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Metabolic syndrome, obesity and ethnicity—The SAMINOR Study

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“Labels are intellectually lazy ways that people assert they know you without knowing you”

- Neil deGrasse Tyson

Abstract

Background: Clustering of certain cardiometabolic risk factors is widely known as metabolic syndrome (MetS). MetS is associated with an unhealthy lifestyle and the prevalence is increasing alongside the obesity epidemic, making it an important public health issue. Both MetS and obesity are common in the adult population in rural Northern Norway, which comprises an ethnically mixed population. MetS is defined using ethnicity-specific cut-offs for waist circumference, but there is much uncertainty with respect to obesity and ethnicity.

Methods: Using various regression models we analysed data from the SAMINOR Study, comprising SAMINOR 1 (2003–2004) and SAMINOR 2 (2012–2014). We examined the change in prevalence of MetS between these two time points by sex and Sami/non-Sami ethnicity, and estimated the mortality of MetS, obesity-metabolic phenotypes, and continuous obesity measures. Next, we modelled the ethnic-specific relationships between metabolic markers and obesity measures. Finally, we examined the correlation between body mass index (BMI) and height, estimated a sample-specific height-corrected weight index and compared it in Sami and non-Sami.

Results: The prevalence of MetS increased over time and was present in more than one third of the population in 2012–2014. The increase differed by sex, but not ethnicity. MetS was associated with a 50% increased cardiovascular disease (CVD) mortality. In men, metabolically healthy obesity was associated with a three-fold increase in CVD mortality compared to metabolically healthy non-obesity. The association was linear and positive for all obesity measures regardless of metabolic health status in men. However, there were only weak associations between metabolically healthy obesity and mortality in women. We found no evidence of ethnic-specific relationships between obesity measures and metabolic markers. Because height differs in Sami and non-Sami, BMI comparisons are biased.

Conclusion: Cardiometabolic health is deteriorating in rural Northern Norway. This development is not influenced by ethnicity. Previous findings of ethnic differences in obesity may be invalid.

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Abbreviations

ABSI	A body shape index
ATC	Anatomical Therapeutic Chemical Classification System
ATP-III	Adult Treatment Panel III
BMI	Body mass index
CHD	Coronary heart disease
CI	Confidence interval
CVD	Cardiovascular disease
DAG	Directed acyclic graph
FFA	Free fatty acids
GEE	Generalised estimating equations
HDL	High-density lipoprotein
HR	Hazard ratio
IDF	International Diabetes Federation
MAR	Missing at random
MCAR	Missing completely at random
MetS	Metabolic syndrome
MHAO	Metabolically healthy abdominal obesity

MHNAO	Metabolically healthy non-abdominal obesity
MHNO	Metabolically healthy non-obesity
MHO	Metabolically healthy obesity
MUAO	Metabolically unhealthy abdominal obesity
MUNAO	Metabolically unhealthy non-abdominal obesity
MUNO	Metabolically unhealthy non-obesity
MUO	Metabolically unhealthy obesity
NMAR	Not missing at random
SAMINOR	The Population-based Study on Health and Living Conditions in Regions with Sami and Norwegian Populations
SD	Standard deviation
T2DM	Type 2 diabetes mellitus
WC	Waist circumference
WHO	World Health Organization
WHtR	Waist-to-height ratio

Brief definitions

Abdominal obesity	Waist circumference ≥80/88 cm in women and ≥94/102 cm men
Cardiometabolic disease	Diseases of the cardiovascular or endocrine system linked to metabolic syndrome, most common e.g. atherosclerotic heart disease and type 2 diabetes mellitus
Ethnicity	A population group defined from sharing certain sociocultural characteristics
General obesity	Body mass index ≥30 kg/m^2
Glucose	A simple sugar, circulating in the blood as an essential source of energy
HDL cholesterol	Cholesterol that is carried by high-density lipoprotein, often referred to as “the good cholesterol”
Hypertension	Elevated systolic and/or diastolic blood pressure
Metabolic syndrome	Clustering of certain risk factors for cardiometabolic disease
Obesity measures	Clinical measurements of body fatness, often crude proxy measures, such as body mass index, waist circumference, a body shape index, and waist-to-height-ratio
Triglycerides	An ester of glycerol and three fatty acids; the major constituent of body fat

List of papers

The following papers, ordered and referred to by Roman numerals, are included in this thesis:

I. Michalsen VL, Kvaløy K, Svartberg J, Siri SRA, Melhus M, Broderstad AR. Change in prevalence and severity of metabolic syndrome in the Sami and non-Sami population in rural Northern Norway using a repeated cross-sectional population-based study design: the SAMINOR Study. BMJ Open. 2019; 9(6):e027791.

II. Michalsen VL, Wild SH, Kvaløy K, Svartberg J, Melhus M, Broderstad AR. Obesity measures, metabolic health and their association with 15-year all-cause and cardiovascular mortality in the SAMINOR 1 Survey: a population-based cohort study. Submitted to BMC Cardiovascular Disorders.

III. Michalsen VL, Braaten T, Kvaløy K, Melhus M, Broderstad AR. Relationships between metabolic markers and obesity measures in two populations that differ in stature—The SAMINOR Study. Obes Sci Pract. 2020; 6:324–39.

IV. Michalsen VL, Coucheron DA, Kvaløy K, Melhus M. Sex-specific height-correction of weight in a population with ethnic groups that differ in stature—the SAMINOR 1 Survey: a cross-sectional study. Manuscript ready for submission to a journal.

1 Introduction

The medical literature has long suggested that type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD) originate from a "common soil", meaning that they have overlapping distal causes (1). During the last 30 years, the incidence and mortality of CVD have decreased alongside a decrease in traditional risk factors such as smoking, hypertension and cholesterol (2). However, the prevalence of obesity and T2DM, two known risk factors of CVD, have increased (2–4). Between 1980 and 2010 the mortality burden of these two conditions almost doubled (5). The pathological impact of obesity and T2DM on CVD takes many years to develop, and some worry has been expressed regarding future CVD trends (6).

The clinical overlap between obesity, T2DM and CVD is often referred to as "cardiometabolic disease". It demands specialist knowledge in endocrinology and cardiology, and in some cases also nephrology, hepatology and gynaecology, explaining why a new medical subspecialty of "cardiometabolic medicine" has been proposed (7). The antecedent of cardiometabolic disease is believed to be a cluster of risk factors known as metabolic syndrome (MetS) (8). Hence, to prevent further escalating development of cardiometabolic disease, updated data on population prevalence of MetS, development and risks are important for public health.

This thesis examines the epidemiology and mortality regarding MetS and obesity in rural Northern Norway, a region comprising a mixed-ethnic population. Therefore, two core variables—MetS and ethnicity—a biological condition and a sociocultural concept, respectively, are emphasised. The scientific validity of both MetS and ethnicity is controversial and hence will be introduced thoroughly, ensuring a theoretical understanding necessary for critical evaluation of the findings and implications of this thesis.

1.1 Metabolic syndrome

The sedentary, calorie-rich life in modern societies has given rise to a phenotype: MetS. It is not a disease, but a premorbid condition. MetS is associated with a more than 5-fold increased

risk of T2DM (9) and a doubled risk of CVD (9,10). Other conditions linked to MetS include some cancers, polycystic ovary syndrome, non-alcoholic fatty liver disease, and sleep apnoea (8). By definition, MetS comprises the following five risk factors, or components: elevated triglycerides, reduced high-density lipoprotein (HDL) cholesterol, elevated fasting glucose, elevated systolic or diastolic blood pressure, and increased waist circumference (WC) (11). No unifying understanding of the pathophysiology of MetS exists, but research suggests that dysfunctional adipose tissue and insulin resistance are core factors (8). There is much controversy and confusion around MetS. Therefore, in this first chapter, I start with a thorough introduction.

1.1.1 History

In the last century, clinicians and researchers have observed that certain biochemical and clinical risk factors for CVD coexist in individuals. This has given rise to many similar-sounding syndromes, such as the hypertension-hyperglycaemia-hyperuricaemia syndrome, metabolic trisyndrome, plurimetabolic syndrome and the syndrome of affluence, among others (12). In 1923, Kylin described a syndrome of hypertension, hyperglycaemia, and hyperuricemia (13). In 1956, Vague made observations of two distinct phenotypes of obesity, the android and gyneoid (i.e., “apple” and “pear” shapes), linking the former to T2DM and heart disease (14). In 1967, Avogaro described an association between hyperlipidaemia, T2DM and obesity in six patients (15). In 1981, the term ‘das metabolisches Syndrome’ was first used in a German medical journal (16). In 1989, Kaplan described ‘The Deadly Quartet’ as the co-occurrence of abdominal obesity, dyslipidaemia, hypertension and impaired glucose tolerance (17). A report even exists as far back as 1641 on a carbohydrate-induced hypertriglyceridemia syndrome, or Tulp syndrome, named after the Dutch doctor who described it (18). However, Gerald Reaven’s seminal 1988-paper—“Role of insulin resistance in human disease” —is viewed as the first etiological recognition of the condition (19). A few years later, Stern proposed the “common soil” hypothesis, suggesting that CVD and T2DM arise from a common antecedent, namely MetS (1).

1.1.2 Definition

All proposed definitions of MetS are consensus definitions from various expert groups. Table 1 provides a summary of the definitions including the detailed criteria. The World Health Organization's (WHO) 1998-definition required a hyperinsulinemic euglycaemic clamp technique for determining insulin resistance (20). The European Group for the Study of Insulin Resistance (EGIR) suggested WC as a measure of central obesity, and fasting insulin for determining hyperinsulinemia/insulin resistance (21). Both these definitions have been termed "glucocentric" because they required the presence of insulin resistance (22). A few years later, two new "obesogenic" definitions were published. In 2001, the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (NCEP-ATP-III, often referred to as ATP-III) suggested that abdominal obesity should replace direct measures of insulin, and no components were required to fulfil the criteria for MetS (23). In 2005, the International Diabetes Federation (IDF) suggested that abdominal obesity, defined by ethnic-specific cut-offs, should be an obligatory component (22). The same year, the American Health Association and National Heart, Lung, and Blood Institute modified the 2001 ATP-III criteria with minor alterations in the cut-offs for glucose (24). Finally, in 2009, the International Diabetes Federation Task Force on Epidemiology and the Prevention, National Heart, Lung, and Blood Institute, the American Heart Association, the World Heart Federation, the International Atherosclerosis Society, and the International Association for the Study of Obesity joined forces and published a "harmonised" definition of MetS to be used in research. This definition was a further adoption of the original ATP-III criteria and included ethnic-specific cut-offs in the abdominal obesity criteria (11).

Some researchers suggest diagnosing MetS using fewer biomarkers. For instance, the triglycerides/HDL cholesterol ratio is associated with insulin resistance (25–27), future T2DM (28) and CVD (27). The hypertriglyceridemic waist, defined as having both abdominal obesity and hypertriglyceridemia, is a simple marker of visceral obesity associated with MetS and future CVD (29). Conversely, some suggest adding biomarkers to the definition, such as high low-density lipoprotein cholesterol, hyperuricemia, fatty liver and high sensitivity C-reactive protein (30,31).

Table 1. Definitions of metabolic syndrome.

WHO (1998)	EGIR (1999)	ATP-III (2001)	IDF (2005)	Modified ATP-III (2005)	Harmonised ATP-III (2009)
Glucose intolerance, IGT, DM and/or insulin resistance, plus ≥2 of the following:	Insulin resistance or fasting hyperinsulinaemia, plus ≥2 of the following:	≥3 of the following:	Central obesity (as measured by WC, with ethnic-specific cut-offs), plus ≥2 of the following:	≥3 of the following:	≥3 of the following:
Central obesity: WHR >0.90 men and >0.85 women, and/or BMI >30 kg/m^2	Central obesity: WC >94 cm in men and >80 cm in women	Abdominal obesity: WC >102 cm in men, >88 cm in women		Abdominal obesity: WC >102 cm in men, >88 cm in women	Abdominal obesity: Population- and country-specific definitions
TG ≥1.70 mmol/L and/or low HDL-C <0.9 mmol/L men, <1.0 mmol/L women	TG >2.0 mmol/l or HDL cholesterol <1.0 mmol/l or on treatment	TG ≥1.70 mmol/L	TG ≥1.70 mmol/L or on specific treatment	TG ≥1.70 mmol/L, or on specific treatment	TG ≥1.70 mmol/L, or on specific treatment
Insulin resistance		HDL-C <1.0 mmol/L in men, <1.30 mmol/L in women	HDL-C <1.03 mmol/L in men, <1.29 mmol/L in women or on specific treatment	HDL-C <1.0 mmol/L in men, <1.30 mmol/L in women, or om specific treatment	HDL-C <1.0 mmol/L in men, <1.30 mmol/L in women, or om specific treatment
Arterial BP ≥160/90 mmHg	Arterial BP >140/90 mmHg or on treatment	Systolic BP ≥130 or diastolic BP ≥85 mmHg	3. Systolic BP ≥130 or diastolic BP ≥85 mmHg or on specific treatment	Systolic BP ≥130 or diastolic BP ≥85 mmHg, or on specific treatment	Systolic BP ≥130 or diastolic BP ≥85 mmHg, or on specific treatment
Impaired glucose regulation or DM	FPG >6.1 mmol/l, but nondiabetic	FPG ≥ 6.1 mmol/L	FPG ≥5.6 mmol/L or DM	FPG ≥5.6 mmol/L or on specific treatment	FPG ≥5.6 mmol/L or on specific treatment
Microalbuminuria					

WHO = World Health Organization, EGIR = European Group for the Study of Insulin Resistance, IDF = International Diabetes Federation, ATP-III = Adult Treatment Panel III, BP = blood pressure, FPG = fasting plasma glucose, DM = diabetes mellitus, TG = triglycerides, HDL = high density lipoprotein cholesterol, WC = waist circumference, WHR = waist-to-hip ratio, BMI = body mass index.

1.1.3 Epidemiology

Worldwide, studies have estimated the prevalence of MetS in the adult population ranging from 12% to 49%, and typically around 25–30% (32–36). Repeated national cohorts in the US, China and South Korea show consistent trends of an increasing prevalence of MetS (33–35). Based on data from 2011–2016, the overall prevalence in the US seemed to plateau around 35% with a particularly high prevalence increase among young adults (37). Abdominal obesity increased drastically in this age group (34–37).

Three demographic variables influence the prevalence of MetS: age, sex and ethnicity. MetS increases with age (38–40), but the age effect is stronger in women than in men. After the age of 50 years, women typically surpass men in having the highest prevalence (38–40). Regarding ethnicity and MetS, which will be introduced thoroughly later, literature suggests a higher prevalence of MetS in ethnic minorities compared to the majority population (39,41). Both population-level (sociocultural, governmental, and institutional differences) and individual level (biological and sociocultural differences) factors are suggested causes of ethnic differences in MetS (41)

In Norway, three large population-based cohorts cover Mid- and Northern Norway: The HUNT Study, the Tromsø Study, and the SAMINOR Study. In 1995–1997 in Mid-Norway, the HUNT Study showed a prevalence of MetS at 29.6% and 25.9% using the IDF- and ATP-III definition, respectively in adults aging 20–89 years (42). In 2006–2008, the ATP-III prevalence was 23.5% in the HUNT Study (43). The two HUNT studies used different cut-offs for the glucose component, making it challenging to compare figures. Estimates from the Tromsø Study, conducted in the largest city in Northern Norway, showed that the ATP-III prevalence was 14.1% in 1995–1996 in adults aging 25–98 years (44) and 22.5% in 2007–2008 in adults aging 30–87 years (45). However, the first study did not include the glucose component at all in the definition of MetS. The SAMINOR 1 Survey, conducted in rural areas of Northern (and parts of Mid-) Norway in 2003–2004 in adults aging 36–79 years, showed a prevalence of 25.7% according to the IDF-definition, with no ethnic differences (Sami vs non-Sami) (46).

1.1.4 Criticism

Metabolic risk factors coexist more often than by chance, and the clustering increase with increasing levels of obesity and/or insulin (47–49). Nevertheless, MetS as a diagnosis has been subject to much criticism from the scientific community (50–53), which may be summarised as follows: 1) there is loss of information in dichotomisation of risk factors; 2) the cut-offs are more or less arbitrary; 3) evidence of a single underlying mechanism is lacking; and 4) MetS does not seem to provide any predictive value of future disease occurrence beyond the sum of its components (50–53).

Dichotomisation of risk does not capture the dynamic and continuous relationship between risk and disease, and the cut-offs have varying strength of scientific evidence or are even arbitrary (50,51). Dichotomisation of continuous variables causes loss of information, reduction of statistical power, and may disturb the direction and magnitude of associations between outcome and predictor (54,55). Using the ATP-III definition (see Table 1 in Section 1.1.2), 16 different component combinations are possible, which all qualify for a diagnosis of MetS (50). Ultimately, this questions whether MetS represents a distinct entity (50). The proposed definitions probably fail to recognise the same phenotype, and they ignore individuals with ≤ 2 risk factors and individuals with levels just below the cut-offs (51).

Factor analysis examining a potential single underlying factor for MetS show conflicting results (31,56–58). Much debate has centred around the role of obesity vs insulin resistance (22,59–61). Reaven proposed that insulin resistance connected the single metabolic risk factors, but obesity was not included in MetS (at that point called Syndrome X) (19). Later, the association between high fasting insulin levels and metabolic risk was established in population studies (47,48). However, obesity increasingly gained attention as a central component (61–63). Reaven was, surprisingly, a major critic of MetS. His main objection was that MetS, defined in any way, did not attempt to explain the clustering, but rather function as a diagnostic tool for risk prediction—and in respect to this it underperformed (52). Undoubtedly, MetS is associated with a long-term increased *relative* risk of CVD, but several studies have shown that MetS is outperformed by other *absolute* risk calculators (for instance the Framingham Risk Score) (50–52,64–66). Further, studies show that MetS is no longer an

independent predictor of CVD or coronary heart disease (CHD) when controlling for its individual components (67,68). Hence, the current dichotomous definitions of MetS does not offer more information than "the sum of its individual components" (67,68).

Different aims warrant different definitions: physiologists want to explain the biological process; epidemiologists describe statistical associations; and clinicians aim for a definition that is both practical and useful for identifying the risk of future disease (22,69,70). In a philosophical and epistemological analysis of MetS, Federspil et al. state: "Thus, a syndrome that was initially formed on the basis of a causal definition was later identified on the basis of a descriptive definition and used for mainly clinical purposes" (70). All proposed MetS definitions are timely criticised for mixing underlying potential etiologic factors (obesity and insulin resistance/hyperinsulinemia) with secondary consequences (hypertension, dyslipidaemia and impaired glucose tolerance) (61).

1.1.5 Defence

Some argue that the lack of a single underlying aetiology is no problem, because the aetiology is multifactorial, as is the case of many lifestyle-related disorders (71). MetS is not registered as a disease in the International Statistical Classification of Diseases and Related Health Problems, 10th revision. However, MetS is useful as a clinical phenotype because it warns physicians and patients alike of a lifetime risk of both T2DM and CVD. Some argue that MetS has raised attention to the often over-looked, non-traditional CVD risk factors (71,72). Further, decades of research on MetS has turned the attention from the mere physical to the metabolic features following obesity (73).

In 2019, the Endocrine Society, comprising the American Diabetes Association and the European Society of Endocrinology, published a clinical guideline for what was called "elevated metabolic risk" (74). This was the first formal alteration to the definition of MetS since 2009. The expert collaboration explicitly discarded the term "metabolic syndrome". They aimed to raise attention to preventative identification of individuals with future risk of both CVD and T2DM, and not yet another attempt at defining a clinical entity. However, the definition of being at elevated metabolic risk was almost identical to the harmonised ATP-III

definition (with two exceptions: the cut-off for diastolic blood pressure was lowered from 85 to 80 mmHg, and the presence of T2DM was regarded as a separate entity). The Endocrine Society explicitly stated that the dichotomisation of continuous risk, the equal weighting of components and the linearity assumptions were still major causes of concern. After three decades, it is interesting that a major health organisation recognised the common antecedents of both T2DM and CVD, while at the same time discarded MetS as a distinct entity.

1.1.6 Continuous score

Parallel with the debates on how to define MetS, and partly driven by them, continuous MetS scores have been developed. Some techniques have relied on the sample distribution of the components, such as a sum of Z-scores (75). A study showed that an increase of one standard deviation (SD) in a MetS Z-score was associated with a relative risk of 3.7 for T2DM incidence and 1.4 to 1.8 for CVD incidence and coronary mortality (76). Using a quintile-based approach generating a sum score ranging from zero to 60, a study showed that this outperformed the ATP-III definition in predicting T2DM (77). A discrete score may be calculated by counting the number of dichotomised MetS components present (with a sum score ranging from zero to five). This score was positively associated with risk of CVD and all-cause mortality in a study (78), and with body mass index (BMI) and insulin resistance in another study (79). However, all of these scores assume equal weighting of the components. Principal component analysis and factor analysis, on the other hand, allows for unequal loading of each component. Both have been used to create a score and test the validity of MetS as a single entity. Studies have shown that one SD increase in continuous scores created using principal component analysis is associated with a substantially increased risk of T2DM (80) and CVD (80,81). Studies using confirmatory factor analysis have shown that MetS can be regarded as a valid entity (31,58,76).

Using confirmatory factor analysis, Gurka et al. constructed a MetS severity score (https://metscalc.org/) using a random sample of 6870 U.S. men and women aged 20–65 of White, Black and Hispanic ethnicities, resulting in sex- and ethnic-specific scores, which were transformed into Z-scores for interpretability (mean 0, SD 1) (58). The scores correlated well with high-sensitivity C-reactive protein, insulin resistance, and uric acid. Applied on

other U.S. cohorts, the MetS severity Z-score was associated with increased risk of future occurrence of CHD (82) and T2DM (83) independently of its individual components, as opposed to the dichotomous ATP-III MetS definition. That is, the MetS severity Z-score offered more than the sum of its components. In a randomised controlled trial of patients with prediabetes, favourable 1-year changes in MetS severity Z-score were associated with reduced risk of T2DM and CVD in patients receiving metformin or lifestyle modification (84). The MetS severity Z-score has been found useful in populations outside the U.S. as well. It was inversely associated with kidney function in a large Korean population-based cohort (85), showed satisfying predicative capabilities regarding carotid plaque in an Argentinian cohort (86), and was used as an effect measure in a randomised controlled trial for supervised exercise conducted on patients with T2DM in Italy (87).

1.1.7 Aetiology and pathophysiology

The aetiology of MetS is multifactorial and likely a combination of genetic predisposition and environmental factors. Modern society, in affluent countries particularly, is dominated by an abundance of calorie-dense processed food, sedentary behaviour with little physical activity, and chronic stress. The prevailing view is that these environmental exposures initiate a cascade leading to metabolic abnormalities at a varying degree, partly determined by individual variability in body composition, insulin resistance and adipose tissue tolerance (88–90). Genetic studies of MetS are few, but indicate that MetS may be a complex polygenic trait (91). Low birth weight and epigenetic modifications are also associated with MetS, and will be discussed below in Section 1.1.8.

Two endocrine factors are central in the proposed pathophysiology of MetS: insulin and adipose tissue. These are interconnected in a complex and dynamic fashion involving many biological pathways, which are not fully understood. A full review is beyond the scope of this thesis. Here, I will only provide a brief overview of the proposed pathophysiology of MetS, starting with Figure 1 illustrating the involved tissues. However, note that biological pathways and relationships have not been drawn in the figure and that the figure is by no means exhaustive concerning the pathophysiology of MetS.

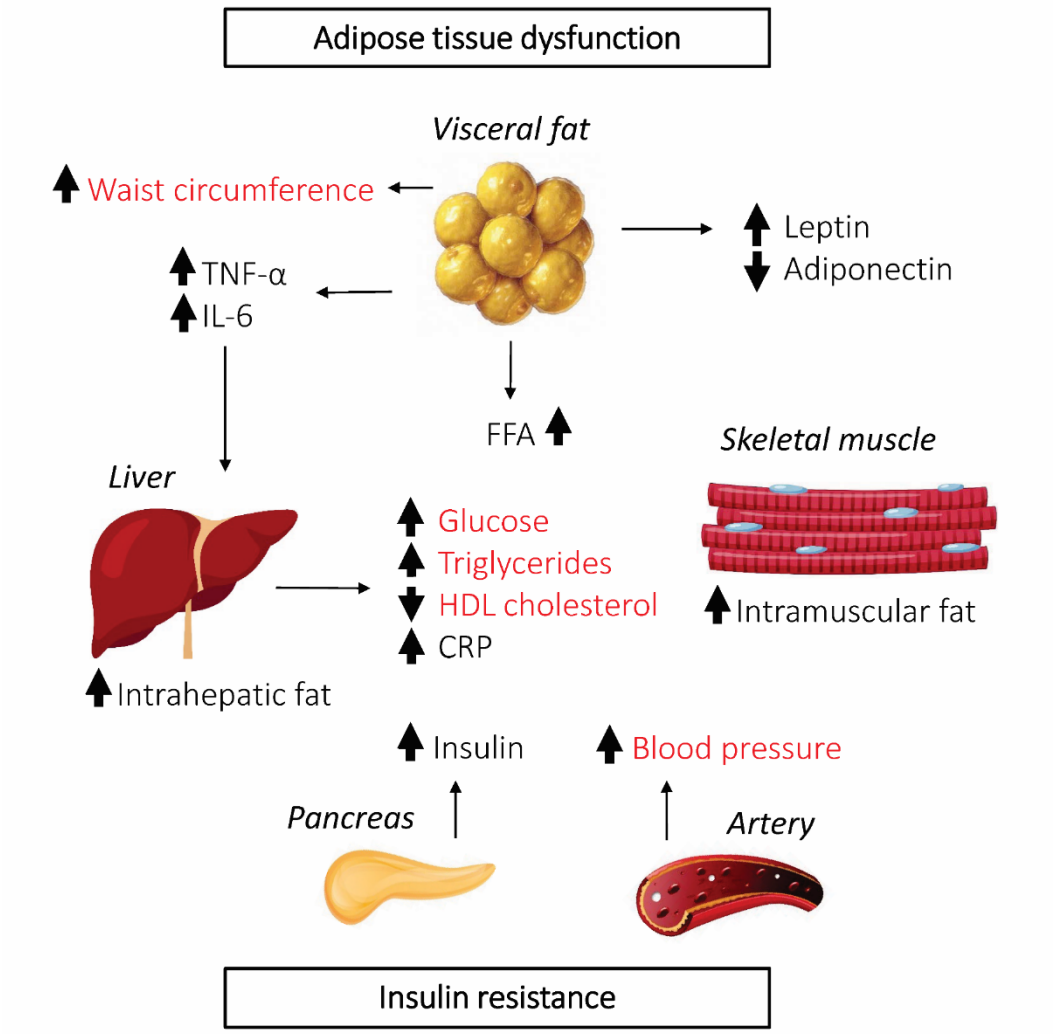

Figure 1. A simplified illustration of relevant tissues and molecules involved in the proposed pathophysiology of metabolic syndrome. The components included in the formal definition of metabolic syndrome are coloured in red. Illustrations used in the figure were downloaded from www.mostphotos.com. FFA = free fatty acids. CRP = C-reactive protein. HDL = high-density lipoprotein. TNF-α = tumor necrosis factor α. IL-6 = interleukin 6.

Insulin is an anabolic hormone produced by β-cells in the pancreas, which has profound effects on the carbohydrate and lipid metabolism (92). Insulin is released in response to increased blood glucose and stimulates the storage of energy surplus, mainly as glycogen in the liver and triglycerides in adipose tissue (88,92). Free fatty acid (FFA) regulation in adipose tissue is involved in glucose regulation (92,93). Postprandial insulin inhibits lipolysis

in adipose tissue, decreasing FFA flux, which in turn inhibits the gluconeogenesis in the liver (less synthesis of glucose). In the fasting state, insulin levels drop, resulting in less inhibition of lipolysis in adipose tissue, causing an increase in FFA, which in turn stimulates gluconeogenesis (more synthesis of glucose). This fine-tuned balance keeps the blood glucose levels within a normal range in healthy individuals. However, in some individuals, this physiologic response becomes dysfunctional (88).

When peripheral tissue fails to respond adequately to insulin, it is by definition insulin resistant. Reaven suggested that insulin resistance was the mechanism behind the common cluster of metabolic risk factors (19). The β-cells' compensatory ability to secrete insulin could explain why individuals with various degrees of insulin resistance have similar glucose levels. The hyperinsulinemic and insulin-resistant state could explain the secondary metabolic abnormalities, at least to some extent: β-cells that failed to compensate for worsening insulin resistance, would, due to less inhibition from insulin, result in an increase in FFA, hyperglycaemia, and ultimately T2DM (19). Thirty years later, many molecular mechanisms have been proposed as underlying causes of insulin resistance in peripheral tissue, such as inflammatory factors (tumour necrosis factor α, C-reactive protein, interleukines), adipokines (leptin, adiponectin), free radicals and oxidative stress (94). Adipose tissue is well-known as a metabolically active endocrine organ with an ability to produce a range of adipokines (for instance adiponectin) that may affect the sensitivity to insulin (88,92). Insulin-resistant adipose tissue may cause a chronic flux of FFA, possibly leading to fat deposition (triglycerides) in the liver and skeletal muscle (93).

Dysfunctional adipose tissue is closely related to insulin resistance (88–90,95). In periods of overnutrition, adipose tissue may fail to expand normally and/or become dysfunctional. Expansion of visceral adipose tissue, i.e. intra-abdominal fat, as opposed to subcutaneous fat, is commonly followed by metabolic deterioration (90,96). Some suggest that subcutaneous adipose tissue may function as a buffer for a surplus of triglycerides that, when exceeded, spill over into visceral and ectopic fat deposition (96). This expanded, dysfunctional visceral adipose tissue is highly metabolically active, secreting adipokines and inflammatory cytokines that contribute to a systemic, low-grade inflammation (90). Conversely, the

concentration of the anti-inflammatory molecule adiponectin decreases (90). Genetics, sex, age and ethnicity have been suggested as non-modifiable factors influencing an individual's susceptibility to store fat as visceral adipose tissue (90). The large variability seen in visceral fat depositions between individuals has been connected to the "personal fat threshold" theory for T2DM (97), which proposes that everyone has a tolerance to weight gain that when exceeded, cardiometabolic disease develops (96). In other terms, some individuals tolerate excess nutrition and weight gain surprisingly well, metabolically speaking, whereas others do not and develop metabolic abnormalities. This has led to the concept of metabolically healthy obesity, which I will expand on in greater detail later.

Hypertension is the one component of MetS that has the weakest link to the proposed mechanisms. However, research suggests that visceral adipose tissue and insulin resistance/hyperinsulinemia may cause hypertension through renal sodium reabsorption, activation of the sympathetic nervous system and the renin-angiotensin system and/or structural changes in the kidneys due to fat depositions (89,90,95). Finally, there is evidence that MetS may be regarded a pro-thrombotic state due to alterations in the haemostatic system, such as dysfunction in the endothelium, fibrinolysis and platelets (95).

Neither insulin resistance nor visceral adipose tissue fully explain MetS. In a study, insulin resistance correlated well with elevated triglycerides, increased fasting glucose and low HDL cholesterol, but the (adjusted) correlations between insulin resistance and increased WC and hypertension were weak (98). Only 56–71% of individuals with MetS were insulin-resistant, and 13–17% of insulin-resistant individuals did not have MetS (98). A study showed that visceral adipose tissue measured using a computer tomography scan was a good predictor of IDF-defined MetS in women, but not in men (99). Surprisingly, subcutaneous fat was the best predictor of IDF-defined MetS in men. Further, among those not having IDF-MetS, but who reported a cardiovascular event, 55% had an elevated visceral fat percentage (99).

In summary, the literature suggests that the pathophysiology of MetS comprises a dysfunctional relationship between insulin and adipose tissue, which causes a range of secondary metabolic and vascular abnormalities including hyperglycaemia, dyslipidaemia,

hypertension, and a pro-inflammatory and pro-thrombotic state. Overnutrition from excess calorie intake and/or lack of physical activity are viewed as primary causes of MetS, although there may be individual variability in the ability to store energy surplus without dysfunction in adipose tissue and insulin resistance.

1.1.8 Ethnicity and obesity

The cut-offs for WC and BMI for prediction of metabolic abnormalities differ by ethnicity (100). Table 2 displays the ethnic-specific cut-offs for WC in the ATP-III criteria for MetS.

Table 2. Ethnic-specific cut-offs for waist circumference

Population/ethnic group	**Cut-off value**
Europid, Middle Eastern, Mediterranean, Sub-Saharan African	
Women	≥80 cm
Men	≥94 cm
Asian, Central and South American	
Women	≥80 cm
Men	≥90 cm
Chinese	
Women	≥80 cm
Men	≥85 cm
Japanese	
Women	≥90 cm
Men	≥85 cm
U.S. American/Canadian	
Women	≥88 cm
Men	≥102 cm

This table has been adapted from Alberti *et al.* (2009) (11).

The background for introducing ethnic-specific cut-offs stems from research showing that people of different ethnicities, for instance Asian, African, Polynesian, European, and Hispanic, may differ in amount of lean mass and fat mass, and in distribution of fat mass (visceral/ectopic vs subcutaneous) at the same BMI or WC (101,102). For instance, people of Asian ethnicity have greater fat mass at the same BMI and more visceral fat at the same WC

than people of European ethnicity, which has led to lower cut-offs for WC and BMI concerning prediction of metabolic abnormalities or overweight/obesity in people of Asian ethnicity (101–103). The motivation for introducing ethnic-specific cut-offs is to identify people with the same amount of visceral fat mass and cardiometabolic risk. In the harmonised ATP-III definition of MetS, Alberti et al. recognises these issues (11). However, it is not clear which cut-offs should be applied on people of mixed ethnicity or people of a specific ethnicity that resides in a different region (11).

In a comprehensive review published in 2012, Wells provides a thorough analysis of proposed explanations of ethnic variability of adiposity and risk of T2DM and CVD (101). A core question is whether environment or genes contribute to the observed variability in body composition. Researchers have suggested both a "thrifty phenotype" and a "thrifty gene" hypothesis. Neel's thrifty gene hypothesis in the 1960s suggested that repeated cycles of feast and famine have forced a selection of genes that enhance survival in short periods of famine, but promote cardiometabolic disease in the modern era of "chronic feast" (101). However, there do not exist systematic distinctions in genotypes between population groups/ethnicities (104), and most cardiometabolic diseases have polygenic traits (101).

In 1977, Anders Forsdahl, a Norwegian professor of primary care, Anders Forsdahl showed using population data from Finnmark County (i.e., some of the same areas included in this thesis) that infant mortality correlated with atherosclerotic disease in middle age (105). In 1992, Hales and Barker suggested the "thrifty phenotype" hypothesis stating that early life adaptation to poor nutrition put low birth weight individuals at poor odds of tolerating high nutrition environments later in life, and consequently were predisposed to Syndrome X (i.e., MetS), T2DM and CVD (106). This has been supported by a large body of research, maintaining the "thrifty phenotype" theory as a plausible mechanism for the common soil mechanism of chronic cardiometabolic disease (107). Recent scientific advances using animal models, in vitro studies and human studies suggest that the mechanism behind the "thrifty phenotype" is due to epigenetic changes induced in utero (108). Other environmentally driven explanatory factors proposed for ethnic variability in adiposity include: climate (e.g., increased fat mass to protect against cold stress); long-term food availability (e.g., observed as

population changes in stature); dietary quality (e.g., genetic adaptation to lactose tolerance in populations that practice dairy farming); infections (e.g., favouring certain cytokines or fat depots that has survival advantages against various infections); and culture (e.g., ritual fattening in some societies) (101). These factors correlate with geography and, consequently, ethnicity, and may change across time and space (101).

WHO supports the use of both BMI and WC as risk measures of future disease (102,103,109,110). Weight is a commonly used proxy of body fat; however, weight is expected to vary between individuals merely due to height differences. Stature differs between the sexes, populations, and ethnic groups. Therefore, WHO suggested the BMI (weight/height^2) as a practical tool for comparing adiposity independent of stature between and within populations, albeit admitting its limitations (109). BMI is recognised as being a poor marker of body composition, and it is not perfectly independent of height, particularly in women (111). Abdominal obesity, as measured by WC, is recognised as a better predictor of visceral fat, and, possibly, future cardiometabolic disease (102,112). However, WC is not height-corrected, and several different cut-offs for subgroups of sex and ethnicity exist (Table 2), which makes comparisons across multi-ethnic populations unsatisfactory. Waist-to-height ratio (WHtR, WC divided by height) has been suggested as a valid predictor of future disease that may be independent of sex and ethnicity (100,112). Because BMI and WC are highly correlated, Krakauer et al. recently created a body shape index (ABSI) from simple anthropometrics such as height, weight and WC (113). The ABSI is approximately independent of height, weight and BMI.

In summary, ethnicity is a marker of environmental factors and possibly genetic factors, which seem to affect body composition, adiposity distribution and metabolic load capacity. Epidemiologists have developed simple obesity measures, but these may have limited comparability regarding underlying obesity across populations.

1.1.9 Metabolically healthy obesity

The relationship between metabolic risk and obesity is complex and heterogeneous (114). Women typically have more subcutaneous fat and fat stored in the lower limbs than men, who

typically have more visceral fat (114–116). Sex hormones play a central role, as postmenopausal women start to store fat in a male-type pattern, explaining some of the increased CVD risk in women after menopause (114). Independent of sex, people with the same value of BMI may have remarkably different body composition and metabolic manifestations (115,116). But neither BMI nor WC sufficiently distinguish between the different compartments of fat (117), perhaps explaining why some people with obesity are insulin sensitive, and why some people who are insulin resistant have a normal weight (118). Likewise, MetS appear in normal weight individuals (119,120), and some people with obesity do not have MetS (120).

The notion of having a BMI ≥30 kg/m^2 while at the same time being metabolically healthy, is several decades old and based upon the relatively common finding of obesity without metabolic abnormalities such as insulin resistance (121). Metabolically healthy is typically defined as having a normal insulin sensitivity, absence of MetS, its components, obvious visceral fat accumulation, and any other obesity-related disease. In 1999–2004 in the U.S. adult population, approximately 1 out of 3 people with obesity were categorised as metabolically healthy (120). Researchers raised questions as to whether weight loss in this subgroup is beneficial or detrimental (121).

Since then, several large meta-analyses have shown that compared to people with metabolically healthy normal weight or non-obesity, people with metabolically healthy obesity (MHO) have increased risks of future T2DM (122), CVD (123–125) and mortality (123,125), with higher relative risks for T2DM than CVD (approximately 4.0 vs 1.25-1.60, respectively). However, risks were lower for people with MHO than for people with metabolically unhealthy obesity (MUO), however. Evidence suggests that people with MHO have less visceral and ectopic fat compared to people with MUO, despite having similar amounts of total body fat. Weight gains, visceral fat particularly, have been associated with conversion from MHO to MUO (126,127). The mortality in metabolically healthy abdominal obesity (MHAO) has also been examined in several studies with varying results (128–130). In a comprehensive review from 2019, Smith et al. reports more than 30 different definitions of MHO, and argues that there are very few truly metabolically healthy individuals with obesity,

if defined as having no metabolic abnormalities including insulin sensitivity and normal liver fat content (131).

Extrapolation between multiple categories of BMI or WC usually shows J- or U-shaped associations with mortality (132,133). Despite well-known limitations with defining cut-offs for BMI and WC, most research on the apparent benign nature of excess body fat in metabolically healthy individuals has been performed in categories of obesity. However, BMI or WC may have a functional relationship with mortality not reflected well by crude dichotomies, as dichotomisation of continuous predictors causes loss of information and statistical power (55). How these continuous relationships are in strata of metabolic health, i.e. MetS, is not known.

1.1.10 Prevention and treatment

Both prevention and treatment of MetS are based on lifestyle changes (74,134,135). All individuals with MetS should avoid excessive calorie intake, improve the quality of their food, and increase their daily physical activity. Evidence indicates that a "heart-healthy" diet such as the Mediterranean diet rich in fibre and unsaturated fats (e.g., vegetables, legumes, nuts, fish and seafood) and low in sugar, refined carbohydrates and saturated fats (e.g., sugar-sweetened beverages, refined grain and meat products) is beneficial (134,135). Heavy alcohol drinking should be abstained from, and smoking cessation is strongly recommended. Further, there is strong evidence that physical activity ameliorates components of MetS in a dose-response relationship; at least 30-60 minutes of physical activity daily (e.g., brisk walking) has been recommended (134).

In 2019, the Endocrine Society published a clinical guideline for prevention of CVD and T2DM in people with "elevated metabolic risk" (74), as previously described in Section 1.1.5. The guideline suggests that people with elevated metabolic risk (i.e., MetS) should go through a global assessment of 10-year absolute risk of CVD (e.g., national risk calculators) (74). Individuals with one or two components should be re-evaluated every third year and adhere to a general lifestyle recommendation. When lifestyle changes is not successful, relevant drugs for dyslipidaemia, hypertension and elevated fasting glucose (prediabetes) such as statins or

fenofibrates, blood pressure-lowering drugs (not beta blockers or thiazide diuretics, which may worsen insulin resistance) and metformin, respectively, may be prescribed (74,135).

In patients with obesity, a weight loss of 5–10% the first year should be the aim (74,134,135). However, in practice, dieting is hard, especially in a long-term perspective. Potential reasons for failure to lose weight with calorie-restricted diets include changes in metabolic rate, loss of lean mass, hormonal alterations in appetite, altered gut microbiota, and psychological factors (136). The most realistic goals may be to prevent obesity in the general population, and to prevent a progression from metabolically healthy to metabolically unhealthy in people who already have obesity (136).

