Healthy diet indicator and metabolic syndrome in the Czech Republic, Russia and Poland: cross-sectional findings from the Health, Alcohol and Psychosocial factors in Eastern Europe (HAPIEE) study

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Thesis submitted for the degree of Doctor of Philosophy

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2015

Declaration

I, Peijue Huangfu, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

In Eastern Europe, cardiovascular disease (CVD) mortality is high, but the causes of this remain poorly understood. Metabolic syndrome (MetS) is a risk factor for CVD and is thought to be partly determined by diet. However, few studies have examined the prevalence of MetS and the associations between dietary quality and MetS in Eastern European populations.

This cross-sectional study used data from the baseline wave of HAPIEE study— 21519 randomly selected adults aged 45-69 years. MetS was defined using the ATP III definition. Healthy Diet Indicator (HDI) was derived using WHO 2003 recommendations: each component was scored from 0 (worst) to 10 (best adherence) and the total score ranged from 0 (worst) to 70 (best dietary quality). Anthropometric data and blood samples were collected during clinic visits.

Prevalence of MetS was high in the Czech Republic (men: 37.1%, women: 35.7%), Russia (20.8%, 36.3%), and Poland (27.9%, 28.6%). In logistic regression, adherence to total HDI score was not associated with risk of MetS (P>0.05), but higher HDI was associated with lower risk of having raised blood pressure in the pooled sample (OR per 10 unit increase in HDI=0.82, 95% CI: 0.72-0.94). A better adherence to recommended protein intake was consistently associated with lower risk of having high blood glucose in three countries (Czech Republic: OR per 1 unit increase in protein score=0.87, 95% CI: 0.80-0.94; Russia: 0.93, 0.88-0.99; Poland: 0.82, 0.75-0.89), and also associated with lower risk of MetS (0.92, 0.86-0.98) and central obesity (0.90, 0.84-0.96) in Poland.

Findings showed that MetS prevalence was high and diet quality was moderate to poor. Findings also provide some support for the beneficial role of diet quality (especially moderate protein intake) in lowering MetS prevalence. Future longitudinal studies should examine whether higher adherence to HDI reduces the risk of MetS and CVD.

Acknowledgements

First, I would like to thank my supervisors, Dr Hynek Pikhart, Dr Anne Peasey, and Professor Eric Brunner. I very much appreciate their help and support during the 4-year PhD programme.

Second, I would like to thank my coach Olga Vikhireva, for her invaluable advice, support and encouragement at the end of my PhD.

I would also like to thank HAPIEE study group, especially Andrea and Denes for their kind support for the past years.

I would like to thank my dear friends in this department especially Tuba, Silvia, Jemima, Carolina, and Ula. Without their continuous support, warmness, and kindness I would not get through the tough process of PhD, I very much cherish their friendships. I would also like to thank Gyuri, who was great company during my Master's degree.

I would like to thank David, my fiancé, for his love, support, and patience. I very much appreciate his continuous motivation and support.

Most importantly, I would like to thank my parents, for their strict upbringing and tough love. I also appreciate their unconditional support and encouragement thorough my life so far. It is them, who give me the strength to face all the challenges and difficulties ahead.

This thesis is dedicated to my parents and my first teacher Xiping Ji.

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Abbreviations

AACE – American Association of Clinical Endocrinologists

AHA/NHLBI – American Heart Association/National Heart, Lung, and Blood Institute

ATP III – Third Report of Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults

BMI – body mass index

BMR – basal metabolic rate

CTSU – Clinical Trial Service Unit and Epidemiological Studies Unit

CVD – cardiovascular disease

DBP – diastolic blood pressure

DRI – dietary reference intake

EGIR – European Group for the Study of Insulin Resistance

EI – energy intake

EPIC – European Prospective Investigation into Cancer and Nutrition

FFQ – Food Frequency questionnaire

FINE – Finland, Italy, The Netherlands, Elderly

GEMCAS – German Metabolic and Cardiovascular Risk Project

HALE – Healthy Ageing: a Longitudinal study in Europe

HAPIEE – Health, Alcohol and Psychosocial factors in Eastern Europe

HDI – healthy diet indicator

HDL-C – high-density lipoprotein cholesterol

IDF – International Diabetes Federation

IFG – impaired fasting glucose

IGT – impaired glucose tolerance

MDC – Malmo Diet and Cancer

MetS – metabolic syndrome

MONICA – MONItoring trends and determinants in CArdiovascular disease

NCEP – National Cholesterol Education Program

NHANES – National Health and Nutrition Examination Survey

OR – odds ratio

PONS – Polish Norwegian Study

PCOS – polycystic ovary syndrome

RDAs – Recommended Dietary Allowances

SBP – systolic blood pressure

SENECA – Survey in Europe on Nutrition and the Elderly: a Concerted Action

SEP – socioeconomic position

T2DM – type II diabetes mellitus

TG – triglycerides

WC – waist circumference

WHO – World Health Organisation

Chapter 1 Introduction

The term metabolic syndrome (also called as Syndrome X or the Deadly quartet) refers to a cluster of conditions which occur more commonly among individuals with insulin resistance, and it was first put forward by Reaven in 1988.[1;2] The conditions include abdominal obesity, hyperglycaemia, high blood pressure, and dyslipidaemia. Metabolic syndrome has been shown to be a risk factor for cardiovascular disease and type 2 diabetes, and is also related to other metabolic abnormalities and diseases.[3-5] Over the past three decades, the prevalence of metabolic syndrome increased worldwide, and its definitions and pathophysiology have been widely discussed.[3-6]

The prevalence of metabolic syndrome is relatively high worldwide. In Europe, about 25% of adults are thought to have metabolic syndrome;[7] while in the United States (U.S.) and Latin America, the prevalence is higher—among older adults (>60 years) its prevalence is thought to be over 40% in the U.S.[8] In addition, the prevalence of metabolic syndrome is believed to be increasing worldwide in parallel with the rising prevalence of obesity and type 2 diabetes.[7;9] Most metabolic syndrome patients are thought to be at higher risk of having cardiovascular disease, because the clinical features of metabolic syndrome are also cardiovascular disease risk factors.[10] A systematic review and meta-analysis found that metabolic syndrome is associated with an 80% increased risk of cardiovascular disease events and mortality;[11] moreover, metabolic syndrome is also associated with increased total mortality.[12] Therefore, in order to prevent various adverse life events, tackling metabolic syndrome is an important global public health issue.

Despite reductions in premature mortality in Western Europe, total and cardiovascular disease mortality increased in Central and Eastern Europe between 1970s to 1980s, and cardiovascular disease accounted for almost 60% of the gap in life-expectancy between Western Europe and Central and Eastern Europe.[13] Since the dissolution of Soviet Union, and the start of social and political transformation in Central and Eastern Europe after 1989, cardiovascular disease mortality decreased dramatically in the Czech Republic and Poland in early 1990s, but not in Russia.[14] It has been hypothesised that changes in diet are one reason for this reduction.[14;15] Since the late 1990s to early 2000s, cardiovascular mortality in the Czech Republic and Poland continued to fall and further reduced the gap with Western Europe, but the incidence in Russia has remained far above the European average.[16;17] However, few

population studies have investigated the reasons for the differences between these countries in cardiovascular mortality trends. The HAPIEE (Health, Alcohol and Psychosocial factors in Eastern Europe) study was set up at the start of 2000s to investigate the wider determinants of cardiovascular disease and other chronic conditions in the Czech Republic, Russia, and Poland.[18] Metabolic syndrome, as a risk factor for cardiovascular disease, has been examined in some studies in this region. A few studies have investigated the prevalence of metabolic syndrome in the Czech Republic, Russia, and Poland.[19-25] Despite the limited research and non-unified definition used in previous studies, prevalence of metabolic syndrome (and its components) was estimated to be high in this region. For example, one previous report using HAPIEE data estimated that over 70% individuals aged ≥45 years were overweight or obese (BMI>25kg/m^2) in the Czech Republic, Russia, and Poland.[26] Since obesity is one of the underlying risk factors for metabolic syndrome, the prevalence of metabolic syndrome is also likely to be high in Central and Eastern Europe, but it is still not well described. Thus, metabolic syndrome, as well as its related risk factors, needs further examination in the Central and Eastern Europe.

Metabolic syndrome and some of its components (central obesity and insulin resistance) are thought to be associated with demographic factors (age, sex), socioeconomic position, lifestyle behaviours (diet, physical activity), and genetic factors.[27;28] Some of these, such as dietary factors, are modifiable. In addition, it is believed that the prevalence of central obesity, insulin resistance, and metabolic syndrome can be reduced by interventions targeting physical inactivity and unhealthy diet, and such interventions have been found to have short-term success in clinical trials with both intensive and less intensive procedures.[29-34]

High energy intake is not the only link between diet and metabolic disorders, and some food groups and nutrients might be particularly important for preventing metabolic syndrome and its components. For example, fruit and vegetable intake was found to have protective effects on inflammation markers due to the combination of antioxidants and minerals, and it could further prevent cardiovascular risk factors.[35;36] Therefore, examining components of diet rather than energy intake alone is important in understanding the relationship between diet and metabolic syndrome.

Previous work, including one from the HAPIEE study,[37] showed that the intake of saturated fatty acids, sugar, and protein is very high in the Czech Republic, Russia, and Poland, whilst the consumption of fruits and vegetables and fibres is low.[38] High intake of saturated fatty acids and protein is associated with increased risk of

metabolic syndrome,[39;40] and high intakes in fruits and vegetables, fibre and whole grain are associated with decreased risk of metabolic syndrome.[41-46] However, there are a number of limitations of examining how single nutrients relate to health outcomes. In recent years, dietary pattern research has been increasingly used to overcome these limitations.[47;48] However, to the author's knowledge, no study has investigated associations between dietary factors/patterns and metabolic syndrome in the Czech Republic, Russia, and Poland.

The main aim of this thesis is thus to at least partly fill this gap and to investigate the prevalence of metabolic syndrome in the HAPIEE study populations (in the Czech Republic, Russia, and Poland), to explore the dietary patterns using Healthy Diet Indicator (HDI, described in detail in Chapter 4) in these populations, and to examine the association between HDI and the risk of metabolic syndrome and its components. The findings of this thesis will contribute to scarce research on health in Central and Eastern Europe, and potentially contribute to policies which ultimately aim at reducing diet-related non-communicable diseases.

The thesis is structured as follows: Chapter 2 provides a literature review on the history and prevalence of metabolic syndrome, and describes its pathophysiology, main debates, and its risk factors. It then provides an extensive literature review of studies examining how dietary patterns relate to metabolic syndrome. In Chapter 3, the aims and objectives of this thesis are presented; in Chapter 4, the study design, statistical power, and analytical methods used in this thesis are explained in detail, followed by the results of the study in Chapter 5. In Chapter 6, methodological issues, comparisons with previous studies, potential explanations of findings and their implications are discussed. Finally in Chapter 7 the final conclusions of this thesis are presented.

Chapter 2 Literature review

2.1 Historical background of metabolic syndrome

As early as the beginning of the 20th century, scientists have been trying to describe a very common coexistence of several metabolic disorders, which we know today as metabolic syndrome.

The first descriptions of the clustering of various components of the metabolic syndrome trace back to the 1920s and 1930s when Banting and Best discovered insulin.[49] During the First World War, some physicians started to believe that there was a relationship between blood pressure and diabetes mellitus among adults, and began to explore the mechanisms of such a relationship.[50] In 1936, Himsworth first divided patients with diabetes mellitus into insulin-sensitive and insulin-resistant groups. This could be seen as a milestone in metabolic research history.[51] After about 20 years, Vague was the first person who distinguished android obesity (where fat is localised around the waist and in the upper body, commonly seen in men) from gynaecoid obesity (obesity where fat is localised in the lower half of the body, commonly seen in women).[52] He also believed that there was a connection between android obesity and the development of diabetes, hypertension, gout and atherosclerosis; moreover, he suggested that android obesity plays an important role in cardiovascular disease. At the same time, other researchers also emphasised how android obesity related to the development of dyslipidaemia and hyperglycaemia.[53]

Sarafidis and Nilsson reported that since 1960s, researchers have published their findings on a variety of multifaceted metabolic disorders using different names: metabolic trisyndrome, plurimetabolic syndrome, syndrome of affluence, metabolic syndrome, syndrome X, deadly quartet, and insulin resistance syndrome.[54] In 1981, based on epidemiological and pathophysiological data, Hanefeld and Leonards (1981), as summarised by Sarafidis (2006), described a 'metabolic syndrome' which included type 2 diabetes mellitus, hyperinsulinaemia, obesity, hypertension, hyperlipidaemia, gout and thrombophilia. They also hypothesised that the 'metabolic syndrome' was caused by both genetic and environment factors (eg lack of physical exercise).[54]

In 1988, Reaven raised the profile of metabolic syndrome by naming it 'syndrome X'.[1] Based on observations of hospital patients, he believed that insulin resistance was the common aetiological factor for impaired glucose tolerance (IGT),

hyperinsulinaemia, high levels of very low-density lipoprotein, high level of triglycerides, low levels of high-density lipoprotein cholesterol (HDL-C) and hypertension. He also claimed that individuals with 'syndrome X' have a high risk of developing atherosclerosis. Moreover, he emphasised the important role of genetic and environmental factors in relation to the severity of insulin resistance. Later, Kaplan added central adiposity to 'syndrome X', and claimed that a group of disorders including central adiposity, IGT, hypertriglyceridaemia, and hypertension, played a critical role in development of cardiovascular disease and named it as 'the Deadly Quartet'.[55] From the 1990s onwards, the terms 'insulin resistance syndrome', 'metabolic syndrome', and 'syndrome X', were the most commonly used to describe this group of disorders, and the term metabolic syndrome becoming widely accepted. In the next section, the most commonly used definitions of metabolic syndrome in practice and research will be described in detail.

2.2 Definitions of metabolic syndrome

Several definitions of metabolic syndrome have been proposed during the past 15 years by organisations including the World Health Organisation (WHO), the European Group for the Study of Insulin Resistance (EGIR), the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood cholesterol in Adults (ATP III), the American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), and the International Diabetes Federation (IDF) (see Table 1).

In 1998, the WHO consultation proposed a working definition of metabolic syndrome, and in 1999 published a finalised definition by changing the systolic blood pressure cut-off point from 160mmHg to 140 mmHg (see Table 1).[56] According to the WHO definition, a patient with insulin resistance plus two additional metabolic abnormalities (obesity, hypertension, dyslipidaemia, or microalbuminuria) could be diagnosed as having metabolic syndrome. In the same year, EGIR published a modified definition (see Table 1).[57] EGIR agreed with WHO that insulin resistance is likely to be the major cause of metabolic syndrome, and they suggested to use the term 'insulin resistance syndrome' instead of 'metabolic syndrome', because it contains non-metabolic components (eg, blood pressure). They defined insulin resistance as being in the top quartile of fasting insulin among the non-diabetic population; this was used in order to

avoid the need for expensive and burdensome euglycaemic clamp[i] measures used in the WHO definition. In addition, two more abnormal features are required among central obesity, high blood pressure, and dyslipidaemia, and fasting plasma glucose. However, the EGIR definition is only suitable for non-diabetic populations. The cut-points for triglycerides and HDL-C were modified, since the report from the Second Joint Task Force of European and other Societies on Coronary Prevention suggested that the fasting triglycerides >2.0mmol/L and/or an HDL-C<1.0mmol/L could predict higher risk of coronary heart disease.[59] In their definition, central obesity was an important component of the diagnosis criteria, and it was measured using waist circumference instead of waist-hip ratio, because it was much easier to measure and better correlated with intra-abdominal visceral adipose tissue accumulation and metabolic abnormalities.[60] EGIR removed the microalbuminuria criteria from the list, because it has not been universally shown to be linked with insulin concentrations.[61;62] Finally, EGIR suggested that a minimum number of abnormalities in the syndrome is practical for most epidemiological research use, which lead the further thoughts from other institutions. In 2001, the National Cholesterol Education Program (NCEP) produced a third version of clinical updates on cholesterol management (ATP III). Unlike previous versions, ATP III maintains the attention of the intensive treatment for patients with coronary heart disease, but also emphasises the focus on the prevention of coronary heart disease among people with multiple metabolic risk factors. Subsequently a definition of metabolic syndrome was proposed by ATP III.[63] The purpose of ATP III was to identify the risk factors for coronary heart disease— consequently, it does not have a prerequisite of insulin resistance. The ATP III diagnosis of metabolic syndrome required three out of five components believed to be the major components of metabolic syndrome (central obesity, hypertriglyceridaemia, low HDL-C, hypertension, and elevated fasting glucose). It was still believed that central obesity was an important component, and the cut-points were modified by using National Institutes of Health clinical guidelines of obesity.[64] ATP III revised the definition of high blood pressure and changed the cut-points for triglycerides back to the WHO 1999 definition and allowed for the diagnosis of the metabolic syndrome among diabetes patients. NCEP acknowledged racial and ethnic differences in risk factors for coronary heart disease, but suggested that the observed

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[i] During the procedure, the plasma insulin concentration is acutely raised and maintained at 100 μU/ml by a continuous infusion of insulin. Meanwhile, the plasma glucose concentration is held constantly at basal levels by a variable glucose infusion. When the steady-state is achieved, the glucose infusion rate equals glucose uptake by all the tissues in the body and is therefore a measure of tissue insulin sensitivity. The hyperinsulinemic clamps are often used to measure insulin resistane..[58]

evidence was not sufficient for changing the general guidelines. Therefore, the ATP III definition of metabolic syndrome is thought to be more suitable for Caucasian compared with other ethnic groups (see Table 1).

In 2005, AHA/NHLBI and IDF proposed revised definitions of metabolic syndrome.[65;66] The AHA/NHLBI definition, central obesity was not required as an obligatory criteria, and it only modified the ATP III criteria slightly (fasting plasma glucose ≥5.6 mmol/L). These two modified versions are quite similar to ATP III version. Specifically, the IDF definition made central obesity (high waist circumference) an obligatory component in the definition, and first proposed that different ethnic cut-points of waist circumference are needed, but other requirements are exactly the same as ATP III. In addition, the cut-points of central obesity are different between IDF and AHA/NHLBI (see Table 1).

In 2009, AHA/NHLBI and IDF agreed on a unified definition of metabolic syndrome.[3] They reached an agreement that central obesity would not be an obligatory component of metabolic syndrome but emphasised ethnic differences of central obesity, and kept the ATP III requirement of three abnormal findings out of five for a person to qualify for the metabolic syndrome (see Table 1).

There are also some other definitions suggested by different institutions. For example, in 2003, American Association of Clinical Endocrinologists (AACE) proposed a modified definition called as 'insulin resistance syndrome'.[67] Components of this definition included impaired glucose tolerance, elevated triglycerides, reduced HDL-C, elevated blood pressure, and obesity. However, no specified number of factors was stipulated for the diagnosis, but specific clinical judgement was required (this definition has not been showed in Table 1).

Both WHO and EGIR definition included the measurement of insulin resistance as a prerequisite component of metabolic syndrome, but these measurements are not routinely available in clinical practice, especially in population studies. Moreover, studies have shown that ATP III and AHA/NHLBI definitions are stronger predictors of cardiovascular disease risk than other definitions, and ATP III is the most commonly used definition in research. By considering the above aspects, the ATP III definition is by far the most practical definition in population health studies, and it was therefore used in this thesis.[68;69]

Table 1 Definitions of metabolic syndrome

Risk factors	WHO(1999)[56]	EGIR(1999)[57]*	ATP III(2001)[63]	AHA/NHLBI(2005)[65]	IDF(2005)[66]	Unified AHA/NHLBI & IDF(2009)[3]
Insulin resistance	T2DM,IFG,IGT, or lowered insulin sensitivity[1] Plus any 2 of the following	Top quartile of fasting insulin values among the nondiabetic population Plus any 2 of the following	None Any 3 of the following 5 components	None Any 3 of the following 5 components	None	None Any 3 of the following 5 components
Body weight	waist:hip ratio >0.90(male), > 0.85 (female) or BMI> 30 kg/m^2	WC ≥ 94 cm (male) or ≥ 80 cm (female).	WC ≥ 102 cm (male) or ≥ 88 cm (female)	WC ≥ 102cm (male), ≥ 88 cm (female)	WC ≥ 94cm (male), or 80cm (female) or BMI is >30 kg/m^2 [2] Plus any 2 of the following 4 components	WC- population/country specific definitions [4]
Blood pressure	≥140/90 mmHg	≥ 140/90 mmHg or treated for hypertension	≥ 130/85 mmHg	≥ 130/85 mmHg, or on antihypertensive drug treatment in a patient with a history of hypertension	≥ 130/85 mm Hg, or treated for hypertension.	≥ 130/85 mm Hg, or treated for hypertension.
Dyslipidaemia	TG≥1.695 mmol/L or HDL-C≤ 0.9 mmol/L (male), ≤ 1.0 mmol/L (female)	TG > 2.0 mmol/L or HDL-cholesterol < 1.0 mmol/L	TG ≥ 1.7 mmol/L	TG ≥ 1.7 mmol/L or on drug treatment for elevated TG	TG ≥1.7 mmol/L, or specific treatment for this lipid abnormality.	TG ≥1.7 mmol/L, or specific treatment for this lipid abnormality.

Risk factors	WHO(1999)[56]	EGIR(1999)[57]*	ATP III(2001)[63]	AHA/NHLBI(2005)[65]	IDF(2005)[66]	Unified AHA/NHLBI & IDF(2009)[3]
		or treated for dyslipidaemia	HDL-C < 1.03 mmol/L (male) or < 1.29 mmol/L (female)	HDL-C < 1.03 mmol/L (male) or <1.29 mmol/L (female) Or on drug treatment for reduced HDL-C	HDL-C: < 1.03 mmol/L (male), or < 1.29 mmol/L (female), or specific treatment for this lipid abnormality	HDL-C: < 1.03 mmol/L (male), or < 1.29 mmol/L (female), or specific treatment for this lipid abnormality
Fasting plasma glucose	--	≥ 6.1 mmol/L	≥ 6.1 mmol/L (including diabetes)	≥ 5.6 mmol/L or on drug treatment for elevated glucose	≥ 5.6 mmol/L, or previously diagnosed T2DM	≥ 5.6 mmol/L, or previously diagnosed T2DM
Other	Microalbuminuria[3]	--	--	--	--	--

Abbreviation: T2DM- type 2 diabetes mellitus, IFG- impaired fasting glucose, IGT- impaired glucose tolerance, BMI- body mass index, TG- triglycerides, HDL-C- high density lipoprotein cholesterol, WC- waist circumference

[1] Insulin sensitivity measured under hyperinsulinaemic and euglycaemic conditions, glucose uptake in the lowest quartile for the back ground population under investigation.

[2] When BMI is >30 kg/m², central obesity can be assumed and waist circumference does not need to be measured

[3] Microalbuminuria: urinary albumin excretion ratio ≥ 20 µg/min or albumin:creatinine ratio ≥ 30 mg/g

[4] It is recommended that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available

*Unlike all other definitions restricted to non-diabetic persons

2.3 Prevalence of metabolic syndrome

The lack of diagnostic concordance among metabolic syndrome definitions and its individual components makes it difficult to compare metabolic syndrome prevalence across different studies and different countries. In the following sections, the estimated prevalence of metabolic syndrome worldwide will be discussed first, then in the countries studied in HAPIEE: the Czech Republic, Russia, and Poland.

2.3.1 Worldwide prevalence of metabolic syndrome using different definitions

In 2004, Cameron, Shaw, and Zimmet summarised the prevalence of metabolic syndrome in different populations using three definitions: WHO, ATP III, and EGIR (see Figures 1 and 2).[70]

Figure 1 displays the data on prevalence of metabolic syndrome defined by ATP III and WHO definitions in selected countries in the 2000s. The prevalence varies from 11% to 35% depending on the definition and population used. Prevalence was higher in men than in women using the WHO definition, but this gender difference was not seen when using ATP III definition. In addition, the prevalence in men was higher when using WHO definition compared to ATP III.

Figure 2 shows the comparison of metabolic syndrome prevalence using EGIR and WHO definitions. Firstly, similar to the WHO definition, the prevalence of metabolic syndrome was higher in men than in women when using EGIR definition. Secondly, the prevalence in both men and women are higher when using the WHO definition than EGIR; however, in some studies, one or more components of metabolic syndrome in either EGIR or WHO definition were not included in the used definition, which made these estimates less comparable. For example, in the study among 22-73 years men and women conducted in Italy, the waist-hip ratio component was not included in the WHO definition and waist circumference was not included in the EGIR definition, these could both reduce the true prevalence using both definitions and making it difficult to predict the difference of the distribution.

In addition, one study in Mauritius showed the prevalence of metabolic syndrome using all three definitions. The prevalence of metabolic syndrome was the highest using the WHO definition in both men and women (20.9% and 17.6% respectively),

compared with ATP III (men: 10.6%; women: 14.7%) and EGIR (men: 9.0%; women: 10.2%).[70]

Ko et al examined the prevalence of metabolic syndrome among Hong Kong Chinese using WHO, ATP III, and EGIR definitions.[71] Of 1513 participants aged 18-66 years, the prevalence was highest when using the WHO definition (13.4%), followed by ATP III (9.6%) and EGIR (8.9%). This confirmed the findings from Cameron et al.[70]
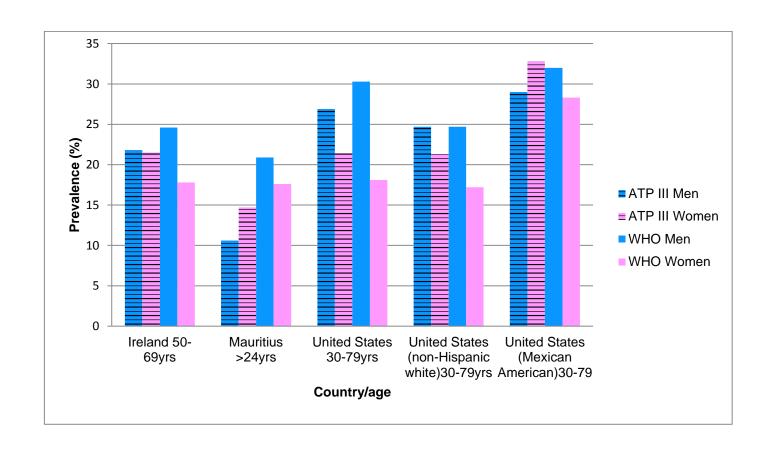
Figure 1 Prevalence of metabolic syndrome using ATP III and WHO definitions (adapted from Cameron, Shaw, Zimmet[70])
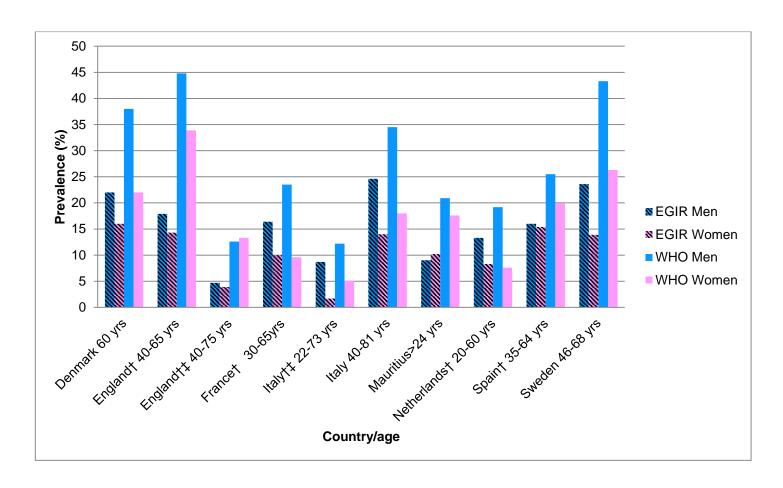
Figure 2 Prevalence of metabolic syndrome using EGIR and WHO definitions (adapted from Cameron, Shaw, Zimmet[70])

†This value is not comparable due to one or more components of the metabolic syndrome not being measured for the WHO criteria.

‡Obesity was omitted from the definition of metabolic syndrome in the EGIR criteria.

Since 2005, several new definitions of metabolic syndrome have been proposed, and they are AHA/NHLBI, IDF, and Unified AHA/NHLBI & IDF as aforementioned (see Table 1). These definitions kept the five basic components of metabolic syndrome as ATPIII for its simplicity and practical advantage, but modified the cut-points of some components. For example, AHA/NHLBI modified the glucose level in response to the updates from American Diabetes Association criteria.[65] The IDF writing group suggested that central obesity and insulin resistance are highly correlated, and that central obesity could be used instead, with specific ethnic threshold.[66] Later, both AHA/NHLBI and IDF groups agreed not to have central obesity as a prerequisite component in the unified definition in order to resolve the differences in definitions.[3] These new definitions have been compared with each other and with ATP III definition in the U.S., Sweden, Germany, and Greece.

In the National Health and Nutrition Examination Survey (NHANES) 1999-2002, among a total of 3601 people aged ≥20 years, Ford found that the age-adjusted prevalence of metabolic syndrome in men was 34.4%, and 34.5% in women when using ATP III definition, while the prevalence increased slightly when using IDF definition (40.7% in men and 37.1% in women).[72]

Nilsson, Engstrom and Hedblad found that among 5,047 Swedish people aged 46 to 68 years who enrolled in the Malmo Diet and Cancer (MDC) study between 1991 and 1994, the prevalence of metabolic syndrome was the highest when using IDF definition (21.9%), followed by 20.7% when using ATP III and 18.8% when using EGIR.[73]

In the German Metabolic and Cardiovascular Risk Project (GEMCAS) which conducted in 2005, Moebus et al compared prevalence of metabolic syndrome using ATP III, AHA/NHLBI 2005, and IDF definitions; among 35,869 primary care patients aged 18-99 years.[74] The age-standardised prevalence was the lowest when using ATP III definition (18.7%) and the highest when using IDF definition (30.7%).

Another similar comparison study was conducted in a Mediterranean population in Greece between 2003 and 2004.[69] Athyros et al compared the metabolic syndrome prevalence using four different definitions (ATP III, AHA/NHLBI 2005, IDF, and Unified AHA/NHLBI & IDF) among a total of 9,669 Greek adults aged ≥18 years. The age-adjusted prevalence of metabolic syndrome was similar when using ATP III and AHA/NHLBI 2005 (24.5% and 26.3% respectively), and the prevalence were higher when using IDF and Unified AHA/NHLBI and IDF (43.4% and 45.7% respectively).

The evidence above showed that the prevalence of metabolic syndrome is high worldwide, although the estimates vary by populations and definition. Moreover, the prevalence is higher when using WHO and IDF definition in the same population compared with other definitions.

2.3.2 Prevalence of metabolic syndrome and its components in the Czech Republic, Russia, and Poland

Recently several studies have examined prevalence in the Central and Eastern Europe, for example in Hungary,[75] Slovakia,[76] and Croatia.[77]. Studies have suggested that the prevalence of metabolic syndrome is high (>24%) in these countries. However, studies on the prevalence of metabolic syndrome are still scarce in Central and Eastern European population. In the following section, the studies on the prevalence of metabolic syndrome in the countries in which HAPIEE study was conducted are summarised.

The Czech MONICA (MONItoring trends and determinants in CArdiovascular disease) study showed 24.4% of women had metabolic syndrome and 32.0% of men aged between 25 and 64 years.[19;25] Another study conducted among 805 aged between 18 and 65 years in three regions of the Czech Republic showed that 22.9% of women and 32.5% of men had metabolic syndrome when using the IDF definition.[25] Other studies among Czech population have focused on the prevalence of components of metabolic syndrome. From 1985 to 2007/8, among men, BMI increased from 27.0 to 28.5kg/m^2; among both men and women, the mean systolic blood pressure decreased (in men: 135.8 to 132.5mmHg; in women: 131.6 to 126.6mmHg), as well as the mean diastolic pressure (in men: 85.9 to 84.4mmHg; in women: 82.5 to 80.6mmHg); further, the prevalence of hypertension (defined as systolic blood pressure≥140mmHg, and/or diastolic blood pressure≥90mmHg) decreased in total population from 47.1% to 43.6% and from 42.5% to 37.3% in women, however, there was no change among men. In the study, blood pressure was measured by standard mercury sphygmomanometers, and the first and fifth Korotkoff sounds were recorded as systolic blood pressure and diastolic blood pressure to the nearest 2mmHg. Final blood pressure was recorded as the average of the first two readings. However, the blood pressure readings may be biased by differences in investigator technique. Moreover, there was a mild decline for mean HDL-C level in men (from 1.35 to 1.30mmol/L) but no change in women; the high prevalence of dyslipidaemia (defined as total cholesterol≥5mmol/L or HDL-C <1mmol/L in men and <1.2mmol/L in women or use of lipid-lowering drug) was observed throughout the

surveys, and it decreased in both men (from 87.5% to 73.8%) and women (85.2% to 62.9%).[78]

Few studies have examined metabolic syndrome prevalence in Russia. Jones et al examined the prevalence of metabolic syndrome among a sample of 146 people aged 25-89 years in Kuzmolovsky, Russia.[20] They found the prevalence of metabolic syndrome was 54.1% using ATP III definition; however, the sample size was small and the sample was not representative because it was selected in the only one clinic in a local area by inviting patients who came to the clinic, which introduced substantial selection bias by including unhealthy participants only. Several years later, a cross-sectional study of 3555 participants aged 18-90 years was conducted in Arkhangelsk, Northwest Russia, and investigated the prevalence of metabolic syndrome using IDF definition.[21] The prevalence was 9.5% in men and 23.5% in women. However, the prevalence could have been underestimated because of using HbA1c (≥6.1%) instead of plasma glucose (≥6.1mmol/L) as the hyperglycaemia criteria. A level of ≥6.1% in HbA1c is equivalent to a level of plasma glucose level ≥7.1mmol/L;[79] therefore, the cut-point used for HbA1c underestimated the prevalence of hyperglycaemia and metabolic syndrome. In the same year, Sidorenkov et al investigated the prevalence of metabolic syndrome by comparing three definitions – ATP III, IDF, and AHA/NHLBI – in the same study sample.[22] The age-standardised prevalence was highest among women by using IDF definition (23.1%), followed by AHA/NHLBI (20.6%) and ATP III (19.8%), while in men the prevalence was highest by using AHA/NHLBI (13.7%), followed by ATP III (11.5%) and IDF (11.0%). However, in this latter study, the prevalence of the metabolic syndrome may have been underestimated since the glucose level was measured by serum glucose instead of plasma glucose.

In Poland, the prevalence of metabolic syndrome was also investigated in several studies. Szurkowska and colleagues found that the prevalence of metabolic syndrome among 40989 Poles aged 25-97 years was 16.2% in men and 20.9% in women when using the ATP III definition.[23] In the Polish Norwegian Study (PONS), researchers found that among 3862 people, the prevalence of metabolic syndrome was 49.9% in men and 34.3% in women when using the Unified AHA/NHLBI & IDF definition; central obesity was the most common abnormality with a prevalence of 75.1%, followed by high blood pressure (71%), glucose intolerance (37.3%), high triglycerides (21.2%), and low HDL-C (15.9%).[80] In a study of 8006 men and 10577 women aged 40 and 50 years from Wroclaw, Poland, Ilow and colleagues found that the prevalence of

metabolic syndrome was 35.9% in men and 22.9% in women when using the Unified AHA/NHLBI and IDF definition.[24] They also found that metabolic syndrome was significantly more common in men than women, and among older group (=50 years old) than younger group (=40 years old). The most frequent components of metabolic syndrome among 40 years old women was central obesity (36.1%) and high blood pressure (27.3%), while in the 50 years old group, the prevalence was 62.6% and 55.3% respectively. In this study, researchers also compared the prevalence of metabolic syndrome using two definitions- IDF and Unified AHA/NHLBI & IDF. The prevalence of metabolic syndrome and its components was significantly lower when using IDF definition compared to the Unified definition.

The Czech Republic, Russia, and Poland are the countries included in the HAPIEE study as well as this thesis. The literature above showed the prevalence of metabolic syndrome to vary considerably, suggesting that assessment of prevalence of metabolic syndrome in these countries using a multi-centre study, such as HAPIEE study, with representative samples, standardised data collection procedures, and well-designed laboratory measures, will considerably advance understanding of the metabolic syndrome in the region.

The evidence in both section 2.3.1 and 2.3.2 showed that the prevalence of metabolic syndrome varies between populations and criteria used. Comparing prevalence between definitions, IDF and Unified AHA/NHLBI & IDF showed a higher prevalence of metabolic syndrome compared to other definitions. Ford tested the agreement of metabolic syndrome diagnosis using IDF and ATP III and the percent agreement was high in both men (89.8%) and women (96.0%); moreover, when using IDF definition, 5.8% of the participants had been diagnosed with metabolic syndrome but not when using ATP III definition. The prevalence difference between two definitions could be explained by the obligatory of central obesity in IDF and the lower threshold of waist circumference in IDF (≥90cm for men and ≥80 for women) compared to ATP III (≥102cm for men and ≥88cm for women).[72] Moebus et al found that the largest disagreement among definitions was between ATP III and IDF.[74] Despite the large disagreement between IDF and most commonly used definition (ATP III), the prediction level of different definitions on other chronic disease has been described. A study from Greece reported that the use of the IDF definition resulted in increased labelling of elderly subjects with the diagnosis of metabolic syndrome without identifying more subjects at high risk for stroke.[81] Athyros et al found that metabolic syndrome by the use of ATP III definition predicted cardiovascular disease better than

the use of other definitions.[69] Also, in the Malmo Diet and Cancer study, better prediction of cardiovascular disease event by metabolic syndrome was found using the ATP III definition.[73] In summary, by comparing the agreement and predicted level of other chronic diseases with definitions, the ATP III definition is potentially more suitable for disease detection at the population level.

2.4   Concepts and debates of metabolic syndrome

Metabolic syndrome, as a constellation of risk factors for cardiovascular diseases and type 2 diabetes, has been discussed in studies for decades.[82] However, the pathogenesis of metabolic syndrome is still not fully understood. There are two essential research aspects related to the pathophysiology of metabolic syndrome: 1), whether insulin resistance is the major underlying risk factor for the metabolic syndrome; and 2) whether obesity is the main cause of multiple metabolic disorders which constitutes the metabolic syndrome.[5] Furthermore, there has been important debate on whether metabolic syndrome has some additional predictive effect in comparison to its individual components. The literature related to these three issues will be summarised below.

2.4.1   Insulin resistance in the aetiology of the metabolic syndrome

The metabolic interaction between glucose and fatty acids is thought to be important for development of insulin resistance and metabolic syndrome.[83] In adipose tissue, when the glucose circulation increases, the pancreas secretes more insulin in order to maintain euglycaemia; meanwhile, insulin suppresses fatty acid release from adipose tissue. Therefore, a high glucose level normally leads to a low non-esterified fatty acids level in plasma. In muscle, when more glucose becomes available, muscle tissue utilises glucose rather than fatty acids. In between meals, the glucose level falls, the pancreas secrets less insulin, but the non-esterified fatty acid level increases. At this point, fatty acids in muscle are oxidised in order to suppress the uptake and oxidation of glucose, which could preserve the glucose for other tissue use (eg, brain).

In insulin resistant subjects, glucose uptake is not stimulated by insulin as normal, leading to hyperinsulinaemia. Normally, insulin inhibits gluconeogenesis in the liver when the glucose level is high (eg, after meals). But among insulin resistant subjects, the inhibiting function by insulin is not effective, which results in a further increase of glucose level by gluconeogenesis. The impaired insulin function will also result in the failure of suppressing fatty acids release from the adipose tissue.

It has been proposed that insulin resistance is a physiological adaptation to obesity that limits fat deposition and leads to weight stabilisation.[84]Insulin resistance is one of the components of metabolic syndrome,[1] and it is the most accepted hypothesis of the pathophysiology of the metabolic syndrome.[82] Some researchers proposed that insulin resistant syndrome is the same as metabolic syndrome,[67] because they believed that insulin resistance is the root cause of metabolic syndrome. To some extent, this view is supported. According to the Framingham Offspring studies, most metabolic syndrome patients were insulin resistant.[85] Reaven believed that a defect in insulin function can further cause several other abnormalities. Specifically, it can lead to an increased level of triglyceride, a decreased level of HDL-C, and elevated blood pressure.[86] According to DeFronzo and Ferrannini, insulin resistance has two main stages which are obesity and type 2 diabetes, and both of these stages are the components of metabolic syndrome.[87] It is believed that insulin resistance can cause metabolic disorders, such as high level of triglycerides and blood glucose. It is a major component of metabolic syndrome; however, there is still a lack of evidence to show if insulin resistance is the major cause of every component of metabolic syndrome.

2.4.2 Obesity in the aetiology of the metabolic syndrome

The worldwide rising prevalence of obesity paralleled the increasing prevalence of metabolic syndrome.[88] Obesity is associated with risk of cardiovascular disease, premature mortality, and some metabolic disorders, such as type 2 diabetes, hypertension, and dyslipidaemia.[89] Researchers have found that it is the products, released by adipose tissue, that play important roles in metabolic disorders. One of the products released by adipose tissue is non-esterified fatty acid. Insulin can suppress the activity of hormone-sensitive lipase. When insulin level is low, the enzyme hormone-sensitive lipase can enhance the hydrolysis of triglycerides, and release more non-esterified fatty acid. Among obese people, their tissue is resistant to insulin actions, which leads to surprisingly high levels of non-esterified fatty acid levels.[90] In this way, insulin resistance and obesity are connected.

One of the components of metabolic syndrome is central obesity (abdominal obesity). One study showed that central obesity was more strongly associated with metabolic syndrome than the whole body obesity, but the reasons for this were not understood.[91] Moreover, studies show a strong relationship between central obesity and metabolic risk factors.[92-96] Pouliot and colleagues found that centrally obese men are more likely to have atherogenic metabolic traits, and they also suggested that central obesity especially the measurement of waist circumference is a strong predictor of metabolic

complications.[60;97] According to Lemieux and colleagues, around 80% of men who were centrally obese had elevated triglycerides level, and they also suggested that a hypertriglyceridaemic waist can predict metabolic abnormalities.[98] Also, central obesity is thought to be one of the causes of insulin resistance because a high percentage of body fat can decrease insulin sensitivity.[99] Consequently central obesity may be one of the causes of metabolic syndrome.

2.4.3   Controversies surrounding metabolic syndrome

Debates on metabolic syndrome have been continuing for decades. The major issues include the validity of its naming and its utility as a practical clinical tool, these have been discussed in previous sections (see Section 2.1 and 2.2); mostly important, is its predictive value. Researchers question whether metabolic syndrome can forecast cardiovascular events, diabetes or disease progression any better than its components.[88]

Three meta-analyses conducted in 2006, 2007, and 2010, showed that metabolic syndrome is an important risk factor for cardiovascular disease, and that metabolic syndrome was associated with increased cardiovascular and all-cause mortality.[11;100;101] However, comparison of the effects of metabolic syndrome and its components has not been discussed systematically. Scatter and colleagues found that metabolic syndrome and its components are associated with risk of type 2 diabetes, but no association was found in relation to vascular risk.[102] Reaven recently suggested that metabolic syndrome should no longer to be used.[103] He argued that it is simply the additive effect of several adverse factors together (under the heading 'metabolic syndrome') that predict higher risk of cardiovascular disease rather than any additional effect associated with the clustering of conditions together—he argued that there is no evidence for metabolic syndrome effect above its additive value. The debate still continues and more research is needed to justify whether metabolic syndrome should still be used and whether it has additional value compared with the sum of its individual components—central obesity, high blood pressure, high triglycerides, low HDL-C, and high plasma glucose.

However, metabolic syndrome still has its unique value in clinical diagnosis. One of the most important reasons of introducing metabolic syndrome into medical research and practice is to amplify the awareness of the increased risk associated with obesity and to target the sedentary life-styles and unhealthy diets in modern society.[5]

Therefore, metabolic syndrome might still be important as a clinical tool, and as a predictor of adverse life events.

2.5 Risk factors for metabolic syndrome

Identifying risk factors for metabolic syndrome is important to ultimately prevent and reverse metabolic syndrome. In addition to diet, the main focus of this thesis, there are other risk factors for metabolic syndrome which may affect the association between diet and metabolic syndrome. These factors will be used as the covariates in the analysis of the association between diet and metabolic syndrome in this thesis, and the existing evidence of their association with metabolic syndrome and its components will be briefly discussed in the following sections. These factors are gender, age, socioeconomic position, health behaviours, BMI and weight gain, hormones change, family history, and other diseases.

