Meat (see photo 4) *

17a
17b   17c

Suitable for - Fruit crumble and other puddings and desserts

Not for - Puddings WITH custard, sauce, yoghurt, or ice cream combined *

LATE

14

	18b	18c
18a		
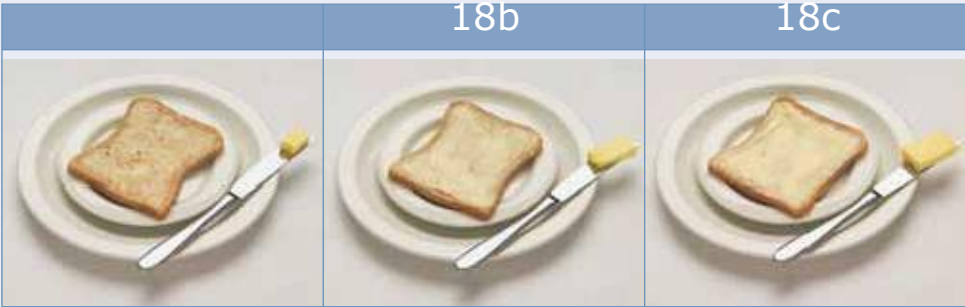
Suitable for – Butter, margarines, and spreads on bread only

	19b	19c
19a		

Suitable for – Meat or minced meat stews WITHOUT vegetables
Not for – Meat stews WITH vegetables (see photo 5)

	20b	20c
20a		

Suitable for – Shepherd's pie and similar dishes or lasagne

EXAMPLE

Food/Drink	Description and Preparation	Amount
LUNCH		
Beef cass. Potatoes Vegetables Dessert Tea	<u>Canteen at work</u> Beef casserole (onion and carrots) Mashed potatoes Boiled cabbage Rhubarb crumble Custard Tea bag Milk - semi-skimmed (no sugar)	Photo 5b 2 scoops Photo 14a Photo 17b 2 small ladles 1 plastic cup 1 tbsp
TEA – between lunch time and evening meal		
Sandwich Spread Filling Apple Tea Chocolate	Brown bread, large, sliced loaf St. Ivel Utterly Butterly Grated cheddar cheese and tomato Small Braeburn - ate skin as lunch with whole milk Cadbury s Dairy Milk - small bar	1 medium slice thick spread 1/2 x Photo 2c 2 slices 1 fruit 1 large mug 3 tbsp milk 1 (49g)
EVENING MEAL		

Chicken & vegetable stir-fry	Skinless and boneless chicken breast, packaged, 300-gram rawVegetable oil 1 large carrot, 2 spring onions 1 small courgette, 1 med. red pepper, 4 oz button mushrooms 2 tsp grated ginger, 1 tbsp soy sauce, 1 tbsp sherry	Ate ½ of this recipe
Rice	White rice, boiled	4 heaped tbsp
Fruit yoghurt	Muller Fruit Corner - strawberry	1 carton (175g)
red wine	Cabernet Sauvignon (14.5% alcohol)	1 large wine glass (270 ml)

16

DATE / /	DAY OF THE WEEK:	

BEFORE BREAKFAST		
Food/Drink	Description and Preparation	Amount

BREAKFAST		
Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time		
Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night		
Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

END OF DAY No. 1

20

DATE	/	/	DAY OF THE WEEK:	

BEFORE BREAKFAST		
Food/Drink	Description and Preparation	Amount

BREAKFAST		
Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time		
Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night		
Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

24

DATE	/	/	DAY OF THE WEEK:	

BEFORE BREAKFAST		
Food/Drink	Description and Preparation	Amount

BREAKFAST		
Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time		
Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night		
Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

28

DATE	/ /	DAY OF THE WEEK:	

BEFORE BREAKFAST		
Food/Drink	Description and Preparation	Amount

BREAKFAST		
Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time		
Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night		
Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

32

DATE	/	/	DAY OF THE WEEK:	

BEFORE BREAKFAST		
Food/Drink	Description and Preparation	Amount

BREAKFAST		
Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time		
Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night		
Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

DATE	/	/	DAY OF THE WEEK:	

BEFORE BREAKFAST

Food/Drink	Description and Preparation	Amount

BREAKFAST

Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time

Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night

Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

DATE	/	/	DAY OF THE WEEK:	

BEFORE BREAKFAST		
Food/Drink	Description and Preparation	Amount

BREAKFAST		
Food/Drink	Description and Preparation	Amount

MID MORNING – between breakfast time & lunch time		
Food/Drink	Description and Preparation	Amount

LUNCH		
Food/Drink	Description and Preparation	Amount

TEA – between lunch time & the evening meal		
Food/Drink	Description and Preparation	Amount

EVENING MEAL		
Food/Drink	Description and Preparation	Amount

LATER EVENING – up to last thing at night		
Food/Drink	Description and Preparation	Amount

ANYTHING ELSE? Between meal snacks and drinks NOT already written in before		
Food / Drink	Description and Preparation	Amount
Chocolate		
Toffees, sweets		
Crisps, peanuts		
other snacks		
Beer, wine		
Sherry, spirits		
Other cold drinks		
Tea, coffee		
Other hot drinks		
Ice cream		
Anything else?		

Space to write in the recipe or ingredients of any home-made dishes, take-away meals etc. that you have mentioned but not described previously. Where applicable, please list amounts of ingredients and brand names. **Please indicate the amount or proportion consumed by yourself.**

GENERAL QUESTIONS ABOUT YOUR FOOD/DRINK *LAST WEEK*

1. *Which type of milk did you most often use last week?*
Select one only.

☐ Whole/full cream   ☐ Soya

☐ Semi-skimmed   ☐ Other:

☐ Skimmed/fat free   ☐ No milk used

Do you know the fat percentage (%) of your milk? _____

Was this milk: ☐ pasteurized? ☐ UHT? ☐ sterilized? ☐ dried?

2. *How much milk did you usually have in tea, coffee and on your cereal?*

	A lot of A lot	Average	Hardly any	No milk used
Tea:	☐	☐	☐	☐
Coffee:	☐	☐	☐	☐
Cereal:	☐	☐	☐	☐

3. *Did you drink decaffeinated tea or coffee?*

	Always	Sometimes	Never
Tea:	☐	☐	☐
Coffee:	☐	☐	☐

4. *Which types of fat did you use last week for baking, frying, spreading and on salads?* **If you are not sure which category to indicate, check packaging for the exact name, fat content and brand and fill in this information.**

Type of fat, spread or margarine	Brand and name of product	Spreading	Frying	Baking	Salads
Butter					

Spreadable butter					
Dairy spread (e.g., I can't believe it's not butter)					
Polyunsaturated spread (sunflower, soya or *egan)					

4. *(Continued.)*

Type of fat, spread or margarine	Brand and name of product	Spreading	Frying	Baking	Salads
Low fat spread (less than 60% fat)					
Olive oil-based spread					
Other soft margarine or spread – 1					
Other soft margarine or spread – 2					
Hard margarine					
Vegetable oil - 1	*Type:*				
Vegetable oil - 2	*Type:*				
Lard					
White vegetable fat					
Dripping or animal fat					
Other					

5. *Which type of bread did you eat most often last week?*
   Select one only.

☐ White   ☐ Soft grain
☐ Granary   ☐ Brown
☐ Wholemeal   ☐ Wheatgerm
Other: _____

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6. *Did you eat butter, margarine or spread last week?*
Please tick boxes below to show whether you ate it on toast, bread, sandwiches, in rolls or on crackers:

	Toast	Bread	Sandwiches	Rolls	Crackers
Always					
Sometimes					
Never					
Don't know					

7. *How thickly did you spread butter, margarine etc. on bread or crackers?*

☐ Thick   ☐ Medium

☐ Thin   ☐ None

8. *If you ate grilled, fried, barbecued, or roast meat last week, howwell cooked was it?* **Please tick the boxes.**

	Beef, lamb, pork	Poultry
Well done or dark brown		
Medium		
Lightly cooked or rare		
Did not eat meats cooked by these methods		
Did not eat these meats		

9. *If you ate meat last week, what did you do with the visible fat?*
Please note that meat includes beef, lamb, pork, ham, andbacon.

☐ Ate all the fat   ☐ Ate most of the fat

☐ Ate some of the fat   ☐ Ate as little as possible

☐   ☐

Did not eat meat   No fat eaten

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10. *If you ate poultry last week, did you eat the skin? **Please note that poultry includes chicken, duck, goose, and game birds.***

☐ Yes   ☐ No

☐ Sometimes   ☐ Did not eat poultry

11. *If you had gravy last week, were the meat juices, pan residues or dripping put into the gravy?*

☐ Yes   ☐ No   ☐ Sometimes

☐ Don't know   ☐ Did not eat gravy

12. *Was salt usually added to your food during cooking last week?*

☐ Yes   ☐ No   ☐ Don't know

Did you usually add salt to your food at the table last week?

☐ Yes   ☐ No   ☐ Don't know

Did you regularly use a salt substitute (e.g., LoSalt) last week?

☐ Yes   ☐ No   ☐ Don't know

If YES, which brand?

13. *Did you eat the skin on fruit? **Please tick boxes.***

	Apple	Pear
Skin eaten		
Skin not eaten		

Fruit not eaten		

14. *Please name any vitamins, minerals or other food supplements taken on each day of last week.* **Please write down all the details from each packet/container or enclose label(s). Give the number of tablets taken on each day.**

Brand	Name	Strength	Tablet capsule tsp.	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Boots	High strength vitamin C	100 mg	Tablet	1	1		2	1	1	1

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15. *Which types of water did you consume last week?*
   Please give information for both HOT and COLD drinks.

Water type	Hot drinks	Cold drinks
%Ap water (unfiltered)		
Filtered water - hard water filter		
Filtered water – other		
Bottled water – *brand:*		
Other water – *brand:*		

16. *Were any of the following foods which you ate last week produced* **organically** *(without pesticides)?* **Please tick the necessary box(es).**

☐ Vegetables, homegrown   ☐ Vegetables, purchased
☐ Fruit, homegrown   ☐ Fruit, purchased
☐ Milk and dairy products   ☐ Cereal or cereal products, bread
☐ Meat   ☐ No organic foods eaten

This space has been left for you to tell us about anything else which you feel is important about your food/drink intake last week.

Please bring the diary back with you to the clinicfor your health screening appointment.

Thank you very much for your help in completing such a detailed record.

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Imperial College London

Airwave Health Monitoring Study

Standard protocol for food diary coding

Previous version

20/12/16This version:

30/01/18

Developed by: Jennifer Griffin, Anwar AlBaloul, Aleksandra Kopytek Nutrition and Dietetics Research Group

Dietplan7.00.52 nutritional software programme (*Forestfield Software Ltd, Horsham, UK*)

Contents   **Page**

16.0   Introduction:

The following pages provide an outline of how to input and code the food diaries from the AIRWAVE study.

The primary aim of this protocol is to reduce error and to standardise code and portion selection.

Please read through before you start to code and input the food diaries. You will also need to refer to the i) AIRWAVE code book, ii) AIRWAVE portion size document and iii) Food base portion size document. These documents are within the NUTRI-TECH share drive.

All coders should keep a weekly log of any issues regarding code / portion selection to discuss at the weekly meeting.