1.2 Ethnicity

1.2.1 Semantics and terminology

Ethnicity (from the Greek word “ethnos”, translating to “folk” or “people”) is regarded a sociocultural construct (137), meaning that it is not found in an objective reality, but is an abstract concept collectively developed by society (138). Ethnic groups are population groups that are characterised by one or more factors from the following non-exhaustive list: language, culture, religion, skin colour, diet, nationality or geography (137). Such sociocultural characteristics may have biological implications through their effects on disease and health, making ethnicity a relevant and common proxy variable (i.e., representing something else) in modern epidemiology. Which factors that characterise an ethnicity vary greatly. For instance, in the U.S., black skin colour is a characteristic of the ethnic Black population, while Jews are characterised by their religious beliefs. Geographic origin is a common characteristic of many ethnicities, e.g. South-Asian and Latin-American ethnicity.

The epidemiologist Raj Bhopal has written comprehensively about the challenges with ethnicity as a variable in epidemiology (137,139–142). He recommends that categorisation of ethnic groups should be as specific as necessary, and the terminology should reflect this (137). As an example, Bhopal discusses the broad term “Asian”: do we mean Indians,

Chinese, Mongols, Koreans or Syrians? Albeit all qualify for the term Asian, these population groups have quite different social and cultural impacts on health.

1.2.2 Use in epidemiology

Several researchers have proposed principles for how to use ethnicity in health research (142–144). These include explicitly specifying the research purpose, describing the ethnic categories, not using it as a proxy for genetic variation, considering all relevant confounders (especially socioeconomic status), not using stigmatising terminology, and tailoring of the criteria to the specific purpose. Principally, ethnicity is used as an instrument for something unmeasured that is thought to affect health (e.g., a diet, a lifestyle, discrimination, a gene), and is interpreted as a risk *marker* in epidemiology, not a risk *factor* (137). Equality of health is an important value in democratic societies, and a main argument for studying ethnicity is that health differences between subgroups in the population must be quantified in order for policy-makers and health professionals to reduce differences (137).

However, ethnicity is a problematic variable to study. Its fluid, imprecise and ill-defined inherent qualities make the risks of measurement error and misclassification potentially large. There might be overlap between categories (mixed-ethnic groups), further diluting the "effects" of ethnicity. Bhopal has pointed out that most ethnic-related epidemiologic research is based on a weak theoretical foundation (142). Epidemiologic studies with ethnicity is a "black box", referring to the hidden mechanisms in the associations between ethnicity and other variables (137). Hence, interpretation of e.g., a coefficient for ethnicity in regression models demand knowledge of the specific characteristics that define the ethnicity that is studied (145).

1.2.3 Ethnic groups in Northern Norway

Northern Norway comprises several population groups, or ethnicities. Apart from other nationalities (Swedes, Russians, Thai, Somali etc.), inhabitants in Northern Norway may be divided into three main ethnicities: Norwegian, Sami, and Kven. All are Norwegian citizens.

The Sami people are regarded as an ethnic minority and indigenous people by the Norwegian Government and have distinct languages that belong to the Uralic language family, as well as distinct and various cultures. Traditionally, the Sami were occupied with nomadic reindeer herding, hunting, fishing and farming, but there are only a few Sami reindeer herders and fishermen today. It is assumed that the Sami population in Norway consists of 50 000 people, but this number is anecdotal. Most Sami live in Norway, but the Sami also inhabit northern parts of Sweden, Finland and the Kola Peninsula in the Russian Federation, a cultural region known as Sápmi.

The Kven people is an ethnic minority of descendants of Finnish immigrants in the 1700s and 1800s. They are not recognized as indigenous, but was granted national minority status in 1996 (146). The Kven have their own language, which also belongs to the Uralic language family. The size of the Kven population is not known, but thought to be much lower than that of the Sami population.

From the 19th century through the first half of the 20th century, the Sami and Kven in Norway experienced a strong effort of governmental assimilation, which in Norwegian was called "fornorskning", literally meaning "norwegianisation" (147). Among others this included sending Sami and Kven children to boarding schools where Sami and Kven languages were prohibited to use. Throughout the same period and inspired by social Darwinism, Sami and Kven people were objects to research that had the purpose of proving their inferiority as a "race" (147). Sami and Kven ethnicity became associated with shame. Consequently, language, culture and identity have been diluted through generations in both Sami and Kven, making many people not aware of their Sami or Kven background.

In 2019, a public health report from the northernmost county in Norway, Troms and Finnmark (random sampling of adults, 43.5% participation rate), showed that almost four in ten individuals in this population had some connection to either Sami or Kven ethnicity (148). Among these, approximately 30% were categorised as Sami, 20% as Kven, 16% as both Sami and Kven, and 5% as having Sami speaking grandparents. One in four who reported some connection to either Sami or Kven ethnicity did not provide further answers on language and

ethnic background, and were thus not possible to place in an ethnic category (148). This illustrates the complicated and mixed composition of ethnicity in this population.

Most epidemiological research on the Sami population in Norway the last 10–20 years has compared Sami to non-Sami in data from population surveys conducted specifically in areas with an assumed high proportion of Sami inhabitants (146,149,150). In a recent systematic review of research from mainly Norway and Sweden, the somatic health of Sami people was overall similar to non-Sami people (151). Specifically, there are no or small differences in T2DM (152–154), CVD (155,156) and risk factors for CVD (157). One study found a similar prevalence of IDF-defined MetS in 2003–2004 (46). However, Sami people have slightly higher BMI (women particularly) than non-Sami people (158).

1.3 Aim of thesis

In summary, MetS is a common, but preventable health issue with complex associations with obesity and ethnicity. There is a knowledge gap on the development of this issue in rural Northern Norway. Thus, the overall aim of this thesis was to examine the epidemiology of MetS and relationships between obesity and ethnicity in rural Northern Norway. Specifically, we aimed to:

1. examine the sex- and ethnicity-specific change over time in the prevalence and severity of MetS in rural Northern Norway (Paper I),
2. examine the association between MetS and metabolic-obesity phenotypes, and all-cause and CVD mortality, and between continuous obesity measures and all-cause and CVD mortality specifically for metabolically healthy and metabolically unhealthy (Paper II),
3. examine the influence of ethnicity on the relationships between metabolic markers and obesity measures (Paper III), and
4. examine the correlation between BMI and height, develop a height-corrected weight index in this population, and compare ethnic figures of this index (Paper IV).

2 Materials and methods

2.1 The SAMINOR Study

In 2001, the Ministry of Health established the Centre for Sami Health Research at the Department of Community Medicine, UiT The Arctic University of Norway, due to a lack of knowledge on the health and living conditions of the Sami people in Norway. The centre is responsible for the Population-based Study on Health and Living Conditions in Regions with Sami and Norwegian Populations—the SAMINOR Study. To date, two waves of data collection have been completed. Information on Norwegian, Sami and Kven ethnicity was collected in both surveys. However, the main settlement regions for Kven people were not included in the surveys as the intention was to study the Sami people in particular.

The first survey, the SAMINOR 1 Survey (hereafter called SAMINOR 1) was conducted in 2003–2004 by the centre in collaboration with the Norwegian Institute of Public Health (146). Data from SAMINOR 1 was used in all four papers of this thesis. The second survey, the SAMINOR 2 Survey, was carried out in 2012–2014 by the centre alone, and comprised two parts. The first part, the SAMINOR 2 Questionnaire Survey, was conducted in 2012 (149). Data from the first part was, however, not used in this thesis.

The second part, the SAMINOR 2 Clinical Survey (hereafter called SAMINOR 2), was conducted in 2012–2014 (150). Data from this second part was used in Paper I. Participants in both SAMINOR 1 and SAMINOR 2 were identified using the personal identification number that is mandatory for all inhabitants in Norway, allowing for linkage with national registries if participants consented to it. Both surveys comprised self-administered questionnaires on health issues, lifestyle and ethnicity, a standardised, clinical examination and blood samples.

2.1.1 SAMINOR 1

The national census of 1970 posed questions regarding Sami and Kven ethnicity in selected areas of Northern Norway. Being the latest national register to collect ethnicity data, this census was used as a basis to determine the geographical areas to be included in SAMINOR 1. However, as the ethnicity questions were included only in parts of the regions with

assumed Sami inhabitants today, historical and local knowledge were also applied. The goal was to include geographical areas expected to have at least 5% Sami inhabitants. In six of the 24 included municipalities, only parts of the municipality were included. In Troms and Finnmark County (formerly two separate counties, Troms County and Finnmark County) the following municipalities were included: Karasjok, Kautokeino, Porsanger, Tana, Nesseby, Lebesby, Alta, Loppa, Kvalsund, Kåfjord, Kvænangen, Storfjord, Lyngen, Skånland and Lavangen. In Nordland County, the following municipalities were included: Tysfjord, Evenes, and parts of Hattfjelldal (Hattfjelldal), Grane (Majavatn) and Narvik (Vassdalen). In Trøndelag County (formerly two separate counties, Nord-Trøndelag and Sør-Trøndelag), the following were included: the municipality of Røyrvik, and parts of Namsskogan (Trones and Furuly), Snåsa (Vinje) and Røros (Brekken).

All inhabitants in the included geographical areas ageing 30 and 36–78/79 years were invited. In total, 27 987 women and men were invited to SAMINOR 1, of which 16 865 (60.6%) participated by answering at least one questionnaire or attending clinical examinations. Initially, an initial questionnaire, a screening questionnaire, and an additional questionnaire were sent out consecutively. Only those who handed in the initial questionnaire and said they wanted a clinical examination, received an invitation together with the screening questionnaire. After data collection in the four first municipalities, it was evident that the logistics of the questionnaires caused a reduction in attendance rate. Therefore, the logistics were changed such that in the rest of the municipalities, a combined questionnaire with the two first questionnaires was included in the invitation to the clinical examination. The additional questionnaire was handed out when participants attended the clinical examination. However, data from the additional questionnaire was not used in this thesis. In Troms and Finnmark, invitees who did not attend the clinical examinations, received a new invitation to attend a couple of months later. In Nordland and Trøndelag, no second chance was offered. Information was given in Norwegian and Northern-Sami languages. In the municipalities Kautokeino, Karasjok, Porsanger, Tana, Nesseby, Lyngen and Kåfjord, invitees were offered questionnaires in both languages. In all other municipalities, only the Norwegian questionnaire was used. Details on study logistics are found in a previous publication (146).

Information on the following lifestyle factors were obtained from the questionnaire (answer options in parenthesis): education (total number of school years); diabetes (yes/no); angina pectoris (yes/no); previous stroke (yes/no); previous heart attack (yes/no); use of blood pressure-lowering drug (currently/previously, but not now/never); use of cholesterol-lowering drug (currently/previously, but not now/never); use of insulin (currently/previously, but not now/never); use of glucose-lowering drug in tablet format (currently/previously, but not now/never); daily smoking (currently/previously/never); leisure-time physical activity during the last year by a modified Saltin-Grimby Physical Activity Level scale (reading, watching television, or engaging in sedentary activities/at least 4 hours a week of walking, bicycling, or other types of physical activity/at least 4 hours a week of participating in recreational athletics or heavy gardening/regular, vigorous training or participating in competitive sports several times a week) (159); alcohol consumption during the last year (never/not this year/a few times during this year/1 time per month/2-3 times per month/1 time per week/2-3 times per week/4-7 times per week). In addition, participants were asked to list any medication they had used within the last 4 weeks, which later were coded with Anatomical Therapeutic Chemical Classification System (ATC) codes.

2.1.2 SAMINOR 2

Due to limited resources, only ten of the 24 municipalities mentioned above were included in SAMINOR 2: Kautokeino, Karasjok, Porsanger, Tana, Nesseby, Kåfjord, Storfjord, Lyngen, Skånland and Evenes (150). Figure 2 shows the areas included in SAMINOR 1 and SAMINOR 2. All 12 455 inhabitants aged 40–79 years were invited, of which 6004 (48.2%) participated. Three to four weeks before survey start, eligible participants received an information pamphlet about the survey by mail. Two weeks before start, they received an invitation with details on appointment time, information and a questionnaire, and halfway through the collection period, a reminder was sent to non-responders. All information was given in Norwegian. In addition, information about the survey was also provided in Northern-Sami and Kven languages in some municipalities. Details on study logistics are found in a previous publication (150). Information on the following lifestyle factors was obtained from the questionnaire (answer options in parenthesis): education (total number of school years); diabetes (yes/no); use of blood pressure-lowering drug (currently/previously, but not

now/never). Note that the question on diabetes were not posed identical in the surveys. In SAMINOR 1, the question was “Do you have or have you had diabetes (“sugar sickness”)?” In SAMINOR 2, the question was “Have you ever been diagnosed with diabetes (elevated blood sugar levels)?” Participants who replied “yes” to the diabetes questions in the surveys, were assumed to have T2DM as ~90% of cases of diabetes are T2DM (160).

2.1.3 Clinical examination

Both surveys had trained personnel that performed all clinical measurements and blood sampling using similar procedures. WC was recorded to the nearest centimetre at the umbilicus with the participant standing and breathing normally. Height and weight were measured to the nearest 0.1 cm and 100 g, respectively, using an electronic scale with participants wearing light clothing and no shoes. In SAMINOR 1, blood pressure was measured using a Dinamap-R automatic device (Critikon, Tampa, Florida, USA), whereas CARESCAPE V100 monitor (GE Healthcare, Milwaukee, Wisconsin, USA) was used in SAMINOR 2. Blood pressure was measured following at least 2 min of seated rest and with their arms resting on a table. With one-minute intervals, three measurements were recorded and the average of the last two measurements was used. Blood samples were non-fasting and drawn by venepuncture in a seated position. Triglycerides, HDL cholesterol and glucose were measured by an enzymatic method (Hitachi 917 autoanalyzer, Roche Diagnostic, Switzerland) in SAMINOR 1 (146), while a homogeneous enzymatic colourimetric method (Roche/Hitachi Cobas 8000B system, Roche Diagnostics GmbH, Mannheim, Germany) was used in SAMINOR 2 (150).

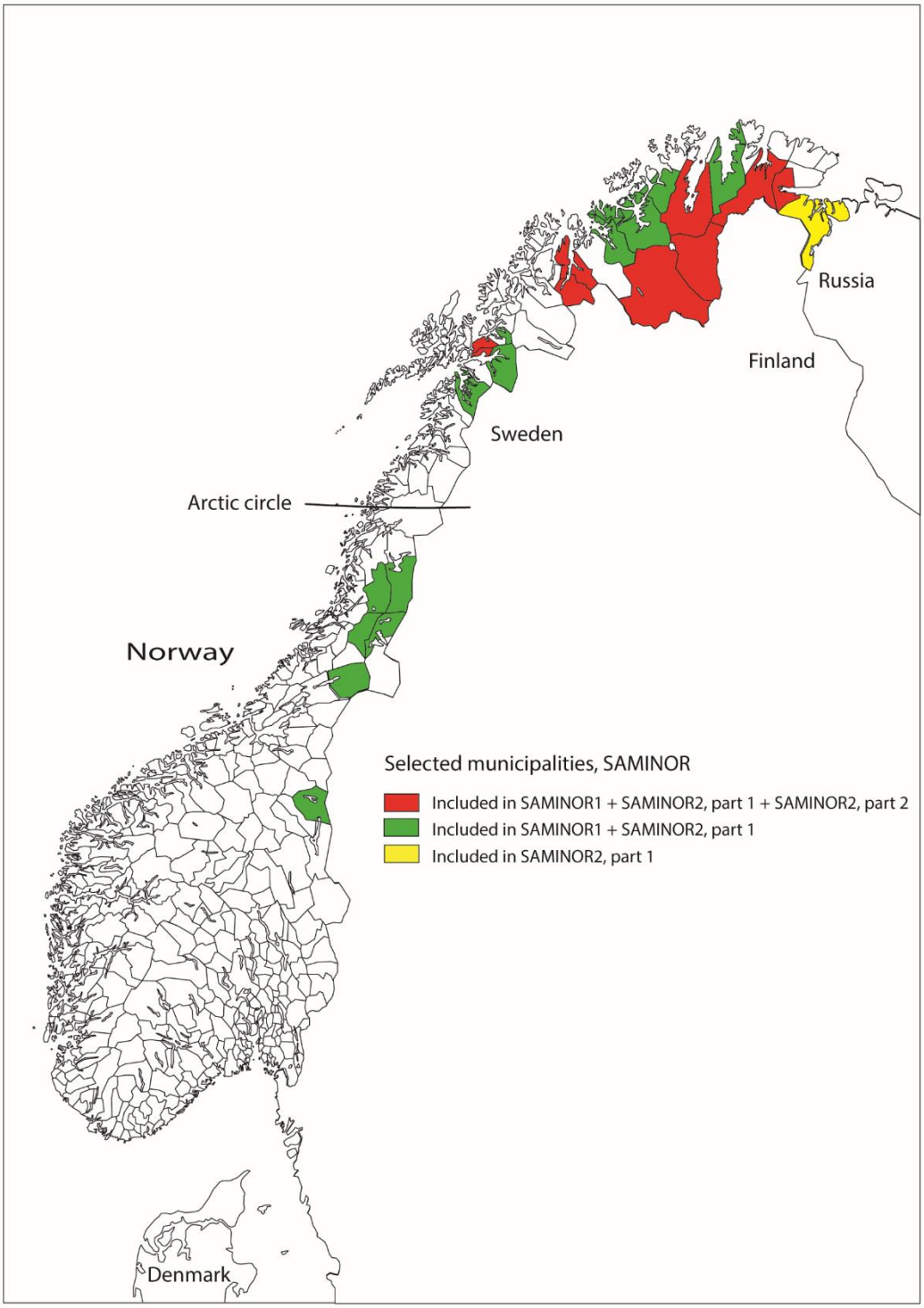

Figure 2. Selected municipalities in the SAMINOR Study.

2.2 Registry data

In Paper II, survey data from SAMINOR 1 was linked with mortality data from the Norwegian Cause of Death Registry, administered by the Norwegian Institute of Public Health. It issues official cause of death statistics and has a coverage of more than 98% (161). The data we used comprised date of death and underlying cause of death, coded using the International Statistical Classification of Diseases and Related Health Problems, 10th revision. In Paper II we also used emigration data from the National Population Register, provided by Statistics Norway. The datasets were linked using the personal identification number, and was facilitated by Statistics Norway.

2.3 Variables

2.3.1 MetS, metabolic markers and metabolic health

In Papers I–III, we included the same core components of MetS: triglycerides, HDL cholesterol, glucose, systolic and diastolic blood pressure, and WC. In Paper IV, we examined obesity only and did not include any measure of MetS or its components.

In Paper I, we examined MetS in its original dichotomous form, defined according to the harmonised ATP-III criteria from 2009 (11) (see Table 1 in Section 1.1.2). We chose the European cut-offs for WC (see Table 2 in Section 1.1.8). The cut-off for serum glucose was set to ≥7.8 mmol/L because blood samples were taken in a non-fasting state, and national guidelines state there is a high risk of T2DM if glucose is above this value two hours after an oral glucose tolerance test (160,162). Presence of any three of the following five qualified for a diagnosis of MetS:

1. Hypertension: systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg or current use of medication for high blood pressure.
2. Abdominal obesity: WC ≥80 cm in women and ≥94 cm in men
3. Elevated non-fasting serum glucose ≥7.8 mmol/L. Participants with self-reported T2DM (all who responded “yes” to the diabetes questions were assumed to have T2DM) were also considered to have elevated glucose.

4. Reduced non-fasting serum HDL cholesterol: <1.3 mmol/L in women and <1.0 mmol/L in men.
5. Elevated non-fasting serum triglycerides ≥1.7 mmol/L.

In Paper I, we also included the MetS severity Z-score developed by Gurka et al. (58). As shown in Section 1.1.6, this score has been validated against future cardiometabolic disease occurrence and offer predictive capabilities independently of its individual components. The formula for MetS severity Z-score for Non-Hispanic White men and women are, respectively,

$$Z_{\text{men}} = -5.4559 + 0.0125W - 0.0251H + 0.0047S + 0.8244\ln(T) + 0.0106G$$
$$Z_{\text{women}} = -7.2591 + 0.0254W - 0.0120H + 0.0075S + 0.5800ln(T) + 0.0203G$$

where *W* is WC in centimetres, *H* is HDL cholesterol in mg/dl, *S* is systolic blood pressure in mmHg, *T* is for triglycerides in mg/dl and *G* is for glucose in mg/dl (58). Glucose, HDL cholesterol and triglycerides were converted from mmol/L to mg/dl before calculation of the severity Z-score.

In Paper II, MetS was central in the definition of metabolic health. Absence of MetS or any cardiometabolic disease (that is, diabetes, angina pectoris, stroke or myocardial infarction) or prescribed drugs for cardiometabolic disease (that is, prescribed drugs for high blood pressure, hyperglycaemia or dyslipidaemia, see definitions below) were defined as metabolically healthy. The presence of any of the aforementioned was defined as metabolically unhealthy. We used the same definition of MetS in Paper I and Paper II.

In Paper III, we examined the relationships between various obesity measures (see below) and components of MetS, except for WC. These metabolic markers were kept in their continuous form in order to model the functional relationships.

2.3.2 Obesity measures

We used both categorical and continuous versions of general and abdominal obesity measures. BMI was calculated as weight in kg divided by height in metres raised to the power

of two (kg/m^2). In Paper II and IV, general obesity was defined as having a BMI ≥30 kg/m^2 (109). In Paper II, abdominal obesity was defined as having a WC ≥88 cm in women and ≥102 cm in men. Note that this cut-off is higher than the cut-off used in the MetS definition. The cut-offs originate from a WHO report that recommends two action levels for WC (110): ≥80 cm in women and ≥94 cm in men (level 1, increases the risk of metabolic complications), and ≥88 cm in women and ≥102 cm in men (level 2, substantially increases the risk of metabolic complications). The first action level is commonly used in the MetS definition (see Table 2 in Section 1.1.8. The second action level is commonly used to define abdominal obesity for general purposes. In Paper III, waist-to-height ratio (WHtR) was calculated as WC in cm divided by height in cm. In Paper II, we also used a body shape index (ABSI), which is calculated using the following formula (113):

$$ABSI = \frac{W}{BMI^{2/3}\, h^{1/2}}$$

Where W is waist circumference and h is height. The ABSI is a measure of abdominal obesity created to be independent of weight and height, and was used in Paper II because there is a high correlation between BMI and waist circumference.

2.3.3 Obesity-metabolic phenotypes

In Paper II, obesity-metabolic phenotypes were created by cross-classifying metabolic health status (see Section 2.3.1) by general and abdominal obesity status (see Section 2.3.2). Note that in the creation of abdominal obesity phenotypes, the WC criterion was removed in the definition of MetS for metabolic health status, such that any given two of the remaining four components qualified for a diagnosis of MetS.

Table 3. General obesity phenotypes.

	BMI <30 kg/m^2	**BMI ≥30 kg/m^2**
Absence of MetS, cardiometabolic disease, and prescribed drug for cardiometabolic disease	Metabolically healthy non-obesity (MHNO)	Metabolically healthy obesity (MHO)
Presence of MetS or cardiometabolic disease or prescribed drug for cardiometabolic disease	Metabolically unhealthy non-obesity (MUNO)	Metabolically unhealthy obesity (MUO)

Table 4. Abdominal obesity phenotypes.

	WC <88/102* cm	**WC ≥88/102* cm**
Absence of MetS, cardiometabolic disease, and prescribed drug for cardiometabolic disease	Metabolically healthy non-abdominal obesity (MHNAO)	Metabolically healthy abdominal obesity (MHAO)
Presence of MetS or cardiometabolic disease or prescribed drug for cardiometabolic disease	Metabolically unhealthy non-abdominal obesity (MUNAO)	Metabolically unhealthy abdominal obesity (MUAO)

*The cut-off of 88 and 102 cm was used in women and men, respectively.

2.3.4 Covariates

In Paper II and in Paper III, we adjusted the estimates for the following covariates: education, alcohol consumption, smoking, leisure-time physical activity, and prescribed drugs (Paper III only). In both Paper II and Paper III, leisure-time physical activity was categorised into three categories: sedentary (first alternative), light (second alternative) and medium/hard (third and fourth alternative merged due to a low number in the latter category). In Paper II, the potential

for residual confounding was regarded as particularly large, such that we categorised alcohol consumption during the last year and daily smoking with three levels. Alcohol consumption during the last year was categorised into "weekly", "less than weekly" and "never/not last year", whereas daily smoking was categorised into "currently", "previously", and "never". In Paper III, alcohol consumption during the last year was dichotomised into "weekly" vs "less than weekly" and smoking was dichotomised into "current smoker" vs "not current smoker".

In Paper II and Paper III, three drug variables were created: current use of cholesterol-lowering drug, current use of blood pressure-lowering drug, and current use of glucose-lowering drug. This was done by carefully combining responses to the drug-specific questions and the ATC codes of drugs that had cholesterol/blood pressure/glucose-lowering (side) effects. We included the ATC codes together with self-report in categorisation of current drug use to limit potential misclassification or residual confounding in the analyses. Criteria for being categorised as a current user of cholesterol-lowering drugs were: 1) responding "currently" to the question regarding use of cholesterol-lowering drug, or 2) reporting use of one or several drugs with the following ATC-codes: C10AA01 (simvastatin), C10AA03 (pravachol), C10AA05 (atorvastatin). Criteria for being categorised as a current user of glucose-lowering drugs were: 1) reporting "currently" to the question regarding use of insulin or glucose-lowering drug, or 2) reporting use of one or several drugs with the following ATC-codes: A10AB04 (humalog), A10BA02 (metformin). Criteria for being categorised as a current user of blood pressure-lowering drug were: 1) reporting "currently" to the question regarding use of blood pressure-lowering drug, or 2) reporting use of one or several drugs with the following ATC-codes (which either have blood pressure-lowering main effects or blood pressure-lowering side effects): C01BC04 (flecainide), C01DA02 (nitroglycerine), C01DA08 (isosorbide dinitrate), C01DA14 (isosorbide mononitrate), C02CA04 (α-blocker), C03AA03 (hydrochlorthiazide), C03CA01(furosemide) C07AA05 (β-blocker), C07AA07 (β-blocker), C07AB02 (β-blocker), C07AB03 (β-blocker), C08CA01 (calcium antagonist), C08CA05 (calcium antagonist), C08DA01 (calcium antagonist), C08DB01 (calcium antagonist), C09AA01 (angiotensin converting enzyme inhibitors), C09AA02 (angiotensin converting enzyme inhibitors), C09AA03 (angiotensin converting enzyme inhibitors), C09CA01 (angiotensin II receptor blocker).

2.3.5 Ethnicity

Northern Norway comprises a mixed-ethnic population. The SAMINOR Study collected self-reported information on Norwegian, Sami and Kven ethnicity, but due to the design of the study, we chose to not include Kven ethnicity as a category in the analyses. The geographical areas chosen for the SAMINOR Study were included due to having a substantial proportion of Sami inhabitants, while large Kven settlement areas were not included. Thus, the Kven participants in the SAMINOR Study cannot be considered representative. Therefore, we compared Sami to non-Sami ethnicity in this thesis.

The same ethnicity questions were posed in both SAMINOR 1 and SAMINOR 2 (146,150). Three domains were covered: language spoken at home, ethnic background, and self-perceived ethnicity. Multiple answers from the following list were allowed: Norwegian, Sami, Kven, other. The questions were posed as follows:

- What language do/did you, your parents and your grandparents use at home?
- What is your, your father's and your mother's ethnic background?
- What do you consider yourself to be?

In total, this produced eleven replies on ethnicity (six for language, three for background, one for self-perceived ethnicity). Defining Sami ethnicity is no straight-forward task. Therefore, several definitions were used in both main analyses and sensitivity analyses. These were as follows:

- *Objective language criteria and subjective criteria.* A participant was categorised as Sami if they answered Sami as 1) home language for at least one of their grandparents, parents, or themselves, and 2) their own ethnic background or self-perceived ethnicity. All others were categorised as non-Sami. This definition was used in the main analyses in Paper I, III and IV, and in a sensitivity analysis in Paper II.
- *Only subjective criteria*. A participant was categorised as Sami if they answered Sami as 1) their own ethnic background, or 2) their self-perceived ethnicity. All others were categorised as non-Sami. This definition was used in the main analysis in Paper II.

- *Self-perceived ethnicity*. A participant was categorised as Sami if they considered themselves Sami. All others were categorised as non-Sami. This definition was used in a sensitivity analysis in Paper I.
- *Number of Sami marks*. A three-level category of ethnicity was created by counting the number of "Sami answers": a) Answered Sami on all eleven questions, b) answered Sami on one to ten questions, and c) answered Sami on no questions. This definition was used in sensitivity analyses in Paper I and III.

In all these definitions, participants were categorised as Sami regardless of having reported other languages/ethnicities in addition to Sami. Further, the non-Sami group may include participants with Sami background, as those who did not meet the specific criteria, were categorised as non-Sami.

2.3.6 Mortality

In Paper II, mortality was the endpoint. The underlying cause of death was coded with the International Statistical Classification of Diseases and Related Health Problems, 10th revision. The outcome variables of interest were all-cause mortality and CVD mortality. The latter was defined as all deaths from causes I00–I99, which cover all diseases of the circulatory system.

2.4 Paper I

2.4.1 Study sample and design

Paper I had a repeated cross-sectional design, allowing us to examine the *population change* in the prevalence of MetS. The source population was the ten municipalities included in both SAMINOR 1 and SAMINOR 2, age range 40–79 years. The overall sample thus included individuals who had participated either in only the first survey, only the second survey, or in both surveys. The final sample comprised 6308 participants from SAMINOR 1 and 5866 participants from SAMINOR 2, whereof 3110 had participated in both surveys (Figure 3). Table 5 shows basic characteristics of the invited sample, attendees to the clinical examination, and the final analytical sample.

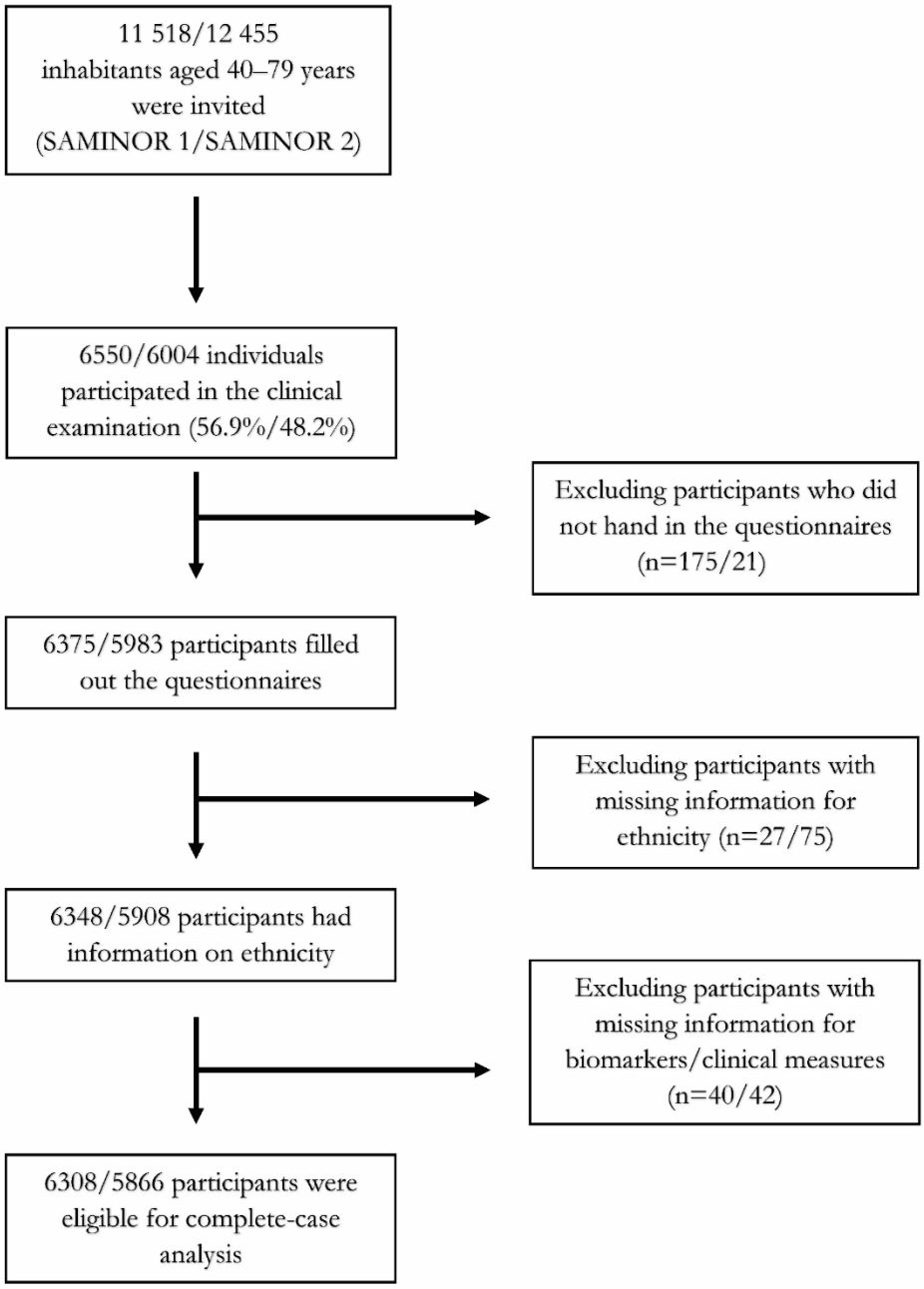

Figure 3. Flow chart of sample selection in Paper I.

Table 5. Basic characteristics of the invited sample in SAMINOR 1 and SAMINOR 2, attendees to the clinical examination, and the final analytical sample in Paper I.

	SAMINOR 1			SAMINOR 2		
	Invited	Met to clinical examination	Analytical sample	Invited	Met to clinical examination	Analytical sample
Total	11 518	6550 (56.9%)	6308 (54.8%)	12 455	6004 (48.2%)	5866 (47.1%)
Sex						
Men	5987 (52)	3089 (47)	2982 (47)	6469 (52)	2747 (46)	2684 (46)
Women	5531 (48)	3461 (53)	3326 (53)	5986 (48)	3257 (54)	3182 (54)
Age						
Mean (SD)	56.3 (10.5)	56.3 (10.1)	56.3 (10.0)	57.9 (10.8)	59.4 (10.5)	59.4 (10.4)
Marital status*						
Single/ unmarried	2597 (22)	1171 (18)	1121 (18)		722 (12)	699 (12)
Married	6537 (57)	4128 (63)	3979 (63)		3401 (57)	3344 (57)
Cohabitant					859 (15)	845 (15)
Widow(er)	897 (8)	488 (7)	460 (7)		389 (7)	383 (7)
Divorced	1264 (11)	656 (10)	644 (10)		533 (9)	539 (9)
Separated	222 (2)	107 (2)	104 (2)			
Missing	1	0	0		80	56
Education (years)						
Mean (SD)		10.7 (4.1)	10.8 (4.0)		12.0 (4.0)	12.0 (4.0)
Missing		446	419		273	240
Ethnicity						
Sami		2281 (36)	2268 (36)		2410 (41)	2396 (41)
Non-Sami		4067 (64)	4040 (64)		3498 (59)	3470 (59)
Missing		202	0		96	0

Categorical variables are given in frequency (percentage) and continuous variables are given in mean (standard deviation, SD). *Marital status was obtained from the national population register in SAMINOR 1 and self-reported in SAMINOR 2. In SAMINOR 1, married and same-sex partnerships were merged.

2.4.2 Statistical analysis

The statistical analysis is described step-by-step in the published paper. Details will not be repeated, but I elaborate on the reasons for choosing the respective methods. We used STATA version 15.1 (StataCorp, College Station, TX, USA) for the statistical computing and *R* version 3.4.2 *(*R Core Team 2017, R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria, https://www.R-project.org/) in making all graphs. We examined the change over time in the prevalence and severity of MetS by using generalised estimating equations (GEE) regression models. Analyses were stratified by sex and ethnicity, adjustment was made primarily for age, and potential ethnic differences in change over time were assessed with interaction analyses. We chose GEE because some of the observations correlated as some individuals participated twice. This excluded common statistical methods that assumes independent data. GEE treats the within-subject correlations as a nuisance and adjusts for the correlation by assuming a "working correlation matrix" (163). However, GEE is robust against the use of wrong working correlation matrix. An alternative to GEE was mixed models, which treats the within-subject correlations by estimating different intercepts and/or slopes. However, coefficients and standard errors differ between GEE and mixed models in logistic regression particularly (i.e., dichotomous outcomes, such as MetS). GEE produces "population averaged" coefficients, whereas logistic mixed models produce subject-specific coefficients (164). Of the two, GEE is recommended for dichotomous outcomes in population studies (164). Therefore, logistic (MetS) and linear (MetS severity Z-score) GEE regression were used in the analysis. Note that we also chose to age standardise the overall prevalence estimates in each survey using the direct method and the 2013 European standard population. This allows for direct comparison with other studies that standardise against the same standard population.

Some additional analyses were performed for this thesis (i.e., not published in the paper). We repeated the GEE models for change in MetS and abdominal obesity from SAMINOR 1 to SAMINOR 2 in strata of sex, disregarding ethnicity. Hence, overall age-adjusted prevalences for men and women are reported. The sex-specific prevalence of MetS and abdominal obesity (defined according to both action levels, see Section 2.3.2) by 10-year age groups were

graphically visualised. We also present sex-specific kernel density distribution of WC in both surveys.

2.5 Paper II

2.5.1 Study sample and design

Paper II had a longitudinal, prospective cohort design as we linked baseline data from SAMINOR 1 in 2003–2004 to the Norwegian Cause of Death Registry ending 31st December 2018. The final sample comprised 12 815 participants (Figure 4). Table 6 shows basic characteristics of the invited sample, attendees to the clinical examination, and the final analytical sample.

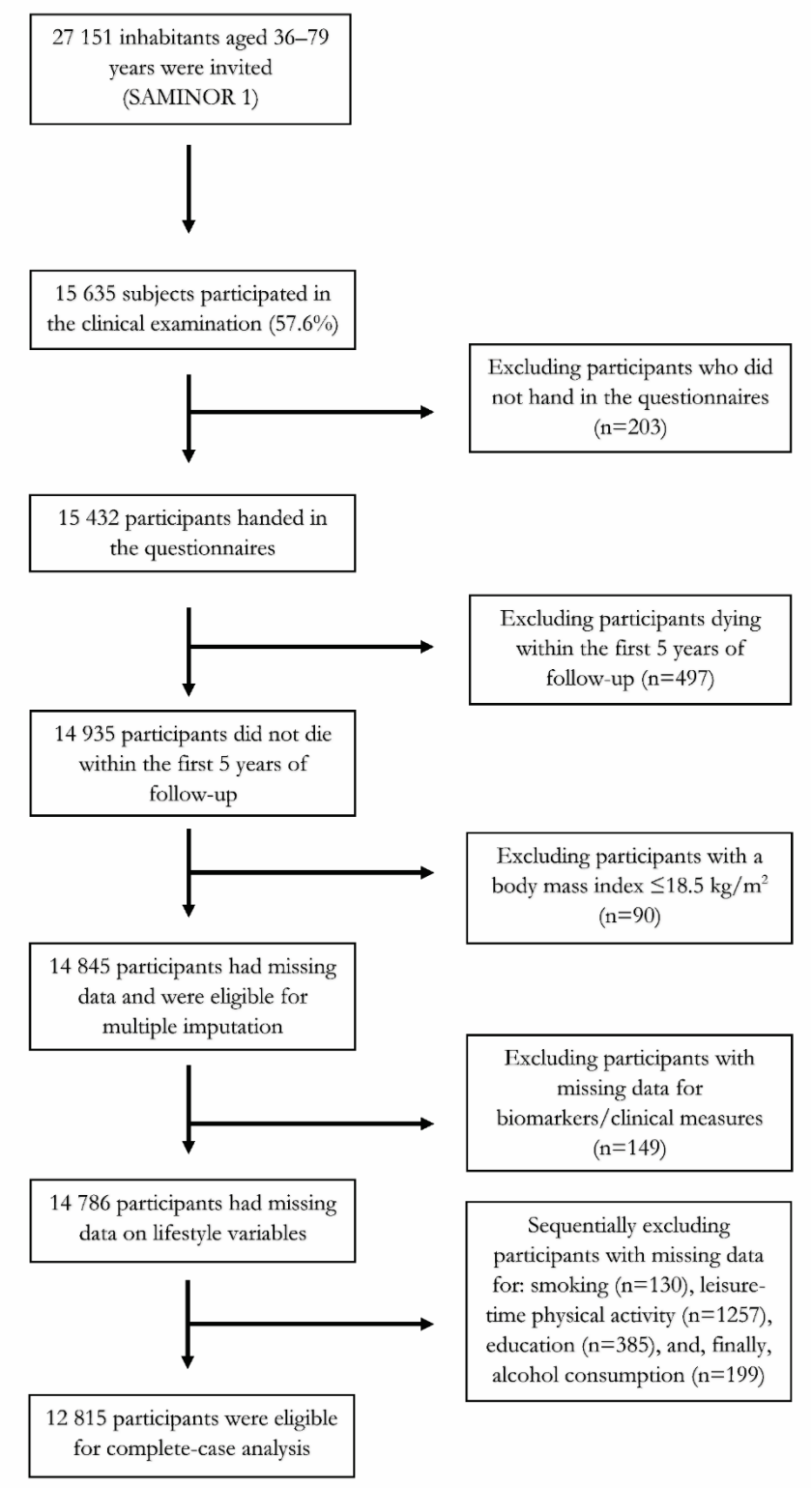

Figure 4. Flow chart for sample selection in Paper II.

Table 6. Basic characteristics of the invited sample in SAMINOR 1, attendees to the clinical examination, and the final analytical sample in Paper II.