2.5.1 Gender

Gender differences in several components of metabolic syndrome, namely central obesity, lipid concentration, and hypertension, have been often discussed in published studies. It is well known that menopause is a critical point of cardiovascular health among women compared with men.[104;105] Before menopause, women tend to accumulate more fat in the lower body gluteal area (thighs and bottom), while later they tend to accumulate more fat in upper body area (centrally obese).[106;107] Moreover, women tend to store fat subcutaneously, while men tend to store fat viscerally, and this gender difference may be due to a greater amount of fatty acid uptake in the visceral area in men compared with women after eating.[108] However, after menopause, women start having increasing risk of metabolic abnormalities, such as central obesity and hypertension. Among postmenopausal women, body fat distribution shifts to a more male pattern with fat stored viscerally.[107;109] Post-menopausal women have also been found to have higher risk of hypertension compared to their pre-menopausal counterparts.[110] Dallongeville et al compared the importance of components of metabolic syndrome in men and women, they found that high waist circumference and low HDL-C were the most important contributor to metabolic syndrome in women, while raised blood pressure was the most important contributor to metabolic syndrome in men.[111] Furthermore, NHANES also showed a higher increase of prevalence of metabolic syndrome in women (23.5%) than among men (2.2%) in 10 years time.[112]

2.5.2 Age

Older age is a risk factor for many health outcomes, and as well as metabolic syndrome and its components. According to researchers in the United States, the prevalence of metabolic syndrome increases by age.[8;27] Among men, the prevalence of metabolic syndrome reached a peak at 60 years of age, while in women at the age of 70 years. In both men and women, the dramatic increase in metabolic syndrome prevalence from age 30-40 years old is paralleled with the increase of prevalence in overweight and obesity. Carnethon and colleagues found that the risk of metabolic syndrome increased with age in the Coronary Artery Risk Development in Young Adults study during the 15-year follow-up.[113] In addition, with the increasing age, insulin resistance, hypertension, other hormonal alterations, and visceral adipose tissue become more common among adults, which is the other important pathogenesis of developing metabolic syndrome.[27;114-116]

2.5.3 Socioeconomic position

Low socioeconomic position (SEP) is another risk factor for metabolic syndrome. Occupation, income, education and wealth across the life (from childhood to adulthood) are the most commonly used measures of SEP in relation to metabolic syndrome.

Childhood socioeconomic position

One of the commonly used measures of childhood SEP is father's occupation. The British Regional Heart Study, Medical Research Council National Survey of Health and Development, and Whitehall II study showed that lower father's occupation in childhood was associated with higher risk of metabolic syndrome.[117-119] However, neither of the latter two studies showed a significant association between father's occupation and metabolic syndrome among men.

Apart from father's occupation, other predictors of childhood SEP have been used, such as housing condition. Researchers using data from the Newcastle Thousand Families Study found that poor housing conditions at age 5 and 10 years were not associated with metabolic syndrome score among adults aged 49-51.[120;121] Another predictor is parental possessions. A study based on Chinese Guangzhou Biobank Cohort Study suggested that parental possessions were inversely associated with metabolic syndrome risk among Chinese women aged over 50 years.[122]

In the United States, researchers derived a cumulative score in the Atherosclerosis Risk in Communities study by summing up the values of parental education at the time of birth, parental occupation, parental occupational role, and parental home ownership. They showed that low childhood SEP predicted higher risk of metabolic syndrome among 45-64 years old women but not among men.[123;124]

Adulthood socioeconomic position

Education is one of the main indicators for adulthood SEP. The Medical Research Council National Survey of Health and Development study, World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease population survey, and another Finnish study, all consistently showed that lower education was associated with higher risk of metabolic syndrome.[118;125;126] In addition, this social gradient is much stronger among women than men.[122;127-131] However, some studies found that there was no association between educational level and metabolic syndrome among men nor women.[27;119]

Income is used in several different forms as a measure of SEP, specifically, poverty income ratio, personal income, and household income. Poverty income ratio is the ratio of family income to federal poverty line. It is believed to be a better measure than income by some researchers because it takes family size and inflation into account.[132] A study based on NHANES showed that women aged between 46 and 65 years with income level below the poverty line (poverty income ratio less than 1) have almost 5 times higher risk of having metabolic syndrome compared with their counterparts in the top poverty income ratio group, but the similar association was not found in men.[128] The relationship between personal income, household income, and metabolic syndrome is similar to the one of education. Specifically, income level is inversely associated with risk of metabolic syndrome, and the association is more common in women rather in men.[27;119;125;130;133]

Other measures of adulthood SEP include employment grade and house ownership. The association between employment grade and house ownership, and household wealth, and metabolic syndrome showed similar results as the association of education and income.[117;119;125;127;134-136]

In summary, a variety of predictors of childhood SEP and adulthood SEP have been used. Generally, there was a social gradient in relation to risk of metabolic syndrome and SEP—the higher the SEP, the lower the risk of having metabolic syndrome. Moreover, this gradient was much stronger among women than men.

2.5.4 Health behaviours

Health behaviours are thought to be related to many chronic diseases, such as cardiovascular disease, diabetes, as well as metabolic syndrome. It is argued that physical inactivity, smoking and sleeping duration are all risk factors for metabolic syndrome.

Physical inactivity

Physical inactivity is reported to be a risk factor for metabolic syndrome. According to NHANES study, men with a sedentary lifestyle have 50% higher risk of metabolic syndrome compared to their peers who were physically active.[27] Another study showed that having 3 hours/week of moderate or vigorous leisure time physical activity could halve the risk of metabolic syndrome compared to having a sedentary lifestyle among men.[137] Another study showed that participants having no moderate or vigorous physical activity during leisure time had about two-fold of higher risk of having metabolic syndrome compared to their peers with 150 min/week physical activity, however, the analyses in this study were not adjusted for BMI.[138] Several other studies showed consistent results that increased physical activity can be a protective factor for metabolic syndrome and other risk factors of cardiovascular disease, although the analyses were not adjusted for BMI in the models; instead, some of them included dietary intakes (eg, fat intake, alcohol intake, energy intake) as covariates in the analyses.[113;139-141]

Smoking

Smoking is another risk factor for metabolic syndrome. A Taiwanese study showed that former (35.3%) or current smokers (34.6%) had higher prevalence of metabolic syndrome than never smokers (10.8%).[142] A Japanese study showed that smoking increased the risk of metabolic syndrome, central obesity, raised triglycerides, and low HDL-C.[143] A Chinese study found that current smokers have increased incidence of raised triglycerides and low HDL-C compared to non-smokers; furthermore, ex-smokers who had quitted smoking for more than 13 years ago had decreased risk of having new metabolic syndrome event.[144] Furthermore, Slagter et al also found that current smokers had higher risk of having metabolic syndrome in Dutch men and women. Wilsqaard and Jacobsen found that smoking more than 20 cigarettes/day was associated with increased risk of having metabolic syndrome among men and women in a Norwegian longitudinal study.[145]

Sleeping duration

Both short and long sleeping duration have been related to metabolic syndrome. Researchers from The Nurses Health Study suggested that restriction of sleeping hours may be a risk factor of diabetes.[146] In NHANES I, less than 5 hours sleep and more than 9 hours sleep was also associated with higher risk of having diabetes after a 10 years follow-up.[147] Moreover, lack of sleep was also found associated with obesity and hypertension.[148-150] However, it was argued that the association between lack of sleep and higher risk of obesity was overestimated; instead, daytime sleepiness (due to lack of sleep) and physical inactivity result in a lower energy expenditure than energy intake.[151] Horne suggested that an intervention of 10 minutes of exercise per day could obtain the same effect as sleeping for one or more hours in reducing body fat among children.[152] In 2013, Ju and Choi conducted a systematic review and meta-analysis on sleep duration and metabolic syndrome risk among adults.[153] They suggested that less than 6 hours/day sleepers had higher risk of having metabolic syndrome among 12 cross-sectional and 3 cohort studies, while more than 8 hours/day sleepers also had higher risk of having metabolic syndrome among 11 cross-sectional studies, and 2 cohort studies. However, the associations between sleep duration and metabolic syndrome (and its components) are moderate; and it could be confounded by other lifestyle factors, such as, physical activity, energy intake/expenditure.[153] Furthermore, lack of sleep may also impair immunity and further leads to inflammatory response and metabolic syndrome.[154] Therefore, the effect of sleeping duration on metabolic syndrome and its components still needs further investigation.

2.5.5 BMI and weight gain

Studies showed that higher BMI and weight gain over time are associated with the risk of having some components of metabolic syndrome—high blood pressure, high triglycerides, and high blood glucose.[155;156]

Atlantis et al found that weight gain was associated with higher risk of metabolic syndrome in an Australian longitudinal study.[157] Also in the Coronary Artery Risk Development in Young Adults study, BMI was a significant predictor of metabolic syndrome risk in all sex and race groups (black and white).[113] Weight gain was associated with increased risk of metabolic syndrome in the study. Moreover, the strong predictive value of BMI and weight gain over 15 years on metabolic syndrome

did not change when excluding central obesity as a component of metabolic syndrome.

2.5.6 Hormones changes

Imbalanced sex hormones may represent a risk factor for metabolic syndrome. Specifically, during menopause, reduction of estrogen production leads to some metabolic disorders. According to a meta-analysis by Neugarten and colleagues, menopause was associated with all the components of metabolic syndrome.[158]

In addition, polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders. The PCOS also can result in obesity, type 2 diabetes, and high cholesterol levels which are the components of metabolic syndrome. Because PCOS and metabolic syndrome share insulin resistance as an important element in their pathophysiology, it may explain some of the gender differences in metabolic syndrome over time.[159] Glueck and colleagues found the surprising result that the incidence of metabolic syndrome in newly diagnosed PCOS patients to be 46%, which indicates a higher overlap among metabolic syndrome and PCOS patients.[160] Nestler et al found the prevalence of the metabolic syndrome was 43% among PCOS patients diagnosed after a 3-year period and it was nearly twofold higher than the age-adjusted prevalence rate of 24% in women in the general population.[161]

Studies also showed that low testosterone level also associated with increased prevalence of metabolic syndrome components, such as hypertension in men.[158;162;163]

2.5.7 Family history

Family history may through both genetic and environmental pathways be important in the prevention of metabolic syndrome. A study used family history of diabetes and cardiovascular disease and childhood BMI to predict metabolic syndrome in adulthood.[164] Results showed that after adding family history to BMI, the predicted probability of adult metabolic syndrome rose from 29% to 52% among adults who were overweight as children. In addition, another study in the U.S. showed that people with moderate and high familial diabetes risk had higher risk of having metabolic syndrome compared to the average familial risk (Odds ratios: 1.41-1.62, 1.58-1.79, respectively; the strata of the familial risk was determined by how close and how many relatives were not well).[165]

2.5.8   Other health conditions

There are some other health conditions which are considered as risk factors for metabolic syndrome. For example, obstructive sleep apnoea was independently associated with risk of metabolic syndrome, and non-alcoholic fatty liver disease was seen as a feature of metabolic syndrome;[166;167] however, the link and pathogenesis between these health conditions and metabolic syndrome still need to be investigated further.[168;169]

Apart from the risk factors discussed above, diet is another factor thought to be an important underlying risk factor for metabolic syndrome, and it is also the main exposure of this thesis. In the following section, nutrition in health research, dietary patterns in health research, dietary patterns in relation to metabolic syndrome and its components will be described and existing evidence will be summarised.

2.6   The history of nutrition in health research

For hundreds of years, the possible effects of nutrition on health have been considered important in society. In L'Orange's book in 2002, a note from Hippocrates said, 'Leave your drugs in the chemist's pot if you can cure the patient with food'.[170] This quote shows that the importance of food and nutrition in health has been discussed throughout history.

During Medieval and Tudor periods, eating fresh fruit was not recommended because it was thought to cause fever.[171] Pregnant women were described as having a 'sickness' of craving for fresh fruits, which could be explained by the bodies physiological need of vitamin C. Another vitamin deficiency was discovered by the Newfoundland fishermen. Fishermen reporting 'night blind', now known as a symptom of vitamin A deficiency, were instructed to immediately cook and eat cod liver (which contains high levels of vitamin A).

In the 16th and 17th century, the recommended remedy of scurvy was a mix of oranges, lemons, and scurvy grass, but the cause of it was still unknown.[171] Until 1795, lemon-juice was introduced as a scurvy remedy, and deaths from scurvy dropped dramatically from 1,754 in 1760 to 1 in 1806 in a naval hospital. Drummond estimated the diet records of a working man's family (north of England) in the 18th century and suggested the family was well nourished.[172] He also suggested that the South-Eastern European diet (consisted of little meat, whole-grain bread, think vegetable stews, and

goat's cheese) at the time provided local people sufficient nutrients (eg, calcium, iron, vitamins) for a healthy and strong body.

The first official recorded dietary recommendation was the lemon juice requirement in the rations of British sailors in 1835 to prevent scurvy.[173;174] Subsequently, in 1862, Smith estimated that a 3000kcal of energy from food and 80g of protein per day could prevent starvation in response to the British Government as referred by Harper.[173] In the following 50–60 years, some dietary recommendations based on observing protein or energy intake were proposed, and scientists increasingly realised that some food are protective and especially important for certain population (eg, infants and children). In 19th century, nutrition science was more advanced than former times.[171] Scientists investigated nitrogen, and began realising that protein was an important nutrient for human health.[175] Moreover, scurvy was accepted as a deficiency disease of certain dietary factors, and experiments were implemented on animals for other nutrient deficiency diseases.

From the early 20th century, there was a big improvement in scientific knowledge on vitamins.[176] For example, scientists for the first time found that rickets was associated with lack of vitamin D intake and exposure to sunlight. Moreover, vitamin A, carotene, vitamin E, and vitamin K were first discovered; essential fatty acids were first related to early development in experimental studies of rats. Drummond suggested that a "basic intake of essential protective foods" for the population should be ensured, and suggested a food pattern comprised of wholemeal bread, sufficient vegetables and potatoes, and dairy products (cheese or milk).[172]

During World War II, the rationing run by the UK government was designed to ensure a fair supply of food in all strata of the population.[177] The government also introduced some special measures in order to meet the specific dietary requirements, such as in deficiencies of thiamine and calcium. There were also some food policies for population with special needs. For example, the National Milk Scheme operated from 1940, which provided pregnant woman and children from birth to age five with one pint of milk at a reduced price or free of charge; the Vitamin Scheme entitled pregnant women to a daily concentrated orange juice (contained 25mg of vitamin C) and cod liver oil or supplement tablets (containing 4000IU vitamin A, 800IU vitamin D, and 250mg calcium phosphate). Moreover, the nutritional status of the UK population was under close observation by the Ministry of Health via running food surveys, clinical surveys, and adult body weight surveys.[177]

In 1943, the full report of Recommended Dietary Allowances (RDAs) was published by the American Dietetic Association.[178] RDAs was one of the first dietary guidelines aimed at preventing diseases and improving dietary quality in the entire population. Since then, organisations proposed different dietary recommendations to improve people's health. From the second half of the 20th century, the affluent diet was doubted to be healthy for the first time.[179] It was suggested that after World War II, people in affluent countries were at higher risk of chronic diseases at middle-age. Furthermore, scientists began to compare fat intake and ischaemic heart disease mortality in different countries.[179]

In the early 1990s, Popkin proposed the nutrition transition concept.[180] He believed that nutrition patterns had shifted and would shift in the future in parallel with economic, demographic, and epidemiological changes. He suggested that nutrition transition affects and is affected by two other historic transitions: demographic and epidemiological transitions. The demographic transition indicates the shift from a pattern of high fertility and high mortality to a pattern of low fertility and low mortality, while the epidemiological transition is the shift from a pattern of high prevalence of infectious diseases associated with malnutrition, famine, and poor sanitation, to a pattern of high prevalence of chronic diseases associated with modern lifestyle. In addition, five nutrition patterns are summarised by Popkin in chronological order, but any pattern is not specifically restricted to a certain historical period and could be the characteristic of any geographic or socioeconomic subpopulations: Pattern 1 is collecting food, which was characterised by a diet with high intake of carbohydrates and fibre but low in saturated fat among hunter-gatherer populations; Pattern 2 is famine, characterised by scarcity of food; Pattern 3 is receding famine, characterised by increasing intake of fruits, vegetables, and animal protein while starchy foods (eg, potatoes) become less important; Pattern 4 is nutrition related non-communicable diseases, characterised with a diet high in total fat, cholesterol, sugar and other refined carbohydrates and low in polyunsaturated fatty acids and fibre, also accompanied by an increasingly sedentary life; Pattern 5 is behavioural change, and it is the result of changes in diet in order to prevent degenerative diseases and prolong health. Western high-income countries, such as the U.S., the United Kingdom, and other Western European countries, have changed from a receding famine to degenerative diseases pattern, then to the behavioural change with health conscious pattern among at least some subpopulations (eg, higher educated population). In Eastern Europe, the intake of saturated fats accounted for 25% of the energy intake, which could be explained by moving from receding famine to nutrition related non-

communicable diseases pattern. This is because saturated fats impairs plasma cholesterol levels, which may result in the development of metabolic disorders,[181] For example, in Russia, between 1970s and 1990s, the consumption of starchy food (eg, potatoes) and cereals declined while the consumption of sugar and red meat increased a lot.[182] In addition, the change of diet also accompanied increasing obesity prevalence. The nutrition transition has occurred worldwide, and it will likely continue in different populations accompanying economic changes.

The development of nutritional epidemiology as a discipline was influenced by both the nutritional and epidemiological transitions. It is originally based on the influential role of diet on disease occurrence.[183] Until 1980s, scientists still mostly focused on sanitation and nutrients deficiencies in the general population in the last 3 decades, the focus moved to the prevention of chronic diseases in the developed world, as well as some developing countries.[183]

Studies have since found that some particular foods (eg, fruits and vegetables, cereals) or nutrients (eg, fat) are associated with the risk of some non-communicable diseases, such as cardiovascular diseases, type 2 diabetes, and cancer.[184-189] For example, a systematic review of cohort studies showed that increased intake of monounsaturated fatty acids was associated with lower risk of coronary heart disease, while the increased intake of trans fatty acids was associated with higher risk of coronary heart disease.[185] A systematic review and meta-analysis showed that the increased consumption of green leafy vegetables was associated with lower risk of having type 2 diabetes.[186] Another systematic review and dose-response meta-analysis showed that for an increase of three servings of daily whole grain intake, the risk of developing colorectal cancer decreased.[187]

Apart from examining the association between a single/specific foods or nutrient consumption and health, the relationship between a combination of foods—so called 'dietary patterns'—and health outcomes has also been investigated. Dietary patterns account for the fact that people eat meals containing multiple components instead of a single food or nutrient. In the next section, dietary pattern research will be discussed.

2.7   Dietary patterns in health research

Dietary pattern research has become popular in recent years due to some limitations of traditional methodology (ie, examining association between single or a few nutrients and health outcomes) in nutritional epidemiology. First, people eat meals

rather than single nutrients, and the interactions between the components of a diet and certain disease risk can be ignored when only examining a single nutrient or food study. For example, non-haem ferric iron (Fe^{3+}) is not easily absorbed in the human body; instead, it needs to be reduced to Fe^{2+} before absorption in the intestine; while vitamin C from food helps with the transformation from Fe^{3+} to Fe^{2+}.[190] Second, some nutrients are highly intercorrelated (eg, when magnesium is low in the body, potassium is also low), which makes it difficult to examine their separate effects because the degree of independent variation of the nutrients is markedly reduced when they are entered into a model simultaneously. Also, the effect of a single nutrient may be too small to detect, but the cumulative effects of several nutrients (eg, some minerals and fibres are often consumed together) may be sufficiently large to be detectable.[48;191]

Because of its advantages, studying dietary patterns has received considerable attention in the past three decades. In general, dietary pattern studies can be divided into two categories: a priori and a posteriori dietary pattern studies. 'A priori' studies evaluate the adherence to a pre-defined dietary patterns or dietary guidelines (also known as score-based), while 'a posteriori' studies involve statistical methods to derive patterns within different populations (also known as post-hoc).

2.7.1   A priori dietary patterns

A priori dietary patterns approaches are often based on dietary recommendations of foods and/or nutrients. There are many different a priori dietary scores, however, there are four main dietary quality scores which are commonly used and modified in nutrition studies: the Healthy Eating Index, the Dietary Quality Index, the Mediterranean Diet Score, and the Healthy Diet Indicator.[192] The Healthy Eating Index, the Dietary Quality Index, and the Healthy Diet Indicator are created based on dietary guidelines or recommendations on a daily basis, while the Mediterranean Diet Score was inspired by the low risk of coronary heart diseases and cancer in Mediterranean regions. These four dietary quality scores will be described below in detail.

Healthy Eating Index

The Healthy Eating Index was proposed by Kennedy and colleagues in 1995.[193] Ten components were included in the original index: components 1 to 5 are five major food groups based on the daily serving recommendations from the U.S. Department of Agriculture Food Guide Pyramid—grains, vegetables, fruits, milk, meat; Component

6 and 7 are daily total fat and saturated fat intake as percentage of total energy intake; Component 8 and 9 are cholesterol and sodium intake per day; and component 10 is based on food variety over a 3-day period. Each component has a score ranging from 0 to 10 and a total score ranges from 0 to 100 (see Table 2). A higher score in Healthy Eating Index represents a better dietary quality. In 2005, a new version of Healthy Eating Index was developed to reflect the emphasis on increasingly important aspects of diet. The Healthy Eating Index-2005 (new version of Healthy Eating Index) included 9 adequacy components (ie, intake of certain food should be enough in order to provide the nutrients that the body needs): total fruit (score 0-5), whole fruit (score 0-5), total vegetables (score 0-5), dark green and orange vegetables and legumes (score 0-5), total grains (score 0-5), whole grains (score 0-5), milk (score 0-10), meat and beans (score 0-10), and oils (score 0-10); also it included 3 moderation components (ie, certain nutrients are recommended to have a limited intake): saturated fat (score 0-10), sodium (score 0-10), and calories from solid fat, alcohol, and added sugars (score 0-20) (see Table 3). The total score of Healthy Eating Index-2005 still ranges from 0 to 100.[194;195] In April 2013, a new update of Healthy Eating Index-2010 was published to reflect the new release of Dietary Guidelines for Americans-2010 and revised the United States Department of Agriculture Food Patterns to emphasize the importance of seafood intake and limitations of refined grains.[196] In the Healthy Eating Index-2010, total fruits, whole fruit, total vegetables, total grains, sodium, milk, and meat and beans were carried forward from Healthy Eating Index-2005, only the milk was renamed to dairy and meat and beans was renamed to total protein foods. In the Healthy Eating Index-2010, the "Empty Calories" was used instead of "Calories from solid fats, alcohol, and added sugars"; dark green and orange vegetables and legumes was modified to "greens and beans"; seafood and plant proteins were newly added; fatty acids replaced saturated fats and oils; and total grains was replaced by refined grains (see Table 4).

Table 2 Healthy Eating Index-1995[193]

Components	Score range	Highest score (daily)	Lowest score (daily)
Grains	0-10	6-11servings=10	0 serving=0
Vegetables	0-10	3-5 servings=10	0 serving=0
Fruits	0-10	2-4 servings=10	0 serving=0
Milk	0-10	2-3 servings=10	0 serving=0
Meat	0-10	2-3 servings=10	0 serving=0
Total fat	0-10	≤30% =10	≥45% =0
Saturated fat	0-10	<10% =10	≥15%=0
Cholesterol	0-10	<300mg=10	≥450mg=0
Sodium	0-10	<2400mg=10	≥4800mg=0
Variety	0-10	16 kinds of food items over 3-day period=10	≤6 food items over a 3-day period=0

Table 3 Healthy Eating Index-2005[194;195]

	Components	Score range	Highest score	Other scores	Lowest score
Adequacy	Total fruit (include100% juice)	0-5	≥0.8 cup eq/1000 kcal=5		No fruit
	Whole fruit (except juice)	0-5	≥0.4 cup eq/1000 kcal=5		No whole fruit
	Total vegetables	0-5	≥1.1 cup eq/1000 kcal=5		No vegetables
	Dark green and orange vegetables and legumes	0-5	≥0.4 cup eq/1000 kcal=5	The score was calculated proportionately	No dark green or orange vegetables or legumes
	Total grains	0-5	≥3.0 oz eq/1000 kcal=5		No grains
	Whole grains	0-5	≥1.5 oz eq/1000 kcal=5		No whole grains
	Milk	0-10	≥1.3 cup eq/1000 kcal=10		No milk
	Meat and beans	0-10	≥2.5 oz eq/1000 kcal=10		No meat or beans
	Oils	0-10	≥12 g/1000 kcal=10		No oil
Moderation	Saturated fat	0-10	≤7% of the energy intake =10	=10%=8 (other scores are calculated proportionally)	≥15% of energy=0
	Sodium	0-10	≤0.7g /1000 kcal	=1.1g/1000 kcal=8 (other scores are calculated proportionally)	≥2.0g /1000 kcal
	Calories from solid fats, alcoholic beverages, and added sugars	0-20	≤20% of energy	calculated proportionally	≥50% of energy

Table 4 Healthy Eating Index-2010[196]

	Components	Score range	Highest score	Lowest score
Adequacy	Total fruit (include100% juice)	0-5	≥0.8 cup eq/1000 kcal=5	No fruit
	Whole fruit (except juice)	0-5	≥0.4 cup eq/1000 kcal=5	No whole fruit
	Total vegetables	0-5	≥1.1 cup eq/1000 kcal=5	No vegetables
	Greens and beans	0-5	≥0.2 cup eq/1000 kcal=5	No dark green vegetables or beans and peas
	Whole grains	0-10	≥1.5 oz eq/1000 kcal=5	No whole grains
	Dairy	0-10	≥1.3 cup eq/1000 kcal=10	No dairy
	Total protein foods	0-5	≥2.5 oz eq/1000 kcal=5	No protein foods
	Seafood and plant proteins	0-5	≥0.8 oz eq/1000 kcal=5	No seafood or plant proteins
	Fatty acids	0-10	(PUFAs + MUFAs)/SFA>2.5	(PUFAs + MUFAs)/SFA≤1.2
Moderation	Refined grains	0-10	≤1.8 oz eq/1000 kcal	≥4.3 oz eq/1000 kcal
	Sodium	0-10	≤1.1g /1000 kcal	≥2.0g/1000 kcal
	Empty calories	0-20	19% of energy	≥50% of energy

Dietary Quality Index

The Dietary Quality Index was developed by Patterson and colleagues in 1994 and aimed to measure overall diet related to chronic diseases using dietary recommendations from the American Committee on Diet and Health.[197;198] Eight dietary elements were included: intake of total fat, saturated fatty acid, cholesterol, fruit and vegetables, grains and legume, protein, sodium, and calcium. For each element, score 0, 1, and 2 was assigned: 0 was assigned to participants who achieved the nutrition goal, while a 2 score was assigned when they have not achieved it. The total index score ranges from 0 to 16, where a lower score represent a better dietary quality (see Table 5). In 1999, a revised Diet Quality Index was proposed by Haines, Siega-riz, and Popkin.[199] The Diet Quality Index Revised version aimed at reflecting current dietary guidance and incorporates improved methods of estimating food servings. Iron intake was newly added in the revised Diet Quality Index. Moreover, two new scores—dietary diversity and dietary moderation—were also added in order to measure the dietary structure. The dietary diversity score was developed to capture the consumption of 4 different food groups: grains, vegetables, fruits, and meat/dairy. The dietary moderation score was developed based on four dietary elements: added sugar, discretionary fat, sodium intake, and alcohol intake (see Table 6).

Table 5 Diet Quality Index-1994[198]

Components	Highest score	Score range	Lowest score
Total fat	>40%=2	0-2	≤30%=0
Saturated fatty acid	>13%=2	0-2	<10%=0
Cholesterol	>400mg=2	0-2	<300mg=0
Fruits and vegetables	0-2 servings=2	0-2	≥5 servings=0
Breads, cereals, and legumes	0-3 servings=2	0-2	≥6 servings=0
Protein	>150% RDA=2	0-2	≤100% RDA=0
Sodium	>3400mg=2	0-2	≤2400mg=0
Calcium	<2/3 DRI*=2	0-2	≥DRI=0

*DRI: dietary reference intake

Table 6 Diet Quality Index Revised-1999[199]

Components	Score range	Highest score	Other score	Lowest score
Total fat	0-10	≤30%=10	>30,≤40%=5	>40%=0
Saturated fatty acid	0-10	≤10%=10	>10, ≤13%=5	>13%=0
Cholesterol	0-10	≤300mg=10	>300, ≤400mg=5	>400mg=0
Fruit	0-10	2-4 servings		
Vegetables	0-10	3-5 servings		
Grains	0-10	6-11 servings	Calculated proportionally according to the recommended intake	
Calcium	0-10	% adequate intake value for age		
Iron	0-10	% 1989 RDA for age		
Dietary diversity score	0-10	Any food group out of 4 has a maximum point of 2.5(out of 10 in total). The score was calculated proportionally.		
Dietary moderation score	0-10	Any component out of 4 has a maximum point of 2.5 (out of 10 in total). Each component has score cut-points at 2.5, 1.5, 1.0, and 0.		

Mediterranean Diet Score

The Mediterranean diet has been supported by institutions since early 1990s due to its suspected beneficial effects in certain populations.[200] The highest life expectancy and the lowest prevalence of coronary heart disease, certain cancers, and some other diet-related chronic diseases in 1960s were observed in Crete, most of Greece, and southern Italy. Moreover, studies showed that some dietary patterns which share the similarities with Mediterranean diet have been associated with low risk of some chronic diseases. In 1995, Trichopoulou proposed the Mediterranean Diet Score based on a traditional Mediterranean diet which is characterised by a high intake of fruits and vegetables, legumes and nuts, cereals, fish, and olive oil (as the main source of fat), but a low intake of saturated fats, a low-to-moderate intake of dairy products, a low red meat intake, and a regular and moderate alcohol intake during meals.[201] The Mediterranean Diet was revised in 2003 and now included nine components: vegetables, legumes, fruits and nuts, fish, meat, poultry, dairy products, ethanol, and ratio of monounsaturated lipids to saturated lipids.[202] As beneficial components, vegetables, legumes, fruits and nuts, fish, and ratio of monounsaturated lipids to saturated lipids, a score of 1 was assigned to participants who have a consumption at or above the median intake, while score of 0 was assigned to those whose consumption was below the median intake; as detrimental components, meat, poultry, and dairy products, a score of 1 was assigned to participants who have a consumption below the median intake, while score of 0 was assigned to whom have a consumption at or above the median intake. For ethanol, a score of 1 was assigned to men who have a consumption between 10 and 50 gram per day, and women who have a consumption between 5 and 25 gram per day, otherwise a 0 score was assigned. In total, the Mediterranean Diet Score ranges from 0 to 9, with a high score representing a better quality diet (see Table 7).

Table 7 Mediterranean Diet Score-2003[202]

Components	Score range	Highest score	Lowest score
Vegetables	0-1		
Legumes	0-1	Beneficial components: if a person's consumption is <u>above</u> the median, a score 1 is assigned.	If a person's consumption is <u>below</u> the median, a score 0 is assigned.
Fruits and nuts	0-1		
Fish	0-1		
Monosaturated lipds:saturated lipids	0-1		
Meat	0-1	Detrimental components: if a person's consumption is <u>below</u> the median, a score 1is assigned.	If a person's consumption is <u>above</u> the median, a score 0 is assigned.
Poultry	0-1		
Dairy products	0-1		
Ethanol	0-1	Men: 10-50g/day= 1 Women: 5-25g/day=1	Men: <10 or >50g/day=0 Women: <5 or 25g/day=0

Healthy Diet Indicator

The Healthy Diet Indicator was first developed by Huijbregts and colleagues in 1997.[203] The Healthy Diet Indicator was developed based on World Health Organisation (WHO) daily dietary guidelines for the prevention of chronic diseases.[204] There are nine components in the Healthy Diet Indicator: saturated fatty acids, polyunsaturated fatty acids, protein, complex carbohydrates, dietary fibre, fruits and vegetables, pulses/nuts/seeds, monosaccharides and disaccharides, and cholesterol. Each component was generated into a dichotomous variable: a score of 1 was assigned to participants who have daily consumption of food within the recommended range, otherwise a score of 0 was assigned. The total score of Healthy Diet Indicator ranges from 0 to 9 (see Table 8). In 2003, WHO updated the daily dietary guidelines for the prevention of chronic disease, and 15 dietary factors were included in the guidelines: total fat, saturated fatty acids, polyunsaturated fatty acids, n-6 polyunsaturated fatty acids, n-3 polyunsaturated fatty acids, trans fatty acids, monounsaturated fatty acids, total carbohydrate, free sugars, protein, cholesterol, sodium chloride, fruits and vegetables, total dietary fibre, non-starch polysaccharides.[205] In Table 9, the HDI score adapted to the updated WHO guidelines is shown.

Table 8 Healthy Diet Indicator-1997[203]

Components	Score range	Highest score (daily)	Lowest score (daily)
Saturated fatty acids	0-1	0-10% of energy intake	>10%
Polyunsaturated fatty acids	0-1	3-7%	<3% or >7%
Protein	0-1	10-15%	<10% or >15%
Complex carbohydrates	0-1	50-70%	<50% or >70%
Dietary fibre (g)	0-1	27-40g	<27g or >40g
Fruits and vegetables (g)	0-1	≥400g	<400g
Pulses, nuts, seeds (g)	0-1	≥30g	<30g
Monosaccharides and disaccharides	0-1	0-10%	>10%
Cholesterol (mg)	0-1	0-300mg	>300mg

Table 9 Healthy Diet Indicator adapted to updated WHO guidelines-2003

Components	Score range	Highest score (daily)	Lowest score (daily)
Saturated fatty acids	0-1	0-10% of energy intake	>10%
Polyunsaturated fatty acids	0-1	6-10%	<6% or >10%
Protein	0-1	10-15%	<10% or >15%
Complex carbohydrates	0-1	50-70%	<50% or >70%
Dietary fibre (g)	0-1	27-40g	<27g or >40g
Fruits and vegetables (g)	0-1	≥400g	<400g
Pulses, nuts, seeds (g)	0-1	≥30g	<30g
Monosaccharides and disaccharides	0-1	0-10%	>10%
Cholesterol (mg)	0-1	0-300mg	>300mg

The above four most popular 'a priori' dietary patterns vary in both their components and score system. The Healthy Eating Index, Diet Quality Index, and Healthy Diet Indicator include a mix of components in both nutrients and foods, while the Mediterranean Diet Score includes foods and a ratio of monosaturated lipids and saturated lipids.

Although the components in these dietary indices and patterns are different from each other, there are still some specific foods/nutrients included in all patterns; they are fruits, vegetables, cholesterol, sodium, and saturated/unsaturated fatty acids. In the Healthy Eating Index, Diet Quality Index, and Healthy Diet Indicator, the scoring is based on dietary guidelines to set certain cut-points for each component, while the Mediterranean Diet Scale used the group median as the cut-points for each dietary component (except for ethanol). The disadvantages of using the median as cut-points have been widely discussed.[206] Since the median is not based on any scientific guidelines, the value of the cut-point does not necessarily reflect a healthy cut-off value; moreover, the median would differ in different populations and studies, which makes comparison between studies difficult. The Healthy Diet Indicator, defined by Huijbregts[203] in 1997 and adapted it to WHO 2003 guidelines,[205] is the main explanatory variable used in this thesis, and its use in health research to date is summarised in the section 2.8.

2.7.2 A posteriori dietary patterns

A posteriori dietary patterns are derived using statistical methods, and are not based on any predefined dietary guidelines. The statistical methods included so far in population studies are factor analysis, principal components analysis, cluster analysis, and reduced rank regression. Although these three methods share the same aim in dietary pattern research, they are different in some ways. Factor analysis and principal component analysis are essentially dealing with the same problems in the data, however, factor analyses analyse covariance while principal component analyse variance. In addition, principal component analysis assumes that the components derived depend on the observed measures, while factor analysis has a reversed direction- observed measures are based on latent factors. Reduced rank regression is very different from the aforementioned two methods, it accounts for a priori information on the pathways between predictors (dietary factors) and responses (health outcome).[207] The summary of literature on posteriori dietary patterns and metabolic syndrome will be discussed in section 2.10.

2.7.3 Strengths and limitations of a priori and a posteriori dietary patterns

The strengths and limitations of a priori and a posteriori dietary patterns have been discussed for the past two decades. A priori dietary patterns and a posteriori including nutrients, food group, or a mix of both could represent total diet in study population; moreover, both methods can be used to examine the association between dietary patterns and health outcomes. Apart from this, there are some more advantages of using a priori dietary patterns in research. First, a priori dietary patterns are score-based indices which are typically easier to calculate and interpret. Second, a priori dietary patterns are based on dietary guidelines which made it easy to reproduce the dietary patterns in different population (eg, different countries) and to compare the dietary intake status between different studies. The advantages of using a posteriori dietary patterns in research are: first, the patterns can describe the variation in food intake based on the correlation between different food intakes; second, in cluster analysis, people with similar dietary intake patterns are separated to same group; third, in reduced rank regression, it also helps understand the pathways between diet and health outcomes.

Both a priori and a posteriori methods have limitations. A priori dietary pattern methods are often dichotomise/categorised dietary data, therefore lose potentially valuable information; second, the different food groups are typically equally weighted partitions (eg, fruit group, nut group), this assumes that certain components in diet are equally important. A posteriori dietary patterns differ in different datasets, which makes it difficult to make comparison between studies; secondly, there are subjective decisions to make while deriving dietary patterns using statistical methods—for example, grouping the dietary factors (eg, including potato in the vegetable group or not), the forms of the input variables (eg, portions/grams/percentage of energy intake), selecting the final patterns (eg, using eigenvalue>1).

2.8 Healthy Diet Indicator and health outcomes

Since the Healthy Diet Indicator (HDI) was proposed in 1997, over the past two decades, its association with a variety of different health outcomes has examined, such as mortality, cognitive function, and cancer risks. The characteristics of epidemiological studies using HDI as a dietary exposure are summarised in Table 10.

The association between HDI and mortality was first examined in western European populations, and later in other populations.[203;208-210] Huijbregts and colleagues found

that people with higher adherence to HDI (in Finland, the Netherlands, and Italy) had 13% less risk of all-cause death compared with those with lower adherence to HDI after 20 years follow-up (RR=0.87, 95%CI: 0.77-0.98).[203] Knoops and colleagues examined the association between HDI and 10-year mortality in HALE project (Healthy Ageing: a Longitudinal study in Europe).[208] They also showed a mild inverse association between high HDI score and all-cause mortality (HR=0.89, 95%CI: 0.81-0.98). However, in some small population studies, the mild protective effect of high HDI score on mortality was not found. Sjogren and colleagues found no association between HDI score and all-cause mortality or cardiovascular disease mortality in a Swedish population sample.[209] A Polish study showed that women aged 75-80 years with lower HDI score had 39% lower of the risk of all-cause death, but the association was not found among men.[210]

The association between HDI and cognitive function was also investigated in several studies. Huijbregts et al found that an increased HDI score was associated with lower prevalence of mild cognitive impairment (OR=0.87, 95%CI: 0.77-0.99).[211] Correa Leite et al also found that a better HDI score was associated with a lower prevalence of cognitive deficit (OR=0.85, 95%CI: 0.77-0.93).[212]

Cade et al and Berentzen et al investigated HDI score in relation to cancer risks.[213;214] Cade et al did not find that HDI score was associated with breast cancer risk after 9-year follow-up.[213] In addition, Berentzen et al's study showed that the adherence to HDI was not associated with overall cancer risk, smoking-related cancer risk, or alcohol-related cancer risk.[214]

Apart from the aforementioned health outcomes, some studies also focused on the association between HDI and biomarkers. In the Framingham Heart Study and SENECA (Survey in Europe on Nutrition and the Elderly: a Concerted Action) study, Haveman-Nies and colleagues showed that people with HDI score greater than 3 had smaller waist circumference and lower body mass index than people with HDI score less than 3.[215]

Other studies have investigated HDI and health outcomes using specific population group, such as diabetes patients and children.[216-218] In addition, Rodrigues et al and Cade et al investigated the association between HDI and socioeconomic status.[219;220] The details of these studies are presented in Table 10.

Since 1997, the effect of HDI on health has not been investigated in Central and Eastern European Countries. Apart from the aforementioned mortality study in

Poland, to the author's knowledge, there is only one study focused on the dietary adherence on HDI in the Czech Republic, Russia, and Poland.[37] Using data from HAPIEE study, Boylan et al showed a low adherence to HDI in the above regions with mean HDI score ranging from 1.0 to 1.7 out of a total score of 7. Few participants met HDI guidelines on complex carbohydrates, pulses or nuts, and the intake of saturated fatty acids, sugar, and protein exceeded the WHO's recommendation limits.

Table 10 Healthy diet indicator in health research

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Huijbregts et al. (1997)[203]	Cohort study	20 years	Finland, Italy, the Netherlands (5 cohorts)	Sample size: 3045 Age: 50-70yrs Sex: Men	Mortality	Cross check dietary history	Based on WHO guideline 1990. 9 components: SFA, PUFA, protein, complex carbohydrates, dietary fibre, fruits and vegetables, pulses/nuts/seeds, monosaccharides and disaccharides, cholesterol.	HDI was associated with increased risk of mortality.
Huijbregts et al. (1998)[211]	Cross-sectional study	n/a	Finland, The Netherlands, and Italy	Sample size:1049 Age: 70-91yrs Sex: men.	Cognitive function (Mini-Mental State Examination), a score of 23 or lower was used to indicate cognitive impairment	Cross check dietary history	Same Huijbregts et al. (1997)	HDI score was inversely associated with mild cognitive impairment.

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Cade et al. (1999)[221]	Cross-sectional study	n/a	UK	Sample size:15191 Age: 35-69yrs Sex: women	Same Huijbregts et al. (1997) excluded cholesterol	FFQ	Direct costs and indirect costs	Increased costs was associated with higher dietary score
Correa Leite et al. (2001)[212]	Cross-sectional study	n/a	Italy	Sample size: 1651 Age : >=65 yrs Sex: men and women	Cognitive function (cognitive deficit)	FFQ	Same Huijbregts et al. (1997)	HDI score was associated with lower prevalence of cognitive deficit.

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Haveman-Nies A et al. (2001)[215]	Cross-sectional study (multi-centred)	n/a	U.S., Belgium, Denmark, Italy, The Netherlands, Portugal, Spain, Switzerland	Sample size:1110 Age: 70-77yrs Sex: men and women	Serum albumin, haemoglobin, BMI, waist circumference	FFQ & dietary history method	Same Huijbregts et al. (1997)	Waist circumference and BMI were significant lower in people with high HDI score (>3) compared to the low HDI counterparts (≤3).
Knoops et al. (2006)[208]	Cohort study (multi-centred)	10 years	Belgium, Denmark, France, Greece, Italy, The Netherlands, Portugal, Spain, Switzerland, Finland	Sample size: 3093 Age: 70-90 yrs Sex: men and women	All-cause mortality	Dietary history	Same Huijbregts et al. (1997)	HDI score was inversely associated with mortality. SFA intake was positively associated with mortality. The intake of fibres and fruits and vegetables was inversely associated with mortality.

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Rodrigues et al. (2008)[220]	Cohort study	10 years	Portugal	Sample size: 10020 households Age: all Sex: men and women	Education, urbanisation, household income, expenditures on outside home food	Data food networking (food availability from surveys)	Revised version of HDI: added sodium and alcohol in the HDI. Also, they revised the cut-points of PUFA, and fibre in accordance with the new 2003 WHO/FAO guidelines.	Households whose head had higher education, living in more urbanised areas, from the Azores region, and with higher income or higher expenditure on outside home food were more likely to have a low-quality diet (either low HDIr or Mediterranean Adequacy Index score)
Sjogren et al. (2010)[209]	Cohort	10 years	Sweden	Sample size:1221 Age:70yrs Sex: men	All-cause mortality and CVD mortality	7-day dietary record	Based on WHO 2003. HDI was modified under the guidelines advocated by the Swedish recommendations (-1-8 scores). HDI includes SFA, PUFA, protein, total carbohydrates, sucrose, fibre, fruit and vegetables, cholesterol, fish (9 components)	No association between HDI and all-cause or CVD mortality

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Frackiewicz et al (2010)	Cohort study	Not clear	Poland(Warsaw)	Sample size: 411 Age: 75-80 yrs Sex: men and women	All-cause mortality	3-day food intake	Same Huijbregts et al. (1997)	the risk of all-cause mortality was statistically significantly lower in women with lower HDI and DQI-R compared to women with higher quality of diet. A similar tendency was shown for MDS indicator.
Cade et al (2011)	Cohort study	9yrs	UK	Sample size: 33731 Age:35-69 yrs at baseline Sex: women	Breast cancer	FFQ	HDI was based on WHO 2003 10 components: total fatty acids, saturated fatty acids, polyunsaturated fatty acids, total carbohydrates, non-starch polysaccharides, fruits and vegetables, protein, cholesterol, salts.	HDI was not associated with breast cancer risk
Jennings et al (2011)	cross-sectional study	n/a	UK	Sample size: 1700 Age: 9-10 yrs Sex: boys and girls	Weight status	4-day food diary	HDI score were modified to be reflective of children's diets	High HDI score was associated with improved weight status. Comparing extreme quintiles of HDI scores were associated with lower waist circumference and

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Berentzen et al 2013	Cohort study	12.7 yrs	The Netherlands	Sample size: 35555 Age: 20-65 yrs at baseline Sex: men and women	Overall Cancer Risk, smoking related cancer, alcohol-related cancer	FFQ	Based on WHO 2003. 7 components: SFA, PUFA, cholesterol, protein, dietary fibre, fruits and vegetables, free sugars.	Adherence to the HDI was not associated with reduced overall cancer risk or smoking-related cancer, or alcohol-related cancer
Kim et al (2013)	cross-sectional study		Korea	Sample size: 110 consecutive outpatients with type 2 diabetes. Age: mean age 55 yrs Sex: men and women	HbA1C, fasting plasma glucose, postprandial 2-h glucose	24h dietary recall	Same Huijbregts et al. (1997)	HDI was correlated with HbA1c, fasting plasma glucose, and postprandial 2h glucose

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Murray et al (2013)	cross-sectional study	n/a	Ireland	Sample size: 111 Caucasian adults(65 with type 2 diabetes). Age: 30-75 yrs Sex: men and women	n/a	3-day dietary diary	Same Huijbregts et al. (1997)	HDI was significantly lower among people with type 2 diabetes compared to people without.
Atkins et al (2014)[222]	Cohort study	11.3 years	UK	Sample size: 3328 Age: 60-79 years Sex: men	CVD and all-cause mortality, CVD and CHD events	FFQ	Same Huijbregts et al. (1997) but modified PUFA, fibre, and fruits/vegetable intake.	HDI score was not associated with any outcome of interest. But higher HDI score was associated with lower HDL-C, less chance being smokers, heavy drinkers, manual social class or obese, and had lower energy intake, and C-reactive protein level. Following the cholesterol guidelines was associated with lower risk of CVD mortality.