EXCLUSION CRITERIA for coding:
- Less than one day completed
- Meal replacement diet
- Incomplete diaries are coded but incomplete days are not e.g., if days 1-6 are complete but day 7 is does not follow the same pattern as the previous days. Therefore days 1-6 are coded but 7 is not

If a diary cannot be coded due to any of the above, it needs to be logged into the MASTER LOG excel file, sheet 'Diaries to be excluded'.

Diaries with missing gender and/or date of birth should be logged in the Master Log excel file, sheet 'Missing Gender - DOB

2.0 General questions

Recording the answers to the questions in page 45-50 of the food diary

- Open the file: \\wmdi-nutritech\Dietary assessment protocol files for shared access / general questions

- The participant responses to questions 3, 8, 12, 14 and 16 are recorded in this spread sheet.
- The responses to the questions have been coded – the codes are detailed in the top row or in the comment box.
- <u>Only one</u> value should be entered per cell.
- <u>Please ignore column U, as this no longer applies to current protocol.</u>
- In column 'V', enter the number of days that the diary has been completed for.
- Please ignore column 'W', as this information no longer applies to current protocol.
- In column X enter the date of the first day in the food diary

Using the answers recorded in page 45-50 of the food diary to aid codeselection

Initially, select the food codes based on what the participant has written in the actual food diary. Refer to the general questions to assist selection of code/portion when information provided by the diary is insufficient.

Q. 1 MILK - type

The answers recorded here detail the type of milk used by the participant. This should be the type of milk that you input unless another type is written in the daily diet entry. If this section is incomplete, assume UKN 12-313 'Semi-skimmed milk pasteurized' consumed, unless otherwise stated in the food diary.

MILK - amount

Details the amount of milk to input unless otherwise written in the daily entry (n.b. these are in grams therefore specific gravity does not need to be applied):

	A lot (g)	Average (g)	Hardly any (g)
Tea	40	30	23
Coffee	64	43	30
Cereal	175	123	91

Source: Foodbase 75th / 50th / 25th centile values 'all age groups' mixed gender. Values calculated by combing the recording portion sizes for semi-skimmed and whole milk and then divided by two and rounded to the nearest whole number.

If this section is incomplete, assume 'medium' amount consumed unless otherwise stated in the food diary.

- Tea - add milk (semi-skimmed, average amount) if milk is recorded elsewhere in the diary
- Cereal - add milk (semi-skimmed, average amount) if milk is recorded elsewhere in the diary.

Exception: if there is a specific pattern to consumption, e.g., every evening 'tea' written without milk – then do not include milk.

TYPE OF TEA /COFFEE

This should be the type of tea / coffee that you input unless another type is written in the daily diet entry. Check if the respondent has indicated when they have caffeinated drinks or not.

If they have not indicated in the food diary which type of drinks are consumed and have filled in the back of the diary – please enter as follows:

Answer:	Tea	coffee
Always decaffeinated	USF A000006	USF A000005

Sometimes decaffeinated	Use decaffeinated code when indicated in the diary, otherwise use standard default code	Use decaffeinated code when indicated in the diary, otherwise use standard default code
Never decaffeinated	Refer to the Airwave code book for standard and default codes.	Refer to the Airwave codebook for standard and default codes.

If this section is incomplete assume caffeinated versions are consumed, unless otherwise stated in the food diary.

FATS

Details the type of fat to input unless otherwise written in the diary entry. If this section is not completed, assume UKN 17-655 Butter, spreadable consumed unless otherwise stated in the food diary.

BREAD

This provides details of the type of bread to enter unless otherwise written in the daily entry. If this section is not completed use code UKN 11-1145 White bread, average. If the respondent has toast, use the toasted code. There is no toasted code for granary bread, so the bread code 11-461 must be used.

NOTE: Brown bread is no longer available in the UK –Always code wholemeal breadQ.6 FATS – frequency of use

States if the participant used butter, margarine or spread (as selected in Q.4) when they ate bread / toast / crackers / rolls.

Answer =	Enter as:
Always	Always add butter / spread as Q.4/Q.7 when the item is mentioned
Sometimes	Code when specified in the diary
Never	Never enter butter or spread on any of these items unless recorded in the daily entry.
Don't know	Never enter butter or spread on any of these items unless recorded in the daily entry.

If this section is not completed apply 'sometimes' option.

FATS – quantity used on bread and crackers

This gives an indication of the amount in grams used on bread and crackers, unless the participant has stated another quantity or referred to the photo images. Refer to the portion size algorithm. NB. This refers to the serving size per slice/side of bread e.g., one bread roll = 2 sides

If participant recorded usage on a **'cracker'** use 50% of the quantity

Answer =	Enter as:
thick	14g
medium	10g
thin	7g

Source: Food base (1) serving 25th / 50th / 75th centile

If this section is not completed, assume 'medium' amount is consumed unless otherwise stated in the food diary.

MEAT – level of cooking

This information only needs to be recorded in the Excel spreadsheet.

MEAT – amount of fat eaten

Answer =	Enter as:
Ate all the fat	Select a code that states 'lean and fat' every time meat is eaten.
Ate some of the fat	Every time meat is eaten, enter 50% of the reported weight as a code that states, 'lean and fat' and 50% as a code that states 'lean'or 'meat only'. i.e., *sirloin beef steak fried 230g* enter as: 115g UKN 18-066 beef, sirloin steak, fried, lean 115g UKN 18-067 beef, sirloin steak, fried, lean, and fat
Ate most of the fat	Every time meat is eaten, enter 75% of the reported weight as a code that states, 'lean and fat' and 25% as a code that states 'lean'or 'meat only'. i.e., *sirloin beef steak fried 230g* enter as:

	57.5g UKN 18-066 beef, sirloin steak, fried, lean
	172.5g UKN 18-067 beef, sirloin steak, fried, lean, and fat
Ate as little as possible	Every time meat is eaten enter 25% of the reported weight as a code that states, 'lean and fat' and 75% as a code that states 'lean'or 'meat only'.
	i.e., *sirloin beef steak fried 230g*
	enter as:
	172.5g UKN 18-066 beef, sirloin steak, fried, lean
	57.5g UKN 18-067 beef, sirloin steak, fried, lean, and fat
Did not eat meat	n/a
No fat eaten	Select a code that states 'lean' every time meat is eaten.

If this section is incomplete, apply '*Ate some of the fat*' option.

POULTRY – amount of skin eaten

Answer =	Enter as:
yes	Select option for 'meat and skin' every time poultry is eaten
sometimes	Every time poultry is eaten enter 50% of the reported weight as a code that states, 'meat and skin' and 50% as a code that states 'without /no skin / meat only'.
no	Select option for 'without /no skin' every time poultry is eaten
Did not eat poultry	n/a

If this section is not completed apply 'sometimes' option.

GRAVY

	Enter as:
With juices / pan residues	RCP AR00008 homemade beef gravy made with meat fat juices added

Without juices / pan residues	UKN 17-311 Gravy instant granules made up with water
Sometimes	Every time gravy is consumed enter the recorded portion as UKN 17-311
Don't know	Enter as default: UKN 17-311 Gravy instant granules made up with water

Default code if not stated use UKN 17-725 Gravy instant granules made up with water

Q12. SALT

This information only needs to be recorded in the Excel spreadsheet. No salt added at the table or to cooking water should be included.

NB. Default code for all vegetables boiled – select the code stating '<u>unsalted water'</u> unless optionnot available.

(Ref: methodology as NDNS 2008/09 -2009/10-sodium intake excludes cooking and table salt).

FRUIT

This tells you if the participant eats the skin/peel on fruits where it is edible.

Answer:	**Apple**	**Pear**
Skin eaten	UKN 14-012 Apples, eating, average, raw	UKN 14-190 Pears, average, raw
Skin not eaten	UKN 14-014 Apples, eating, average, raw, peeled	UKN 14-192 Pears, average, raw, peeled

If this section is not completed apply 'Skin eaten' option.

Vitamins and supplements

This information only needs to be recorded in the Excel spreadsheet.

WATER

	Hot drinks	Cold drinks
Tap water (unfiltered)	ENTER: UKN 17-377 water, distilled	
Filtered water - hard water filter		
Filtered water - other		
Bottled water	ENTER: USF A000001 mineral water	

If this section is incomplete, assume tap water only consumed unless otherwise stated in the food diary.

Q. 16 Organic foods

This information only needs to be recorded in the Excel spreadsheet.

REGISTRATION SCREEN:

Max number of days: 7

Max number of mealsper day: 8

Max courses per meal:

blank

of day 1: as per date recorded in day one of the food diary. (The date does not always register on DietPlan, to ensure it does do not press 'entre' key always click continue and check thegrid.)

Date: to show the date of diary input.

Type: select intake diary from drop down screen

Reference values 'none'

Enter mealtimes: 'no'

COMPOSITION SCREEN:

Database selection

Click on 'add item'
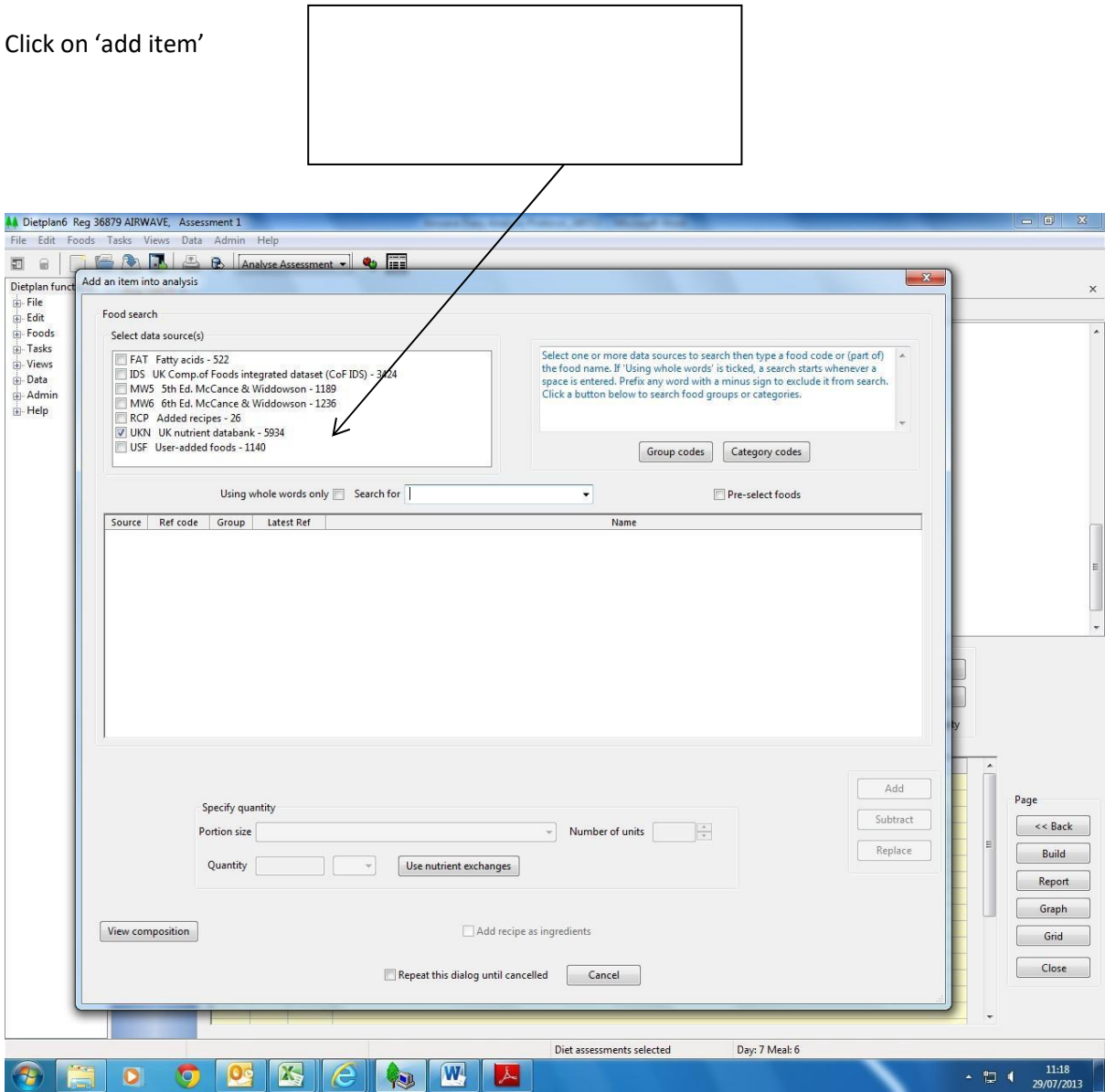
Entering meals
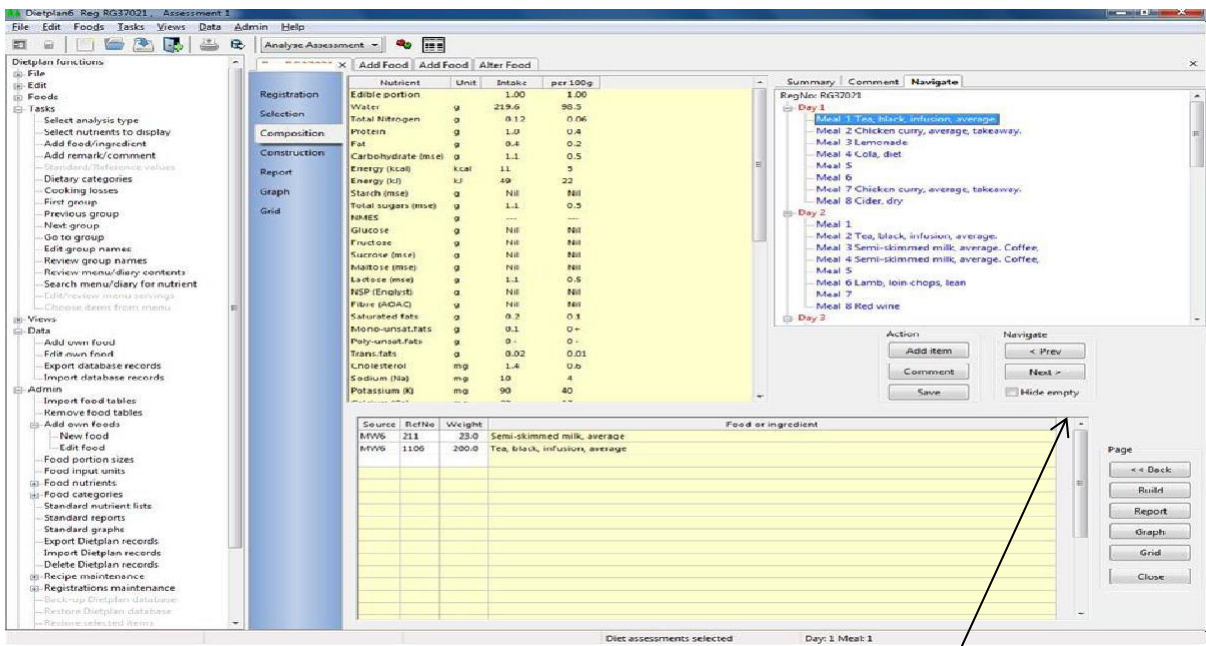
Diet plan	**Food diary section**
Meal 1	before breakfast
Meal 2	breakfast
Meal 3	Mid-morning
Meal 4	lunch
Meal 5	tea
Meal 6	evening meal
Meal 7	later evening
Meal 8	'Anything else'.

Start from day 1 meal 1 and enter the items as written in the diary

Remember to save your work as you go to avoid any data loss.

General rules

- ✓ UKN is the default database. Only use RCP and USF databases if it is a food from the codebook.
- ✓ Never select a code for an item that states' (fats only)' at the end of the description.
- ✓ Items such as drinks and sandwiches should be broken into their constituent parts (see 3.2 Foods and meals not in the database)
- ✓ Items should be coded in the form in which they were eaten e.g., raw tomato / boiled potato where possible unless option not available.

Algorithm for code selection:
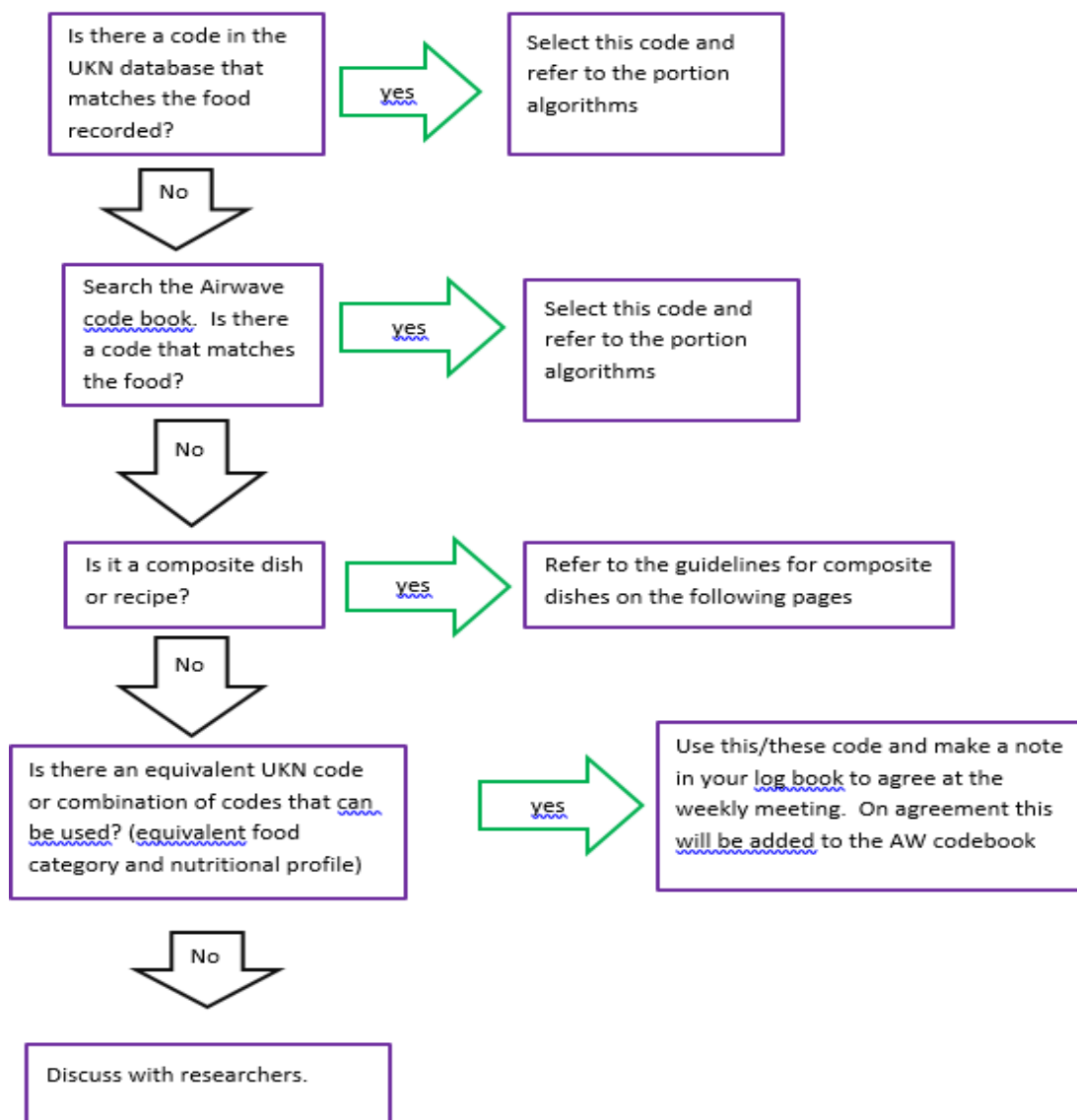
4.1 Composite Dishes:

The following items should be broken into their constituent parts where possible:

- Hot beverages (except those made up with water)
- Sandwiches
- Home cooked meal when full recipe provided
- Homemade burgers

o Example 1:

Instant coffee with semi-skimmed milk and white sugar

Enter as:
UKN 17-159 instant, made up with water
UKN 12-313 Semi-skimmed, pasteurised milk, average
UKN 17-063 sugar, white

Rules for entering composite dishes:

1. Canned ready meals: i.e., spaghetti, soup, beans etc.

Select UKN code, which states 'canned –reheated'.

2. Dish stated as 'homemade 'and where a recipe is provided:

Enter all ingredients as the amount consumed and in their correct state– i.e., cooked / raw directlyinto the assessment (i.e., do not set up a separate recipe code).

3. Dish stated as 'homemade' and complex* recipe provided: i.e., ingredients are not available in their correct state in the database AND the recipe provided is not comparable to those in the UKN database. Check the standard recipes used if listed in McCance (2).

*e.g., recipe with full quantities provided, but difficult to estimate actual proportion

eaten.In this situation, a recipe should be set up using the 'Recipe analysis' option:

The code for the recipe should be the participant code prefixed by AW.

If multiple recipes are required for one participant, then add 'a', 'b', 'c'… etc..., at the end of thecode.

e.g., AW44399a

The recipe name should state the description of the dish and the participant code

e.g., Fruit cake – recipe for AW44399

Please ensure that the correct 'group code' is assigned to the recipe.

Please note these recipes should **not** be included in the Airwave codebook as they are unique to each participant.

4. Dish stated as 'homemade 'and no recipe provided

Select UKN code, which states a 'homemade' version of this dish, if available.

5. Ready/Microwave meal (including ready to eat pizza, pies) with brand name provided:

Check the retailer / manufacturer website and select the closest equivalent code from diet plan that reflects the food eaten and the macronutrient profile.

NB: this may involve selecting two or more codes to combine to provide a similar food/nutrient profile.

See below for how to match foods not on the database.

6. Fast food burgers:

Enter as the complete food (e.g., Big Mac etc.)

If there is not a code in UKN database, please check the excel Airwave codebook. If there is no codein the codebook then a recipe will be required (see recipe set up protocol).

7. Retail sandwiches:

Do not use sandwiches in dietplan, match the sandwich to those online. Sandwiches can be found on Tesco and Waitrose websites. Use Waitrose for M&S and Waitrose sandwiches only (i.e. Premium/luxury type sandwiches) and Tesco's for all other brands if brand not stated use Tesco as default.

Foods and meals not in the database

- Sandwiches
- Weight watchers/ reduced fat, calorie, sugar etc. meals
- Foods from cafés and fast foods e.g., costa, burger king, KFC etc.