	Invited	Met to clinical examination and consented to linkage	Analytical sample
Total	27 151	15 635 (57.6%)	12 815 (47.2%)
Sex			
Men	14 114 (52)	7501 (48)	6298 (49)
Women	13 037 (48)	8134 (52)	6517 (51)
Age			
Mean (SD)	54.1 (11.6)	54.6 (11.2)	53.6 (10.7)
Marital status*			
Single	3472 (24)	2931 (19)	2388 (19)
Married	15 175 (56)	9804 (63)	8187 (64)
Widow(er)	1826 (7)	1012 (6)	678 (5)
Divorced	3054 (11)	1599 (10)	1322 (10)
Separated	623 (2)	289 (2)	240 (2)
Missing	1	0	0
Education (years)			
Mean (SD)		11.2 (3.9)	11.4 (3.9)
Missing		962	0
Ethnicity			
Sami		3386 (22)	2931 (23)
Non-Sami		11 997 (78)	9884 (77)
Missing		252	0

Categorical variables are given in frequency (percentage) and continuous variables are given in mean (standard deviation, SD). *Marital status was obtained from the national population register in SAMINOR 1. Married and same-sex partnerships were merged.

2.5.2 Statistical analysis

The statistical analysis is described step-by-step in the published paper. Details will not be repeated, but I elaborate on the reasons for choosing the respective methods. We used *R* version 3.6.2 (R Core Team 2019, R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria, https://www.R-project.org/). In Paper II, we regressed all-cause and CVD mortality (outcomes) on MetS and metabolic-obesity phenotypes (categorical predictors) with Cox proportional hazards regression

(hereafter referred to as Cox), while adjusting for relevant confounders. Effect modification by sex and ethnicity was assessed. We analysed both complete case data (N=12 815) and data with missing data (N=14 845) that were imputed using multiple imputation. We performed similar analyses with continuous obesity measures (BMI, WC, ABSI) as predictors and tested for interactions with metabolic health status. The final result was visualised graphically with separate curves for metabolically healthy and metabolically unhealthy.

Three main mechanisms of nonresponse to survey items exist: missing-completely-at-random (MCAR), missing-at-random (MAR) or not-missing-at-random (NMAR) (165). Principally, complete-case analysis is valid if missing data is MCAR (not dependent on observed or missing values) and may be biased if it is MAR (only dependent on observed variables) or MNAR (dependent on missing values) (165). For instance, nonresponse to smoking may depend on sex (dependent on *observed* values, i.e., MAR), or dependent on a specific category of smoking (dependent on the *missing* values, i.e., NMAR). Multiple imputation is a recommended method for imputing missing values and assumes that data is MAR (165,166). Briefly, multiple imputation is a statistical procedure that fills in missing values by predictive models using observed data. In order to maintain uncertainty in the imputed values, this is performed many times (typically 20–100 times), creating many datasets, which are analysed individually, and finally, the results are pooled. In Paper II, we performed multiple imputation as a sensitivity analysis due to a large number of missing data in the covariates. Continuous variables (e.g., glucose, triglycerides, WC) were imputed using predictive mean matching, dichotomous variables (e.g., stroke, angina) with logistic regression, and categorical variables with multinomial logit model (e.g., smoking) or ordered logit model (e.g., alcohol consumption, leisure-time physical activity).

The nature of the data in Paper II (that is, time-to-event) demanded appropriate regression methods that account for censoring (death or emigration), which is why we chose Cox proportional hazard regression. A main assumption of Cox is the proportional hazard assumption, which means that the independent variables should not interact with time. This was tested for and dealt with appropriately using stratification for covariates that violated the proportionality assumption. We had to overcome the potential for non-linearity in the

relationship between the continuous predictors (BMI, WC, ABSI) and mortality. Alternative solutions included categorisation of the continuous predictor or application of flexible methods such as fractional polynomials or splines. Categorising continuous predictors in regression models are not recommended due to loss of power and information (55,167). We chose restricted cubic splines as recommended by Harrell in *Regression Modelling Strategies* (167). Splines are piecewise polynomials that are connected at "knots" at specified values of the variable. Restricted cubic splines are piecewise cubic polynomials that are linear at each tail because the fit is often poor at each tail. Model fitting of restricted cubic splines is described in more detail in the paper.

We performed some additional analyses for this thesis (i.e., not published in the paper). First, we investigated how many participants had the MHO phenotype if the definition of metabolically healthy excluded *any* metabolic abnormalities, i.e., no components of MetS (in addition to no previous history of cardiometabolic disease or prescribed drugs for cardiometabolic disease, as in the definition used for the main analysis). Second, we estimated the adjusted hazard ratio (HR) of quartiles of MetS severity Z-score for all-cause and CVD mortality, using the 1st quartile of MetS severity Z-score as the reference group.

2.6 Paper III

2.6.1 Study sample and design

Paper III had a cross-sectional design and used data from SAMINOR 1 with a final study sample of 13 921 participants (Figure 5). Table 7 shows basic characteristics of the invited sample, attendees to the clinical examination, and the final analytical sample.

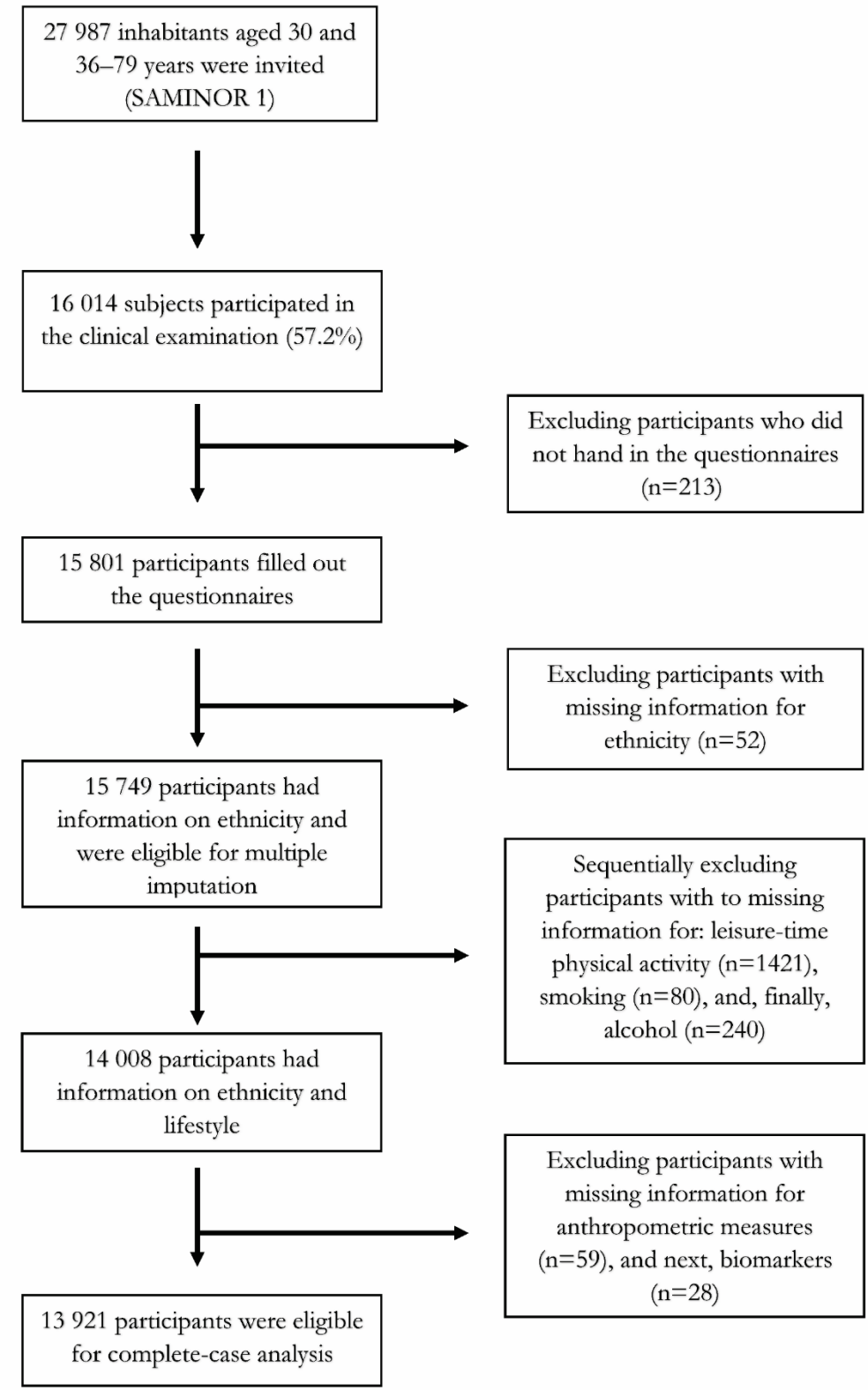

Figure 5. Flow chart for sample selection in Paper III.

Table 7. Basic characteristics of the invited sample in SAMINOR 1, attendees to the clinical examination, and the final analytical sample in Paper III and Paper IV.

	Invited	Met to clinical examination	Analytical sample Paper III	Analytical sample Paper IV
Total	27 987	16 014 (57.2%)	13 921 (49.7%)	15 717 (56.2%)
Sex				
Men	14 541 (52)	7639 (48)	6797 (48)	7504 (48)
Women	13 446 (48)	8375 (52)	7124 (52)	8213 (52)
Age				
Mean (SD)	53.4 (12.2)	54.1 (11.5)	53.5 (11.3)	54.1 (11.5)
Marital status*				
Single	7057 (25)	3144 (20)	2714 (20)	3069 (20)
Married	15 394 (55)	9937 (62)	8736 (63)	9767 (62)
Widow(er)	1826 (7)	1015 (6)	783 (6)	986 (6)
Divorced	3071 (11)	1619 (10)	1426 (10)	1600 (10)
Separated	638 (2)	299 (2)	262 (2)	295 (2)
Missing	1	0	0	0
Education (years)				
Mean (SD)		11.2 (3.9)	11.4 (3.9)	11.3 (3.9)
Missing		985	391	951
Ethnicity				
Sami		3480 (22)	3032 (22)	3470 (22)
Non-Sami		12 271 (78)	10 889 (78)	12 247 (78)
Missing		263	0	0

Categorical variables are given in frequency (percentage) and continuous variables are given in mean (standard deviation, SD). *Marital status was obtained from the national population register in SAMINOR 1. Married and same-sex partnerships were merged.

2.6.2 Statistical analysis

The statistical analysis is described step-by-step in the published paper. Details will not be repeated, but I elaborate on reasons for choosing the respective methods. We used STATA 15.1 (StataCorp, College Station, TX, USA). In Paper III, we regressed metabolic markers (continuous outcomes) on obesity measures (continuous predictors) while adjusting for relevant confounders. The primary interest was the influence of ethnicity on this relationship, and how additional adjustment for height influenced the coefficient for ethnicity. Height was relevant because obesity measures are dependent on height and the ethnic groups differ

substantially in height on a population level. Analyses were stratified by sex in models in case of evidence of effect modification by sex on obesity measures. We used regression with fractional polynomials as the method for the data analysis because the functional relationship between metabolic markers and obesity measures may not be linear, an assumption of standard linear regression. In this paper, a large number of models were fitted, which increased the risk of false positive findings. Therefore, we chose fractional polynomial regression over spline regression to reduce the risk of overfitting, which is reported to be more common in the latter method (168). Because there was a large number of missing data in the covariates, we performed multiple imputation as a sensitivity analysis (N=15 749), see description of multiple imputation in Section 2.5.2. Because maximum likelihood is not possible to use in the fractional polynomial model selection procedure with multiple imputation, we used the "mfpmi" function in STATA (169). This function utilises log-likelihood type tests. Both this technique and fractional polynomial regression are described in more detail in the published paper.

2.7 Paper IV

2.7.1 Study sample and design

Paper IV had a cross-sectional design and used data from SAMINOR 1. The final study sample comprised 15 717 participants (Figure 6). Table 7 shows basic characteristics of the invited sample, attendees to the clinical examination, and the final analytical sample.

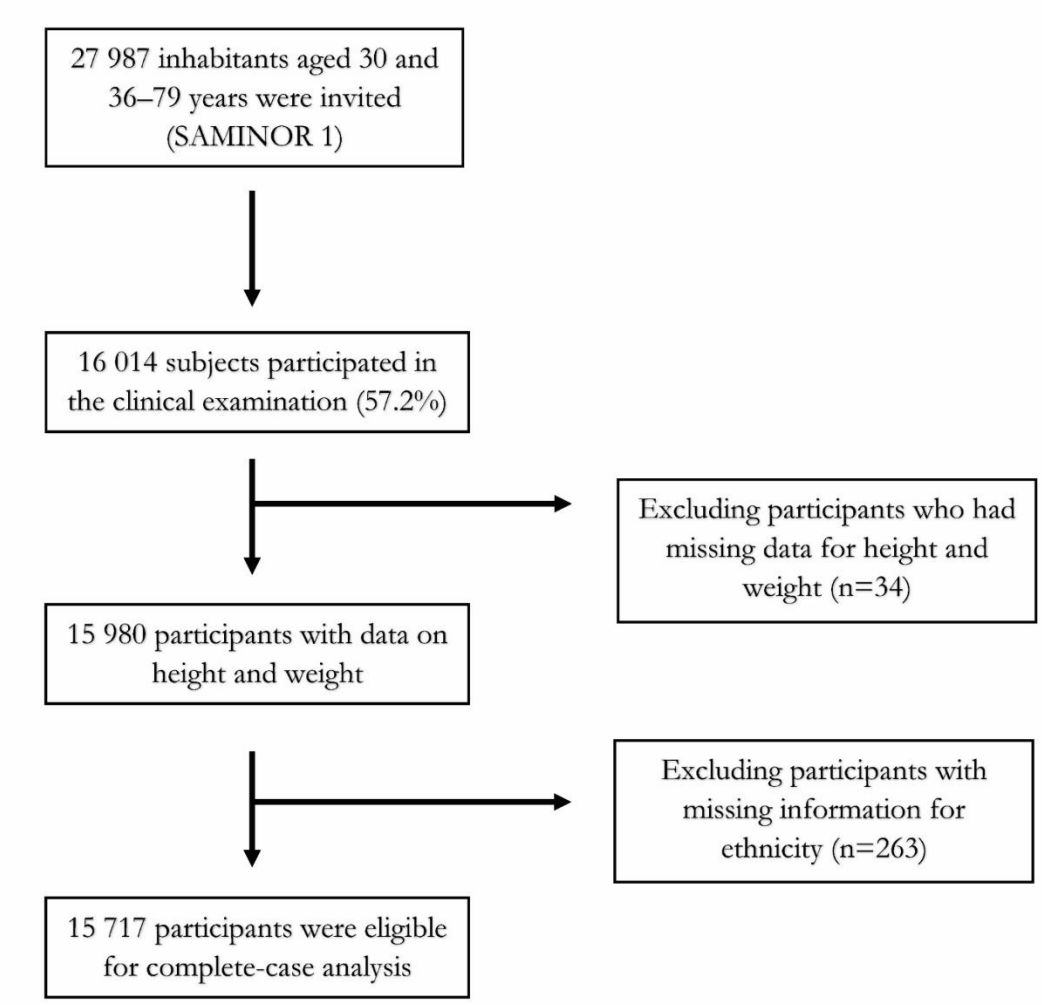

Figure 6. Flow chart for sample selection in Paper IV.

2.7.2 Statistical analysis

In Paper IV, we used *R* version 4.0.0 (R Core Team 2020, R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria, https://www.R-project.org/). We performed simple descriptive statistics with kernel density plots and scatter plots displaying the data. The main analytical part comprised log-log regression (that is, logarithmic transformation of both predictor and exposure), where log(weight) was regressed on log(height). The slope or β coefficient in this regression was then used as the power *p* in weight/height^p (Benn index). According to Benn, this index is

approximately uncorrelated with height for the given population (170). We compared means of obesity measures (BMI and Benn index) across the ethnic groups (t-test) and correlations between obesity measures and height and weight (Pearson's product-moment correlation). We examined potential interactions between *p* and sex, and *p* and ethnicity. All analyses were accordingly stratified by sex.

2.8 Ethical considerations

Written informed consent was obtained from all participants in the SAMINOR Study. The project that this thesis builds upon has been approved by the SAMINOR Project Board and The Regional Committee for Medical and Health Research Ethics (reference: 2017/1974/REK North).

Aside from the formal ethical approvals needed to perform this research, some additional considerations are discussed. The Declaration of Helsinki states that "medical research with a vulnerable group is only justified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable group. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research" (171). Ethnic minority groups, such as the Sami and Kven, may be defined as vulnerable groups. The Sami has been object to unethical research inspired by eugenics, e.g., skull measuring to prove their intellectual deficit and inferiority as a "race" (172,173). After the Second World War, the eugenics movement and the ideology of social Darwinism were defeated. Today, it is not legal to register ethnicity in national registries in Norway. Surveys intended for research may however pose questions related to ethnicity.

Ethnicity as a label of group belonging has replaced "race", its premise being that ethnic differences in health primarily is explained by social and cultural determinants (137). In this perspective, the use of ethnic labelling in research can be justified. In this thesis, we study not only the Sami, but a population in Northern and Mid Norway of which the Sami comprise approximately 20–40%, depending on the definition of ethnicity and geographical areas included (146,150). The pressing ethical question in this thesis is whether it is justifiable and necessary to disaggregate the data on ethnicity (e.g., publish prevalence of MetS separate for

Sami and non-Sami) in order to perform the research. The alternative would be to perform the research on the population as one unit, ignoring ethnicity. In 2020, the Norwegian National Human Rights Institution published a report that recommended disaggregated health statistics on Sami ethnicity from a human-rights perspective (174). However, potential risks and challenges with collecting and using Sami ethnicity for statistical purposes were discussed thoroughly, as ethnic health data may be harmful despite the human-rights benefit.

In 2019, the Sami Parliament adopted ethical guidelines for Sami health research, emphasising the importance of cultural knowledge, respect and Sami co-determination (175). No guidelines or recommendations regarding specifically how to perform statistical analysis with Sami data exists, although several international recommendations for responsible use of ethnic data have been published (142–144,176). Given the historic backdrop, modern health research that involves labelling research participants as Sami and non-Sami call for continuous re-evaluation of the ethical concerns at all research stages from design to publication.

3 Results

In this chapter, I summarise the results of the papers. Details are found in the published papers. The results of the additional analyses performed exclusively for this thesis are also provided.

3.1 Paper I

The aim of Paper I was to examine the sex- and ethnicity-specific change over time in the prevalence and severity of MetS in rural Northern Norway. Sex- and ethnicity-stratified analyses of 6308 participants in SAMINOR 1 (2003–2004) and 5866 participants in SAMINOR 2 (2012–2014) showed that the largest age-adjusted increases in MetS prevalence were found in men: from 29.9% (95% CI: 27.2–32.5) to 38.1% (35.3–40.9) in Sami and from 30.2% (28.1–32.2) to 37.7% (35.3–40.0) in non-Sami ($p<0.001$ in both). In women, the change was of smaller magnitude: from 35.2% (32.4–37.9) to 39.2% (36.5–41.9) in Sami ($p=0.019$) and from 33.5% (31.5–35.5) to 34.0% (31.8–36.1) in non-Sami ($p=0.73$). We found no evidence of effect modification by ethnicity, meaning that the change in prevalence of MetS did not differ significantly by ethnicity. Hence, despite a statistically significant increase in MetS prevalence in Sami women but not in non-Sami women, we do not have evidence to reject the null hypothesis of no difference between the two groups. To the contrary, we found evidence of an interaction with ethnicity in models with MetS severity Z-score, with slightly larger increases in Z-score for Sami than for non-Sami (p for interaction=0.024 in women and p for interaction <0.001 in men). The effect estimate was larger in men than in women.

Figure 7 shows the prevalence of MetS in SAMINOR 1 and SAMINOR 2 according to 10-year age groups and sex. Overall in women, the age-adjusted prevalence of MetS changed from 34.1% (32.5–35.7) in SAMINOR 1 to 36.0% (34.4–37.7) in SAMINOR 2 and was not statistically significant ($p=0.07$). Overall in men, the age-adjusted prevalence of MetS increased from 29.9% (28.3–31.5) to 37.8% (36.0–39.6) ($p<0.001$).

Figure 7. Sex-specific prevalence of MetS by 10-year age groups in SAMINOR 1 (2003–2004) and SAMINOR 2 (2012–2014).

The proportion fulfilling the criteria for abdominal obesity (≥80 cm in women and ≥94 cm in men) increased markedly between the surveys in all subgroups of sex and ethnicity. Figure 8 shows sex-specific kernel density distribution of WC and proportion with abdominal obesity according to the two cut-offs (see Section 2.3.2). Overall in women, the age-adjusted proportion with a WC ≥80 cm increased from 69.0% (67.3–70.6) to 88.0% (86.8–89.1) ($p<0.001$). Overall in men, the age-adjusted proportion with a WC ≥94 cm increased from 45.8% (44.0–47.6) to 70.7% (69.0–73.4) ($p<0.001$).

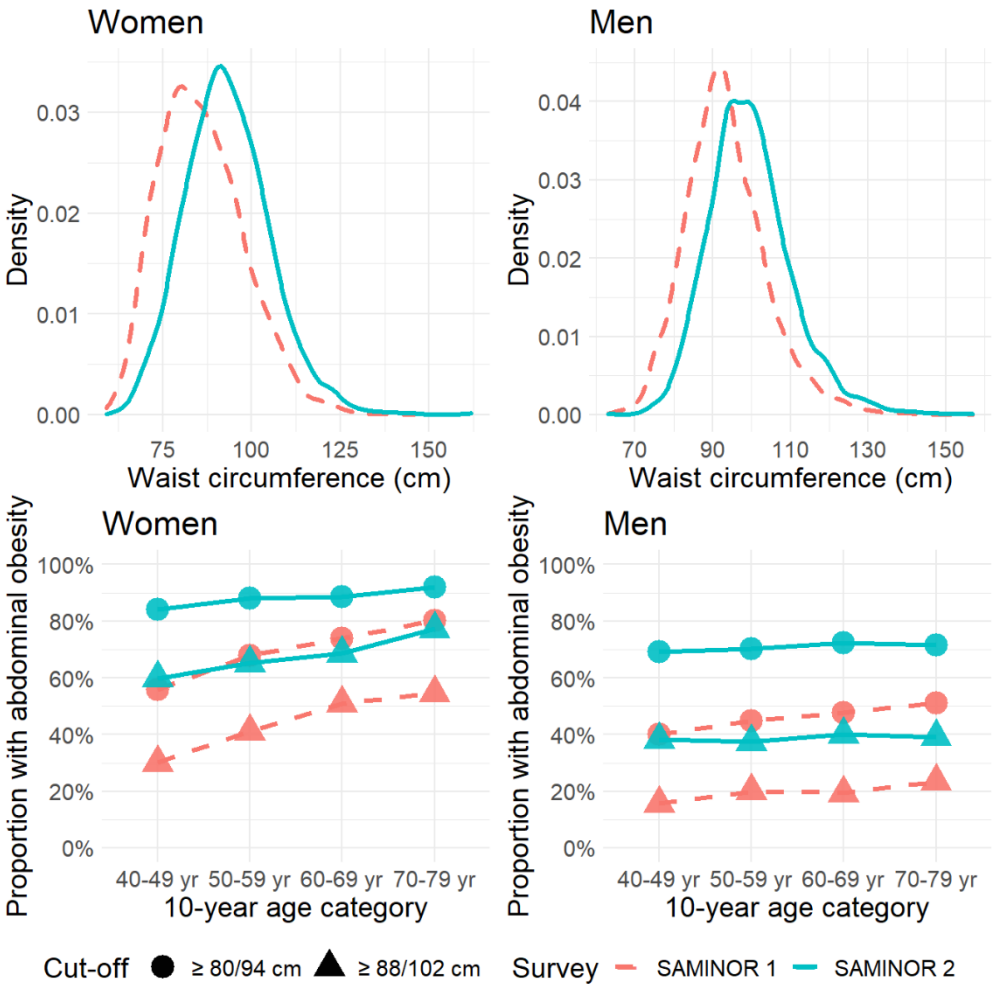

Figure 8. Sex-specific kernel density distribution of WC and proportion with abdominal obesity (both action levels, see section 2.3.2) by 10-year age categories in SAMINOR 1 (2003–2004) and SAMINOR 2 (2012–2014).

In a sensitivity analysis, the abdominal obesity component was excluded from the ATP-III-MetS definition, which left only Sami men with a minor increase in prevalence of MetS (Supplementary Table 1). Sensitivity analyses exploring alternative ethnicity categorisations (self-perceived ethnicity and count of ethnic markers) showed overall similar patterns as in the original analyses (Supplementary Table 2).

3.2 Paper II

The aim of Paper II was to examine the association between MetS and metabolic-obesity phenotypes, and all-cause and CVD mortality, and between continuous obesity measures and

all-cause and CVD mortality specifically for metabolically healthy and metabolically unhealthy participants. Analyses of 12 815 participants with complete case data from SAMINOR 1 showed that the MHO phenotype was present in 7.8% of women and 5.8% of men. Compared to the other general obesity phenotypes, the MHO phenotype had a higher proportion with Sami ethnicity. Median follow-up time was 15.3 and 15.2 years, with 596 and 938 deaths in women and men, respectively. Men and women with MetS had an approximately 50% higher 15-year risk of CVD mortality than those without MetS. We found effect modification by sex in the relationship between obesity phenotypes and CVD mortality (p=0.05 for general and p=0.02 for abdominal obesity). In women, the MHO group had an adjusted HR (95% CI) of 1.05 (0.38–2.88) for CVD mortality relative to the MHNO group. The corresponding estimate in men was 2.92 (1.71–5.01).

We found no evidence of effect modification by ethnicity defined with the subjective criteria (main analysis) or with the objective language criteria plus the subjective criteria (sensitivity analysis) (see Section 2.3.5 for details on definitions). In the main analysis, the following p-values from likelihood ratio tests were found in models of all-cause mortality: ethnicity x MetS, p=0.38; ethnicity x general obesity phenotypes, p=0.40; ethnicity x abdominal obesity phenotypes, p=0.23. In models of CVD mortality, the corresponding p-values were 0.87, 0.25, and 0.80. Ethnicity was not associated with all-cause mortality (HR 1.03 for Sami vs non-Sami, p=0.56) or to CVD mortality (HR 0.96 for Sami vs non-Sami, p=0.73). In the sensitivity analysis using an alternative ethnicity categorisation (see Section 2.3.5), the following p-values from likelihood ratio tests were found in models for all-cause mortality: ethnicity x MetS, p=0.26; ethnicity x general obesity phenotypes, p=0.17; ethnicity x abdominal obesity phenotypes, p=0.09. In models of CVD mortality, the corresponding p-values were 0.89, 0.12, and 0.69. Ethnicity was not associated with all-cause mortality (HR 1.03 for Sami vs non-Sami, p=0.60) or to CVD mortality (HR 0.98 for Sami vs non-Sami, p=0.85). Importantly, regression adjustment for ethnicity had no impact on the coefficients for the exposures in the main analysis or in the sensitivity analysis.

Restricted cubic spline regression showed curvilinear associations between BMI/WC and all-cause mortality irrespective of metabolic status and sex. Figure 9 and 10 show that

corresponding relationships with CVD mortality were linear, with differing slopes by sex and metabolic status, in women and men, respectively. In men, ABSI was linearly associated with both all-cause and CVD mortality. Figure 9 and 10 also show models not adjusting for metabolic health.

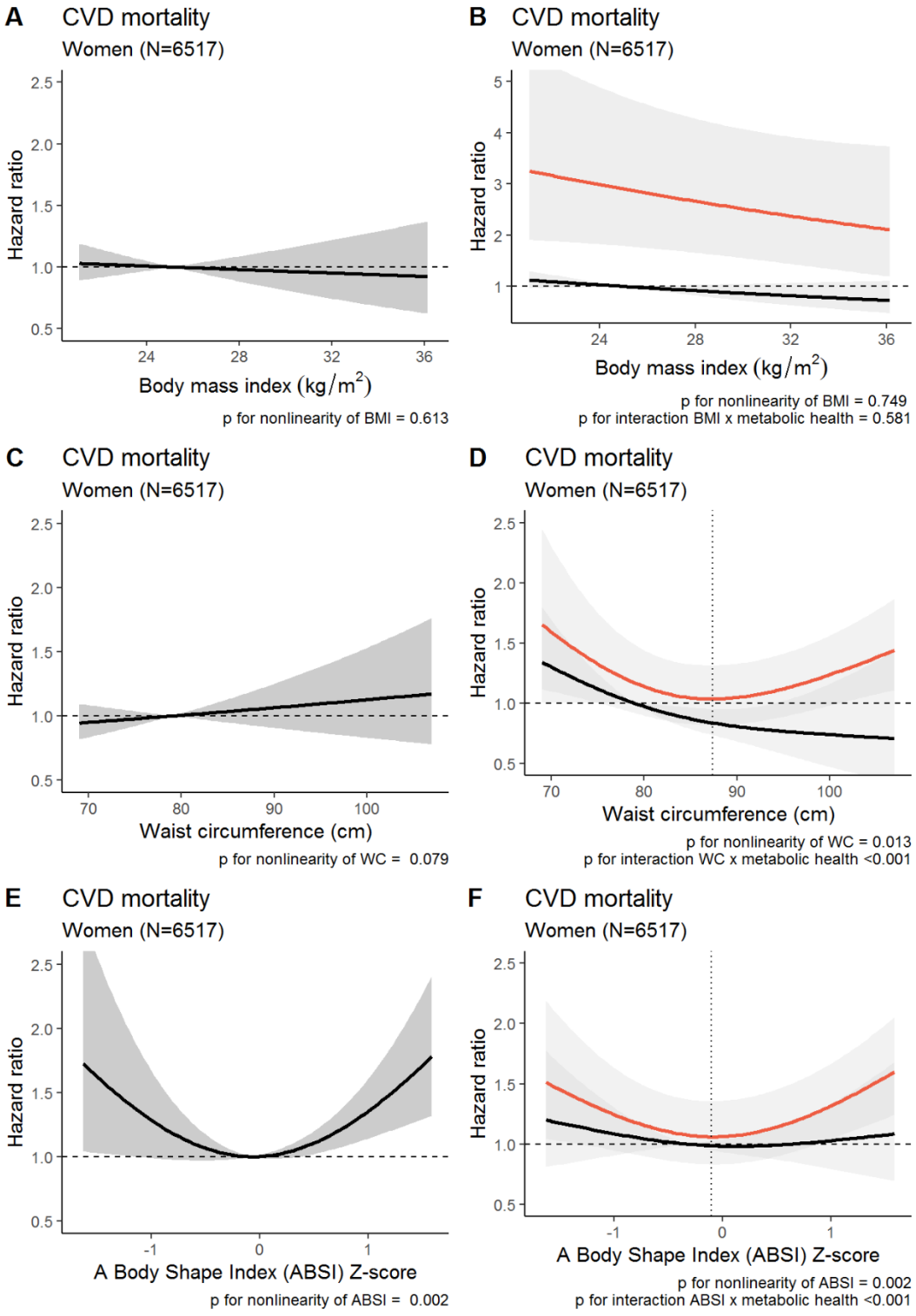

Figure 9. CVD mortality vs body mass index, waist circumference and a body shape index not adjusted for metabolic health (panels A, C and E, respectively) and according to metabolic health status (panels B, D and F, respectively, with black and red curves representing metabolically healthy and unhealthy, respectively) in 6517 women participating in SAMINOR 1 (2003–2004).

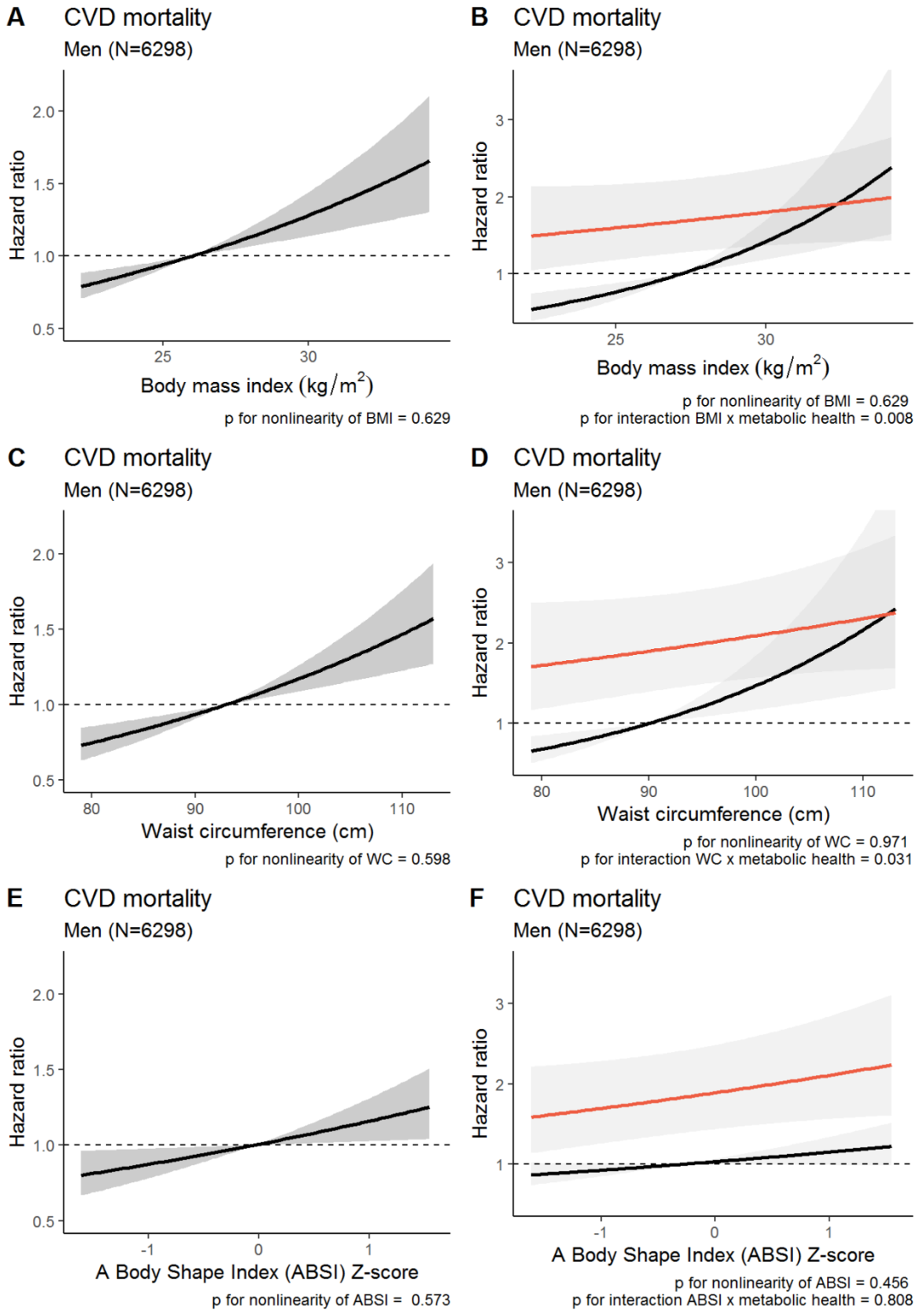

Figure 10. CVD mortality vs body mass index, waist circumference and a body shape index not adjusted for metabolic health (panels A, C and E, respectively) and according to metabolic health status (panels B, D and F, respectively, with black and red curves representing metabolically healthy and unhealthy, respectively) in 6298 men participating in SAMINOR 1 (2003–2004).

Unpublished results show that MHO, defined as general obesity without *any* metabolic abnormalities, was very uncommon in this population: 8 participants (0.1%) fulfilled the criteria. MHAO defined as abdominal obesity without *any* metabolic abnormalities was more common: 377 participants (4.1%) fulfilled the criteria. In models of MetS severity Z-score vs all-cause/CVD mortality, the 1st quartile of MetS severity Z-score was the reference group. In women, the HRs (95% CI) for all-cause mortality were 0.73 (0.58–0.94) for the 2nd quartile, 0.92 (0.72–1.16) for the 3rd quartile, and 1.15 (0.91–1.45) for the 4th quartile. Corresponding figures in men were 1.00 (0.81–1.24), 0.98 (0.80–1.22) and 1.12 (0.91–1.37), respectively. Regarding CVD mortality, the HR (95% CI) in women was 0.60 (0.36–1.03) for the 2nd quartile, 1.03 (0.64–1.66) for the 3rd quartile, and 1.30 (0.82–2.07) for the 4th quartile. Corresponding figures in men were 1.43 (0.91–2.25), 1.50 (0.96–2.33) and 2.03 (1.33–3.11). These estimates were adjusted for age, leisure-time physical activity, alcohol consumption, smoking and education.

3.3 Paper III

The aim of Paper III was to examine the influence of ethnicity on the relationships between metabolic markers and obesity measures. Analyses of 13 921 participants with complete case data from SAMINOR 1 showed that the relationships between components of MetS, i.e., metabolic markers, and obesity measures, i.e. BMI, WC and WHtR, did not differ by ethnicity (no interaction). On average, the non-Sami were approximately six cm taller than the Sami. At the same values of BMI, WC or WHtR, levels of metabolic markers differed only marginally between Sami and non-Sami. Levels of metabolic markers were in general more favourable for Sami than for non-Sami at any given BMI or WHtR, and less favourable at any given WC. However, these minute differences were mostly eliminated by height adjustment.

3.4 Paper IV

The aim of Paper IV was to examine the correlation between BMI and height, develop a height-corrected weight index in this population, and compare ethnic figures of this index. Analysis of 15 717 participants with complete case data from SAMINOR 1 showed a modest, negative correlation between BMI and height. The correlation was stronger in women than in

men. Log-log-regression gave estimates of *p* (95% CI) in Benn index (weight/height^p) of 1.29 (1.21–1.38) in women and 1.90 (1.83–1.98) in men. We found evidence of effect modification by sex, meaning that the power *p* differed between men and women (p-value for interaction <0.001). Figure 11 shows kernel density distribution of BMI and Benn index in Sami and non-Sami women and men. Mean BMI was higher in Sami vs non-Sami: 28.2 kg/m^2 vs 27.4 kg/m^2, respectively, in women (p< 0.001), and 27.8 kg/m^2 vs 27.6 kg/m^2, respectively, in men (p=0.016). However, the Benn index did not differ in Sami vs non-Sami: 38.7 kg/m$^{1.29}$ vs 38.4 kg/m$^{1.29}$, respectively, in women (p=0.164) and 29.3 kg/m$^{1.90}$ vs 29.1 kg/m$^{1.90}$, respectively, in men (p=0.114).

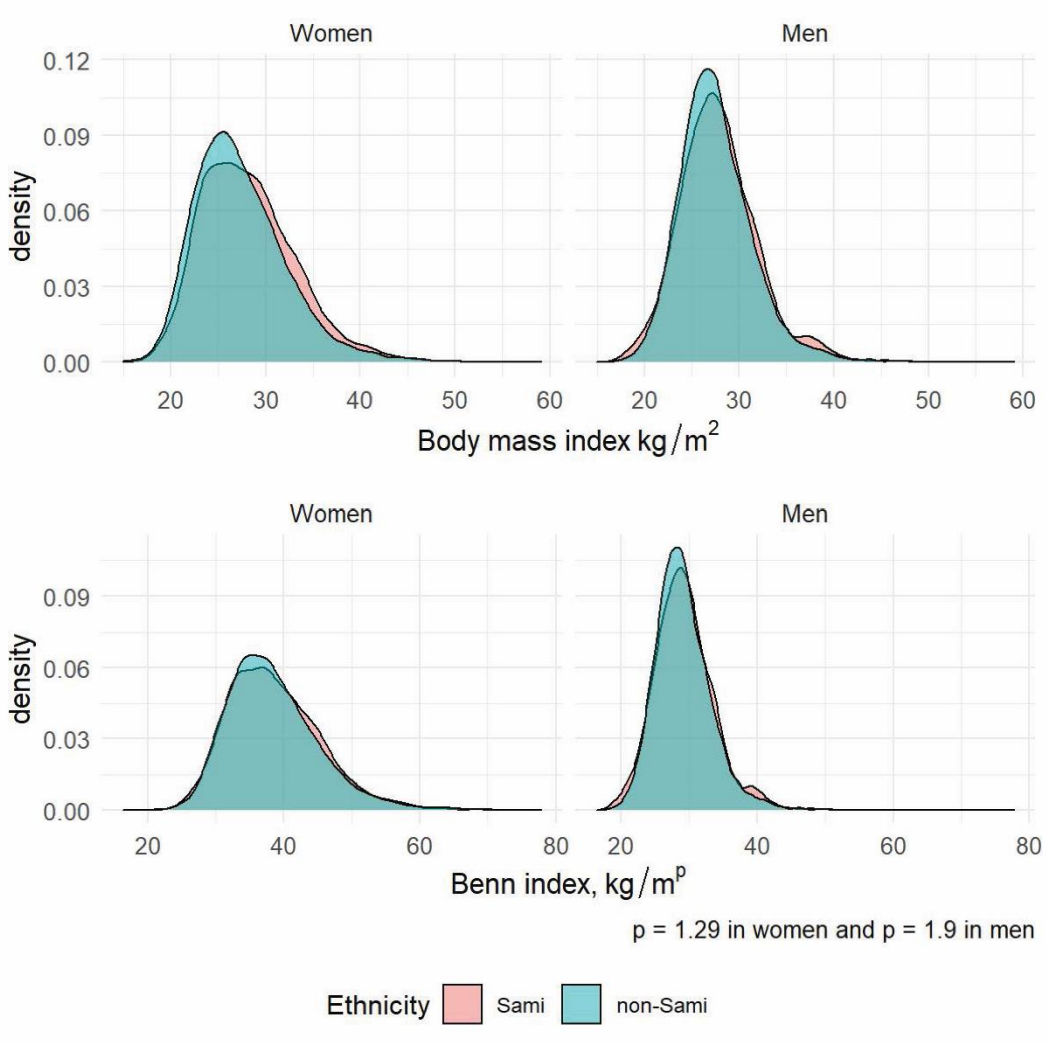

Figure 11. Kernel density distribution of body mass index and Benn index in Sami and non-Sami women and men in SAMINOR 1 (2003–2004).