Authors (year)	Study type	Follow-up time	Country	Sample characteristics	Outcome /exposure	Dietary assessment method	Exposure (HDI forms)	Results
Santos et al (2014)[223]	Cross-sectional studies (Household Budget Surveys)	n/a	Portugal	Sample size*: 1990:3733 1995:3588 2000:4003 2005:4294 Age: >18years Sex: men and women	Education level, family income, eating out expense, region, urbanisation level	An open questionnaire and subsequently recorded into 500 codes	Same as Rodrigues et al. (2008)	Education level, eating out expenses were inversely associated with HDI score, only among the solitary men, education level was positively associated with HDI score.

*Household surveys including years of 1990, 1995, 2000, and 2005.

Abbreviations: WHO- World Health Organisation; HDI- Healthy Diet Indicator; SFA- saturated fatty acids; PUFA- polyunsaturated fatty acids; FFQ- food frequency questionnaire; CVD- cardiovascular disease

2.9 HDI in relation to metabolic syndrome and its components

In this section, the literature on HDI and its dietary components in relation to metabolic syndrome will be discussed first; then the literature on HDI and its dietary components in relation to components of metabolic syndrome will be discussed. Finally, some literature on other a priori dietary patterns (Healthy Eating Index, Diet Quality Index, and Mediterranean Diet Score) in relation to metabolic syndrome will be discussed.

2.9.1 HDI, components of HDI and metabolic syndrome

To the author's knowledge, there is only one study examining HDI and metabolic syndrome. Alkerwi et al conducted a cross-sectional study among 1349 Europid adults aged 18-69 years in Luxembourg to examine the relationship between dietary factors and metabolic syndrome risk.[224] The dietary score developed by the authors was called as Diet Quality Index according to WHO dietary recommendations on prevention of chronic diseases—the dietary reference base of the HDI.[205] In Alkerwi et al's study, the HDI was consisted of 13 components: saturated fatty acids, polyunsaturated fatty acids, monounsaturated fatty acids, overall fat consumption, n-6:n3 fatty acids, cholesterol, total carbohydrates, simple sugars, total daily energy intake, Na, fruits and vegetables, total fibre, and soluble fibre. However, no association was found between HDI and metabolic syndrome risk (unified AHA/NHLBI&IDF definition).

Apart from this study on HDI and metabolic syndrome, some studies have examined the association between dietary components of HDI and metabolic syndrome. In the following sections, the intake of saturated fatty acids, polyunsaturated fatty acids, protein, complex carbohydrate, dietary fibre, fruits and vegetables, pulses/nuts/seeds, and monosaccharides/disaccharides in relation to metabolic syndrome risk will be discussed.

Saturated fatty acids

Two studies have examined the association between saturated fatty acids intake and metabolic syndrome risk. Hosseini-Esfahani et al found that the high intake of saturated fatty acids was associated with increased risk of metabolic syndrome (modified ATPIII definition- waist circumference≥95cm in both sexes) among 2510 Iranian adults aged 19 to 70 years.[225] De Oliveira et al also found that high saturated fatty acids intake (more than 10% of the daily total energy intake) was associated with

twofold risk of having metabolic syndrome (modified ATP III definition-glucose≥100mg/dL) compared to their counterparts among 305 Brazilian adults.[46]

Polyunsaturated fatty acids

Only one study has been found on polyunsaturated fatty acids intake and metabolic syndrome. Alkerwi et al found no association between polyunsaturated fatty acid intake (preferable intake: 6-10% of total energy intake) and metabolic syndrome risk among 1349 Europid adults aged 18-69 years in Luxembourg.[224]

Protein

Two studies have examined protein intake in relation to metabolic syndrome risk. Damiao et al examined dietary intakes and metabolic syndrome risk among 151 Japanese-Brazilians aged 40-79 years at the baseline.[226] After 7 years follow-up, they found that the protein intake was higher among men with metabolic syndrome compared to those without; moreover, the study also showed that people with higher red meat intake (mostly protein and fat) was associated with 4.7 folds higher risk of having metabolic syndrome compared to those with lower intake, however, the association disappeared after adjusting for saturated fatty acids and protein. In addition, Alkerwi et al found that the protein intake lower than 10% or higher than 15% of total energy intake was significantly associated with 56% higher risk of having metabolic syndrome among 1349 Europid adults aged 18-69 years in Luxembourg.[224]

Complex carbohydrate

Four studies have examined the carbohydrate intake in relation to metabolic syndrome. Kim et al conducted a study among 910 middle-aged Korean adults and found that high intake of dietary carbohydrate was associated with increased risk of metabolic syndrome in women but not in men.[227] In another Korean study, similar results were found. Song et al examined the association between carbohydrate intake and metabolic syndrome risk among 6845 Korean adults aged 30-65 years in the Fourth Korea National Health and Nutrition Examination Survey (KNHANES 2007-2009).[228] They found that high energy intake from carbohydrate was associated with increased risk of metabolic syndrome (modified ATP III definition) among men, but the association was not found among women. Moreover, high intake of refined grains and white rice were associated with increased risk of metabolic syndrome in women but not in men.

However, Kouki et al found no association between white bread intake and risk of metabolic syndrome among either men or women aged 57-78 years in Dose Responses to Exercise Training study.[45] In addition, Alkerwi et al also found no association between total carbohydrates intake (preferable intake: 55-75% of energy intake) and metabolic syndrome risk among 1349 Europid adults aged 18-69 years in Luxembourg.[224]

Dietary fibre

Three studies have examined the dietary fibre intake and metabolic syndrome risk. McKeown et al examined the association between dietary factors and the prevalence of metabolic syndrome among 2834 subjects aged 26-82 years in the Framingham Offspring Study.[44] They found that people with higher cereal fibre intake were 38% less likely to have metabolic syndrome compared to those with lower intake. Hosseini-Esfahani et al also found that the low intake of dietary fibre was associated with high risk of metabolic syndrome among 2510 Iranian adults aged between 19 and 70 years.[225]

However, Alkerwi et al found no association between total fibre intake or soluble fibre intake (preferable intake: >25g/day and >10g/day respectively) and metabolic syndrome risk among 1349 Europid adults aged 18-69 years in Luxembourg.[224]

Fruits and vegetables

Seven studies have examined the fruits and vegetable intake in relation to metabolic syndrome. Esmaillzadeh et al found that people with higher consumption of fruits was associated with 34% lower risk of having metabolic syndrome (ATP III definition), and people with higher consumption of vegetables was associated with 30% lower risk of having metabolic syndrome compared to their counterparts among 486 Iranian female teachers aged 40-60 years.[42] De Oliveira et al also found that people having more than 3 servings of fruits per day was associated with 48% less risk of having metabolic syndrome (modified ATP III definition- glucose≥100mg/dL) compared to people have less than 3 servings in a Brazilian study consisted of 305 adults aged ≥35 years.[46] In addition, Kouki et al found that high intake of vegetables was associated with decreased risk of metabolic syndrome (ATP III definition) among women (n=671) and men (n=673) aged 57-78 years after adjusting for age, alcohol consumption and smoking in the Dose Responses to Exercise Training study.[45] However, after adding education and maximal oxygen uptake in the model, no association between vegetable intake and risk of metabolic syndrome was found. The similar results were

found between non-root vegetables and metabolic syndrome risk. Moreover, the study also showed that high berries intake was associated with decreased risk of metabolic syndrome among men, but this association was not found in women. Also, Yoo et al found that people with no metabolic syndrome component (ATP III definition) have much higher fruit and vegetables intake compared to those with 1-2 components of metabolic syndrome among 1181 adults aged 19-38 years in the Bogalusa Heart Study.[229]

However, some studies found no association between fruit/vegetables intake and metabolic syndrome risk. Alkerwi et al found no association between fruits and vegetables intake (preferable intake: ≥400g/day) and metabolic syndrome risk among 1349 Europid adults aged 18-69 years in Luxembourg.[224] Moreover, Lutsey et al found no association between fruit and vegetable intake and metabolic syndrome (AHA/NHLBI definition) risk among 9514 adults (mean age was 54 at baseline) in the Atherosclerosis Risk in Communities Study after 9 years follow-up.[230] Another Iranian study also showed the similar results.[225]

Pulses, nuts, and seeds

In total, four studies examined the associations between pulses/nuts/seeds intake and metabolic syndrome risk. Kouki et al found that people with high intake of legumes and nuts was associated with 40% less risk of having metabolic syndrome compared to those with lower intake among men (n=673) aged 57-78 years, but the association was not found in women (n=671).[45] O'Neil et al found that tree nut consumers had a lower prevalence of metabolic syndrome compared to the non-consumers among 13292 adults aged ≥19 years in the 1999-2004 NHANES.[231] Fernandez-Montero et al examined the association between tree nut consumption and risk of metabolic syndrome (Unified AHA/NHLBI & IDF definition) among 9887 adults (mean age from 37-41 years) in the Seguimiento Universidad de Navarra, University of Navarra Follow-up (SUN) cohort.[232] They found that women who had ≥2 servings/week of nut had 69% less risk of having metabolic syndrome compared to the non-consumers, but the association was not found among men. In the study, they also stratified the sample by health professionals. Among health professionals, higher consumption of nuts was associated with lower risk of metabolic syndrome, but this association was not found in non-health professionals. Ibarrola-Jurado et al also found that high nut intake was associated with decreased risk of metabolic syndrome (Unified AHA/NHLBI & IDF definition) among 7210 participants with mean age of 67 years in the PREvencion con DIeta Mediterranea (PREDIMED) study.[233]

Monosaccharides and disaccharides

Two studies examined the association between sugar intake and metabolic syndrome risk. For example, Alkerwi et al found that sugar intake higher than 10% of the total daily energy intake (preferable intake: <10% of energy intake) was associated with 73% less risk of having metabolic syndrome among 1349 Europid adults aged 18-69 years in Luxembourg.[224] Also, Kouki et al found that high sugar intake was associated with decreased risk of metabolic syndrome among men aged 57-78 years in Dose Responses to Exercise Training (DR's EXTRA) study, and the association disappeared after adjusting for education and maximal oxygen consumption.[45]

Cholesterol

Only one study was found on cholesterol intake and metabolic syndrome risk. Alkerwi et al found no association between cholesterol intake (preferable intake: <300mg/day) and metabolic syndrome risk among 1349 Europid adults aged 18-69 years in Luxembourg.[224]

In the following section, the relationship between HDI and components of metabolic will be discussed.

2.9.2 HDI and components of metabolic syndrome

To the author's knowledge, there are few studies examined HDI and components of metabolic syndrome. For example, a cross-sectional study conducted in the U.S., Belgium, Denmark, Italy, the Netherlands, Portugal, Spain, and Switzerland among 1110 men and women aged between 70 and 77 years showed that waist circumference was significant lower among people with high HDI score compared to those with low HDI score;[215] moreover, Kim et al found that high HDI score was associated with low fasting plasma glucose among 110 consecutive middle aged outpatients with type 2 diabetes.[216]

In the next section, other a priori dietary patterns (Healthy Eating Index, Diet Quality Index, and Mediterranean Diet Score) in relation to metabolic syndrome and its components will be discussed.

2.9.3 Other a priori dietary patterns and metabolic syndrome

Three studies have examined the association between Healthy Eating Index and metabolic syndrome risk. For example, Nicklas and colleagues investigated the

association between Healthy Eating Index-2005 and cardiovascular risk factors in NHANES 2001-2008 data.[234] They found that participants with the highest dietary quality of Healthy Eating Index-2005 were 35% less likely to have metabolic syndrome (ATP III definition) compared to those with the lowest dietary quality among 18,988 people aged ≥19 years. Silva and colleagues have compared the Healthy Eating Index score between individuals with metabolic syndrome (ATPIII definition) and those without among 246 Brazilian.[235] Results showed that people without metabolic syndrome had higher score in total Healthy Eating Index score, total fat score, and diet variety score. In addition, the Whitehall II study showed that the adherence to Alternative Healthy Eating index (a revision of Healthy Eating Index) was associated with metabolic syndrome reversion after 5 years follow-up among 339 metabolic syndrome patients.[236]

Two studies have examined the association between Diet Quality Index and metabolic syndrome risk. Gregory and colleagues examined Dietary Quality Index- International (a revision of Dietary Quality Index) in relation to metabolic syndrome (Unified AHA/NHLBI definition) among 1,220 Guatemalan young adults (mean age: 32 years).[237] However, they found no association between Dietary Quality Index-International and metabolic syndrome. The similar results were found in a Mexican study.[238] Ramirez-Vargas et al found no protective effect of high Dietary Quality Index score on metabolic syndrome among 325 Mexican aged 35-65 years.

In 2010, a meta-analysis was conducted by Kastorini and colleagues on 50 studies relating Mediterranean diet to metabolic syndrome. It suggested that adherence to a Mediterranean diet was associated with a 50% reduction in the metabolic syndrome.[239] In 2013, Esposito and colleagues conducted an updated systematic review on Mediterranean diet and metabolic syndrome. They confirmed that the adherence to Mediterranean diet was associated with decreased risk of metabolic syndrome, and Mediterranean diet should be provoked worldwide.[240]

Kouki et al examined reaching dietary recommendations including the vegetables intake more than 400g/day, fish more than 2 servings/week, fibre more 14g/1000 kcal, saturated fatty acids less than 10% of daily total energy intake in relation to metabolic syndrome (ATP III definition) risk.[241] A 5-points dietary score was constructed based on the adherence to the above dietary factors. They found that high score was associated with decreased risk of metabolic syndrome.

The above studies showed that better adherence to the Healthy Eating Index, and Mediterranean diet were associated with lower metabolic syndrome risk. However, the studies reported no association between adherence to Dietary Quality Index and metabolic syndrome but they were small studies and the inconclusive results could be due to insufficient study power. In the next section, literature on the relationship between a priori dietary patterns and components of metabolic syndrome will be summarised.

2.9.4 Other a priori dietary patterns and components of metabolic syndrome

Many studies have investigated the association between Healthy Eating Index and components of metabolic syndrome. For example, Nicklas et al found that participants with the highest dietary quality in Healthy Eating Index-2005 were 35% less likely to have high waist circumference, 26% less likely to have elevated blood pressure, and 21% less likely to have decreased HDL-C, compared to those with lowest dietary quality in the NHANES 2001-2008 among 18,988 individuals aged ≥19. No association was found between Healthy Eating Index-2005 and triglycerides or blood glucose.[234] Tande et al investigated the relationship between Healthy Eating Index and central obesity among 15,658 US adults aged ≥20 years.[242] They found that each 10-unit increase in Healthy Eating Index was associated with 8.3% lower risk of central obesity in women and 14.5% lower risk in men. However, Asghari found no association between Health Eating Index-2005 and waist circumference.[243] In an Iranian study consisted of 9568 adults aged ≥19 years, women with higher Healthy Eating Index scores had lower values of systolic blood pressure.[244] A French study consisted of 5081 men and women aged 35-61 years showed that higher Healthy Eating Index score was associated with lower blood pressure among men.[245]

Some studies have examined the Diet Quality Index and components of metabolic syndrome. For example, Zamora and colleagues found that better adherence to Dietary Quality Index was associated with greater increase in HDL-C among 4,381 people in Coronary Artery Risk Development in Young Adults study.[246] Gregory et al examined Dietary Quality Index- International (a revision of Dietary Quality Index) in relation to metabolic syndrome (Unified AHA/NHLBI definition) among 1220 Guatemalan young adults(mean age: 32 years).[237] However, they found that high score in Dietary Quality Index-International was associated with increasing waist circumference.

An increasing body of evidence has showed the protective effect of Mediterranean diet on metabolic syndrome components. For example, Kastorini et al conducted a systematic review and meta-analysis on Mediterranean diet and components of metabolic syndrome.[239] This study showed that high adherence to Mediterranean diet was associated with low waist circumference, high HDL-C, low diastolic blood pressure, and low blood glucose. Mediterranean diet score was inversely associated with waist circumference.[247] Some recent studies have also confirmed the results from the previous meta-analysis.[247;248]

2.9.5 Summary of the role of a priori dietary measures and their role on metabolic syndrome

Based on a small number of studies on HDI and metabolic syndrome risk, high HDI was associated with smaller waist circumference and lower blood glucose level, but was not associated with metabolic syndrome risk. More studies have examined the separate dietary components of HDI score in relation to metabolic syndrome. High saturated fatty acid, carbohydrate intake and low fibre intake were associated with increased risk of metabolic syndrome; both low protein and high protein intake was associated with increased risk of metabolic syndrome; high intake of fruits, vegetables, nuts, and sugar was associated with decreased risk of metabolic syndrome; and no association was found between polyunsaturated fatty acids or cholesterol intake and metabolic syndrome risk. However, the above results are differ between studies, which may due to different study design methods (eg, different sample size, different metabolic syndrome definition/measures, age difference, and ethnicity differences).

Studies on other a priori dietary patterns and metabolic syndrome were also reviewed. The highly protective effect of Mediterranean diet on metabolic syndrome has been supported, while the protective effect of Healthy Eating Index and Diet Quality Index on metabolic syndrome was not consistently found.

In the next few sections, a posteriori dietary patterns and metabolic syndrome will be discussed.

2.10 A posteriori dietary patterns and metabolic syndrome

In the following section, a posteriori dietary patterns—healthy food pattern, prudent dietary pattern, and western food pattern—and metabolic syndrome risk will be discussed (see Table 11).

2.10.1 A posteriori dietary patterns and metabolic syndrome

'Healthy food patterns' have been found to be protective against having metabolic syndrome. These favourable dietary patterns are mainly characterised by high consumption of low fat products, such as fish, vegetables, legumes, whole grains cereals, fruits, fruit juices, poultry, and tea. The healthy food pattern in the ATTICA study (3042 Greeks aged 18 to 89 years) was associated with a lower risk of metabolic syndrome after adjusting for smoking status, years of education, income, use of medication and BMI.[249] A study of 486 Iranian women showed that healthy food pattern characterised by high consumption in fruits, tomatoes, poultry, legumes, cruciferous and green leafy vegetables, other vegetables, tea, fruit juices, and whole grains, was also associated with lower odds of having metabolic syndrome.[250] According to Taiwan National Health and Nutrition Examination Survey, a food pattern including lean meat, egg, soybean, vegetables, dark green vegetables, carrot, fruit, seaweed, and mushroom was associated with decreased metabolic syndrome risk among Taiwanese women.[251] However, a study among Brazilian low-income adults showed no protective effect of healthy pattern characterised by whole dairy items, fresh juices, whole breads, fruits, non-starchy vegetables, homemade popcorn and fish on metabolic syndrome risk.[252] Comparing study results from different regions, regardless of the differences of dietary habits due to cultures, a healthy pattern consisting of protein, vegetables, fruits and legumes can be seen as a protective food pattern against metabolic syndrome.

Another dietary pattern called the 'prudent pattern' was identified by two studies—one cross-sectional study conducted among urban Mexican men and women aged 20-70, and the other, a cohort study conducted in US among 9514 people aged 45-64.[230;253] The prudent dietary pattern is similar to the healthy food pattern aforementioned. It is characterised by high consumptions of vegetables, fruits, legumes, fish, poultry and low consumptions in pastries, refined cereals, and cookies. However, neither of these studies found any association between prudent food pattern and risk of metabolic syndrome.

Table 11 Characteristics of reviewed studies examining associations between a posteriori dietary patterns and metabolic syndrome

Authors, year	Study type	Country	n	Age (yrs), Sex	Definition	Dietary assessment	Dietary pattern identification methods
Panagiotakos et al. 2007[249]	Cross-sectional study	Greece	3042	18-89 M/F	NCEP ATP III	FFQ	PCA
Leite and Nicolosi 2009[254]	Cross-sectional study	Italy	1052	42-74 M/F	NCEP ATP III	24h recall & FFQ	Cluster analysis
Denova-Gutierrez et al. 2010[253]	Cross-sectional study	Mexico	5240	20-70 M/F	NCEP ATP III	FFQ	Factor analysis
DiBello et al. 2009[255]	Cross-sectional study	Samoan island	1508	18+	NCEP ATP III	24h recall &FFQ	PLS
Sonnenberg et al. 2005[256]	Cohort study	US	1615	18-76 F	NCEP ATP III	FFQ	Cluster analysis
Fabiana Castillo Marsola et al. 2011[252]	Cross-sectional study	Brazil	237	35+ M/F	NCEP ATP III	24h recall &FFQ	Varimax rotation
Esmaillzadeh et al. 2007[250]	Cross-sectional	Iran	486	40-60 F	NCEP ATP III	FFQ	PCA

Authors, year	Study type	Country	n	Age (yrs), Sex	Definition	Dietary assessment	Dietary pattern identification methods
Lutsey et al. 2008[230]	Cohort study	US	9514	45-64 M/F	rNCEP	FFQ	PCA
Yeh et al. 2011[251]	Cross-sectional	Taiwan	5647	18+ M/F	IDF	FFQ	RRR
Song and Joung2011[257]	Cross-sectional study	Korea	4730	20+ M/F	NCEP ATP III (IDF ethnicity-specific values for waist circumference)	24h recall	Cluster analysis
Duffey et al[258]	Cohort study	US	4161	18-30 M/F	NCEP ATP III	Dietary history	Cluster analysis
Min et al[259]	Cross-sectional study	Korea	371	30-50 M/F	IDF	24h recall, 2-day diet record	Factor analysis
Sahay et al	Cross-sectional study	Croatia	1442	Not clear	Not clear	FFQ	PCA

Abbreviation: M- Male; F- Female; FFQ- Food Frequency Questionnaire; PCA- Principal Component Analysis; RRR- Reduced Rank Regression; PLS-Partial least squares regression.

The 'western food pattern' is characterised by high intake of pastries, refined cereals/grains, red meat, processed meat, sweets, desserts, potatoes, and low consumptions in whole grain cereals, seafood, low-fat dairy products was found as an unfavourable dietary pattern in three studies. In the Mexican Health Workers Cohort Study, Denova-Gutierrez et al found that western food pattern was associated with increased risk of metabolic syndrome.[253] A cohort study based on Atherosclerosis Risk in Communities project showed that western food pattern was positively associated with incidence of metabolic syndrome.[230] Among Iranian women, a western food pattern increased the odds of having metabolic syndrome, and was consistent with the results from other studies.[250]

Several food patterns, such as high glycaemic index and high-fat pattern (including red or white meat and meat products, and potatoes), animal products pattern (including meat, eggs, and dairy products), high-protein/fat pattern, or empty calorie pattern (higher intakes of total fat, calories, and sweetened beverages and lowest intakes of dietary fibre and vegetables) have been identified and all shared similarities with western food pattern. Moreover, these food patterns were associated with higher odds of having metabolic syndrome.[249;253;254;256] However, according to Panagiotakos et al, dietary patterns characterised by dairy products and eggs are not associated with metabolic syndrome risk.[249] A food pattern called 'modern food pattern' which is similar to western food pattern showed borderline negative effects on metabolic syndrome risk among both Samoans and American Samoans.[255]

Apart from the patterns described above in this section, several more specific food patterns were investigated in various studies. A food pattern typified by alcohol beverages was generated in Greek ATTICA study.[249] It showed that higher alcohol consumption was positively associated with the risk of having metabolic syndrome, while no such association was found in a Korean study.[257] Leite and Nicolosi found that people with higher consumption of starch food pattern (rich in starch, vegetal proteins and Na) had 80% greater likelihood of having metabolic syndrome when compared to the common group (close to the overall mean expected intakes-moderately low in fat, and moderately high in carbohydrate); meanwhile, a food pattern that consisted of vegetables, legumes, and fruits, showed no association with metabolic syndrome risk.[254]

Several studies compared different food patterns to traditional food and their association with metabolic syndrome risk. These traditional food patterns include food

patterns in Samoan Island, Brazil, Iran, and Korea. But no significant protective effect was found for metabolic syndrome.[250;252;255;257]

Only one study from Korean National Health and Nutrition Examination Survey compared the associations between dietary patterns and metabolic syndrome using different definitions of metabolic syndrome, but no difference was found.[257]

In addition to studies focusing on association between metabolic syndrome and dietary patterns, there are many studies evaluating role of dietary patterns on the components of metabolic syndrome. The next section will review these.

2.10.2 A posteriori dietary patterns and components of metabolic syndrome

A posteriori dietary patterns and central obesity

Studies have used waist circumference, waist:hip ratio and BMI, as measures of central obesity to investigate relationship between this component of metabolic syndrome and dietary pattern.

Some studies showed that western dietary pattern was significantly associated with higher odds of having central obesity when using ATPIII criteria (waist circumference ≥102cm in men and 88cm in women),[250;253] while another study did not show any significant association between western dietary pattern and central obesity.[252] In addition, dietary patterns with high glycaemic index and high-fat products and alcohol increased the risk of being obese (waist circumference ≥102/88 cm),[249] while Delavar et al's study did not find this.[260] According to Denova-Gutierrez et al,[253] high animal protein/fat pattern was also associated with higher risk of having central obesity. A healthy food pattern and prudent dietary pattern was generally protective for central obesity.[250;252;253;260]

When using EGIR criteria for central obesity (waist circumference ≥94/80 cm), results showed that there was no significant association between low-fat and high fibre food pattern and obesity, but food pattern called fibre bread was inversely associated with the risk of having central obesity among men.[261]

Williams et al found that a food pattern characterised with high intake of green vegetables, fruits, fish, and low intake of fried food, processed meat was negatively correlated with waist: hip ratio.[262] When using BMI as a measure of central obesity, cereals intake pattern has been found to be negatively associated with obesity, while a pattern characterised by frequent intakes of confectionery and chocolate but low

intake of vegetables was positively correlated with the risk of having higher risk of central obesity.[262;263]

A posteriori dietary patterns and hypertension

Blood pressure is another component of metabolic syndrome. Two different thresholds for hypertension are used in definitions of metabolic syndrome, with ≥130/85 mmHg, adopted by ATP III, rNCEP and IDF,[63;264;265] and WHO and EGIR using ≥140/90 mmHg. In this review, only papers with the NCEP ATP III, rNCEP, and IDF definition of hypertension were found, and consequently reviewed.

The association between dietary patterns and hypertension differs between countries. Esmaillzadeh and colleagues identified a healthy food pattern among Iranian women aged 40-60, and showed it was associated with lower odds of having elevated blood pressure, while western food pattern was associated with higher odds of having elevated blood pressure.[250] However, another cross-sectional study conducted in Iran, found no association between healthy food pattern and hypertension.[260] This difference may be due to different sample sizes and different statistical methods. A Mexican study also showed no significant association between prudent dietary pattern (similar to the healthy food pattern) and hypertension, while western pattern modestly increased the risk of hypertension.[253] A Brazilian cross-sectional study showed that there was no association between either western or healthy dietary pattern and elevated blood pressure.[252] However, this Brazilian study used a low income population. Dibello and other researchers identified a 'modern' dietary pattern similar to the western pattern, among American Samoans and Samoans, but this was not associated with hypertension.[255] Panagiotakos et al found that a low-fat food pattern was associated with reduced risk of high systolic blood pressure (>130 mmHg), and higher alcohol consumption was associated with higher risk of having elevated systolic pressure.[249]

A posteriori dietary patterns and dyslipidaemia

Most studies investigating the association between dietary pattern and dyslipidaemia focused on the separate effects of triglycerides and HDL-C. Only a study by Wirfalt et al looked at the association with dyslipidaemia as a whole.[261] Among women, a white bread food pattern was associated with higher risk of dyslipidaemia, however, this association was attenuated when adjusted for fatty acid ratio and intake of some micronutrients. Among men, a fibre bread pattern remained modestly associated with lower risk of dyslipidaemia.

Panagiotakos and colleagues found that low-fat food pattern was positively associated with HDL-C level.[249] Williams et al found that a dietary pattern typified by high consumption of green vegetables, fruits, fish, and low consumption of fried food and processed meat, was positively correlated with HDL-C level.[262] A study conducted by Delavar et al showed that healthy food pattern characterised by low-fat products was correlated with high HDL-C level.[260] Moreover, Esmaillzadeh et al showed healthy food pattern was associated with high HDL-C.[250] The Samoan study identified a 'Neo-traditional' pattern characterised by high intake of crab/lobster, coconut products, taro, and low intake of processed foods including potato chips and soda.[255] Higher intake of this pattern was associated with lower risk of having low HDL-C among American Samoans. In addition, a food pattern characterised by high intake of dairy products and eggs was positively correlated with HDL-C level.[260] However, according to a Mexican study, a prudent pattern was not associated with low HDL-C levels.

Dietary patterns characterised by high glycaemic index and high-fat and alcohol were negatively correlated with HDL-C level according in a Greek study.[249] A western food pattern was found to have an adverse effect on the risk of lower HDL-C.[253;266] However, high glycaemic index and high-fat pattern were not associated with HDL-C level.[260]

A healthy food pattern was negatively correlated with triglycerides level,[250;260] but another study found no association.[252] Moreover, no association between prudent pattern and risk of high triglycerides level was found in a Mexican study.[253]

The western food pattern was significantly associated with higher risk of having high triglycerides level,[250;253;266] but some studies found no association.[252] According to Panagiotakos et al (2007), dairy products, eggs and alcohol pattern were positively associated with triglycerides level, but Delavar et al found an inverse relationship between them.[260] McNaughton et al[267] also found that patterns characterised by high consumption of white bread, sweetened drinks, lower consumption of vegetables and red meat and cabbage were positively associated with triglycerides level. A negative association was found between triglycerides level and low-fat products pattern.[249;262]

A posteriori dietary patterns and fasting plasma glucose

A study conducted in Cyprus and the Greek Islands showed that a low-fat food pattern was associated with lower fasting blood glucose level, while a study of similar population showed inconsistent results.[249;263] Delavar et al, Marsola and Esmaillzadeh

et al found that healthy food pattern was associated with lower fasting blood glucose level.[250;252;260] Denova-Gutierrez et al[253] showed that the western pattern food was associated with higher fasting blood glucose, while several other studies did not find significant results.[250;252]

2.10.3 Summary of the role of a posteriori dietary pattern and their role on metabolic syndrome

According to the reviewed articles, healthy food pattern/prudent food pattern was generally associated with a lower risk of metabolic syndrome, while western food pattern was associated with a higher risk of metabolic syndrome and its components. However, not all studies found this.

2.11 Diet in Central and Eastern European countries

There are only a few studies on nutrition status in the study countries. The diet in this region has been known to have high in energy and fat intake, but low in fruit and vegetable intake.[268-270] This may be because the climate in some areas which is not suitable for planting fruits and vegetables, and it may also be due to the previous political focus on increasing protein intake (eg, meat and dairy products).[271]

After the collapse of the Former Soviet Union, the food market and consumption in the Central and Eastern Europe faced a nutrition transition. After 1989, subsidies on meat and animal fats ended, which resulted in a decline of fat intake in these countries.[272] Conversely, consumption of fruits and vegetables increased during this time. Moreover, due to the economic and marketing reform, prices for some food increased within short periods of time, and this could be the reason certain food (such as fresh fish) has not been widely consumed.

The Household Budget Survey was conducted to examine the dietary changes in the region.[273] The energy intake was found to increase in 1980s in the Czech Republic and Poland, then after 1990, it reduced until 1994-1995, and the consumption increased after this. Moreover, between 1989 and 1997, in the Czech Republic, beef consumption decreased by 7kg per capita, while the chicken consumption increased by 6kg per capita, but consumption of processed meat stayed high in the 1990s.[273;274] In addition, more households started using new cooking methods, such as deep fried food. The food pattern in Russia transformed from high consumption of bread and potato in 1950s to a high consumption of red meat, milk, and sugar in late 1980s.[182] In 1985, a study showed that compared with U.S. participants, Russian participants

had higher intake of saturated fatty acids, but lower intake of polyunsaturated fatty acids and protein.[275] The results from the Russian Longitudinal Monitoring Survey showed that despite the slight decrease of total energy intake, the fat and protein intake both decreased among Russian adults, potentially due to increased prices of dietary sources of protein and fat.[276] Moreover, among the main food groups (including fruits and vegetables, meat and fish, dairy, bread, fats, sugar, and eggs), consumption decreased except for potato consumption between early 1990s and early 2000s.[277;278]

However, very limited research on recent diet quality has been done in the region.

2.12 Literature review summary and gaps in research

Metabolic syndrome was found to be highly prevalent and strongly associated with cardiovascular disease events and mortality. This is likely that diet could play a critical role in reducing prevalence of metabolic syndrome, as well as other diseases. However, existing evidence is limited and little is known about metabolic syndrome prevalence and diet quality in Eastern European countries.

In the literature, evidence of a priori dietary patterns in relation to metabolic syndrome needs to be developed further, especially on HDI and metabolic syndrome research. HDI has been recognised as a useful predictor for dietary quality and it has been used in international comparison studies in relation to mortality. According to the few available studies on HDI and metabolic syndrome risk, high HDI score was not associated with metabolic syndrome, but was associated with smaller waist circumference and lower blood glucose. However, to the author's knowledge, there are only three studies on HDI and metabolic syndrome risk. The sample sizes of these three studies were small (ranging from 110 to 1349), while one of the studies used a non-random sampling design, which makes it difficult to compare their results and interpret the findings. Although more studies have been done on dietary components of HDI and metabolic syndrome, the inconsistent results were possibly due to different study characteristics. Therefore, a large population study in different countries using a consistent design is needed to better understand the association between HDI and metabolic syndrome, especially in Eastern Europe.

In the posteriori dietary patterns research, the names and composition of dietary patterns are numerous among studies but, in general, available literature suggest that healthy food pattern has a positive effect on risk of metabolic syndrome (and its

components), while western food pattern has an adverse effect; but some inconsistent results have been reported.

To the author's knowledge, no study of dietary patterns and metabolic syndrome has been done in Central and Eastern European Countries, and there are only few studies on metabolic syndrome related topics. Moreover, there is no cross-country study with a large enough sample size to compare the association between dietary patterns and metabolic syndrome in several countries. These gaps can be, at least partially, filled by the current study. In addition to filling some gaps in research of metabolic syndrome, this thesis also focuses on novel methodological aspects of nutritional research. HDI has been used in previous studies almost exclusively as dichotomous, and in this thesis, a continuous HDI score with a total score of 70 will be used in order to capture the valuable dietary information.

As highlighted previously, a substantial proportion of the European population are estimated to be affected by metabolic syndrome and its components. This suggests that the present study would have important public health implications, since dietary habits as well as other unhealthy lifestyle behaviours identified could be potentially modified. Before designing dietary interventions to reduce metabolic syndrome across Europe, it is important to explore the relationships between different dietary patterns and metabolic syndrome in a more diverse number of populations. There is a lack of such evidence particularly in Central and Eastern European countries. In this thesis, dietary pattern and metabolic syndrome in Central and Eastern European countries, and its related potential risk factors will be discussed in detail, with the aim of providing valuable evidence for policy makers.

Chapter 3 Aims and objectives of this thesis

3.1 Aims

There are three main aims of this thesis. The first aim is to examine the prevalence of metabolic syndrome in the Czech Republic, Russia, and Poland. The second aim is to further examine how different dietary patterns among these countries relate to social and demographic factors (age, sex, SEP, smoking, physical activity). The third aim is to evaluate the association between HDI score and risk of metabolic syndrome and its components.

3.2 Objectives

By addressing the first aim of the thesis, the specific objectives are:

1. To examine the prevalence of metabolic syndrome and its components in the Czech Republic, Russia, and Poland.
2. To examine how metabolic syndrome prevalence relates to demographic factors (age, sex, SEP) and health behaviours (smoking and physical activity) in the Czech Republic, Russia, and Poland.

By addressing the second aim of the thesis, the specific objective is:

3. To examine and compare dietary patterns in the Czech Republic, Russia, and Poland using the HDI; and to further examine HDI in relation to age, sex, SEP, smoking, and physical activity in each country.

By addressing the third aim of the thesis, the specific objectives are:

4. To examine the associations between the HDI and risk of metabolic syndrome and its components in the Czech Republic, Russia, and Poland.
5. To examine the associations between dietary components of the HDI and risk of metabolic syndrome and its components in the Czech Republic, Russia, and Poland.
6. To examine the associations between HDI scores and metabolic syndrome and its components in the pooled dataset by combining three countries together.

7. To compare the sample characteristics, and associations between HDI score and metabolic syndrome risk using the complete case and imputed data sources.

3.3 Hypotheses

In response to the objectives, I hypothesised that:

1. The prevalence of metabolic syndrome and its components is relatively high in the Czech Republic, Russia, and Poland compare with Western European countries.
2. The prevalence of metabolic syndrome is higher in men than women in the Czech Republic and Poland, but it is higher in women than men in Russia; it increases with older age and lower SEP. Non-smokers have lower prevalence of metabolic syndrome compared with smokers and past-smokers; physically active participants have lower prevalence than physically less active ones.
3. The study samples have on average a low HDI score, especially low scores for saturated fatty acids, dietary fibres, protein, cholesterol, and sugar. HDI score increases with older age, higher SEP, and increased physical activity. Women have a higher adherence to HDI compared with men, and non-smokers have a higher adherence to HDI compared with ex- and current smokers.
4. A higher HDI score is associated with lower risk of metabolic syndrome and its components, namely, central obesity, raised blood pressure, high triglycerides, low HDL-C, and high blood glucose level.
5. A higher score in HDI individual dietary components is associated with lower risk of metabolic syndrome and its components.
6. A higher HDI score is associated with lower metabolic syndrome risk in the pooled dataset, and the magnitude of associations is similar to the country specific sample analyses.
7. The sample characteristics are similar between imputed and restricted sample for main analyses, and the positive association between higher HDI and lower metabolic syndrome risk is similar to the association found in restricted sample.

Chapter 4 Methods

4.1 Introduction to the HAPIEE study

This thesis used data from the baseline survey of the HAPIEE (Health, Alcohol and Psychosocial factors In Eastern Europe) cohort study. The baseline survey was first conducted in the Czech Republic, Russia, and Poland in 2002-2005. The study consists of three cohorts in six centres in the Czech Republic (Havirov/Karvina, Hradec Kralove, Jihlava, Krometiz, Liberec, and Ústí nad Labem), Russia (Novosibirsk), and Poland (Krakow). The planned sample size for each country was 10,000 men and women aged 45-69 years at baseline. The study sample was randomly selected and stratified by gender and 5-year age-groups. Subjects were selected from population registers in the Czech Republic and Poland, while the Russian sample was selected from electoral lists. In total, 28,945 adults aged 45-69 years were recruited, including 13,617 men and 15,328 women.[18]

The baseline survey included structured questionnaires and a medical examination that took place in a clinic. The questionnaires covered health, lifestyle, food frequency (in the last 3 months prior to interview), socioeconomic circumstances, psychosocial factors, quality of life of retired persons, and psychosocial environment at work of those still employed. The medical examination included a fasting venous blood sample, measurement of height, weight, leg length, waist and hip circumference, blood pressure, lung function and cognitive function testing. In the Czech Republic and Poland, questionnaires were completed at home, and then participants were invited for a clinical examination in the clinics. In Russia, participants completed both questionnaire and the clinical examination in the clinics. Therefore, compared with Russia, in the Czech Republic and Poland a slightly smaller proportion of participants had both data on questionnaire and clinical examination (82% and 87% respectively). The response rates in the wave 1 of HAPIEE study were 55% in the Czech Republic and 61% in both Russia and Poland (See Table 12).

Table 12 Response rates in the HAPIEE study

Country	N (men)	N (women)	Total participants	Eligible participants	Response rate
Czech Republic	4123	4734	8857	16100	55%
Russia	4264	5096	9360	15340	61%
Poland	5230	5498	10728	17590	61%
Total	13617	15328	28945	49030	

In the following sections, the analytical sample for this PhD thesis will be described, along with the definition of metabolic syndrome and its components, the dietary data used, study power, analytical methods used, and ethical issues.

4.2   Analytical sample

A series of exclusion criteria were used to prepare the data for use in this thesis (see Figure 3, Figure 4, and Figure 5 showing the flow charts for each country). First, the minority of subjects younger than 45 years old or older than 70 years old at baseline were excluded (84 in the Czech Republic, 59 in Russia, and 19 in Poland). Second, since body weight is needed in order to calculate extreme nutrient intake (described in section 4.5), subjects with missing body weight were excluded (34 in the Czech Republic, 0 in Russia, and 21 in Poland). Third, subjects with more than 15 lines of the FFQ missing were excluded from the sample (436 in the Czech Republic, 14 in Russia, and 276 in Poland).[37] Fourth, those who answered 'No' to the question 'Are the foods and drinks listed in the previous table representative of the foods and drinks that you consumed in the last 3 months', but did not give any details of other foods that are typically eaten more than once a week were excluded (232 in the Czech Republic, 29 in Russia, and 378 in Poland). Moreover, subjects with extreme nutrient values, based on predicted energy expenditure, were identified and excluded (150 in the Czech Republic, 56 in Russia, and 66 in Poland); this will be explained in more detail in section 4.7.1. After the exclusion of extreme energy values, subjects were excluded if they: reported eating more than 65 portions per day (mean: 32.2, SD: 9.5; "65" was more than 6 times of standard deviation of the mean); reporting eating 'more than 6 portions/day' on 5 or more occasions (mean: 0.5, SD: 0.9; "5" was around 5 times of standard deviation of the mean); or if the majority of diet intake was tea, coffee, or sugar (102 in the Czech Republic, 48 in Russia, and 28 in Poland). In addition, subjects with at least one missing component of metabolic syndrome (1866 in the Czech Republic, 246 in Russia, and 1395 in Poland) were excluded. Finally,

subjects with any missing data for covariates were excluded (893 in the Czech Republic, 120 in Russia, and 874 in Poland; covariates were education level, smoking status, leisure physical activity, sports time, working activity, family history of diabetes and stroke, medication for at least one of abnormalities (ie, high cholesterol, diabetes, high blood pressure)). The final sample with complete data consisted of 5060 subjects in the Czech Republic, 8788 in Russia, and 7671 subjects in Poland aged 45-69 years old.
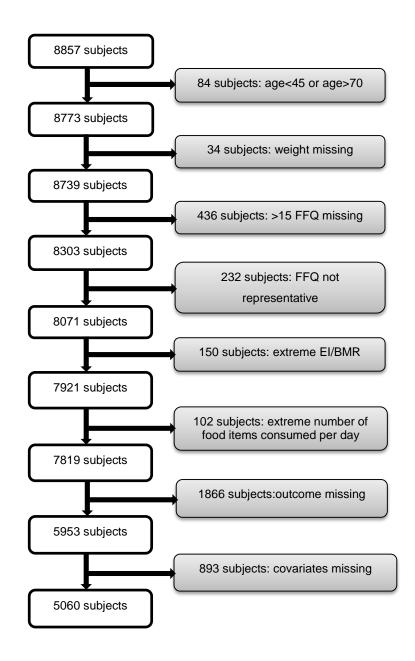
Figure 3 Analytical sample selection in the Czech Republic

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┌─────────────────┐
│  9360 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  59 subjects: age<45 or age>70   │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  9301 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  14 subjects: >15 FFQ missing    │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  9287 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  29 subjects: FFQ not            │
         │        │  representative                  │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  9258 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  56 subjects: extreme EI/BMR     │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  9202 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  48 subjects: extreme number of  │
         │        │  food items consumed per day     │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  9154 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  246 subjects:outcome missing    │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  8908 subjects  │
└────────┬────────┘
         │        ┌──────────────────────────────────┐
         ├───────▶│  120 subjects:covariates missing │
         ▼        └──────────────────────────────────┘
┌─────────────────┐
│  8788 subjects  │
└─────────────────┘
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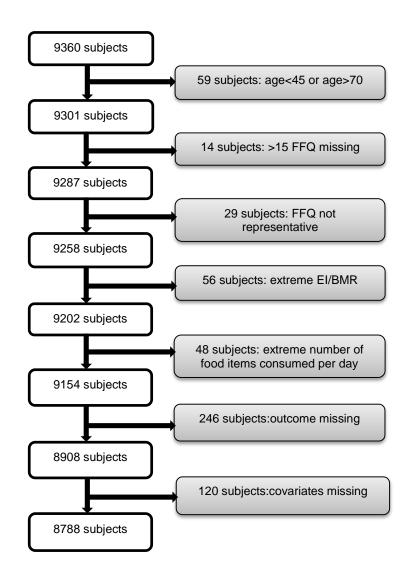
Figure 4 Analytical sample selection in Russia
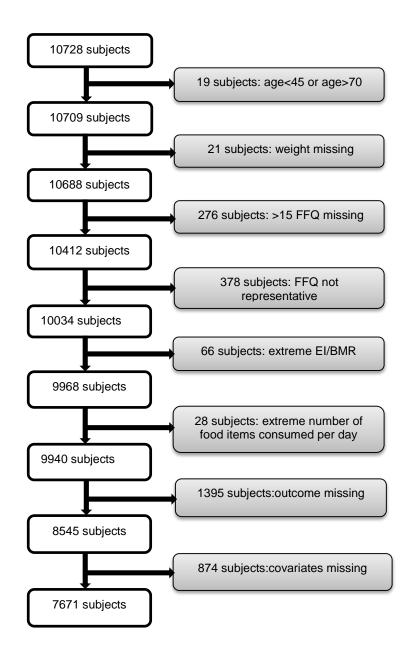
Figure 5 Analytical sample selection in Poland

4.3 Metabolic syndrome and its components in the HAPIEE study: definition and methods of measurement

Metabolic syndrome and its components are the main outcome measures in this thesis. Metabolic syndrome was defined using the ATP III definition.[63] Components of ATP III metabolic syndrome are central obesity, raised blood pressure, high triglycerides, low HDL-C, and raised blood glucose. In this thesis, the ATP III definition was slightly modified for raised blood pressure, this minor modification will be described below. Each outcome was coded as a dichotomous variable. In the following paragraphs, data collection methods and definitions of these parameters will be described.