How to code

- Find the nutritional information:
    1. Check Airwave codebook for item
    2. Check Portion Information folder: \\\\wmdi-nutritech\Dietary assessment protocol\Filesfor shared access\Portion information\retail & fast-food portion info
    3. Check retailer's website
    4. Search online

- Calorie match (see screen shot below)
    1. Click 'use nutrient exchanges' button
    2. Choose kcal,
    3. Type in the number of calories you want to match in 'exchange value'

4. Click 'view composition'
5. If the protein, carbohydrates, sugars, fat are with 10% this amount can be used

If outside of 10%

- Check what nutrient is outside of the 10% range, e.g., protein is too low
- Add foods using the **ingredients list** (only include foods if they are on the ingredient list)
    1. If more protein is required add more of the protein source
    2. If carbohydrates are required, add more of the carbohydrate source
        - Be careful as some e.g., pasta, bread also contain protein
        - If sugar is needed add sugar.
            - There are different types of sugar. Some products have ingredients, which code as sugar e.g., inverted sugar, white sugar and honey, glucosefructose syrup so only code white sugar. **Be mindful of adding sugar, asit will increase carbohydrates.**

Where possible do not simply increase sugar by coding 'white sugar',try alternative methods e.g., using canned or jar sauces, which by nature are higher in sugar.

- If fat is needed add oil or fat (from the source of fat in the product), check saturated fat.
    - One type of fat may not be suitable, both palm oil and rapeseed oil may be required.
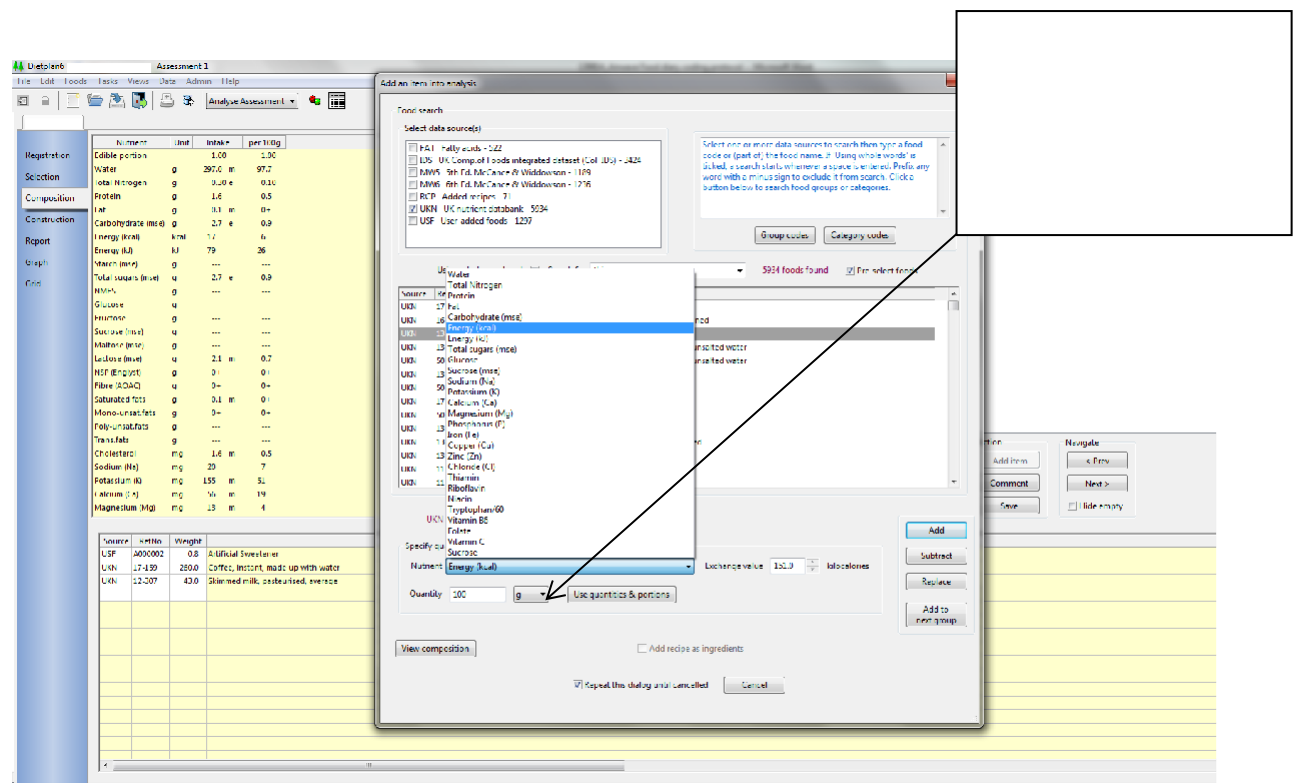
Some foods e.g., Burger King Burger's, pasta salads, Subway, sandwiches must be coded separately

- Code the main ingredients using the ingredient list

1. Calorie match the ingredients using their primary nutrient

    E.g., a ham salad sandwich

    - Calorie match bread to carbohydrates
    - Calorie match ham to protein
    - Add green salad portion as for homemade sandwich
2. Compare fats, carbohydrates, sugar, protein for the meal to nutritional information
3. Adjust weights of ingredients so nutrients are with 10%
4. Some extra ingredients from the ingredients list may need to be to be added e.g., oil or sugar

Tips

- Weights do not always match exactly this does not matter if the nutrients do
- For the first few 'real' diaries have a go and ask for them to be checked
- Sandwiches – use Tesco's for all sandwiches and Waitrose for Waitrose and M&S and premium/ luxury sandwiches
- You may need to use more than one type of the same food e.g., sponge cake and fatless sponge

8.   Homemade sandwiches:

Unless otherwise stated:

Two x medium slices of bread (as per general questions response or default code)

Fat spread (if stated or stated in general questions) – NB quantity for each slice

Filling: unless otherwise stated use 'average' amounts for cheese / meats / fish / egg.

Unless otherwise stated 20g lettuce / 34g tomato / 23g cucumber

'Salad' – default portion 20g of 'green salad' (UKN 15-648) other editions to sandwiches use ~15g.

Mixed Salads

If there is not enough information provided to be able to enter the weight of each vegetable included use 'green salad' UKN 15-648, see codebook for default portion sizes.

Not all the different cooking options for each food type are available in Dietplan, therefore a comparable cooking method may need to be selected if the one recorded in the food diary is not available.

Vegetables

'steamed' or 'microwaved'	- enter as boiled 'unsalted water' if 'steamed' not available
'Stir fried'	- if fried option not available enter as 'raw' (select type of oil as specified in the general questions as the 'average amount', refer to the codebook for the default code)
'Stir fried' in cook in sauce	- enter as boiled 'unsalted water' if 'steamed' not available
'roasted'	- select 'baked' or grilled if available + oil (select type of oil as specified in the general questions as the 'average amount', refer to the codebook for the default code)
'casseroled' or 'stewed'	- select 'boiled'

'boiled' = default cooking method unless vegetables are eaten as part of a salad

Meat / fish

'steamed'	- enter as 'casseroled' or 'stewed' if 'steamed' not available
'fried'	- select 'grilled' + oil if fried option not available (select type of oil as specified in the general questions as the 'average amount', refer to the codebook for the default code)
'Stir fried in cook in sauce'	- enter as 'casseroled' or 'stewed'
'roast'	- enter as 'grilled' if 'roast' option not available
'grilled'	- enter as 'roast' if 'grilled' option not available

Some fish e.g., tuna steak does not have a cooked code so the raw must be

used. Default cooking methods if not specified:

Potato, root vegetables, peas - 'boiled' unsalted water

Meat and fish – grilled

- If the raw weight of a food is given the cooked weight needs to be calculated and entered Dietplan.
- If the weight is written in the 'amount' column <u>we assume this is a cooked weight</u> unless it is part of recipe

<u>Weight Gain</u>

- Foods which gain weight upon cooking (they expand when cooked)
  - E.g., pasta, rice, couscous, lentils

- Find the water gain in McCance and Widdowson's the Composition of Foods
- The number given is the <u>percentage of water gained,</u> this means the amount of water added. Therefore, if it gives +144 water gain the total is x2.44

  - E.g., Dried pasta boiled +123%
    200g dry pasta, water gain 123%
    200 x 2.23

= <u>446g boiled pasta</u>

Or (an alternative method)
200g + 123%

  - E.g., Dried rice boiled +172%
    241g dry rice, water gain 172%
    241 x 2.72

= <u>655.52g boiled rice</u>

Or (if using calculator)
241 + 172%

<u>Water loss</u>

- Foods which lose weight upon cooking
  - E.g., meat, fish
- Find the water loss in McCance and Widdowson's the Composition of Foods
- The number given is the <u>% of water lost</u> during cooking
  - E.g., Raw stewing beef -36%
    450g stewing beef, water loss -36%
    450g x 0.36 = 162g lost

$$= 450\text{g raw stewing beef - 162g loss}$$
$$= \underline{288\text{g eaten}}$$

Or if using a calculator 450 – 36% = 288g

- E.g., Raw chicken casseroled

  175g stewing beef, water loss -25%

  175g x 0.25 = 43.75g lost

  $= 175\text{g raw chicken} - 43.75\text{g loss}$

  $= \underline{131.25\text{g eaten}}$

  <u>or if using a calculator 175g – 25% = 131.25g</u>

<u>Tips</u>

- Code foods in the form they are eaten e.g., we eat chicken cooked so it must be coded cooked
- Some foods e.g., tuna steak only have raw code in Dietplan, so the raw code must be used
- Water loss does not have to be calculated for vegetables in a recipe

All sausages to be entered as cooked weights. Unless specified otherwise e.g., brand and weight asthe following weights and NOT those stated in the UKN dietplan6 dataset.

Default sausage weights (each):

	raw	cooked
Thick	47g	35g
Cocktail	12g	9g
Thin	25g	19g
Premium (e.g., 'best' / 'finest' / taste the difference'	65g	49g

(Based on average supermarket weight per sausage recorded in Food base data)

Default cooked weight is not stated: 34g (average thick, thin, and premium)

Conversion of liquids to grams:

- Liquids have a specific gravity so 100ml is not always 100g
- Conversion factors must be used as weight must be coded
- Used for milk, cream, ice cream, egg, oils, fizzy drinks, 100% fruit juices, alcoholic drinks
- Do not use for water, squash, tea, coffee

<u>How to calculate the conversion factor</u>

- All conversion factors are after the contents page in the Food Portion Sizes book (orange book)
- Multiple value in 'specific gravity' column by the ml given

E.g., 200ml of whole milk

       Conversion factor 1.031

              200ml x 1.031

                    = <u>206.2g milk</u>

E.g., 330ml can cola

       Conversion factor 1.04

              330ml x 1.04

                    = <u>343.2g cola</u>

<u>Tips</u>

- If the respondent has used a small amount e.g., 3tbs of milk the conversion factor does not need to be used
- The weights of milk for tea and coffee in section 1.2 **do not** need a conversion factor
- If the amount has been given in ounces, litres or pints convert to ml first then use conversion factor (values are at the top of the same page as the conversion factors)
- Weights of glasses and cups are given in ml in this document
- Some alcoholic drinks have pints and half pints in the drop down, these already have the conversion factor, so it does not need to be calculated again
- Be careful of yogurt as the respondent sometimes puts 125ml or 500ml, they probably mean 1 pot which is 125g or 500g, so the conversion factor does not need to be used
- If a volume of food is given check the food density pdf in \\WMDI-NUTRITECH\Dietary Analysis\Airwave\Files for shared access\Portion information

Spoon volumes not listed in the FSA book:

       Serving spoon = 40ml. MAFF Food Atlas (5)

       Ladle = 120ml (mean volume of the two serving spoons featured in MAFF Food Atlas (5))

If a participant enters 'spoon' but does not specify what size, then apply appropriate default sizes:

Meat in sauce / vegetables – tablespoons

Vinegar / herbs / spices / sugar - teaspoons

Cup: For tea / coffee and other hot drinks, refer to portion algorithm.