4 Discussion of methods

There are many potential sources of systematic and random error that may hamper the validity of the results. The aim of epidemiology is to provide *valid* estimates of disease occurrence and of causal relationships (177). Valid estimates reflect parameters that exist outside the sample and are not distorted by systematic errors—so-called biases. "Outside the sample" refers to the source population (i.e., internal validity) or even outside the source population (i.e., external validity). The source population in this thesis is adults ageing 30 and 36/40–79 years in the 24 (or 10) municipalities in rural Northern Norway included in the surveys. Sampling variation is inevitable in sampled data and may cause random error. A valid estimate is an unbiased estimate that did not occur merely due to chance (177). For a more thorough description of the concepts involved, I refer the reader to text books in epidemiology, such as *Modern Epidemiology* by Kenneth Rothman, Sander Greenland and Timothy Lash (177).

4.1 Study design

The results of this thesis rely on observational data that are inherently prone to bias. However, due to the nature of the research questions, an experimental design was not feasible. In Paper I and IV, we examined descriptive public health questions. The research questions in Paper II and III were potentially of causal nature, but randomisation of the exposures (MetS/obesity and ethnicity) is not possible. The aim of Paper I was to provide information on temporal change in the prevalence of a public health issue. We used a repeated, cross-sectional design because we were interested in change in prevalence in the *population* in the given areas and not in *individuals*, which differentiate this design from a longitudinal design with repeated measures on all individuals. The design provides a snap-shot of the public health situation within the given geographical areas and age groups at two points in time. In Paper II, we used a longitudinal, prospective cohort design, which allows for an assessment of temporality of events and avoiding reverse causality. A limitation of this design is the lack of repeated measures of the exposures (obesity and MetS), which allowed us to evaluate the effect of exposure status at baseline only. Paper III and Paper IV were cross-sectional studies. In Paper

III, a longitudinal design would have enabled us to examine the obesity measure's predictability of future metabolic abnormalities.

4.2 Internal validity

Three main biases threaten the internal validity of observational studies: confounding, selection bias and information bias. The first two may be visualised using a directed acyclic graph (DAG), a methodology developed for causal inference (177,178). Causality is the goal of many sciences, including epidemiology (177–179). According to Rothman, a cause is a condition with two main qualities: it precedes a disease, and in its absence, the disease does not occur (at the given time point) (177). Using expert knowledge on relationships between variables, it is possible to visualise the research question using simple drawings, and from a set of mathematical rules determine which covariates to adjust for, or not, in order to obtain unbiased estimates. The word *acyclic* in directed acyclic graph means that the relationships between variables cannot include feedback-loops (an exposure cannot cause itself). Figure 12 illustrates a typical DAG.

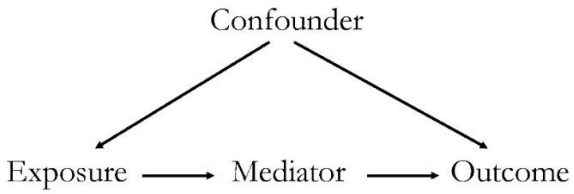

Figure 12. Illustration of a directed acyclic graph (DAG).

4.2.1 Confounding

Observational data regularly show non-causal associations between two variables, which may rise under influence from a third variable: a confounder. The distortion induced by confounding may be very large, making control for confounders an important part of observational data analysis (177). Rothman provides three criteria for a confounder: it must 1) be a risk factor for the disease, 2) be associated with the exposure, and 3) not be affected by the exposure (i.e. not a mediator, see Figure 12) or the disease (i.e. the outcome in Figure 12)

(177). Controlling for confounding may be performed in regression adjustment, stratification or restriction.

Age is a strong risk factor for disease and perhaps the most important confounder in epidemiology (177). We controlled for age in Paper I–III, but not in Paper IV. Age affects the relationship between height and weight (180), but we were not primarily interested in a perfect allometric model independent of age and other factors, but an alternative version to the BMI allowing for comparisons across a range of heights in the sample. In Paper I, we were primarily interested in a descriptive comparison between subgroups, and not necessarily interested in explaining potential ethnic differences (except for that confounded by age) and hence did not include additional confounders. Incorrect modelling of continuous confounders, such as age, e.g., assuming a linear relationship when there is a nonlinear, functional relationship, may bias the estimate (181). Therefore, we allowed for non-linearity in age in Paper II (non-parametrically using age as the time scale) and in Paper III (adding a squared term, age^2).

Residual confounding describes the situation where a confounder has been adjusted for, but some confounding is still present (177). This is typical for continuous or discrete variables that are crudely categorised, e.g., physical activity and smoking, the alternatives being e.g., total energy expenditure and pack-years. Adjustment for lifestyle confounders in Paper II had a modest effect on mortality estimates of obesity phenotypes/MetS, with an exception for smoking, which had a marked confounding effect on CVD mortality, in men particularly. The HR of MHO vs MHNO increased from 2.68 to 3.03 for CVD mortality when adjusting for smoking, reflecting on the higher proportion of current smokers in the reference group. In women, those with MHO did not have a significantly increased CVD mortality even when adjusting for confounders (unadjusted HR 1.08, smoking-adjusted HR 1.12). Several potential sources of errors were discussed in the paper. Residual confounding by smoking has been suggested a particularly important bias that may explain obesity paradoxes (132,182). The SAMINOR data included self-reported information on number of cigarettes smoked per day and years of daily smoking that could have provided better confounding adjustment. However, these variables had a large number of missing values (~60% in ever-smokers),

which indicates that the information is probably biased. Restriction may remove confounding (177). The HR for CVD mortality in women with MHO was 1.05 when adjusting for smoking, but increased to 1.48 when restricting analyses to never-smokers. A similar increase in the HR was seen in men. However, in sample sizes of 1800 men and 2400 women, the 95% CI were very wide and included the null (HR 1.0), reflecting uncertainty in the estimates. In conclusion, there was too weak evidence to reject the null-hypothesis of similar CVD mortality in MHO and MHNO. Nevertheless, this suggests residual confounding, as confounding from smoking is not possible in true never-smokers.

In reality, differentiating between confounders and mediators may be a difficult task that warrants expert knowledge in the specific field (177). The difference between a confounder and a mediator according to causal DAG theory is the direction of the arrow linking it with the exposure. In the causal relationship between exposure *X* and outcome *Y*, covariate *Z* is a confounder given

$$X \leftarrow Z \rightarrow Y$$

However, covariate *Z* is a mediator given

$$X \rightarrow Z \rightarrow Y$$

Controlling for a mediator (*Z*) may lead to biased results if the aim is to estimate the total effect of the exposure (*X*) on the outcome (*Y*). "Correct" interpretation of ethnicity in regression models may demand adjustment for mediators, depending on the research question (145). Ethnicity cannot be caused by, or temporally follow, e.g., lifestyle habits such as smoking and leisure-time physical activity (e.g., one does not become Sami by increasing physical activity). On the contrary, ethnicity may affect e.g., lifestyle habits (e.g., being a part of Sami reindeer culture increases physical activity), which may be causally related to obesity and MetS. Hence, these variables are technically mediators on the pathway between ethnicity and outcomes.

In Paper III, we estimated the "effect" of Sami ethnicity on the relationship between obesity and metabolic markers that was not confounded by nor mediated through other variables. Hence, we aimed to estimate the *direct* effect of Sami ethnicity, not the total effect (145). Reiterating, "effect" in this context refers to the regression coefficient and not a causal effect, because ethnicity is principally used as a proxy variable in epidemiology (see Section 1.2.2). Sophisticated methods such as mediation analysis may be used to quantify how much of the effect of ethnicity is mediated through certain variables, i.e., the *indirect* effect. However, we were not interested in the indirect effect. Some argue that including mediators in the model may suffice to estimate the direct effect of ethnicity (145). On the contrary, adjustment for mediators may induce bias, e.g., from unmeasured confounders between the mediator and the outcome (183). However, assessing the totality of the data and the minute effects of ethnicity in any circumstance, adjusted or not, a potential bias from mediator-adjustment is likely small in Paper III. Therefore, the application of mediation analyses would probably not have produced a different conclusion, but perhaps answered a different question.

4.2.2 Selection bias

Selection bias may hamper study validity if the selected sample used in a study differs from the source population with respect to exposures and/or outcomes (177). Selection bias typically happens at the design stage of a study, but may also be introduced through exclusion of participants, loss-to-follow-up, and adjustment or stratification on variables.

"Healthy participation bias" describes the situation when respondents are healthier, e.g., live longer and have fewer diseases, than nonrespondents. This has been reported in the US National Health Interview Survey (184) and the HUNT Study (185). The latter is a large population-based health survey in Trøndelag County (formerly Nord-Trøndelag County), which is a county in Mid Norway and partly overlaps with the southernmost areas in SAMINOR 1. In SAMINOR 1, the response rate (or proportion, technically) was 60.6% (146). The response was lower in SAMINOR 2 (48.2% response rate) (150). No studies have evaluated non-response bias in the SAMINOR Study, but given knowledge from other similar surveys it is probably present. As seen in Table 5–7 in Section 2, the invited samples had lower mean ages, higher proportions of men, and higher proportions of single/unmarried

people than those that attended the clinical examination. This suggests that non-responders were younger, more often men and unmarried compared to responders.

Collider bias (or collider stratification bias) is a special type of selection bias that may be introduced by design or analysis (186). It may cause biased prevalence estimates and may distort associations between variables, particularly between two traits that both cause selection into a study (186). Technically, a collider is a variable that is a common cause of two or more exposures, as illustrated below:

$$X \rightarrow Y \leftarrow Z$$

Conditioning on the collider *Y*, either through selection, stratification or regression adjustment, may open a non-causal pathway between the two exposures *X* and *Z* and create a spurious association (187). The bias may cause a positive, negative or absent association between *X* and *Z*. If there is no association between *X* and *Z*, an association may be created; if there is an association between *X* and *Z*, it may be changed (187). If *X* and *Z* both have either positive or negative effect on *Y*, then conditioning on *Y* will typically create a negative association between *X* and *Z*. If *X* and *Z* have different effects on *Y*, conditioning on *Y* will typically create a positive association between *X* and *Z* (187). Collider bias was mentioned in Paper II and is described in further detail in Section 5.3.

Collider bias may be induced by design. The SAMINOR Study has had a strong Sami profile in the media and is led by a Sami research centre (Centre for Sami Health Research). Assuming this has motivated people with Sami ethnicity particularly to participate, or even discouraged people who do not have Sami ethnicity from participation, this may have induced collider bias in the surveys if healthy participation bias is also present:

Ethnicity → Participation in the SAMINOR Study ← Health status

Given that the DAG above is true, by using SAMINOR data we are conditioning on a collider. Given that Sami ethnicity and being healthy both are positively associated with participation in SAMINOR, a negative association between the two may arise due to collier

bias. That is, the data may show that Sami have poorer health than non-Sami. This could in theory explain the modest ethnic differences in MetS found in Paper I. However, it may be argued that Sami people are less willing to participate because of e.g., mistrust towards researchers due to the collective memory of past assimilation policy and unethical research. This may have induced a positive association between Sami ethnicity and health, meaning that the ethnic differences in MetS may be larger than what was shown in Paper I. Descriptive statistics (means, proportions, rates) may be adjusted e.g., using weights to control for under- or overrepresentation of Sami in the sample, but this demands knowledge of the number of Sami people in the population. However, this size is unknown.

Missing data, i.e., non-response to survey items, is not technically a selection bias, but if reasons for non-response is informative it may induce selection bias. The easiest way to handle missing data is to exclude participants that lack information on items, that is, to perform a complete-case analysis (177). This reduces statistical power, and may cause severe bias if participants with missing data differ from participants with complete-case data. In Paper I and Paper IV the exclusion of missing data was negligible (<5%). In the main analysis in Paper III, we ad hoc imputed responses that were missing for drug and diabetes questions by recoding missing to no-use/disease free, based on an assumption that those who did not reply these did so because the questions were not relevant. Although frequently used in epidemiologic analysis, this method lacks scientific validity and may have caused bias. As shown in Paper II, most participants with missing data for drug and disease questions were categorised as metabolically unhealthy by other determinants, which indicates that the assumption made in Paper III may be wrong. We showed in Paper II that those with missing data were older, had higher proportion of women, had higher mortality, and a higher proportion of metabolically unhealthy phenotypes (MUNO and MUO), indicating that missing data was dependent on variables in the data (i.e., MAR). Therefore, in both Paper II and III, we performed multiple imputation of missing data as a sensitivity analysis. The results did not differ substantially compared to the complete-case analysis. Therefore, if there was any bias present it was small in magnitude. Alternatively, the mechanism of missing data was NMAR, making the imputed models wrong. However, it is impossible to know which of the two alternatives is correct.

Loss-to-follow-up in longitudinal studies may also induce selection bias, if reasons for drop-out is informative (dependent on exposure, particularly) (177). Paper II had a longitudinal design with linkage to the Norwegian Cause of Death Registry, which has >98% coverage (161). The registry does not cover those who have emigrated, which is why we censored participants who emigrated at some point during the follow up, using official emigration records from Statistics Norway. If emigration was related to the exposure, it could have caused bias, however, we have no reason to believe emigration was related to obesity phenotypes. Only 48 participants in the analytical sample of 12 815 participants emigrated during the follow-up period. In conclusion, we do not believe that loss-to-follow-up and censoring have created any bias in Paper II.

4.2.3 Information bias

Information bias describes the distortion that occurs due to errors in measurement or estimation of information (177). Measurement error of discrete variables is termed misclassification. The direction of the bias depends on whether it is differential or non-differential. Differential misclassification occurs when the misclassification is dependent on the actual values of the variable, whereas non-differential misclassification is not dependent on the values of the variable (177). Non-differential misclassification usually biases the results toward the null ("no effect"), whereas differential misclassification may over- or underestimate effects.

In this thesis, misclassification is probably present to some degree in most variables due to information gathering through self-reported questionnaires. The self-reported questions regarding heart attack (188), stroke (188) and leisure-time physical activity (189) are the only questionnaire variables used in this thesis that have been validated against objective measures. Misclassification of confounders typically give rise to residual confounding (177), and was discussed in detail with regards to smoking status in Section 4.2.1. Misclassification of exposures or outcomes is most crucial and may happen if a participant with MetS or obesity gets labelled as not having MetS or obesity, or if a Sami participant gets labelled as non-Sami. When evaluating potential misclassification of MetS and ethnicity, it becomes clear that the ontology of both may be questioned. Section 1.1.4 was dedicated to criticism of MetS, with

the lack of an underlying unifying entity as one major criticism. Assuming there exists no single entity of MetS, misclassification clearly becomes a major bias. Even if there is a single biological entity underlying MetS, the arbitrary cut-offs probably misclassify people.

Each MetS component has a cut-off designed to capture a more-or-less defined biological entity. Misclassification may be present in blood biomarkers particularly due to the non-fasting state of the blood samples. HDL cholesterol varies minimally according to fasting stage (190,191). Triglycerides may change up to 20% after a meal (190) and maximally increase by 0.3 mmol/L in non-fasting state (191). According to the Third Report of the NCEP-ATP III, "borderline high" triglycerides are present at ≥1.7 mmol/L and "high" triglycerides at ≥2.1 mmol/L (23). It is likely that some participants had higher triglycerides than they would have had in a fasting state. Differential misclassification is present if people with normal triglycerides were categorised with elevated triglycerides. Therefore, an alternative cut-off (≥2.1 mmol/L) was applied in sensitivity analyses in Paper I and Paper II. This reduced the prevalence of MetS by 5–10% depending on subgroup and survey, but it did not change the final conclusion of the study.

As described in detail in Section 1.1.7, blood glucose levels are highly dependent on time since last meal. We could not apply the cut-off for fasting glucose at 5.6 mmol/L, as this would have grossly misclassified people with normal glucose metabolism as abnormal. There are no valid cut-offs for random glucose. Alternative measures such as simply fasting glucose, HbA1c (glycated haemoglobin, reflects 6–12 week average glucose) or a 2-hour oral glucose tolerance test (diagnostic of impaired glucose tolerance) would have provided better information on prediabetic glucose levels. We chose a cut-off for random glucose at ≥7.8 mmol/L, which is the cut-off for prediabetes after a 2-hour oral glucose tolerance test. However, depending on time since last meal, this may misclassify participants in both directions. In SAMINOR 2, we had information on HbA1c, but could not use it in the analyses due to the need for comparability with SAMINOR 1. However, for the purpose of assessing bias in this thesis, I categorised prediabetes (a high risk category for future T2DM) according to both HbA1c (≥6.0%) (162) and random glucose (≥7.8 mmol/L) in the analytical sample from SAMINOR 2 used in Paper I (5866 participants). However, 742 participants

with diabetes (defined as self-reported or HbA1c ≥6.5%) were removed. Results are shown below in a cross-table (Table 8).

Table 8. Cross-table of prediabetes defined according to Hb1Ac and random glucose in 5124 participants free from diabetes in SAMINOR 2 (2012–2014)

		Random glucose (mmol/L)	
		<7.8	*≥7.8*
HbA1c (%)	*<6.0*	4480	73
	≥6.0	539	32

Of 571 participants classified as prediabetic by HbA1c, only 32 (5.6%) participants were classified as prediabetic by random glucose, indicating an extremely low sensitivity. To the contrary, of 105 participants classified as prediabetic by random glucose, 32 (30.5 %) participants actually had prediabetes according to the HbA1c test, indicating a very low positive predictive value. However, these statements assume HbA1c is the gold standard for diagnosing prediabetes, and that prediabetes is the diagnostic aim with respect to the glucose cut-off used in the MetS definition. Because prediabetes (and T2DM) are heterogeneous conditions with varying degrees of insulin resistance and β-cell failure, fasting glucose, 2-hour oral glucose tolerance test and HbA1c will most likely identify different pathologies (192). An alternative cut-off for random glucose is ≥11.1 mmol/L, which per definition is T2DM if present together with T2DM symptoms (e.g., polydipsia, polyuria, weight loss) (160,162). In Paper I and Paper II, we performed a sensitivity analysis using this cut-off. The resulting prevalence of MetS was approximately 0.5 percentage points lower than that defined using 7.8 mmol/L as cut-off for glucose.

Obesity is typically referred to as a category or dichotomy (109,110). However, the cut-offs for BMI and WC are somewhat arbitrary. The cut-offs for BMI stem from visual inspection of mortality vs BMI (109). The cut-offs for the two action levels of WC (see Section 2.3.2) were determined on the basis of predicting a BMI-level of 25 kg/m^2 (cut-offs ≥80/94 cm, action level 1), and a BMI-level of 30 kg/m^2 (cut-offs ≥88/102 cm, action level 2) (193). The cut-offs for WC were later shown to predict an increased metabolic risk (action level 1) and a substantially increases metabolic risk (action level 2) (194). However, the cut-offs have not been validated against actual adiposity levels. In Paper I and Paper II, we used the cut-offs for

action level 2 in defining MetS in sensitivity analysis. In Paper I, the prevalence of MetS decreased by 5–10% using this cut-off. Sensitivity analyses in Paper II including the more conservative cut-offs for triglycerides, glucose and WC in defining MetS and obesity phenotypes showed increased mortality estimates, perhaps indicating some misclassification with regards to the underlying pathology of MetS and obesity.

Information on prescribed drugs was collected through the self-administered questionnaire containing specific questions (e.g., "do you use medications for high blood pressure?"). These variables may be susceptible to information bias if e.g., participants do not know why they use a specific drug. In Paper II and III, we included ATC-codes in the categorisation of drug use (see Section 2.3.4). Analyses of the full SAMINOR 1 data (Paper II and III had different analytical samples, hence the choice of analysing the full data), showed that this reclassified 433 "non-users" of blood pressure-lowering drug and 53 with missing data as "current users" of blood pressure-lowering drug. Similarly, we reclassified 19 and 3 participants, respectively, as "current users" of cholesterol-lowering drug, and 7 and 3 participants, respectively, as "current users" of glucose-lowering drug. Reclassification was most common for blood pressure-lowering drug likely due to the broad list of possible medications with blood pressure-lowering effects or side-effects. We did not include these ATC-codes in the categorisation of hypertension for use as a criterion in diagnosing MetS (Paper I), but we used the ATC-code-enhanced categories for determining the broad category of metabolically unhealthy (Paper II) and for confounder adjustment (Paper III). This ensured no over-diagnosis of hypertension due to drug use with minimal blood pressure effects in Paper I, but less misclassification of metabolic health in Paper II, and reduced residual confounding from prescribed drug use in Paper III.

Misclassification of ethnicity is probable, but hard to address. There may not exist strict borders between the crude dichotomies of Sami and non-Sami, as described in Section 1.2.3. As with MetS, the underlying characteristics of Sami ethnicity is undefined, or at least rarely explicitly defined. This may sound obscure because Sami (or any other ethnicity for that sake) usually have some tacit but obvious meaning in society. Society's definition of Sami ethnicity is not being challenged, but for interpretation in epidemiology, the specific characteristics of

ethnicity should be defined. The validity of a variable can be evaluated only if we know what it is intended to measure. In Section 5.5, this is being discussed in detail.

Due to previous assimilation and unethical research, answering questions about ethnicity may be traumatic, intrusive or shameful, leaving these questions unanswered or incorrectly answered. “Successful” assimilation may also have removed Sami identity from families. Therefore, people of Sami ethnicity may not report their Sami background. The misclassification would in that case be differential (Sami misclassified as non-Sami), which could either under- or overestimate effects or associations. However, there are no studies examining reasons to report or not report on ethnic background in population surveys in Northern Norway. Hence, this would be speculation.

If people with a connection to Sami ethnicity do not identify as Sami, then it may be correct to categorise them as non-Sami for research purposes. Assuming Sami ethnicity is a sociocultural determinant dependent on participation in Sami culture, misclassification bias occurs if we categorise people who do not identify with Sami culture as Sami. When defining Sami ethnicity with the most common criteria in this thesis (objective language criteria and subjective criteria, see Section 2.3.5), people are categorised as Sami if they report Sami language use in their family and their own ethnic background as Sami, yet report Norwegian as their only self-perceived ethnicity. Figure 13 shows that among 3960 participants categorised as Sami in the full SAMINOR 1 data (excluding those who failed to reply any ethnicity-related questions) using the definition above, 655 (16.5%) participants perceived themselves as Norwegian only. If these 655 participants do not participate in Sami culture, they are misclassified given that participation in Sami culture is what we intend to measure.

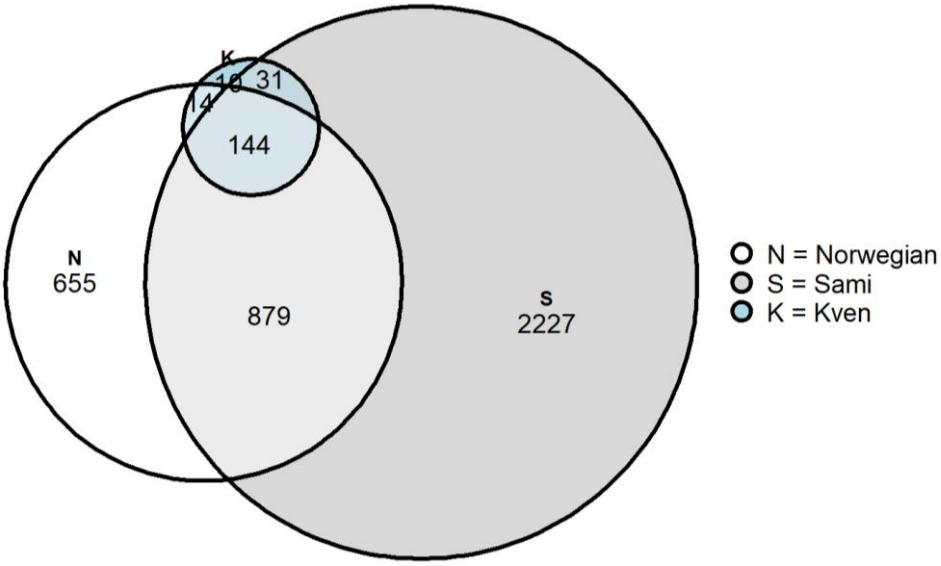

Figure 13. Self-perceived ethnicity among 3960 participants in SAMINOR 1 who were defined as Sami using the definition with an objective language criteria in addition to a subjective criterion comprising either Sami as own ethnic background or Sami as self-perceived ethnicity.

We addressed misclassification of ethnicity in several sensitivity analyses in the papers. Changing the definition of ethnicity had very little or no influence on the results. Importantly, the conclusions in the papers were not dependent on definition of ethnicity. Therefore, misclassification of ethnicity does not seem to be a substantial bias in this thesis.

Summarising this subsection on internal validity, I believe that the results of the papers have adequate validity for the source population, i.e., the included municipalities in the SAMINOR Study. The biggest threat to the internal validity, however, is probably selection bias. The ethnic comparisons seem valid, assuming participation was not dependent on ethnic belonging.

4.3 Random error

Epidemiologic studies rely on population samples, which inevitably are affected by variation (177). This sampling variation creates an unpredictable randomness to the data, which may be a source of error leading to false associations or estimates. Null hypothesis significance testing with a resulting p-value is widely used as an aid in determining whether a statistic is

compatible with the hypothesis or occurred due to chance (177), and were also extensively used throughout this thesis. Significance testing has received negative attention (177,195–197), particularly due to dichotomising results into "statistically significant" and "not statistically significant" on the basis of the arbitrary p-value cut-off of 0.05. Because the p-value is based on sample size and variance, it typically decreases with increasing sample size. In sample sizes of several thousand participants, such as in the SAMINOR Study, even small differences may become highly significant. Therefore, we put more emphasis on a qualitative evaluation of estimates, confidence limits and the totality of evidence rather than focusing on single "statistically significant" results. For instance, the single finding in Paper III showing a significantly lower systolic blood pressure in Sami than non-Sami at the same value of obesity measure, which we have no explanation for, is probably either a chance finding or a clinically insignificant finding. This is supported by the fact that all other metabolic markers were similar between the two groups.

Stratification can have a large impact on variation, efficiency and precision (177). In Paper I, we stratified "blindly" on sex and ethnicity, dividing the crude data in four groups before the analysis. This may be defended on the basis that we were in fact interested in sex- and ethnicity-specific estimates. But stratification may be a source of random error. A more sophisticated approach would be to test for e.g., interaction with sex and ethnicity, respectively, and then stratify and present data accordingly. Therefore, in Paper II–IV, we implemented this approach. In Paper II and III, we ran a very high number of models between several exposures and several outcomes, including interaction analyses and sensitivity analyses. Fractional polynomials, especially combined with testing for interactions, examines dozens of possible transformations and interactions, making multiple testing a particular relevant issue (168). This amplifies the risk of false positive findings, which may be approached with corrections of p-values (e.g., Bonferroni-correction) (198). Another recommended approach is to make careful evaluations of effect sizes and clinical significance instead of statistical significance, and make qualitative evaluations of biological/epidemiological plausibility of associations (198). We chose the latter approach, as we were first and foremost interested in directions and magnitudes of potential associations and not whether or not there was *any* association. From a sober evaluation of the ethnic

differences or associations in this thesis it is concluded that they were either clinically insignificant or possibly chance findings. This conclusion is drawn upon the inconsistent patterns, weak associations or lack of robustness when tested in sensitivity analyses.

4.4 Interaction

A statistical interaction occurs if the association between *X* and *Y* differs in strata of a third variable *Z*, often termed an effect modifier (177). We tested several different relationships for interactions with sex (Paper II–IV) and ethnicity (Paper I–IV). Presence of interactions was judged based on model comparisons with likelihood ratio tests except for in Paper I, where we used GEE regression, which is a quasi-likelihood model that is not possible to perform likelihood ratio tests on (163). Interactions in Paper I were judged based on the significance of coefficients of the interaction terms. The analyses showed that MetS development over time, obesity phenotypes vs mortality, and height vs weight interacted with sex, but not with ethnicity. We did not assess, for instance, interactions between MetS/obesity phenotypes and age with regards to mortality, which could have revealed relevant findings. However, we adhered to the project protocol which had a main focus on sex and ethnicity.

4.5 Model misspecification

The GEE regression method used in Paper I has some assumptions. Correct specification of correlation structure assumes that missing data is MCAR. However, the study was not set up as a longitudinal study aiming to interpret change in MetS in individual participants, so technically, there was no missing data. GEE was chosen to adjust for the possibly correlated observations within the same individuals (164). Misspecification of correlation structure may give biased results (163). In our data, we only had two measurements (SAMINOR 1 and SAMINOR 2), i.e., there was only one correlation for each repeated observation and therefore no need for a correlation structure, making misspecification of correlation structure not an issue (163).

In Paper II, we used Cox regression. The proportional hazard assumption was assessed using Schoenfeld residuals. Smoking status was stratified due to non-proportional hazards;

however, this had little impact on the main variable of interest (the exposure). In Paper III and IV, we relied on linear regression models, which assumes linearity of covariates, normality and homoscedasticity of residuals, and absence of collinearity. We examined all assumptions thoroughly, adding robust standard errors and transforming the dependent variables in cases of heteroscedasticity and non-normality of residuals. In Paper III, we examined departure from the linearity assumption between independent and dependent variables by applying fractional polynomials to the continuous predictors. Likewise, in Paper II we handled non-linearity with restricted cubic splines.

4.6 External validity

Results with external validity are generalisable, meaning they are valid for people outside the source population. In Paper I, Paper III and Paper IV, there was a specific focus on evaluating some aspect of Sami ethnicity. The geographical areas included in Paper I, Paper III and Paper IV differed. Only 10 of the total 24 municipalities were included in Paper I, whereas Paper II and Paper III included all 24 municipalities. If the results are externally valid, it means that the results relating to Sami ethnicity can be generalised to people with Sami ethnicity outside of the regions included in the analysis, e.g., Sami in Norway or Sami in Sweden, Finland or Russia. There are many undefined factors related to Sami ethnicity, i.e., environmental and sociocultural determinants of health, and these probably vary within the whole Sami population and between regions and countries that differ in culture, access to health care, ethnic discrimination, climate etc. In conclusion, the results of Paper I, III and IV are not generalisable for the whole Sami population.

In Paper II, ethnicity was neither an effect modifier nor a confounder of the MetS/obesity phenotypes-mortality relationship, such that the analysis was based on the population as a whole. In “Modern Epidemiology”, Rothman, Greenland and Lash, discuss scientific generalisability as an extension of external validity to a target population, i.e., as generalised scientific statements about cause and effect (177). They argue that causal questions do not need a representative sample in order to be generalizable; further, representativeness may actually hamper internal validity e.g., through poor confounder control (177). The question of external validity in Paper II may therefore relate to whether the causal effect of MetS/obesity

on mortality is valid in a broader sense, not necessarily whether the population sample is representative of other target populations. For instance, residual confounding by smoking is probably hampering the internal validity of the estimates (for women, particularly). The restricted sample of never-smokers are not representative of any real population, but the estimates in this sample may nevertheless be the most valid and generalisable with regards to the cause-effect estimates.

5 Discussion of results

5.1 Summary of results

We found an overall increasing prevalence of MetS over ten years in selected municipalities in rural Northern Norway, particularly among men (Paper I). Ethnic differences were absent or of insignificant magnitude. The increase in prevalence of MetS was driven primarily by increases in the proportion with abdominal obesity. Further, we found that MetS increased the 15-year CVD mortality by 50% in this population (Paper II). Men with MHO had increased CVD mortality compared to men with MHNO, whereas women with MHO did not have increased CVD mortality. The relationships between all-cause/CVD mortality and BMI/WC/ABSI differed by sex and metabolic health status. Ethnicity did not influence these relationships. We did not find evidence of ethnic-specific relationships between metabolic markers and obesity measures (Paper III). However, we show very marginal differences in levels of metabolic markers at the same values of obesity measures, which were eliminated by height-adjustment. Further, we found that comparisons of BMI in Sami vs non-Sami give biased estimates due to the negative correlation between height and BMI, particularly in women (Paper IV). A sample-derived weight-for-height index (Benn index) did not differ between Sami and non-Sami.

5.2 Epidemiology of MetS

In Paper I, we discussed the development of MetS in perspective of international and local trends. We commented on the confusion that exists in epidemiologic studies when using various definitions, cut-offs, fasting vs non-fasting blood samples and methods for age correction. Reiterating from Chapter 1, abdominal obesity plus 2 or more other components must be fulfilled to get a diagnosis of MetS according to the IDF definition. Broderstad et al. showed that the crude point-prevalence of IDF-defined MetS in SAMINOR 1 (2003–2004) was 27.5% in men and 29.5% in women (46). Overall, the IDF-defined prevalence of MetS did not differ between the ethnic groups when accounting for age by stratification, albeit with some differences in some age groups (46). However, these findings followed no consistent pattern. The prevalence of IDF-defined MetS was somewhat lower than the ATP-defined

prevalence of MetS in the same data from Paper I. A comparison cannot be made, however, as the previous study included all 24 municipalities in SAMINOR 1 (46), whereas we only included the 10 municipalities that overlapped with SAMINOR 2.

A major weakness with most of the continuous scores developed for MetS is that they are sample-derived, including the MetS severity Z-score. Hence, the validity of the scores across different cohorts and populations is questionable and the interpretation is not necessarily useful. For instance, the mean MetS severity Z-score in Sami men in 2012–2014 was 0.50. That is, Sami men had on average a MetS severity Z-score that was half a standard deviation higher than the mean among adult U.S. men (20–64 years) in the NHANES cohort (1999–2010) (58). This is not immediately useful information. Further, the Z-score was developed on fasting blood samples, whereas the SAMINOR Study only provided non-fasting blood samples. Importantly, it was developed based on the clustering of the MetS components, as opposed to predictive capabilities of future outcomes. Nevertheless, promising studies show that the Z-score is independently associated with future T2DM and coronary heart disease in U.S. cohorts (82,83). In this thesis, we found that MetS severity Z-score and 15-year CVD mortality was not significantly associated in women in rural Northern Norway, but they were associated in men: a Z-score in the 4th quartile was associated with twice as high CVD mortality as a Z-score in the 1st quartile.

In Paper I, Sami of both sexes had a statistically larger increase in MetS severity Z-score from the first to the second survey compared to the non-Sami. Sami women had a 0.03 standard deviation higher increase in Z-score than non-Sami; the corresponding figure in men was 0.14. Given the very small difference in absolute terms, in women particularly, and poor predictive capabilities for CVD mortality, it is highly unlikely a difference relevant for public health. In addition, the result was sensitive to alterations in the ethnic categorisation. In Paper I, we speculated whether the findings in men could confer clinical/public health relevance. Although the Z-score was predictive of future CVD mortality, 0.14 standard deviation is a very small difference, with unclear implications. Previous works do not show substantial ethnic differences in cardiometabolic diseases comparing Sami and non-Sami (152–157).

Combining all available information, there is no convincing evidence of differences in prevalence and severity of MetS between Sami and non-Sami in Northern Norway.

We show that the overall prevalence of MetS has increased over time, and in men particularly. Sex differences in MetS are known and relate to both biological (e.g., hormones) and sociocultural factors (e.g., lifestyle) (40). As discussed in Paper I, rural Northern Norway seems to have a higher MetS prevalence than that found in the city of Tromsø in Northern Norway, the largest city in the region. In a recent study, the prevalence of ATP-III defined MetS varied between 22% and 25% from 1994 to 2016 in Tromsø (199). This study used HbA1c ≥6.5% (i.e., diagnostic of T2DM) as the glucose component and ≥88/102 cm in women/men as cut-offs for WC. As mentioned in Section 4.2.3, applying a glucose cut-off diagnostic of T2DM changed the prevalence of MetS by only 0.5%. As shown in Paper I, applying ≥88/102 cm in women/men as cut-offs for WC gave a prevalence of approximately 30% in 2012–2014, which is higher than that found in the new study from Tromsø. In Paper II, we found that MetS increased the CVD mortality by approximately 50% in both women and men. There was no effect modification by ethnicity and adjustment for ethnicity did not influence the regression coefficient. Hence, existing evidence suggests that future epidemiology in Northern Norway should focus on sex and urban-rural differences in MetS.

The association between MetS and mortality was weaker than that found in a previous meta-analysis of 87 studies on MetS and mortality (10). MetS is still a controversial concept (50). It should not replace national 10-year CVD absolute risk assessment tools. However, MetS is a phenotype that is easy to detect and that is predictive of *both* T2DM and CVD, and a plethora of other conditions. As mentioned in Chapter 1, the Endocrine Society recently provided a slightly modified version of the ATP-definition for what they named "elevated metabolic risk" (74). The guideline suggests that people with elevated metabolic risk should improve their lifestyle and go through an assessment for absolute CVD risk using national risk calculators. In Norway, the NORRISK2 calculator for fatal and non-fatal acute cerebral stroke and myocardial infarction would be appropriate for such assessments (200). In 2012–2014, more than a third of men and women ageing 40–79 years in ten rural municipalities in

Northern Norway had MetS and were thus in need of NORRISK2 assessment and lifestyle improvements. This knowledge may interest local public health officials.

5.3 Metabolically healthy obesity

In Paper II, a third of participants with obesity and 6–8% of all participants from SAMINOR 1 (including 24 municipalities in rural Northern Norway) were defined as MHO, which is somewhat higher than most prevalence figures found in a collaborative study from ten European countries (201). However, this study used a different definition of metabolic health. Higher proportions of women than men had MHO, consistent with previous findings (201). In a thorough review, Smith argues that very few people with obesity are truly metabolically healthy (131). In SAMINOR 1, nearly no one (0.1%) could be classified as MHO when we used a very strict definition of metabolic health—that is, obesity without *any* MetS components (in addition to the absence of known cardiometabolic disease or prescribed drugs). Evidently, a strict MHO phenotype is rare. Several prospective studies with follow-up time spanning several decades provide strong evidence that longer duration with obesity increases the risk of MetS and transition from MHO to MUO (202–207). Preventing a transition to metabolically unhealthy in people with obesity is clearly important with respect to future disease and premature mortality prevention.

Approximately 25% of women and 29% of men were defined as MUNO. People with normal weight, yet metabolically unhealthy, are often characterised by visceral adipose tissue, ectopic fat, inflammation and low skeletal muscle mass (208). The phenotype is somewhat underappreciated, but not benign. Men with MUNO had a HR of 2.1 for CVD mortality. In women with MUNO, the HR for CVD mortality was 2.8, which is in stark contrast to the HR of 1.05 for women with MHO. Even in never-smoking women (where confounding from smoking is removed), the HR for CVD mortality was almost twice in MUNO compared to MHO (2.8 vs 1.5). In accordance with previous findings, there is not much evidence supporting normal weight, or lack of obesity, as a marker of good metabolic health (96,208). The public health implication of this is that even people who are not visibly obese may nonetheless be “metabolically obese”. In rural Northern Norway, this may be true for more than a third of the adult population.

We showed how, in men at least, BMI, WC and ABSI increased CVD mortality linearly through their whole range of values with no indications of inflexion points. Interestingly, the results for BMI and WC depended on metabolic health status, with steeper slopes in metabolically healthy. This is worrying, given the large increase in proportion with abdominal obesity found in Paper I. However, the metabolically unhealthy had the highest CVD mortality regardless of BMI, WC or ABSI in both women and men. In women, modelling of the relationship between BMI, WC or ABSI and CVD mortality indicated that metabolic health, or "metabolic obesity", is more detrimental than the mere physical attributes of obesity. In models with categorical obesity phenotypes, women with MUNO and MUNAO (i.e., unhealthy non-obesity) had a HR of 2.77 and 1.86, respectively, for CVD mortality. However, compared to the BMI and WC models, the ABSI models showed that the curve was tilted upwards at the higher end of the scale. ABSI is a good predictor of mortality (113,209) and, in contrast to BMI, negatively associated with lean mass (210). In women, ABSI was the only obesity measure positively associated with CVD mortality at higher ends of the scale in models not adjusted for metabolic health (see Figure 9). Defining obesity phenotypes using the ABSI could have provided clarifying results with respect to healthy obesity. However, to date, there are no valid cut-offs for the ABSI.

The apparent benign nature of MHO in women was discussed thoroughly in the paper. In summary, there is much evidence in the literature that MHO is not benign in women, and there is a great chance that systematic or random error affected the results in this thesis. Both confounding and misclassification bias may have influenced findings, as the HR increased above 1.0 when restricting to never-smokers and when using more conservative cut-offs for WC, triglycerides and glucose. Collider bias has been suggested as a potential cause of obesity paradoxes (182,211,212), and was briefly mentioned in Paper II. In Section 4.2.2, I explained how conditioning on a common cause of two exposures may induce bias in cause-effect relationships. Cardiometabolic diseases (MetS, CVD, T2DM, etc.) have several causes, for instance obesity and genes. Theoretically, when we examine the stratum of metabolically healthy participants, the subgroup with obesity (i.e., MHO) are more likely to have protective genes than the subgroup without obesity (i.e., MHNO). In a simplified world with only two causes of cardiometabolic disease (obesity and genes), MHNO are metabolically healthy

because they do not have obesity, whereas MHO, who have obesity, must be metabolically healthy because of protective genes. Assuming that these genes are protective of both cardiometabolic disease and mortality, an apparent protective effect of obesity (i.e., MHO) occurs. Ideally, we should adjust for such other causes (e.g., genes) of the collider (e.g., cardiometabolic disease), but that is often not possible as these may be unknown or unmeasured. In practice, we may condition on a collider when we stratify by or adjust for metabolic health and thereby induce bias toward the null (i.e., no association).

This does not, however, explain why this bias possibly occurs in women but not in men. Perhaps there are strong risk factors of both cardiometabolic disease and mortality present in women but not in men. There are many known sex differences in cardiometabolic disease (213), and a recent meta-analysis showed some evidence of lower mortality in women with MHO than in men with MHO, although there were too few studies to confidently comment on the differences (125). Hence, the effect modification by sex on the risk of MHO on CVD mortality is probably real, but it is less clear whether the effect estimates and functional relationships in women are reliable or biased towards the null for reasons explained in the paper and above.