4.3.1 Central obesity

Central obesity was defined using waist circumference, and was measured using a tape measure. The tape was pulled taut and applied at the half way point between the costal margin and iliac crest. Participants were asked to breathe out gently and let their arms hang loosely by their sides and look straight ahead. Measurements were taken to the nearest 0.1cm and recorded. Central obesity was defined as waist circumference ≥102 cm in men or ≥88 cm in women.[63]

4.3.2 Raised blood pressure

Blood pressure was measured using an Omron M5-I digital blood pressure monitor. Participants were first asked to sit quietly for 5 minutes before blood pressure taken. For each participant, blood pressure was measured three times with two-minute intervals.

The average values of the last two measurements of systolic and diastolic blood pressure were used. Where one blood pressure reading was missing, blood pressure was calculated as the average of the two available measurements if the difference between these two measurements was less than 10mmHg, otherwise the value remained as missing; where only one blood pressure reading was available, the measurement was assumed to be missing, due to its expected imprecision. Raised blood pressure was defined as systolic blood pressure≥130mmHg or diastolic blood pressure≥85mmHg.[63] In this thesis, subjects that had been told by the doctor as having hypertension were also classified as having raised blood pressure; this is a minor modification of the original ATP III definition.

4.3.3 High triglycerides and low HDL-C

The venous blood sample was taken from participants' arm using venepuncture. In the Czech Republic, lipid concentrations in serum were measured on a Roche COBAS MIRA auto-analyser, using a conventional enzymatic method with reagents from Boehringer Mannheim Diagnostics and Hoffman-La Roche. In Russia, lipid concentrations in serum were measured using an auto-analyser FP 901 (Finland) using an enzymatic method with reagents from Biocon Diagnostic (Germany). In Poland, serum lipid analysis was conducted using a Modular P and Hitachi 917 analyser (Roche) using dedicated Roche reagents. All laboratories in the HAPIEE study were certified, and the assay methods were calibrated and with internal quality control. High level of triglycerides was defined as ≥1.7 mmol/L and low HDL-C was defined as <1.03 mmol/L in men or <1.29 mmol/L in women.[63]

4.3.4 High plasma blood glucose

In the Czech Republic, blood glucose was measured from capillary blood by Reflotron. In Russia, blood glucose was measured from serum. In Poland, blood glucose was measured in plasma. However, the glucose level described in ATP III metabolic syndrome criteria was based on plasma glucose.[63] In order to harmonise the glucose measures among the three HAPIEE centres, the capillary blood glucose in the Czech sample and the serum blood glucose in Russian sample were recalculated to plasma glucose equivalent values using the formula suggested by European Society of Cardiology and European Association for the Study of Diabetes (see Table 13).[279] Subjects with extreme plasma glucose level were investigated with other related variables such as diabetes diagnosis and treatment of diabetes. In the Czech sample, two participants with glucose level greater than 20mmol/L had no diagnosis of diabetes and no treatment of diabetes records; therefore, their glucose level were recoded to missing. When blood glucose level drops to 2.22mmol/L, an apparent impairment would occur, but no emergency case was reported during clinical examinations.[280] Therefore, values of plasma glucose level less than 2.22mmol/L were recoded to missing. Raised plasma blood glucose was defined as ≥6.1 mmol/L.[63]

Table 13 Conversion factors between plasma and other vehicles for glucose values [ii]

Plasma glucose (mmol/L) = 0.558 + 1.119 X whole blood glucose (mmol/L)
Plasma glucose (mmol/L) = 0.102 + 1.066 X capillary blood glucose (mmol/L)
Plasma glucose (mmol/L) = - 0.137 + 1.047 X serum glucose (mmol/L)

Standardised plasma glucose by using measurements from Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU) laboratory

Since the methods of collection and analysis of blood glucose were different in the three countries, standardising plasma glucose concentrations is needed to enable comparison between centres and reduce systematic error. A random sample of 3242 blood glucose samples selected from all three cohorts were analysed in the CTSU laboratory, at Oxford University (987 from the Czech Republic, 1283 from Russia, and 972 from Poland). A standardised plasma glucose measure was calculated using the plasma glucose levels from CTSU, the local plasma glucose levels based on local laboratories measurements, and conversion factors from Table 13. This strategy was only adopted in the Czech and Polish samples because a continuous value of plasma glucose was unavailable from Russian sample. Russian investigators only provided the binary variable defining whether glucose levels were <6.1 mmol/L or ≥6.1 mmol/L. However, the sensitivity and specificity between the CTSU and local measurements were also investigated (see Table 14). As the CTSU measurements were treated as the 'gold standard', samples have a glucose ≥6.1 mmol/L from the CTSU laboratory were treated as the true/confirmed cases. Table 14 shows that 216 samples were found have glucose level ≥6.1mmol/L among 388 samples which were identified ≥ 6.1mmol/L by the local laboratory. In addition, 50 samples were found have glucose level ≥ 6.1mmol/L among samples were identified having glucose level <6.1mmol/L (851 in total), and these samples were assumed to be falsed categorised into '<6.1mmol/L'. Therefore, the sensitivity of the local laboratory measurements was 216/266 or 81.2%. This means that among samples have a true value of ≥6.1mmol/L, 81.2% of these were found have glucose level ≥6.1mmol/L by the local laboratory. The specificity of the local laboratory measurements was 801/973 or 82.3%, indicating

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[ii] Adapted from Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary[279]

that 82.3% among the samples which have true glucose level < 6.1mmol/L were identified correctly. Given the available binary plasma glucose data, the calculation based on equation modelling could not be achieved in Russian sample. Therefore, in the following section, the detailed methods for calculating the standardised plasma glucose in the Czech and Polish samples are explained.

Table 14 Sensitivity and specificity of high blood glucose in randomly selected Russian sample

| Local laboratory measurements | CTSU measurements | | Total |
	Yes	No	
Yes	216	172	388
No	50	801	851
Total	266	973	1239

Sensitivity = 216/266 = 81.2%
Specificity = 801/973 = 82.3%

For the purpose of this thesis, the glucose level analysed in CTSU is considered the 'gold standard' because it was analysed in the same laboratory, and it has been used in a number of other studies. Thus, it is important to compare the local measurement to the 'gold standard' values. First, the correlation coefficient between local and CTSU glucose levels was calculated for both countries (see Figure 6 and Figure 7). A strong linear relationship between local and CTSU glucose level was found in both Czech and Polish samples. The correlation coefficients between local and CTSU glucose level were large: 0.84 and 0.94 in Czech and Polish sample, respectively; a value of 1 would indicate perfect correlation

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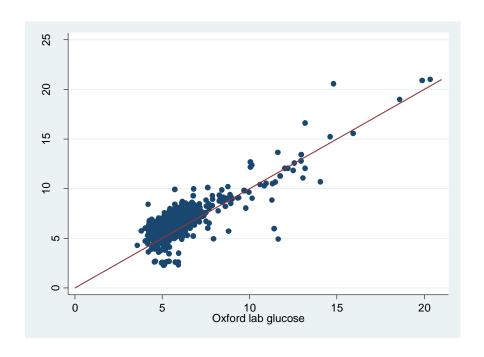
Figure 6 Correlation between local and CTSU glucose level in Czech sample
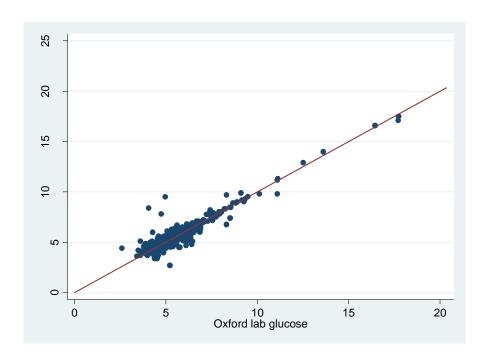
Figure 7 Correlation between local and CTSU glucose level in Polish sample

Although a strong linear relationship between two measurements was shown, it did not necessarily mean the two measures agree.[281] Therefore, Bland-Altman plots were also created to check agreement between the two measurements in the Czech and Polish samples (See Figure 8 and Figure 9). Three horizontal lines in both figures show the mean difference between the two measurements, and the mean difference plus and minus 2 times the standard deviation (limits of agreement). In the Czech sample, 765 (out of 938) participants had lower results of blood glucose in CTSU than in local lab, and 569 participants (out of 971) in Polish sample. The mean differences between two measures were -0.62 and -0.06 in the Czech and Polish samples, respectively; in addition, in both samples, the 95% confidence intervals for limits of agreement were small, especially in the Polish sample. This could be due to the Reflotron test of blood glucose being imprecise compared with the plasma glucose measurements (see Table 15). Therefore, there is a bias between the CTSU (gold standard) and local lab glucose results, although no noticeable variation could be found in agreement among the range of glucose results.
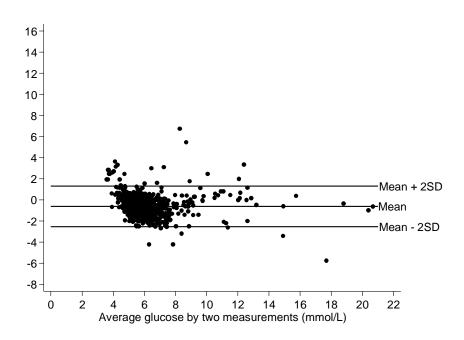
Figure 8 Bland-Altman plot: the agreement of blood glucose between local and CTSU measurements in Czech sample
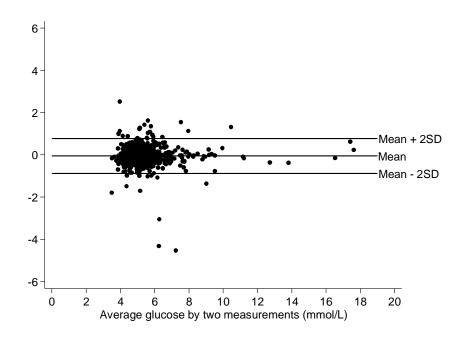
Figure 9 Bland-Altman plot: the agreement of blood glucose between local and CTSU measurements in Polish sample

Table 15 Agreement statistics between local glucose level and CTSU glucose level

	N	Mean difference	Lower limit of agreement (95% CI)	Upper limit of agreement (95% CI)
Czech sample	938	-0.62	-2.84 (-2.65, -2.43)	1.31 (1.20, 1.41)
Polish sample	971	-0.06	-0.88 (-0.93, -0.84)	0.77 (0.72, 0.81)

Cook's distance was also calculated for both samples to identify outliers, and a Cook's distance value > 1 was used to classify an outlier.[282] However, in both samples, no outliers were identified.

Finally, robust regression was used to generate equations to estimate the standardised plasma glucose values for all participants. In linear regression models, CTSU glucose levels were used as the dependent variable and local glucose levels used as the independent variable; polynomials were also added into these models to achieve a better model fit. In the Polish sample, a simple linear model was selected due to a linear relationship between local and CTSU glucose level. In the Czech

sample, first, a model including a square polynomials was performed in order to achieve a better model fit; however, when adding another cubit polynomial in the model, the model fit was significantly better compared to the model only included a square polynomials (P<0.001 from a likelihood ratio test). Finally, by comparing the statistics of model fit (R-square, RMSE, and F-test) and likelihood ratio test statistics, a model including square and cubic polynomials was selected for the Czech sample:

Czech Republic: Standardised glucose=-1.766local+ 0.251local^2 - 0.007local^3 +8.375

Poland: Standardised glucose=0.967local+ 0.232

4.3.5 Metabolic syndrome

Metabolic syndrome was constructed using the component measures described in sections 4.3.1-4.3.4. To be classified as having metabolic syndrome, participants must have at least three of the following:[63]

1. *Central obesity (waist circumference ≥102 cm in men or ≥88 cm in women);*
2. *High blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or have been told by the doctor that has hypertension);*
3. *High triglycerides (≥1.7 mmol/L);*
4. *Low HDL-C (<1.03 mmol/L in men or <1.29 mmol/L in women);*
5. *High plasma blood glucose (≥6.1 mmol/L).*

4.4 HDI score and its components

The Healthy Diet Indicator (HDI) is the main dietary exposure in this thesis. HDI was calculated on the basis of the WHO recommendations.[205] The dietary data was collected using food frequency questionnaire (FFQ).[283] The FFQ was adapted from the FFQ used in Whitehall II study,[284] and has been validated. There were slightly different numbers of food items in each country due to the inclusion of country-specific dishes. In total, there were 136 items in the Czech Republic, 147 in Russia, and 148 in Poland. Portion size was specified for each item and country specifically. Participants were asked how often, on average, they had consumed such portion of the item during the last three months. There were 9 possible responses for each item ranging from 'never or less than once per month' to 'six or more times per day'. The full English version of FFQ with the additional country specific items marked can be found in Appendix I. The strategy of dealing with missing data in FFQ will be explained in section 4.7.1.

Based on the FFQ, the frequency of food intake was converted into daily food consumption. Next, the nutrient content of specific food was multiplied with standard portion of the food in order to calculating nutrient intakes. In calculating the nutrient intake, the food composition data was mainly based on the McCance & Widdowson's (2002) tables. Food composition was also obtained using country specific food composition tables, the United States Department of Agriculture Nutrient Data database, International table of glycaemic index and glycaemic load values, and manufacturer data.[285-288]

In the WHO recommendations,[205] there were 15 dietary components. In the HAPPIE study, 9 components were selected on the basis of the data collected in the FFQ: saturated fatty acids, n-3 polyunsaturated fatty acids, n-6 polyunsaturated fatty acids, trans fatty acids, protein, mono and disaccharides, dietary fibre, fruits and vegetables, and cholesterol.[203]

In this thesis, a short version of HDI was created, which included 7 dietary factors: saturated fatty acids, polyunsaturated fatty acids, protein, mono and disaccharides, dietary fibre, fruits and vegetables, and cholesterol. Compared with the original development of HDI, n-3 polyunsaturated fatty acids and n-6 polyunsaturated fatty acids were combined as one component—polyunsaturated fatty acids; furthermore, trans fatty acids was omitted. The polyunsaturated fatty acids are commonly used as the different fatty acids measures (n-3/6 polyunsaturated fatty acids) do not typically provide additional information compared with the single combined measure. The short version was created to aid comparisons with findings from other cohorts, because the dietary factors included measures that most studies should have, so making comparison between different studies easier.

In the original HDI, each component has a dichotomous score: 0 (not meeting the recommendation) and 1 (meeting the recommendation). Recently, it has been suggested that adherence to recommended level should be treated as continuous measure, with closer adherence given a higher score.[289] This continuous scoring system was used in this thesis. In the short version of HDI, each component has a score ranging from 0-10 (0 represents the worst adherence, 10 represents the best adherence). The total score of the HDI has a range of 0-70, with0 representing worst adherence and 70 representing the best adherence (see Table 16).

Table 16 Short version of the healthy diet indicator

Components	Scores		
	0	0-10	10
Saturated fat(energy%)	>15	10< x ≤15	≤10
PUFA(energy%)	>16	0≤ x <6 or 10≤ x <16	6≤ x ≤10
Protein(energy%)	>25	0≤ x <10 or 15< x ≤25	10≤ x ≤15
Mono and disacharides(energy%)	>30	10< x ≤30	≤10
Dietary fibre(NSP)(g/day)	=0	0< x <20	≥20
Fruits and vegetables(g/day)	=0	0< x <400	≥400
Cholesterol(mg/day)	>400	300< x ≤400	≤300

4.5 Other variables in the study

As well as the main exposure (HDI score and its components) and outcome (metabolic syndrome and its components) variables, other variables were included in analyses as potential confounders or effect modifiers. These were age, sex, education level, current economic activity, smoking status, number of hours in leisure time physically demanding activities, number of hours engaging in sports, weight, energy intake, and alcohol intake. In the following sections, the definition of these variables will be described.

Age was used both as a continuous and categorical variable. When used as a categorical variable, it was categorised to age groups (1) 45-49, (2) 50-54, (3) 55-59, (4) 60-64, and (5) 65-69 years. Sex was used as a binary variable with two categories of (1) men and (2) women.

Education was categorised into 4 groups according to the highest completed level: (1) no formal education, incomplete primary or complete primary education, (2) vocational education, (3) secondary education, and (4) university education.

Working activity was grouped into 4 categories: (1) non-pensioner working, (2) non-pensioner not working, (3) pensioner working, and (4) pensioner not working.

Smoking status was grouped into 3 categories: (1) smokers, (2) past smokers, and (3) never smokers.

Physical activity was classified on the basis of number of hours per day spent on physically demanding activities in leisure time, and it was grouped into 4 categories: (1) <1h/d, (2) ≥1 and <2h/d, (3) ≥2 and <3h/d, and (4) ≥3h/d. In the Czech Republic,

there is only one measure on number of hours per day spent on physically demanding activities in leisure time, while in Russia and Poland, most individuals have 2 measures: a winter and a summer estimate. Therefore, in these two study samples, where winter and summer values were given, the average value of two was used; and where only one of the values of two was available, the available one was used as the final value. Another physical activity measure was classified on the basis of number of hours per day engaging in sports, and it was grouped into 3 categories: (1) 0, (2) >0 and ≤1h/d, (3)>1h/d. Where more than 8 hours per day was reported as hours per day spent on physically demanding activities in leisure time or engaging in sports, these values were recoded to missing values (89 and 20 observations respectively).

Body weight was used in the calculation of basal metabolic rate (BMR) to identify extreme energy intake, therefore, data cleaning on weight variable was necessary. There are two weight measures in the HAPIEE study, self-reported weight and clinically examined weight. Cleaning of weight measure was thus done in two steps. First, some implausible values were removed. Second, the clinical weight measure was used as 'gold standard'; however, some participants (in the Czech and Polish sample) had clinical measure missing because they did not visit the clinics. Therefore, self-reported weight was used together with clinical weight measure in order to calculate an objective weight measure using regression equation. These two steps will now be explained below. In the self-reported weight, extreme values were coded to missing (self-reported weight>200kg). In addition, one participant had weight and height data incorrectly transcribed as each other, and this was corrected. There were also some other further potentially 'extreme' values in both self-reported height and weight. However, after data checking based on the comparison of clinical measures, energy intake, age, health status (diabetes, high cholesterol, or hypertension presented or not), it showed that these potentially 'extreme' values were plausible because of their reasonable energy intake, height, and health status. For example, one person with self-reported weight less than 40kg, but she also had 1.48m height, and diagnosed diabetes; thus the low body weight was assumed to be plausible. Because of potential reporting bias in self-reported weight, linear regression models including objective weight, self-reported weight, sex, age, and education level were used to predict the objective weight. After the calculation, the correlation coefficient between the predicted objective weight and self-reported weight was 0.98. This predicted objective weight was then used to replace the missing data in clinical examined weight, and used in further analyses as a measure of personal weight.

Thus, participants without the calculated body weight was excluded from the analytical sample from the very early stage of sample selection (see Section 4.2).

Family history of stroke and diabetes were used as the binary variables: (1) having parents/sibling suffering from stroke/diabetes, and (2) having no parents/siblings suffering from stroke/diabetes.

Medication for at least one of the abnormalities (ie, high cholesterol, diabetes, high blood pressure) was used as a binary variable: (1) yes: have medication for at least one of the abnormalities, and (2) have no medication for any of the abnormalities.

Energy intake was calculated based on FFQ and local food composition data, and was used as a continuous variable with unit of kcal/day.[37] Alcohol intake also calculated from FFQ and was used as a continuous variable with unit of gram/day.

4.6 Study power

The HAPIEE study is the largest population study in the Central and Eastern Europe, and its large sample size is expected to provide enough study power to examine the association between HDI score and metabolic syndrome risk. Because the diagnosis of metabolic syndrome depends on the clinical measures, participants who were absent in clinical examination were excluded. In the main analyses, a complete cases sample was used. The number of subjects excluded from the final sample could likely reduce the study power. Therefore, the study power was calculated for the complete cases sample.

Assuming the confidence interval is at 95%, and the odds ratios (OR) in comparing metabolic syndrome risk in the bottom quintile of HDI score (the exposed group) to the risk in the top quintile of HDI score (the unexposed group) are 1.25, 1.50, and 2.00, the study powers were calculated accordingly. As shown in Table 17, study power for most of the study samples are above 85% apart from the Czech sample with OR of 1.25.[250] However, in the main analyses of the thesis, the HDI score was used as a continuous variable, thus, the study power in each study sample would be even higher. Therefore, assuming a moderate effect size, all three current study samples have sufficient study power to examine the association between HDI score and metabolic syndrome risk.

Table 17 Study power calculations in the Czech, Russian, and Polish samples

OR	Study power (95% CI)		
	Czech Republic	Russia	Poland
1.25	71%	91%	87%
1.50	99%	>99.9%	>99.9%
2.00	>99.9%	>99.9%	>99.9%

4.7   Analytical methods used in the thesis

In the following sections, analytical methods including strategies on dealing with missing data, and detailed statistical methods used in this thesis will be described step by step.

4.7.1   Missing data and outliers

Missing data in FFQ

After excluding subjects with more than 15 missing lines in FFQ, in the remaining dietary data, if there were missing data, the items left blank in FFQ were intermittent, which means the items were most probably not consumed.[183;290-292] The decision was taken to change these remaining missing items to zero intakes. As well as cleaning the data, this also reduced the number of missing variables and increased the number of subjects included in the further statistical analyses. The zero intake settings within the missing items could cause misclassification of the food intake, and the alternative way of avoiding the misclassification is imputation. However, since the left-blank items were not random (it could be due to items not consumed or participant not remembering the intake).

Identification of outliers in FFQ

The outliers in FFQ nutrients intake was identified on the basis of predicted energy expenditure. The predicted energy expenditure was based on the ratio of energy intake (EI) to basal metabolic rate (BMR) (ie, EI/BMR). BMR was calculated based on the equations by Schofield in 1985 which was summarised in Human Energy Requirements by Food and Agriculture Organisation (See Table 18).[293] The equations are based on subjects' age, sex, and body weight. The Schofield equation has been criticised for its overestimation of BMR populations, especially tropical and Asian populations, due to its inclusion of disproportioned Italian subjects in the study sample (Italians have a higher BMR than other populations).[294] However, compared with the

newly developed equations, it has the best performance[295] and has been used in multiple European population studies.[296;297] Subjects with clinical weight variable missing were excluded from the study sample before BMR calculation. After the calculation of EI/BMR ratio, subjects within the top and bottom 0.5% of the ratio were assumed to have extreme nutrient intake, and have been excluded from the study sample.[298;299] This method of identifying implausible nutrient intake has been used in European Prospective Investigation into Cancer and Nutrition (EPIC) study, and previously in papers using data from the HAPIEE study, ie, the same sample as this thesis.[37;298] Although a higher cut-point than 0.5 was suggested in population studies with similar sample sizes, it may not suitable for studies with FFQs.[300] Moreover, exclusion of top and bottom 0.5% of the ratio could also retain greater number of valuable data.

Table 18 Equations for estimating BMR from body weight adapted from Human Energy Requirements[293]

Age (years)	BMR: kcal/day
Males	
30-60	11.472kg+873.1
>=60	11.711kg+587.7
Females	
30-60	8.126kg+845.6
>=60	9.082kg+658.5

Missing data on outcome and covariates

In the thesis, metabolic syndrome and its components are the main outcomes. The clinical measures including blood pressure, waist circumference, HDL-C, triglycerides, and blood glucose were collected during the clinic visit, participants who did not attend the clinic had missing values on these measures. After the previous exclusion on age, FFQ, and extreme food intake, as shown in Table 19, a large proportion of participants did not have the metabolic syndrome measures, between 16-20% in the Czech Republic, and around 13% in Poland. In Russia, because both the questionnaire and the examination were completed in the clinic, there were fewer missing values (<3%). Among people with missing data on metabolic syndrome measures, 1316 Czechs, 3 Russians, and 1333 Poles had missing data due to their non-attendance of the clinic examination on sites.

The missing patterns for other variables used in the thesis (see section 4.5) are needed to be understood. As shown in Table 20, less than 8% of participants had

missing values on covariates in the Czech Republic, while the proportion was less than 1% in Russia, and less than 5% in Poland.

One way of dealing with missing data is omitting the observations with missing data, ie complete case analyses. In a complete case scenario, the final sample size in this thesis would be 5,060 in the Czech Republic, 8,788 in Russia and 7,671 in Poland after a loss of 34.5%, 0.04%, and 22.8% of participants in the Czech Republic, Russia, and Poland, respectively. However, by omitting subjects with any missing data, the study power would be reduced, and the precision (the confidence intervals) of the estimates could be worse (wider). An alternative approach—multiple imputation—for dealing with missing data is popular because it can increase study sample size and may produce unbiased results. In the following section, the assumptions required for multiple imputation will be explained.

Table 19 Percentages of missing data on outcomes in the Czech Republic, Russia, and Poland

Country	Variable	Missing	%
Czech Republic **(n=7819)**	Waist circumference	1,317	16.84
	Plasma glucose	1,549	19.81
	SBP[iii] 1st reading	1,318	16.86
	SBP 2nd reading	1,324	16.93
	SBP 3rd reading	1,331	17.02
	DBP[iv] 1st reading	1,317	16.84
	DBP 2nd reading	1,325	16.95
	DBP 3rd reading	1,331	17.02
	HDL-C	1,620	20.72
	Triglycerides	1,603	20.5
Russia **(n=9154)**	Waist circumference	3	0.03
	Plasma glucose	228	2.49
	SBP 1st reading	3	0.03
	SBP 2nd reading	5	0.05
	SBP 3rd reading	6	0.07
	DBP 1st reading	4	0.04
	DBP 2nd reading	5	0.05
	DBP 3rd reading	10	0.11
	HDL-C	30	0.33
	Triglycerides	32	0.35
Poland **(n=9940)**	Waist circumference	1,333	13.41
	Plasma glucose	1,338	13.46
	SBP 1st reading	1,333	13.41
	SBP 2nd reading	1,348	13.56
	SBP 3rd reading	1,359	13.67
	DBP 1st reading	1,333	13.41
	DBP 2nd reading	1,349	13.57
	DBP 3rd reading	1,360	13.68
	HDL-C	1,338	13.46
	Triglycerides	1,341	13.49

[iii] SBP: systolic blood pressure
[iv] DBP: diastolic blood pressure

Table 20 Percentage of missing data on covariates in the Czech Republic, Russia, and Poland

Country	Variable	Missing	%
Czech Republic (n=7819)	Education	22	0.28
	Smoking	71	0.91
	Working activity	63	0.81
	Leisure activity	238	3.04
	Hours in engaging sports	214	2.74
	Medication for high blood pressure	39	0.5
	Medication for abnormal cholesterol	66	0.84
	Medication for diabetes	26	0.33
	Family history of stroke	590	7.55
	Family history of diabetes	575	7.35
Russia (n=9154)	Education	0	0
	Smoking	0	0
	Working activity	0	0
	Leisure activity	69	0.75
	Hours in engaging sports	12	0.13
	Medication for high blood pressure	0	0
	Medication for abnormal cholesterol	0	0
	Medication for diabetes	0	0
	Family history of stroke	49	0.54
	Family history of diabetes	49	0.54
Poland (n=9940)	Education	6	0.06
	Smoking	28	0.28
	Working activity	17	0.17
	Leisure activity	91	0.92
	Hours in engaging sports	496	4.99
	Medication for high blood pressure	64	0.64
	Medication for abnormal cholesterol	42	0.42
	Medication for diabetes	23	0.23
	Family history of stroke	262	2.64
	Family history of diabetes	292	2.94

There are three possible distributions for missing data: 'missing completely at random', 'missing at random', and 'missing not at random'.[301] 'Missing completely at random' means the missing data is a random subset of the existing observed data. That is, the probability of an observation missing is not related to the unobserved value itself or to the values of any observed variables or values, so that the distribution of the missing data is similar to the observed data. For example, the laboratory samples were lost in transit from the local clinic to the certified laboratory, the lost samples has no systematic differences compared to the non-lost samples. 'Missing at random' means that there might be some systematic differences between the missing data and the observed data, and the differences could be explained by other observed variables. For example, the participants dropped out of the study because of their medical conditions and the medical condition was recorded in the questionnaire, so that the participants stayed in the study are healthier compared to the dropouts. 'Missing not at random' means that the missing data cannot be fully explained by the observed data, that is even after taking into account of the observed data, the systematic differences remain between the missing data and observed data. For example, in the self-reported questionnaire collection, some people did not respond to the household income question, this is because people did not want to reveal their income no matter low or high; even after taking into account of the education variable, the income variable was still difficult to predict because of the lack of information on other variables, such as house ownership or postcode. The assumption for using multiple imputation is that missing data are 'missing completely at random' or 'missing at random'.

Unfortunately, there is no formal statistical test using the available data to examine whether data is 'missing at random' or 'missing not at random'.[301] Therefore, the reason for missing data can only be based on the background knowledge of the study.

In the HAPIEE study, the majority of missing data is for outcome measures. Usually, people who do not come to the clinics are less healthy compared to participants who come to the clinic.[302] This means that the missing data might be dependent on/explained by the observed variables in the dataset; for example, age and diagnosis of chronic diseases. In order to check the differences between participants with missing data and those with complete data, a sensitivity analysis was performed in comparing the characteristics of these two groups (see Table 21, Table 22, and Table 23).

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In the Czech Republic, participants excluded from the final sample were older, less educated, less physically active, but with higher total energy intake and alcohol intake; they tended to have family history of stroke and diabetes, and medication for at least one of abnormalities (ie, high cholesterol, diabetes, and high blood pressure). On the other hand, there was no difference in terms of gender and smoking status (see Table 21).

In Russia, participants excluded from sample were also older and less educated; included more pensioners not working, and were more likely to be ex- or current smokers. Furthermore, they had higher energy and alcohol intake. However, there was no difference in terms of physical activity, family history of stroke or diabetes, or medication (see Table 22).

In Poland, as in the other two countries, excluded participants from the final sample were older; they also had lower level of physical activity and were more likely to be ex- or current smokers. But among two groups, there was no difference in gender, education, working activity, energy/alcohol intake, family history of stroke/diabetes, and medications (see Table 23).

In summary, the final study sample included people who were younger, with higher SEP, and with healthier lifestyle. Therefore, the systematic difference between the observed data and unobserved data may be explained by the observed variables. In addition, previous HAPIEE research suggested that the non-respondents were also due to the incorrect home address contacts or living at their official home address, which would assume the missing data were 'missing completely at random'.[18] Thus, the exclusion strategy for the complete-cases analysis may introduce some selection bias in the final study sample. However, in the multiple imputation, the assumption of 'missing at random' or 'missing completely at random' is still questionable. Both the complete case analysis and multiple imputation have limitations. Therefore, the main analyses were conducted on complete case dataset, and only sensitivity analysis comparing results from two methods have been done on multiply imputed dataset.

Table 21 Characteristics of participants according to their inclusion in complete case analyses in the Czech Republic

Variable (mean and SD, or % as indicated)		Excluded (N=2703)	In sample (N=5060)	P*
		Mean (SD)	Mean (SD)	
Age		58.6 (7.4)	57.9 (7.0)	<0.001
Energy intake (Kcal/d)		2062.2 (847.4)	2010.3 (625.1)	0.002
Alcohol intake (g/d)		7.2 (13.0)	8.4 (13.5)	<0.001
		%	%	
Sex	Men	46.8	46.3	0.236
	Women	53.2	53.7	
Education	Primary or lower	13.9	11.6	0.001
	Vocational	38.1	36.6	
	Secondary	35.0	37.4	
	University	13.1	14.4	
Working activity	Working:non-pensioner	45.2	48.4	0.007
	Not working:non-pensioner	0.9	0.6	
	Working:pensioner	8.5	7.5	
	Not working:pensioner	45.5	43.5	
Sports time	0 hour	34.6	28.5	<0.001
	0-1 hour	43.7	45.5	
	>1 hour	21.7	26.0	
Leisure activity	<1 hour	39.4	33.3	<0.001
	1-2 hours	23.9	25.8	
	2-3 hours	18.4	21.4	
	>3 hours	18.3	19.6	
Smoking	Current smoker	26.6	26.4	0.432
	Past smoker	28.8	30.1	
	Never smoker	44.6	43.6	
Family history of stroke	Yes	32.0	29.5	0.017
	No	68.0	70.5	
Family history of diabetes	Yes	38.1	33.8	<0.001
	No	61.9	66.3	
Medication	Yes	53.3	49.1	<0.001
	No	46.7	50.9	

*For continuous variables, t-test was applied, while for categorical variables, chi-square test was applied.

Table 22 Characteristics of participants according to their inclusion in complete case analyses in Russia

Variable (mean and SD, or % as indicated)		Excluded (N=366)	In sample (N=8788)	P*
		Mean (SD)	Mean (SD)	
Age		59.7 (8.3)	58.0 (7.0)	<0.001
Energy intake (Kcal/d)		3099.4 (1255.5)	2527.8 (760.6)	<0.001
Alcohol intake (g/d)		7.9 (17.5)	5.4 (12.5)	<0.001
		%	%	
Sex	Men	52.1	45.0	<0.001
	Women	47.9	55.0	
Education	Primary or lower	14.3	10.1	0.005
	Vocational	24.7	26.7	
	Secondary	32.3	34.4	
	University	28.7	28.9	
Working activity	Working:non-pensioner	32.42	39.3	<0.001
	Not working:non-pensioner	0.96	1.1	
	Working:pensioner	16.48	18.6	
	Not working:pensioner	50.14	40.9	
Sports time	0 hour	70.5	72.0	0.644
	0-1 hour	12.6	12.4	
	>1 hour	16.9	15.7	
Leisure activity	<1 hour	19.1	15.8	0.072
	1-2 hours	22.4	25.6	
	2-3 hours	25.8	24.7	
	>3 hours	32.7	33.9	
Smoking	Current smoker	30.49	28	0.015
	Past smoker	16.21	13.44	
	Never smoker	53.3	58.56	
Family history of stroke	Yes	24.8	23.6	0.504
	No	75.2	76.4	
Family history of diabetes	Yes	13.9	12.0	0.150
	No	86.1	88.0	
Medication	Yes	37.0	36.4	0.752
	No	63.1	63.6	

*For continuous variables, t-test was applied, while for categorical variables, chi-square test was applied.

Table 23 Characteristics of participants according to their inclusion in complete case analyses in Poland

Variable (mean and SD, or % as indicated)		Excluded (N=2269)	In sample (N=7671)	P*
		Mean (SD)	Mean (SD)	
Age		57.9 (7.3)	57.6 (6.9)	0.029
Energy intake (Kcal/d)		2161.7 (770.0)	2176.5 (639.0)	0.358
Alcohol intake (g/d)		2.7 (9.1)	2.8 (7.2)	0.840
		%	%	
Sex	Men	48.0	49.1	0.311
	Women	52.0	50.9	
Education	Primary or lower	11.7	11.5	0.659
	Vocational	21.3	21.1	
	Secondary	39.3	38.5	
	University	27.7	28.9	
Working activity	Working:non-pensioner	41.4	42.1	0.849
	Not working:non-pensioner	1.7	1.6	
	Working:pensioner	6.6	6.6	
	Not working:pensioner	50.3	49.8	
Sports time	0 hour	32.2	29.0	0.003
	0-1 hour	36.0	36.1	
	>1 hour	31.9	34.9	
Leisure activity	<1 hour	33.6	27.8	<0.001
	1-2 hours	28.7	30.7	
	2-3 hours	19.4	21.9	
	>3 hours	18.3	19.6	
Smoking	Current smoker	36.3	30.4	<0.001
	Past smoker	27.1	28.8	
	Never smoker	36.6	40.9	
Family history of stroke	Yes	17.8	17.5	0.686
	No	82.2	82.6	
Family history of diabetes	Yes	22.1	21.1	0.253
	No	77.9	78.9	
Medication	Yes	53.2	53.0	0.923
	No	46.9	47.0	

*For continuous variables, t-test was applied, while for categorical variables, chi-square test was applied.

In the multiple imputation, it is advisable to include all the variables that are included in the final model in the imputation model, including the interaction terms.[301] In the study sample, effect modifiers were only found in the Czech sample, but not in Russian and Polish samples; therefore, the interaction term was included in the imputation model. For the outcome measures (metabolic syndrome and its components), the following measures were included: three readings of both systolic and diastolic blood pressure, triglyceride and HDL-C level, the standardised plasma glucose (see Section 4.3.4), and waist circumference. For the covariates, the variables below were included: smoking (current smoker, past smoker, never smoker), hours/day spent on leisure activity (<1 hour, 1-2 hours, 2-3 hours, >3 hours), hours/day engaging physical activity (0 hour, 0-1 hour, >1 hour), working activity (working:non-pensioner, not working:non-pensioner, Working:pensioner, not working:pensioner), education (primary school or no formal education, vocational, secondary, university), medication for blood pressure/cholesterol/diabetes (yes, no), family history on stroke and diabetes (yes, no).

Chained equation multiple imputation was performed.[303] There is no gold-standard for the number of imputed datasets which need to be created. However, creating at least 20 datasets is preferable in order to decrease the sampling variability from the imputation process.[301] Therefore, twenty imputations were performed in this thesis. The sensitivity analyses comparing individuals with complete and incomplete data, and regression results in the imputed dataset will be presented in Section 5.6.1.

4.7.2   Confounders, effect modifiers, and mediators

A confounder is associated with both the exposure and outcome, but it is not on the causal pathway between the exposure and outcome. Confounders can over- and under-estimate the unadjusted association between the exposure and outcome.[304] Moderating variable (also called an effect modifier), is a variable that affects the magnitude of an exposure association across strata of another variable.[304] A mediator is a variable that associated with the exposure and outcome, and is on the causal pathway between them.[305]

Not accounting for such covariates could introduce bias into the findings of this thesis, and they were thus included in the main statistical analysis in Chapter 5.

The potential confounders and effect modifiers were chosen initially on a-priori basis from the literature background. The potential confounders were then related to metabolic syndrome and then HDI. The potential confounders were finally selected

as those both associated with the outcome (metabolic syndrome) and exposure (HDI). Potential effect modifiers were also tested using Likelihood Ratio Tests by comparing model including and excluding the potential effect modifiers. If the model including effect modifier yielded a significantly better model fit, the effect modifier was chosen for the final analyses. The details of potential confounders and effect modifiers (related to objectives 2 and 3) in this thesis will be described in section 5.5.

4.7.3 Statistical methods used in examining the association between HDI and metabolic syndrome

As discussed in section 4.6 and 4.7.1, in the main analyses of this thesis complete case analyses were used (ie, observations with missing values on exposure, outcomes, and other covariates were excluded from the analyses). In the following section, the statistical methods used to examine the relationship between HDI and metabolic syndrome will be explained by following the order of seven objectives stated in section 3.2.

To achieve objective 1 (examining the prevalence of metabolic syndrome and its components in the Czech Republic, Russia, and Poland): the prevalence of metabolic syndrome and its components were calculated by country and sex. The descriptive statistics including means and standard deviations of metabolic syndrome components—waist circumference, blood pressure (systolic and diastolic blood pressure), triglycerides, HDL-C, and plasma glucose (only in the Czech and Polish samples)—were calculated by country and sex. The means of each metabolic syndrome component (in continuous form) were compared by t-tests within countries to explore any sex difference. (See Section 5.2)

To achieve objective 2 (examining how metabolic syndrome prevalence relates to demographic factors and health behaviours in the Czech Republic, Russia, and Poland)**:** the association between prevalence of metabolic syndrome and its components and the following categorical variables including education level, smoking status, hours of engaging leisure activity per day, hours of engaging in sports per day, working activity, family history of diabetes and stroke, and medication of at least one of the abnormalities (ie, high cholesterol, diabetes, high blood pressure) were calculated by country, and prevalence was compared using chi-square test. (See Section 5.3)

To achieve objective 3 (examining and comparing dietary patterns in the Czech Republic, Russia, and Poland using the HDI): The summary statistics including mean,

median, and standard deviation of HDI and its dietary components were calculated stratified by country and sex. The sex differences in each country were examined using t-test for HDI total score, and Wilcoxon rank-sum test for components of HDI score.

The means of the HDI total score was compared using one way ANOVA according to demographic (age group and sex) and sample characteristics (education level, smoking status, hours of engaging leisure activity per day, hours of engaging in sports per day, working activity, family history of diabetes and stroke, and medication of at least one of the abnormalities (ie, high cholesterol, diabetes, high blood pressure)) and stratified by country. The HDI total score was also related to alcohol and daily energy intake using linear regression (see Section 5.4).

To achieve objective 4 *(examining the associations between the HDI and risk of metabolic syndrome and its components in the Czech Republic, Russia, and Poland):* The potential confounders and interaction terms in the relationship of HDI and metabolic syndrome including age, sex, education level, smoking status, hours of engaging leisure activity per day, hours of engaging in sports per day, working activity, family history of diabetes and stroke, and medication of at least one of the abnormalities (ie, high cholesterol, diabetes, high blood pressure) were first tested using logistic regression modelling and Likelihood ratio test. (See Section 5.5)

Logistic regression was used to assess the relationship between HDI and metabolic syndrome and its components. Model 1 only included HDI and metabolic syndrome to calculate the crude effect size. Model 2 was adjusted for age and sex. In model 3, other potential confounders were also included (education level, smoking status, hours of engaging leisure activity per day, hours of engaging in sports per day, working activity, family history of diabetes and stroke, and medication of at least one of the abnormalities (ie, high cholesterol, diabetes, high blood pressure) (see Section 5.6.1).

To achieve objective 5 *(examining the associations between dietary components of the HDI and risk of metabolic syndrome and its components in the Czech Republic, Russia, and Poland)*: logistic regression was used to examine the association between the 7 individual dietary components of HDI (saturated fatty acids, polyunsaturated fatty acids, protein, mono and disaccharides, fruits and vegetables, dietary fibre, and cholesterol) and metabolic syndrome, by country. As stated in the previous paragraph, three regression models were performed in each case (from

unadjusted to fully adjusted for all potential confounders and inclusion of all effect modifiers) (see Section 5.6.2).

To achieve objective 6 *(examining the associations between HDI scores and metabolic syndrome and its components in the pooled dataset by combining three countries together)* logistic regression was used to examine the association between HDI scores and metabolic syndrome and its components in the pooled dataset by combining three countries together. The variable 'country' was added as a potential confounder in the final analysis (see Section 5.6.3).

To achieve objective 7 *(compare the sample characteristics, and associations between HDI score and metabolic syndrome risk using the complete case and imputed data sources):* multiple imputation was performed using chained equations. The sample characteristics were compared between the complete and imputed datasets. Logistic regression was used to assess the association between HDI and metabolic syndrome risk in the imputed dataset (see Section 5.7.1).

4.8 Ethical issues

The HAPIEE study was approved by University College London Hospital Research Ethics Committee Alpha in the United Kingdom and by the local ethics committees in all participating centres.[18] All participants gave written informed consent before contributing to the data collection (health questionnaire and medical examination).

Chapter 5 Results – metabolic syndrome and HDI in the HAPIEE study

This chapter presents the main results of this thesis, including descriptions of the sample characteristics, prevalence of metabolic syndrome, prevalence of metabolic syndrome components, and HDI score distributions. It then presents analyses examining the relationship between HDI and with covariates, confounders and effect modifiers, and the association between HDI scores and metabolic syndrome (and its components). Main results will be conducted using both complete case and multiply imputed datasets, and these results will be compared.