If a '<u>cup</u>' is used to <u>measure liquids other than hot</u> **drinks take the default volume to be 250ml** (UK cooks measure) and apply specific gravities as appropriate. See food density pdf [\\wmdi-nutritech\Dietary assessment protocol files for shared access \Portion information\food density

Other arbitrary measures:

'a handful' of Fruit (not berries) and vegetables code 80g (reference carbs & cals is unsure)

'a handful' of raspberries, blueberries, and bilberries code

40g'a handful' of nuts and dried fruits code 30g

'a splash of oil' code 5g

'a drizzle of salad dressing' = 10g (25th percentile for salad dressing see reference Food base)

Imperial measures: Conversion of imperial measures to grams are in the FSA Food Portion Sizes book (3) (page viii).

Note that 1cl = 10ml, so they might say 75cl of wine which is 750ml which is a standard bottle.

5.0 Portion size algorithms

Algorithm for portion size estimation – hot drinks
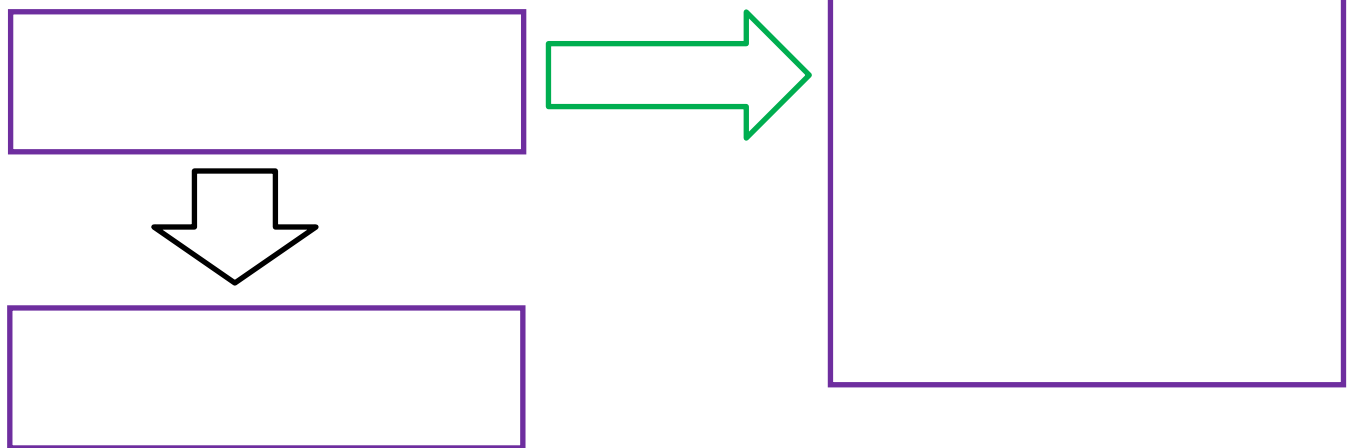
NB:

Adding milk to hot drinks

Tea / coffee entered as the cup / mug volume (i.e., 190 / 260ml) then add the milk.

e.g., mug of tea with average milk

Tea infusion average 260g + semi skimmed milk pasteurised average 30g

Sugar in drinks

If a participant records '1 sugar' – enter 1 level teaspoon (=4g sugar).

Algorithm for portion size estimation – cold / ambient / alcoholic drinks described by a glass.

Algorithm for portion size estimation – cold / ambient / alcoholic drinks described by a bottle orcan.

```
┌─────────────────────┐        ┌─────────────────────┐
│                     │  ═══>  │                     │
│                     │        │                     │
└─────────────────────┘        └─────────────────────┘
          │                              ▲
          ▼                              │
┌─────────────────────┐        ┌─────────────────────┐
│                     │  ═══>  │                     │
│                     │        │                     │
└─────────────────────┘        └─────────────────────┘
          │                              │ No
          ▼                              ▼
```

Use default volume of average and apply specific gravities as required.

330ml can (non-alcoholic)

390ml can (lager, cider, bitter) – mean average of small and large can.

330ml bottle (beer / cider / lager)

Non-alcoholic (based on FSA portion sizes):Can = 330ml

Small carton = 200ml

Large bottle = 1ltr

Medium bottle = 500ml

Small bottle = 250ml

Alcoholic:

Wine – small bottle = 375ml (FSA ½ bottle). Large bottle = 750ml

Beer / lager / cider: (based on common sizes listed at Sainsbury's / Tesco 02/08/13):

Small bottle = 275ml

Medium / regular bottle = 330ml

Large bottle = 1lt

Small can = 330ml

Medium can = 390ml

Large can = 450ml

Algorithm for portion size estimation – food: canned and tinned, when recorded as a proportion ofa can /tin.

Has respondent referred a specific brand / tin size? Eg. Half a Heinz 400g tin of beans?

yes →

Refer to the manufacturer or retailer website (e.g., Sainsbury's, Tesco) to find the appropriate tin weight.

No ↓

Select from default tin size*: non-drained weights.

Fish:

Tuna - 160g

Salmon - 105g

Sardine –

120g

Vegetables / pulses:

Tomatoes – 400g

Sweet corn kernels –

165gPeas (not mushy) –

300g Mushy peas – 300g

Beans (not baked) –

400gBaked beans –

415g Other:

Soup – 400g

Spaghetti in sauce –

400gFruit – 415g

*Based on most common tin size featured on

Sainsbury's & Tesco website 02/08/13

→

Enter the 'drained weight' /'edible portion' of the portion of the can eaten.

If you would normally consume the medium in which the food is canned the drained weight would = 100%.

e.g., baked beans, tinned tomatoes, soup, mushy peas, items tinned in tomato sauce and tinned fruit would = 100%.

If you would not normally eat the medium in which the food is canned (e.g., oil and brine) you need to calculate the drained weight:

Tuna / sardines / salmon canned in oil or brine = 82%

Sweet corn canned in water / salted water = 82%

Chickpeas / tinned beans canned in water / salt water = 60%

Example calculation:

Half a 400g can of chickpeas

= 400g/2 = 200g

= 200g x 0.60 = 120g (weight to enter)

Algorithm for portion size estimation FOOD (NOT canned / tinned):

Has respondent referred to images page 9-15? → **yes** → Refer to 'portion weights sheet' * (see notes below)

↓ **No**

Has respondent referred a packet or size of a branded product? i.e., a magnum ice cream or tin of soup? → **Yes** → Refer to the manufacturer or retail website to estimate portion size

↓ **No**

Is it an individual food item? i.e., slice of bread? → **Yes** → Is it in the UKN? database? → **Yes** → Is the portion size indicated by the participant? i.e medium?
- → **Yes** → Enter this weight
- → **No** → Estimate the portion size using the portion sizes recorded on other days - i.e., what portion size would be consistent with this participants intake. Enter 'medium' or 'average' as default.

Is it an individual food item? ↓ **No**

Is it listed in the foodbase portion guide? → **No** → Is it listed in the Carbs and Cals book? → **Yes** → Enter this weight

Is it in the UKN? database? ↓ **No** → Is it listed in the Carbs and Cals book?

Is it listed in the Carbs and Cals book? ↓ **No**

Is it listed in the foodbase portion guide? ↓ **Yes**

Is the portion size indicated by the participant? i.e medium?
- ↓ **Yes** → Enter this weight
- ↓ **No** → Estimate the portion size using the portion sizes recorded on other days - i.e., what portion size would be consistent with this participants intake. Enter 'medium' or 'average' as default.

Is there a default weight stated in the Airwave code book?
- → **Yes** → Enter this weight
- → **No** → Is it in the FSA food portion sizes book?
  - ↓ **Yes** → Enter this weight
  - ↓ **No** → Seek advice from the supervisor

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*Notes to the Airwave food portions

Check that you select the portion size relative to the food type. For example, picture set 14 related to salad and boiled leaf vegetables,

e.g., photo 14a = 51g for boiled spinach

= 15g for lettuce

- If a participant has only referred to one portion size against 2 foods that are from different food groups:

Eg.   Chicken in curry sauce & boiled rice   8b

Select portion 8b for the rice (131g) and select the 'b' size portion for the chicken curry, in this example it would be 19b (115g).

- If a participant has only referred to one portion size against 2 foods that are from the same food group:

EG.   Carrots, broccoli, green beans   13c

Select 13c = 107g divide by 3 = 36g per type of vegetable

6.0 Error checking

- Save the assessment
- Check the following against the diary you have inputted:
  - ✓ Registration code is the same as the code on the front of the diary you have inputted
  - ✓ Meal occasions have been entered in the correct meal number (1-8)
  - ✓ Codes represent the foods in the diary
  - ✓ Portion sizes are entered correctly
  - ✓ Any changes are saved
- Select 'grid'

Click 'grid'
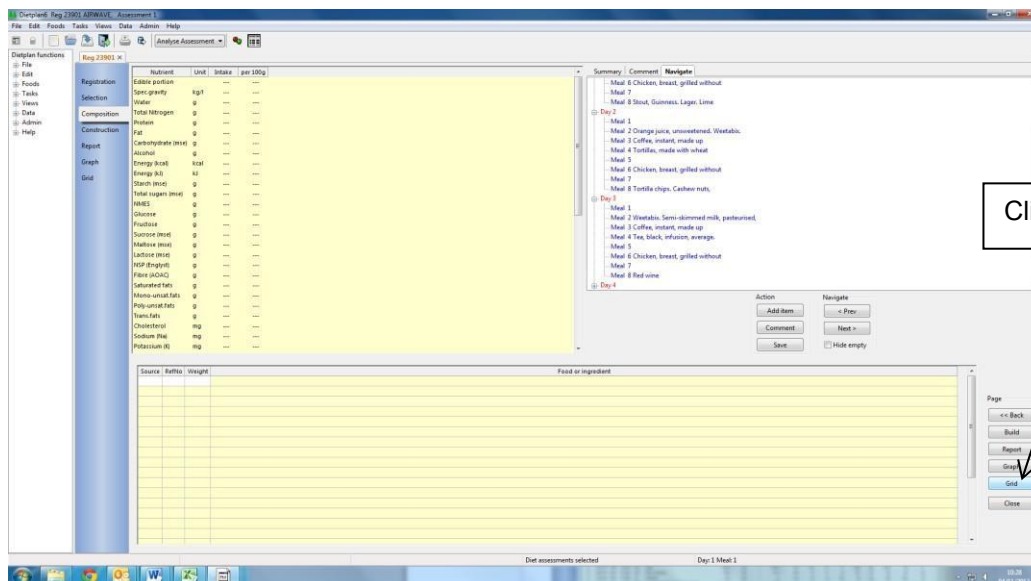
When grid view opens you can double check foods and quantities:

Click 'quantity' – this will arrange all items by quantity. Check down the rows to make sure all quantities are appropriate to the foods selected. NB. Changes cannot be made in this view.