5.4 Ethnicity and obesity measures

The relationship between ethnicity and obesity is confusing. Table 2 in Section 1.1.8 displayed the different cut-offs for WC used in the MetS definition (11). Semantically speaking, ethnicity in this context is more or less synonymous with geography. The table contains ethnicities from single countries (Japan, China, Canada/USA), from larger regions (Europe, Middle East) and from continents (South America). Some of these groups are wide and unspecific, as there may be heterogeneity within the groups with respect to body composition and fat mass (100,101). WHO has called for more research as WC cut-offs should be population-specific (102). However, too specific cut-offs may not provide an added benefit, but rather add to the confusion. Previous studies in Northern Norway have raised the question whether Sami people should have specific cut-offs for WC (46,158). We did not find evidence of ethnic-specific relationships between obesity measures and metabolic markers in Sami and non-Sami (Paper III). Ethnicity is a vague concept that may entail many different

determinants of health, ranging from purely socially derived groups (e.g., based on language) to groups based on physiological characteristics (e.g., because of adaptations to the environment) (101,137). Therefore, some ethnic groups may need specific cut-offs for WC, while others do not. Use of a single cut-off across populations has many benefits, such as being able to compare figures between various populations, but there may be a trade-off with respect to predictive abilities. However, this was not an issue with Sami/non-Sami ethnicity.

In Paper III, we gained insight regarding height and its relationship with BMI in this population. Building on this insight, we found in Paper IV that the height difference between Sami and non-Sami has consequences when comparing BMI between the groups, as BMI has a weak negative correlation with height. Previous studies have found that the Sami have higher proportions of obesity than non-Sami (158,214). However, this difference may be explained by inadequacies with BMI as a population measure of relative weight. In the SAMINOR Study, there are no actual measures of body fatness (e.g., imaging with dual X-ray absorptiometry, computer tomography, or ultrasound). Measures of obesity are thus based on simple anthropometric measures of height, weight and body circumferences. These basic proxies of obesity fail to provide nuanced and detailed information on adipose tissue, which is a very complex biological organ (116). Therefore, the actual levels of body fatness are unknown in this population.

In the next section, I attempt to dissect ethnicity as an epidemiological variable. Sami ethnicity may not be one single category, but several categories, including a category of mixed ethnicity. This is probably true for many ethnicities around the world, further confusing the relationship between ethnicity and obesity. Wells recognised this problem (see Section 1.1.8) and suggested a more sophisticated model for body composition variability across all ethnicities (101). The model is based on an objectively measured body composition variable, based on e.g., fat mass, height, and birth weight among others, which would ideally capture genetic and environmental influence on adiposity and cardiometabolic risk entirely independent of ethnic belonging (101).

5.5 A critical reflection on Sami ethnicity

I find that there are three main issues with the use of Sami vs non-Sami ethnicity in population studies in rural Northern Norway. First, Sami and non-Sami are not mutually exclusive groups with respect to the underlying sociocultural determinants of health that ethnicity is intended to measure as an epidemiological variable. Second, the underlying sociocultural determinants of health underlying Sami ethnicity are rarely described in research, making interpretation of results a challenge. Third, due to the variability of the various sociocultural determinants of health within Sami people as a group, there is a large possibility of heterogeneity of risk.

Regarding the first issue, it has been shown that various aspects of Sami ethnicity (language connection, self-identification, geography) are unevenly distributed and partially overlapping (215). The choice of criteria for defining Sami ethnicity thus impacts the final group in terms of size, geography and partly characteristics such as household income and self-rated health (215). Evidently, Sami ethnicity is a heterogeneous cluster comprising several subgroups with different characteristics. Therefore, Sami and non-Sami cannot be viewed as mutually exclusive population groups. Generally speaking, the use of non-terms (e.g., non-Sami) is discouraged because non-terms are not descriptive and does not label a group with its own distinctive features (216). This can be said for the non-Sami in this thesis.

The second issue must be solved for better interpretation of results. Which sociocultural determinants of health are underlying Sami ethnicity? It may comprise exposure from a specific culture such as reindeer herding and a traditional diet comprising reindeer meat and fatty fish. Sami ethnicity correlates with geography, which is associated with distance to health services and higher education. Sami people may be exposed to ethnic discrimination and bullying (217), which may interact with e.g., geography (minority vs majority area) or use of Sami language. Sami ethnicity is associated with lower stature, as shown in this thesis. Nonetheless, all the above mentioned factors are distributed with variance within the Sami people, and may overlap with non-Sami people. For instance, only a minute fraction of Sami people is involved in traditional reindeer-herding, and there are variations in diet between and within Sami and non-Sami partly due to an interaction with geography (coastal vs inland)

(218). Hence, there is heterogeneity in the distribution of many sociocultural determinants of health when creating mutually exclusive groups for statistical analysis. As discussed in Section 4.2.3, this may hamper validity of results due to misclassification.

Finally, an overlooked issue is the potential for heterogeneity of risk *within* the Sami population. For instance, Sami people living in urban areas (e.g., the cities of Tromsø, Trondheim and Oslo), may have a different risk profile than Sami in rural areas, which may differ from Sami occupied as reindeer-herders. Theoretically, there may be larger sociocultural differences between subgroups of Sami people than between Sami and non-Sami people. The characteristics of Sami ethnicity may vary according to age, as the oldest Sami today grew up in a society where Sami culture had a completely different status than it has today (147). Further, many Sami growing up in the first half of the 20th Century were sent to boarding school as part of the assimilation process (147,219). Qualitative differences in risk profile within an ethnic group may cancel each other out, resulting in no apparent risk associated with the group. This is a real challenge for public health, as research on ethnicity needs to balance pragmatism with "truth-telling" in deciding the level of specificity for population subgroups (220).

The Sami Parliament's criteria for the electoral register have inspired the most used definition of Sami ethnicity in research the recent years (objective language criteria and subjective criteria, see Section 2.3.5). A definition that resembles the Sami community's politically accepted definition may be viewed as a strength. However, there are concerns regarding the scientific validity of ethnicity classifications that are intended for administrative purposes (139). The use of language in ethnic group labelling in Northern Norway can be traced to the National Censuses more than a century ago. However, making Sami language, which has been harshly opposed (partly successfully) by previous Governmental assimilation policies (147), an obligatory criterion in defining Sami ethnicity will exclude Sami people who lack the language connection. A recent bibliometric study showed that self-identification of ethnicity is most common in ethnicity-related health research internationally (216). It may be recommended for pragmatic and theoretical reasons (140). As discussed in Section 4.2.3, perceiving oneself as Sami may be the best way to ensure that the participant is exposed to

Sami culture, which is most often what we want to measure in epidemiologic studies of lifestyle-related diseases such as MetS. From this logic, a self-perceived ethnic categorisation may have been the better choice in this thesis, e.g., with three categories including Sami, mixed and Norwegian/non-Sami ethnicity. Having said that, sensitivity analyses showed that the different definitions of ethnicity, including self-perception, did not influence the conclusions in the studies.

In this thesis, I do not find convincing evidence of substantial influence of ethnicity on the epidemiology of MetS in the mixed-ethnic, rural population in Northern Norway. This is certainly a positive conclusion. However, ethnicity is a black box both semantically and ontologically speaking when used in epidemiology. If we do not express what we want to measure using ethnicity as a variable in epidemiologic research, we will not be able to interpret it or know for who the results are valid. Future research in this field will be challenged by finding the right level of specificity (220) and at the same time avoiding data dredging, random error and sample size issues when drawing up the borders between ethnic groups in Northern Norway.

6 Conclusion

Over a 10-year period, the age-adjusted prevalence and the severity of MetS increased in a selected area in rural Northern Norway, particularly in men. This development was not influenced by ethnicity. The increase in MetS was mainly driven by a large increase in the proportion with abdominal obesity. Over a 15-year period, people with MetS had a 50% higher CVD mortality compared to people without MetS. Approximately a third of people with obesity was defined as metabolically healthy, i.e., MHO. The CVD mortality of MHO differed by sex: men with MHO had almost three times higher CVD mortality than men with MHNO, but the corresponding figure in women showed no association with CVD mortality. Residual confounding, misclassification, and collider bias could explain the surprising finding in women. In both metabolically healthy and unhealthy men, BMI, WC and ABSI were linearly associated with CVD mortality. In both sexes, metabolically unhealthy people had the highest CVD mortality, irrespective of BMI, WC or ABSI. Ethnicity did not influence change in MetS, the mortality of MetS or obesity-metabolic phenotypes, or the relationships between metabolic risk markers and obesity measures. However, Sami and non-Sami differed in height. Because of the weak negative correlation between BMI and height, comparisons of obesity as classified by BMI is biased between Sami and non-Sami. We estimated a sample-specific height-corrected weight index (weight in kg/height in cm raised to the power of 1.29 in women and 1.90 in men) that was independent of height. This index did not differ in Sami and non-Sami, suggesting previous findings of higher obesity prevalence in Sami are invalid.

7 Public health implications and future perspectives

This thesis shows that the population in rural regions in Northern Norway have a high prevalence of MetS and one in three are in need of CVD risk assessment. This knowledge should interest local public health officials, as MetS is both preventable and treatable by changes in lifestyle. However, it should be emphasised that MetS is not a disease by itself, and it is not the case that a third of the adult population has an undiagnosed disease. MetS is a cluster of cardiometabolic risk, more or less poorly defined. But it is evident that the cardiometabolic risk burden is high in this region. Increases in BMI, WC or ABSI should be avoided. People who already have obesity should make efforts to avoid development of "metabolic obesity". Men should particularly pay attention to their lifestyle and health status. These recommendations should be followed independent of ethnicity.

Based on this thesis it is recommended that future epidemiologic research with Sami ethnicity should aim for methodological improvement of ethnic categorisation, selection, and measures of obesity. Regarding ethnic categorisation, this should be performed with the potential for heterogeneity of risk in mind. Presence of selection bias of the collider bias type could be examined for instance with a range of plausible different weights for Sami ethnicity. Future obesity research with the ethnicity-perspective in this area should aim to replicate the methods used in Paper IV or in other ways improve methods for obesity comparisons.

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Paper I

BMJ Open

Change in prevalence and severity of metabolic syndrome in the Sami and non-Sami population in rural Northern Norway using a repeated cross-sectional population-based study design: the SAMINOR Study

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ABSTRACT

Objective To examine the change in both the prevalence and severity of metabolic syndrome (MetS) in the Sami and non-Sami in Northern Norway due to a lack of knowledge regarding the development of MetS in this population.

Design Repeated cross-sectional study.

Setting The study is based on data from the SAMINOR 1 Survey (2003–2004, n=6550) and the SAMINOR 2 Clinical Survey (2012–2014, n=6004), conducted in 10 municipalities in Northern Norway.

Participants Men and women aged 40–79 years were invited. We excluded participants not handing in the questionnaire and with missing information concerning ethnicity questions or MetS risk factors resulting in a final sample of 6308 (36.0% Sami) subjects in SAMINOR 1 and 5866 (40.9% Sami) subjects in SAMINOR 2.

Outcome measures MetS prevalence was determined using the harmonised Adult Treatment Panel III (ATP-III) criteria, and severity was assessed with the MetS severity Z-score. Generalised estimating equations with an interaction term (survey × ethnicity) were used to compare prevalence and severity between the two surveys while accounting for partly repeated measurements.

Results The overall, age-standardised ATP-III-MetS prevalence was 31.2% (95% CI: 29.8 to 32.6) in SAMINOR 1 and 35.6% (95% CI: 34.0 to 37.3) in SAMINOR 2. Both the ATP-III-MetS prevalence and the mean MetS severity Z-score increased between the surveys in all subgroups, except the ATP-III-MetS prevalence in non-Sami women, which remained stable. Over time, Sami men showed a slightly larger increase in MetS severity than non-Sami men (p<0.001): the score increased by 0.20 (95% CI: 0.14 to 0.25) and 0.06 (95% CI: 0.01 to 0.10) in Sami and non-Sami men, respectively. Abdominal obesity increased markedly between the surveys in all subgroups.

Conclusion The prevalence and severity of MetS increased over time in rural Northern Norway. Abdominal obesity appeared to drive the increase in ATP-III-MetS prevalence. Sami men had a slightly larger increase in severity than non-Sami.

Strengths and limitations of this study

- This study included data from two cross-sectional surveys with acceptable attendance rates and relatively high proportions with Sami ethnicity.
- The change in metabolic syndrome (MetS) over time was examined using generalised estimating equations, thus accounting for repeated measures and obtaining population averaged regression coefficients.
- Ethnic differences were detected in MetS risk with a continuous severity score that were not detectable with the dichotomous definition of MetS.
- A wide range of sensitivity analyses with respect to the diagnostic criteria and ethnic classification were conducted to ensure the internal validity of the study.
- The results cannot be generalised to the entire Sami and non-Sami population, and we were not able to include potential confounders such as physical activity and diet.

INTRODUCTION

The co-occurrence of hypertension, abdominal obesity, impaired fasting glucose, low high-density lipoprotein (HDL) cholesterol and increased triglyceride is known as metabolic syndrome (MetS).[1] MetS is viewed as a state of excess adiposity and insulin resistance[1] that increases the risk of cardiovascular disease[2] and type 2 diabetes mellitus (T2DM).[3] The worldwide prevalence of obesity has doubled since 1980[4]; however, excess visceral adiposity is associated with cardiometabolic abnormalities in both obese and non-obese individuals.[5] Ethnic differences in body composition related to cardiometabolic abnormalities further complicate this relationship.[6] The dichotomous definition

of MetS has been criticised for being a crude marker of risk that more likely operates on a continuous scale, and for the lack of consensus regarding the ethnic-specific cut-offs for abdominal obesity.[7] Recently, Gurka *et al* constructed a sex- and ethnicity-specific continuous MetS severity Z-score[8] that predicts coronary heart disease[9] and T2DM,[10] independently of the individual MetS risk factors.

Northern Norway is inhabited by Norwegians, Sami and Kven. The Sami is an ethnic minority living in Sápmi, a settlement area covering northern parts of Norway, Sweden, Finland and Russia, and is regarded as indigenous people in Norway. The Sami culture has traditionally centred around reindeer herding, farming, fishing and hunting, but nowadays few are left in these occupations. Internationally, indigenous and minority groups have elevated prevalences of chronic lifestyle diseases compared with majority populations,[11] but little to no differences in the prevalences of cardiovascular disease and MetS (using the International Diabetes Federation definition) have been found in Sami and non-Sami in Norway.[12–14] However, recent data have shown unfavourable prevalences of obesity (women) and T2DM (women and men) among Sami when compared with non-Sami.[15 16]

We used the most up-to-date consensus definition of MetS, which is the harmonised Adult Treatment Panel-III (ATP-III) criteria,[17] in addition to the MetS severity Z-score,[8] to examine the prevalence and severity of MetS in Sami and non-Sami at two points in time and to examine whether variations in MetS prevalence and severity differed by ethnicity.

METHODS

We used data from two cross-sectional surveys of the Population-based Study on Health and Living Conditions in Regions with Sami and Norwegian Populations—The SAMINOR Study, which is run by the Centre for Sami Health Research (CSHR) at UiT The Arctic University of Norway. The first survey (SAMINOR 1) was carried out in collaboration with the National Institute of Public Health during 2003–2004 in 24 municipalities in Northern and Central Norway.[18] The SAMINOR 2 Clinical Survey (SAMINOR 2) was carried out during 2012–2014 in 10 of the municipalities included in SAMINOR 1.[19] The present analyses are restricted to these 10 municipalities.

In both surveys, all inhabitants from these 10 municipalities who (1) were registered in the National Registry and (2) aged 40–79 years were invited to participate. Of all the inhabitants invited in SAMINOR 1 (n=11 518) and SAMINOR 2 (n=12 455), 6550 (56.9%) and 6004 (48.0%) individuals, respectively, attended the clinical examination and signed an informed consent (3872 participated in both surveys). The SAMINOR Project Board and The Regional Committee for Medical and Health Research Ethics approved this study.

Patient and public involvement

During the planning of the SAMINOR Study, CSHR consulted with the Sami Parliament. In addition, researchers/health workers who are either Sami or work in Sami core areas were consulted in order to meet the needs of the Sami community. In the case of abnormal findings during the examination, participants were encouraged to visit their primary physician. We intend to report the results of this study to decision makers, regional health establishments and authorities. An important aim of CSHR has always been to give the knowledge back to the participants of the study, often through popular science forums, meetings and lectures.

Self-administered questionnaire

In both surveys, information on the duration of education (years), use of blood pressure (BP) medication (currently/previously, but not now/never), DM (yes/no), alcohol consumption, physical activity and diet was taken from a self-administered questionnaire. The questions on DM were not identical (SAMINOR 1: *Do you have or have you had diabetes?* SAMINOR 2: *Have you ever been diagnosed with diabetes (elevated blood sugar levels)?*). We did not include information on self-reported alcohol consumption, physical activity or diet in the analyses, as these questions were not similar enough for comparison.

Information on ethnic background cannot be recorded in Norwegian registries or medical records, but it can be solicited for research purposes. Three main aspects of ethnicity—language, ethnic background and self-perceived ethnicity—were explored in the questionnaire through a total of 11 questions: *What language do/did you/your mother/your father/[all 4 of] your grandparents speak at home?; What is your/your father's/your mother's ethnic background?; What do you regard yourself as?* Response options were: Norwegian, Sami, Kven or other, and participants could choose more than one answer. In order to be categorised as Sami, participants had to respond that (1) their own ethnic background or self-perceived ethnicity was Sami, and (2) the home language for at least one of their grandparents, parents or themselves was Sami. All participants who did not meet these criteria were categorised as non-Sami.

Clinical examination

Trained personnel performed all clinical measurements and blood sampling using similar procedures in both surveys. BP was taken with a Dinamap-R automatic device (Criticon, Tampa, Florida, USA) in SAMINOR 1 and a CARESCAPE V100 monitor (GE Healthcare, Milwaukee, Wisconsin, USA) in SAMINOR 2, following at least 2 min of seated rest, with participants' arms resting on a table. Three BP measurements were recorded at 1 min intervals; the average of the second and third measurements was used in the analyses. Waist circumference (WC) was recorded to the nearest centimetre at the umbilicus, with the participant standing and breathing normally. Non-fasting blood samples were drawn by venipuncture,

with participants in a seated position. In SAMINOR 1, serum was sent by mail and analysed consecutively at the Ullevål University Hospital, Oslo. In SAMINOR 2, serum was frozen on site at −20°C and sent to the biobank in Tromsø, where it was stored at −70°C and later analysed at the University Hospital of North Norway, Tromsø. Lipids and glucose were measured by an enzymatic method (Hitachi 917 autoanalyzer, Roche Diagnostic, Switzerland) in SAMINOR 1, and with a homogeneous enzymatic colorimetric method (Roche/Hitachi Cobas 8000B system, Roche Diagnostics GmbH, Mannheim, Germany) in SAMINOR 2.

Criteria for MetS

MetS was defined using the harmonised ATP-III criteria, which state that a combination of any three of the following five risk factors qualifies for a diagnosis of MetS[17]:

1. Hypertension: systolic BP ≥130 mm Hg, diastolic BP ≥85 mm Hg or current use of BP medication.
2. Abdominal obesity: WC ≥80 cm in women and ≥94 cm in men, as recommended for a European population.[5]
3. Elevated non-fasting serum glucose ≥7.8 mmol/L. We chose this cut-off as it is a proxy for pre-diabetes defined by an oral glucose tolerance test.[20] Participants with self-reported DM were also considered to have elevated glucose.
4. Reduced non-fasting serum HDL cholesterol: <1.3 mmol/L in women and <1.0 mmol/L in men.
5. Elevated non-fasting serum triglycerides ≥1.7 mmol/L.

Common approaches when estimating the severity of MetS include to simply count the number of risk factors (0–5) with levels above the cut-offs or to sum up Z-scores of the five risk factors. However, these methods do not take into account the need for different weighting of risk factors in discrete ethnic groups and the two sexes. Nor have these methods been validated regarding future disease occurrence. Therefore, we chose to estimate the severity of MetS based on an ethnicity and sex-specific, continuous Z-score (https://metscalc.org/) developed by Gurka *et al* in 2014. This score was constructed through confirmatory factor analyses to determine the weighted contribution of the five MetS risk factors to a latent MetS factor, with data from the NHANES survey on US adults aged 20–65 years.[8] The score correlates with high levels of high-sensitivity C reactive protein, uric acid and insulin resistance,[8] and predicts coronary heart disease[9] and T2DM[10] independent of its individual components. It operates like a Z-score, with mean 0 and SD 1, meaning that a score above/below 0 indicates a higher/lower severity of MetS than the average US adult aged 20–65 years. The score has been useful when applied in populations outside the USA as well.[21–23] No cut-offs are available for the score, but this is less important in our study as our intention was to compare figures in the two ethnic groups. We used the sex-specific formula for non-Hispanic-whites for both Sami and non-Sami,[8] assuming similar weighting of risk factors.

Final study sample

Of the 6550 and 6004 individuals who participated in SAMINOR 1 and SAMINOR 2, we excluded those who did not fill in the questionnaire (SAMINOR 1 n=175/SAMINOR 2 n=21); those with missing information on all ethnicity questions (n=27/n=75); and those with missing information on one or several MetS risk factors (systolic and diastolic BP, WC, glucose, HDL cholesterol and triglycerides, n=40/n=42). Thus, the final analyses included 6308 and 5866 participants, respectively. Some of these participants had missing information on education (SAMINOR 1 n=419/SAMINOR 2 n=240), use of BP medication (n=105/n=221) and DM (n=351/n=138).

Statistical analyses

All analyses were stratified by sex. Sample characteristics are presented for Sami and non-Sami participants in the two surveys; continuous variables are given as mean (SD) or median (IQR) where appropriate; categorical variables are given as numbers (percentage). In order to allow for comparison with international data, the overall prevalence for each survey was age-standardised by the direct method, using a European standard population from 2013. We compared values in the two surveys for ATP-III-MetS prevalence, MetS severity Z-score and all five MetS risk factors (seven outcomes in total) with generalised estimating equation regression models with an exchangeable working correlation matrix.[24] This method gives population averaged regression coefficients while accounting for dependencies between repeated measures, as 3110 individuals participated twice (25.5% overlapping observations). The MetS severity Z-score was log-transformed in models with a skewed distribution of the model residuals. In order to make all values positive, we added 2.5, and then transformed these using the natural logarithm. Mean Z-scores were transformed back for presentation in tables. First, in order to compare values in the two surveys among Sami and non-Sami participants separately, the models were stratified by ethnicity and run with age and survey as covariates. We calculated the age-adjusted prevalence or mean of all seven outcomes using the 'marginal' command in STATA, holding age constant at the sex-specific mean age in both surveys together (57.49 years for women, 58.15 years for men). Second, we tested whether variations in ATP-III-MetS prevalence and MetS severity Z-score differed by ethnicity, by using interaction terms (ethnicity x survey) in models that were not stratified by ethnicity. The interaction term was excluded from a model if p≥0.05. All statistical tests had a two-sided significance level of 0.05.

Sensitivity analyses

In order to avoid spurious conclusions, we performed a wide range of sensitivity analyses, as recommended in ethnic health research.[25] We repeated the analyses with

1. Alternative cut-offs for ATP-III-MetS risk factors: (1) WC ≥88 cm in women and ≥102 cm in men; (2) excluding WC, so those having ≥3 of 4 remaining risk factors

qualified as ATP-III-MetS; (3) glucose ≥11.1 mmol/L; (4) triglycerides ≥2.1 mmol/L.[26]
2. A 'healthier' sample, excluding participants that currently used BP or DM medication (tablets or insulin), or if they reported ever having had a myocardial infarction, angina pectoris or DM.
3. Two alternative measures of ethnicity: (1) answered 'Sami' on all 11 questions, answered 'Sami' on 1–10 questions, did not answer 'Sami' on any question; (2) solely based on self-perceived ethnicity.
4. Stratification by geographical regions (Inland Finnmark County, coastal Finnmark County and Troms/Nordland County).
5. Adjustment for education.

We used STATA V.15.1 for all statistical analyses. Graphics were created using the 'ggplot2' package for the open-source statistical software R V.3.4.2 (The R Foundation for Statistical Computing, URL https://www.R-project.org/).

RESULTS

The proportion of Sami in SAMINOR 1 and SAMINOR 2 was 36.0% and 40.9%, respectively. On average, the SAMINOR 2 participants were older than the SAMINOR 1 participants, had a longer education, higher prevalence of self-reported DM and larger WC (table 1).

The overall, age-standardised prevalence of MetS was 31.2% (95% confidence interval [CI]: 29.8 to 32.6) in SAMINOR 1 and 35.6% (95% CI: 34.0 to 37.3) in SAMINOR 2 (data not shown).

The age-adjusted proportion of hypertension decreased modestly from SAMINOR 1 to SAMINOR 2, whereas the proportion of abdominal obesity increased markedly in all four strata of sex and ethnicity (between +15.3 percentage points (pp) and +26.4 pp). The proportion of elevated triglycerides increased markedly among both Sami women (+4.2 pp) and men (+9.1 pp). Both ATP-III-MetS prevalence and MetS severity Z-score increased in all strata of sex and ethnicity, except for ATP-III-MetS

Table 1 Sample characteristics stratified by sex, ethnicity and survey, given in mean (SD) or n (%)

	Sami participants		Non-Sami participants	
	SAMINOR 1	SAMINOR 2	SAMINOR 1	SAMINOR 2
Women	**n=1150**	**n=1283**	**n=2176**	**n=1899**
Age (years)	55.5 (10.2)	58.5 (10.4)	56.5 (10.1)	59.1 (10.7)
Education (years)	10.8 (4.7)	12.5 (4.4)	10.9 (3.8)	12.3 (4.0)
Waist circumference (cm)	86.5 (12.0)	93.6 (12.1)	85.6 (12.0)	92.9 (12.0)
Systolic BP (mm Hg)	130.6 (21.6)	130.0 (19.3)	133.0 (20.1)	131.1 (18.6)
Diastolic BP (mm Hg)	72.7 (10.3)	71.7 (9.2)	73.0 (10.5)	72.3 (9.0)
Triglycerides (mmol/L)*	1.36 (0.98)	1.40 (0.90)	1.35 (0.92)	1.40 (0.90)
Glucose (mmol/L)*	5.29 (1.07)	5.30 (1.10)	5.29 (1.09)	5.20 (1.00)
HDL cholesterol (mmol/L)	1.45 (0.37)	1.45 (0.41)	1.49 (0.40)	1.55 (0.45)
Self-reported diabetes mellitus	53 (4.8)	104 (8.3)	113 (5.6)	156 (8.5)
Current use of BP medication	270 (23.8)	352 (28.5)	556 (26.0)	550 (30.0)
Men	**n=1118**	**n=1113**	**n=1864**	**n=1571**
Age (years)	56.3 (10.1)	59.8 (10.3)	56.4 (9.8)	60.3 (10.2)
Education (years)	10.3 (4.1)	11.4 (3.8)	10.9 (3.7)	11.8 (3.6)
Waist circumference (cm)	92.5 (10.6)	98.6 (10.6)	93.9 (10.2)	100.2 (10.7)
Systolic BP (mm Hg)	135.4 (20.0)	134.6 (18.0)	136.1 (17.6)	135.1 (17.2)
Diastolic BP (mm Hg)	78.3 (10.0)	77.0 (9.9)	78.2 (10.0)	77.8 (9.4)
Triglycerides (mmol/L)*	1.55 (1.27)	1.70 (1.20)	1.58 (1.14)	1.50 (1.10)
Glucose (mmol/L)*	5.42 (1.02)	5.40 (1.10)	5.41 (1.15)	5.40 (1.10)
HDL cholesterol (mmol/L)	1.27 (0.36)	1.23 (0.38)	1.28 (0.34)	1.28 (0.38)
Self-reported diabetes mellitus	48 (4.5)	107 (9.8)	75 (4.3)	146 (9.4)
Current use of BP medication	236 (21.5)	308 (29.0)	408 (22.3)	483 (31.9)

The SAMINOR 1 Survey (2003–2004, n = 6308) and the SAMINOR 2 Clinical Survey (2012–2014, n = 5866).
All blood samples are non-fasting. Continuous variables are given as mean (SD) unless otherwise indicated. Categorical variables are given as n (%). For some variables, the total adds up to a lower number due to missing data. The maximum number missing (n=419) was for 'education' in SAMINOR 1.
*Median (IQR) due to right-skewed data.
BP, blood pressure; HDL, high-density lipoprotein.

in non-Sami women, which remained unchanged. In absolute numbers, ATP-III-MetS prevalence increased the most among Sami and non-Sami men (+8.2 pp and +7.5 pp, respectively, p<0.001 for both), whereas MetS severity Z-score increased the most among Sami women and Sami men (+0.13 and +0.21, respectively, p<0.001 for both) (table 2).

In the models assessing whether variations in ATP-III-MetS prevalence and MetS severity Z-score between the surveys differed by ethnicity, interactions between ethnicity and survey were found for MetS severity, with Sami men having a larger increase than non-Sami men (p<0.001) (table 3). From the first to the second survey, the score increased by 0.20 (95% CI: 0.14 to 0.25) in Sami men and 0.06 (95% CI: 0.01 to 0.10) in non-Sami men (data not shown). In women, the interaction term between ethnicity and survey was also significant (p=0.024), but the difference in effect size was negligible (table 3).

Abdominal obesity increased across all age groups in all strata of sex and ethnicity between the surveys (figure 1). The MetS severity Z-score increased more in Sami men than in non-Sami men (figure 2).

Overall, sensitivity analyses, including alternative ethnic classifications, region and education, did not change the conclusions (data not shown). Results in Sami women were sensitive to alterations in cut-offs for ATP-III-MetS risk factors. Excluding abdominal obesity from the ATP-III-MetS criteria left only Sami men with a minor increase in prevalence (+3.5 pp, p=0.014) (see the online supplementary table 1). The interaction between ethnicity and survey for MetS severity was confirmed in the 'healthier' sample (in women and men) and using alternative ethnicity classifications (only in men) (data not shown).

DISCUSSION

From 2003–2004 to 2012–2014, we observed an increase in both the prevalence (based on ATP-III criteria) and the severity of MetS in rural Northern Norway. The increases in prevalence were largest in men and were confirmed by sensitivity analyses. Non-Sami women had stable measures of MetS prevalence, but a small increase in MetS severity. Sami of both sexes had a slightly larger increase in MetS severity than non-Sami; this finding was most pronounced and most robust in men. Abdominal obesity increased markedly in all strata of sex and ethnicity.

Strengths and limitations

The relatively large sample size (n=6308 and n=5866) is a strength of our study, and we had an acceptable attendance rate (54.8% and 47.1%). In general, non-attendance was high among men aged 40–49 years. We could not evaluate ethnicity-specific non-attendance rates, as national registers do not record ethnicity. Due to design issues and varying response rates across municipalities, the SAMINOR 1 sample includes a lower proportion of people from Sami majority areas in Finnmark County and a higher proportion from Northern Troms County as compared with the SAMINOR 2 sample. These different geographic and ethnic compositions challenge our ability to compare the samples, nor can we generalise the results of this study to the entire Sami and non-Sami population. Analyses of participants excluded due to missing data (n=242 in SAMINOR 1, n=138 in SAMINOR 2) revealed that they were older, had lower education and had a slightly worse cardiometabolic profile; we could not determine if this varied by ethnic belonging. An important weakness in our study is that blood samples were non-fasting, as the time schedule was distributed during the entire day. Lipid levels vary little according to fasting state, except mean triglycerides levels, which have been found to vary around 20% between different fasting states.[24] A more important issue is that using non-fasting glucose as a diagnostic tool is not valid regarding neither pre-diabetes nor diabetes. HbA1c was available in SAMINOR 2 only, such that in order for us to make comparisons between the surveys, we had to choose non-fasting glucose. Other weaknesses included self-reported DM status and drug use and the lack of socioeconomic factors other than education. However, the internal validity of this study is high. We performed a wide range of sensitivity analyses with alterations in cut-offs for MetS risk factors, restricted samples and ethnic classification. We assumed that the prevalence and severity of MetS could be defined in the same way in Sami and non-Sami, thus, our results would be invalid if these assumptions were revealed to be incorrect. Despite the limitations, we believe that we have added novel information on cardiometabolic health by utilising a MetS severity Z-score.

Comparison with other studies

The overall ATP-III-MetS prevalences we report in this study from rural Northern Norway were much higher than that reported in the sixth survey of the Tromsø Study (2007–2008, 22.6%), which sampled from an urban area in Northern Norway.[27] Thus, regional differences in MetS may be larger than ethnic differences in MetS in rural areas. Consequently, public health efforts to reduce the burden of MetS risk factors should focus more on the region than on ethnicity. The ATP-III-MetS prevalences we found were also higher than those reported in other Arctic populations, such as the Greenland Inuit,[28] the Yup'ik Eskimo[29] and indigenous Nenets women in Russia.[30] However, valid comparisons of MetS prevalences are challenging due to differences in study years, age distributions, MetS criteria and fasting versus non-fasting blood samples. Decreases in hypertension and increases in abdominal obesity have been reported both nationally and internationally.[31–33] Abdominal obesity, which appeared to be the driving force behind the increased ATP-III-MetS prevalences in our study, was present in nearly 90% of women and in more than two-thirds of men in 2012–2014. The cut-offs for waist circumference that we used are quite strict, such that we found a large proportion with abdominal obesity with only one or no

Table 2 Age-adjusted proportion or mean (95% CI) of five MetS risk factors, ATP-III MetS and MetS severity Z-score in Sami and non-Sami in the SAMINOR 1 Survey (2003–2004, n=6308) and the SAMINOR 2 Clinical Survey (2012–2014, n=5866)

	Sami participants			Non-Sami participants		
	SAMINOR 1	SAMINOR 2		SAMINOR 1	SAMINOR 2	
Women	**n=1150**	**n=1283**	**P value***	**n=2176**	**n=1899**	**P value***
Hypertension, %	60.2 (57.0 to 63.4)	54.7 (51.7 to 57.6)	0.004	64.2 (62.0 to 66.5)	57.7 (55.3 to 60.2)	<0.001
Abdominal obesity, %	73.2 (70.6 to 75.9)	88.5 (86.8 to 90.2)	<0.001	66.7 (64.7 to 68.7)	87.7 (86.2 to 89.2)	<0.001
Elevated glucose, %	7.5 (6.0 to 9.0)	8.5 (6.9 to 10.1)	0.29	8.3 (7.2 to 9.5)	8.8 (7.5 to 10.1)	0.57
Reduced HDL cholesterol, %	35.4 (32.6 to 38.1)	33.6 (31.1 to 36.1)	0.28	32.4 (30.5 to 34.4)	26.3 (24.4 to 28.3)	<0.001
Elevated triglycerides, %	35.0 (32.2 to 37.8)	39.2 (36.5 to 41.8)	0.018	31.3 (29.4 to 33.3)	32.8 (30.7 to 35.0)	0.26
ATP-III MetS, %	35.2 (32.4 to 37.9)	39.2 (36.5 to 41.9)	0.019	33.5 (31.5 to 35.5)	34.0 (31.8 to 36.1)	0.73
MetS severity Z-score, mean†	−0.01 (−0.06 to 0.03)	0.12 (0.08 to 0.17)	<0.001	−0.06 (−0.09 to −0.02)	−0.01 (−0.05 to 0.03)	0.024
Men	**n=1118**	**n=1113**		**n=1864**	**n=1571**	
Hypertension, %	69.5 (66.6 to 72.3)	63.4 (60.4 to 66.3)	0.001	72.4 (70.3 to 74.5)	67.7 (65.3 to 70.0)	0.001
Abdominal obesity, %	44.2 (41.3 to 47.1)	66.7 (64.0 to 69.4)	<0.001	46.9 (44.6 to 49.2)	73.3 (71.1 to 75.4)	<0.001
Elevated glucose, %	8.3 (6.7 to 9.9)	11.4 (9.4 to 13.3)	0.007	8.5 (7.3 to 9.8)	9.7 (8.2 to 11.2)	0.18
Reduced HDL cholesterol, %	21.1 (18.7 to 23.5)	22.6 (20.2 to 25.0)	0.33	19.6 (17.8 to 21.4)	19.6 (17.6 to 21.5)	0.97
Elevated triglycerides, %	42.5 (39.6 to 45.4)	51.6 (48.6 to 54.5)	<0.001	43.3 (40.9 to 45.5)	45.0 (42.5 to 47.5)	0.27
ATP-III MetS, %	29.9 (27.2 to 32.5)	38.1 (35.3 to 40.9)	<0.001	30.2 (28.1 to 32.2)	37.7 (35.3 to 40.0)	<0.001
MetS severity Z-score, mean	0.29 (0.24 to 0.34)	0.50 (0.45 to 0.55)	<0.001	0.31 (0.28 to 0.35)	0.37 (0.33 to 0.41)	0.036

Survey-specific proportions or means (95% CI) are age-adjusted post-estimated marginal means from GEE models, holding age constant at the sex-specific mean in both surveys together (57.49 years for women, 58.15 years for men). The GEE logistic or linear regression models were stratified by ethnicity and run with age and survey as covariates.
*P values for the survey, that is, p value for change in proportion or mean from SAMINOR 1 to SAMINOR 2.
†Geometric means due to the log-transformed outcome.
ATP-III, Adult Treatment Panel III; GEE, generalised estimating equation; HDL, high-density lipoprotein; MetS, metabolic syndrome.

Table 3 Sex-stratified GEE models examining potential interactions between survey and ethnicity for ATP-III MetS and MetS severity Z-score

	ATP-III MetS		MetS severity Z-score	
	OR (95% CI)	P value	β (95% CI)	P value
Women				
Survey				
SAMINOR 2 vs SAMINOR 1	1.08 (0.99 to 1.18)	0.095	0.02 (0.01 to 0.04)	0.010
Ethnicity				
Sami vs non-Sami	1.16 (1.03 to 1.30)	0.011	0.02 (–0.01 to 0.04)	0.14
Survey × ethnicity				
SAMINOR 2 × Sami	—		0.03 (0.00 to 0.05)	0.024
Age (per 10 years)	1.37 (1.30 to 1.45)	<0.001	0.09 (0.08 to 0.10)	<0.001
Men				
Survey				
SAMINOR 2 vs SAMINOR 1	1.43 (1.29 to 1.58)	<0.001	0.06 (0.01 to 0.10)	0.021
Ethnicity				
Sami vs non-Sami	1.00 (0.89 to 1.13)	0.95	–0.02 (–0.07 to 0.04)	0.62
Survey × ethnicity				
SAMINOR 2 × Sami	—		0.14 (0.07 to 0.21)	<0.001
Age (per 10 years)	1.06 (1.00 to 1.12)	0.034	–0.04 (–0.06 to 0.02)	0.001

We tested whether the change in ATP-III MetS and MetS severity Z-score differed by ethnicity, by using interaction terms (ethnicity × survey) in GEE logistic or linear models that included age, survey and ethnicity as covariates. Analyses were not stratified by ethnicity. The interaction term was excluded from a model if p≥0.05. In women, the MetS severity Z-score was log-transformed. When interpreting the coefficients for survey and ethnicity in the models for MetS severity Z-score, one should be aware that these must be interpreted together with the interaction term.
ATP-III, Adult Treatment Panel III; GEE, generalised estimating equation; MetS, metabolic syndrome.

additional MetS risk factors. Nevertheless, general obesity (body mass index ≥30 kg/m^2), without MetS, is known as metabolically healthy obesity and has been reported to confer significant risk of cardiovascular disease and T2DM in long-term follow-up studies.[34 35] As research has indicated that metabolically healthy obesity is an unstable condition,[36] efforts should be made to prevent weight gain and promote weight loss in all obese individuals, regardless of MetS presence.

Possible implications of ethnic differences

The ethnic differences in the change of MetS severity from 2003–2004 to 2012–2014, were more robust in men than in women. The MetS severity increased by 0.20 (95% CI: 0.14 to 0.25) in Sami men and 0.06 (95% CI: 0.01 to 0.10) in non-Sami men, which is a modest difference. However, in a longitudinal study it was shown that irrespective of baseline MetS severity Z-scores, individuals with a change of ≥0.5 in this score had an increased risk of T2DM compared with those with a change of ≤0.[10] Moreover, in a cohort study that followed nearly 300 000 individuals for 25 years, subtle elevations in metabolic risk factors (obesity, glucose and triglycerides) were observed decades before T2DM onset.[37] Thus, even minor differences may be indicative of future differences in DM. As the differences between Sami and non-Sami men are small in our study, we are reluctant to speculate in detail what the implications of the results are. But, a few previous findings are interesting in the light of our results. In 1974–1975, Sami in Finnmark County had a reduced risk of T2DM compared with non-Sami.[14] However, in 2012–2014, a study from Northern Norway, including parts of Finnmark, Troms and Nordland counties, reported that Sami had a higher prevalence of self-reported T2DM than non-Sami; this was evident in both sexes.[16] Conversely, no ethnic differences in the 10-year risk of non-fatal cardiovascular disease or self-reported myocardial infarction was found in rural Northern Norway.[12 38] In fact, both ATP-III-MetS and MetS severity Z-score have stronger associations with T2DM than with coronary heart disease.[2 3 9 10] The MetS severity Z-score has the highest factor loadings for HDL cholesterol and triglycerides,[8] which probably explains why this score increased more among Sami, as there was ethnic heterogeneity in the distribution of these two MetS risk factors. In sum, available research may indicate a more detrimental metabolic development associated with T2DM in Sami than in non-Sami men.