5.1 Sample characteristics

Table 24 shows the sample characteristics in relation to covariates (stratified by sex) for the Czech Republic, Russia, and Poland. The mean age in three study samples was similar, and ranged from 57.3 years in Polish women to 58.4 years in Czech men. The proportion of participants in each age group was similar in three countries, with slightly more participants in the older age groups. More participants from Russia and Poland had a university degree than those from the Czech Republic (31.7% in men and 26.5% in women in Russia, 30.4% in men and 27.3% in women in Poland, compared with 18.5% in men and 11.1% in women in the Czech Republic). The prevalence of smoking was high in three study samples (over 25% in each of the three combined sex samples, results not shown), and smoking was more frequent in men compared with women, especially in Russia (49.7% in men and 10.2% in women). Women were more physically active compared with men during leisure time in all countries; 24.9% of Czech women participated in more than 3 hours/day of leisure activity compared with 13.5% of Czech men—the trend was similar in the other two countries. In Poland, around 35% of men and women spent more than 1 hour per day participating in sports, compared with 25% of Czechs and 15% of Russians. Most of the non-pensioners had a job at the time of interview in all three countries; among pensioners, more men had a job compared to women, and more Russian pensioners had a continued job after retirement compared with the other two study samples (Russia: 39.5% in men and 25.2% in women, results are not shown in the table). In the Czech Republic and Poland, around half of the men and women took at least one medication for high blood glucose, diabetes, or high cholesterol, while less Russian men than women took medication (25.6% in men, and 45.4% in women). Czech men and women had the most cases of family history of diabetes (32.1% in men, 35.5% in

women), followed by Poles (19.6% in men and 22.2% in women) and Russians (9.6% in men, and 14.0% in women). Around 30% of Czech men and women had a family history of stroke, compared with less than 20% in Russia and Poland, although 28.1% of Russian women reported a family history. More women had a family history of diabetes or stroke in all countries compared with men. The daily alcohol intake was much higher in men than women in all three study samples (Czech Republic: 14.1/3.4 g/day (men/women mean alcohol intake); Russia: 10.4/1.3 g/day; Poland: 4.5/1.1 g/day). Russian men and women had the highest daily energy intake compared with the other two countries, and men had higher energy intake than women in all three countries (Czech Republic: 2076.1/1944.2 kcal/day (men/women mean daily energy intake); Russia: 2765.7/2354.4 kcal/day; Poland: 2287.2/2076.6 kcal/day).

Table 24 Sample characteristics in the Czech Republic, Russia, and Poland

	Czech Republic				Russia				Poland			
	Men (N=2355)		Women (N=2705)		Men (N=3972)		Women (N=4816)		Men (N=3773)		Women (N=3898)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	58.4	0.1	57.4	0.1	58.2	0.1	58.0	0.1	58.1	0.1	57.3	0.1
Alcohol intake (g/day)	14.1	16.8	3.4	6.3	10.4	17.0	1.3	3.5	4.5	9.2	1.1	4.0
Energy intake (Kcal/day)	2076.1	629.8	1944.2	640.2	2765.7	819.5	2354.4	713.2	2287.2	673.3	2076.6	621.4
	N	%	N	%	N	%	N	%	N	%	N	%
Age group (%)												
45-49	379	16.1	510	18.9	636	16.0	863	17.9	630	16.7	770	19.8
50-54	433	18.4	570	21.1	782	19.7	931	19.3	743	19.7	847	21.7
55-59	456	19.4	507	18.7	862	21.7	1039	21.6	820	21.7	811	20.8
60-64	521	22.1	653	24.1	764	19.2	898	18.6	771	20.4	756	19.4
65-70	566	24.0	465	17.2	928	23.4	1085	22.5	809	21.4	714	18.3
Education (%)												
Primary or lower	115	4.9	473	17.5	450	11.3	451	9.4	341	9.0	547	14.0
Vocational	1034	43.9	807	29.8	868	21.9	1474	30.6	1028	27.2	579	14.9
Secondary	771	32.7	1125	41.6	1394	35.1	1,614	33.5	1257	33.3	1706	43.8
University	435	18.5	300	11.1	1260	31.7	1277	26.5	1147	30.4	1066	27.3
Smoking (%)												
Current smoker	699	29.7	635	23.5	1976	49.7	492	10.2	1289	34.2	1034	26.5
Past smoker	908	38.6	615	22.7	975	24.5	210	4.4	1398	37.1	823	21.1
Never smoker	748	31.8	1455	53.8	1021	25.7	4114	85.4	1086	28.8	2041	52.4
Leisure time activity (%)												
<1 hour/d	953	40.5	735	27.2	888	22.4	507	10.5	1359	36.0	777	19.9
1-2 hours/d	639	27.1	666	24.6	1152	29.0	1098	22.8	1163	30.8	1180	30.3
2-3 hours/d	445	18.9	630	23.3	937	23.6	1232	25.6	716	19.0	957	24.6
>3 hours/d	318	13.5	674	24.9	995	25.1	1979	41.1	535	14.2	984	25.2
Sports (%)												
0 hour/d	685	29.1	756	28.0	2809	70.7	3524	73.2	1074	28.5	1152	29.6
0-1 hour/d	1070	45.4	1237	45.7	508	12.8	577	12.0	1369	36.3	1,399	35.9
>1 hour/d	600	25.5	712	26.3	655	16.5	715	14.8	1330	35.3	1347	34.6

	Czech Republic				Russia				Poland			
	Men (N=2355)		Women (N=2705)		Men (N=3972)		Women (N=4816)		Men (N=3773)		Women (N=3898)	
	N	%	N	%	N	%	N	%	N	%	N	%
Working activity												
Working:non-pensioner	1241	52.7	1211	44.8	1827	46.0	1611	33.5	1722	45.6	1493	38.3
Not working:non-pensioner	4	0.2	25	0.9	4	0.1	95	2.0	7	0.2	113	2.9
Working:pensioner	200	8.5	182	6.7	846	21.3	784	16.3	282	7.5	222	5.7
Not working:pensioner	910	38.6	1287	47.6	1295	32.6	2326	48.3	1762	46.7	2070	53.1
Medication												
Yes	1152	48.9	1336	49.4	1015	25.6	2184	45.4	1910	50.6	2152	55.2
No	1203	51.1	1369	50.6	2957	74.5	2632	54.7	1863	49.4	1746	44.8
Family history of diabetes												
Yes	755	32.1	959	35.5	383	9.6	674	14.0	738	19.6	866	22.2
No	1600	67.9	1746	64.6	3589	90.4	4142	86.0	3035	80.4	3032	77.8
Family history of stroke												
Yes	627	26.6	864	31.9	728	18.3	1352	28.1	566	15.0	772	19.8
No	1728	73.4	1841	68.1	3244	81.7	3464	71.9	3207	85.0	3126	80.2

5.2 Prevalence of metabolic syndrome and its components in the HAPIEE study

In this section, the results for prevalence of metabolic syndrome in respond to Objective 1 (see Section 3.2) are shown. Table 25 shows the descriptive results of individual components of metabolic syndrome by country and sex. Men had larger waist circumference compared with women in the three countries (P<0.001). In men, Czechs had the largest waist circumference (98.0cm), followed by Poles (97.7cm), and Russians (94.1cm); in women, Russian had the largest waist circumference (91.8cm) followed by Czechs (88.7cm), and Russians (87.7cm). Czech and Polish men had higher systolic and diastolic blood pressure compared with Czech and Polish women (P<0.001), while Russian men and women had very similar blood pressure readings (Czech Republic: 144.2/90.8mmHg in men and 134.3/87.0mmHg in women; Russia: 142.7/90.3mmHg in men and 142.9/89.9mmHg in women; Poland: 142.4/88.1mmHg in men and 134.3/84.5mmHg in women). Men had higher triglycerides in the Czech and Polish samples (P<0.001), while Russian women had slightly higher level of triglycerides compared with men (P<0.001) (Czech Republic: 2.1mmol/L in men and 1.7mmol/L in women; Russia: 1.5mmol/L in men and 1.6mmol/L in women; Poland: 1.8mmol/L in men and 1.5mmol/L in women). For HDL-C (the 'healthy' cholesterol), women had higher levels compared with men in all countries (P<0.001). For plasma glucose, men had higher level than women in the Czech and Polish samples (P<0.001). Because glucose level in Russia was a binary variable (≥6.1mmol/L or not), its relationship to sex is described below in the prevalence section.

Table 26 shows the prevalence of metabolic syndrome by country and sex. In the Czech Republic and Poland, men and women had a similar prevalence of metabolic syndrome (Czech sample: 37.1% in men and 35.7% in women, P=0.316; Polish sample: 27.9% in men and 28.6% in women, P=0.532); while in Russia, women had higher prevalence of metabolic syndrome compared with men (20.8% in men and 36.3% in women, P<0.001). In all three countries, the prevalence of having raised blood pressure was high—over 50% in all subsamples (Czech Republic: 73.7% in men and 58.2% in women; Russia: 62.4% in men and 65.5% in women; Poland: 66.1% in men and 54.5% in women). The prevalence of central obesity was high, especially in women, the statistics were 50.4%, 60.9%, and 47.0% among Czech, Russian, and Polish women, respectively; while among men, they were 33.9%, 25.1%, and 32.3%, respectively. The prevalence of high triglycerides was high, and

the prevalence was higher among men compared with women in the Czech Republic and Poland (Czech Republic: 50.3% in men and 38.2% in women; Poland: 41.4% in men and 31.3% in women), while in Russia, the prevalence was lower among men (26.3% in men and 31.4% in women). In all countries, the prevalence of having low HDL-C was higher among women than men, and especially in Russia, where the prevalence among women was around 3 times higher than men (20.3% in women and 5.4% in men). The prevalence of having a high blood glucose was higher among men than women in all countries (P<0.001).

Table 27 shows the prevalence of each component of metabolic syndrome among participants with metabolic syndrome by country and sex. In all countries, the most frequent abnormality was blood pressure (Czech Republic: 94.3% in men, and 88.0% in women; Russia: 92.6% in men, and 91.0% in women; Poland: 91.8% in men and 86.8% in women). Central obesity was another commonly occurring component among participants with metabolic syndrome, especially among women in all three countries (Czech Republic: 67.4% in men, and 87.5% in women; Russia: 72.3% in men, and 93.0% in women; Poland: 74.7% in men, and 90.6% in women). Around 85% of Czech men and 79.1% of Czech women with metabolic syndrome had high triglycerides level, followed by 82.3% in Polish men and 75.3% in Polish women, and 78.2% in Russian men and 70.9% in Russian women. In Russia, almost 80% of men with metabolic syndrome had high glucose, although the proportion in women was lower (62.8%), while the percentages in the Czech and Polish sample were lower than in Russian sample (Czech Republic: 49.7% in men and 38.4% in women; Poland: 53.0% in men and 40.5% in women). Low HDL-C was more common in the Czech and Polish samples (Czech Republic: 57.4% in men, and 68.0% in women; Poland: 45.9% in men, and 60.5% in women). In Russia, the proportion of women with metabolic syndrome having low HDL-C was more than double that of men (18.3% in men, and 44.8% in women).

Table 25 Mean value of each component of metabolic syndrome by country and sex in the HAPIEE study

	Czech Republic					Russia					Poland				
	Men (N=2355)		Women (N=2705)			Men (N=3972)		Women (N=4816)			Men (N=3773)		Women (N=3898)		
	Mean	SD	Mean	SD	P*	Mean	SD	Mean	SD	P*	Mean	SD	Mean	SD	P*
Waist circumference (cm)	98.0	10.3	88.7	12.9	<0.001	94.1	12.1	91.8	13.2	<0.001	97.7	10.6	87.7	12.1	<0.001
SBP (mmHg)	144.2	18.7	134.3	19.6	<0.001	142.7	23.1	142.9	25.9	0.743	142.4	20.3	134.3	21.3	<0.001
DBP (mmHg)	90.8	10.7	87.0	10.9	<0.001	90.3	13.3	89.9	13.4	0.122	88.1	11.8	84.5	11.5	<0.001
Triglycerides (mmol/L)	2.1	1.4	1.7	0.9	<0.001	1.5	0.8	1.6	0.8	<0.001	1.8	1.1	1.5	0.8	<0.001
HDL-C (mmol/L)	1.3	0.3	1.5	0.4	<0.001	1.5	0.5	1.6	0.5	<0.001	1.3	0.3	1.6	0.4	<0.001
Plasma blood glucose (mmol/L)	5.9	1.5	5.7	1.3	<0.001	n/a	n/a	n/a	n/a	n/a	5.6	1.5	5.3	1.3	<0.001

*P-value from t-test ** SBP:systolic blood pressure ***DBP: diastolic blood pressure

Table 26 Prevalence of metabolic syndrome and its components in the HAPIEE sample

	Czech Republic					Russia					Poland				
	Men (N=2355)		Women (N=2705)			Men (N=3972)		Women (N=4816)			Men (N=3773)		Women (N=3898)		
	N	%	N	%	P*	N	%	N	%	P*	N	%	N	%	P*
Metabolic syndrome	873	37.1	966	35.7	0.316	827	20.8	1748	36.3	<0.001	1054	27.9	1114	28.6	0.532
Raised blood pressure	1735	73.7	1575	58.2	<0.001	2480	62.4	3154	65.5	0.003	2494	66.1	2126	54.5	<0.001
Central obesity	799	33.9	1363	50.4	<0.001	997	25.1	2935	60.9	<0.001	1220	32.3	1831	47.0	<0.001
High triglycerides	1184	50.3	1034	38.2	<0.001	1044	26.3	1510	31.4	<0.001	1561	41.4	1220	31.3	<0.001
Low HDI-C	646	27.4	875	32.4	<0.001	216	5.4	976	20.3	<0.001	708	18.8	1018	26.1	<0.001
Raised blood glucose	610	25.9	473	17.5	<0.001	1210	30.5	1368	28.4	0.035	831	22.0	584	15.0	<0.001

*P-value from chi-square test.

Table 27 The proportion of components of metabolic syndrome among participants with metabolic syndrome

	Czech Republic		Russia		Poland	
	Men (%)	Women (%)	Men (%)	Women (%)	Men (%)	Women (%)
Raised blood pressure	94.3	88.0	92.6	91.0	91.8	86.8
Central obesity	67.4	87.5	72.3	93.0	74.7	90.6
High triglycerides	85.0	79.1	78.2	70.9	82.3	75.3
Low HDL-C	57.4	68.0	18.3	44.8	45.9	60.5
High glucose	49.7	38.4	79.8	62.8	53.0	40.5

5.3 The association between sample characteristics and metabolic syndrome

In this section, in response to Objective 2, the prevalence of metabolic syndrome will be presented in relation to sample characteristics.

Table 28 shows the prevalence of metabolic syndrome in relation to the covariates used in the thesis. Lower alcohol intake was associated with metabolic syndrome only in Russian sample (P<0.001), not in the other two. This may due to the sex difference in alcohol consumption in Russian men and women (see Table 24), and it will be discussed in Chapter 6 Contrary to expectation, lower energy intake was associated with metabolic syndrome in three countries (P<0.002). In all countries, the prevalence of metabolic syndrome was higher with older age (P<0.001), with a peak of over 25% in the 65-69 years age group in all three study samples. There were no significant sex difference in prevalence of metabolic syndrome in the Czech and Polish sample (P=0.316 and P=0.532, respectively), but in the Russian sample, more women had metabolic syndrome than men (P<0.001). Prevalence of metabolic syndrome was also associated with education level (P<0.001): metabolic syndrome was more prevalent among participants with lower education in the Czech sample, especially those with vocational (41.2%) and secondary (32.7%) education; however, in Russian and Polish samples, although prevalence among those with secondary education was also higher (36.3% in Russian sample, 38.4% in Polish sample), the prevalence among participants with vocational and university education was similar (Russia: 26.5% with vocational education, 25.7% with university education; Poland: 22.1% with vocational education, 23.2% with university education), and those with primary or lower education had the lowest prevalence in these two samples (11.5% in Russia and 16.4% in Poland). In all three countries, prevalence of metabolic syndrome was significantly associated with smoking status: interestingly among people with metabolic syndrome, there were more never smokers than both past smokers and current smokers having metabolic syndrome (non-smokers: 41.3% in the Czech sample, 68.6% in the Russian sample, and 41.6% in the Polish sample). Leisure time activity was not significantly associated with metabolic syndrome in the Russian and Polish sample, but was associated in the Czech sample (P=0.001); among subjects with metabolic syndrome, 35.2% of them undertook <1 hour/day leisure activity, followed by 24.5% of those with 1-2 hours/day, 21.3% with >3 hours/day, and 19.0% with 2-3 hours/day. Hours spent participating in sports was significantly associated with metabolic syndrome in three countries (P<0.001): in the Czech sample, around

42.9% people with metabolic syndrome had 0-1 hour/day spent on sports, 33.4% did not spend any time on sports, and the rest had >1 hour/day spent on sports; while in Russia, most people with metabolic syndrome had no hour spending on sports (75.6%), 10.9% with 0-1hour/day, and 13.5% with >1 hour/day; in Poland, the more hours spent on sports was associated with lower risk of metabolic syndrome (>1 hour/day: 34.7%; 0-1 hour/day: 33.4%; 0 hour/day: 32.0%). Working activity was also associated with metabolic syndrome. In three countries, over half of the participants with metabolic syndrome were pensioners who were not working at the moment (55.3% in the Czech sample, 51.8% in the Russian sample, 61.6% in the Polish sample), and around one third were non-pensioners who were working (36.7% in the Czech sample, 29.3% in the Russian sample, and 29.8% in the Polish sample). However, unlike the other two samples, among participants with metabolic syndrome, in the Russian sample, there were more working pensioners compared with the other two samples (7.0% in the Czech sample, 17.8% in the Russian sample, and 7.4% in the Polish sample). In all three study samples, more participants with metabolic syndrome used at least one medication for high blood pressure, diabetes, or high cholesterol (P<0.001). Family history of diabetes and stroke was also associated with metabolic syndrome in all three countries (P<0.05).

Table 28 Sample characteristics in relation to metabolic syndrome by country

	Czech Republic			Russia			Poland		
	No (N=3221)	Yes (N=1839)	P*	No (N=6213)	Yes (N=2575)	P*	No (N=5503)	Yes (N=2168)	P*
	Mean(SD)	Mean (SD)		Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Alcohol intake (g/day)	8.6 (13.2)	7.9 (13.9)	0.067	6.0 (13.3)	4.0 (10.6)	<0.001	2.8 (6.9)	2.7 (8.2)	0.597
Energy intake (kcal/day)	2026.6 (635.9)	1968.8 (642.1)	0.002	2589.7 (799.8)	2421.0 (752.7)	<0.001	2199.0 (654.6)	2132.5 (656.9)	<0.001
	%	%		%	%		%	%	
Age group									
45-49	77.2	22.8	<0.001	80.7	19.3	<0.001	83.0	17.0	<0.001
50-54	72.2	27.8		73.7	26.3		76.5	23.5	
55-59	61.2	38.8		67.7	32.4		68.4	31.6	
60-64	56.6	43.4		67.6	32.4		68.2	31.8	
65-69	54.0	46.0		66.2	33.8		63.6	36.4	
Sex									
Male	62.9	37.1	0.316	79.2	20.8	<0.001	72.1	27.9	0.532
Female	64.3	35.7		63.7	36.3		71.4	28.6	
Education									
Primary or lower	51.7	48.3	<0.001	67.0	33.0	<0.001	60.0	40.0	<0.001
Vocational	58.8	41.2		70.9	29.1		70.3	29.7	
Secondary	68.3	31.8		68.9	31.1		71.9	28.1	
University	73.5	26.5		73.9	26.1		77.3	22.7	
Smoking									
Current smoker	65.1	34.9	0.001	82.2	17.8	<0.001	75.9	24.1	<0.001
Past smoker	59.8	40.3		68.9	31.1		68.2	31.8	
Never smoker	65.5	34.5		65.6	34.4		71.2	28.9	
Leisure time activity									
<1 hour/d	61.6	38.4	0.001	71.4	28.6	0.102	71.2	28.8	0.706
1-2 hours/d	65.5	34.5		72.5	27.5		71.9	28.1	
2-3 hours/d	67.5	32.5		69.6	30.4		72.7	27.3	
>3 hours/d	60.5	39.5		69.8	30.2		71.2	28.8	
Sports									

	Czech Republic			Russia			Poland		
	No (N=3221)	Yes (N=1839)	P*	No (N=6213)	Yes (N=2575)	P*	No (N=5503)	Yes (N=2168)	P*
0 hour/d	57.3	42.7	<0.001	69.3	30.7	<0.001	68.9	31.1	<0.001
0-1 hour/d	65.8	34.2		74.1	25.9		73.9	26.1	
>1 hour/d	66.8	33.2		74.7	25.3		71.9	28.1	
Working activity									
Working:non-pensioner	72.5	27.5	<0.001	78.0	22.0	<0.001	79.9	20.1	<0.001
Not working:non-pensioner	34.5	65.5		73.7	26.3		79.2	20.8	
Working:pensioner	66.2	33.8		71.8	28.2		68.1	31.9	
Not working:pensioner	53.8	46.2		63.1	36.9		65.2	34.8	
Medication **									
Yes	48.4	51.7	<0.001	50.8	49.2	<0.001	59.8	40.2	<0.001
No	78.5	21.5		82.1	17.9		85.2	14.9	
Family history of diabetes									
Yes	57.9	42.1	<0.001	63.3	36.7	<0.001	64.4	35.6	<0.001
No	66.6	33.4		71.7	28.3		73.7	26.3	
Family history of stroke									
Yes	59.8	40.2	<0.001	66.4	33.6	<0.001	68.7	31.3	0.006
No	65.3	34.7		72.0	28.0		72.4	27.6	

*P-value: chi-square tests**Medication was defined as having at least one of the medication for high blood pressure, high glucose, or high cholesterol.

5.4 HDI in the HAPIEE study

In this section, in response to the Objective 3, the distribution of HDI and its components will be described, along with relationships between HDI and covariates. The total HDI score was approximately normally distributed in each country, while the components of HDI were slightly skewed.

Table 29 shows the mean, standard deviation, and median of HDI total score and its components by country and sex. There were sex differences in the components of HDI in each country, but overall women had higher HDI (a healthier diet) in all three countries. In the Czech sample, women had an 0.2 units higher total HDI score compared with men (P<0.001); women also had a higher (healthier) score in saturated fats, protein, fruits and vegetables, fibre, and cholesterol, while men had higher score in sugar; there was no difference on polyunsaturated fats score between men and women. In Russia, women also had an 0.2 units higher HDI total score compared with men (P<0.001); Russian women also had higher score in saturated fats, protein, fruits and vegetables, and cholesterol compared to men, while men had higher score in polyunsaturated fats, sugar, and fibre intake. In Poland, women had 0.2 units higher HDI total score compared to men (P<0.001); Polish women had higher score in saturated fats, protein, fruit and vegetables, and cholesterol, while men had higher score in polyunsaturated fats and sugar; there was no difference of fibre intake between men and women.

Table 29 Average HDI by country and sex

	Czech Republic							Russia							Poland						
	Men (N=2355)			Women (N=2705)				Men (N=3972)			Women (N=4816)				Men (N=3773)			Women (N=3898)			
	Mean	SD	Median	Mean	SD	Median	P*	Mean	SD	Median	Mean	SD	Median	P*	Mean	SD	Median	Mean	SD	Median	P*
HDI	4.6	0.7	4.6	4.8	0.7	4.9	**<0.001**	4.3	0.6	4.3	4.5	0.7	4.4	**<0.001**	4.2	0.7	4.1	4.4	0.7	4.3	**<0.001**
SFA	3.2	3.2	2.5	4.0	3.4	3.5	**<0.001**	2.4	3.0	0.7	2.9	3.3	1.7	**<0.001**	2.1	3.0	0.1	2.8	3.3	1.3	**<0.001**
PUFA	9.5	1.0	10.0	9.4	1.1	10.0	0.162	9.3	1.8	10.0	8.8	2.3	10.0	**<0.001**	8.3	1.4	8.4	8.0	1.5	8.1	**<0.001**
Protein	6.4	2.6	6.7	7.1	2.5	7.5	**<0.001**	7.0	2.4	7.3	7.2	2.5	7.7	**<0.001**	6.4	2.4	6.6	6.7	2.3	6.9	**<0.001**
Sugar	4.6	2.8	4.6	3.0	2.7	2.6	**<0.001**	6.1	2.2	6.2	4.9	2.5	5.1	**<0.001**	4.5	2.6	4.5	3.2	2.6	2.9	**<0.001**
Fruit & vegetables	8.2	2.5	10.0	9.1	1.9	10.0	**<0.001**	7.8	2.3	8.3	8.3	2.2	9.4	**<0.001**	8.5	2.2	10.0	8.9	1.9	10.0	**<0.001**
Fibre	7.6	2.1	7.7	8.2	2.0	8.8	**<0.001**	8.3	1.7	8.6	8.1	1.8	8.4	**<0.001**	8.4	1.8	10.0	8.4	1.8	10.0	0.717
Cholesterol	6.8	4.1	10.0	7.8	3.7	10.0	**<0.001**	2.3	3.8	0	4.5	4.5	3.0	**<0.001**	3.8	4.3	1.6	5.7	4.3	7.0	**<0.001**

*T-test was performed for HDI (total score), Wilcoxon rank-sum test was performed for the components of HDI scores because of the assumption of normality was not met

Table 30,Table 31, and Table 32 show the correlations between the HDI components by country. Saturated fatty acids score and other components of HDI were significantly but weakly correlated (P<0.003), except for fruit and vegetable score (P=0.129). For example, in all countries, saturated fatty acids and polyunsaturated fatty acids scores were weakly negatively but significantly correlated (β=-0.167 in the Czech sample, β=-0.133 in the Russian sample, and β=-0.176 in the Polish sample); saturated fatty acid scores were positively correlated with protein in both Czech (β=0.069) and Russian (β=0.031) samples, but in the Polish sample, the correlation was in the opposite direction (β =-0.126). Moreover, saturated fatty acid and cholesterol scores were moderately positively correlated in the Russian sample (β=0.474), but the correlation was slightly weaker in the Czech (β=0.348) and Polish (β=0.380) samples, but remained significant (P<0.001). Polyunsaturated fatty acids and other components of HDI were all weakly but significantly correlated (P<0.05): for example, it was weakly negatively correlated with protein (β=-0.133 in the Czech sample, β=-0.185 in the Russian sample, β=-0.073 in the Polish sample). The protein score was weakly and significantly correlated with other scores of components of HDI except with fruit and vegetable in the Russian sample and cholesterol in the Polish sample. Moreover, the correlation with sugar was consistently stronger in all three study samples (β=-0.387 in the Czech sample, β=-0.230 in the Russian sample, β=-0.278 in the Polish sample). Sugar score was negatively and significantly correlated with fibre and cholesterol scores, and moderately correlated with fruits and vegetables in the Czech and Polish samples (β=-0.423 in the Czech sample and β=-0.426 in the Polish sample; P<0.001 for both). Fruits and vegetables score was strongly positively correlated with fibre score in all three samples (β=0.725 in the Czech sample, β=0.697 in the Russian sample, and β=0.705 in the Polish sample; P<0.001), and it was weakly negatively correlated with cholesterol score in all three countries (P<0.001). Fibre and cholesterol scores were weakly negatively correlated in all countries (β=-0.255 in the Czech sample, β=-0.354 in the Russian sample, β=-0.281 in the Polish sample; P<0.001 for all samples). In summary, the consistent relationship found in the three study samples were the positive correlations between saturated fatty acids and cholesterol score, and between fruit and vegetable score and fibre scores.

Table 30 Correlation coefficients between components of HDI in the Czech sample (N=5060)

	SFA	PUFA	Protein	Sugar	F & V	Fibres	Cholesterol
SFA*	1.000						
PUFA*	-0.167	1.000					
P value	*<0.001*						
Protein	0.069	-0.133	1.000				
P value	*<0.001*	*<0.001*					
Sugar	-0.341	0.116	-0.387	1.000			
P value	*<0.001*	*<0.001*	*<0.001*				
F & V*	0.200	0.051	0.082	-0.423	1.000		
P value	*<0.001*	*<0.001*	*<0.001*	*<0.001*			
Fibre	0.253	0.032	0.154	-0.313	0.725	1.000	
P value	*<0.001*	*0.022*	*<0.001*	*<0.001*	*<0.001*		
Cholesterol	0.348	-0.131	0.169	-0.179	-0.110	-0.255	1.000
P value	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	

*Abbreviations: SFA- saturated fats; PUFA- Polyunsaturated fats; F&V: Fruit and

Table 31 Correlation coefficients between components of HDI in the Russian sample (N=8788)

	SFA	PUFA	Protein	Sugar	F & V	Fibres	Cholesterol
SFA*	1.000						
PUFA*	-0.133	1.000					
P value	*<0.001*						
Protein	0.031	-0.185	1.000				
P value	*0.003*	*<0.001*					
Sugar	-0.198	-0.125	-0.230	1.000			
P value	*<0.001*	*<0.001*	*<0.001*				
F & V*	-0.016	-0.039	-0.003	-0.245	1.000		
P value	*0.129*	*<0.001*	*0.783*	*<0.001*			
Fibre	-0.045	0.025	0.105	-0.083	0.697	1.000	
P value	*<0.001*	*0.021*	*<0.001*	*<0.001*	*<0.001*		
Cholesterol	0.474	-0.142	0.143	-0.170	-0.165	-0.354	1.000
P value	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*	

*Abbreviations: SFA- saturated fats; PUFA- Polyunsaturated fats; F&V: Fruit and

Table 32 Correlation coefficients between components of HDI in the Polish sample (N=7671)

	SFA	PUFA	Protein	Sugar	F & V	Fibres	Cholesterol
SFA*	1.000						
PUFA*	**-0.176**	**1.000**					
P value	*<0.001*						
Protein	**-0.126**	**-0.073**	**1.000**				
P value	*<0.001*	*<0.001*					
Sugar	**-0.274**	**0.280**	**-0.278**	**1.000**			
P value	*<0.001*	*<0.001*	*<0.001*				
F & V*	**0.133**	**0.105**	**0.038**	**-0.426**	**1.000**		
P value	*<0.001*	*<0.001*	*0.001*	*<0.001*			
Fibre	**0.147**	**0.078**	**0.154**	**-0.354**	**0.705**	**1.000**	
P value	*<0.001*	*<0.001*	*<0.001*	*<0.001*	*<0.001*		
Cholesterol	**0.380**	**-0.215**	**0.010**	**-0.119**	**-0.126**	**-0.281**	**1.000**
P value	*<0.001*	*<0.001*	*0.376*	*<0.001*	*<0.001*	*<0.001*	

*Abbreviations: SFA- saturated fats; PUFA- Polyunsaturated fats; F&V: Fruit and

Table 33 shows the associations between total HDI score and a range of covariates. In all countries, HDI score was higher in older adults (P<0.001); women had higher HDI score than men (P<0.001); and never smokers and past smokers had a higher HDI score compared with current smokers (P<0.001). In both Czech and Polish samples, HDI score increased with longer time spent on leisure activity and engagement in sports (P<0.001), but such associations were not found in Russia (P=0.398), where HDI score was lower with more time spent on sports engagement (P<0.001). In the Czech and Russian samples, the HDI score decreased with higher education level (P=0.043 in the Czech sample, P=0.009 in the Russian sample), but in Poland education was not associated with HDI score (P=0.445). Subjects taking at least one medication for high blood pressure, cholesterol, or diabetes had a lower HDI score than those who did not in the Czech sample (P<0.001). However, in the Russian and Polish samples, HDI scores were lower among subjects not taking medication (P<0.001). Those with a family history of diabetes had higher HDI score compared with those without (P<0.001), but this was not significant among Czechs (P=0.153). In the Czech and Polish samples, subjects with family history of stroke had higher HDI score compared with those without (P=0.007 in the Czech sample, P=0.032 in the Polish sample), but this association was not found among Russians (P=0.297).

Finally, HDI score was associated with working activity (P<0.001), and a high HDI score was correlated with lower alcohol consumption per day, and total energy intake per day in all countries (P<0.001).

Table 33 Sample characteristics in relation to HDI total score in the HAPIEE study

Covariates		Czech Republic (N=5060)		Russia (N=8788)		Poland (N=7671)	
		HDI mean (SD)	P*	HDI mean (SD)	P *	HDI mean (SD)	P *
Age group	45-49	46.3(7.1)	<0.001	42.9(6.3)	<0.001	42.0(6.4)	<0.001
	50-54	46.9(6.8)		43.3(6.4)		42.2(6.5)	
	55-59	47.4(6.9)		44.0(6.9)		43.0(6.6)	
	60-64	48.2(7.0)		44.4(6.9)		43.4(6.5)	
	65-69	48.2(6.9)		45.1(7.2)		43.7(6.8)	
Sex	Men	46.3(7.2)	<0.001	43.1(6.5)	<0.001	42.0(6.5)	<0.001
	Women	48.5(6.5)		44.7(7.0)		43.7(6.6)	
Smoking	Current smoker	46.2(7.1)	<0.001	42.5(6.4)	<0.001	41.7(6.5)	<0.001
	Past smoker	47.7(6.9)		43.7(6.6)		43.2(6.5)	
	Never smoker	48.1(6.7)		44.8(6.9)		43.5(6.6)	
Leisure activity	<1 hour/d	47.1(7.1)	<0.001	44.1(6.9)	0.398	42.3(6.8)	0.015
	1-2 hours/d	47.4(6.8)		44.1(6.8)		43.3(6.5)	
	2-3 hours/d	47.6(6.9)		43.9(6.8)		43.1(6.6)	
	>3 hours/d	48.0(6.8)		43.9(6.8)		42.9(6.4)	
Sports time	0 hour/d	46.7(7.1)	<0.001	44.2(6.9)	<0.001	42.0(6.4)	<0.001
	0-1 hour/d	47.6(6.9)		43.8(6.4)		43.2(6.8)	
	>1 hour/d	48.2(6.7)		43.3(6.9)		43.3(6.5)	

Covariates		Czech Republic (N=5060)		Russia (N=8788)		Poland (N=7671)	
		HDI mean (SD)	P*	HDI mean (SD)	P *	HDI mean (SD)	P *
Working activity	Working:non-pensioner	46.6(6.9)	**<0.001**	43.0(6.3)	**<0.001**	42.2(6.4)	**<0.001**
	Not working:non-pensioner	49.5(6.4)		43.5(6.8)		42.8(7.0)	
	Working: pensioner	47.7(6.9)		43.9(6.6)		42.9(6.6)	
	Not working: pensioner	48.4(6.8)		44.9(7.2)		43.5(6.7)	
Education	Primary or lower	48.0(7.1)	**0.043**	44.6(7.3)	**0.009**	43.0(6.6)	0.445
	Vocational	47.4(7.0)		44.2(6.8)		42.5(6.4)	
	Secondary	47.6(6.7)		43.7(6.8)		43.1(6.7)	
	University	46.9(7.1)		43.9(6.7)		42.9(6.6)	
Medication**	Yes	48.3(6.8)	**<0.001**	43.5(6.6)	**<0.001**	41.9(6.4)	**<0.001**
	No	46.7(6.9)		44.8(7.0)		43.7(6.7)	
Family history of diabetes	Yes	47.7(7.0)	0.153	44.4(6.8)	**0.043**	43.2(6.8)	**0.014**
	No	47.4(6.9)		43.9(6.8)		42.8(6.6)	
Family history of stroke	Yes	47.9(6.8)	**0.007**	44.1(6.9)	0.297	43.2(6.6)	**0.032**
	No	47.3(7.0)		43.9(6.8)		42.8(6.6)	
		r		r		r	
Alcohol intake (g/day)		-0.147	**<0.001**	-0.078	**<0.001**	-0.080	**<0.001**
Energy intake (kcal/day)		-0.130	**<0.001**	-0.236	**<0.001**	-0.223	**<0.001**

*P-value for trend using linear regression for age group, leisure activity, sports time, education; P-value for correlation coefficient (r) for alcohol intake and energy intake; P-value from t-test for sex, medication, family history of diabetes, family history of stroke; P-value from one-way ANOVA for smoking, working activity.

**At least have one medication for blood pressure, diabetes, or cholesterol

5.5 Potential confounders, mediators, and effect modifiers

According to the previous analyses conducted in sections 5.2 and 5.4, which examined metabolic syndrome and HDI in relations to covariates. The following variables were therefore chosen as potential confounders in each study sample (ie, variables associated with both the exposure and outcome but not on the causal pathway).

- Czech Republic:
    - *Age group*
    - *Sex*
    - *Smoking status*
    - *Leisure activity*
    - *Sports time*
    - *Working activity*
    - *Education*
    - *Medication for blood pressure, diabetes, or cholesterol*
    - *Family history of stroke*
    - *Energy intake*
- Russia:
    - *Age group*
    - *Sex*
    - *Smoking status*
    - *Sports time*
    - *Working activity*
    - *Education*
    - *Medication for blood pressure, diabetes, or cholesterol*
    - *Family history of diabetes*
    - *Alcohol intake*
    - *Energy intake*
- Poland:
    - *Age group*
    - *Sex*
    - *Smoking status*
    - *Sports time*
    - *Working activity*
    - *Medication for blood pressure, diabetes, or cholesterol*

- *Family history of diabetes*
- *Family history of stroke*
- *Energy intake*

Mediators are also the important elements in the epidemiological studies. However, mediators were not considered in this thesis due to the cross-sectional study design, which are not recommended to test for mediation.[306]

Potential effect modifiers were also tested using interaction tests. These analyses suggested that sex was not effect modifier in the association between HDI and metabolic syndrome in any of three countries (Czech Republic: P=0.37; Russia: P=0.21; Poland: P=0.63). Therefore, analyses between HDI and metabolic syndrome were carried out without sex stratification. Moreover, country was not a significant effect modifier in the association between HDI and metabolic syndrome either (P=0.115), but country specific analyses were carried out due to some country specific methodological designs, and combined analyses conducted in addition (see Section 5.6.3). Education and energy intake were found to be effect modifiers in the association between HDI and metabolic syndrome in the Czech sample; however, this was not found in Russia or Poland.

In order to facilitate the comparison among countries, the regression model in the main analyses included all the confounders and interaction terms which had been found in any country. Therefore, in multivariable regression models, adjustment was made for the following: age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake were included. Interaction terms were also included between education and HDI, and between energy intake and HDI. In the pooled analyses, a categorical variable indicating country was also added in the final model as a potential confounder.

5.6 Association between HDI and metabolic syndrome (and its components) in the HAPIEE study

In the following sections, the results in response to Objective 4 are presented. To investigate the associations between HDI (and its components) and metabolic syndrome (and its components), three models were performed: first, a crude (unadjusted) model; second, a model adjusted for age group and sex; and finally a

model additionally adjusted for a range of other potential confounders (smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake) and effect modifiers (education and energy intake).

5.6.1   HDI total score and metabolic syndrome—country specific results

Table 34 shows the association between total HDI score and metabolic syndrome and its components by country. In the Czech sample, HDI total score was not associated with metabolic syndrome, high blood pressure, low HDL-C, or high glucose. A higher score of total HDI (healthier diet) was associated with higher risk of central obesity and lower risk of high triglycerides in the unadjusted model (OR:1.15, 95%CI(1.06,1.24), P<0.001; 0.91(0.84,0.99),P=0.029), but both associations were fully attenuated after adjustment for potential confounders. In the Russian sample, a higher HDI score was associated with higher risk of having metabolic syndrome (1.11 (1.04,1.19),P=0.003), high blood pressure (1.12 (1.05,1.20), P<0.001), central obesity (1.09 (1.02,1.16), P=0.007), high triglycerides (1.07 (1.00,1.15), P=0.045), and low HDL-C (1.11 (1.02,1.21), P=0.020) in the unadjusted models, but these associations were fully attenuated in the adjusted models. In Polish sample, a higher HDI total score was associated with higher risk of metabolic syndrome (1.18 (1.09,1.27), P<0.001), high blood pressure (1.17 (1.07,1.28), P<0.001), central obesity (1.15 (1.07,1.23), P<0.001), low HDL-C (1.14 (1.07,1.23), P<0.001), and high glucose (1.14 (1.05,1.24), P=0.001). After adjusting for age group and sex, the associations between HDI and metabolic syndrome (1.12 (1.04,1.21), P=0.003), high blood pressure (1.14 (1.06,1.22), P=0.001), low HDL-C (1.09 (1.01,1.19), P=0.033), and high glucose (1.16 (1.06,1.27), P=0.001) remained significant although attenuated. However, after full adjustment, these associations were fully attenuated.

In the next section, the association between individual components of HDI and metabolic syndrome and its components will be presented.

Table 34 The association between HDI score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.05 (0.97,1.14)	0.260	0.99 (0.91,1.08)	0.843	1.00 (0.78,1.28)	0.974
High blood pressure	1.04 (0.96,1.13)	0.332	1.05 (0.96,1.15)	0.282	0.97 (0.74,1.28)	0.838
Central obesity	1.15 (1.06,1.24)	**0.001**	1.00 (0.91,1.08)	0.926	1.11 (0.86,1.42)	0.425
High TG	0.91 (0.84,0.99)	**0.029**	0.94 (0.87,1.02)	0.151	0.92 (0.72,1.16)	0.472
Low HDL-C	0.98 (0.90,1.06)	0.587	0.93 (0.85,1.02)	0.103	0.88 (0.69,1.13)	0.312
High glucose	1.04 (0.94,1.14)	0.454	1.04 (0.94,1.15)	0.467	0.95 (0.72,1.24)	0.708
Russia						
Metabolic syndrome	1.11 (1.04,1.19)	**0.003**	1.00 (0.93,1.07)	0.937	1.03 (0.83,1.28)	0.804
High blood pressure	1.12 (1.05,1.20)	**<0.001**	1.05 (0.98,1.12)	0.185	0.83 (0.62,1.12)	0.225
Central obesity	1.09 (1.02,1.16)	**0.007**	0.92 (0.86,0.98)	**0.015**	1.00 (0.80,1.25)	0.978
High TG	1.07 (1.00,1.15)	**0.045**	1.02 (0.96,1.10)	0.490	1.01 (0.82,1.25)	0.913
Low HDL-C	1.11 (1.02,1.21)	**0.020**	1.00 (0.91,1.10)	0.956	1.01 (0.77,1.32)	0.959
High glucose	1.05 (0.98,1.12)	0.178	1.02 (0.95,1.09)	0.663	0.96 (0.78,1.18)	0.678
Poland						
Metabolic syndrome	1.18 (1.09,1.27)	**<0.001**	1.12 (1.04,1.21)	**0.003**	0.91 (0.73,1.14)	0.404
High blood pressure	1.15 (1.07,1.23)	**<0.001**	1.14 (1.06,1.22)	**0.001**	0.81 (0.62,1.04)	0.097
Central obesity	1.14 (1.07,1.23)	**<0.001**	1.03 (0.96,1.10)	0.456	0.85 (0.68,1.06)	0.140
High TG	1.02 (0.95,1.10)	0.568	1.05 (0.98,1.13)	0.153	1.05 (0.85,1.30)	0.650
Low HDL-C	1.14 (1.05,1.24)	**0.001**	1.09 (1.01,1.19)	**0.033**	1.04 (0.83,1.31)	0.710
High glucose	1.17 (1.07,1.28)	**<0.001**	1.16 (1.06,1.27)	**0.001**	0.92 (0.72,1.18)	0.526

[a]HDI total score with 10-unit increment
[b]model 1: unadjusted model
[c]model 2: adjusted for age group and sex
[d]model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

5.6.2 HDI components, metabolic syndrome, and its components – country specific results

This section presents associations between each of the seven components of HDI score (saturated fatty acids, polyunsaturated fatty acids, protein, sugar, fruit and vegetable, fibre, and cholesterol) and metabolic syndrome and its components (in response to Objective 5).

Table 35 shows the association between a one unit increase in saturated fatty acids score and risk of metabolic syndrome and the components of metabolic syndrome in three study samples. In the Czech sample, saturated fatty acids score was not associated with risk of metabolic syndrome nor its components, except high blood glucose. After adjusting for potential confounders and including interaction terms, a one unit increase in saturated fatty acids score was associated with 8% increased risk of having high blood glucose (1.08 (1.01,1.16), P=0.036) in the Czech sample. In the Russian sample, higher saturated fatty acids score was associated with a slightly increased risk of some components of metabolic syndrome in unadjusted models: for example, a one unit increase in saturated fatty acids score was associated with 4% increased risk of having a low HDL-C level. However, these associations were fully attenuated after adjustment for potential confounders. In the Polish sample, the association between saturated fatty acids score and metabolic syndrome and its components was similar to the Russian sample in the unadjusted model. However, unlike the Russian sample, the fully adjusted model in the Polish sample showed some significant associations: a one unit increase in saturated fatty acid score was associated with higher risk of having high triglycerides (1.06 (1.00,1.12), P=0.048) and high blood glucose (1.07 (1.00,1.15), P=0.043), but associated with lower risk of having central obesity (0.93 (0.88,0.99), P=0.017) after adjusting for all confounders and including the effect modifiers.

The association between polyunsaturated fatty acids score and risk of metabolic syndrome and its components is shown in Table 36. In the Czech sample, a higher score in polyunsaturated fatty acids was associated with higher risk of high blood pressure in the unadjusted and age and sex adjusted models. However, in the fully adjusted model, the association was fully attenuated. No other association was found in the Czech sample. In the Russian sample, a higher polyunsaturated fatty acid score was weakly associated with lower risk of metabolic syndrome and its components: for example, a higher score of polyunsaturated fatty acids were associated with lower

risk of metabolic syndrome in the age and sex adjusted model (0.97 (0.95,0.99), P=0.012). However, these associations were attenuated fully after adjusting for confounders. In the Polish sample, higher score in polyunsaturated fatty acids was associated with lower risk of having low HDL-C, but the association with HDL-C was not significant in the fully adjusted model, while the association with lower risk of having high triglycerides was only significant after adjusting for more confounders (0.91 (0.83,1.00), P=0.043).