Check the date has been registered by Dietplan and is correct

Note the total at the bottom of the 'Energy kcal' column – this can be used to double check the mean kcal intake per day. Range should be approx. 1500 – 3000kcal

'back' takes to the composition screen to allow any changes to be made.

7.0 Log the diary as complete

o   Open the file via shared drive: [\\wmdi-nutritech\Dietary assessment protocol files for shared access / logging of food diaries in-out/020414_MASTER_FD_LOG].

o   Search for the registration code and input the participant date of birth, gender, and the date the diary was entered into Dietplan and your initials in the designated columns (highlighted in orange).

References:

1. Food Standards Agency. Foodbase 2005 [30.08.13]. Available from:http://www.foodbase.org.uk/results.php?f_report_id=82.
2. Food Standards Agency. McCance and Widdowson's: The composition of foods. 6thSummary ed. Cambridge: Royal Society of Chemistry; 2002
3. Food Standards Agency. Food Portion Sizes. 3rd ed. London: TSO; 2010.
4. Charrondiere R, Haytowitz D, Stadlmayr B. FAO/ FOODS Density Database Version 2.0. FAO;Rome, Italy, 2012
5. Nelson M, Atkinson M, Meyer J: *A Photographic Atlas of Food Portion Sizes*. London: MAFFPublications; 1997
6. Cheyette C, Balolia Y. Carbs and cals and protein and fats 1st ed. United Kingdom: ChelloPublishing; 2010.

Practice some matching, weight changes on cooking and conversion factors

Try coding these foods (create new analyses using registration your initials foods e.g., KLfoods)
- Sainsbury's chicken and sweetcorn sandwich
- Weight watcher's lasagne
- Costa lemon muffin
- Supermarket bought chicken pasta salad
- Burger King Double Whopper
- Dolmio Light sauce

Try calculating the weight change of these foods

- 500g raw mince beef
- 100g raw back bacon
- 88g raw pasta
- Risotto recipe had third 224g rice, 550ml stock, 84g onions, 150g mushrooms
- Lasagne had a quarter 130g vegetables, 300g raw minced beef, 200g tomatoes, 450g water, garlic clove, herbs, 200g raw lasagne, 400g cheese sauce

Try calculating the weight in grams of these foods

- 200ml of semi-skimmed milk
- 3 pints of lager
- 250ml ice cream
- 1 glass red wine
- 250ml Tesco's chocolate milk shake

Figure 3.1 Snapshot of Airwave Health Monitoring Study Codebook

Figure 3.2 Snapshot of Airwave Health Monitoring Study Food Base Portions Guide

The alcohol by volume % (ABV) of an alcoholic beverage can differ across different brands and beverage type. From example the ABV % in wine can vary from 9 – 14 % depending on the brand and fermentation techniques. A standard ABV was designated for each alcoholic beverage surveyed within the AHMS and UK Biobank touchscreen questionnaire. This standard was derived from several sources including consumer surveys detailing the ABVs of commonly consumed alcoholic beverages [1:4]. The standardmeasures for each alcoholic beverage are as specified in the AHMS and UK Biobank touchscreen surveys.

Key Formulas

1 unit of alcohol = 10ml or 8g of Pure Alcohol; Standard Measure (ml) x ABV (%) = Alcohol (ml); Alcohol (ml) / 10 = Alcohol (units); Alcohol (units) * 8 = Alcohol (g)

Reference Table of Alcohol Content in Standard Measures of Several Alcoholic Beverages

Beverage	Standard Measure (ml)	ABV (%)	Alcohol (ml)	Alcohol (units)	Alcohol (g)
Red Wine	125	13.0	16.2	1.6	12.8
White/Sparkling Wine	125	12.0	15.0	1.5	12.0
Fortified Wine	50	20.0	10.0	1.0	8.0
Beer/Stout/Cider	568	5.0	29.3	2.9	23.4
Spirits	25	40.0	10.0	1.0	8.0

References

1. Cook, M., Parker, E. & Griffiths, C. (2020) Review of typical ABV levels in beer, cider and wine purchased for the 'in home' market. [Online] 1–17. Available from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/893741/Review_of_typical_ABV_levels_in_beer_cider_and_wine_purchased_for_the_in_home_market.pdf?fbclid=IwAR0j6wvY0NQ85b7BFUk2xe3Js7h-WnafzsLe7voAEpLn-UNgH5hg18.
2. https://www.drinkaware.co.uk/tools/unit-and-calorie-calculator
3. https://www.nhs.uk/live-well/alcohol-support/calculating-alcohol-units/

A5.1 Figure 5.1 Sample Procedure Airwave Health Monitoring Study
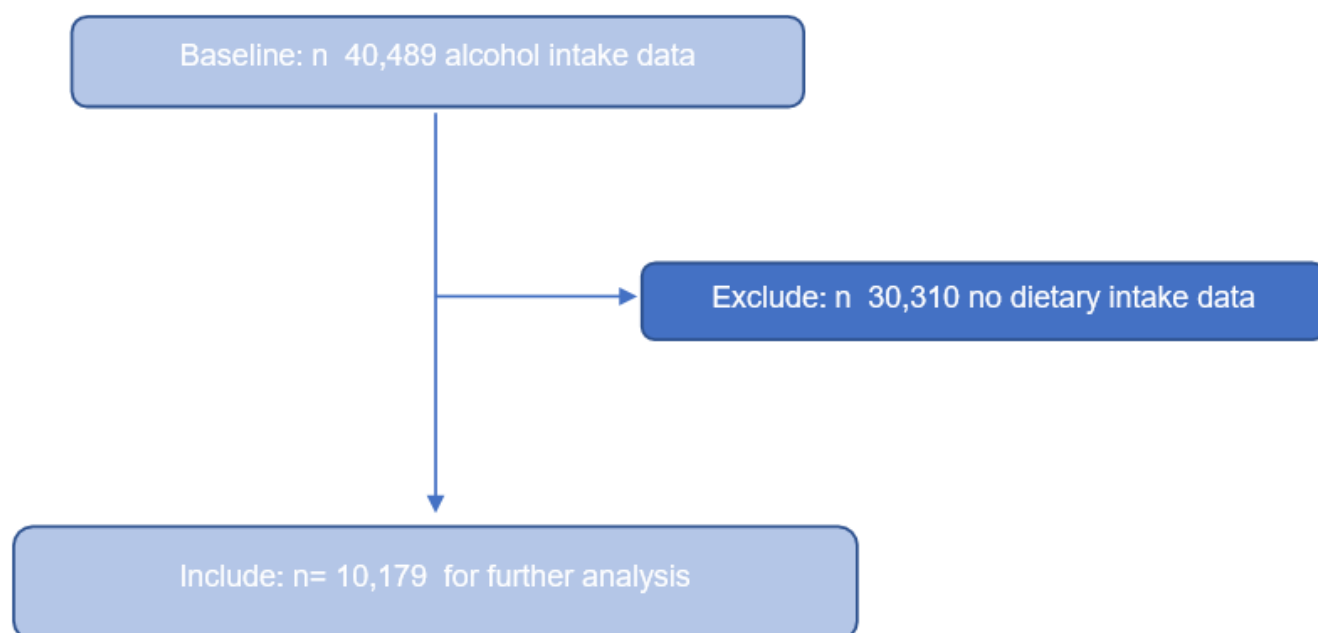
Figure 5.1: Sampling procedure for Airwave Health Monitoring Study cohort studied in Chapter 5

A5.2 Figure 5.2 Sample Procedure UK Biobank Cohort
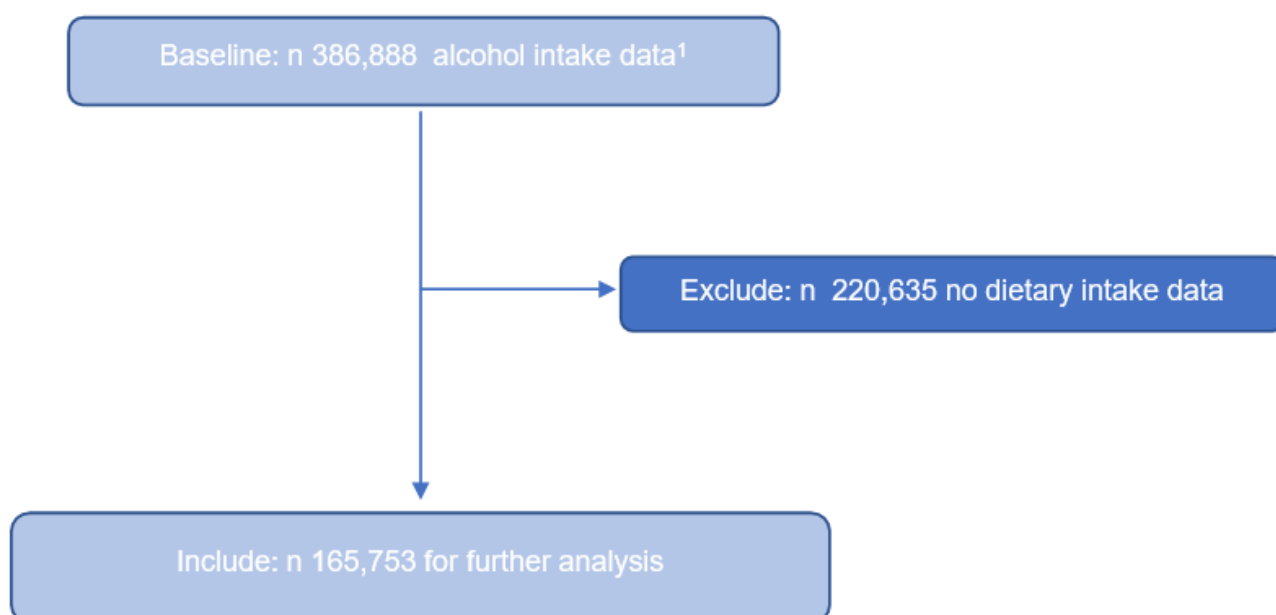
Figure 5.2: Sampling procedure for UK Biobank cohort studied in Chapter 5. Keys 1 – includes non-drinkers and currentdrinkers with quantitative alcohol intake data.

Table 5.1 Dietary Profile According to Drinking Pattern				
		Binge	**Non-Binge**	**p**
Total = 9389	**n (%)**	3262 (34.7)	6127 (65.3)	<0.001
Drinker				
Moderate 1	**n (%)**	17 (0.5)	3086 (50.4)	<0.001
Moderate 2		514 (15.7)	1847 (30.1)	<0.001
Moderate 3		734 (22.5)	746 (12.2)	0.01
Heavy		1997 (61.3)	448 (7.3)	<0.001
Energy Intake				
TEI (kcal)	**Mean (SD)**	2081 (496)	1180 (479)	<0.001
Energy Density (g/kcal)		0.67 (0.17)	0.71 (0.20)	<0.001
Nutrient Intake				
%TEI Carbohydrate	**Mean (SD)**	40.6 (6.1)	45.6 (6.0)	<0.001
% TEI Total Fat		31.8 (5.3)	34.1 (5.4)	<0.001
% TEI Saturated Fat		11.4 (2.7)	12.5 (2.9)	<0.001
% TEI Protein		16.7 (3.0)	17.4 (3.5)	<0.001
Fibre (g/1000kcal) [†]		6.4 (1.9)	7.6 (2.1)	<0.001
% TEI Alcohol[¥]	**Median (IQR)**	10.0 (6.9)	3.1 (3.9)	<0.001
DASH Score	**Mean (SD)**	2.4 (1.3)	2.5 (1.3)	<0.001
Abbreviations: TEI – Total Energy Intake; DASH Dietary Approaches to Stop Hypertension; SD – Standard Deviation, IQR – Interquartile Range Keys: 1 - Non-Starch Polysaccharide Fibre; 2 – TEI from alcoholic beverages: * p < 0.05 – significant. Statistical Test: ANOVA adjusted for age and sex – normally distributed variables, Kruskal-Wallis Test for non-parametric variables.				