Possible explanations for ethnic differences

Prior to a discussion on possible explanations for the ethnic differences, we emphasise that they are quite small. In an international perspective, it is not common to observe such small differences between an indigenous population and the majority reference population. We

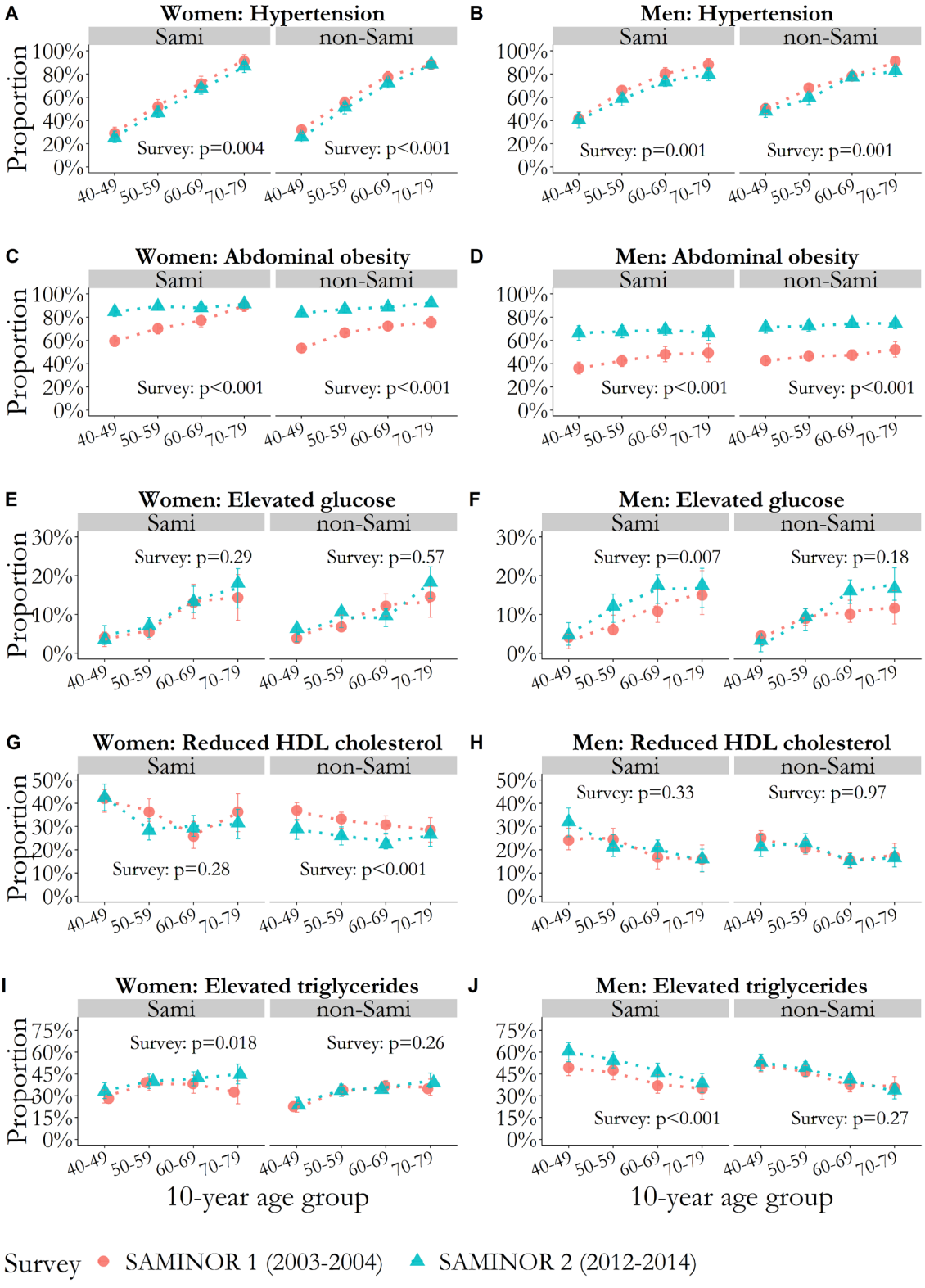

Figure 1 Proportion with values above the cut-off for each cardiometabolic risk factor comprising metabolic syndrome (A–J), per 10-year age group, with vertical error bars (95% CI). P values for the survey are age-adjusted and were obtained with GEE logistic regression. Models were stratified by sex and ethnic group. (A and B) Hypertension defined as systolic blood pressure ≥130 mm Hg, diastolic blood pressure ≥85 mm Hg or current use of blood pressure medication. (C and D) Abdominal obesity defined as waist circumference ≥80 cm in women and ≥94 cm in men. (E and F) Elevated glucose defined as glucose ≥7.8 mmol/L or self-reported diabetes mellitus. (G and H) Reduced HDL cholesterol defined as HDL cholesterol <1.3 mmol/L in women and <1.0 mmol/L in men. (I and J) Elevated triglycerides defined as triglycerides ≥1.7 mmol/L. GEE, generalised estimating equation; HDL, high-density lipoprotein.

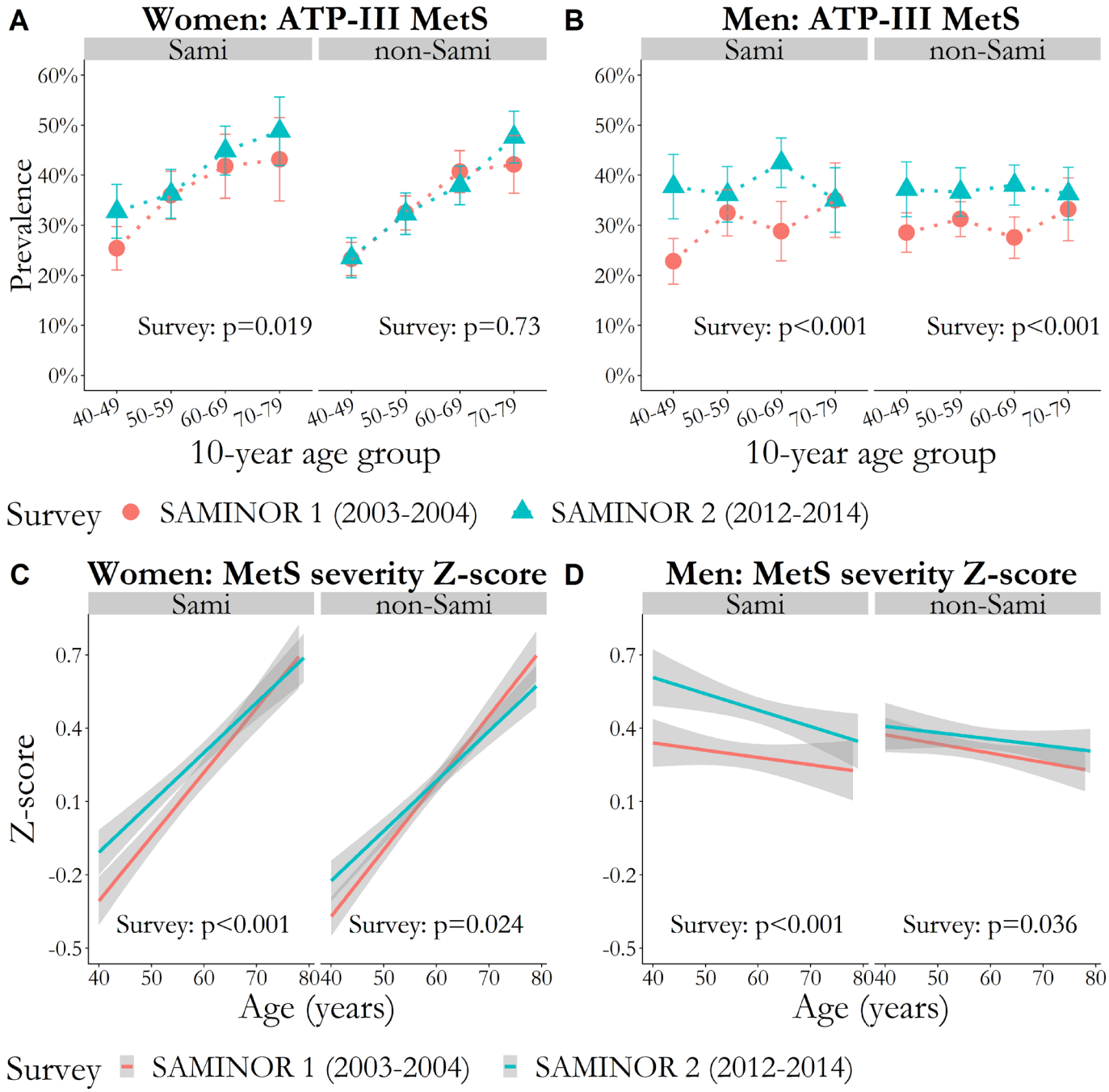

Figure 2 P values for survey are age-adjusted and were obtained with GEE logistic or linear regression. Models were stratified by sex and ethnic group. (A and B) Prevalence of MetS defined by the harmonised ATP-III criteria, per 10-year age group with vertical error bars (95% CI). (C and D) Mean of MetS severity Z-score as a function of age with 95% CI bands shaded in grey. ATP-III, Adult Treatment Panel III; GEE, generalised estimating equation; MetS, metabolic syndrome.

speculate that our positive findings may be explained by the fact that the Sami and non-Sami mostly live side-by-side in the same geographical areas. Thus, important social determinants of health, such as education, job opportunities and health services, should be equally available independent of ethnicity. We also reiterate that regional differences may be of a much larger magnitude than the ethnic differences[27] and this calls for continued public health surveillance in rural Northern Norway. Further, in an effort to explain ethnic health differences, one should keep in mind that ethnicity comprises an interplay between lifestyle, geography, culture and possibly genetics. It is likely that lifestyle factors such as diet and physical activity—which are strongly associated with MetS development[39]—mediate, at least to some degree, the (weak) association between ethnicity and MetS. There are some studies on differences in physical activity and dietary habits in Sami and non-Sami,[40–42] but they are both insufficient (ie, no information on the total level of physical activity) and cross-sectional. Unfortunately, we

were not able to include such variables in our analyses. A complex facet of ethnicity is represented by potential differences in body composition[6]; thus, if such a difference exists between Sami and non-Sami, it could have led us to misclassify some participants as obese. For instance, the Greenland Inuit have a more favourable cardiometabolic profile and lower amounts of visceral adipose tissue at the same level of obesity as Danes.[43 44] On average, Sami have a shorter stature than non-Sami, and when adjusting for waist-to-height-ratio, the differences in T2DM between Sami and non-Sami in SAMINOR 2 were eliminated.[16] Finally, we emphasise that there is heterogeneity in all aspects comprising ethnicity within the Sami population, just as there is heterogeneity between the Sami and the non-Sami. Our results suggest that further research on the ethnic differences in the adiposity-related MetS risk profile in rural Northern Norway is warranted.

CONCLUSION

We found a high burden of MetS in rural Northern Norway. From 2003–2004 to 2012–2014, both the prevalence (ATP-III-MetS) and the severity (Z-score) of MetS increased in the 10 selected municipalities. The largest increases in prevalence were observed in Sami and non-Sami men. In Sami men, the increase in MetS severity was slightly larger than in non-Sami. Abdominal obesity appeared to be the driving force behind the increase in ATP-III-MetS and should be a public health target regardless of ethnicity or MetS presence.

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Patient consent for publication We used data fromparticipants that have consented to participate in the SAMINOR Study. Patient consent for publication specifically is not required.

Ethics approval The SAMINOR Project Board and The Regional Committee for Medical and Health Research Ethics approved this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data that support the findings of this study are available from the SAMINOR Study (www.saminor.no), but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are however available upon reasonable request to the SAMINOR Project Board and with permission of the Regional Committee for Medical and Health Research Ethics.

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Supplementary Table 1. Sensitivity analyses of the age-adjusted prevalence of ATP-III MetS and mean of MetS severity Z-score in Sami and non-Sami in SAMINOR 1 (2003-2004) and SAMINOR 2 (2012-2014), with altered MetS definitions and restricted samples, including tests of potential interactions between survey and ethnicity using GEE models.

	Sami participants			non-Sami participants			p-value for interaction (survey x ethnicity)[b]
	SAMINOR 1	SAMINOR 2	p-value[a]	SAMINOR 1	SAMINOR 2	p-value[a]	
Women							
ATP-III MetS: Waist ≥88 cm, %	28.9 (26.3, 31.5)	35.3 (32.7, 37.9)	<0.001	27.3 (25.5, 29.2)	30.2 (28.1, 32.2)	0.022	0.12
ATP-III MetS: Excluded waist criteria, %	16.6 (14.4, 18.7)	16.3 (14.2, 18.3)	0.82	14.2 (12.8, 15.7)	13.5 (11.9, 15.0)	0.42	0.91
ATP-III MetS: Glucose ≥11.1 mmol/L, %	34.6 (31.9, 37.4)	38.7 (36.0, 41.4)	0.018	32.6 (30.6, 34.5)	33.4 (31.2, 35.5)	0.54	0.22
ATP-III MetS: Triglycerides ≥2.1 mmol/L, %	29.2 (26.6, 31.8)	31.2 (28.7, 33.8)	0.20	27.4 (25.5, 29.3)	26.9 (24.9, 28.9)	0.67	0.32
ATP-III MetS: "Healthier" sample, %	20.4 (17.4, 23.4)	28.9 (25.9, 31.9)	<0.001	21.0 (18.8, 23.2)	23.3 (20.9, 25.6)	0.13	0.03
MetS Z-score: "Healthier" sample, mean	-0.15 (-0.21, -0.11)	0.06 (0.01, 0.11)	<0.001	-0.20 (-0.24, -0.17)	-0.07 (-0.11, -0.03)	<0.001	0.025
Men							
ATP-III MetS: Waist ≥102 cm, %	21.8 (19.4, 24.2)	29.6 (26.9, 32.3)	<0.001	21.7 (19.8, 23.5)	28.8 (26.5, 31.0)	<0.001	0.62
ATP-III MetS: Excluded waist criteria, %	14.4 (12.4, 16.5)	17.9 (15.7, 20.2)	0.014	13.5 (11.9, 15.0)	15.6 (13.8, 17.4)	0.057	0.47
ATP-III MetS: Glucose ≥11.1 mmol/L, %	28.3 (25.6, 30.9)	37.4 (34.6, 40.2)	<0.001	29.3 (27.2, 31.4)	37.2 (34.9, 39.6)	<0.001	0.47
ATP-III MetS: Triglycerides ≥2.1 mmol/L, %	23.7 (21.2, 26.1)	31.3 (28.4, 33.8)	<0.001	23.5 (21.6, 25.4)	30.2 (28.0, 32.5)	<0.001	0.74
ATP-III MetS: "Healthier" sample, %	20.0 (17.0, 23.0)	27.8 (24.6, 31.1)	<0.001	23.0 (20.6, 25.4)	30.0 (27.0, 32.8)	<0.001	0.53
MetS Z-score: "Healthier" sample, mean	0.10 (0.04, 0.16)	0.36 (0.30, 0.41)	<0.001	0.17 (0.12, 0.21)	0.24 (0.19, 0.29)	0.017	<0.001

GEE = generalised estimating equation. CI = confidence interval. MetS = metabolic syndrome. HDL = high-density lipoprotein. A "healthier" sample was constructed by excluding participants if they currently used blood pressure medication or diabetes medication or if they reported ever having had a myocardial infarction, angina pectoris or diabetes mellitus. Survey-specific proportions or means (95% CI) are age-adjusted post-estimated marginal means from GEE models, holding age constant at the sex-specific mean for the entire sample (i.e. both surveys).

[a]P-values for survey, i.e. p-value for change in proportion or mean from SAMINOR 1 to SAMINOR 2. The GEE logistic or linear regression models were stratified by ethnicity and run with age and survey as covariates.

[b]P-values for the interaction term (survey x ethnicity) in GEE models not stratified by ethnicity. P<0.05 indicates that the change in outcome over time differs by ethnic group.

Supplementary Table 2. Sensitivity analyses for the age-adjusted prevalence of ATP-III MetS and mean of MetS severity Z-score according to two alternative ethnic categorisations in SAMINOR 1 (2003-2004) and SAMINOR 2 (2012-2014), including tests of potential interactions between survey and ethnicity using GEE models.

	Female participants				Male participants			
Metabolic syndrome dichotomized								
	SAMINOR 1	SAMINOR 2	p for survey[a]	OR (95% CI)[b]	SAMINOR 1	SAMINOR 2	p for survey[a]	OR (95% CI)
Count								
0 Sami	32.7 (30.5-34.9)	32.3 (29.9-34.7)	0.77	Ref.	30.2 (27.8-32.5)	38.0 (35.3-40.7)	<0.001	Ref.
1-10 Sami	35.5 (32.5-38.5)	39.0 (36.3-41.7)	0.063	1.22 (1.08-1.37)	29.2 (26.4-32.1)	38.1 (35.2-40.9)	<0.001	1.00 (0.88-1.14)
11 Sami	35.9 (32.1-39.6)	39.5 (34.8-44.2)	0.17	1.23 (1.05-1.44)	30.2 (26.6-33.9)	37.1 (31.8-42.3)	0.016	0.99 (0.83-1.18)
Self-identification								
Norwegian	33.1 (31.1-35.1)	34.3 (32.1-36.5)	0.38	Ref.	30.3 (28.2-32.4)	36.6 (34.2-39.0)	<0.001	Ref.
Sami	34.1 (30.7-37.5)	39.4 (36.0-42.7)	0.013	1.14 (1.00-1.31)	31.1 (27.7-34.6)	37.7 (34.1-41.3)	0.004	1.04 (0.91-1.20)
Mixed	38.4 (34.1-42.7)	37.4 (33.5-41.3)	0.73	1.18 (1.02-1.37)	27.9 (23.9-31.9)	41.8 (37.3-46.2)	<0.001	1.04 (0.89-1.21)
MetS severity Z-score								
	SAMINOR 1	SAMINOR 2	p for survey[a]	β (95% CI)[b]	SAMINOR 1	SAMINOR 2	p for survey[a]	β (95% CI)
Count								
0 Sami	0.09 (0.04 to 0.13)	0.13 (0.08 to 0.17)	0.15	Ref.	0.33 (0.28 to 0.37)	0.38 (0.33 to 0.42)	0.09	Ref.
1-10 Sami	0.16 (0.11 to 0.22)	0.25 (0.21 to 0.30)	0.004	0.09 (0.04 to 0.15)	0.31 (0.26 to 0.36)	0.45 (0.40 to 0.50)	<0.001	0.08 (-0.00 to 0.16)
11 Sami	0.19 (0.12 to 0.27)	0.23 (0.14 to 0.32)	0.41	0.10 (0.03 to 0.17)	0.25 (0.18 to 0.32)	0.47 (0.38 to 0.56)	<0.001	0.16 (0.06 to 0.26)†
Self-identification								
Norwegian	-0.07 (-0.10 to -0.03)	0.01 (-0.03 to 0.05)	<0.001	Ref.	0.32 (0.28 to 0.36)	0.36 (0.32 to 0.40)	0.12	Ref.
Sami	-0.01 (-0.06 to 0.05)	0.12 (0.06 to 0.18)	<0.001	0.03 (0.01 to 0.05)	0.29 (0.23 to 0.36)	0.49 (0.42 to 0.56)	<0.001	0.16 (0.07 to 0.24)†
Mixed	0.04 (-0.04 to 0.12)	0.08 (0.01 to 0.16)	0.35	0.03 (0.01 to 0.05)	0.29 (0.22 to 0.37)	0.51 (0.44 to 0.59)	<0.001	0.17 (0.07 to 0.28)†

Count definition of ethnicity: 11 Sami = answered 'Sami' on all 11 questions, 1-10 Sami = answered 'Sami' on 1–10 questions, 0 Sami = did not answer 'Sami' on any question.
Self-identification of ethnicity: Norwegian = answered only 'Norwegian' as self-perceived ethnicity, Sami = answered only 'Sami' as self-perceived ethnicity, Mixed = all others.
[a]Age-adjusted p-value for change in survey using GEE models stratified by ethnic groups.
[b]OR (95% CI) for each ethnic category adjusted for survey and age, using GEE models.
†Interaction ethnicity*survey significant/below 0.05-level

Paper II

Obesity measures, metabolic health and their association with 15-year all-cause and cardiovascular mortality in the SAMINOR 1 Survey: a population-based cohort study

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Abstract

Background: The mortality of metabolic—obesity phenotypes has been thoroughly studied, but it is not known if or how the association between mortality and body mass index (BMI), waist circumference or a body shape index (ABSI) differ in strata of cardiometabolic health status.

Methods: We linked data on 12,815 men and women aged 36—79 years from the SAMINOR 1 Survey with mortality data from the Norwegian Cause of Death Registry. We defined metabolically healthy and unhealthy as having zero and ≥1, respectively, of the following: MetS, pre-existing diabetes or cardiovascular disease (CVD), or prescribed drugs for high blood pressure, hyperglycaemia or dyslipidaemia. We defined general and abdominal obesity as BMI ≥30 kg/m^2 and waist circumference ≥88 cm (women) or 102 cm (men), respectively, and cross-classified these categories with metabolic status to create metabolically healthy non-obese and obese (MHNO and MHO) and metabolically unhealthy non-obese and obese (MUNO and MUO) phenotypes. We used Cox regression to estimate the hazard ratio (HR) for all-cause and CVD mortality for 1) the four phenotypes and 2) BMI, waist circumference and ABSI fitted with restricted cubic splines. We adjusted for age and lifestyle, and tested for interactions with sex and metabolic status (only continuous measures).

Results: The MHO phenotype was present in 7.8% of women and 5.8% of men. During a median follow-up of 15.3/15.2 years, 596/938 women/men had died, respectively. The MUNO and MUO groups had higher mortality than the MHNO group. Sex and phenotypes interacted with respect to CVD mortality: relative to the MHNO group, the MHO group had an adjusted HR (95% confidence interval) for CVD mortality of 1.05 (0.38–2.88) in women and 2.92 (1.71–5.01) in men. We found curvilinear associations between BMI/waist circumference and all-cause mortality irrespective of metabolic status. Corresponding relationships with CVD mortality were linear and the slope differed by sex and metabolic status. ABSI was linearly and positively associated with all-cause and CVD mortality in men.

Conclusion: The relationships between BMI, waist circumference or ABSI and mortality differed by sex, metabolic status and cause of death. Poor metabolic health substantially increases mortality regardless of obesity status.

Keywords: Abdominal obesity. A body shape index. All-cause mortality. Body mass index. Cardiovascular mortality. Metabolically healthy obesity. Metabolic syndrome. Obesity. Waist circumference.

1 Background

The prevalence of obesity doubled between 1980 and 2015 in more than 70 countries (1). Obesity is a strong driver of a cluster of risk factors known as metabolic syndrome (MetS). MetS is etiologically linked to insulin resistance and visceral adipose tissue that promotes a proinflammatory and prothrombotic state, making it an antecedent of both cardiovascular disease (CVD) and type 2 diabetes mellitus (2). At least half of the cardiovascular risk linked to obesity is mediated through metabolic risk factors (3,4). In Europe, approximately 7–19% of people with obesity do not have MetS, so-called metabolically healthy obesity (MHO) (5). Accumulating evidence strongly suggests that, compared to the metabolically healthy normal-weight group, people with MHO are at increased risk of CVD (6–8), type 2 diabetes mellitus (9,10), and mortality (11,12).

A body mass index (BMI) ≥30 kg/m^2 is commonly used to define obesity in populations of European ancestry, but BMI is a crude marker of body fat distribution. Waist circumference is a better measure of the visceral adipose tissue that is particularly strongly associated with cardiometabolic disease (13). BMI and waist circumference usually show J- or U-shaped associations with mortality (14,15). This may indicate a functional relationship not reflected well by crude dichotomies, as dichotomisation of continuous predictors cause loss of information and statistical power to demonstrate associations (16). However, BMI and waist circumference are usually highly correlated. Krakauer et al. developed a body shape index (ABSI), which is a measure of central obesity that has a low correlation with BMI (17).

To the best of our knowledge, no studies have examined the relationships between continuous measures of BMI, waist circumference or ABSI and mortality by metabolic health status. We aimed to examine these relationships using a population-based multi-ethnic sample of adult women and men from rural Northern Norway, which has high prevalence of both general and abdominal obesity and MetS (18,19).

2 Methods

2.1 Data

We used the national 11-digit personal identity number linking individual data from the three following sources: baseline information on participants in the SAMINOR 1 Survey (the first survey of the Population-based Study on Health and Living Conditions in Regions with Sami and Norwegian Populations—the SAMINOR Study), mortality data from the Norwegian Cause of Death Registry, and information on emigration from Statistics Norway.

The population of Northern Norway includes people of Norwegian, Sami and Kven (descendants of Finnish immigrants in the 18th and 19th Century) ethnicity. The Sami is an ethnic minority and acknowledged as an indigenous people. Traditionally, the Sami inhabited Northern parts of Norway, Sweden, Finland and the Kola Peninsula in the Russian Federation.

The SAMINOR Study is a population-based study designed to investigate the health and living conditions in regions of Norway with an assumed proportion of at least 5—10% Sami inhabitants. The Centre for Sami Health Research at UiT The Arctic University of Norway and the Norwegian Institute of Public Health conducted the SAMINOR 1 Survey in 2003—2004 in 24 rural municipalities mainly in northern parts of Norway. Clinical measurements, blood samples and self-administered questionnaire data were collected on men and women aged 36—79 years. Of 27,151 invited individuals, 16,455 (60.6%) participated and consented to have their data linked to medical and national registries. Survey details have been reported previously (20).

2.2 Clinical measurements

The following measurements of each participant were made by trained personnel: waist circumference, recorded to the nearest centimetre at the umbilicus, the participant standing and breathing normally; height and weight, measured to the nearest 0.1 cm and 100 g, respectively, using an electronic scale with participants wearing light clothing and no shoes; and blood pressure, measured with a Dinamap-R automatic device (Critikon, Tampa, Florida, USA). Blood pressure was measured after a 2-minute seated rest, and three measurements with 1-minute intervals were recorded. The first measurement was discarded and the average of the second and third was used. Trained personnel performed venepuncture with the participant in a seated position and non-fasting blood samples were centrifuged within 1.5 hours. Serum was sent by overnight post to the laboratory at Ullevål University Hospital, Oslo. Lipids and glucose were measured by an enzymatic method (Hitachi 917 autoanalyzer, Roche Diagnostic, Switzerland)

2.3 Lifestyle and disease variables

Participants were asked to fill in a questionnaire from which we obtained the following information (answer options in parenthesis): education (total number of school years); diabetes (yes/no); angina pectoris (yes/no); previous stroke (yes/no); previous heart attack (yes/no); use of blood pressure-lowering drug (currently/previously, but not

now/never); use of cholesterol-lowering drug (currently/previously, but not now/never); use of insulin (currently/previously, but not now/never); use of glucose-lowering drug in tablet format (currently/previously, but not now/never); smoking (currently/previously/never); alcohol consumption (never/not this year/a few times during this year/1 time per month/2-3 times per month/1 time per week/2-3 times per week/4-7 times per week). Alcohol consumption was categorised into "weekly alcohol consumption", "less than weekly alcohol consumption" and "never/not last year". Leisure-time physical activity was measured by a self-reported modified Saltin-Grimby Physical Activity Level scale (reading, watching television, or engaging in sedentary activities/at least 4 hours a week of walking, bicycling, or other types of physical activity/at least 4 hours a week of participating in recreational athletics or heavy gardening/regular, vigorous training or participating in competitive sports several times a week) (21). The Saltin-Grimby Physical Activity Level scale has been used in many Nordic populations and has shown acceptable validity regarding objectively measured physical activity (21). Leisure-time physical activity was categorised into "sedentary" (the first option), "light" (the second option) and "moderate-hard" (the last two options merged). Participants were also asked to list any medication they had used within the last four weeks and the information was combined with information from drug-specific questions, details are found elsewhere (22).

The questionnaire also included questions (11 in total) on use of language at home by grandparents, parents and participants, ethnic background for parents and participants, and the participants' self-perceived ethnicity (one or more of these alternatives were allowed: Norwegian, Sami, Kven, and other). Participants were categorised as Sami if they answered Sami as 1) their self-perceived ethnicity or 2) their own ethnic background. All others were categorised as non-Sami.

2.4 Independent variables

We defined MetS according to the 'harmonised' Adult Treatment Panel-III definition, with some adaptations (23). At least three of the following five components had to be present:

hypertension, defined as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg or current use of antihypertensive drug;

elevated random glucose, defined as random serum glucose ≥7.8 mmol/L or self-reported diabetes;

increased waist circumference, defined as waist circumference ≥80 cm in women and ≥94 cm in men;

hypertriglyceridemia, defined as random serum triglycerides ≥1.7 mmol/L; and

lowered HDL cholesterol, defined as random serum HDL cholesterol <1.3 mmol/L in women and <1.0 mmol/L in men.

Participants were categorised as metabolically unhealthy if they had any of the following, as recommended by Smith et al. (24):

MetS (for abdominal obesity phenotypes, the MetS definition was modified to the presence of any given two or more components excluding increased waist circumference);

self-reported diabetes, stroke, angina pectoris, or myocardial infarction;

self-reported current treatment for high blood pressure, hyperglycaemia or dyslipidaemia.

General and abdominal obesity were defined as BMI ≥30 kg/m^2 and waist circumference ≥88 cm in women and ≥102 cm in men, respectively. The following general obesity phenotypes were created: metabolically healthy non-obesity (MHNO); metabolically unhealthy non-obesity (MUNO); metabolically healthy obesity (MHO); and metabolically unhealthy obesity (MUO). The following abdominal obesity phenotypes were created: metabolically healthy non-abdominal-obesity (MHNAO); metabolically unhealthy non-abdominal-obesity (MUNAO); metabolically healthy abdominal obesity (MHAO); and metabolically unhealthy abdominal obesity (MUAO).

In addition to using BMI and waist circumference to define general and abdominal obesity, respectively, we also used them as continuous variables (BMI in kg/m^2 and waist circumference in cm). Due to the high correlation between BMI and waist circumference (0.88 in women and 0.86 in men), we also applied ABSI as developed by Krakauer et al. (17):

$$ABSI = \frac{waist\ circumference}{BMI^{2/3}\ height^{1/2}}$$

The ABSI was transformed to a Z-score for interpretability by subtracting the sex-specific mean and dividing by the sex-specific standard deviation. ABSI was not used as a determinant of categorical obesity because of the lack of validated cut-offs.

2.5 Outcome variables

Mortality data comprised date of death and underlying cause of death, coded using the International Statistical Classification of Diseases and Related Health Problems, 10th revision. The study period started at the date of study entry (between 14th January 2003 and 5th March 2004) and ended at date of death (the event), date of emigration (censored) or the end of follow-up 31st December 2018 (censored), whichever occurred first. The outcome variables of interest were all-cause mortality and CVD mortality (death from causes I00-I99).

2.6 Missing data and exclusions

Figure 1 shows a flow chart describing the cohort selection. We excluded 497 participants who died within the first 5 years of follow-up and 90 participants with a BMI ≤18.5 kg/m^2 to avoid the potential for reverse causality (14). Because information on pre-existing disease or prescribed drugs was not necessary for the categorisation, we did not exclude participants with missing data for these variables. However, most participants with missing data for these variables were categorised into a metabolically unhealthy group by other determinants (Table 1). After exclusions, the complete case analytical sample comprised 12,815 participants, 47.2% of the invited sample.

2.7 Statistical analysis

Sample characteristics were described in strata of sex and metabolic–obesity phenotype and reported as mean (SD) and frequency (percentage) as appropriate. One-way analysis of variance and Pearson's χ^2 test were used to compare characteristics across the phenotypes. We calculated age-standardised mortality rates using the direct method and the 2013 European standard population.

In separate models for each pair of outcome and exposure, we modelled the relationships between all-cause mortality and CVD mortality (outcomes) and MetS, general obesity phenotypes and abdominal obesity phenotypes (exposures) using Cox proportional hazard regression. We tested interactions between exposures and sex, and between exposures and ethnicity, and compared models with and without interaction terms using the likelihood ratio test. Interaction was considered present if $p<0.05$. There were no significant interactions with ethnicity, but we found evidence of interactions between sex and general ($p=0.02$) and abdominal ($p=0.05$) obesity phenotypes for CVD mortality. Therefore, all models were stratified by sex. Attained age was set as the time-scale as recommended in observational studies (25), hence, all models were inherently and non-parametrically controlled for age (model 1). Further adjustments were made for smoking (model 2), plus leisure-time physical activity, education and alcohol consumption (model 3). Sami ethnicity is primarily regarded a sociocultural category in this cohort, and neither interacted with nor affected the beta coefficient for the exposures in the models, and was therefore not included in the models. The proportional hazard assumption was evaluated using Schoenfeld residuals. In models with all-cause mortality, non-proportional hazards for smoking status were handled by allowing separate baseline hazards for subgroups of the data, i.e. stratified Cox models. We reported adjusted hazard ratios (HR) with 95% confidence intervals (CI) for each pair of outcome and exposure.

Next, in separate models, we fitted BMI, waist circumference and ABSI as continuous variables using restricted cubic splines against all-cause and CVD mortality, respectively, while adjusting for the same covariates as in model 3 above, in addition to metabolic health. Fitting three knots provided the lowest Akaike information criterion and were thus sufficient, as recommended by Harrell (26). We assessed non-linearity by testing models with the linear term against models with both linear and a cubic spline term using likelihood ratio test. Non-linearity was considered present if $p<0.05$. We also assessed interaction between metabolic health status and BMI/waist circumference/ABSI using likelihood ratio tests. If there was a significant interaction, we kept the interaction term in the model; if there was no interaction, metabolic health status was kept in the model as a covariate. Adjusted HR (95% CI) of all-cause and CVD mortality, respectively, were plotted against BMI, waist circumference and ABSI, respectively, with separate curves for metabolically healthy and unhealthy, using the sex-specific sample median of BMI, waist circumference or ABSI as reference values. In models with a significant interaction, metabolically healthy with the sex-specific sample median of BMI, waist circumference or ABSI were used as reference.

We used *R* version 3.6.2 for Windows for statistical computing (27). Code and output is found in the supplementary material.

2.8 Sensitivity analysis

We excluded 1) ever-smokers and 2) participants with pre-existing diseases (or prescribed drugs for cardiometabolic disease) in sensitivity analyses. Furthermore, we analysed data with more conservative cut-offs for MetS-components: waist circumference (≥88/102 cm in women/men), random triglycerides (≥2.1 mmol/L), and random glucose (≥11.1 mmol/L). We also repeated the analyses in the full sample, adjusting for sex. Finally, we used multiple imputation to address missing data on at least one variable for 2030 participants (13.7%). The variables with the largest proportion of missing data were found for leisure-time physical activity (n=1322, 8.9%) and education (n=881, 5.9%). Characteristics differed between participants with complete and missing data (Supplementary Table 1). The mechanism for missing information was assumed to be missing-at-random (28). We used a rich set of relevant variables, performed 20 imputations, and pooled the data according to Rubin's rules using the 'mice' package in *R* (29). Because metabolic health is a known mediator of the relationship between obesity and mortality, we also ran the analyses of continuous BMI/waist circumference/ABSI vs mortality without adjusting for metabolic health.

3 Results

After median follow-up of 15.3 years in 6517 women and 15.2 years in 6298 men (12,815 in total), 596 (9.1%) and 938 (14.9%) had died, respectively. In both women and men, the prevalence of MetS was 29.7%. Proportions categorised as metabolically unhealthy (defined as either having MetS, pre-existing disease or prescribed drugs) were 44.7% in women and 47.0% in men. Proportions having general obesity were 27.0% in women and 23.5% in men, and proportions having abdominal obesity were 39.0% in women and 21.1% in men.

Table 1 and 2 describe the prevalence of the four general obesity phenotypes and the distributions of characteristics across the phenotypes in women and men, respectively. Compared to the other groups, men and women with MHO were relatively young, with a higher proportion of people with Sami ethnicity, a lower proportion of current smokers, and a higher proportion of people who reported being sedentary in their leisure-time (but lower than in people with MUO). Supplementary Table 2 and 3 describe the distribution and characteristics of the four abdominal obesity phenotypes. Patterns of characteristics were generally similar to those reported for general obesity phenotypes.

The proportion of deaths during follow-up were comparable in people with MHO and people with MHNO, but they differed in the distribution of causes of death (Table 1 and 2). In general, the proportion of death from CVD was lowest in the MHNO group.

Figure 2 shows that the lowest mean mortality rates in men occurred in the MHNO and MHNAO groups, whereas in women, the metabolically healthy phenotypes regardless of obesity status had the lowest mortality rates.

Table 3 and Table 4 show the hazard ratios (HR) from Cox proportional hazards models for all-cause mortality and CVD mortality in women and men, respectively. Men and women with MetS had an approximately 50% higher 15-year risk of CVD mortality than those without MetS. The 15-year mortality in the subgroups with MHO and MHAO compared to the respective metabolically healthy non-obese groups differed markedly between the sexes, particularly for CVD mortality, with significant interactions with sex differences in the beta coefficient for MHO and MHAO primarily. We found that obesity, regardless of metabolic health, markedly increased CVD mortality in men, but there was no association in women. In the metabolically healthy, all-cause mortality was reduced in obese women (general and abdominal, respectively) compared to non-obese women. In both sexes, the mortality associated with metabolically unhealthy obesity phenotypes (MUNO, MUNAO, MUO, MUAO) were higher for CVD-specific death than for all-cause mortality.

Figure 3 and 4 (panels A and C) show curvilinear relationships between all-cause mortality and BMI (panel A) and waist circumference (panel C) in women and men, respectively. Figure 3 and 4 (panels E) show curvilinear and linear relationships between all-cause mortality and ABSI in women and men, respectively. Figure 3 and 4 (panels B, D and F) show marked sex-differences in the relationships with CVD mortality for BMI (panel B), waist circumference (panel D) and ABSI (panel F). Interactions were present between metabolic health status and obesity measures in CVD models (except in panel 3B and 4F). In men, all obesity measures had positive, strong associations with CVD mortality. We found stronger associations (steeper slopes) in metabolically healthy than unhealthy groups in models with BMI and waist circumference, but not in models with ABSI. In women, BMI had negative associations with CVD mortality. The association between waist circumference or ABSI and CVD mortality differed by metabolic health status.

3.2 Sensitivity analysis

Supplementary Table 4, 5 and 6 show the results of the sensitivity analyses. In never-smokers, most associations between general and abdominal obesity phenotypes and mortality were stronger than those observed in the whole cohort, but several estimates included 1.0 in the CI. Contrary, in participants without pre-existing disease or prescribed drugs, most estimates were strongly attenuated and not statistically significant (except men with MHO

and MHAO) compared to those observed in the whole cohort. Using more conservative cut-offs for MetS resulted in increased estimates, and the apparent protective effect of MHO and MHAO in women was attenuated towards the null and was no longer statistically significant. In sex-adjusted analyses, HR (95%) for all-cause mortality compared to the reference groups were 0.92 (0.71–1.20) for MHO and 0.92 (0.72–1.17) for MHAO, respectively. Analysis of multiply imputed data gave similar results compared to the complete case analysis. Supplementary Figure 1 and 2 of "unadjusted" obesity vs mortality models show overall patterns similar with the primary analyses. An exception was seen for models with CVD mortality in women, which showed no association with BMI or waist circumference, but a curvilinear association with ABSI indicating significantly higher mortality at higher ends of the scale.

4 Discussion

We followed almost 13,000 adults for 15 years and found that metabolically unhealthy status was associated with a higher CVD mortality than metabolically healthy status irrespective of obesity status. We found curvilinear associations between BMI (women and men), waist circumference (women and men) or ABSI (women) and all-cause mortality regardless of metabolic health status. However, in men, the relationship between ABSI and all-cause mortality was linear. Corresponding relationships between these three continuous obesity measures and CVD mortality differed by both sex and metabolic health status. Ethnicity had no impact on the results.

To our knowledge, this study is the first to examine the relationship between continuous measures of BMI, waist circumference or ABSI and mortality according to metabolic health status. A recent study of a Japanese population by Izumida et al. examined the relationships between four categories of BMI and 18-year mortality according to MetS status (30). The relationship between BMI categories and all-cause and CVD mortality were J-shaped in metabolically unhealthy people, whereas no associations were found in metabolically healthy people. In contrast, we show that the relationships between BMI and CVD mortality in a Norwegian population differ by sex: with no or negative association in women and positive association in men. A meta-analysis of 21 prospective studies showed that compared to the MHNO group, the HR for CVD in women with MHO were lower than those in men with MHO (HR 1.71 vs 2.15, respectively) (31). However, the meta-analysis included few sex-stratified studies. In a recent Iranian study, neither women nor men with persistent MHO status had increased HR for CVD incidence compared to the non-obese comparison group (32). However, among women and men who transitioned from MHO to MUO, only men had an increased HR compared to the non-obese comparison group (32). In the study by Izumida et al., the authors adjusted for sex, whereas we found an interaction, but only regarding CVD mortality. The association between BMI/waist circumference and all-cause mortality was U-shaped in both sexes. Although the HR of MHO for all-cause mortality differed by sex (HR of 0.63 in women and 1.25 in men), there was no evidence of statistically significant effect modification. In sensitivity analyses, the (sex-adjusted) HR (95% CI) of MHO was 0.92 (0.71–1.21).

The amount of visceral adipose tissue may differ between people with the same value of BMI or even waist circumference, and men typically have more visceral adipose tissue than women (13). This may have contributed to the sex-differences in associations between obesity measures and CVD mortality in women and men. A recent UK Biobank study including nearly 300,000 men and women without CVD at baseline showed that BMI had J-shaped associations with CVD events and mortality in both sexes (33). In men, the association with CVD events was linear when restricted to non-smokers. Residual confounding when adjusting for crude smoking categories has been pointed out as a potential cause of obesity paradoxes (34). We also show that when the analyses were restricted to non-smokers, most estimates increased, and women with MHO had a HR of approximately 1.50 for CVD mortality, albeit non-statistically significant due to low power. Importantly, in the UK Biobank study, all measures of central obesity, including waist circumference, and fat mass were positively associated with CVD mortality in both sexes (33).