Table 35 The association between saturated fatty acids score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.01 (0.99,1.02)	0.544	1.01 (0.99,1.02)	0.524	1.04 (0.98,1.11)	0.218
High blood pressure	0.99 (0.98,1.01)	0.518	1.01 (0.99,1.02)	0.535	1.02 (0.95,1.09)	0.616
Central obesity	1.01 (0.99,1.02)	0.476	0.99 (0.98,1.01)	0.433	1.03 (0.96,1.10)	0.391
High TG	0.99 (0.98,1.01)	0.379	1.00 (0.98,1.02)	0.940	1.03 (0.97,1.09)	0.358
Low HDL-C	1.01 (1.00,1.03)	0.120	1.01 (0.99,1.03)	0.288	0.96 (0.90,1.02)	0.212
High glucose	1.00 (0.98,1.02)	0.630	1.00 (0.98,1.02)	0.793	1.08 (1.01,1.16)	**0.036**
Russia						
Metabolic syndrome	1.03 (1.02,1.05)	**<0.001**	1.01 (1.00,1.03)	0.086	0.99 (0.93,1.05)	0.764
High blood pressure	1.05 (1.03,1.06)	**<0.001**	1.03 (1.02,1.05)	**<0.001**	0.94 (0.88,1.00)	0.069
Central obesity	1.03 (1.01,1.04)	**<0.001**	1.00 (0.99,1.01)	0.983	0.98 (0.92,1.04)	0.447
High TG	1.02 (1.01,1.03)	**0.007**	1.01 (1.00,1.03)	0.128	0.96 (0.90,1.01)	0.120
Low HDL-C	1.04 (1.02,1.06)	**<0.001**	1.03 (1.01,1.05)	**0.008**	1.01 (0.94,1.09)	0.825
High glucose	1.01 (1.00,1.03)	0.097	1.01 (0.99,1.02)	0.478	0.96 (0.91,1.02)	0.190
Poland						
Metabolic syndrome	1.05 (1.03,1.06)	**<0.001**	1.03 (1.02,1.05)	**<0.001**	1.02 (0.96,1.08)	0.557
High blood pressure	1.04 (1.03,1.06)	**<0.001**	1.03 (1.02,1.05)	**<0.001**	1.02 (0.95,1.09)	0.645
Central obesity	1.03 (1.01,1.04)	**<0.001**	1.01 (0.99,1.02)	0.498	0.93 (0.88,0.99)	**0.017**
High TG	1.02 (1.01,1.04)	**0.003**	1.03 (1.01,1.04)	**<0.001**	1.06 (1.00,1.12)	**0.048**
Low HDL-C	1.04 (1.03,1.06)	**<0.001**	1.04 (1.02,1.05)	**<0.001**	1.00 (0.94,1.06)	0.955
High glucose	1.03 (1.01,1.05)	**0.002**	1.02 (1.00,1.04)	**0.027**	1.07 (1.00,1.15)	**0.043**

[a]Saturated fats score with one unit increment
[b]model 1: unadjusted model
[c]model 2: adjusted for age group and sex
[d]model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

Table 36 The association between polyunsaturated fatty acids score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.03 (0.97,1.08)	0.347	1.03 (0.97,1.09)	0.306	1.04 (0.91,1.19)	0.570
High blood pressure	1.07 (1.02,1.13)	**0.009**	1.07 (1.01,1.13)	**0.015**	1.00 (0.87,1.16)	0.966
Central obesity	1.01 (0.96,1.06)	0.746	1.02 (0.97,1.08)	0.414	0.97 (0.85,1.12)	0.694
High TG	1.02 (0.97,1.07)	0.458	1.01 (0.96,1.07)	0.622	1.00 (0.88,1.13)	0.946
Low HDL-C	0.97 (0.92,1.03)	0.329	0.98 (0.93,1.03)	0.419	0.99 (0.87,1.13)	0.880
High glucose	1.01 (0.94,1.07)	0.875	1.00 (0.94,1.07)	0.966	1.05 (0.90,1.22)	0.564
Russia						
Metabolic syndrome	0.96 (0.94,0.98)	**<0.001**	0.97 (0.95,0.99)	**0.012**	0.98 (0.91,1.05)	0.516
High blood pressure	0.97 (0.95,0.99)	**0.013**	0.97 (0.95,0.99)	**0.004**	0.98 (0.90,1.06)	0.585
Central obesity	0.94 (0.92,0.96)	**<0.001**	0.97 (0.95,0.99)	**0.010**	0.97 (0.90,1.05)	0.459
High TG	1.00 (0.98,1.02)	0.866	1.00 (0.98,1.02)	0.867	0.99 (0.92,1.06)	0.769
Low HDL-C	0.93 (0.91,0.96)	**<0.001**	0.96 (0.94,0.99)	**0.003**	0.94 (0.86,1.02)	0.149
High glucose	0.98 (0.96,1.00)	0.057	0.97 (0.95,0.99)	**0.010**	0.96 (0.89,1.03)	0.208
Poland						
Metabolic syndrome	0.98 (0.95,1.01)	0.210	1.00 (0.97,1.04)	0.833	0.97 (0.88,1.07)	0.515
High blood pressure	1.00 (0.97,1.03)	0.942	1.02 (0.99,1.05)	0.258	1.02 (0.91,1.14)	0.760
Central obesity	1.01 (0.97,1.04)	0.722	1.05 (1.02,1.09)	**0.002**	1.01 (0.92,1.12)	0.771
High TG	0.99 (0.96,1.02)	0.446	0.98 (0.95,1.01)	0.216	0.91 (0.83,1.00)	**0.043**
Low HDL-C	0.94 (0.90,0.97)	**<0.001**	0.95 (0.91,0.98)	**0.005**	0.95 (0.86,1.05)	0.353
High glucose	1.06 (1.02,1.10)	**0.006**	1.08 (1.03,1.12)	**<0.001**	1.06 (0.94,1.18)	0.344

[a]Polyunsaturated fats score with one unit increment
[b]model 1: unadjusted model
[c]model 2: adjusted for age group and sex
[d]model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

Table 37 shows the association between protein score and risk of metabolic syndrome and its components. In the Czech sample, a higher protein score was associated with lower risk of metabolic syndrome and its components. However, the effects were weakened after adjusting for confounders and the inclusion of the effect modifiers, except for the association with lower risk of having high blood glucose (0.87 (0.80,0.94), P<0.001). Similar results were also found in Russia: a one unit increase in protein score was associated with 7% lower risk of having high blood glucose (0.93 (0.88,0.99), P=0.022). In the Polish sample, in the fully adjusted model, higher score in protein was significantly associated with not just lower risk of having high blood glucose (0.82 (0.75,0.89), P<0.001), but also metabolic syndrome (0.92 (0.86,0.98), P=0.015), and central obesity (0.90 (0.84,0.96), P=0.002).

The association between sugar score and risk of metabolic syndrome and its components is shown in Table 38. In the Czech sample, a higher score in sugar intake was associated with higher risk of metabolic syndrome and most components in the unadjusted model. For example, after adjusting for confounders and including effect modifiers, a higher score in sugar intake was only associated with a higher risk of having high blood glucose (1.11 (1.03,1.19), P=0.008). Higher sugar score was also significantly associated with lower risk of having low HDL-C in the fully adjusted model (0.93 (0.87,1.00), P=0.048). In the Russian sample, the higher sugar score was significantly associated with higher risk of having high blood pressure (1.10 (1.02,1.18), P=0.011) as well as high glucose (1.12 (1.05,1.19), P=0.001) in the fully adjusted model. Higher sugar score was also associated with lower risk of having low level of HDL-C (0.93 (0.91,0.95), P<0.001), but was only significant in the unadjusted model. In the Polish sample, a one unit increase in the sugar score was associated with 23% increased risk of having high blood glucose in the fully adjusted model (1.23 (1.15,1.32), P<0.001)—double the increased risk seen in the Czech and Russian samples.

Table 37 The association between protein score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	0.95 (0.92,0.97)	**<0.001**	0.93 (0.91,0.95)	**<0.001**	0.94 (0.87,1.01)	0.093
High blood pressure	0.94 (0.92,0.97)	**<0.001**	0.94 (0.92,0.96)	**<0.001**	0.98 (0.90,1.06)	0.556
Central obesity	0.98 (0.96,1.00)	**0.044**	0.94 (0.92,0.97)	**<0.001**	0.98 (0.91,1.06)	0.634
High TG	0.97 (0.95,0.99)	**0.002**	0.97 (0.95,1.00)	**0.023**	1.00 (0.93,1.07)	0.985
Low HDL-C	0.98 (0.96,1.00)	0.086	0.97 (0.95,0.99)	**0.011**	0.95 (0.88,1.02)	0.149
High glucose	0.89 (0.87,0.91)	**<0.001**	0.89 (0.86,0.91)	**<0.001**	0.87 (0.80,0.94)	**<0.001**
Russia						
Metabolic syndrome	0.93 (0.92,0.95)	**<0.001**	0.92 (0.90,0.94)	**<0.001**	0.97 (0.91,1.03)	0.292
High blood pressure	0.95 (0.93,0.96)	**<0.001**	0.94 (0.92,0.96)	**<0.001**	0.98 (0.91,1.05)	0.547
Central obesity	0.94 (0.93,0.96)	**<0.001**	0.92 (0.90,0.93)	**<0.001**	0.94 (0.88,1.00)	0.055
High TG	0.96 (0.94,0.98)	**<0.001**	0.96 (0.94,0.98)	**<0.001**	0.97 (0.92,1.04)	0.409
Low HDL-C	0.98 (0.96,1.01)	0.162	0.97 (0.95,0.99)	**0.017**	1.01 (0.93,1.10)	0.769
High glucose	0.92 (0.90,0.93)	**<0.001**	0.91 (0.90,0.93)	**<0.001**	0.93 (0.88,0.99)	**0.022**
Poland						
Metabolic syndrome	0.91 (0.89,0.93)	**<0.001**	0.91 (0.89,0.93)	**<0.001**	0.92 (0.86,0.98)	**0.015**
High blood pressure	0.92 (0.90,0.94)	**<0.001**	0.93 (0.91,0.95)	**<0.001**	1.05 (0.98,1.14)	0.176
Central obesity	0.94 (0.92,0.95)	**<0.001**	0.93 (0.91,0.95)	**<0.001**	0.90 (0.84,0.96)	**0.002**
High TG	0.95 (0.93,0.97)	**<0.001**	0.96 (0.94,0.98)	**<0.001**	0.95 (0.89,1.01)	0.116
Low HDL-C	0.99 (0.97,1.01)	0.455	0.99 (0.96,1.01)	0.236	0.94 (0.88,1.01)	0.073
High glucose	0.83 (0.81,0.85)	**<0.001**	0.84 (0.82,0.86)	**<0.001**	0.82 (0.75,0.89)	**<0.001**

[a] Protein score with one unit increment
[b] model 1: unadjusted model
[c] model 2: adjusted for age group and sex
[d] model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

Table 38 The association between sugar score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.06 (1.03,1.08)	**<0.001**	1.06 (1.04,1.08)	**<0.001**	1.04 (0.97,1.12)	0.249
High blood pressure	1.08 (1.05,1.10)	**<0.001**	1.04 (1.02,1.07)	**<0.001**	1.04 (0.96,1.12)	0.375
Central obesity	1.03 (1.01,1.05)	**0.005**	1.08 (1.05,1.10)	**<0.001**	1.06 (0.99,1.14)	0.081
High TG	1.04 (1.02,1.06)	**<0.001**	1.02 (1.00,1.04)	0.116	1.00 (0.93,1.07)	0.975
Low HDL-C	0.98 (0.96,1.00)	0.064	0.99 (0.97,1.01)	0.405	0.93 (0.87,1.00)	**0.048**
High glucose	1.13 (1.10,1.15)	**<0.001**	1.11 (1.08,1.14)	**<0.001**	1.11 (1.03,1.19)	**0.008**
Russia						
Metabolic syndrome	1.01 (0.99,1.03)	0.497	1.05 (1.03,1.07)	**<0.001**	1.04 (0.97,1.11)	0.231
High blood pressure	1.04 (1.02,1.06)	**<0.001**	1.06 (1.04,1.08)	**<0.001**	1.10 (1.02,1.18)	**0.011**
Central obesity	0.98 (0.96,1.00)	**0.014**	1.07 (1.05,1.09)	**<0.001**	1.00 (0.94,1.07)	0.948
High TG	0.99 (0.97,1.01)	0.380	1.01 (0.99,1.03)	0.500	1.00 (0.94,1.07)	0.973
Low HDL-C	0.93 (0.91,0.95)	**<0.001**	0.99 (0.96,1.01)	0.346	0.94 (0.86,1.02)	0.161
High glucose	1.06 (1.04,1.08)	**<0.001**	1.06 (1.04,1.08)	**<0.001**	1.12 (1.05,1.19)	**0.001**
Poland						
Metabolic syndrome	1.04 (1.02,1.06)	**<0.001**	1.05 (1.03,1.07)	**<0.001**	1.04 (0.98,1.10)	0.235
High blood pressure	1.05 (1.03,1.06)	**<0.001**	1.03 (1.01,1.05)	**0.002**	1.02 (0.95,1.09)	0.537
Central obesity	1.01 (0.99,1.02)	0.413	1.04 (1.02,1.06)	**<0.001**	1.02 (0.96,1.09)	0.477
High TG	1.03 (1.02,1.05)	**<0.001**	1.02 (1.00,1.03)	0.074	1.01 (0.95,1.07)	0.821
Low HDL-C	0.97 (0.95,0.99)	**0.002**	0.99 (0.97,1.01)	0.222	1.00 (0.94,1.07)	0.909
High glucose	1.17 (1.14,1.19)	**<0.001**	1.16 (1.14,1.19)	**<0.001**	1.23 (1.15,1.32)	**<0.001**

[a]Sugar score with one unit increment
[b]model 1: unadjusted model
[c]model 2: adjusted for age group and sex
[d]model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

Table 39 shows the association between dietary score for fruits and vegetables and risk of metabolic syndrome and its components. In the Czech sample, higher score for fruit and vegetable intake was significantly associated with 5% higher risk of having central obesity (1.05 (1.03,1.08), P<0.001), and a 4% higher risk of having low HDL-C (1.04 (1.01,1.07), P=0.004) in the unadjusted model. However, the associations were fully attenuated after including all potential confounders and effect modifiers. In the Russian sample, higher fruit and vegetable score was associated with higher risk of having metabolic syndrome (1.04 (1.02,1.06), P<0.001), central obesity (1.04 (1.02,1.06), P<0.001), higher triglycerides (1.04 (1.02,1.06), P<0.001), low HDL-C (1.04 (1.02,1.07), P=0.002), and high glucose level (1.03 (1.01,1.05), P<0.002) in the unadjusted models. However, after adjustment all potential confounders and effect modifiers, the only association still significant was a higher risk of having high glucose level (1.07 (1.00,1.14), P=0.044). In the Polish sample, score in fruits and vegetable intake was found associated only with higher risk of having metabolic syndrome (1.03 (1.00,1.05), P=0.040), central obesity (1.04 (1.02,1.07), P<0.001), and low HDL-C (1.03 (1.00,1.06), P=0.030) in the unadjusted model, the association with metabolic syndrome (1.03 (1.00,1.05), P=0.036) and central obesity (1.03 (1.00,1.05), P=0.023) remained significant in the age-sex adjusted models, and was no longer significant in the fully adjusted model. Interestingly, in both the Czech and Polish samples, higher fruit and vegetable score was associated with 3% and 4% higher risk of having high glucose level, respectively, in the age and sex adjusted model. However, unlike in Russia, these associations were no longer significant in the fully adjusted model.

Table 40 shows the association between fibre score and risk of metabolic syndrome and its components. In the Czech sample, higher fibre score was only significantly associated with higher risk of having low HDL-C in the unadjusted model (1.03 (1.00,1.06), P=0.027), while in the age-sex adjusted model, the higher fibre score was associated with lower risk of having central obesity (0.97 (0.94,1.00), P=0.034). However, these associations were fully attenuated after adjusting for all potential confounders and effect modifiers. In the Russian sample, higher fibre score was associated with lower risk of having central obesity (0.96 (0.94,0.98), P=0.001) in the unadjusted model, and increased higher risk of having high triglycerides (1.03 (1.01,1.06), P=0.013) and high glucose level (1.03 (1.00,1.06), P=0.049) in the age-sex adjusted model. However, after including all the confounders and effect modifiers, these associations were attenuated. In the Polish sample, higher fibre score was significantly associated with higher risk of having central obesity (1.03 (1.00,1.06), P=0.022) and low HDL-C (1.04 (1.01,1.07), P=0.017), and the results remained

significant after adjusted for age and sex. However, this association was attenuated in the fully adjusted model. Thus, there were no significant association between fire score and metabolic syndrome or its components in the fully adjusted model in any of the samples.

Table 41 shows the association between cholesterol score and risk of metabolic syndrome and its components. In the Czech sample, in the unadjusted model, higher cholesterol score was associated with higher risk of having central obesity (1.01 (1.00,1.03), P=0.045), but lower risk of having high triglycerides (0.98 (0.97,1.00), P=0.019) and low HDL-C (0.98 (0.97,1.00), P=0.020), but after adjusting for age and sex, only the protective association with low HDL-C remained significant (0.98 (0.96,0.99), P=0.002); after adjusting for all potential confounders and including effect modifiers, this association was no longer significant (0.97 (0.92,1.02), P=0.201). In the Russian sample, higher cholesterol score was associated with greater risk of metabolic syndrome (1.03 (1.02,1.04), P<0.001), high blood pressure (1.02 (1.01,1.03), P<0.001), central obesity (1.04 (1.03,1.05), P<0.001), and low HDL-C (1.04 (1.03,1.06), P<0.001), but these associations were all attenuated after adjusting for age and sex. In the fully adjusted model, higher cholesterol score was only significantly associated with higher risk of having metabolic syndrome (1.06(1.01,1.11), P=0.030), a finding not duplicated in the Czech or Polish samples. In the Polish sample, in the unadjusted model, higher cholesterol intake was associated with higher risk of having metabolic syndrome (1.02 (1.01,1.03), P=0.001), high blood pressure (1.02 (1.01,1.03), P=0.001), and central obesity (1.02 (1.01,1.03), P=0.001) as in the Russian sample. In addition, higher score for cholesterol intake was also associated with low HDL-C (1.02 (1.00,1.03), P=0.011). After adjusting for age and sex, only the association with high blood pressure (1.02 (1.01,1.03), P=0.002) remained significant. In the fully adjusted models, the with high blood pressure was no longer significant and higher cholesterol score was only associated with higher risk of having high glucose level (1.09 (1.03,1.15), P=0.002) although this association was not discovered in the Czech nor Russian samples.

Table 39 The association between fruit and vegetable score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.03 (1.00,1.05)	0.055	1.02 (0.99,1.05)	0.184	1.01 (0.93,1.10)	0.793
High blood pressure	1.00 (0.97,1.02)	0.734	1.02 (0.99,1.05)	0.244	1.07 (0.98,1.17)	0.147
Central obesity	1.05 (1.03,1.08)	**<0.001**	1.01 (0.98,1.04)	0.458	1.02 (0.94,1.11)	0.627
High TG	0.98 (0.95,1.00)	0.085	1.00 (0.97,1.02)	0.794	0.97 (0.89,1.05)	0.393
Low HDL-C	1.04 (1.01,1.07)	**0.004**	1.03 (1.00,1.06)	0.059	1.01 (0.93,1.09)	0.871
High glucose	1.02 (0.99,1.05)	0.266	1.03 (1.00,1.07)	**0.045**	1.04 (0.95,1.13)	0.439
Russia						
Metabolic syndrome	1.04 (1.02,1.06)	**<0.001**	1.03 (1.01,1.05)	**0.007**	1.05 (0.98,1.13)	0.150
High blood pressure	0.99 (0.98,1.01)	0.608	1.00 (0.98,1.02)	0.854	0.98 (0.91,1.05)	0.547
Central obesity	1.04 (1.02,1.06)	**<0.001**	1.01 (0.99,1.03)	0.416	0.99 (0.92,1.06)	0.726
High TG	1.04 (1.02,1.06)	**<0.001**	1.04 (1.02,1.06)	**<0.001**	1.06 (0.99,1.13)	0.084
Low HDL-C	1.04 (1.02,1.07)	**0.002**	1.01 (0.98,1.04)	0.362	1.01 (0.92,1.11)	0.802
High glucose	1.03 (1.01,1.05)	**0.002**	1.04 (1.02,1.07)	**<0.001**	1.07 (1.00,1.14)	**0.044**
Poland						
Metabolic syndrome	1.03 (1.00,1.05)	**0.040**	1.03 (1.00,1.05)	**0.036**	1.02 (0.95,1.09)	0.614
High blood pressure	1.00 (0.98,1.02)	0.790	1.01 (0.99,1.04)	0.330	1.02 (0.94,1.09)	0.678
Central obesity	1.04 (1.02,1.07)	**<0.001**	1.03 (1.00,1.05)	**0.023**	1.03 (0.96,1.10)	0.432
High TG	0.98 (0.96,1.01)	0.143	1.00 (0.97,1.02)	0.671	1.01 (0.95,1.08)	0.774
Low HDL-C	1.03 (1.00,1.06)	**0.030**	1.02 (0.99,1.05)	0.164	0.99 (0.92,1.06)	0.704
High glucose	1.03 (1.00,1.06)	0.082	1.04 (1.01,1.07)	**0.009**	1.07 (0.99,1.16)	0.075

[a] Fruit and vegetable score with one unit increment
[b] model 1: unadjusted model
[c] model 2: adjusted for age group and sex
[d] model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

Table 40 The association between fibre score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.00 (0.97,1.03)	0.986	0.99 (0.96,1.02)	0.464	1.01 (0.92,1.11)	0.777
High blood pressure	0.99 (0.97,1.02)	0.664	1.00 (0.97,1.03)	0.938	1.08 (0.97,1.20)	0.142
Central obesity	1.00 (0.98,1.03)	0.759	0.97 (0.94,1.00)	**0.034**	0.99 (0.90,1.09)	0.850
High TG	0.98 (0.95,1.01)	0.141	0.99 (0.96,1.02)	0.458	0.95 (0.87,1.04)	0.311
Low HDL-C	1.03 (1.00,1.06)	**0.027**	1.02 (0.99,1.05)	0.127	1.00 (0.91,1.09)	0.927
High glucose	1.00 (0.97,1.04)	0.882	1.01 (0.97,1.04)	0.658	1.10 (0.99,1.22)	0.089
Russia						
Metabolic syndrome	1.00 (0.97,1.02)	0.832	1.02 (0.99,1.04)	0.228	1.04 (0.95,1.14)	0.366
High blood pressure	0.98 (0.96,1.01)	0.141	0.99 (0.97,1.02)	0.486	0.97 (0.88,1.07)	0.570
Central obesity	0.96 (0.94,0.98)	**0.001**	0.99 (0.96,1.02)	0.465	0.95 (0.87,1.04)	0.290
High TG	1.03 (1.00,1.05)	0.055	1.03 (1.01,1.06)	**0.013**	1.07 (0.98,1.17)	0.115
Low HDL-C	0.98 (0.95,1.01)	0.237	1.01 (0.97,1.04)	0.761	0.97 (0.86,1.09)	0.604
High glucose	1.02 (1.00,1.05)	0.094	1.03 (1.00,1.06)	**0.049**	1.09 (1.00,1.19)	0.059
Poland						
Metabolic syndrome	1.02 (0.99,1.05)	0.198	1.02 (0.99,1.05)	0.198	1.00 (0.91,1.09)	0.951
High blood pressure	1.00 (0.98,1.03)	0.790	1.00 (0.98,1.03)	0.858	1.05 (0.96,1.16)	0.307
Central obesity	1.03 (1.00,1.06)	**0.022**	1.03 (1.01,1.06)	**0.018**	1.01 (0.93,1.10)	0.764
High TG	1.00 (0.97,1.02)	0.904	1.00 (0.97,1.02)	0.895	1.01 (0.93,1.10)	0.788
Low HDL-C	1.04 (1.01,1.07)	**0.017**	1.04 (1.01,1.07)	**0.015**	0.99 (0.90,1.08)	0.800
High glucose	1.03 (0.99,1.06)	0.119	1.02 (0.99,1.06)	0.145	1.06 (0.96,1.17)	0.277

[a]Fibre score with one unit increment
[b]model 1: unadjusted model
[c]model 2: adjusted for age group and sex
[d]model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

Table 41 The association between cholesterol score[a] and metabolic syndrome in the HAPIEE study by country

	Model 1[b]		Model 2[c]		Model 3[d]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.00 (0.98,1.01)	0.747	0.99 (0.98,1.01)	0.218	1.03 (0.98,1.09)	0.213
High blood pressure	1.00 (0.99,1.02)	0.769	1.00 (0.99,1.02)	0.561	1.00 (0.94,1.06)	0.911
Central obesity	1.01 (1.00,1.03)	**0.045**	1.00 (0.98,1.01)	0.667	1.04 (0.99,1.10)	0.119
High TG	0.98 (0.97,1.00)	**0.019**	0.99 (0.97,1.00)	0.076	1.03 (0.98,1.08)	0.319
Low HDL-C	0.98 (0.97,1.00)	**0.020**	0.98 (0.96,0.99)	**0.002**	0.97 (0.92,1.02)	0.201
High glucose	1.00 (0.98,1.02)	0.931	1.00 (0.98,1.02)	0.928	1.05 (0.99,1.11)	0.129
Russia						
Metabolic syndrome	1.03 (1.02,1.04)	**<0.001**	1.00 (0.99,1.01)	0.959	1.06 (1.01,1.11)	**0.030**
High blood pressure	1.02 (1.01,1.03)	**<0.001**	1.01 (1.00,1.02)	0.197	1.02 (0.97,1.08)	0.395
Central obesity	1.04 (1.03,1.05)	**<0.001**	0.99 (0.98,1.00)	0.271	1.03 (0.98,1.08)	0.303
High TG	1.01 (1.00,1.02)	0.185	0.99 (0.98,1.01)	0.376	1.00 (0.95,1.05)	0.972
Low HDL-C	1.04 (1.03,1.06)	**<0.001**	1.01 (0.99,1.02)	0.342	1.02 (0.96,1.08)	0.494
High glucose	1.01 (1.00,1.02)	0.110	1.00 (0.99,1.01)	0.512	1.03 (0.98,1.08)	0.261
Poland						
Metabolic syndrome	1.02 (1.01,1.03)	**0.001**	1.01 (1.00,1.02)	0.181	1.02 (0.98,1.07)	0.295
High blood pressure	1.02 (1.01,1.03)	**0.001**	1.02 (1.01,1.03)	**0.002**	1.01 (0.96,1.06)	0.797
Central obesity	1.02 (1.01,1.03)	**0.001**	0.99 (0.98,1.00)	0.200	1.00 (0.96,1.04)	0.920
High TG	1.00 (0.99,1.01)	0.950	1.01 (1.00,1.02)	0.157	1.02 (0.98,1.06)	0.394
Low HDL-C	1.02 (1.00,1.03)	**0.011**	1.01 (0.99,1.02)	0.421	0.96 (0.92,1.01)	0.094
High glucose	1.00 (0.99,1.02)	0.704	1.00 (0.99,1.02)	0.835	1.09 (1.03,1.15)	**0.002**

[a]cholesterol score with one unit increment
[b]model 1: unadjusted model
[c]model 2: adjusted for age group and sex
[d]model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

5.6.3 HDI scores and metabolic syndrome – the pooled results

The associations found between HDI score and risk of metabolic syndrome and its components in the pooled dataset (combining all three countries together) are shown in Table 42 (in respond to Objective 6). With the exception of the risk of high blood pressure, higher HDI total score was associated with higher risk of having metabolic syndrome and its other components, but these associations were fully attenuated after adjusting for confounders and effect modifiers. A higher HDI total score was still associated with lower risk of having high blood pressure after adjusting for confounders and adding effect modifiers (0.82 (0.72,0.94),P=0.005). Higher score in polyunsaturated fatty acid was associated with lower risk of having central obesity, low HDL-C, but higher risk of high glucose, but after full adjustment, only the association with lower risk of having low HDL-C (0.93 (0.88,0.98), P=0.012). A higher score for protein was associated with lower risk of metabolic syndrome and components in the unadjusted model, but in the fully adjusted model the protective association was only significant for metabolic syndrome (0.94 (0.90,0.98), P=0.002), central obesity (0.94 (0.90,0.97),P=0.001), and high glucose (0.87 (0.83,0.90), P<0.001). However, a higher score in sugar was found associated with higher risk of having metabolic syndrome (1.04 (1.00,1.08), P=0.039), high blood pressure (1.07 (1.02,1.11), P=0.002), and high glucose (0.87 (0.83,0.90), P<0.001) in the fully adjusted model. Higher score in fibre was associated in the fully adjusted model with higher risk of having metabolic syndrome (1.04 (1.00,1.09), P=0.047) and high glucose (1.08 (1.03,1.13), P=0.001). A higher score in fruits and vegetables was only associated with higher risk of having high blood glucose (1.07 (1.01,1.13), P=0.018) in the fully adjusted model. Finally, a higher score in cholesterol was associated with higher risk of having metabolic syndrome (1.04 (1.01,1.07), P=0.003) and high blood glucose (1.07 (1.04,1.10), P<0.001).

Table 42 The association between HDI score and its dietary components score and metabolic syndrome in the HAPIEE study (pooled dataset)

	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
HDI total score	**(per-10 unit)**					
Metabolic syndrome	1.17 (1.12,1.22)	**<0.001**	1.09 (1.04,1.13)	**<0.001**	0.96 (0.85,1.09)	0.558
High blood pressure	1.13 (1.09,1.18)	**<0.001**	1.09 (1.05,1.14)	**<0.001**	0.82 (0.72,0.94)	**0.005**
Central obesity	1.12 (1.08,1.17)	**<0.001**	0.98 (0.94,1.02)	0.323	0.96 (0.85,1.09)	0.554
High TG	1.07 (1.03,1.12)	**0.001**	1.07 (1.03,1.12)	**0.001**	0.98 (0.87,1.10)	0.760
Low HDL-C	1.17 (1.11,1.22)	**<0.001**	1.10 (1.05,1.16)	**<0.001**	0.94 (0.82,1.07)	0.349
High glucose	1.08 (1.03,1.13)	**0.001**	1.05 (1.01,1.10)	**0.029**	0.99 (0.87,1.13)	0.890
SFA[d]	**(per-one unit)**					
Metabolic syndrome	1.04 (1.03,1.04)	**<0.001**	1.02 (1.01,1.03)	**<0.001**	1.01 (0.98,1.05)	0.475
High blood pressure	1.03 (1.02,1.04)	**<0.001**	1.03 (1.02,1.04)	**<0.001**	0.98 (0.95,1.02)	0.408
Central obesity	1.02 (1.01,1.03)	**<0.001**	1.00 (0.99,1.01)	0.810	0.97 (0.94,1.01)	0.136
High TG	1.02 (1.01,1.03)	**<0.001**	1.02 (1.01,1.03)	**<0.001**	1.01 (0.98,1.05)	0.387
Low HDL-C	1.04 (1.03,1.05)	**<0.001**	1.03 (1.02,1.04)	**<0.001**	0.98 (0.95,1.02)	0.369
High glucose	1.01 (1.00,1.02)	**0.020**	1.01 (1.00,1.02)	0.153	1.03 (0.99,1.07)	0.135
PUFA[e]	**(per-one unit)**					
Metabolic syndrome	0.99 (0.98,1.01)	0.431	1.00 (0.98,1.02)	0.889	0.97 (0.92,1.02)	0.242
High blood pressure	1.01 (0.99,1.02)	0.445	1.00 (0.99,1.02)	0.834	0.99 (0.94,1.05)	0.739
Central obesity	0.98 (0.96,0.99)	**0.003**	1.00 (0.98,1.02)	0.937	0.99 (0.94,1.04)	0.613
High TG	1.01 (0.99,1.02)	0.396	1.00 (0.99,1.02)	0.750	0.97 (0.92,1.02)	0.240
Low HDL-C	0.96 (0.94,0.98)	**<0.001**	0.97 (0.95,0.99)	**0.001**	0.93 (0.88,0.98)	**0.012**
High glucose	1.02 (1.00,1.04)	**0.025**	1.02 (1.00,1.04)	0.079	0.99 (0.94,1.05)	0.767
Protein	**(per-one unit)**					
Metabolic syndrome	0.93 (0.92,0.94)	**<0.001**	0.92 (0.91,0.93)	**<0.001**	0.94 (0.90,0.98)	**0.002**
High blood pressure	0.94 (0.93,0.95)	**<0.001**	0.94 (0.93,0.95)	**<0.001**	1.01 (0.96,1.05)	0.809
Central obesity	0.95 (0.94,0.96)	**<0.001**	0.93 (0.92,0.94)	**<0.001**	0.94 (0.90,0.97)	**0.001**
High TG	0.95 (0.94,0.96)	**<0.001**	0.96 (0.95,0.97)	**<0.001**	0.98 (0.94,1.02)	0.266
Low HDL-C	0.97 (0.96,0.99)	**<0.001**	0.96 (0.95,0.98)	**<0.001**	0.97 (0.93,1.01)	0.123
High glucose	0.90 (0.89,0.91)	**<0.001**	0.90 (0.89,0.91)	**<0.001**	0.87 (0.83,0.90)	**<0.001**
Sugar	**(per-one unit)**					

	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Metabolic syndrome	1.02 (1.01,1.04)	**<0.001**	1.04 (1.03,1.05)	**<0.001**	1.04 (1.00,1.08)	**0.039**
High blood pressure	1.05 (1.04,1.06)	**<0.001**	1.04 (1.03,1.06)	**<0.001**	1.07 (1.02,1.11)	**0.002**
Central obesity	1.01 (1.00,1.02)	**0.033**	1.06 (1.05,1.07)	**<0.001**	1.02 (0.99,1.06)	0.164
High TG	1.00 (0.99,1.01)	0.353	0.99 (0.98,1.00)	**0.015**	1.01 (0.98,1.04)	0.570
Low HDL-C	0.93 (0.92,0.94)	**<0.001**	0.95 (0.94,0.96)	**<0.001**	0.98 (0.95,1.02)	0.433
High glucose	1.13 (1.12,1.15)	**<0.001**	1.13 (1.12,1.15)	**<0.001**	1.13 (1.09,1.17)	**<0.001**
Fibre	(per-one unit)					
Metabolic syndrome	1.03 (1.02,1.05)	**<0.001**	1.03 (1.02,1.04)	**<0.001**	1.04 (1.00,1.09)	**0.047**
High blood pressure	0.99 (0.98,1.01)	0.274	1.00 (0.99,1.02)	0.477	1.00 (0.96,1.05)	0.843
Central obesity	1.04 (1.02,1.05)	**<0.001**	1.01 (1.00,1.02)	0.091	1.02 (0.98,1.06)	0.267
High TG	1.02 (1.01,1.03)	**0.003**	1.03 (1.01,1.04)	**<0.001**	1.02 (0.98,1.06)	0.341
Low HDL-C	1.06 (1.05,1.08)	**<0.001**	1.05 (1.03,1.06)	**<0.001**	1.01 (0.96,1.05)	0.745
High glucose	1.01 (0.99,1.02)	0.261	1.02 (1.00,1.03)	**0.010**	1.08 (1.03,1.13)	**<0.001**
Fruit and vegetables	(per-one unit)					
Metabolic syndrome	1.00 (0.98,1.01)	0.723	1.00 (0.98,1.01)	0.692	1.02 (0.97,1.07)	0.444
High blood pressure	0.99 (0.97,1.00)	0.121	0.99 (0.97,1.00)	0.113	1.03 (0.97,1.09)	0.344
Central obesity	0.99 (0.98,1.01)	0.365	0.99 (0.98,1.01)	0.333	0.98 (0.93,1.03)	0.435
High TG	1.00 (0.98,1.01)	0.531	1.00 (0.98,1.01)	0.516	1.01 (0.96,1.06)	0.759
Low HDL-C	1.01 (0.99,1.03)	0.217	1.01 (0.99,1.03)	0.226	1.00 (0.95,1.06)	0.978
High glucose	1.01 (1.00,1.03)	0.123	1.01 (1.00,1.03)	0.111	1.07 (1.01,1.13)	**0.018**
Cholesterol	(per-one unit)					
Metabolic syndrome	1.03 (1.02,1.03)	**<0.001**	1.01 (1.01,1.02)	**<0.001**	1.04 (1.01,1.07)	**0.003**
High blood pressure	1.02 (1.01,1.02)	**<0.001**	1.01 (1.01,1.02)	**<0.001**	1.00 (0.97,1.03)	0.973
Central obesity	1.02 (1.02,1.03)	**<0.001**	0.99 (0.99,1.00)	0.061	1.03 (1.00,1.05)	0.053
High TG	1.02 (1.01,1.02)	**<0.001**	1.02 (1.01,1.03)	**<0.001**	1.02 (0.99,1.05)	0.121
Low HDL-C	1.04 (1.03,1.05)	**<0.001**	1.03 (1.02,1.04)	**<0.001**	0.98 (0.95,1.01)	0.107
High glucose	0.99 (0.99,1.00)	**0.039**	0.99 (0.98,1.00)	**0.004**	1.07 (1.04,1.10)	**<0.001**

[a] model 1: unadjusted model
[b] model 2: adjusted for age group and sex
[c] model 3: adjusted for age group, sex, country, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI
[d] SFA: saturated fatty acids
[e] PUFA: polyunsaturated fatty acids

5.7   Sensitivity analyses

5.7.1   Multiple imputation

In this section, in response to Objective 7, the results from restricted and imputed samples are presented and descriptively compared. The means of metabolic syndrome component measures including three readings of systolic and diastolic blood pressure, waist circumference, triglycerides, HDL-C, and glucose were very similar in both the complete case and imputed data (see Table 43 & Table 44). Similarly, the proportions of Russians with a glucose level higher than 6.1mmol/L were similar in both sources of data (see Table 43).The distributions of covariates among complete case data and imputed data were also similar (see Table 44).

Table 43 Descriptive statistics of complete data and imputed data

	Czech Republic		Russia		Poland	
	Complete data	**Imputed data**	**Complete data**	**Imputed data**	**Complete data**	**Imputed data**
	N=5060	**N=7819**	**N=8788**	**N=9154**	**N=7671**	**N=9940**
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)
Systolic blood pressure 1	144.3 (143.7,144.8)	144.6 (144.1,145.2)	148.0 (147.5,148.6)	148.0 (147.5,148.6)	144.2 (143.6,144.7)	144.3 (143.8,144.8)
Systolic blood pressure 2	139.7 (139.2,140.3)	140.0 (139.5,140.5)	143.9 (143.4,144.4)	143.9 (143.4,144.4)	139.2 (138.7,139.6)	139.3 (138.8,139.7)
Systolic blood pressure 3	138.1 (137.6,138.7)	138.3 (137.8,138.8)	141.7 (141.2,142.3)	141.7 (141.2,142.2)	137.5 (137.0,137.9)	137.6 (137.1,138.0)
Diastolic blood pressure 1	90.2 (89.9,90.5)	90.2 (89.9,90.5)	91.9 (91.6,92.3)	91.9 (91.6,92.2)	87.8 (87.5,88.1)	87.9 (87.7,88.2)
Diastolic blood pressure 2	89.0 (88.7,89.3)	89.1 (88.8,89.4)	90.6 (90.3,90.9)	90.6 (90.3,90.9)	86.5 (86.2,86.7)	86.5 (86.3,86.8)
Diastolic blood pressure 3	88.5 (88.2,88.8)	88.5 (88.2,88.8)	89.5 (89.2,89.8)	89.5 (89.2,89.7)	86.1 (85.8,86.3)	86.2 (85.9,86.4)
Waist circumference	93.0 (92.7,93.3)	93.3 (93.0,93.7)	92.8 (92.6,93.1)	92.8 (92.6,93.1)	92.6 (92.3,92.9)	92.6 (92.4,92.9)
Triglycerides	1.9 (1.8,1.9)	1.9 (1.9,2.0)	1.5 (1.5,1.5)	1.5 (1.5,1.5)	1.7 (1.6,1.7)	1.7 (1.6,1.7)
HDL-C	1.4 (1.4,1.4)	1.4 (1.4,1.4)	1.5 (1.5,1.5)	1.5 (1.5,1.5)	1.4 (1.4,1.4)	1.4 (1.4,1.4)
Standardised blood glucose*	5.8 (5.7,5.8)	5.8 (5.7,5.8)	70.7 (70.0,71.6) (no)	71.8 (70.9,72.7) (no)	5.4 (5.4,5.5)	5.4 (5.4,5.5)
			29.3 (28.3,30.3) (yes)	28.2 (27.3,29.1) (yes)		

*standardised blood glucose: the Russian sample was not standardised using CTSU measurements, and statistics in Russian sample were described by proportion of having high blood glucose or not due to the binary nature of the blood glucose data from Russia.

Table 44 Descriptive results on covariates in complete data and imputed data

Covariates		Czech Republic		Russia		Poland	
		Complete data % (95%CI)	Imputed data % (95%CI)	Complete data % (95%CI)	Imputed data % (95%CI)	Complete data % (95%CI)	Imputed data % (95%CI)
Smoking	Current smoker	26.3 (25.1,27.5)	26.4 25.2,27.6)	28.1 (27.2,29.0)	28.2 (27.3,29.1)	30.3 (29.3,31.3)	30.3 (29.3,31.3)
	Past smoker	30.1 (28.8,31.4)	30.1 (28.8,31.4)	13.5 (12.8,14.2)	13.6 (12.9,14.3)	29.0 (27.9,30.0)	29.0 (27.9,30.0)
	Never smoker	43.6 (42.3,45.0)	43.5 (42.2,44.9)	58.4 (57.4,59.5)	58.2 (57.2,59.2)	40.8 (39.7,41.9)	40.8 (39.7,41.9)
Leisure activity	<1 hour	33.3 (32.0,34.6)	33.4 (32.1,34.7)	15.9 (15.1,16.7)	15.9 (15.2,16.7)	27.8 (26.9,28.9)	27.8 (26.9,28.9)
	1-2 hours	25.8 (24.6,27.0)	25.8 (24.6,27.0)	25.6 (24.7,26.5)	25.5 (24.6,26.4)	30.5 (29.5,31.6)	30.5 (29.5,31.6)
	2-3 hours	21.2 (20.1,22.3)	21.2 (20.1,22.4)	24.7 (23.8,25.6)	24.7 (23.8,25.6)	21.8 (20.9,22.7)	21.8 (20.9,22.7)
	>3 hours	19.7 (18.6,20.8)	19.6 (18.5,20.7)	33.8 (32.9,34.8)	33.9 (32.9,34.9)	19.8 (18.9,20.7)	19.8 (18.9,20.7)
Sports time	0 hour	28.5 (27.3,29.8)	28.5 (27.3,29.7)	72.1 (71.1,73.0)	72.0 (71.1,72.9)	29.0 (28.0,30.0)	29.0 (28.0,30.0)
	0-1 hour	45.6 (44.3,47.0)	45.6 (44.2,47.0)	12.3 (11.7,13.1)	12.4 (11.7,13.0)	36.1 (35.0,37.2)	36.1 (35.0,37.2)
	>1 hour	25.9 (24.7,27.1)	25.9 (24.7,27.2)	15.6 (14.8,16.4)	15.6 (14.9,16.4)	34.9 (33.8,36.0)	34.9 (33.8,36.0)
Working activity	Working:non-pensioner	48.5 (47.1,49.9)	48.5 (47.1,49.8)	39.1 (38.1,40.1)	38.9 (37.9,39.9)	41.9 (40.8,43.0)	41.9 (40.8,43.0)
	Not working:non-pensioner	0.6 (0.4,0.8)	0.6 (0.4,0.8)	1.1 (0.9,1.4)	1.1 (0.9,1.3)	1.6 (1.3,1.9)	1.6 (1.3,1.9)
	Working:pensioner	7.6 (6.9,8.4)	7.5 (6.9,8.3)	18.5 (17.7,19.4)	18.6 (17.8,19.4)	6.6 (6.0,7.1)	6.6 (6.0,7.1)
	Not working:pensioner	43.3 (42.0,44.7)	43.4 (42.1,44.8)	41.2 (40.2,42.2)	41.4 (40.4,42.4)	50.0 (48.8,51.1)	50.0 (48.8,51.1)
Education level	Primary or lower	11.5 (10.7,12.4)	11.6 (10.8,12.5)	10.3 (9.6,10.9)	10.3 (9.7,11.0)	11.6 (10.9,12.3)	11.6 (10.9,12.3)
	Vocational(apprenticeship)	36.3 (35.0,37.6)	36.4 (35.1,37.7)	26.6 (25.7,27.6)	26.6 (25.7,27.5)	20.9 (20.1,21.9)	20.9 (20.1,21.9)
	Secondary	37.6 (36.2,38.9)	37.5 (36.1,38.8)	34.2 (33.2,35.2)	34.2 (33.2,35.1)	38.6 (37.5,39.7)	38.6 (37.5,39.7)

Covariates		Czech Republic		Russia		Poland	
		Complete data % (95%CI)	Imputed data % (95%CI)	Complete data % (95%CI)	Imputed data % (95%CI)	Complete data % (95%CI)	Imputed data % (95%CI)
	University(degree)	14.6 (13.7,15.6)	14.5 (13.6,15.5)	28.9 (27.9,29.8)	28.9 (28.0,29.8)	28.8 (27.8,29.9)	28.8 (27.8,29.9)
Medication for blood pressure	Yes	34.6 (33.3,35.9)	34.6 (33.3,35.9)	32.1 (31.1,33.0)	32.0 (31.0,32.9)	37.9 (36.8,39.0)	37.9 (36.8,39.0)
	No	65.4 (64.1,66.7)	65.4 (64.1,66.7)	67.9 (67.0,68.9)	68.0 (67.1,69.0)	62.1 (61.0,63.2)	62.1 (61.0,63.2)
Medication for cholesterol	Yes	25.2 (24.0,26.4)	25.2 (24.0,26.4)	8.5 (8.0,9.1)	8.5 (7.9,9.1)	30.1 (29.1,31.1)	30.1 (29.1,31.1)
	No	74.8 (73.6,76.0)	74.8 (73.6,76.0)	91.5 (90.9,92.0)	91.5 (90.9,92.1)	69.9 (68.9,70.9)	69.9 (68.9,70.9)
Medication for diabetes	Yes	9.6 (8.9,10.5)	9.6 (8.8,10.4)	4.6 (4.2,5.1)	4.6 (4.1,5.0)	9.7 (9.0,10.3)	9.7 (9.0,10.3)
	No	90.4 (89.5,91.1)	90.4 (89.6,91.2)	95.4 (94.9,95.8)	95.4 (95.0,95.9)	90.3 (89.7,91.0)	90.3 (89.7,91.0)
Family history on stroke	Yes	29.4 (28.2,30.7)	29.5 (28.2,30.7)	23.7 (22.8,24.6)	23.8 (22.9,24.7)	17.4 (16.6,18.3)	17.4 (16.6,18.3)
	No	70.6 (69.3,71.8)	70.5 (69.3,71.8)	76.3 (75.4,77.2)	76.2 (75.3,77.1)	82.6 (81.7,83.4)	82.6 (81.7,83.4)
Family history on diabetes	Yes	33.8 (32.5,35.1)	33.9 (32.6,35.2)	12.0 (11.4,12.7)	12.2 (11.5,12.9)	20.9 (20.0,21.8)	20.9 (20.0,21.8)
	No	66.2 (64.9,67.5)	66.1 (64.8,67.4)	88.0 (87.3,88.6)	87.8 (87.1,88.5)	79.1 (78.2,80.0)	79.1 (78.2,80.0)

After the imputation, the prevalence of metabolic syndrome and its components was examined in both complete case and imputed data (see Table 45). These were found to be similar: in the Czech Republic, the prevalence of metabolic syndrome and its components were slightly higher in the imputed data than the complete data; in Poland, the similar pattern was found except the cholesterol measures; in Russia, the prevalence was slightly lower in the imputed data.