Table 5.2 Distribution of Drinker Types Across Alcoholic Beverage Preference Groups						
AHMS Total = 9389	Moderate 1	Moderate 2	Moderate 3	Heavy	All= 9389	*p*
Wine n (%)	1560 (32.9)	1271 (26.8)	770 (16.2)	1146 (24.1)	4747 (50.5)	*ns*
Beer	1067 (30.1)	820 (23.2)	538 (15.2)	1113 (31.4)	3538 (37.7)	*ns*
Spirits	476 (43.1)	270 (24.4)	172 (15.6)	186 (16.8)	1104 (11.8)	<0.001
UK Biobank = 146,713	Moderate 1	Moderate 2	Moderate 3	Heavy	All= 152,595	*p*
Wine n (%)	23,702 (21.5)	35,974 (32.6)	21,255 (19.2)	29,467 (26.8)	110,398 (72.3)	*ns*
Beer	5668 (16.3)	8742 (25.1)	6081 (17.5)	14,274 (41.1)	34,765 (24.7)	0.001
Spirits	2506 (33.7)	1860 (25.0)	1116 (15.0)	1950 (26.3)	7432 (3.0)	*ns*

Table adapted from Klarin et al. Supplementary Table 5 [362]

rsid	Gene* (If Applicable)	EA	NEA	EAF	GLGC HDL-C Beta	GLGC HDL-C SE	GLGC HDL-C P
					SNP Info for Polygenic Risk Score		
rs629301	CELSR2	T	G	0.7742	-0.0418141	0.003055	1.24E-42
rs267733	ANXA9	G	A	0.1366	0.021253	0.003721	1.12E-08
rs4745	EFNA1	T	A	0.4876	0.0032689	0.002627	0.213339
rs12145743	RRNAD1	G	T	0.3121	0.0172277	0.003003	9.67E-09
rs1801274	FCGR2A	G	A	0.4842	-0.008375	0.003521	0.01739
rs1011731	DNM3	A	G	0.5598	0.01474	0.002632	2.17E-08
rs4650994	C1orf220	A	G	0.4916	-0.0191952	0.002588	1.21E-13
rs1689800	NA	G	A	0.3391	-0.0246067	0.00269	5.90E-20
rs340874	NA	C	T	0.5061	-0.0035915	0.002579	0.163757
rs2785990	NA	T	C	0.6852	-0.014979	0.002757	5.55E-08
rs2642438	MOSC1	G	A	0.7619	0.0268468	0.007873	0.0006493
rs4846914	GALNT2	A	G	0.5506	0.04942	0.002735	5.69E-73
rs1077514	ASAP3	T	C	0.8219	0.009854	0.003426	0.004029
rs12027135	TMEM57	T	A	0.5089	0.004503	0.002572	0.080033
rs12748152	NA	T	C	0.07209	-0.0434434	0.004945	1.56E-18
rs4660293	PABPC4	G	A	0.208	-0.0398414	0.003183	6.07E-36
rs2479409	NA	A	G	0.6582	0.009488	0.002691	0.0004227
rs2131925	DOCK7	T	G	0.6477	0.0104456	0.002711	0.0001166
rs7515577	EVI5	A	C	0.8166	0.0041697	0.003333	0.210993
rs2862954	ERLIN1	C	T	0.405	0.01617	0.002691	1.88E-09
rs2255141	GPAM	G	A	0.7281	-0.0267435	0.00288	1.60E-20
rs7076938	NA	T	C	0.7253	0.0187491	0.002851	4.84E-11
rs10885997	PNLIPRP2	G	A	0.4093	-0.008117	0.002801	0.003763
rs1891110	FAM24B	A	G	0.5487	0.004137	0.002556	0.105611
rs10904908	NA	G	A	0.4456	0.0117	0.002568	5.20E-06
rs970548	MARCH8	C	A	0.2421	0.0259897	0.002982	2.86E-18
rs1832007	AKR1C4	G	A	0.1381	-0.0088966	0.003745	0.017517
rs41274050	A1CF	T	C	0.007148	-0.037601	0.015145	0.01304
rs10761731	JMJD1C	T	A	0.4199	0.0129375	0.002597	6.33E-07
rs7901016	CCDC109A	C	T	0.06978	-0.0219525	0.005542	7.45E-05
rs2068888	NA	A	G	0.4701	0.0227842	0.002581	1.05E-18
rs2923084	NA	G	A	0.2006	-0.011837	0.003249	0.0002697
rs746463	ZC3H12C	T	C	0.6892	-0.01657	0.002847	5.87E-09
rs964184	NA	C	G	0.8478	0.111711	0.00355	2.60E-217
rs11603023	PHLDB1	C	T	0.5788	-0.008335	0.002583	0.001254
rs7941030	NA	C	T	0.38	0.02413	0.002612	2.52E-20
rs11220462	ST3GAL4	A	G	0.1453	-0.02103	0.004439	2.18E-06
rs1037378	PDE3B	A	G	0.5357	-0.0150186	0.00255	3.89E-09
rs10128711	SPTY2D1	C	T	0.6911	0.003188	0.00314	0.3098996
rs16928809	SLC22A18	A	G	0.08745	-0.02877	0.004529	2.12E-10
rs3136441	F2	C	T	0.1514	0.03992	0.003853	3.74E-25
rs174546	FADS1	T	C	0.3121	-0.041822	0.002804	2.68E-50
rs35169799	PLCB3	T	C	0.05893	-0.03914	0.005394	3.98E-13
rs12801636	PCNXL3	A	G	0.2339	0.0118095	0.003019	9.17E-05
rs622082	IGHMBP2	G	A	0.3102	-0.0171778	0.002773	5.86E-10
rs499974	NA	A	C	0.184	-0.02622	0.003336	3.85E-15
rs10861661	RIC8B	C	A	0.2332	-0.01689	0.003127	6.65E-08
rs7134594	MMAB	T	C	0.5261	0.0300993	0.002587	2.74E-31
rs11065987	NA	G	A	0.3804	-0.023166	0.002825	2.42E-16
rs1169288	HNF1A	C	A	0.3325	0.014331	0.002836	4.33E-07
rs4759375	SBNO1	T	C	0.1087	0.0505695	0.005331	2.42E-21
rs4765127	FAM101A	T	G	0.3294	0.032852	0.003909	4.32E-17
rs838880	NA	T	C	0.6334	-0.028954	0.002667	1.89E-27

rs7134375	NA	A	C	0.4116	0.02065	0.002581	1.26E-15
rs1106766	NA	T	C	0.2121	0.03155	0.003136	8.27E-24
rs61754230	RAB21	T	C	0.01507	-0.0104	0.010402	0.317351
rs7136716	NA	G	A	0.1502	0.0207533	0.003647	1.27E-08
rs4883201	PHC1	G	A	0.115	-0.03036	0.004016	4.06E-14
rs7400722	GAS6	A	G	0.4203	0.0005495	0.003018	0.855534
rs4942486	BRCA2	C	T	0.5158	0.009385	0.002562	0.00025
rs138358301	SLC25A30	G	A	0.003473	-0.01942	0.021211	0.359819
rs797486	NA	A	C	0.8709	-0.0174945	0.00378	3.68E-06
rs4983559	NA	A	G	0.5689	-0.0266641	0.0026	1.11E-24
rs8017377	NYNRIN	A	G	0.4228	0.002696	0.002608	0.3011877
rs7157785	NA	T	G	0.1773	-0.013265	0.003633	0.0002613
rs10483776	FUT8	G	A	0.1638	-0.0199895	0.003454	7.13E-09
rs9646133	NA	T	G	0.3263	0.0088582	0.002736	0.001204
rs13379043	C14orf43	C	T	0.3053	0.017107	0.002858	2.14E-09
rs8014204	PROX2	A	G	0.5702	0.0081899	0.002715	0.002558
rs28929474	SERPINA1	T	C	0.01536	-0.01708	0.010353	0.09892
rs3803357	BAHD1	A	C	0.5429	0.0099063	0.002593	0.0001331
rs2412710	CAPN3	A	G	0.0214	-0.04835	0.008873	5.06E-08
rs2929282	FRMD5	T	A	0.06708	-0.0313856	0.005391	5.83E-09
rs1532085	NA	G	A	0.5907	-0.095557	0.0026	1.17E-295
rs3198697	PDXDC1	T	C	0.3988	-0.0010988	0.034098	0.9743
rs10871454	STX4	T	C	0.369	0.0078753	0.00282	0.005234
rs78074706	ANKS3	A	G	0.02152	-0.0530981	0.008692	1.00E-09
rs1121980	FTO	A	G	0.4278	-0.02014	0.002596	8.57E-15
rs3764261	NA	A	C	0.3127	0.238777	0.002775	0
rs16942887	PSKH1	A	G	0.1336	0.0800568	0.003919	9.85E-93
rs76116020	TMED6	G	A	0.03279	-0.0412576	0.00713	7.19E-09
rs2000999	HPR	A	G	0.2003	-0.007048	0.003415	0.039
rs2925979	CMIP	C	T	0.698	0.04125	0.002759	1.52E-50
rs147032017	ZFPM1	T	C	0.006487	-0.0404114	0.016517	0.014417
rs2070863	SERPINF2	T	C	0.2128	0.005799	0.003236	0.073153
rs7946	PEMT	T	C	0.6667	0.004621	0.002818	0.101
rs704	VTN	A	G	0.4864	-0.0100425	0.002556	8.51E-05
rs11080150	NF1	G	A	0.3257	-0.0023235	0.002727	0.3942275
rs11869286	STARD3	C	G	0.6304	0.0303	0.002819	5.86E-27
rs2074158	DHX58	C	T	0.1867	-0.0201864	0.003784	9.55E-08
rs8077889	MPP3	C	A	0.2017	-0.0061447	0.003176	0.05301
rs72836561	CD300LG	T	C	0.02753	-0.1726104	0.007717	8.12E-111
rs11871606	KPNB1	A	C	0.5019	-0.0134882	0.00256	1.37E-07
rs1801689	APOH	C	A	0.02673	-0.01933	0.007901	0.0144443
rs314253	NA	C	T	0.3507	-8.71E-05	0.002659	0.97388
rs2125345	UNK	C	T	0.3126	0.0075	0.002878	0.009171
rs4129767	PGS1	A	G	0.4879	0.0263751	0.00255	4.58E-25
rs871841	ARHGEF15	C	T	0.5191	0.0029362	0.002656	0.26903
rs7241918	NA	T	G	0.8481	0.0774087	0.003563	1.16E-104
rs8099014	NA	A	C	0.7115	0.0148	0.002835	1.78E-07
rs17782313	NA	C	T	0.2441	-0.0187114	0.002984	3.62E-10
rs6511720	LDLR	T	G	0.1075	0.0241673	0.004115	4.27E-09
rs737337	DOCK6	C	T	0.1197	-0.0583385	0.004215	1.42E-43
rs874628	MPV17L2	G	A	0.2609	0.0005293	0.002914	0.8559
rs10401969	SUGP1	C	T	0.08456	0.011835	0.004627	0.010541
rs731839	PEPD	A	G	0.6336	0.016818	0.002663	2.70E-10
rs201596848	ZNF574	T	C	0.001363	0.0902935	0.034589	0.009041
rs4420638	NA	G	A	0.1797	-0.0802618	0.004055	3.49E-87
rs2303108	ZC3H4	C	T	0.6653	-0.0149234	0.002752	5.86E-08
rs4492602	FUT2	G	A	0.4502	-0.007407	0.002735	0.00677
rs17695224	FPR3	A	G	0.2508	-0.0278325	0.002939	2.81E-21
rs386000	NA	C	G	0.2189	0.05397	0.003991	1.15E-41
rs7248104	INSR	A	G	0.403	0.01217	0.002589	2.59E-06