A high ABSI seemed to be a more consistent predictor of mortality in both women and men compared to a high BMI or waist circumference irrespective of metabolic health status; however, we have not formally compared the models. Studies in a US and four European (Sweden, Finland, Turkey and UK) cohorts have shown that where BMI or waist circumference tend to show curvilinear relationships with mortality, a progressively increasing ABSI corresponds to an increasing mortality (17,35). As opposed to BMI and waist circumference, ABSI was linearly and positively associated with both all-cause and CVD mortality in men. Although ABSI had a curvilinear association with mortality in women, the curve was tilted upwards at the higher end of the scale compared to the curves for BMI and waist circumference. There was no evidence of reduced CVD mortality with increasing ABSI independent of metabolic status, as opposed to the findings for BMI and waist circumference. A small study found that ABSI and BMI were negatively and positively, respectively, associated with fat free mass, or lean mass, indicating that a high ABSI is a good marker of sarcopenic obesity (36). In future studies, it may be interesting to replace BMI with ABSI in defining categorical obesity phenotypes, i.e., define a MHO phenotype from body shape.

Collider bias has been suggested to explain the "obesity paradox": obesity increases mortality and causes cardiometabolic disease, but within strata of cardiometabolic disease, obesity is not associated with mortality or even appears protective in some studies (37,38), as is seen in models with BMI and waist circumference for women in this study. The collider bias is a type of selection bias, that can be introduced through restriction, regression adjustment or stratification on a variable (in this case cardiometabolic status) that is both affected by the exposure (obesity) and share common causes (e.g. genes) with the outcome (death). However, the magnitude and direction of the bias may be difficult to predict, and some suggest it only a partial explanation of the obesity paradox (39).

Izumida et al. defined metabolically healthy as having no MetS components, compared to our definition of two or fewer components. Hence, metabolically healthy people in our study may have been in a transition phase towards full MetS and converted to metabolically unhealthy during the study period. Approximately 50% of people with MHO transition to MUO (4). A study with six repeated measures during 30 years of follow-up showed that duration with MHO was longer in women than in men. Women transitioned back and forth between a healthy and an unhealthy metabolic status while maintaining their obesity status, whereas men with MHO tended to just transition once from a healthy to an unhealthy metabolic status (40). Nevertheless, in a large U.S. cohort of women (N≈90,000), both those with MHO at baseline and those with persistent MHO status over a period of 24 years were at increased risk of CVD compared with the MHNO (41). Hence, even if women spend a longer time in the MHO state before transitioning to MUO than men, MHO may not be a benign state in a perspective of several decades.

Furthermore, in a study with repeated measures, people with MHO had higher all-cause mortality only when compared to people with stable MHNO status identified during several assessments, and not in comparison to the larger group that were MHNO at baseline (42). This serves as a reminder that exposure status in the reference group can change over time and a single measurement at baseline may give biased results. The implications for this study is that the strength of associations may have been under-estimated.

In summary, collider bias, residual confounding by smoking and misclassification may have distorted some of the relationships between obesity and mortality that we observed. The pathways linking obesity, metabolic health and mortality is complex and dynamic, making it a challenge to study using only data measured at a single point in time. Although obesity is heterogeneous in presentation, it is unlikely a healthy state over time, as is evident particularly for the men in our study.

Strengths and limitations

Strengths of the study include the population-based nature of the study, the long follow-up time and standardised measurements of clinical and biochemical variables by trained personnel. Linkage to the high quality Norwegian Cause of Death Registry enabled virtually complete follow-up of total and CVD deaths. We included important confounders, such as physical activity, smoking, alcohol and education. However, we did not have information on occupational physical activity, which may comprise a large part of the total physical activity level throughout the day. Therefore, some residual confounding from physical activity may be present. Further limitations include non-fasting blood samples, and a modest participation rate that may have resulted in 'healthy participation' bias. There are no valid cut-offs for random glucose regarding prediabetes or impaired glucose tolerance. Non-fasting triglycerides reflect increases over fasting values by a maximum of 0.3 mmol/L (43). Inclusion of inflammation markers (e.g. C-reactive protein) and information on non-alcoholic fatty liver disease may have enabled us to categorise more precisely into metabolically healthy vs unhealthy.

5 Conclusion

Metabolically unhealthy people have increased risks of 15-year all-cause and CVD mortality irrespective of obesity status compared to people who were metabolically healthy at baseline. Associations between BMI, waist circumference or ABSI and CVD mortality differed between the sexes, with strong, positive associations in both metabolically healthy and unhealthy men. The relationship between metabolic risk factors and adipose tissue is dynamic and continuous; therefore, efforts should continue to be made to reduce obesity and metabolic abnormalities across the population.

6 Declarations

Ethics approval and consent to participate: This study has been approved by the SAMINOR Project Board and The Regional Committee for Medical and Health Research Ethics (reference: 2017/1974/REK North). Written informed consent was obtained from all participants.

Consent for publication: Not applicable.

Availability of data and materials: The datasets generated and/or analysed during the current study are not publicly available due to privacy regulations. Data from the SAMINOR Study may be made available upon reasonable request

to the SAMINOR Project Board and with permission of the Regional Committee for Medical and Health Research Ethics.

Competing interests: None.

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Authors' contributions: ARB and VLM conceived the idea behind the study. VLM performed all the data analysis and wrote the first draft of the manuscript. SHW aided with the planning of the analysis. SHW, KK, JS, MM and ARB contributed with interpretation of the results and critically revised the manuscript.

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9 Figures

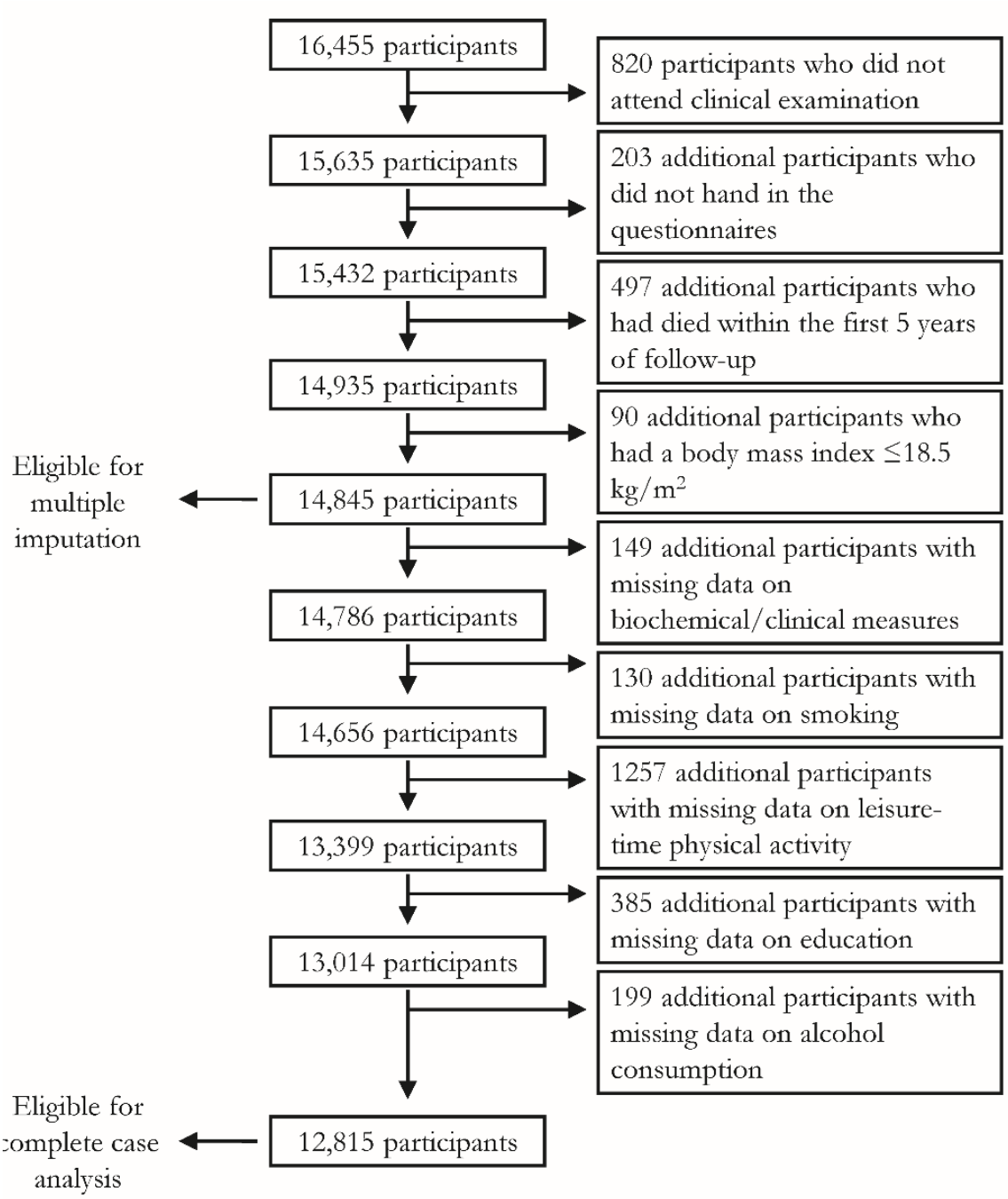


Figure 1. Flow-chart describing cohort selection from SAMINOR 1 participants and patterns of missing data.

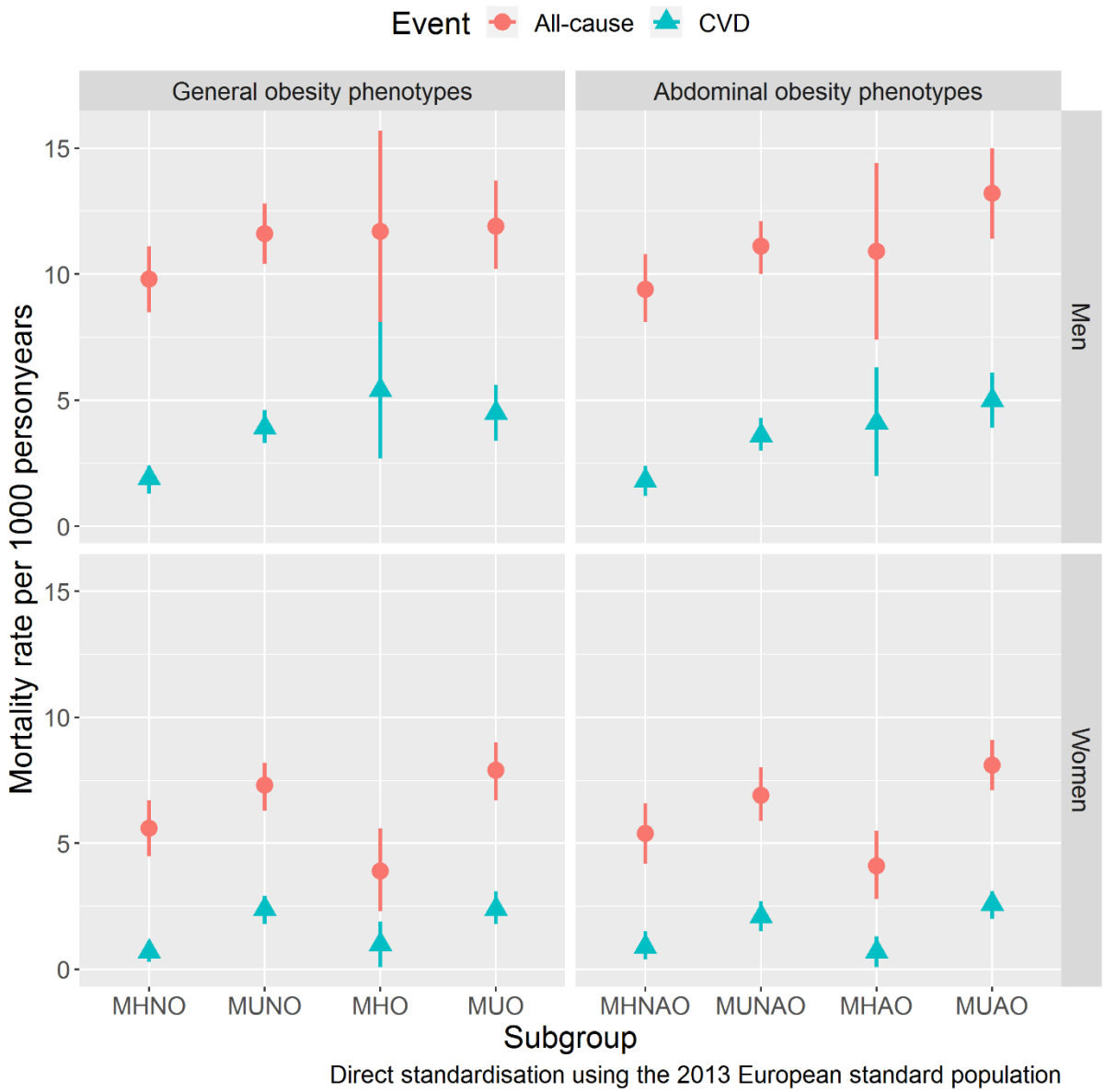


Figure 2. Age-standardised mortality rates per 1000 person-years with 95% CI for all-cause and CVD mortality given by general and abdominal obesity phenotypes. MHNO = metabolically healthy non-obesity, MUNO = metabolically unhealthy non-obesity, MHO = metabolically healthy obesity, MUO = metabolically unhealthy obesity, MHNAO = metabolically healthy non-abdominal obesity, MUNAO = metabolically unhealthy non-abdominal obesity, MHAO = metabolically healthy abdominal obesity, MUAO = metabolically unhealthy abdominal obesity.

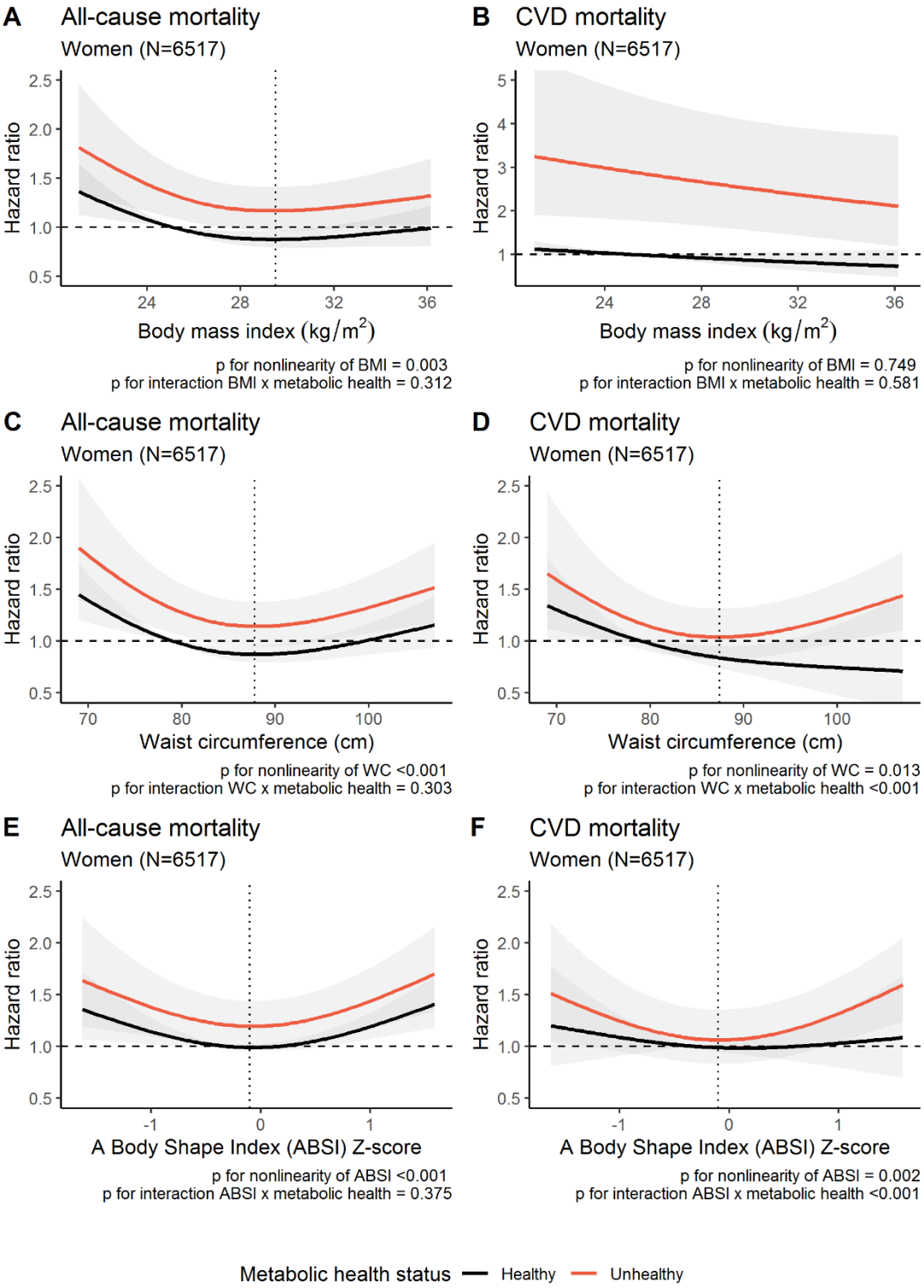


Figure 3. The functional relationships between mortality (all-cause and CVD) and continuous obesity measures (BMI, waist circumference and ABSI) with corresponding hazard ratios with 95% confidence bands in women. The reference of all curves were metabolically healthy women with a BMI of 26.7 kg/m², a waist circumference of 79 cm or an ABSI Z-score of -0.32 (median values for metabolically healthy women). P-values originates from likelihood ratio tests comparing models with/without linear terms/interaction terms. The beta coefficient for metabolic health status was statistically significant in all models. Estimates are predicted for median values of confounders (smoking, leisure-time physical activity, education, alcohol consumption). All models were inherently adjusted for age by using attained age as the time-scale. The vertical, dotted lines represent the nadir of risk. In panel D, the nadir of risk of metabolically healthy and unhealthy differ due to a significant interaction (nadir lower in unhealthy than healthy). Note that panel B has different dimensions on the y-axis than the other panels. ABSI = a body shape index, BMI = body mass index, WC = waist circumference.

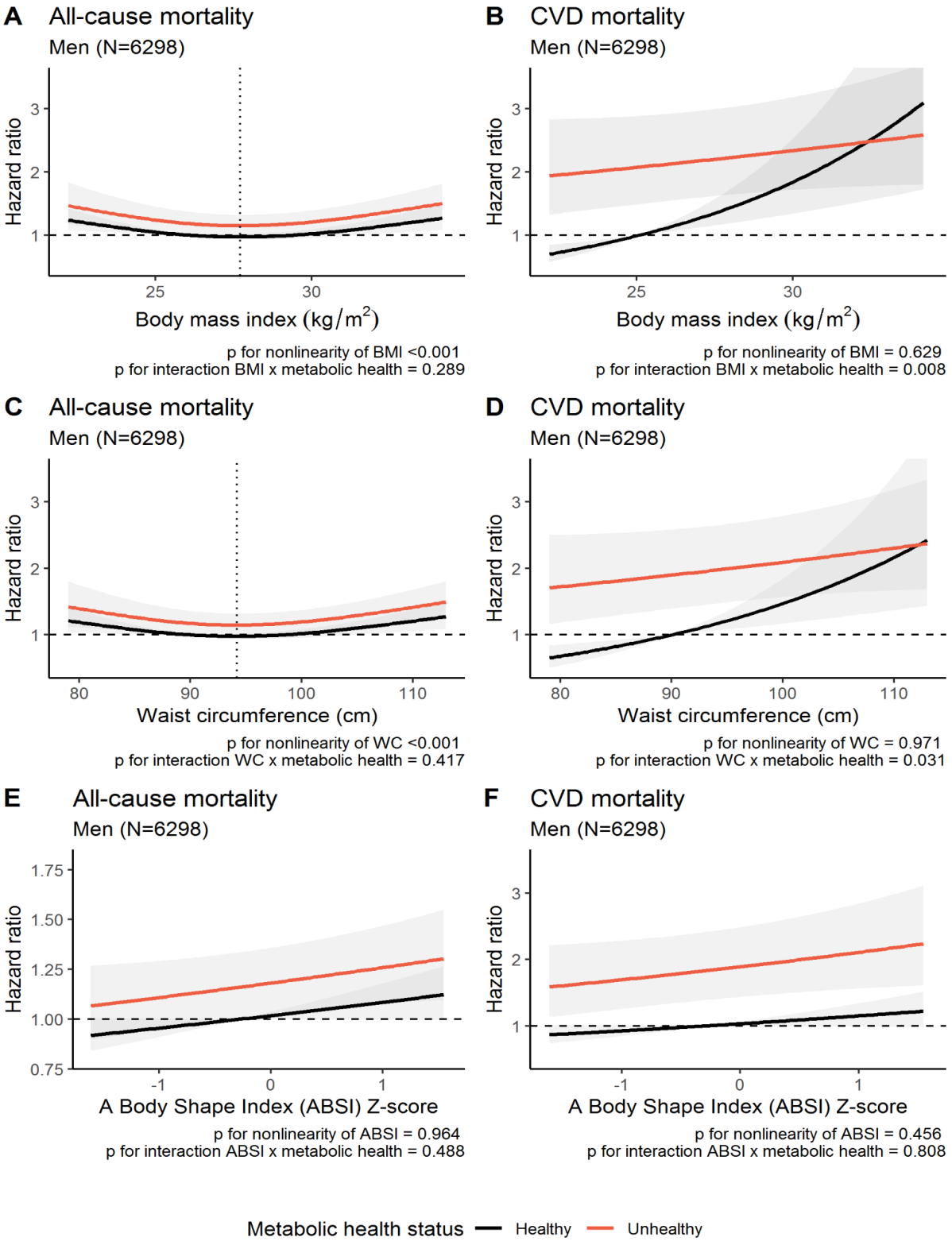


Figure 4. The functional relationships between mortality (all-cause and CVD) and continuous obesity measures (BMI, waist circumference and ABSI) with corresponding hazard ratios with 95% confidence bands in men. The reference of all curves were metabolically healthy men with a BMI of 27.2 kg/m², a waist circumference of 90 cm or an ABSI Z-score of -0.28 (median values for metabolically healthy men). P-values originates from likelihood ratio tests comparing models with/without linear terms/interaction terms. The beta coefficient for metabolic health status was statistically significant in all models. Estimates are predicted for median values of confounders (smoking, leisure-time physical activity, education, alcohol consumption). All models were inherently adjusted for age by using attained age as the time-scale. The vertical, dotted lines represent the nadir of risk. ABSI = a body shape index, BMI = body mass index, WC = waist circumference.

10 Tables

Table 1. Sample characteristics in mean (standard deviation) or frequency (percent) according to general obesity phenotypes in 6517 women in the SAMINOR 1 Survey (2003—2004)

	Metabolically healthy non-obesity (N=3095, 47.5%)	Metabolically unhealthy non-obesity (N=1662, 25.5%)	Metabolically healthy obesity (N=510, 7.8%)	Metabolically unhealthy obesity (N=1250, 19.2%)	Total (N=6517)	p-value
Age (years)	49.4 (9.4)	57.4 (10.7)	52.1 (10.2)	57.4 (11.0)	53.2 (10.8)	<0.001[1]
Ethnicity						<0.001[2]
non-Sami	2462 (79.5%)	1319 (79.4%)	349 (68.4%)	920 (73.6%)	5050 (77.5%)	
Sami	633 (20.5%)	343 (20.6%)	161 (31.6%)	330 (26.4%)	1467 (22.5%)	
Smoking						<0.001[2]
Yes, currently	1063 (34.3%)	588 (35.4%)	120 (23.5%)	277 (22.2%)	2048 (31.4%)	
Yes, previously	948 (30.6%)	481 (28.9%)	192 (37.6%)	441 (35.3%)	2062 (31.6%)	
Never	1084 (35.0%)	593 (35.7%)	198 (38.8%)	532 (42.6%)	2407 (36.9%)	
Died during follow-up	154 (5.0%)	230 (13.8%)	25 (4.9%)	187 (15.0%)	596 (9.1%)	<0.001[2]
Cause of death						<0.001[2]
Malignant tumor	83 (53.9%)	63 (27.4%)	12 (48.0%)	60 (32.1%)	218 (36.6%)	
CVD	16 (10.4%)	73 (31.7%)	5 (20.0%)	58 (31.0%)	152 (25.5%)	
Respiratory	19 (12.3%)	25 (10.9%)	3 (12.0%)	15 (8.0%)	62 (10.4%)	
Other	33 (21.4%)	67 (29.1%)	4 (16.0%)	51 (27.3%)	155 (26.0%)	
Unknown	3 (1.9%)	2 (0.9%)	1 (4.0%)	3 (1.6%)	9 (1.5%)	
Alcohol consumption						<0.001[2]
Weekly	822 (26.6%)	296 (17.8%)	89 (17.5%)	132 (10.6%)	1339 (20.5%)	
Less than weekly	1881 (60.8%)	958 (57.6%)	312 (61.2%)	741 (59.3%)	3892 (59.7%)	
Never/not last year	392 (12.7%)	408 (24.5%)	109 (21.4%)	377 (30.2%)	1286 (19.7%)	
Leisure-time physical activity						<0.001[2]
Sedentary	594 (19.2%)	394 (23.7%)	140 (27.5%)	397 (31.8%)	1525 (23.4%)	
Light	2082 (67.3%)	1100 (66.2%)	324 (63.5%)	751 (60.1%)	4257 (65.3%)	
Moderate-hard	419 (13.5%)	168 (10.1%)	46 (9.0%)	102 (8.2%)	735 (11.3%)	

Education (years)	12.6 (3.9)	10.6 (3.7)	11.6 (4.1)	10.5 (3.9)	11.6 (4.0)	<0.001[1]
General obesity	0 (0.0%)	0 (0.0%)	510 (100.0%)	1250 (100.0%)	1760 (27.0%)	
Metabolic syndrome	0 (0.0%)	948 (57.0%)	0 (0.0%)	990 (79.2%)	1938 (29.7%)	<0.001[2]
Hypertension	802 (25.9%)	1173 (70.6%)	176 (34.5%)	1023 (81.8%)	3174 (48.7%)	<0.001[2]
Increased waist circumference	1274 (41.2%)	1267 (76.2%)	503 (98.6%)	1244 (99.5%)	4288 (65.8%)	<0.001[2]
Low HDL cholesterol	542 (17.5%)	768 (46.2%)	102 (20.0%)	768 (61.4%)	2180 (33.5%)	<0.001[2]
Elevated triglycerides	308 (10.0%)	810 (48.7%)	59 (11.6%)	792 (63.4%)	1969 (30.2%)	<0.001[2]
Hyperglycemia	30 (1.0%)	157 (9.4%)	2 (0.4%)	194 (15.5%)	383 (5.9%)	<0.001[2]
Stroke	0 (0.0%)	68 (4.5%)	0 (0.0%)	37 (3.2%)	105 (1.7%)	<0.001[2]
Missing data	3	166	2	83	254	
Angina pectoris	0 (0.0%)	146 (9.8%)	0 (0.0%)	134 (11.4%)	280 (4.5%)	<0.001[2]
Missing data	3	167	2	73	245	
Myocardial infarction	0 (0.0%)	58 (3.9%)	0 (0.0%)	36 (3.1%)	94 (1.5%)	<0.001[2]
Missing data	3	165	2	80	250	
Diabetes	0 (0.0%)	101 (6.7%)	0 (0.0%)	133 (11.3%)	234 (3.7%)	<0.001[2]
Missing data	3	163	2	74	242	
Blood pressure-lowering drug	0 (0.0%)	713 (43.8%)	0 (0.0%)	629 (50.9%)	1342 (20.8%)	<0.001[2]
Missing data	3	36	2	14	55	
Cholesterol-lowering drug	0 (0.0%)	460 (29.0%)	0 (0.0%)	303 (25.5%)	763 (12.0%)	<0.001[2]
Missing data	3	75	2	60	140	
Glucose-lowering drug	0 (0.0%)	96 (6.3%)	0 (0.0%)	108 (9.3%)	204 (3.2%)	<0.001[2]
Missing data	3	136	2	93	234	

HDL = high-density lipoprotein, CVD = cardiovascular disease.

Continuous variables are reported as mean (standard deviation) and categorical variables are given as frequency (percent). In the final sample, missing data existed only in pre-existing disease and drug variables; in categorisation of metabolic health status, missing was assumed "no", but frequencies of missing are shown in this table. It is evident that most people with missing nevertheless was categorised in an unhealthy group.

[1]One way analysis of variance

[2]Pearson's χ^2 test

Table 2. Sample characteristics in mean (standard deviation) or frequency (percent) according to general obesity phenotypes in 6298 men in the SAMINOR 1 Survey (2003—2004)

	Metabolically healthy non-obesity (N=2972, 47.2%)	Metabolically unhealthy non-obesity (N=1843, 29.2%)	Metabolically healthy obesity (N=363, 5.8%)	Metabolically unhealthy obesity (N=1120, 17.8%)	Total (N=6298)	p-value
Age (years)	51.4 (9.9)	57.8 (10.8)	51.3 (10.1)	55.4 (10.3)	54.0 (10.6)	<0.001[1]
Ethnicity						0.002[2]
non-Sami	2264 (76.2%)	1452 (78.8%)	253 (69.7%)	865 (77.2%)	4834 (76.8%)	
Sami	708 (23.8%)	391 (21.2%)	110 (30.3%)	255 (22.8%)	1464 (23.2%)	
Smoking						<0.001[2]
Yes, currently	1060 (35.7%)	549 (29.8%)	86 (23.7%)	260 (23.2%)	1955 (31.0%)	
Yes, previously	982 (33.0%)	830 (45.0%)	158 (43.5%)	571 (51.0%)	2541 (40.3%)	
Never	930 (31.3%)	464 (25.2%)	119 (32.8%)	289 (25.8%)	1802 (28.6%)	
Died during follow-up	297 (10.0%)	402 (21.8%)	39 (10.7%)	200 (17.9%)	938 (14.9%)	<0.001[2]
Cause of death						<0.001[2]
Malignant tumor	124 (41.8%)	123 (30.6%)	12 (30.8%)	63 (31.5%)	322 (34.3%)	
CVD	56 (18.9%)	135 (33.6%)	18 (46.2%)	75 (37.5%)	284 (30.3%)	
Respiratory	38 (12.8%)	47 (11.7%)	5 (12.8%)	14 (7.0%)	104 (11.1%)	
Other	75 (25.3%)	91 (22.6%)	3 (7.7%)	41 (20.5%)	210 (22.4%)	
Unknown	4 (1.3%)	6 (1.5%)	1 (2.6%)	7 (3.5%)	18 (1.9%)	
Alcohol consumption						<0.001[2]
Weekly	1046 (35.2%)	545 (29.6%)	117 (32.2%)	315 (28.1%)	2023 (32.1%)	
Less than weekly	1691 (56.9%)	1057 (57.4%)	213 (58.7%)	683 (61.0%)	3644 (57.9%)	
Never/not last year	235 (7.9%)	241 (13.1%)	33 (9.1%)	122 (10.9%)	631 (10.0%)	
Leisure-time physical activity						<0.001[2]
Sedentary	602 (20.3%)	417 (22.6%)	93 (25.6%)	339 (30.3%)	1451 (23.0%)	
Light	1571 (52.9%)	1088 (59.0%)	200 (55.1%)	616 (55.0%)	3475 (55.2%)	
Moderate-hard	799 (26.9%)	338 (18.3%)	70 (19.3%)	165 (14.7%)	1372 (21.8%)	
Education (years)	11.7 (3.8)	10.6 (3.7)	11.2 (3.4)	10.8 (3.7)	11.2 (3.8)	<0.001[1]
General obesity	0 (0.0%)	0 (0.0%)	363 (100.0%)	1120 (100.0%)	1483 (23.5%)	

Metabolic syndrome	0 (0.0%)	970 (52.6%)	0 (0.0%)	900 (80.4%)	1870 (29.7%)	<0.001[2]
Hypertension	1271 (42.8%)	1493 (81.0%)	164 (45.2%)	972 (86.8%)	3900 (61.9%)	<0.001[2]
Increased waist circumference	636 (21.4%)	1031 (55.9%)	331 (91.2%)	1097 (97.9%)	3095 (49.1%)	<0.001[2]
Low HDL cholesterol	258 (8.7%)	592 (32.1%)	22 (6.1%)	488 (43.6%)	1360 (21.6%)	<0.001[2]
Elevated triglycerides	825 (27.8%)	1040 (56.4%)	93 (25.6%)	815 (72.8%)	2773 (44.0%)	<0.001[2]
Hyperglycemia	44 (1.5%)	230 (12.5%)	3 (0.8%)	163 (14.6%)	440 (7.0%)	<0.001[2]
Stroke	0 (0.0%)	100 (5.9%)	0 (0.0%)	51 (4.8%)	151 (2.5%)	<0.001[2]
Missing data	6	145	0	52	203	
Angina pectoris	0 (0.0%)	318 (18.6%)	0 (0.0%)	138 (12.9%)	456 (7.5%)	<0.001[2]
Missing data	6	137	0	48	191	
Myocardial infarction	0 (0.0%)	236 (13.7%)	0 (0.0%)	110 (10.2%)	346 (5.7%)	<0.001[2]
Missing data	6	124	0	45	175	
Diabetes	0 (0.0%)	135 (7.9%)	0 (0.0%)	85 (7.9%)	220 (3.6%)	<0.001[2]
Missing data	6	134	0	45	185	
Blood pressure-lowering drug	0 (0.0%)	837 (46.4%)	0 (0.0%)	504 (45.4%)	1341 (21.5%)	<0.001[2]
Missing data	6	38	0	10	54	
Cholesterol-lowering drug	0 (0.0%)	630 (35.6%)	0 (0.0%)	320 (29.5%)	950 (15.4%)	<0.001[2]
Missing data	6	74	0	35	115	
Glucose-lowering drug	0 (0.0%)	131 (7.7%)	0 (0.0%)	66 (6.3%)	197 (3.2%)	<0.001[2]
Missing data	6	141	0	68	215	

HDL = high-density lipoprotein, CVD = cardiovascular disease.

Continuous variables are reported as mean (standard deviation) and categorical variables are given as frequency (percent). In the final sample, missing data existed only in pre-existing disease and drug variables; in categorisation of metabolic health status, missing was assumed "no", but frequencies of missing are shown in this table. It is evident that most people with missing nevertheless was categorised in an unhealthy group.

[1]One way analysis of variance

[2]Pearson's χ^2 test

Table 3. All-cause and CVD mortality according to MetS, general and abdominal obesity phenotypes: Hazard ratios (HR) and 95% confidence intervals (CI) from Cox proportional hazards models of 6517 women in the SAMINOR 1 Survey (2003–2004)

				Model 1		Model 2		Model 3	
	Cases	Person-years	IR	HR	95% CI	HR	95% CI	HR	95% CI
Outcome: All-cause mortality									
Metabolic syndrome									
No	343	68588.7	5.0	Ref.		Ref.		Ref.	
Yes	253	28604.7	8.8	1.14	0.97 – 1.35	1.15	0.97 – 1.35	1.11	0.94 – 1.31
General obesity phenotypes									
Metabolically healthy non-obese	154	46629.4	3.3	Ref.		Ref.		Ref.	
Metabolically unhealthy non-obese	230	24487.6	9.4	1.13	0.92 – 1.40	1.14	0.92 – 1.41	1.11	0.90 – 1.38
Metabolically healthy obese	25	7753.5	3.2	0.64	0.42 – 0.97	0.68	0.44 – 1.04	0.63	0.41 – 0.97
Metabolically unhealthy obese	187	18322.8	10.2	1.17	0.94 – 1.46	1.27	1.02 – 1.59	1.17	0.93 – 1.47
Abdominal obesity phenotypes									
Metabolically healthy non-abdominally obese	119	39259.1	3.0	Ref.		Ref.		Ref.	
Metabolically unhealthy non-abdominally obese	170	20308.6	8.4	1.12	0.88 – 1.43	1.14	0.89 – 1.45	1.12	0.88 – 1.43
Metabolically healthy abdominally obese	42	12571.2	3.3	0.71	0.50 – 1.01	0.75	0.53 – 1.07	0.71	0.50 – 1.02
Metabolically unhealthy abdominally obese	265	25054.5	10.6	1.23	0.99 – 1.55	1.31	1.04 – 1.64	1.22	0.97 – 1.54
Outcome: CVD mortality									
Metabolic syndrome									
No	73	68588.7	1.1	Ref.		Ref.		Ref.	
Yes	79	28604.7	2.8	1.55	1.12 – 2.13	1.53	1.11 – 2.11	1.46	1.06 – 2.02
General obesity phenotypes									
Metabolically healthy non-obese	16	46629.4	0.3	Ref.		Ref.		Ref.	
Metabolically unhealthy non-obese	73	24487.6	3.0	2.86	1.65 – 4.95	2.88	1.66 – 4.99	2.77	1.59 – 4.80
Metabolically healthy obese	5	7753.5	0.6	1.08	0.40 – 2.96	1.12	0.41 – 3.07	1.05	0.38 – 2.88
Metabolically unhealthy obese	58	18322.8	3.2	2.81	1.60 – 4.94	2.93	1.66 – 5.15	2.65	1.49 – 4.72
Abdominal obesity phenotypes									
Metabolically healthy non-abdominally obese	16	39259.1	0.4	Ref.		Ref.		Ref.	
Metabolically unhealthy non-abdominally obese	48	20308.6	2.4	1.90	1.07 – 3.38	1.93	1.09 – 3.43	1.86	1.05 – 3.32
Metabolically healthy abdominally obese	5	12571.2	0.4	0.55	0.20 – 1.50	0.57	0.21 – 1.56	0.54	0.20 – 1.47
Metabolically unhealthy abdominally obese	83	25054.5	3.3	2.25	1.30 – 3.88	2.31	1.34 – 3.99	2.11	1.21 – 3.69

IR = crude incidence rate per 1000 person-years , HR = hazard ratio, CI = confidence interval.

Model 1 is the crude model (all models inherently adjusted for age by using attained age as the time-scale). Model 2 was additionally adjusted for smoking, and model 3 was additionally adjusted for leisure-time physical activity, education and alcohol consumption (model 3). We applied stratified Cox models with separate baseline hazards for subgroups of smoking status to satisfy the proportional hazard assumption in all-cause mortality models.

Table 4. All-cause and CVD mortality according to MetS, general and abdominal obesity phenotypes: Hazard ratios (HR) and 95% confidence intervals (CI) from Cox proportional hazards models of 6298 men in SAMINOR 1 (2003–2004)

				Model 1		Model 2		Model 3	
	Cases	Person-years	IR	HR	95% CI	HR	95% CI	HR	95% CI
Outcome: All-cause mortality									
Metabolic syndrome									
No	627	65040.4	9.6	Ref.		Ref.		Ref.	
Yes	311	27124.8	11.5	1.06	0.93 – 1.22	1.11	0.97 – 1.28	1.10	0.96 – 1.26
General obesity phenotypes									
Metabolically healthy non-obese	297	44234.7	6.7	Ref.		Ref.		Ref.	
Metabolically unhealthy non-obese	402	26321.0	15.3	1.12	0.96 – 1.31	1.18	1.01 – 1.38	1.16	0.99 – 1.35
Metabolically healthy obese	39	5381.8	7.2	1.13	0.81 – 1.57	1.28	0.91 – 1.79	1.25	0.89 – 1.75
Metabolically unhealthy obese	200	16227.8	12.3	1.22	1.02 – 1.46	1.38	1.14 – 1.65	1.33	1.11 – 1.61
Abdominal obesity phenotypes									
Metabolically healthy non-abdominally obese	241	38178.8	6.3	Ref.		Ref.		Ref.	
Metabolically unhealthy non-abdominally obese	430	34896.0	12.3	1.13	0.97 – 1.33	1.20	1.02 – 1.41	1.18	1.00 – 1.38
Metabolically healthy abdominally obese	40	4344.3	9.2	1.12	0.80 – 1.57	1.23	0.88 – 1.73	1.20	0.86 – 1.69
Metabolically unhealthy abdominally obese	227	14746.1	15.4	1.39	1.16 – 1.67	1.53	1.27 – 1.84	1.49	1.23 – 1.79
Outcome: CVD mortality									
Metabolic syndrome									
No	170	65040.4	2.6	Ref.		Ref.		Ref.	
Yes	114	27124.8	4.2	1.43	1.13 – 1.82	1.53	1.20 – 1.94	1.51	1.18 – 1.91
General obesity phenotypes									
Metabolically healthy non-obese	56	44234.7	1.3	Ref.		Ref.		Ref.	
Metabolically unhealthy non-obese	135	26321.0	5.1	1.95	1.42 – 2.68	2.11	1.54 – 2.90	2.08	1.51 – 2.86
Metabolically healthy obese	18	5381.8	3.3	2.68	1.57 – 4.56	3.03	1.77 – 5.19	2.92	1.71 – 5.01
Metabolically unhealthy obese	75	16227.8	4.6	2.40	1.69 – 3.40	2.83	1.98 – 4.03	2.72	1.90 – 3.89
Abdominal obesity phenotypes									
Metabolically healthy non-abdominally obese	47	38178.8	1.2	Ref.		Ref.		Ref.	
Metabolically unhealthy non-abdominally obese	137	34896.0	3.9	1.81	1.30 – 2.54	1.98	1.41 – 2.76	1.94	1.38 – 2.72
Metabolically healthy abdominally obese	15	4344.3	3.5	2.07	1.15 – 3.70	2.28	1.27 – 4.09	2.18	1.21 – 3.92
Metabolically unhealthy abdominally obese	85	14746.1	5.8	2.61	1.82 – 3.74	3.00	2.08 – 4.32	2.89	2.00 – 4.17

IR = crude incidence rate per 1000 person-years, HR = hazard ratio, CI = confidence interval.