Table 45 Prevalence of metabolic syndrome and its components in complete case data and imputed data

	Czech Republic		Russia		Poland	
	Complete case data	Imputed data	Complete case data	Imputed data	Complete case data	Imputed data
	%	%	%	%	%	%
Metabolic syndrome	36.5	37.3	29.3	28.8	28.3	28.8
High blood pressure	65.3	66.2	64.1	64.0	60.2	60.4
Raised waist circumference	42.7	43.9	44.7	44.6	39.8	40.3
High triglycerides	43.9	45.2	29.1	29.0	36.3	36.3
Low HDL-C	30.0	30.4	13.6	13.4	22.5	22.4
High blood glucose	22.0	21.8	29.3	28.2	18.5	18.9

Table 46 presents the association between total HDI score and risk of metabolic syndrome in the imputed datasets. In general, the direction of the association between HDI and metabolic syndrome was consistent between the complete and imputed datasets. In the Czech sample, a ten-unit increase in HDI score was associated with 12% lower risk of having low HDL-C (0.88 (0.80,0.97), P=0.010). Similar to the complete case results, higher HDI score was associated with higher risk of having central obesity but lower risk of having high triglycerides in the unadjusted models; however, the associations were fully attenuated after adjustment for potential confounders. In the Russian sample, a higher HDI score was associated with lower risk of having central obesity (0.91 (0.84,0.98), P=0.012). In the Polish sample, similar to the complete case results, a higher score of HDI was associated with higher risk of having metabolic syndrome (1.18 (1.08,1.28), P<0.001) and high glucose (1.22 (1.11,1.34), P<0.001); the difference is that the effect attenuated to a greater extent after more adjustment in the adjusted models.

To conclude, in the complete data analyses, HDI total score was not associated with metabolic syndrome and or components. The components of HDI score associated with metabolic syndrome in different directions. However, a higher protein score was associated with lower risk of metabolic syndrome and some of its components in all three countries. In the imputed dataset, a higher total HDI score was associated with lower risk of several metabolic syndrome components in the Czech Republic and Russia, but was associated with higher risk of metabolic syndrome and high glucose level in Poland.

Table 46 The association between HDI total score and metabolic syndrome in the HAPIEE study by country (in imputed datasets)

	Model 1[a]		Model 2[b]		Model 3[c]	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Czech Republic						
Metabolic syndrome	1.03 (0.96,1.11)	0.437	0.97 (0.90,1.05)	0.519	0.98 (0.89,1.08)	0.633
High blood pressure	1.04 (0.96,1.12)	0.318	1.04 (0.96,1.13)	0.300	1.00 (0.91,1.10)	0.991
Central obesity	1.10 (1.03,1.18)	**0.006**	0.95 (0.88,1.02)	0.172	1.04 (0.95,1.14)	0.412
High TG	0.91 (0.85,0.97)	**0.008**	0.95 (0.88,1.02)	0.170	0.97 (0.89,1.07)	0.548
Low HDL-C	0.98 (0.90,1.06)	0.547	0.93 (0.86,1.01)	0.088	0.88 (0.80,0.97)	**0.010**
High glucose	1.05 (0.97,1.15)	0.226	1.05 (0.96,1.14)	0.293	1.09 (0.98,1.21)	0.131
Russia						
Metabolic syndrome	1.11 (1.04,1.19)	**0.002**	1.00 (0.94,1.07)	0.973	0.97 (0.89,1.05)	0.425
High blood pressure	1.14 (1.07,1.21)	**<0.001**	1.06 (0.99,1.13)	0.087	1.04 (0.95,1.13)	0.391
Central obesity	1.10 (1.03,1.17)	**0.002**	0.93 (0.87,0.99)	**0.020**	0.91 (0.84,0.98)	**0.012**
High TG	1.08 (1.01,1.15)	**0.032**	1.03 (0.96,1.10)	0.418	0.98 (0.91,1.06)	0.690
Low HDL-C	1.12 (1.03,1.23)	**0.009**	1.01 (0.92,1.11)	0.826	0.99 (0.89,1.09)	0.805
High glucose	1.03 (0.96,1.10)	0.395	1.00 (0.94,1.08)	0.898	0.99 (0.91,1.07)	0.739
Poland						
Metabolic syndrome	1.21 (1.13,1.29)	**<0.001**	1.15 (1.08,1.24)	**<0.001**	1.18 (1.08,1.28)	**<0.001**
High blood pressure	1.17 (1.09,1.24)	**<0.001**	1.15 (1.08,1.23)	**<0.001**	1.09 (1.00,1.19)	0.058
Central obesity	1.15 (1.08,1.22)	**<0.001**	1.04 (0.97,1.10)	0.295	1.07 (0.99,1.15)	0.088
High TG	1.04 (0.98,1.11)	0.195	1.08 (1.01,1.15)	0.028	1.09 (1.00,1.17)	0.040
Low HDL-C	1.15 (1.07,1.24)	**<0.001**	1.11 (1.03,1.19)	0.009	1.14 (1.04,1.24)	0.003
High glucose	1.19 (1.10,1.28)	**<0.001**	1.18 (1.09,1.27)	**<0.001**	1.22 (1.11,1.34)	**<0.001**

[a] model 1: unadjusted model
[b] model 2: adjusted for age group and sex
[c] model 3: adjusted for age group, sex, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, and energy intake; added interaction terms between education and HDI, and energy intake and HDI

5.7.2 Nutrition knowledge, HDI, and metabolic syndrome

In the HAPIEE study, there were two questions examining participants' nutrition knowledge. In one question participants were asked "how do you think eating meat influences human health?", while another asked participants "how do you think eating fruit and vegetables influence human health?". Answers were given as improve strongly, improve slightly, no effect, make it worse slightly, or make it worse strongly. For analyses in this thesis, answers were re-categorised into three groups, improve (health), no effect, and worsen (health).

Table 47 shows the response to nutrition knowledge for meat intake. A small number of subjects had missing data (68, 5, and 60, in the Czech, Russian, and Polish sample, respectively). In the Czech sample, 32.2% participants thought eating meat improved human health, while 49.6% thought it had no effect and 18.1% thought having it worsened health. However, the answer pattern was different in Russian and Polish sample: more than three fifths of the samples thought eating meat could improve health (68.6% in the Russian and 64.7% in Polish sample), and more than one fifth of the samples thought it had no effect on health (22.0% in the Russian and 26.2% in the Polish samples), while the rest thought meat could worsen health (9.5% in the Russian sample and 9.1% in the Polish sample).

Table 48 shows the responses to nutrition knowledge for fruit and vegetable intake. There were some subjects with answer missing data (48, 1, and 44, in the Czech, Russian, and Polish sample, respectively). The pattern of the answers were very similar among three study samples: most participants thought eating fruits and vegetables were good for health (96.1%, 93.4%, and 94.6%, in the Czech, Russian, and Polish sample, respectively), while around 5% of participants thought eating fruits and vegetables had no effect on health (3.2%, 6.2%, and 4.7% in the Czech, Russian, and Polish sample, respectively), and the rest thought the effect was negative.

Table 47 Answers to 'How does meat intake influence human health' in three study samples

View on meat intake	Czech Republic (N=4992)		Russia (N=8783)		Poland (N=7611)	
	N	%	N	%	N	%
Improve	1609	32.2	6022	68.6	4922	64.7
No effect	2478	49.6	1931	22.0	1993	26.2
Worsen	905	18.1	830	9.5	696	9.1

Table 48 Answers to 'How does fruit and vegetable intake influence human health'

View on fruit and vegetables intake	Czech Republic (N=5012)		Russia (N=8787)		Poland (N=7627)	
	N	%	N	%	N	%
Improve	4818	96.1	8206	93.4	7213	94.6
No effect	159	3.2	548	6.2	359	4.7
Worsen	35	0.7	33	0.4	55	0.7

Nutritional knowledge of meat intake was also examined in relation to some components of HDI scores, namely saturated fatty acids, protein, and cholesterol, which are the common nutrients in meat (see Table 49). In the Czech sample, participants who believed the meat intake worsens human health (the 'worsen' group) had higher score in saturated fatty acids (median: 4.2) compared to the 'no effect' group (median: 2.9) and the 'improve' group (median: 2.8). Moreover, participants in the 'worsen' group had slightly higher protein score (median: 7.4) than the 'improve group' (median: 7.1) and the 'no effect group' (median: 6.9). However, the median scores of cholesterol were 10 in all three groups. Compared with the Czech sample, Russians and Poles had lower scores for saturated fatty acids, protein, and cholesterol. In the Russian sample, participants in the 'worsen' group had higher saturated fatty acids score (median: 2.0) compared with those in the 'no effect' (median: 1.5) and 'improve' group (median: 1.1). On the protein score, the three Russian groups had very similar median scores (worsen: 7.6, no effect: 7.5, improve: 7.5); while the cholesterol score was higher in the 'worsen' group (median: 2.5) compared with the 'no effect' (<0.1) and 'improve' group (median: 0). Polish sample had similar scoring pattern compared with the Russian ones: the 'worsen' group had higher median score in saturated fatty acids and cholesterol compare to the other groups, but very similar in protein score.

Table 50 shows the nutrition knowledge of fruits and vegetable intake in relation to the score of fruit and vegetable in the HDI. In three study samples, the medians were similar in three knowledge groups, ranging from 8.5 (Russian 'no effect' group) to 10 (Czech 'improve'/'worsen' group or Polish 'improve').

Table 49 Nutrition knowledge of meat intake and selected HDI components (saturated fats, protein, and cholesterol)

HDI components	View on meat intake	Czech Republic			Russia			Poland		
		Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Saturated fats score	Improve	3.4	3.3	2.8	2.6	3.1	1.1	2.4	3.1	0.6
	No effect	3.5	3.3	2.9	2.8	3.2	1.5	2.4	3.1	0.7
	Worsen	6.8	4.1	4.2	3.1	3.4	2.0	3.1	3.4	1.9
Protein score	Improve	6.7	2.6	7.1	7.1	2.4	7.5	6.5	2.3	6.7
	No effect	6.7	2.6	6.9	7.1	2.5	7.5	6.6	2.3	6.9
	Worsen	7.3	3.9	7.4	7.1	2.6	7.6	6.6	2.5	6.9
Cholesterol score	Improve	6.8	4.1	10	3.3	4.2	0	4.6	4.4	3.7
	No effect	7.0	2.5	10	3.8	4.4	<0.1	4.9	4.4	4.9
	Worsen	8.0	3.5	10	4.5	4.6	2.5	5.6	4.4	6.8

Table 50 Nutrition knowledge of fruit and vegetable intake and fruit and vegetable score

HDI components	View on fruit and vegetable intake	Czech Republic			Russia			Poland		
		Mean	SD	Median	Mean	SD	Median	Mean	SD	Median
Fruit and vegetable score	Improve	8.7	2.2	10	8.0	2.3	8.9	8.8	2.0	10
	No effect	7.8	2.7	9.5	7.8	2.3	8.5	7.9	2.4	9.1
	Worsen	9.0	2.1	10	8.6	1.7	9.0	8.5	2.1	9.7

In Table 51, nutrition knowledge of meat intake was examined in relation to risk of metabolic syndrome using chi square tests. In the Czech sample, around 50% of participants with or without metabolic syndrome thought meat intake had no effect on health, while around 32% thought it could improve health and the rest thought it had a negative effect on health. In the Russian sample, almost 70% of those with or without metabolic syndrome thought meat intake could improve human health, and around 20% thought it had no effect on health, and around 10% thought it worsens health. In the Polish sample, around 65% of those with or without metabolic syndrome thought meat intake improved people's health, and around 25% thought 'no effect' and less than 10% thought 'it worsens health'. The results from the chi square test showed that only in Russian sample, nutrition knowledge of meat intake was associated with risk of metabolic syndrome (P=0.013), but not in the Czech (P=0.136) or Polish sample (P=0.327).

Table 52 shows the nutrition knowledge of fruit and vegetable intake in relation to risk of metabolic syndrome. In all three study countries, over 93% participants in the group of with or without metabolic syndrome believed that having fruit and vegetables could improve health. Results from the chi square tests showed that nutrition knowledge on fruit and vegetable intake was associated with risk of metabolic syndrome in the Czech sample (P=0.033) but not in Russian (P=0.442) and Polish sample (P=0.313).

Table 51 Nutrition knowledge of meat intake and metabolic syndrome

View on meat intake	Czech Republic N=4992			Russia N=8783			Poland N=7611		
	No	Yes	P	No	Yes	P	No	Yes	P
Improve	32.3	32.0	0.136	69.0	67.6	**0.013***	64.8	64.4	0.327
No effect	48.8	51.1		22.2	21.6		26.4	25.7	
Worsen	18.9	16.8		8.9	10.9		8.8	9.9	

*P<0.05

Table 52 Nutrition knowledge of fruit and vegetable intake and metabolic syndrome

View on fruit and vegetable intake	Czech Republic N=5012			Russia N=8787			Poland N=7627		
	No	Yes	P	No	Yes	P	No	Yes	P
Improve	96.6	95.4	**0.033***	93.3	93.7	0.442	94.5	94.8	0.313
No effect	2.7	4.0		6.4	5.9		4.9	4.3	
Worsen	0.8	0.6		0.3	0.5		0.7	0.9	

*P<0.05

In Table 53, nutrition knowledge of meat intake was examined in relation to HDI score. In the Czech sample, participants who believed meat intake worsened human health (mean: 49.4) had higher mean HDI total score compared to those thought meat had no effect (mean: 47.2) or could improve health (mean: 46.8). In the Russian and Polish samples, similar score pattern was found: participants in the 'worsen' group (mean: 44.7 in Russia and 44.2 in Poland) had higher score than the 'no effect' (mean: 44.1 in Russia and 42.6 in Poland) or 'improve' group (mean: 43.8 in Russia and 42.8 in Poland). The results from one-way ANOVA showed that nutritional knowledge on meat intake was associated with HDI score in all three study samples ($P<0.001$, $P=0.003$, and $P<0.001$, in the Czech, Russian, and Polish sample).

In Table 54, nutrition knowledge of fruit and vegetable intake was examined in relation to HDI score. In the Czech sample, participants who believed fruit and vegetable had no effect on health (mean: 45.5) had lower HDI score than those in the 'improve' (mean: 47.5) and 'worsen' (mean: 48.2) groups. While in the Russian sample, the HDI scores were similar in all three groups (mean: 44.0 in 'improve', 44.3 in 'no effect', and 44.3 in 'worsen' group). In Poland, participants in the 'improve' group (mean: 43.0) had higher score than the 'no effect' (mean: 41.6) and 'worsen' (mean: 42.2) group. Results from the one-way ANOVA showed that nutrition knowledge of fruit and vegetable intake was significantly associated with HDI score in the Czech and Polish samples ($P<0.001$), but insignificantly in the Russian sample ($P=0.053$).

Table 53 Nutrition knowledge of meat intake and HDI score

View on meat intake	Czech Republic N=4992			Russia N=8783			Poland N=7611		
	Mean	SD	P	Mean	SD	P	Mean	SD	P
Improve	46.8	6.9	**<0.001***	43.8	6.8	**0.003***	42.8	6.5	**<0.001***
No effect	47.2	6.9		44.1	6.8		42.6	6.5	
Worsen	49.4	6.8		44.7	7.2		44.2	7.0	

*P<0.05

Table 54 Nutrition knowledge of fruit and vegetable intake and HDI score

View on meat intake	Czech Republic N=4992			Russia N=8783			Poland N=7611		
	Mean	SD	P	Mean	SD	P	Mean	SD	P
Improve	47.5	6.9	**0.001***	44.0	6.8	0.053	43.0	6.6	**<0.001***
No effect	45.5	7.4		44.3	7.1		41.6	6.4	
Worsen	48.2	7.0		44.3	6.1		42.2	7.4	

*P<0.05

Based on previous analyses, nutrition knowledge of meat was associated with both risk of metabolic syndrome and HDI total score in the Russian sample only, which indicates that it could be a potential confounder in the association between HDI score and metabolic syndrome. Thus, in the sensitivity analyses, the fully adjusted model included nutrition knowledge on meat intake as an additional potential confounder (see Table 55). After adding nutrition knowledge on meat intake in the final model, the association between higher HDI total score and lower risk of having high blood pressure became significant, but the other results were similar.

Nutrition knowledge of fruit and vegetable intake was also found associated with both risk of metabolic syndrome and HDI score in the Czech sample. Therefore, nutrition knowledge on fruit and vegetable intake was added into the final regression model for a sensitivity analysis (see Table 56). However, the associations were similar.

Table 55 The association between HDI and metabolic syndrome in Russia with nutrition knowledge of meat intake as a confounder

	Model 1[a]		Model 2[b]	
	OR (95% CI)	P	OR (95% CI)	P
HDI total score	(per-10 unit)			
Metabolic syndrome	1.03 (0.83,1.28)	0.804	1.00 (0.81,1.22)	0.974
High blood pressure	0.83 (0.62,1.12)	0.225	**0.77 (0.61,0.98)**	**0.030**
Central obesity	1.00 (0.80,1.25)	0.978	0.94 (0.77,1.16)	0.577
High TG	1.01 (0.82,1.25)	0.913	0.99 (0.81,1.20)	0.889
Low HDL-C	1.01 (0.77,1.32)	0.959	1.00 (0.77,1.30)	0.987
High glucose	0.96 (0.78,1.18)	0.678	1.00 (0.81,1.22)	0.974

[a] model 1: adjusted for age group, sex, country, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, energy intake; added interaction terms between education and HDI, and energy intake and HDI
[b] model 2: model 1+ nutrition knowledge on meat intake

Table 56 The association between HDI and metabolic syndrome in the Czech Republic with nutrition knowledge of fruit and vegetable intake as a confounder

	Model 1[a]		Model 2[b]	
	OR (95% CI)	P	OR (95% CI)	P
HDI total score	(per-10 unit)			
Metabolic syndrome	1.00 (0.78,1.28)	0.974	1.00 (0.78,1.28)	0.972
High blood pressure	0.97 (0.74,1.28)	0.838	0.99 (0.75,1.31)	0.960
Central obesity	1.11 (0.86,1.42)	0.425	1.13 (0.88,1.46)	0.332
High TG	0.92 (0.72,1.16)	0.472	0.92 (0.72,1.17)	0.489
Low HDL-C	0.88 (0.69,1.13)	0.312	0.87 (0.68,1.11)	0.265
High glucose	0.95 (0.72,1.24)	0.708	0.94 (0.72,1.24)	0.667

[a] model 1: adjusted for age group, sex, country, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, energy intake; added interaction terms between education and HDI, and energy intake and HDI
[b] model 2: model 1+ nutrition knowledge on fruit and vegetable intake

5.7.3 Childhood SEP adjustment

Childhood SEP is known to play an important role in diet and metabolic syndrome; however, due to the imperfect/imprecise childhood SEP measure in the HAPIEE study, the childhood SEP measure was only considered in sensitivity analyses. In the HAPIEE study, there was one measure of childhood SEP—household amenities in childhood. Participants were asked "Did you have any of the following items (cold tap water, hot tap water, radio, fridge, own kitchen, own toilet) in your house when you were a child (about 10 years old)". In the analyses, the number of amenities was summed up from 0—6 items. Due to the different distribution of the answers in three study samples, for analytic purposes, the number of amenities in childhood was grouped differently in three study samples in order to achieve a balanced number of subjects in each group. The grouping details can be found in Table 57.

Table 57 The distribution of childhood amenities at 10-year old

Number of amenities	Czech Republic (N=4914)		Number of amenities	Russia (N=8734)		Number of amenities	Poland (N=7481)	
	N	%		N	%		N	%
0—3	1417	28.8	0	818	9.4	0—1	1399	18.7
4	1471	29.9	1	2906	33.3	2	1582	21.2
5	932	19.0	2	2240	25.7	3	1136	15.2
6	1094	22.3	3	955	10.9	4—5	1770	23.7
			4	589	6.7	6	1594	21.3
			5	438	5.0			
			6	788	9.0			

Analyses showed that number of childhood household amenities may be a potential confounder in the association between HDI and risk of metabolic syndrome, thus, the sensitivity analyses were conducted including this as a confounder (see Table 58). In the Czech and Polish samples, no association was found between HDI and risk of metabolic syndrome and its components before or after adjustment on childhood household amenities. While in the Russian sample, after adjusted for childhood household amenities, a ten-unit increase in HDI score was associated with 21% lower risk in having high blood pressure (P=0.047), other associations were similar.

Table 58 Association between HDI[a] and metabolic syndrome adding childhood SEP as an additional confounder

	Model 1[b]		Model 2[c]	
	OR (95% CI)	P	OR (95% CI)	P
Czech Republic				
Metabolic syndrome	1.00 (0.78,1.28)	0.974	0.99 (0.77,1.27)	0.917
High blood pressure	0.97 (0.74,1.28)	0.838	0.97 (0.74,1.29)	0.858
Central obesity	1.11 (0.86,1.42)	0.425	1.15 (0.89,1.49)	0.276
High TG	0.92 (0.72,1.16)	0.472	0.92 (0.72,1.17)	0.494
Low HDL-C	0.88 (0.69,1.13)	0.312	0.87 (0.68,1.11)	0.271
High glucose	0.95 (0.72,1.24)	0.708	0.93 (0.71,1.22)	0.598
Russia				
Metabolic syndrome	1.03 (0.83,1.28)	0.804	0.98 (0.80,1.21)	0.875
High blood pressure	0.83 (0.62,1.12)	0.225	0.79 (0.62,1.00)	**0.047**
Central obesity	1.00 (0.80,1.25)	0.978	0.93 (0.76,1.14)	0.490
High TG	1.01 (0.82,1.25)	0.913	0.97 (0.79,1.18)	0.751
Low HDL-C	1.01 (0.77,1.32)	0.959	1.01 (0.77,1.32)	0.943
High glucose	0.96 (0.78,1.18)	0.678	0.96 (0.79,1.17)	0.691
Poland				
Metabolic syndrome	0.91 (0.73,1.14)	0.404	0.89 (0.72,1.11)	0.307
High blood pressure	0.81 (0.62,1.04)	0.097	0.82 (0.64,1.05)	0.122
Central obesity	0.85 (0.68,1.06)	0.140	0.86 (0.70,1.07)	0.177
High TG	1.05 (0.85,1.30)	0.650	0.98 (0.80,1.22)	0.884
Low HDL-C	1.04 (0.83,1.31)	0.710	0.98 (0.78,1.23)	0.862
High glucose	0.92 (0.72,1.18)	0.526	0.93 (0.72,1.19)	0.539

[a]HDI per 10-unit increment
[b] model 1: adjusted for age group, sex, country, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, energy intake; added interaction terms between education and HDI, and energy intake and HDI
[c] model 2: model 1+ childhood SEP

5.7.4 Not adjusting for energy intake

In order to exclude the possibility of over-adjustment of energy intake in the regression models, sensitivity analyses were conducted in which fully adjusted models were not adjusted for energy intake (see Table 59). Results from regression models without energy intake adjustment were similar to those from the main analyses. The general direction of the association stayed the same, and the magnitude of the effect size became slightly larger, especially in the Russian sample, a 10-unit increase in HDI score was significantly associated with 24% lower risk of having high blood pressure (P=0.020); however, the other associations between HDI and risk of metabolic syndrome and its components remained non-significant.

Table 59 The association between HDI and metabolic syndrome in the fully adjusted model but without energy intake as a confounder

	Czech Republic		Russia		Poland	
	OR (95% CI)	P[a]	OR (95% CI)	P[a]	OR (95% CI)	P[a]
Metabolic syndrome	0.97 (0.76,1.25)	0.839	0.98 (0.80,1.20)	0.834	0.89 (0.72,1.11)	0.293
High blood pressure	0.95 (0.72,1.25)	0.71	0.76 (0.60,0.96)	**0.020[b]**	0.79 (0.62,1.01)	0.057
Central obesity	1.08 (0.84,1.38)	0.548	0.95 (0.78,1.17)	0.635	0.87 (0.71,1.08)	0.198
High triglycerides	0.91 (0.72,1.15)	0.421	0.99 (0.81,1.20)	0.881	1.00 (0.81,1.23)	0.977
Low HDL-C	0.92 (0.72,1.17)	0.491	0.99 (0.76,1.29)	0.951	1.03 (0.83,1.28)	0.785
High glucose	0.91 (0.69,1.18)	0.467	0.94 (0.77,1.14)	0.543	0.87 (0.68,1.12)	0.279

[a] Logistic regression modelling: models were adjusted for age group, sex, country, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake; added interaction terms between education and HDI, [b]$P<0.05$

5.7.5 Menopausal status

The prevalence of metabolic syndrome was examined by stratifying menopausal status among women (see Table 60). There were some missing data on menopausal status in three study samples (9, 3, and 38 cases in the Czech, Russian, and Polish sample respectively). In three study samples, the majority of female participants were postmenopausal (78.4%, 82.2%, and 75%, in the Czech, Russian, and Polish sample, respectively). Generally, the prevalence of metabolic syndrome and its components were higher among postmenopausal women compared to the premenopausal ones, except in Russian and Polish samples, there was no difference on the prevalence of having low HDL-C between the two menopausal status groups.

Analyses showed that menopausal status may be a potential confounder in the association between HDI score and risk of metabolic syndrome, therefore, the sensitivity analyses of including menopausal status in the fully adjusted model among female participants were performed (see Table 61). The direction and the magnitude of the effect were similar before and after this adjustment.

Table 60 Prevalence of metabolic syndrome among women stratified by menopausal status

	Czech Republic					Russia					Poland				
	PRM[a] (N=581)	%	PMP[b] (N=2115)	%	P[c]	PRM[a] (N=855)	%	PMP[b] (N=3958)	%	P[c]	PRM[a] (N=966)	%	PMP[b] (N=2894)	%	P[c]
Metabolic syndrome	123	21.2	839	39.7	<0.001	209	24.4	1,537	38.8	<0.001	141	14.6	961	33.2	<0.001
Raised blood pressure	248	42.7	1,321	62.5	<0.001	436	51.0	2,716	68.6	<0.001	366	37.9	1,735	60.0	<0.001
Central obesity	205	35.3	1,154	54.6	<0.001	448	52.4	2,485	62.8	<0.001	298	30.8	1,509	52.1	<0.001
High triglycerides	149	25.6	881	41.7	<0.001	178	20.8	1,331	33.6	<0.001	188	19.5	1,020	35.2	<0.001
Low HDI-C	164	28.2	706	33.4	0.019	174	20.4	801	20.2	0.940	234	24.2	771	26.6	0.138
Raised blood glucose	62	10.7	410	19.4	<0.001	169	19.8	1,197	30.2	<0.001	61	6.3	516	17.8	<0.001

[a]PRM: premenopausal [b]PMP: postmenopausal [c]P-values from Chi-square tests

Table 61 The association between HDI and metabolic syndrome in women, adjusted for menopausal status

	Czech Republic		Russia		Poland	
	OR (95% CI)	P[a]	OR (95% CI)	P[a]	OR (95% CI)	P[a]
Metabolic syndrome	0.87 (0.65,1.17)	0.348	1.03 (0.79,1.36)	0.805	0.89 (0.67,1.18)	0.409
High blood pressure	0.88 (0.64,1.21)	0.428	0.84 (0.59,1.20)	0.343	0.91 (0.66,1.26)	0.588
Central obesity	1.04 (0.78,1.40)	0.778	0.97 (0.72,1.30)	0.817	0.89 (0.66,1.19)	0.414
High TG	0.79 (0.60,1.05)	0.106	0.98 (0.75,1.27)	0.858	0.89 (0.68,1.17)	0.413
Low HDL-C	0.80 (0.61,1.07)	0.131	1.01 (0.75,1.35)	0.967	1.03 (0.78,1.36)	0.844
High glucose	0.84 (0.61,1.16)	0.288	1.03 (0.79,1.36)	0.808	0.89 (0.65,1.23)	0.483

[a]Logistic regression modelling: models were adjusted for age group, sex, country, smoking status, leisure activity hours per day, hours in engaging sports per day, working activity, education, medication for blood pressure, diabetes, or cholesterol, family history of diabetes, family history of stroke, alcohol intake, energy intake, and menopausal status; added interaction terms between education and HDI, and energy intake and HDI

5.8 Summary

In summary, the prevalence of metabolic syndrome was found to be high in all study samples—in the Czech Republic (37.1% in men and 35.7% in women), Russia (20.8% and 36.3%), and Poland (27.9% and 28.6%). Among the components of metabolic syndrome, raised blood pressure was the most prevalent (Czech Republic: 73.7% in men, and 58.2% in women; Russia: 62.4%, 65.5%; Poland: 66.1%, 54.5%).

The average diet quality as determined by HDI was moderate to poor in the three countries investigated (Czech Republic: mean HDI total score=4.6 in men, 4.8 in women; Russia: 4.3 in men, 4.5 in women; Poland: 4.2 in men, 4.4 in women). The participants tended to have a healthier intake of polyunsaturated fatty acids, protein, fibre, and fruit and vegetables, and an unhealthier intake of other dietary components—especially saturated fatty acids, cholesterol, and sugar. Women generally had a healthier diet pattern compared with men.

HDI was not associated with metabolic syndrome risk after adjusting for potential confounders in any of the three countries investigated (Czech Republic: 1.05 (0.97,1.14); Russia: 1.11 (1.04,1.19); Poland: 1.18 (1.09,1.27)). In the pooled analyses, higher HDI score was associated with lower risk of having high blood pressure only (0.82(0.72,0.94)). However, some associations between HDI components and metabolic syndrome and its components were found. Higher score in saturated fats was associated with greater risk of having high blood glucose and high triglycerides level, but lower risk of having central obesity; higher score in polyunsaturated fatty acids was associated with lower risk of having high triglycerides; higher protein score was associated with lower risk of having high glucose, central obesity, and metabolic syndrome; high sugar score was associated with lower risk of HDL-C but greater risk of having high blood glucose; higher fruit and vegetable score was associated with higher risk of having high blood glucose; and higher cholesterol score was associated with higher risk of having metabolic syndrome and high blood glucose. Among these findings, the most consistent result among countries was the protective association between better adherence to protein intake and low risk of having high blood glucose (Czech Republic: 0.87 (0.80,0.94); Russia: 0.93 (0.88,0.99); Poland: 0.82 (0.75,0.89)).

In sensitivity analyses, the results found in the imputed dataset was largely similar to the results based on the complete case sample except in Polish sample. Participants

with better knowledge of meat intake had healthier intake of saturated fatty acids, protein, and cholesterol.

Chapter 6 Discussion

In this chapter, the main findings of the thesis will be summarised, and the methodological issues of the thesis will be discussed. In addition, the findings of the thesis will be compared with the existing literature. This will include estimates of metabolic syndrome prevalence, HDI scores in the Czech, Russian, and Polish samples, and the association between HDI and metabolic syndrome. The recommendation for the future research will be discussed, followed by the implications for public health.

6.1 Summary of findings

The first objective of this thesis was to examine the prevalence of metabolic syndrome and its components in the three samples. The results showed that the prevalence of metabolic syndrome was high in men and women in the Czech sample (37.1% among men and 35.7% among women), Russian sample (20.8% among men and 36.3% among women), and Polish sample (27.9% among men and 28.6% among women). Of the components of metabolic syndrome, raised blood pressure (systolic blood pressure≥130mmHg or diastolic blood pressure≥85mmHg) was the most prevalent component of metabolic syndrome in men and women: 73.7% and 58.2% in the Czech sample; 62.4% and 65.5% in the Russian sample; and 66.1% and 54.5% in the Polish sample, respectively. Other components of metabolic syndrome were also highly prevalent, especially central obesity (waist circumference ≥102 cm in men or ≥88 cm in women) with 33.9% and 50.4% in the Czech sample, 25.1% and 60.9% in the Russian sample, 32.3% and 47.0% in the Polish sample. High triglycerides (≥ 1.7mmol/L) was also highly prevalent, with 50.3% and 38.2% in the Czech sample, 26.3% and 31.4% in the Russian sample, and 41.4% and 31.3% in the Polish sample. The prevalence of metabolic syndrome and its components were relatively high compared with estimates from Western European countries (eg, 25%),[7] which supported the first hypothesis of this thesis (The prevalence of metabolic syndrome and its components is relatively high in the Czech Republic, Russia, and Poland compare with Western European countries). These findings will be discussed in more detail in Section 6.3.1.

The second objective of this thesis was to examine whether the prevalence of metabolic syndrome was associated with age, sex, SEP, smoking status, and physical activity in the study countries. The results showed that as hypothesised (hypothesis

2) the prevalence of metabolic syndrome was consistently higher in older age in the three study samples. It was also proposed that the prevalence of metabolic syndrome was higher in men than in women in the Czech and Polish sample, but higher in women than men in the Russian sample. The results partially supported the second hypothesis with a slightly higher prevalence in men than in women in the Czech sample, and a more than 15% higher prevalence in women than in men in the Russian sample. However, contrary to expectation, the prevalence was slightly higher in women than in men in the Polish sample. In terms of SEP relations with metabolic syndrome, lower education was associated with higher risk of metabolic syndrome as hypothesis. It was also hypothesised that being a non-smoker or having higher physical activity would be associated with lower risk of metabolic syndrome, and this was supported by the findings in the Czech and Russian samples, while in the Polish sample higher physical activity was associated with slightly higher prevalence of metabolic syndrome.

Objective three of the thesis was to characterise and compare the dietary quality in the three samples. The results showed that the overall diet quality as determined by HDI was moderate to poor in three study samples investigated. The participants tended to have moderate-good adherence to recommended intake of polyunsaturated fatty acids, protein, fibre, and fruit and vegetables, and a poor adherence to the recommended intake of other dietary components—especially, saturated fatty acids, cholesterol, and sugar. The findings of moderate dietary quality and variability of dietary quality scores partially supported hypothesis 3, except for the unexpected high score in dietary fibres (median: 7.7 in men, 8.8 in women in the Czech sample; 8.6 in men, 8.4 in women in the Russian sample; 10.0 in both men and women in the Polish sample) and protein intake (median: 6.7 in men, 7.5 in women in the Czech sample; 7.3 in men, 7.7 in women in the Russian sample; 6.6 in men, 6.9 in women in the Polish sample). In addition, it was also found that Czechs had better adherence to cholesterol intake compared with the other two samples (median: 10.0 in both men and women in the Czech sample; 0 in men, 3.0 in women in the Russian sample; 1.6 in men, 7.0 in women in the Polish sample). The overall dietary quality (in terms of HDI score) was found to be similar between countries (mean: 4.6 in Czech men, 4.8 in Czech women; 4.3 in Russian men, 4.5 in Russian women; 4.2 in Polish men, 4.4 in Polish women), while women generally had a significantly better adherence than men in all three countries (P<0.001); these findings supported hypothesis 3 (The study samples have on average a low HDI score, and women have better adherence to HDI compared with men).

The associations between dietary quality and risk of metabolic syndrome and its components were examined in response to objective 4. However, the results did not support the hypothesised finding (hypothesis 4: a higher HDI score would be associated with lower risk of metabolic syndrome and its components), because no statistically significant association was found between total HDI score and risk of metabolic syndrome or its components in any of the study samples after full adjustment (P>0.05).

Objective 5 considered the associations between the separate dietary components of the HDI and risk of metabolic syndrome and its components. It was hypothesised that a better adherence to recommended levels of dietary components of HDI would be associated with lower risk of having metabolic syndrome and its components. However, associations between adherence to the HDI components and risk of metabolic syndrome components were mixed. On one hand, better adherence to some dietary components was significantly associated with lower risk of metabolic syndrome and its components: for example, a one unit increase in saturated fatty acids score was associated with 7% lower risk of having central obesity in the Polish sample; a one unit increase in polyunsaturated fatty acids score was associated with almost 10% lower risk of having high triglycerides in the Polish sample; and a one unit increase in sugar score was associated with a 7% lower risk of having low HDL-C in the Czech sample. Among all the dietary components, better adherence to protein intake was consistently and significantly associated with lower risk of having high glucose levels in three study samples: a one unit increase in protein score was associated with around 13% decreased risk among Czechs, 7% among Russians, and 18% in Poles; furthermore, in the Polish sample, a one unit increase in protein score was also associated with an 8% decreased risk in metabolic syndrome and 10% in central obesity. On the other hand, a better adherence to some HDI guidelines was significantly associated with increased risk of metabolic syndrome: for example, a one unit increase in saturated fatty acids score was associated with an 8% increased risk of having high blood glucose level in the Czech sample, and a 6% and 7% increased risk of having high triglycerides and high blood glucose in the Polish sample. A one unit increase in sugar score was associated with 10% increased risk of having raised blood pressure in the Russian sample, and it was also associated with 11%, 12%, and 23% increased risk of having high blood glucose in the Czech, Russian, and Polish samples respectively; a one unit increase in fruit and vegetable score was associated with 7% increased risk of having high blood glucose level in the Russian sample; a one unit increase in cholesterol intake was associated with 6% increased

risk of metabolic syndrome in the Russian sample, and 9% increased risk of having high blood glucose level in the Polish sample.

The associations between HDI score and risk of metabolic syndrome and its components were evaluated again in analyses pooling the three countries (in response to objective 6). The results partially supported the hypothesised association (hypothesis 6) between higher HDI score and lower metabolic syndrome risk, and the magnitude of associations was similar to the country specific sample analyses. Similar to results of country-stratified analyses, the directions of the associations between diet quality and metabolic syndrome were not consistent. A better adherence to total HDI score, polyunsaturated fatty acids, and protein was significantly associated with lower risk of metabolic syndrome and its components: for example, a 10-unit increase in HDI score was associated with 18% lower risk of having raised blood pressure; a one unit increase in polyunsaturated fatty acids score was associated with a 7% lower risk of having low HDL-C; a one unit increase in protein score was associated with a 6% lower risk of metabolic syndrome and obesity, and 13% lower risk of having high blood glucose level. In contrast, a one unit increase in sugar score was associated with a 4% increased risk of metabolic syndrome, a 7% increased risk of raised blood pressure, and a 13% increased risk of high blood glucose; a one unit increase in fibre score was associated with a 4% increased risk of metabolic syndrome and an 8% of having high blood glucose; a one unit increase in fruit and vegetable score was associated with a 7% increased risk of having high blood glucose level; a one unit increase in cholesterol intake was associated with a 4% increased risk of metabolic syndrome and 7% in high blood glucose level.

Finally, multiple imputation was conducted and the main analyses repeated using the imputed dataset (objective 7). The sample characteristics were very similar to the complete sample, supporting hypothesis 7. In the imputed analyses, a 10-unit increase in overall HDI score was associated with 12% reduced risk of having low HDL-C in the Czech sample and 9% reduced risk of having central obesity, while in the Polish imputed sample, a 10-unit increase in overall HDI score was associated with 18% and 22% increased risk of having metabolic syndrome and high glucose level, respectively. However, these associations were not found in the combined complete sample, and this did not support hypothesis 7.

Overall, results found were mixed and there was little evidence for a strong association between HDI score (and its components) and metabolic syndrome (and its components). Before comparing the findings in this thesis with the literature, the

methodological issues in this thesis will be considered, and the roles of these issues may play in explaining the findings will be discussed.

6.2   Methodological issues in the thesis

The methodological issues that will be discussed are representativeness, misclassification, residual confounding, missing data, issues related to FFQ, potential over-adjustment, and the cross-sectional study design.

6.2.1   Representativeness

In the HAPIEE study, the participants were randomly selected from population registers in the Czech Republic and Poland, and the Russian sample was selected from electoral list, but the samples were only selected in the urban areas and the response rate was moderate, and these two issues may have affected study findings.

The HAPIEE samples came from six cities in the Czech Republic, one city in Russia, and one city in Poland. The study participants were randomly selected from within the chosen urban areas, thus the study sample would likely be representative of the selected urban areas/communities. However, it could be argued that the study sample was not representative of all urban areas, nor of rural areas in these countries. As such, the prevalence of metabolic syndrome and diet quality reported in this thesis may not reflect the entire countries of Czech Republic, Poland, and Russia. This may be attributed to the urban/rural inequalities in the region;[307] for example, people in urban areas would have better education and more advantage in accessing to health care system.

Another issue related to representativeness is the response rates in the HAPIEE study. The response rates were moderate: 55% in Czech Republic, 61% in both Russia and Poland, and to other large population studies conducted in Western Europe.[308;309] Non-response might be partially due to participants moving homes or participants, but it is likely that a major reason for non-response is unwillingness to participate in the study. Moreover, non-response may be more likely for participants with worse health status.[302] This would lead to underestimate the prevalence of metabolic syndrome, but would not alone affect the association between diet and metabolic syndrome. However, if non-responders also had a particularly unhealthy HDI, then the association between diet and metabolic syndrome would possibly be attenuated to null.

Data for metabolic syndrome (including waist circumference, blood pressure, triglycerides, HDL-C, and blood glucose) could not be measured for a number of participants particularly in the Czech Republic and Poland. In these two countries, participants were visited and questionnaires were administered at home, and they were subsequently invited to the local clinics for a medical examination. While in Russia, both the questionnaires and the examination were completed by the participants in the clinics. The missing data on metabolic syndrome of non-responders are discussed in more detail in section 6.2.4.

6.2.2 Misclassification

Measurement error is a common and important issue in epidemiological studies.[310] It may be introduced into studies by factors including technical errors or fluctuations of the variable over time, leading to single measures incorrectly capturing long-term variables of interest. Measurement error can lead to misclassification, such that exposed persons are classified as unexposed and vice versa. There are two types of misclassification: non-differential and differential misclassification. In the following sections, the impact of these types of misclassification on the study findings will be discussed.

Non-differential misclassification for exposures

When non-differential misclassification occurs in the exposure, the subjects have been misclassified into different exposure group are independent on the outcome and other variables.[310;311] When there is non-differential misclassification in the exposure, the association will be attenuated towards the null.[310] In this thesis, the main explanatory variable was dietary intake, which was captured by FFQ and presented in the continuous form of HDI (1-70 points). FFQ has been commonly used in large epidemiological studies due to its inexpensive cost and easy administration in questionnaires. FFQs evaluate food intake within a specific period of time, for example, the past 3—6 months. However, long-term dietary intake is typically the risk factor of interest in association with outcomes, such as metabolic syndrome. Although compared with other dietary assessment methods, such as dietary reports within 24 hours, FFQs capture a dietary intake for a longer time period; however, this may not reflect long-term dietary habits which take place over years and decades. Moreover, participants were asked the average intake of certain food over a period of time, which may be difficult to accurately recall. Therefore, the use of FFQs may introduce non-

differential misclassification which would have attenuated the association between HDI and metabolic syndrome risk.