rs7255436	ANGPTL4	A	C	0.5207	0.0290316	0.002566	1.14E-29
rs1062062	TBC1D8	T	C	0.1234	0.002406	0.004069	0.5542753
rs6734238	NA	G	A	0.3909	-0.0004142	0.002644	0.875502
rs10490626	NA	A	G	0.06783	0.0035321	0.005241	0.5003
rs2030746	NA	T	C	0.4127	-0.001354	0.002575	0.599073
rs12328675	NA	C	T	0.1197	0.050015	0.003922	3.07E-37
rs2287623	ABCB11	A	G	0.5921	-0.00597	0.002606	0.021957
rs3769823	CASP8	G	A	0.6897	-0.0027072	0.002782	0.33057
rs11694172	FAM117B	G	A	0.1548	-0.0040928	0.045714	0.9287
rs1367117	APOB	A	G	0.2844	-0.01966	0.00285	5.23E-12
rs2972146	NA	T	G	0.67	-0.0359841	0.0028	8.20E-38
rs11553746	ACP1	T	C	0.3288	0.0149362	0.002735	4.71E-08
rs1260326	GCKR	C	T	0.6287	0.0057906	0.002682	0.03081
rs4299376	ABCG8	T	G	0.7127	0.0041769	0.003084	0.17562
rs17189743	TSPYL6	A	G	0.02832	0.0396507	0.007634	2.06E-07
rs364585	NA	G	A	0.6361	0.0072151	0.002743	0.008541
rs2328223	NA	C	A	0.2244	-0.04991	0.039171	0.2026
rs7261862	C20orf173	C	T	0.1768	-0.003868	0.003382	0.2528051
rs6029526	TOP1	A	T	0.5095	0.0037952	0.002605	0.1452033
rs1800961	HNF4A	T	C	0.03085	-0.1396719	0.007304	1.64E-81
rs7679	PCIF1	C	T	0.1685	-0.0561773	0.003411	6.06E-61
rs41302559	PCK1	A	G	0.002059	0.0582471	0.028098	0.03818
rs4809330	ZGPAT	G	A	0.7005	-0.0089263	0.002817	0.0015331
rs6062343	TCEA2	A	G	0.4322	0.0131208	0.002648	7.25E-07
rs35665085	CECR5	A	G	0.04979	0.003913	0.005826	0.501837
rs181362	UBE2L3	T	C	0.254	-0.0281524	0.002979	3.37E-21
rs5763662	MTMR3	T	C	0.03132	0.018	0.00789	0.0225708
rs138777	TOM1	G	A	0.6172	-0.0025528	0.002782	0.358784
rs5756931	PLA2G6	C	T	0.3691	0.01705	0.002814	1.39E-09
rs2076674	SLC25A17	C	T	0.3538	0.0018701	0.002738	0.494551
rs738409	PNPLA3	G	C	0.2313	-0.01208	0.003037	6.99E-05
rs4253772	PPARA	T	C	0.09758	0.00477	0.004516	0.29079
rs2606736	ATG7	T	C	0.599	-0.0009657	0.002602	0.7104984
rs11708067	ADCY5	G	A	0.2068	-0.0153031	0.00321	1.87E-06
rs2290159	RAF1	C	G	0.204	-0.009257	0.003744	0.01342
rs17404153	DNAJC13	T	G	0.1261	0.0030597	0.003937	0.4371
rs645040	NA	T	G	0.7818	-0.0207	0.003094	2.21E-11
rs900399	NA	G	A	0.3824	0.01871	0.002628	1.08E-12
rs9816226	NA	T	A	0.8257	0.0275756	0.00338	3.42E-16
rs7640978	CMTM6	T	C	0.09258	-0.00388	0.004456	0.383911
rs2305637	NBEAL2	T	C	0.1581	-0.0323517	0.004252	2.77E-14
rs146179438	CDC25A	A	C	0.01984	-0.0633901	0.009526	2.85E-11
rs7613875	NA	A	C	0.4941	-0.0215262	0.002632	2.86E-16
rs13326165	STAB1	G	A	0.8052	-0.0246185	0.00324	2.97E-14
rs13315871	PXK	A	G	0.08472	-0.0039354	0.004727	0.40507
rs2602836	LOC100507053	G	A	0.5796	-0.01377	0.002693	3.18E-07
rs13107325	SLC39A8	T	C	0.05057	-0.0737205	0.005813	7.38E-37
rs6054	FGB	T	C	0.003804	-0.0268535	0.020872	0.19824
rs13146272	CYP4V2	A	C	0.6231	0.003435	0.002632	0.191928
rs6831256	DOK7	G	A	0.4412	-0.007848	0.002587	0.002421
rs976002	TMPRSS11E	G	A	0.2259	0.0085285	0.003156	0.006883
rs442177	AFF1	T	G	0.5731	-0.018336	0.002586	1.33E-12
rs13133548	FAM13A	A	G	0.4835	-0.01706	0.002545	2.01E-11
rs4530754	CSNK1G3	A	G	0.5536	0.0053378	0.002677	0.046118
rs26008	FNIP1	C	T	0.9195	0.01586	0.004683	0.0007073
rs1016988	NA	C	T	0.2223	-0.0033999	0.003092	0.27155
rs6882076	TIMD4	C	T	0.626	-0.00159	0.002654	0.549086
rs3351855	FGFR4	A	G	0.292	0.01002	0.003167	0.001558
rs28932178	NSD1	C	T	0.1679	0.0200863	0.003483	8.08E-09
rs6450176	ARL15	A	G	0.2703	-0.0133145	0.003145	2.30E-05

rs9686661	NA	T	C	0.1869	-0.0321721	0.003256	5.05E-23
rs4976033	NA	G	A	0.4248	-0.0146967	0.002584	1.29E-08
rs3846663	HMGCR	T	C	0.3977	0.006229	0.002656	0.01903
rs2745353	RSPO3	T	C	0.5253	-0.0231161	0.002547	1.12E-19
rs9376090	NA	C	T	0.2377	-0.0159672	0.003045	1.57E-07
rs605066	NA	T	C	0.5692	0.0225756	0.002861	3.00E-15
rs4870044	C6orf97	T	C	0.3408	-7.25E-05	0.002881	0.9799163
rs12055786	RGS17	T	C	0.4369	-0.020698	0.002905	1.04E-12
rs1564348	SLC22A1	C	T	0.1517	-0.0028173	0.00353	0.4249
rs3757354	NA	T	C	0.24403	0.003124	0.002971	0.293
rs1800562	HFE	A	G	0.0479	0.007024	0.006024	0.2436
rs201148465	HIST1H1B	C	A	0.001378	0.0211363	0.036292	0.5603
rs2247056	NA	C	T	0.765	0.0131603	0.003394	0.0001055
rs3177928	HLA-DRA	A	G	0.1409	-0.0004877	0.004126	0.9059
rs2814982	NA	T	C	0.1196	-0.0283878	0.003972	8.85E-13
rs2758873	NA	A	G	0.237758	0.045981	0.03972	0.24698
rs998584	NA	A	C	0.4824	-0.025542	0.002652	5.97E-22
rs2239619	NA	A	C	0.619	2.46E-05	0.00271	0.992771
rs1997243	C7orf50	G	A	0.1426	0.0258637	0.003649	1.37E-12
rs38855	MET	G	A	0.4624	0.0100202	0.002564	9.30E-05
rs4731702	NA	T	C	0.4596	0.033021	0.00265	1.22E-35
rs17173637	NA	C	T	0.1449	0.0342042	0.046854	0.4654
rs10282707	SNX13	T	C	0.4261	-0.0270623	0.003077	1.42E-18
rs12670798	DNAH11	C	T	0.2471	0.0014672	0.003057	0.63125
rs4722551	NA	C	T	0.1577	0.007327	0.003626	0.043341
rs4917014	NA	G	T	0.2985	0.0167219	0.002789	2.02E-09
rs702485	DAGLB	G	A	0.4633	0.09697	0.033105	0.003399
rs17145738	NA	T	C	0.1149	0.0425198	0.004038	6.21E-26
rs11776767	PINX1	C	G	0.3719	-0.01077	0.002781	0.000108
rs2293889	TRPS1	G	T	0.6204	0.02887	0.002653	1.38E-27
rs3947	CTSB	A	G	0.2313	0.003957	0.00331	0.2318
rs4871137	NA	T	G	0.6404	-0.02223	0.002771	1.04E-15
rs2954029	NA	T	A	0.4468	0.03518	0.002564	7.47E-43
rs11136341	PLEC	G	A	0.3768	0.0005391	0.003399	0.8739867
rs1495741	NA	A	G	0.7527	-0.0038341	0.002986	0.19917
rs12678919	NA	G	A	0.09741	0.1586	0.00433	9.33E-294
rs10102164	NA	A	G	0.202	-0.0048487	0.00315	0.123798
rs2081687	NA	C	T	0.6624	-0.0026322	0.002694	0.328513
rs626913	NA	C	A	0.5191	0.0025179	0.002545	0.32245
rs9987289	NA	G	A	0.8993	0.09982	0.004376	3.69E-115
rs1883025	ABCA1	T	C	0.2623	-0.066873	0.002891	2.07E-118
rs2274159	DFNB31	G	A	0.48	0.01063	0.002578	3.71E-05
rs635634	NA	T	C	0.1904	0.01658	0.003378	9.20E-07
rs3812594	SEC16A	A	G	0.2375	0.004415	0.003033	0.145444
rs581080	TTC39B	C	G	0.7968	0.0373235	0.003236	8.94E-31
rs3927680	NA	A	T	0.5178	0.01	0.002654	0.0001638
rs67710536	RPS6	C	A	0.1111	0.01532	0.004336	0.0004085
rs3780181	VLDLR	G	A	0.07446	-0.0005274	0.004855	0.9135
rs10968576	LINGO2	G	A	0.2891	-0.0168862	0.002813	1.94E-09
rs77375493	JAK2	T	G	0.001137	-0.2125	0.047737	8.52E-06