Non-differential misclassification for outcomes

When non-differential misclassification occurs in the outcome measure, the effect estimate tends to have wider corresponding confidence intervals and larger p-values.[310] Particularly when the outcome variable is binary, non-differential classification may bias results towards null.[312] In this thesis, metabolic syndrome and its components were the main outcomes. The five components included high blood pressure, central obesity, low HDL-C, high triglycerides, and high blood glucose, all measured during clinic visits. Measurement error is likely to have occurred for each of these. For example, blood pressure is known to vary substantially during the day,[313] so the three measurements of blood pressure during the clinical examination would have imperfectly captured the true average blood pressure. Moreover, the values obtained would also fluctuate depending on the position of the cuff during measurement.[314] Waist circumference was used to measure central obesity, and the use of trained nurses would have minimised measurement error. However, measurement error may have occurred. For example, different temperatures in the clinics may have affected measurement (eg, it would be easier to persuade participants wearing less layers of clothes to measure waist circumference if the room temperature was warmer). The other components of metabolic syndrome used laboratory measurements which differed in each country (see Section 4.3). Therefore, non-differential classification may be introduced in the interested outcome measures, and further affect the precision of the results/association. Several techniques have been adopted to reduce the measurement error and misclassification in plasma glucose level in the thesis (see Section 4.3.4). First, the capillary (Czech sample) and serum (Russian sample) blood glucose was recalculated to plasma equivalent values using recommended equation.[279] Although the technique could reduce the measurement error in glucose measurements, there might be still some residual measurement error. Second, the standard plasma glucose was further calculated for the Czech and Polish sample using equation modelling to further reduce the measurement error between countries; however, this technique was not performed for the Russian sample because the only available glucose variable from Russian collaborators was binary. As explained in section 4.3.4, using CTSU glucose test results as 'gold standard', the sensitivity of the local laboratory measurements was 81.2% and specificity was 82.3%. This showed that there were some misclassification

in the glucose values in the Russian sample, and this may make the results from Russian slightly difficult to compare with the other two samples. However, results from country specific samples did not show distinct difference between countries (see Sections 5.6.1 and 5.6.2). Moreover, in section 5.6.3 the pooled results (combining three study samples together) showed that the direction of the association in the pooled dataset was similar to the country-specific results; differences in results found may be attributed to both the different sample size and measurements used. Furthermore, the measurements of triglycerides, HDL-C, and blood glucose level differs depending on whether participants fasted before giving blood samples. Triglycerides and glucose are known to be sensitive to food intake, while research has suggested that HDL-C concentrations are not affected by food intake.[91;315;316] In the study samples, only the Czech and Polish samples had available data on fasting status. In the Czech sample, 95% of participants fasted before blood sample was taken while only 57% in the Polish sample. Sensitivity analyses was performed by stratifying analyses by fasting status in these two samples. Similar results were found, suggesting that this source of error was unlikely to have substantially affected study findings (results are not shown in this thesis).

Taken together, the above sources of measurement error in the outcomes may have introduced non-differential misclassification in categorising the binary outcomes used, contributing to further attenuation of the association between HDI and metabolic syndrome.

Non-differential misclassification for covariates

Non-differential misclassification could also occur in the covariates, which included smoking status, family history of diabetes, and family history of stroke. First, smokers could under-report their smoking status due to the social pressure. Second, in the thesis, participants had a mean age of 58 years; thus it could be difficult for them to recall clearly about their parents' or even siblings' medical conditions. This may further lead possible misclassification of family history of diabetes and stroke. These covariates were considered potential confounders in the thesis. Thus the non-differential misclassification could have reduced the degree of the confounding control and potentially introducing bias in in adjusted analyses, Misclassification in confounding variables may have led to residual confounding, which will be discussed in more detail in section 6.2.3.

Differential misclassification

The main form of differential misclassification in this thesis is likely to be information bias in the self-reported diet instrument used (FFQ) Recall bias is one of the important forms of information bias, and was likely to have affected reported diet intake (over preceding 3 months). This is likely to have especially affected central obesity, as participants are less likely to be aware of the presence of the other components of metabolic syndrome. For example, participants who were obese may tend to report a healthier diet compared to true intake. Previous research has suggested that obese participants report a healthier diet with more fruit and vegetable and less sugar or fat intake, leading to energy under-reporting.[183] This may have led to an underestimation of the true association between HDI and metabolic syndrome.

6.2.3 Residual confounding

Residual confounding is another issue which could have distorted some of the association between diet quality and metabolic syndrome risk. Normally there are at least two main causes of residual confounding. First, the confounding factors were not measured precisely enough; and second, misclassification occurred among the confounding variables.[317]

In this thesis, the associations found between HDI and metabolic syndrome (though weak and inconsistent) could be attributed to residual confounding. For example, physical activity and alcohol intake were obtained by single measures from self-reported questionnaires, which likely imprecisely measured these complex factors. These and other self-reported confounding factors examined, such as SEP and medical conditions, may have been misclassified (eg, due to genuine lack of awareness, or due to social desirability bias). The adjustment for these potential confounders in this thesis may therefore not have been sufficient to capture the full context of the confounding effects of other social and behavioural factors in the association between HDI and metabolic syndrome.

In order to further investigate if misclassification in SEP have attenuated the finding in this thesis, results from sensitivity analysis including childhood SEP as an additional covariate showed a better adherence to HDI was borderline significantly associated with lower risk of having raised blood pressure in Russian sample, but not in the other two samples. This may imply that childhood SEP is an important factor in the association between HDI and metabolic syndrome. However, including it could also introduce recall bias in the study and further led to misclassification.

6.2.4 Missing data

Missing data is an important factor that reduce the study power and worsen the precision of estimates, and may also bias associations found.[301] In the HAPIEE study, many participants did not come to the clinics to the clinical examination (especially in the Czech and Polish samples), and this led to around 20% of the Czechs and 13% of the Poles having no metabolic syndrome measures. These subjects were excluded from the main analyses (see Section 4.7.1). However, multiple imputation was conducted in sensitivity analysis, under the assumption that the data were "missing at random" (see Section 4.7.1). These sensitivity analyses showed that the sample characteristics of the imputed dataset and the complete case sample were very similar (see Section 5.6.1 & 5.7.1). In the Czech and Russian samples, the direction and the magnitude of the association between HDI total score and metabolic syndrome risk was also largely similar—some differences found in the fully adjusted model in the imputed dataset could be due to the larger sample size compared to the complete-case analyses. However, in the Polish sample, the results from fully adjusted-model in the complete sample (0.92 (0.72,1.18)) and imputed sample (1.22 (1.11,1.34)) were different. This may indicate that in the Polish sample, participants with missing data were possibly not "missing at random". Possibly, participants with missing data were very unhealthy and had very unhealthy diet, thus excluding them had attenuate the association to null.

6.2.5 FFQ

FFQ was the dietary measure used in the HAPIEE study. It is one of the most commonly used methods for collecting dietary intake in the large population studies.[318] However, there are some methodological issues related to the use of which may have affecting the results found in this thesis. First, in order to better capture country-specific food intake, the components of the FFQ differed slightly in the three countries investigated. This could make it difficult to compare the mean intake of certain food groups or nutrients, and therefore HDI comparisons between the countries. For example, Russians and Poles were found to have higher intake of cholesterol, but this may be related to the higher number of cholesterol-related items in the Russian and Polish FFQ compared with the Czech sample. However, the added items were approved by the local nutritionist in order to ensure that diet was appropriately measured in each country.

Second, participants completed the questionnaires in Russia with the assistance of nurses during clinic visits, while in the other two countries participants completed the questionnaire by themselves. Therefore, selective misclassification could have been introduced at the country level. Moreover, in Russia, although the nurses conducted interview on FFQs were trained and certified, it was the nurses' decision on the length and depth of the interview according to the participants' characteristics, which would result in differential misclassification for the recorded food intakes in participants. Third, there may be some seasonal variation in food intake which was not considered in the FFQ design of the HAPIEE study. The impact of seasonal differences may also differ in the different countries and cities investigated.

Another methodological issue in dealing with FFQ would be the missingness of the answers. In this thesis, after excluding participants with more than 15 FFQs answers missing, missing data for a specific food item was assumed to reflect zero intake, rather than reflecting missing data. Although this approach has been long used in nutritional epidemiological studies, in order to preserve the analytic sample size, non-responses may not necessarily always reflect no intake.[183;290-292] Food items on an FFQ may be omitted because the food was not consumed or because of difficulties remembering the frequency and amount of intake, especially since there is no option of 'Don't remember' in FFQs.[183] Studies have showed that older adults tend to leave more FFQ items blank and this may be due to failing memory.[290;319] Ultimately, if the assumption on item missingness was miss-specified, then the food intake might also be misclassified,[290] which would further introduce non-differential misclassification in the study and may bias the association between HDI and metabolic syndrome.

Additionally, some of the confounding factors such as dietary habits may act as underlying factors affecting diet quality. A systematic review showed that eating out of home was associated with higher energy intake, fat intake, and lower intake of vitamin C.[320] Furthermore, a recent Norwegian study found the consistent results, and people constantly eating out had higher intake of sugar compared with those who do not regularly eat out.[321] People are generally less aware of the ingredients they have when eating out, and the food may be less healthy than homemade food (eg, it may have more sugar and fat contents). However, there are no such variables on dietary habits in HAPIEE study to test these potential relationships. Moreover, dieting status is also an important factor when estimating food intake, specifically, women are more likely to be on a diet compare with men. Meal time is also an important factor of dietary

habit which could influence the diet quality. However, there are no such variables in the HAPIEE dataset to reflect the dieting status or dietary habits.

6.2.6 Over-adjustment for energy intake

Another issue regarding the dietary intake may be over-adjustment for energy intake which may lead to an artificial association between HDI and outcome, since the energy intake already has been taken into account while constructing HDI scores. Most of the scores of the HDI components were calculated into the percentage of the total energy intake per day. However, sensitivity analyses by excluding energy intake as a covariate was conducted, and the magnitude and significance of the association between HDI and metabolic syndrome remained the same; therefore, over-adjustment for total energy intake does not appear to be a major explanation of the results found in the thesis.

6.2.7 The cross-sectional study design

Some unexpected results in relation to diet and metabolic syndrome could be attributed to the cross-sectional design of the study. It is not possible to determine the temporal nature of the relationship between HDI and metabolic syndrome using a cross-sectional study. For example, long-term exposure to an unhealthy diet (eg, a high intake of fats and sugars) would be expected to contribute to obesity and thereby type 2 diabetes. These patients are typically advised by doctors to change their diet (eg, to lower low fat and sugar intake). This may explain the unexpectedly higher sugar intake was associated with lower risk of having high blood glucose level (see Section 5.6.2). Studies with follow-up are required in order to better account for reverse causation in explaining an association between HDI and metabolic syndrome. .

6.3 Comparison with other studies and explanation of findings

In this section, the findings from this thesis will be compared with previous research in the order of the objectives stated in Chapter 3 (ie, prevalence of metabolic syndrome, HDI scores, and the association between HDI and metabolic syndrome and its components).

6.3.1   Prevalence of metabolic syndrome and its components (objective 1 & 2)

The prevalence of metabolic syndrome in this study ranged from 20.8% (in Russian men) to 37.1% (in Czech men) in three study samples. There was little sex evidence for sex differences in the prevalence of metabolic syndrome in the Czech and Polish samples (Czech sample: 37.1% in men, 35.7% in women; Polish sample: 27.9% in men, 28.6% in women), while there was a relatively large difference in the Russian sample (20.8% in men compared with 36.3% in women). As shown below, both overall prevalence and sex differences in prevalence do not substantially differ from previous studies in Eastern Europe.

Prevalence of metabolic syndrome in the Czech sample

The slightly higher prevalence of metabolic syndrome among Czech men (37.1%) as compared with Czech women (35.7%) was consistent with other Czech estimates, but higher prevalence in both men than women (32.5% and 29.9% respectively).[25] Metabolic syndrome was defined using IDF in Vosatkova et al's study, and previous research suggested that prevalence may be around 20% higher when using IDF compared with ATPIII as the definition.[69] However, the prevalence was higher in this thesis compared with Vosatkova et al's study, so the choice of definition of metabolic syndrome does not seem to explain the higher prevalence found in the thesis (using ATP III). The main reason for this difference may be that in Vosatkova et al's study the participants were younger (aged from 18 to 65 years) than the sample used in this thesis (45 to 70 years). Previous studies have shown that the prevalence of metabolic syndrome increases with age,[8;27] which was also found in this thesis. Moreover, women have higher risk of having metabolic syndrome and its components after transitioning through menopause.[107;109;110] This may also explain the higher prevalence among women in the thesis compared with the findings in the Vosatkova et al's sample. Indeed, sensitivity analyses in section 5.7.5 showed that the prevalence of metabolic syndrome among premenopausal women in the Czech sample was 21.2%, while among postmenopausal women was 39.7%.

Similarly, it is possible to compare components of metabolic syndrome in the thesis with those from Vosatkova et al's study. In this thesis, raised blood pressure (systolic blood pressure≥130 mmHg or diastolic blood pressure≥85 mmHg) was the most prevalent component of metabolic syndrome in the Czech sample (73.7% in in men and 58.2% in women). In Vosatkova et al's study, the prevalence of having raised blood pressure (defined in the same way) was lower (45% in men, 20% in

premenopausal women, and over 50% in postmenopausal women), potentially explained by the younger age of the sample used.[322] Apart from Vosatkova et al's study, raised blood pressure using the same cut-points as this thesis has not been further investigated in other studies. However, the prevalence of hypertension (systolic blood pressure≥140mmHg or diastolic blood pressure≥90mmHg) was found to be 45.6% in men and 33.0% in women in year 2000/1 in the total population of the Czech MONICA study,[78] compared with 71.9% in men and 51.9% in women in the thesis. Moreover, the average values of both systolic and diastolic blood pressure were higher in this thesis (systolic/diastolic: 144.2/90.8mmHg in men, 134.3/87.0mmHg in women) compared with the Czech MONICA study (131.9/83.7mmHg in men, 125.9/79.3mmHg in women). The most likely reason again could be the younger age of the participants in the MONICA study (mean age: 45 years). Moreover, in the MONICA study, the study sample was mostly from rural areas, while the HAPIEE study sample was selected from urban areas. This region difference may have also contributed to these differences (eg, if rural areas have lower salt intake and/or higher physical activity).[323;324]

The second most prevalent component in the Czech sample found in this thesis was high triglycerides (ie, triglycerides≥1.7mmol/L) (50.3% and 38.2% in men and women respectively). These were higher than the findings in Vosatkova et al's study, where prevalence of having high triglycerides (same definition as above) was 30% in men, 12% in premenopausal women, and 30% in postmenopausal.[25] A similar pattern was also found when comparing the prevalence of having low HDL-C between this thesis (27.4% in men and 32.4% in women) and Vosatkova et al's study (20% in men, 3% in premenopausal women, and 20% in postmenopausal women).[25] As triglycerides increase with age[325] and HDL-C decreases with age,[326] the difference in age between these two studies is again most likely reason for differences in prevalence of high triglycerides and HDL-C levels. In addition, the difference could also due to the differences in laboratory quality control: in the Czech sample, the laboratory was CDC-certified, while certification was not described in Vosatkova et al's study.

In Vosatkova et al's study, prevalence of central obesity was 64% in men, 58% in premenopausal women, and 86% in postmenopausal women;[25] and these were higher than the results from this thesis (33.9% in men and 50.4% in women). These results are however difficult to compare due to different cut-points in two studies. In Vosatkova et al's study, the cut-points were waist circumference ≥94cm in men and ≥80cm in women (compared to ≥102cm in men and ≥88cm in women in ATPIII

definition). Therefore, more subjects would fall into the central obesity category in the IDF definition. The prevalence of having high blood glucose was 25% in men, 6% in premenopausal women, and 27% in postmenopausal women using IDF definition (blood glucose≥5.6mmol/L) in Vosatkova et al's study. With a higher cut-point in blood glucose in the thesis (≥6.1mmol/L), the prevalence found in this thesis was 25.9% in men and 17.5% in women. The prevalence of having high blood glucose was similar and slightly lower in this thesis (especially in women) which may also be due to the different definitions used.

Apart from the Vosatkova et al's, the prevalence of metabolic syndrome and its components in the Czech Republic were not systematically investigated in other studies to the author's knowledge, but some individual components of metabolic syndrome were examined in the MONICA study, namely HDL-C.[78] The HDL-C level was very similar to the findings in this thesis: it was 1.25mmol/L in men and 1.49mmol/L in women in year 2000/1 in Cifkova et al's study, and was 1.3mmol/L in men and 1.5mmol/L in women in the thesis.

Prevalence of metabolic syndrome in the Russian sample

In the thesis, the prevalence of metabolic syndrome in Russian women (36.3%) was similar to the prevalence in the Czech sample, and higher than Russian men (20.8%). These results were higher than previous study conducted in Russia but with different samples/cohorts.[22] However, in a small sample study conducted by Jones et al, the prevalence of metabolic syndrome was 54.1% in the total sample. However, this study had a small sample size (N=146), and recruitment of the participants was not random, which led an over 90% of women in the study sample.[20] Another previous study in Russia (Arkhangelsk) among 3705 participants aged 18-90 years found that women had higher prevalence of metabolic syndrome than men (11.5% in men and 19.8% in women).[22] The lower prevalence found in this study could be due to the use of different biological metabolic measures. For example, the use of HbA1c (≥6.1%) (which equivalent to ≥7.1mmol/L in plasma glucose level) instead of plasma glucose could have resulted in lower prevalence of hyperglycaemia and thus an underestimate of the prevalence of metabolic syndrome.[79] This study also reported a higher prevalence of other components of metabolic syndrome using the ATPIII definition compared with those found in this thesis.[22] For example, the prevalence of central obesity was 37.1% in men and 82.4% in women in the Arkhangelsk study, compared with 25.1% and 60.9% in the thesis respectively; and the prevalence of raised blood pressure, high triglycerides, and low HDL-C, were over 85% in men and women compared with lower

prevalence found in the thesis (raised blood pressure: 62.4% in men and 65.5% in women; high triglycerides: 26.3% in men and 31.4% in women; low HDL-C: 5.4% in men and 20.3% in women). Possible explanations for these differences include the use of a wider age range, differences in age-standardisation procedure, and/or regional differences in prevalence. In Russia, despite the much higher cardiovascular disease mortality in men compared with women, the prevalence of metabolic syndrome in women was found almost double that of men. This may due to the sex difference in alcohol intake, and/or due to the higher smoking prevalence in men.

Prevalence of metabolic syndrome in the Polish sample

In the Polish sample, the prevalence of metabolic syndrome was similar in men and women (27.9% in men and 28.6% in women). Only one previous study was found which examined the prevalence of metabolic syndrome among a Polish population using the ATPIII definition. This study reported a prevalence in men and women of 16.2% and 20.9% respectively.[23] The lower prevalence of metabolic syndrome may be due to the wider age range (25-97 years) compared with the HAPIEE sample (45-70 years). The sample selection was also different: although a large sample size was used (N=40989), the participants were all patients who were not treated for diabetes or coronary artery disease.

In two other Polish studies, different definitions of metabolic syndrome have been used. In the thesis, 66.1% of men and 54.5% of women were defined as having raised blood pressure, 41.4% of men and 31.3% of women with high triglycerides, and 18.8% of men and 26.1% of women with low HDL-C. In the PONS study, Janszky et al also reported a high prevalence of raised blood pressure (70%), but lower prevalence of high triglycerides (20%) and low HDL-C (16%). (Janszky et al. 2011) Moreover, in the study conducted by Ilow and colleagues,[24] they found central obesity (94.8%) and high blood pressure (82.8%) were more common in women, while central obesity (87.5%), high triglycerides (80.9%), and high blood pressure (88.1%) were more common in man. This finding was consistent with the results found in this thesis. Furthermore, they also found that high blood pressure was the most prevalent component of metabolic syndrome in both men and women

Prevalence of metabolic syndrome compared with to different regions

The prevalence of metabolic syndrome was found to differ in the Czech, Polish and Russian samples in this thesis. Previous studies have consistently showed that the prevalence in the U.S. is very high compared with other countries, from 25% to

35%.[8;72] In Europe, Grundy estimated a 25% prevalence of metabolic syndrome.[7] Other studies, using different definitions of metabolic syndrome, have reported prevalence ranges from 18% to 45%.[7;69;70;73;74]

Restricted to the studies using ATPIII definition, the prevalence of metabolic syndrome found in the current study was higher than western European countries: in Ireland, the prevalence was 21.8% in men and 21.5% in women (aged 50-69 years);[327] in Sweden, the total prevalence among people aged 46-68 years was 20.7%;[73] in Germany, the prevalence was 22.7% in men and 18.0% in women among people aged 18-99 years;[74] in Greece, the total prevalence was 24.5% among adults aged ≥18 years.[69] As discussed in the previous sections, the lower prevalence found in these studies might be due to the study samples with a wider age range.[69;74] However, compared with the studies from Ireland and Sweden, which had quite similar aged population to this thesis (45-69 years old), the prevalence in this thesis (except among Russian man: 20.8%) was still higher.

The comparisons between different studies are in general difficult. The differences may be real, and may be due to differences in lifestyle or even genetic differences. It is, however, likely that the differences are influenced by differences in study design, sample characteristics, and data collection. Age seems to be most influential factor because the individual components are mostly driven by the advancing age, which further would drive metabolic syndrome as a whole. It is also likely that the differences in results between studies are the combination of both real differences and differences in methodology.

Prevalence of metabolic syndrome in relation to demographic factors

In this thesis, results showed the prevalence of metabolic syndrome increased with increasing age in the three study samples, and this is consistent with previous studies as described previously.[8;22;27;113;328]

It was also found that the prevalence of metabolic syndrome was slightly higher in men than in women in the Czech sample and this is supported by previous research.[25] While the prevalence was only a little higher in women than men in Polish sample, which was consistent with Szurkowska et al's research, but not with the other two publications from Poland.[23;24;80] In Russian sample, a more than 15% higher prevalence in women than in men was found and this was also supported by previous publications.[21;22]

Previous studies have consistently shown that lower education level is associated with higher risk of having metabolic syndrome in Western countries, and this was supported by the results found in this thesis.[118;125;126]

In the Czech and Russian samples in the thesis, being a non-smoker or having higher physical activity was associated with lower risk of metabolic syndrome, and this was consistent with existing literature.[27;113;137;139-141;143;144] However, in the Polish sample, a higher physical activity was associated with slightly higher prevalence of metabolic syndrome, which was not consistent with the literature. This could be explained by misclassification of the physical activity measure used, and/or reverse causality.

6.3.2 HDI scores (objective 3)

To the author's knowledge, there is only one previous study which examined diet quality using HDI in these three countries, and the study used the same data as this thesis.[37] However, in this study, the HDI score was defined following Huijbregts' original suggestions which consisted of dietary components coded as dichotomous variables [203]. The findings from this thesis therefore build on this study by examining diet quality in greater detail (by examining HDI scores across different age groups, education levels, and other healthy behaviours).

Most previous studies have used the original dichotomous HDI scores, making it difficult to make valid comparison with the results in this thesis. A recent published paper by Jankovic et al (2014) however used a similar continuous version of HDI [289], in a sample of older women in a few European countries and the U.S. The median total HDI score ranged from 42 to 54 in studied countries, which was similar to the findings in the thesis (ie, Czech sample: 46 in men and 49 in women; Russian sample: 43 in men and 44 in women; Polish sample: 41 in men and 43 in women). While the HAPIEE study was included in this paper, it used a sub-sample of older women from three study countries. The median scores in women aged ≥60 years were 48 in the Czech Republic, 42 in both Russia and Poland. This shows the score among Czechs had little difference compared with other countries, but the scores in Russians and Poles were lower.

The studies that used dichotomous scores for HDI components are not perfectly compared with this thesis but they represent valuable source of information about dietary status in different populations. Huijbregts and colleagues found the overall HDI average score was the highest in Italy with values around 4 in different regions, followed by score of 2.5 in the Netherlands, and 1.8 in Finland (scoring range 0-9) [211].

Knoops and colleagues using the SENECA and FINE(Finland, Italy, The Netherlands, Elderly study) data showed that average HDI score in Europe was relatively low with range between 2 and 4 (scoring range 0-9) [208]. Murray et al found the average HDI score was 3.3 in a small sample of non-diabetic Irish participants (scoring range 0-9).[217] Cade et al also found diet quality in the British cohort of women was similar to other European countries, with 55.1% of women having HDI score lower than 5 (ranges from 0-10) [213]. In Asian countries, the diet quality seemed healthier than in the Western Europe; for example, Kim et al found that the average HDI was 5 (with a range from 0-9) among Koreans [216]. Because the number of HDI components was usually different in above reported studies compared to the current data in this thesis, and the scoring systems were different, it is important to be cautious when making comparisons using the HDI total score. Instead, it is necessary to compare the individual components score in these studies compared to the findings in the thesis.

In the current study, participants had better adherence to recommended intake in polyunsaturated fatty acids (median: 10.0 in Czech and Russian men and women; 8.4 in Polish men and 8.1 in Polish women), fruit and vegetables (10.0 in Czech and Polish men and women; 8.3 in Russian men and 9.4 in Russian women), and fibre intake (7.7 in Czech men and 8.8 in Czech women; 8.6 in Russian men and 8.4 in Russian women; 10.0 in Polish men and women), relatively good adherence to recommended intake in protein intake (6.7 in Czech men and 7.5 in Czech women; 7.3 in Russian men and 7.7 in Russian women; 6.6 in Polish men and 6.9 in Polish women), but had worse adherence to recommended intake in saturated fatty acids (2.5 in Czech men and 3.5 in Czech women; 0.7 in Russian men and 1.7 in Russian women; 0.1 in Polish men and 1.3 in Polish women) and sugar intake (4.6 in Czech men and 2.6 in Czech women; 6.2 in Russian men and 5.1 in Russian women; 4.5 in Polish men and 2.9 in Polish women). In terms of the cholesterol intake, Czechs had better compliance to the recommended intake than Russian and Poles (10.0 in Czech men and women; 0 in Russian men and 3.0 in Russian women; 1.6 in Polish men and 7.0 in Polish women).

These results support some findings from previous research in some studies but not all. Huijbregts found that people aged between 50-70 years also had good compliance in polyunsaturated fatty acids and protein intake but bad compliance in saturated fatty acids, sugar, and cholesterol in the Netherlands, Finland, and Italy, however, all three countries showed a low fruit and vegetable intake compared to the WHO recommendation.[203] In contrast to Huijbregts et al's findings, Leite et al had found that

Italians had good compliance to fruit and vegetable intake among people over 65 years old from rural towns, and this was consistent with the findings in this thesis.[254] Furthermore, the results were supported by Knoops and colleagues from the Healthy Ageing: a Longitudinal study in Europe (HALE).[208] In Britain, Cade et al found all participants in the British cohort of women had the fruits and vegetable intake above 400g/day.[213] In South Korea, Kim et al found considering all the components, the greatest compliance in recommended intake for polyunsaturated fatty acids was found, but also in contrast to western populations described by Huijbregts, Koreans also had better compliance for sugar intake.[216]

Compliance with WHO recommendations varied between regions, and sometimes differed within a country in different studies. This could be due to the demographic difference of the samples, for example, depending whether rural or urban area were included, what age range of participants was included, and in which year data were collected. However, it is possible to say the results in this thesis showed findings that generally agreed with majority of previous studies in Europe or even in Asia.

6.3.3   HDI and metabolic syndrome and its components (objective 4, 5, 6 & 7)

The weak and inconsistent association between HDI and metabolic syndrome found in the thesis was consistent with a study conducted in Luxembourg in 2012, which to the author's knowledge is the only study that investigated the association between HDI and metabolic syndrome.[224] The study was based on the data from ORISCAV-LUX national survey in Luxembourg, and used 1349 men and women aged 18-69 in analyses.

Several components of HDI were found to have a protective association with metabolic syndrome or its components in this thesis. The most consistent finding in three study samples was that higher protein score was associated with lower risk of having high blood glucose; furthermore, in Poland, the moderate intake of protein was also associated with lower risk of central obesity and metabolic syndrome. The protective association between moderate protein intake and metabolic syndrome was also found in the Luxembourg study, and was also the only component found to be associated with lower metabolic syndrome risk in the study.[224] Dietary protein includes several food items, such as red meat, white meat, and dairy. A high intake of red meat in particular has long been discussed as being a potential risk to health.[329;330] For example, studies have shown that increased intake of red and process meat was associated with higher risk of metabolic syndrome (among women)[39] and among

those with a high risk of developing future cardiovascular diseases.[40] Two large studies also investigated protein intake in relation to cardiovascular disease mortality. A recent study in the U.S using two large cohort studies and found that high red meat consumption was associated with increased cancer, cardiovascular, and total mortality.[331] Recently, the EPIC study (UK) showed that high processed meat consumption (but not unprocessed red meat) was associated with increased risk of cardiovascular disease mortality.[332] In this thesis, protein intake was associated with metabolic syndrome risk in one country only (Poland), but was associated with having high blood glucose in all three countries. However, total protein intake comes from multiple sources (eg, red meat, white meat, seafood, plant sources, or dairy products) which may have different effects on health and may differ by country. Therefore, the association between protein intake and metabolic syndrome requires in-depth investigation of the specific types of protein.

There are some established underlying biological mechanisms which may explain the relationship between protein intake and blood glucose level. Protein is thought to have a minimal effect on glucose level, but this is only among people who have normal insulin function.[333] However, among people with the insulin deficiency, gluconeogenesis (the conversion of protein to glucose) is much faster than in the normal population, which in turn would result an elevated glucose level. This could explain the association between better adherence to recommended protein intake (ie, moderate rather than low or high intake) and higher blood glucose level in this study.

Better adherence to recommended saturated fatty acid intake was associated with lower risk of having central obesity in Poland. This association is consistent with that of another observational study in the Iran[225] and could be explained by the effects of saturated fatty acids on plasma cholesterol levels, which may result in the development of metabolic syndrome and its components.[181] However, this finding was only observed in the Polish sample, and not in the Russian or the Czech samples, suggesting that this may have been a chance finding. Better adherence to recommended saturated fatty acid intake was also associated with higher risk of having high glucose level in the Czech and Polish sample, and higher risk of having high triglycerides in the Polish sample; the findings were in line those from another observational study by Alkerwi's paper.[224] This found that higher adherence to recommended saturated fatty acids intake was associated with higher risk of metabolic syndrome. Another consistent finding in the thesis is that higher sugar score was associated with higher risk of having high blood glucose in all study samples.

This is also consistent with the findings by Alkerwi: participants with better adherence to recommended sugar intake had higher risk of metabolic syndrome.[224] This at least in part is likely to be explained by the effects of glucose intake on plasma glucose level. This may also in part be due to limitations of the cross-sectional design (whereby those with metabolic syndrome improve their diet following medical advice) (see Section 6.2.7).

A large number of studies have found that high fruit and vegetable intake is associated with lower risk of metabolic syndrome.[42;45;46] However, in the thesis, contrary to expectation, better adherence to recommended fruits and vegetable intake was associated with higher risk of high glucose level and not with metabolic syndrome. This may be explained by the high sugar content of fruit, and/or due to those with impaired glucose metabolism increasing their fruit consumption following medical advice. The later may in part explain the lack of association found with metabolic syndrome. Compared to the existing studies, the sample used in the thesis was substantially larger (5060 in the Czech Republic, 8788 in Russia, and 7671 in Poland), suggesting that the study had sufficient power to detect any existing associations. Comparisons with these studies are difficult due to the different cut-points for fruit and vegetable intake used across the studies.

Similarly, higher adherence to recommended cholesterol intake (ie, lower intake) was associated with higher risk of metabolic syndrome and high blood glucose level in the thesis. Interestingly, Alkerwi et al did not found any associations between cholesterol and metabolic syndrome in their paper.[224] The finding may again be explained by reverse causality.

6.4 Recommendations for future research

Although the analysis of this thesis included large sample from three countries where such analysis has not been done before, there are still many recommendations for future studies.

Because the present study was cross-sectional, and therefore unable to determine the temporal relationship between HDI and metabolic syndromes,[311] future prospective analyses are required. Moreover, repeated dietary measures in longitudinal studies are also recommended to better measure diet and therefore its importance for metabolic health. In addition, since food availability and intake differs

according to season, repeated dietary measures may measure diet across multiple different seasons.

Second, the validation of the FFQ should be further investigated, and its content modified in order to improve its validity in different contexts. For example, validation studies could focus on each food intake in relation to biological measures in different countries separately. One reason is that in the FFQ, even a subtle change of the question could affect the performance of the questionnaire and further affect the results found in association studies.[334] Food consumption may also differ within countries by region, suggesting that FFQs may need to be tailored to account for regional differences.

Third, some unmeasured factors may be important in the relation to diet quality and metabolic syndrome, such as, dieting status. Furthermore, social network and support could be important in determinant diet intake. For example, high frequencies of attending social activities was associated with high carotenoid level in older women;[335] and lack of transportation was associated with higher risk of nutritional risk.[336]

HDI in its current form may not be a sufficient measure of diet quality to predict metabolic syndrome. In the future study, adapting HDI to the local context in the Eastern European countries, or developing a well-weighted scoring system for HDI, would be useful to see if the adjusted HDI would be associated with metabolic syndrome. Further studies could also investigate different diet quality scores which could relate more strongly to metabolic syndrome, such as the Mediterranean diet and diet quality index.

Apart from the unmeasured factors, more precise measures of potential confounding variables should also be included in future studies. For example, objective measures on physical activity rather than self-reported physical activity level may better assess both physical activity level and cardiorespiratory fitness.[45] This is important to measure in order to examine the independent effect of diet on metabolic syndrome risk.

Additionally, the prevalence of having a high blood pressure was found especially high in the study population, this may due to high salt intake.[337-339] However, salt intake was not measured precisely and is very challenging to measure precisely; for example, table and cooking salt are part of many meals, and difficult to distinguish when recalling diet intake. Future studies, with comprehensive measurements of salt

intake could further investigate if salt is the main explanation of the high prevalence of hypertension in this region.

Finally, after using improved measures of both diet and confounding factors, modelling the risk factors together could be useful to examine the relative and independent importance of diet for metabolic syndrome. This may in turn help further explain the cardiovascular disease mortality gap between Eastern and Western Europe.

6.5   Public health implications

Previous studies have suggested that cardiovascular disease prevalence and mortality is high in Eastern Europe. Metabolic syndrome is thought to be an important risk factor for cardiovascular disease,[100] and was found to be highly prevalent in the countries investigated in this thesis. This supports suggestions that tackling metabolic syndrome could reduce cardiovascular disease risk in Eastern Europe.

This thesis also found that the dietary quality was in general moderate to poor in the countries investigated, especially a high intake of saturated fatty acids and cholesterol. Regardless of the relation between HDI and metabolic syndrome, improving diet in the region is likely to have multiple health benefits. Results also suggested that people with better nutrition knowledge had a healthier diet compared with their counterparts. These results indicate that improving the public understanding of diet could be one of the means in improving the population diet intake.

Previous research (including both observational and intervention studies) has suggested that diet is a very important factor for tackling metabolic disorders.[247;340;341] However, results from this thesis did not find strong evidence that a healthy diet (as determined by HDI) is associated with lower risk of metabolic syndrome. However, a number of plausible methodological issues may explain these null findings (see section 6.2).

Despite limited evidence for an association between HDI and metabolic syndrome, some findings have been identified may have potential public health implications. For example, a moderate protein intake was associated with lower risk of having metabolic syndrome and high blood glucose level. This suggests that better adherence to intake of protein may have health benefits in this region.

There are a number of potential means of improving diet quality in the population. Government and related institutions may act to improve nutritional knowledge in the community. Food consumption is also affected by its price and taxation, which also can be targeted to improve the population diet intake. Legislation and incentivisation may also be used such that unhealthy nutrients are reduced during production. For example, reduce salt and fat content in the package food from production. Finally, screening tests for metabolic health may also have a role in order to target those with metabolic disorders for intervention.

Chapter 7 Conclusion

This thesis aimed to estimate the prevalence of metabolic syndrome and investigate the association between dietary quality and risk of metabolic syndrome and its components in three Eastern European countries: the Czech Republic, Russia, and Poland. The findings showed that metabolic syndrome and its components were highly prevalent in each country. HDI was moderate to poor, suggesting room for improvement. Healthy dietary quality (assessed by HDI) was not consistently associated with metabolic syndrome or its components although some findings, such as a moderate protein intake related to lower risk of high blood glucose, suggest potential importance of healthy diet for maintaining metabolic health.

The findings suggest that preventing metabolic syndrome should be a target of public health intervention in Central and Eastern Europe, which in turn would likely contribute to the prevention of cardiovascular disease in this region. Although HDI was not consistently associated with lower risk of metabolic syndrome, there are likely to be a wide range of health benefits of improving diet quality in this region.

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Appendices

Date of questionnaire filled

Day	Month	Year

Health and Life Style

Dietary questionnaire

Name: .... Surname: ....

Study ID

Interviewer code

1. We would like to ask you to estimate your average food use. Please cross the appropriate square in each row of the tables below a number indicating how often, on average, you have eaten the specified amount during the last 3 months.

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Bread and cereals										
White bread, rolls	Medium slice, 1 roll	1	2	3	4	5	6	7	8	9
Dark bread, rolls	Medium slice, 1 roll	1	2	3	4	5	6	7	8	9
Cereals	Medium bowl	1	2	3	4	5	6	7	8	9
Potatoes, rice, pasta, dumplings										
Potatoes boiled or mashed	Medium serving (about 100 g)	1	2	3	4	5	6	7	8	9
Potatoes fried (chips) or roasted	Medium serving (about 100 g)	1	2	3	4	5	6	7	8	9
Rice	Medium serving (about 100 g)	1	2	3	4	5	6	7	8	9
Pasta (spaghetti, noodles)	Medium serving (about 100 g)	1	2	3	4	5	6	7	8	9
Pizza	Medium slice	1	2	3	4	5	6	7	8	9
Roll-dumplings	4 slices	1	2	3	4	5	6	7	8	9
Potato-dumplings(CZ,RU)	4 slices	1	2	3	4	5	6	7	8	9
Groats	Medium serving	1	2	3	4	5	6	7	8	9
Pirog with meat (RU)	4 slices	1	2	3	4	5	6	7	8	9
Pirog with vegetables (RU)	4 slices	1	2	3	4	5	6	7	8	9
Sweet pirog (RU)	4 slices	1	2	3	4	5	6	7	8	9
Dairy products and fats										
Cream, sour cream	50 ml	1	2	3	4	5	6	7	8	9
White yoghurt	1 carton (100-150 ml)	1	2	3	4	5	6	7	8	9
Fruit yoghurt	1 carton (100-150ml)	1	2	3	4	5	6	7	8	9
Milk desserts	1 carton (100-150 ml)	1	2	3	4	5	6	7	8	9
Soft cottage cheese	Medium serving (about 30 g)	1	2	3	4	5	6	7	8	9
Hard cottage cheese	Medium serving (about 30 g)	1	2	3	4	5	6	7	8	9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Low fat soft cheese (CZ,PL)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
High fat soft cheese	Medium serving (about 30g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Hard cheese, processed cheese (CZ, PL)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Hard semi fat cottage cheese (PL)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Hard full fat cottage cheese (PL)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Low fat cottage cheese (RU)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
High fat cottage cheese (RU)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Low/med fat-not hard cheese like feta cheese (Brindza) (RU)	Medium serving (about 30 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Eggs	1 egg	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Margarine (on bread)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Margarine (in food)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Butter (on bread)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Butter (in food)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Mixture of margarine and butter (on bread) (PL)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Mixture of margarine and butter (in food) (PL)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Vegetable oil	1 tablespoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Lard (on bread)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Lard (in food)	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Mayonnaise	1 tablespoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Light mayonnaise (PL)	1 tablespoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Soups, sauces and spreads										
Borsch, shiee, vegetable soup	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Bouillon	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Beetroot soup, white borsch (PL)	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Cabbage soup (PL)	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Bigo (PL)	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Tripe soup (PL)	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Goulash soup (PL)	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Other soups	Medium serving (about 250 ml)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Ketchup	1 tablespoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sauces with meat, pasta, groats (such as gravy or white sauces)	Medium serving	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Marmalade, jam, honey	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sweets and snacks										
Biscuits	1 medium	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Cakes, pies (sweet)	medium slice	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Buns, pastries, doughnuts, muffins	1 piece	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sweets	1 bonbon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Chocolate	1 bar	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Chocolate (pieces), chocolate bars (e.g. Mars) (PL)	1 piece	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Ice cream	one scoop	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Milk pudding	medium serving	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sweet rice	medium serving	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Pancakes	1 pancake	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sweet (fruit) dumplings	4 pieces	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Crisps, crackers and other packet-snacks	1 small packet (25 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Peanuts and other nuts	1 small packet (50 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sugar into coffee, tea	1 teaspoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Sweetener into coffee, tea	1 capsule, 1 tablet	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Drinks										
Milk	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Cocoa (RU,PL)	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Fruit juice	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Fizzy drinks (lemonade, coke, fanta)	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Diet/low calorie fizzy drinks	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Squash	one tablespoon	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Unsweentened mineral water (CZ)	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Tap water, bottle non-mineral water (CZ)	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Coffee	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Tea	2 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Wine	1 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Beer	0.25 l	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Port, sherry, vermouth	1 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Liqueurs	0.5 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Spirits	0.25 dl	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Meat and fish										
Beef : roast, steak, mince, stew or casserole	Medium serving (about 100 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Lamb: roast, chops or stew	Medium serving (about 100 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Pork: roast, chops or stew	Medium serving (about 100 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Poultry	Medium serving (about 100 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9
Rabbit	Medium serving (about 100 g)	☐1	☐2	☐3	☐4	☐5	☐6	☐7	☐8	☐9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Offals (heart, kidney, liver)	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Soft sausages	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Hard sausages	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Soft salami	50 g	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Hard salami (CZ,RU)	50 g	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Ham	about 50 g	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Bacon	2 slices	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Lard from bacon (RU)	2 slices	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Pate	50 g	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Meat pie	Medium serving	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Luncheon meat (CZ,PL)	50 g	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Canned meat	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Meat ravioli (RU)	Serving (10 pieces)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Polish meat dumplings (CZ, PL)	4 pieces	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Fish – fresh, frozen or canned (not in oil)										
Fresh water fish (e.g. carp, pike)	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Salt water white fish (e.g. cod of haddock)	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Oily fish (e.g. mackerel, tuna, salmon, sardines, herring, kippers)	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Other fish										
Fish canned in oil	Medium serving (about 100 g)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9
Fish fingers, fish Afilé (RU,PL)	Medium serving	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7	☐ 8	☐ 9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
	(about 100 g)									
Salted fish (RU,PL)	25 g	□1	□2	□3	□4	□5	□6	□7	□8	□9
Crab, prawns, mussels (sea food)	Medium serving	□1	□2	□3	□4	□5	□6	□7	□8	□9
Fresh fruit										
Apples	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Pears	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Oranges	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Grapefruit	½ medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Mandarins	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Lemons	½ medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Peaches	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Apricots	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Plums	about 100 g	□1	□2	□3	□4	□5	□6	□7	□8	□9
Cherries	about 100 g	□1	□2	□3	□4	□5	□6	□7	□8	□9
Strawberries	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Raspberries	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Red currant	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Black currant	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Blueberries	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Gooseberry	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Kiwi	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Melon	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Pineapple (CZ,RU)	Medium serving	□1	□2	□3	□4	□5	□6	□7	□8	□9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Bananas	(about 100 g) 1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Grapes	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Tinned or bottled fruit	medium serving (about 100g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Dried fruit (e.g. raisins, apricots, apples)	medium serving (about 50g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Vegetables										
Green salad (lettuce)	Medium serving	□1	□2	□3	□4	□5	□6	□7	□8	□9
Spinach	Medium serving	□1	□2	□3	□4	□5	□6	□7	□8	□9
Brussels sprouts (RU,PL)	5 sprouts	□1	□2	□3	□4	□5	□6	□7	□8	□9
Parsley, dill (RU)	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9
Cabbage	Medium serving	□1	□2	□3	□4	□5	□6	□7	□8	□9
Beans	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Lentils	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Dried peas	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Green beans	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Green peas (CZ,RU)	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Turnips, swedes, parsnips (CZ,PL)	Medium serving (about 100 g)	□1	□2	□3	□4	□5	□6	□7	□8	□9
Radish	4 radishes	□1	□2	□3	□4	□5	□6	□7	□8	□9
Celeriac	50 g	□1	□2	□3	□4	□5	□6	□7	□8	□9
Parsley	1 medium	□1	□2	□3	□4	□5	□6	□7	□8	□9

	Amount	6+ per day	4-5 per day	2-3 per day	1 per day	5-6 per week	2-4 per week	1 per week	1-3 per month	Never or less than 1 per month
Cauliflower	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Broccoli	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Carrots	1 medium	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Onion	½ medium	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Leeks	½ medium	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Garlic	1 clove	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Peppers	1 medium	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Tomatoes	1 medium	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Cucumbers	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Aubergine	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Courgette/marrow	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Corn	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Beet-root cooked Russian salad (RU,PL)	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Sauerkraut	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Pickled vegetables, gherkins	Medium serving (about 50 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Mushrooms	Medium serving	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Soya meat	Medium serving (about 100g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9
Mixed frozen vegetables	Medium serving (about 100 g)	□ 1	□ 2	□ 3	□ 4	□ 5	□ 6	□ 7	□ 8	□ 9

2. Are the foods and drinks listed in the previous table representative of the foods and drinks that you consumed in the last 3 months?

     1.   Yes
     2.   No

3. Are there any other foods, which you ate more than once a week?

     1.   Yes
     2.   No

4. **If yes**, please list below

Food name	Usual serving size	Number of times eaten each week

5. What type of milk did you most often use?

     1.   Full cream (3% of fat and more)
     2.   Semi- skimmed (2% of fat)
     3.   Skimmed (about 0.5% of fat)
     4.   Soya milk
     5.   Cream into coffee, tea
     6.   I do not use milk
     7.   I do not know

6. How much milk do you drink each day, including milk with tea, coffee, cereals etc.?

     1.   None
     2.   Less than 250 ml
     3.   More than 250, less than 500 ml
     4.   More than 500 ml, less than 1000 ml
     5.   More than 1000 ml