Model 1 is the crude model (all models inherently adjusted for age by using attained age as the time-scale). Model 2 was additionally adjusted for smoking, and model 3 was additionally adjusted for leisure-time physical activity, education and alcohol consumption (model 3). We applied stratified Cox models with separate baseline hazards for subgroups of smoking status to satisfy the proportional hazard assumption in all-cause mortality models.

Supplementary Table 1. Descriptive characteristics among participants with complete case data and participants with one or more missing data in 14,845 participants in the SAMINOR 1 Survey (2003—2004)

	Complete case (N=12,815)	Missing (N=2030)	Total (N=14,845)	p-value
Age	53.57 (10.74)	58.39 (11.73)	54.23 (11.00)	<0.001[1]
Women	6517 (50.9%)	1254 (61.8%)	7771 (52.3%)	<0.001[2]
Died during follow-up	1534 (12.0%)	480 (23.6%)	2014 (13.6%)	<0.001[2]
Cause of death				0.069[2]
Malignant tumor	540 (35.2%)	137 (28.5%)	677 (33.6%)	
CVD	436 (28.4%)	141 (29.4%)	577 (28.6%)	
Respiratory	166 (10.8%)	56 (11.7%)	222 (11.0%)	
Other	365 (23.8%)	134 (27.9%)	499 (24.8%)	
Unknown	27 (1.8%)	12 (2.5%)	39 (1.9%)	
Weekly alcohol consumption				<0.001[2]
Weekly	3362 (26.2%)	243 (15.3%)	3605 (25.0%)	
Less than weekly	7536 (58.8%)	932 (58.5%)	8468 (58.8%)	
Never/not last year	1917 (15.0%)	417 (26.2%)	2334 (16.2%)	
Missing data	0	438	438	
Sedentary in leisure-time				0.042[2]
Sedentary	2976 (23.2%)	184 (26.0%)	3160 (23.4%)	
Light	7732 (60.3%)	430 (60.7%)	8162 (60.4%)	
Moderate-hard	2107 (16.4%)	94 (13.3%)	2201 (16.3%)	
Missing data	0	1322	1322	
Education	11.41 (3.89)	9.62 (3.42)	11.26 (3.88)	<0.001[2]
Missing data	0	881	881	
Smoking status				0.001[2]
Yes, currently	4003 (31.2%)	621 (32.7%)	4624 (31.4%)	
Yes, previously	4603 (35.9%)	603 (31.7%)	5206 (35.4%)	
Never	4209 (32.8%)	676 (35.6%)	4885 (33.2%)	
Missing data	0	130	130	
Glucose, mmol/L[a]	5.33 (4.91, 5.91)	5.50 (5.02, 6.20)	5.35 (4.93, 5.95)	<0.001[3]

Missing data	0	28	28	
Triglycerides (mmol/L)[a]	1.42 (1.01, 2.04)	1.48 (1.07, 2.14)	1.43 (1.02, 2.05)	<0.001[3]
Missing data	0	10	10	
HDL cholesterol (mmol/L)	1.37 (0.38)	1.38 (0.37)	1.37 (0.38)	0.622[1]
Missing data	0	9	9	
Systolic BP (mmHg)	131.25 (19.68)	136.45 (22.11)	131.96 (20.11)	<0.001[1]
Missing data	0	5	5	
Diastolic BP (mmHg)	75.19 (10.32)	75.88 (11.09)	75.28 (10.43)	0.006[1]
Missing data	0	5	5	
Waist circumference (cm)	89.67 (11.98)	91.00 (12.08)	89.85 (12.00)	<0.001[1]
Missing data	0	28	28	
Height in cm	167.59 (9.45)	163.99 (9.27)	167.10 (9.51)	<0.001[1]
Weight (kg)	77.57 (14.42)	75.72 (14.22)	77.32 (14.41)	<0.001[1]
Angina pectoris	736 (5.9%)	182 (9.8%)	918 (6.4%)	<0.001[2]
Missing data	436	173	609	
Stroke	256 (2.1%)	72 (3.9%)	328 (2.3%)	<0.001[2]
Missing data	457	196	653	
Myocardial infarction	440 (3.6%)	95 (5.2%)	535 (3.8%)	<0.001[2]
Missing data	425	187	612	
Diabetes mellitus	454 (3.7%)	135 (7.3%)	589 (4.1%)	<0.001[2]
Missing data	427	172	599	
Blood pressure-lowering drug	2683 (21.1%)	673 (33.9%)	3356 (22.8%)	<0.001[2]
Missing data	109	46	155	
Cholesterol-lowering drug	1713 (13.6%)	378 (19.6%)	2091 (14.4%)	<0.001[2]
Missing data	255	99	354	
Glucose-lowering drug	401 (3.2%)	111 (6.0%)	512 (3.6%)	<0.001[2]
Missing data	449	170	619	

HDL = high-density lipoprotein, CVD = cardiovascular disease.

Continuous variables are reported as mean (standard deviation) and categorical variables are given as frequency (percent), if not stated otherwise
[a]Median (first quartile, third quartile) [1]Two-sample t-test with equal variance [2]Pearson's χ^2 test [3]Wilcoxon rank sum test

Supplementary Table 2. Sample characteristics in mean (standard deviation) or frequency (percent) according to abdominal obesity phenotypes in 6517 women in the SAMINOR Study (2003—2004)

	Metabolically healthy non-abdominal obesity (N=2600, 39.9%)	Metabolically unhealthy non-abdominal obesity (N=1374, 21.1%)	Metabolically healthy abdominal obesity (N=832, 12.8%)	Metabolically unhealthy abdominal obesity (N=1711, 26.2%)	Total (N=6517)	p-value
Age (years)	49.0 (9.3)	56.5 (10.7)	52.0 (9.9)	57.5 (10.9)	53.2 (10.8)	<0.001[1]
Ethnicity						0.077[2]
non-Sami	2038 (78.4%)	1084 (78.9%)	632 (76.0%)	1296 (75.7%)	5050 (77.5%)	
Sami	562 (21.6%)	290 (21.1%)	200 (24.0%)	415 (24.3%)	1467 (22.5%)	
Smoking						<0.001[2]
Yes, currently	891 (34.3%)	495 (36.0%)	211 (25.4%)	451 (26.4%)	2048 (31.4%)	
Yes, previously	794 (30.5%)	368 (26.8%)	308 (37.0%)	592 (34.6%)	2062 (31.6%)	
Never	915 (35.2%)	511 (37.2%)	313 (37.6%)	668 (39.0%)	2407 (36.9%)	
Died during follow-up	119 (4.6%)	170 (12.4%)	42 (5.0%)	265 (15.5%)	596 (9.1%)	<0.001[2]
Cause of death						<0.001[2]
Malignant tumor	61 (51.3%)	51 (30.0%)	24 (57.1%)	82 (30.9%)	218 (36.6%)	
CVD	16 (13.4%)	48 (28.2%)	5 (11.9%)	83 (31.3%)	152 (25.5%)	
Respiratory	15 (12.6%)	18 (10.6%)	6 (14.3%)	23 (8.7%)	62 (10.4%)	
Other	25 (21.0%)	51 (30.0%)	5 (11.9%)	74 (27.9%)	155 (26.0%)	
Unknown	2 (1.7%)	2 (1.2%)	2 (4.8%)	3 (1.1%)	9 (1.5%)	
Alcohol consumption						<0.001[2]
Weekly	690 (26.5%)	251 (18.3%)	185 (22.2%)	213 (12.4%)	1339 (20.5%)	
Less than weekly	1592 (61.2%)	793 (57.7%)	497 (59.7%)	1010 (59.0%)	3892 (59.7%)	
Never/not last year	318 (12.2%)	330 (24.0%)	150 (18.0%)	488 (28.5%)	1286 (19.7%)	
Leisure-time physical activity						<0.001[2]
Sedentary	497 (19.1%)	292 (21.3%)	206 (24.8%)	530 (31.0%)	1525 (23.4%)	
Light	1745 (67.1%)	931 (67.8%)	539 (64.8%)	1042 (60.9%)	4257 (65.3%)	
Moderate-hard	358 (13.8%)	151 (11.0%)	87 (10.5%)	139 (8.1%)	735 (11.3%)	
Education (years)	12.7 (3.8)	10.8 (3.8)	11.8 (4.1)	10.5 (3.9)	11.6 (4.0)	<0.001[1]

General obesity	60 (2.3%)	95 (6.9%)	450 (54.1%)	1155 (67.5%)	1760 (27.0%)	<0.001[2]
Metabolic syndrome	0 (0.0%)	591 (43.0%)	0 (0.0%)	1347 (78.7%)	1938 (29.7%)	<0.001[2]
Hypertension	600 (23.1%)	946 (68.9%)	277 (33.3%)	1351 (79.0%)	3174 (48.7%)	<0.001[2]
Increased waist circumference	945 (36.3%)	800 (58.2%)	832 (100.0%)	1711 (100.0%)	4288 (65.8%)	<0.001[2]
Low HDL cholesterol	361 (13.9%)	630 (45.9%)	158 (19.0%)	1031 (60.3%)	2180 (33.5%)	<0.001[2]
Elevated triglycerides	167 (6.4%)	631 (45.9%)	88 (10.6%)	1083 (63.3%)	1969 (30.2%)	<0.001[2]
Hyperglycemia	21 (0.8%)	106 (7.7%)	3 (0.4%)	253 (14.8%)	383 (5.9%)	<0.001[2]
Stroke	0 (0.0%)	50 (4.0%)	0 (0.0%)	55 (3.5%)	105 (1.7%)	<0.001[2]
Missing data	3	130	2	119	254	
Angina pectoris	0 (0.0%)	101 (8.1%)	0 (0.0%)	179 (11.2%)	280 (4.5%)	<0.001[2]
Missing data	3	129	2	111	245	
Myocardial infarction	0 (0.0%)	42 (3.4%)	0 (0.0%)	52 (3.3%)	94 (1.5%)	<0.001[2]
Missing data	3	123	2	122	250	
Diabetes	0 (0.0%)	64 (5.1%)	0 (0.0%)	170 (10.6%)	234 (3.7%)	<0.001[2]
Missing data	3	128	2	109	242	
Blood pressure-lowering drug	0 (0.0%)	511 (37.9%)	0 (0.0%)	831 (49.3%)	1342 (20.8%)	<0.001[2]
Missing data	3	26	2	24	55	
Cholesterol-lowering drug	0 (0.0%)	336 (25.3%)	0 (0.0%)	427 (26.3%)	763 (12.0%)	<0.001[2]
Missing data	3	45	2	90	140	
Glucose-lowering drug	0 (0.0%)	64 (5.0%)	0 (0.0%)	140 (8.9%)	204 (3.2%)	<0.001[2]
Missing data	3	89	2	140	234	

HDL = high-density lipoprotein, CVD = cardiovascular disease.

Continuous variables are reported as mean (standard deviation) and categorical variables are given as frequency (percent). In the final sample, missing data existed only in pre-existing disease and drug variables; in categorisation of metabolic health status, missing was assumed "no", but frequencies of missing are shown in this table. It is evident that most people with missing nevertheless was categorised in an unhealthy group.

[1]One way analysis of variance

[2]Pearson's χ^2 test

Supplementary Table 3. Sample characteristics in mean (standard deviation) or frequency (percent) according to abdominal obesity phenotypes in 6298 men in the SAMINOR Study (2003—2004)

	Metabolically healthy non-abdominal obesity (N=2558, 40.6%)	Metabolically unhealthy non-abdominal obesity (N=2408, 38.3%)	Metabolically healthy abdominal obesity (N=297, 4.7%)	Metabolically unhealthy abdominal obesity (N=1035, 16.4%)	Total (N=6298)	p-value
Age (years)	51.3 (9.8)	55.8 (11.0)	53.0 (10.9)	56.8 (10.3)	54.0 (10.6)	<0.001[1]
Ethnicity						<0.001[2]
non-Sami	1931 (75.5%)	1824 (75.7%)	240 (80.8%)	839 (81.1%)	4834 (76.8%)	
Sami	627 (24.5%)	584 (24.3%)	57 (19.2%)	196 (18.9%)	1464 (23.2%)	
Smoking						<0.001[2]
Yes, currently	896 (35.0%)	733 (30.4%)	74 (24.9%)	252 (24.3%)	1955 (31.0%)	
Yes, previously	852 (33.3%)	1007 (41.8%)	126 (42.4%)	556 (53.7%)	2541 (40.3%)	
Never	810 (31.7%)	668 (27.7%)	97 (32.7%)	227 (21.9%)	1802 (28.6%)	
Died during follow-up	241 (9.4%)	430 (17.9%)	40 (13.5%)	227 (21.9%)	938 (14.9%)	<0.001[2]
Cause of death						<0.001[2]
Malignant tumor	104 (43.2%)	130 (30.2%)	13 (32.5%)	75 (33.0%)	322 (34.3%)	
CVD	47 (19.5%)	137 (31.9%)	15 (37.5%)	85 (37.4%)	284 (30.3%)	
Respiratory	29 (12.0%)	48 (11.2%)	6 (15.0%)	21 (9.3%)	104 (11.1%)	
Other	56 (23.2%)	110 (25.6%)	6 (15.0%)	38 (16.7%)	210 (22.4%)	
Unknown	5 (2.1%)	5 (1.2%)	0 (0.0%)	8 (3.5%)	18 (1.9%)	
Alcohol consumption						<0.001[2]
Weekly	914 (35.7%)	710 (29.5%)	99 (33.3%)	300 (29.0%)	2023 (32.1%)	
Less than weekly	1453 (56.8%)	1400 (58.1%)	169 (56.9%)	622 (60.1%)	3644 (57.9%)	
Never/not last year	191 (7.5%)	298 (12.4%)	29 (9.8%)	113 (10.9%)	631 (10.0%)	
Leisure-time physical activity						<0.001[2]
Sedentary	513 (20.1%)	532 (22.1%)	85 (28.6%)	321 (31.0%)	1451 (23.0%)	
Light	1352 (52.9%)	1376 (57.1%)	161 (54.2%)	586 (56.6%)	3475 (55.2%)	
Moderate-hard	693 (27.1%)	500 (20.8%)	51 (17.2%)	128 (12.4%)	1372 (21.8%)	

Education (years)	11.8 (3.7)	10.8 (3.7)	11.1 (3.2)	10.7 (3.8)	11.2 (3.8)	<0.001[1]
General obesity	145 (5.7%)	326 (13.5%)	208 (70.0%)	804 (77.7%)	1483 (23.5%)	<0.001[2]
Metabolic syndrome	0 (0.0%)	1031 (42.8%)	0 (0.0%)	839 (81.1%)	1870 (29.7%)	<0.001[2]
Hypertension	939 (36.7%)	1915 (79.5%)	145 (48.8%)	901 (87.1%)	3900 (61.9%)	<0.001[2]
Increased waist circumference	670 (26.2%)	1093 (45.4%)	297 (100.0%)	1035 (100.0%)	3095 (49.1%)	<0.001[2]
Low HDL cholesterol	100 (3.9%)	804 (33.4%)	12 (4.0%)	444 (42.9%)	1360 (21.6%)	<0.001[2]
Elevated triglycerides	438 (17.1%)	1527 (63.4%)	67 (22.6%)	741 (71.6%)	2773 (44.0%)	<0.001[2]
Hyperglycemia	17 (0.7%)	253 (10.5%)	2 (0.7%)	168 (16.2%)	440 (7.0%)	<0.001[2]
Stroke	0 (0.0%)	103 (4.6%)	0 (0.0%)	48 (4.9%)	151 (2.5%)	<0.001[2]
Missing data	6	148	0	49	203	
Angina pectoris	0 (0.0%)	313 (13.8%)	0 (0.0%)	143 (14.4%)	456 (7.5%)	<0.001[2]
Missing data	6	142	0	43	191	
Myocardial infarction	0 (0.0%)	229 (10.0%)	0 (0.0%)	117 (11.8%)	346 (5.7%)	<0.001[2]
Missing data	6	128	0	41	175	
Diabetes	0 (0.0%)	124 (5.5%)	0 (0.0%)	96 (9.7%)	220 (3.6%)	<0.001[2]
Missing data	6	138	0	41	185	
Blood pressure-lowering drug	0 (0.0%)	858 (36.2%)	0 (0.0%)	483 (47.1%)	1341 (21.5%)	<0.001[2]
Missing data	6	38	0	10	54	
Cholesterol-lowering drug	0 (0.0%)	642 (27.6%)	0 (0.0%)	308 (30.6%)	950 (15.4%)	<0.001[2]
Missing data	6	79	0	30	115	
Glucose-lowering drug	0 (0.0%)	124 (5.5%)	0 (0.0%)	73 (7.5%)	197 (3.2%)	<0.001[2]
Missing data	6	142	0	67	215	

HDL = high-density lipoprotein, CVD = cardiovascular disease.

Continuous variables are reported as mean (standard deviation) and categorical variables are given as frequency (percent). In the final sample, missing data existed only in pre-existing disease and drug variables; in categorisation of metabolic health status, missing was assumed "no", but frequencies of missing are shown in this table. It is evident that most people with missing nevertheless was categorised in an unhealthy group.

[1]One way analysis of variance

[2]Pearson's χ^2 test

Supplementary Table 4. Sensitivity analyses. Hazard ratio (HR) and 95% confidence interval (CI) of metabolic syndrome (MetS), general and abdominal obesity phenotypes for all-cause mortality and CVD mortality in various samples of women in the SAMINOR 1 Survey (2003–2004)

		All-cause mortality						CVD mortality					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Restricted to participants without pre-existing disease or receiving treatment for it (N=4601)	**MetS**												
	No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	Yes	0.95	0.71 – 1.27	0.93	0.69 – 1.25	0.90	0.67 – 1.22	1.65	0.82 – 3.32	1.59	0.79 – 3.19	1.51	0.75 – 3.06
	GOP												
	MHNO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNO	0.68	0.45 – 1.03	0.66	0.44 – 1.00	0.63	0.42 – 0.95	1.11	0.41 – 3.04	1.01	0.37 – 2.79	0.92	0.33 – 2.56
	MHO	0.63	0.41 – 0.97	0.68	0.44 – 1.06	0.63	0.40 – 0.98	1.05	0.38 – 2.91	1.10	0.39 – 3.05	1.01	0.35 – 2.91
	MUO	1.13	0.78 – 1.66	1.19	0.81 – 1.73	1.12	0.76 – 1.65	2.46	1.05 – 5.78	2.58	1.10 – 6.06	2.51	1.06 – 5.98
	AOP												
	MHNAO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNAO	0.93	0.64 – 1.36	0.89	0.61 – 1.31	0.88	0.60 – 1.29	0.51	0.15 – 1.76	0.49	0.14 – 1.69	0.46	0.13 – 1.59
	MHAO	0.71	0.49 – 1.02	0.76	0.53 – 1.09	0.71	0.49 – 1.03	0.53	0.19 – 1.45	0.56	0.20 – 1.55	0.52	0.18 – 1.48
	MUAO	1.05	0.74 – 1.50	1.08	0.76 – 1.54	1.02	0.71 – 1.46	1.65	0.75 – 3.65	1.67	0.75 – 3.70	1.57	0.70 – 3.52
		All-cause mortality						**CVD mortality**					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Restricted to participants who have never smoked (N=2407)	**MetS**												
	No	Ref.				Ref.		Ref.				Ref.	
	Yes	1.47	1.12 – 1.92			1.41	1.07 – 1.85	1.83	1.11 – 3.01			1.77	1.07 – 2.94
	GOP												
	MHNO	Ref.				Ref.		Ref.				Ref.	
	MUNO	1.40	0.95 – 2.08			1.36	0.91 – 2.03	2.95	1.12 – 7.77			2.83	1.06 – 7.52
	MHO	0.58	0.26 – 1.30			0.53	0.23 – 1.19	1.66	0.39 – 7.00			1.48	0.35 – 6.33
	MUO	1.56	1.05 – 2.31			1.40	0.93 – 2.11	3.39	1.29 – 8.91			2.97	1.10 – 8.02
	AOP												
	MHNAO	Ref.				Ref.		Ref.				Ref.	
	MUNAO	1.59	1.02 – 2.48			1.58	1.00 – 2.49	2.15	0.80 – 5.82			2.02	0.73 – 5.54
	MHAO	0.73	0.38 – 1.42			0.69	0.35 – 1.34	0.83	0.20 – 3.50			0.74	0.17 – 3.15
	MUAO	1.50	0.97 – 2.31			1.36	0.87 – 2.13	2.42	0.93 – 6.29			2.10	0.79 – 5.61

		All-cause mortality						CVD mortality					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Original sample size (N=6517), but MetS categorised using conservative cut-offs for waist circumference, triglycerides and glucose	**MetS**												
	No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	Yes	1.33	1.12 – 1.58	1.33	1.12 – 1.59	1.29	1.08 – 1.54	1.74	1.25 – 2.41	1.72	1.24 – 2.39	1.66	1.19 – 2.31
	GOP												
	MHNO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNO	1.32	1.07 – 1.62	1.33	1.08 – 1.64	1.31	1.06 – 1.61	3.38	2.00 – 5.73	3.41	2.01 – 5.77	3.33	1.96 – 5.66
	MHO	0.80	0.56 – 1.15	0.86	0.60 – 1.23	0.81	0.56 – 1.16	1.47	0.64 – 3.38	1.51	0.66 – 3.49	1.44	0.62 – 3.34
	MUO	1.26	1.01 – 1.57	1.38	1.10 – 1.72	1.28	1.02 – 1.61	3.03	1.76 – 5.21	3.16	1.83 – 5.44	2.90	1.66 – 5.07
	AOP												
	MHNAO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNAO	1.12	0.88 – 1.42	1.13	0.89 – 1.44	1.13	0.89 – 1.43	1.98	1.14 – 3.44	2.00	1.15 – 3.48	1.95	1.12 – 3.40
	MHAO	0.78	0.57 – 1.07	0.83	0.61 – 1.14	0.80	0.58 – 1.09	0.64	0.27 – 1.54	0.67	0.28 – 1.60	0.63	0.26 – 1.51
	MUAO	1.23	0.99 – 1.53	1.30	1.04 – 1.62	1.22	0.97 – 1.53	2.30	1.37 – 3.88	2.36	1.40 – 3.98	2.18	1.28 – 3.71
		All-cause mortality						**CVD mortality**					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Multiply imputed data (m=20) of N=7771 women eligible for analysis	**MetS**												
	No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	Yes	1.18	1.03 – 1.35	1.18	1.03 – 1.36	1.14	1.00 – 1.31	1.54	1.19 – 2.00	1.53	1.18 – 1.99	1.46	1.12 – 1.90
	GOP												
	MHNO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNO	1.19	1.00 – 1.42	1.20	1.02 – 1.43	1.18	0.98 – 1.41	2.50	1.63 – 3.84	2.50	1.63 – 3.84	2.45	1.59 – 3.77
	MHO	0.64	0.44 – 0.92	0.69	0.48 – 1.00	0.66	0.45 – 0.95	1.15	0.53 – 2.52	1.20	0.55 – 2.63	1.14	0.52 – 2.50
	MUO	1.20	1.00 – 1.44	1.31	1.09 – 1.58	1.21	1.00 – 1.47	2.74	1.77 – 4.23	2.88	1.86 – 4.46	2.59	1.66 – 4.06
	AOP												
	MHNAO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNAO	1.21	0.99 – 1.49	1.23	1.00 – 1.51	1.21	0.99 – 1.49	2.28	1.39 – 3.73	2.29	1.40 – 3.76	2.23	1.36 – 3.67
	MHAO	0.75	0.56 – 1.01	0.80	0.60 – 1.08	0.77	0.57 – 1.03	1.16	0.58 – 2.30	1.21	0.60 – 2.40	1.12	0.56 – 2.25
	MUAO	1.26	1.05 – 1.53	1.34	1.11 – 1.62	1.26	1.03 – 1.53	2.65	1.66 – 4.24	2.74	1.71 – 4.38	2.49	1.54 – 4.02

CVD = cardiovascular disease, HR = hazard ratio, CI = confidence interval. MetS = metabolic syndrome, ref. = reference, GOP = general obesity phenotypes, AOP = abdominal obesity phenotypes, MHNO = metabolically healthy non-obesity, MUNO = metabolically unhealthy non-obesity, MHO = metabolically unhealthy obesity, MUO = metabolically unhealthy obesity, MHNAO = metabolically healthy non-obesity, MUNAO = metabolically unhealthy non-abdominal obesity, MHAO = metabolically healthy abdominal obesity, MUAO = metabolically unhealthy abdominal obesity.

Model 1 is the crude model (all models inherently adjusted for age by using attained age as the time-scale). Model 2 was additionally adjusted for smoking, and model 3 was additionally adjusted for leisure-time physical activity, education and alcohol consumption (model 3). In all-cause mortality models, we applied stratified Cox with separate baseline hazards for subgroups of smoking status to satisfy the proportional hazard assumption.

Supplementary Table 5. Sensitivity analyses. Hazard ratio (HR) and 95% confidence interval (CI) of metabolic syndrome (MetS), general and abdominal obesity phenotypes for all-cause mortality and CVD mortality in various samples of men in the SAMINOR 1 Survey (2003–2004)

		All-cause mortality						CVD mortality					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Restricted to participants without pre-existing disease or receiving treatment for it (N=4383)	**MetS**												
	No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	Yes	1.05	0.84 – 1.31	1.09	0.87 – 1.36	1.06	0.84 – 1.33	1.16	0.74 – 1.83	1.27	0.80 – 2.01	1.21	0.76 – 1.91
	GOP												
	MHNO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNO	0.99	0.74 – 1.31	1.01	0.76 – 1.35	0.99	0.75 – 1.33	1.01	0.53 – 1.92	1.11	0.58 – 2.13	1.08	0.56 – 2.07
	MHO	1.14	0.82 – 1.59	1.28	0.91 – 1.80	1.22	0.87 – 1.72	2.71	1.59 – 4.63	3.29	1.91 – 5.68	3.09	1.78 – 5.36
	MUO	1.17	0.85 – 1.60	1.30	0.94 – 1.78	1.23	0.89 – 1.70	1.93	1.08 – 3.48	2.30	1.27 – 4.18	2.10	1.15 – 3.83
	AOP												
	MHNAO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNAO	1.13	0.90 – 1.42	1.18	0.94 – 1.49	1.16	0.92 – 1.46	1.36	0.84 – 2.20	1.48	0.91 – 2.39	1.44	0.89 – 2.33
	MHAO	1.14	0.82 – 1.60	1.26	0.90 – 1.77	1.21	0.86 – 1.71	2.19	1.22 – 3.93	2.48	1.37 – 4.47	2.40	1.32 – 4.35
	MUAO	1.27	0.93 – 1.73	1.35	0.99 – 1.85	1.30	0.95 – 1.78	1.49	0.77 – 2.87	1.68	0.87 – 3.25	1.59	0.82 – 3.09
		All-cause mortality						**CVD mortality**					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Restricted to participants who have never smoked (N=1802)	**MetS**												
	No	Ref.				Ref.		Ref.				Ref.	
	Yes	1.10	0.79 – 1.53			1.03	0.73 – 1.44	1.30	0.75 – 2.27			1.22	0.68 – 2.18
	GOP												
	MHNO	Ref.				Ref.		Ref.				Ref.	
	MUNO	1.25	0.88 – 1.78			1.23	0.85 – 1.77	1.79	0.92 – 3.49			1.83	0.92 – 3.63
	MHO	1.95	0.92 – 4.12			1.85	0.87 – 3.91	3.84	1.24 – 11.89			3.78	1.21 – 11.80
	MUO	1.47	0.95 – 2.29			1.35	0.86 – 2.12	2.16	0.98 – 4.76			2.09	0.92 – 4.75
	AOP												
	MHNAO	Ref.				Ref.		Ref.				Ref.	
	MUNAO	1.48	1.02 – 2.15			1.46	1.00 – 2.13	2.81	1.28 – 6.18			3.00	1.35 – 6.68
	MHAO	1.39	0.65 – 2.96			1.37	0.64 – 2.93	3.52	1.05 – 11.77			3.95	1.17 – 13.39
	MUAO	1.62	1.01 – 2.61			1.47	0.89 – 2.42	3.23	1.29 – 8.09			3.20	1.22 – 8.38

		All-cause mortality						CVD mortality					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Original sample size (N=6298), but MetS categorised using conservative cut-offs for waist circumference, triglycerides and glucose	**MetS**												
	No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	Yes	1.21	1.03 – 1.42	1.25	1.06 – 1.46	1.23	1.05 – 1.44	1.60	1.23 – 2.09	1.67	1.28 – 2.18	1.64	1.25 – 2.14
	GOP												
	MHNO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNO	1.18	1.01 – 1.37	1.23	1.06 – 1.43	1.21	1.04 – 1.41	2.24	1.64 – 3.06	2.38	1.74 – 3.26	2.36	1.72 – 3.23
	MHO	1.15	0.86 – 1.54	1.28	0.95 – 1.72	1.26	0.94 – 1.69	2.59	1.59 – 4.23	2.90	1.77 – 4.75	2.84	1.73 – 4.65
	MUO	1.25	1.05 – 1.50	1.40	1.17 – 1.69	1.36	1.13 – 1.64	2.58	1.83 – 3.65	3.01	2.12 – 4.28	2.90	2.04 – 4.14
	AOP												
	MHNAO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNAO	1.20	1.02 – 1.40	1.25	1.07 – 1.46	1.23	1.05 – 1.44	1.94	1.41 – 2.68	2.08	1.50 – 2.87	2.04	1.48 – 2.83
	MHAO	1.23	0.91 – 1.66	1.33	0.98 – 1.80	1.30	0.96 – 1.76	1.93	1.10 – 3.38	2.10	1.20 – 3.68	2.03	1.16 – 3.57
	MUAO	1.42	1.18 – 1.70	1.55	1.29 – 1.86	1.51	1.25 – 1.81	2.73	1.93 – 3.86	3.08	2.17 – 4.38	2.97	2.08 – 4.24

		All-cause mortality						CVD mortality					
		Model 1		Model 2		Model 3		Model 1		Model 2		Model 3	
		HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Multiply imputed data (m=20) of N=7074 participants eligible for analysis	**MetS**												
	No	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	Yes	1.09	0.96 – 1.23	1.13	1.00 – 1.28	1.11	0.98 – 1.26	1.46	1.18 – 1.81	1.54	1.24 – 1.91	1.50	1.20 – 1.87
	GOP												
	MHNO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNO	1.14	0.99 – 1.31	1.21	1.05 – 1.39	1.18	1.02 – 1.36	1.81	1.36 – 2.40	1.87	1.38 – 2.54	1.88	1.40 – 2.51
	MHO	1.12	0.83 – 1.52	1.27	0.94 – 1.72	1.23	0.91 – 1.66	2.42	1.48 – 3.94	2.30	1.38 – 3.83	2.57	1.56 – 4.21
	MUO	1.21	1.03 – 1.43	1.39	1.17 – 1.64	1.33	1.12 – 1.58	2.36	1.73 – 3.22	2.74	1.98 – 3.81	2.61	1.89 – 3.60
	AOP												
	MHNAO	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
	MUNAO	1.12	0.97 – 1.30	1.20	1.03 – 1.39	1.17	1.00 – 1.35	1.73	1.28 – 2.35	1.87	1.38 – 2.54	1.78	1.31 – 2.42
	MHAO	1.15	0.86 – 1.54	1.26	0.94 – 1.69	1.21	0.90 – 1.63	2.11	1.27 – 3.52	2.30	1.38 – 3.83	2.12	1.27 – 3.55
	MUAO	1.34	1.13 – 1.58	1.49	1.26 – 1.76	1.43	1.21 – 1.70	2.44	1.76 – 3.37	2.74	1.98 – 3.81	2.60	1.87 – 3.63

CVD = cardiovascular disease, HR = hazard ratio, CI = confidence interval. MetS = metabolic syndrome, ref. = reference, GOP = general obesity phenotypes, AOP = abdominal obesity phenotypes, MHNO = metabolically healthy non-obesity, MUNO = metabolically unhealthy non-obesity, MHO = metabolically unhealthy obesity, MUO = metabolically unhealthy obesity, MHNAO = metabolically healthy non-obesity, MUNAO = metabolically unhealthy non-abdominal obesity, MHAO = metabolically healthy abdominal obesity, MUAO = metabolically unhealthy abdominal obesity.

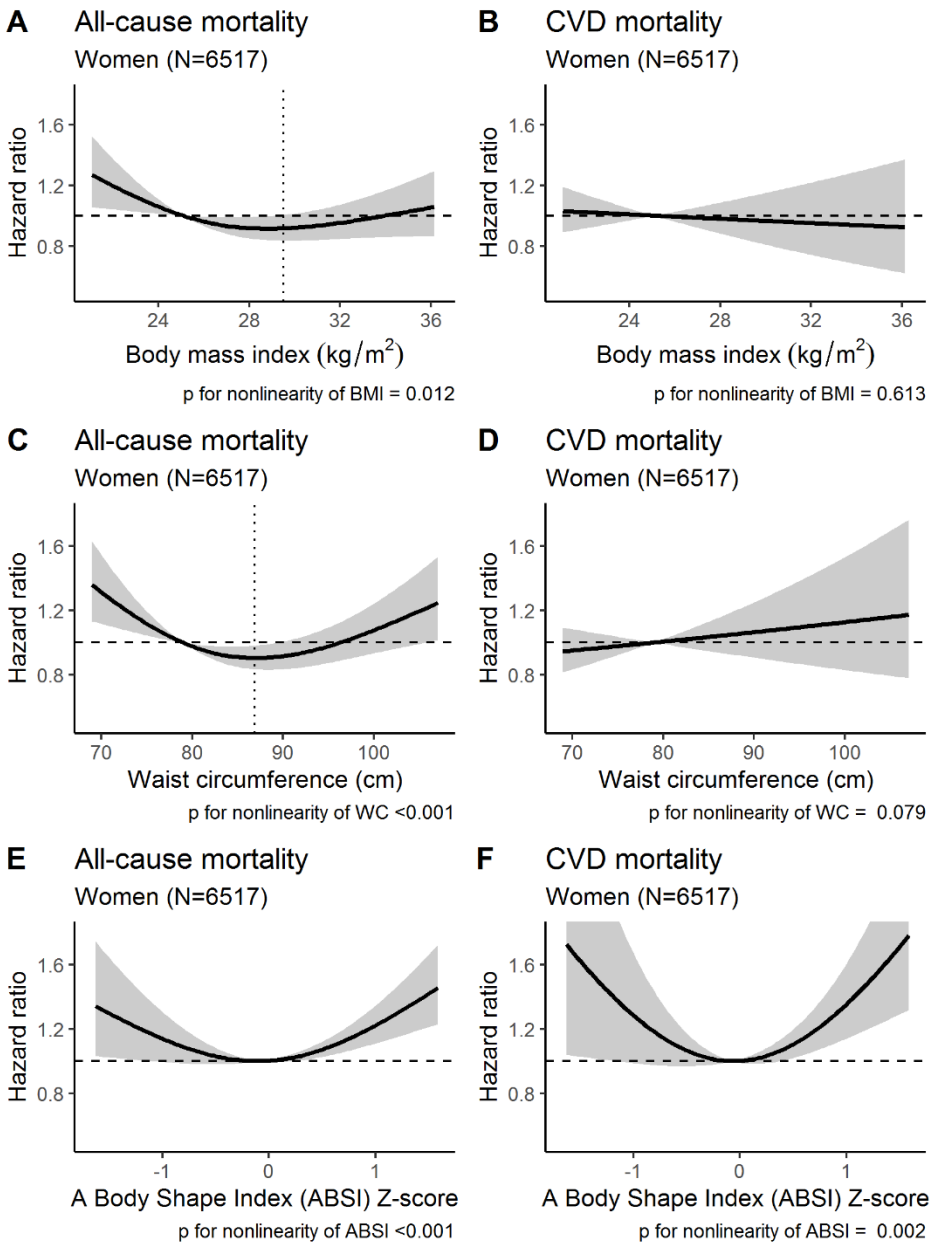
Model 1 is the crude model (all models inherently adjusted for age by using attained age as the time-scale). Model 2 was additionally adjusted for smoking, and model 3 was additionally adjusted for leisure-time physical activity, education and alcohol consumption (model 3). In all-cause mortality models, we applied stratified Cox with separate baseline hazards for subgroups of smoking status to satisfy the proportional hazard assumption.

Supplementary Table 6. All-cause and CVD mortality according to MetS, general and abdominal obesity phenotypes: Hazard ratios (HR) and 95% confidence intervals (CI) from Cox proportional hazards models of 12,815 men and women in SAMINOR 1 (2003–2004)

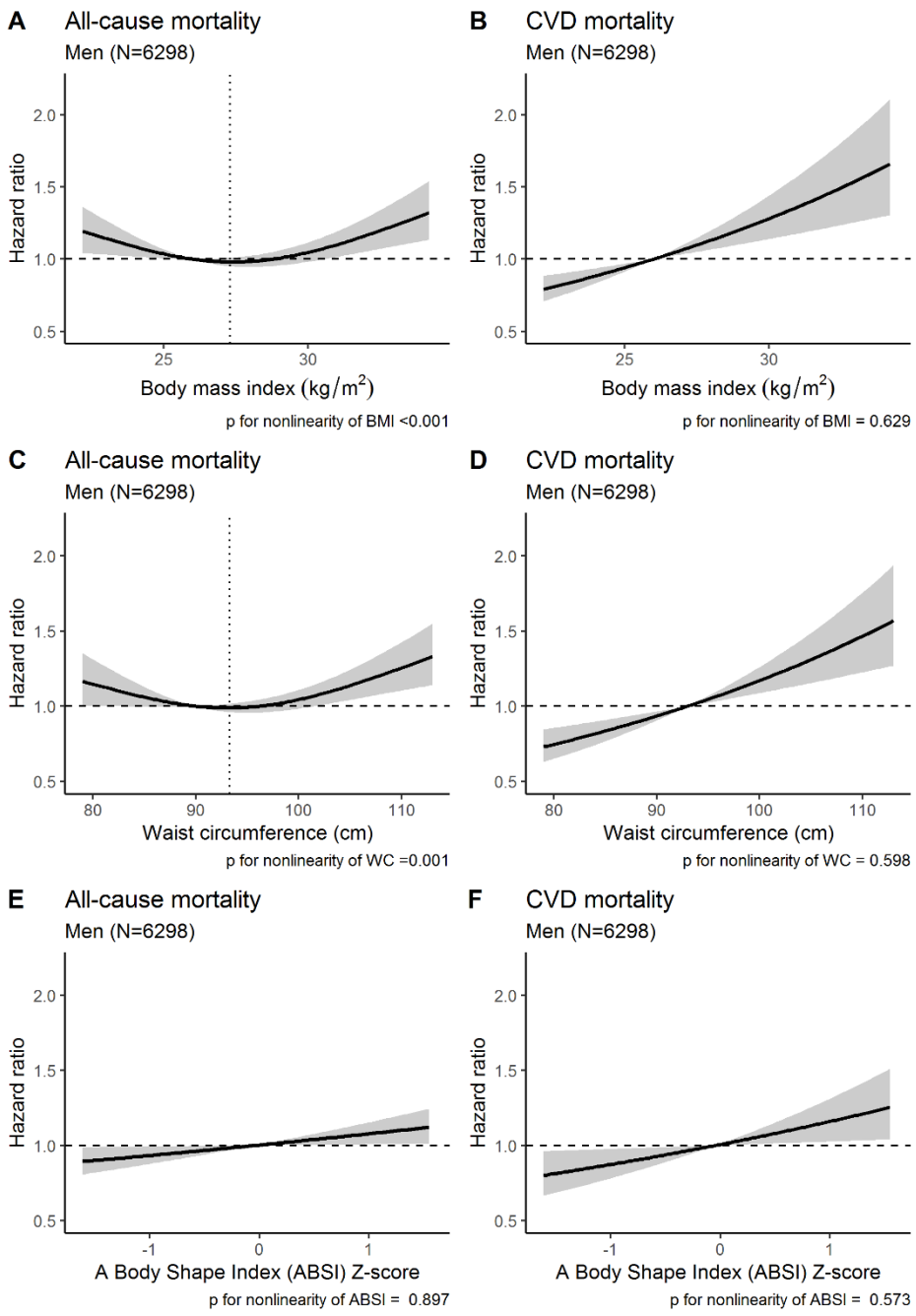
				Model 1		Model 2		Model 3	
	Cases	Person-years	IR	HR	95% CI	HR	95% CI	HR	95% CI
Outcome: All-cause mortality									
Metabolic syndrome									
No	970	133,629.1	7.3	Ref.		Ref.		Ref.	
Yes	564	55,729.5	10.1	1.10	0.99 – 1.22	1.12	1.01 – 1.25	1.10	0.99 – 1.23
General obesity phenotypes									
Metabolically healthy non-obese	451	90,864.1	5.0	Ref.		Ref.		Ref.	
Metabolically unhealthy non-obese	632	50,808.6	12.4	1.13	1.00 – 1.28	1.16	1.03 – 1.31	1.14	1.00 – 1.29
Metabolically healthy obese	64	13,135.3	4.9	0.87	0.67 – 1.13	0.95	0.73 – 1.24	0.92	0.71 – 1.20
Metabolically unhealthy obese	387	34,550.6	11.2	1.20	1.05 – 1.38	1.33	1.15 – 1.53	1.26	1.10 – 1.46
Abdominal obesity phenotypes									
Metabolically healthy non-abdominally obese	360	77,437.9	4.6	Ref.		Ref.		Ref.	
Metabolically unhealthy non-abdominally obese	600	55,204.6	10.9	1.13	0.99 – 1.29	1.17	1.03 – 1.34	1.15	1.01 – 1.32
Metabolically healthy abdominally obese	82	16,915.5	4.8	0.88	0.69 – 1.12	0.95	0.74 – 1.21	0.92	0.72 – 1.17
Metabolically unhealthy abdominally obese	492	39,800.6	12.4	1.33	1.15 – 1.53	1.43	1.24 – 1.65	1.36	1.18 – 1.58
Outcome: CVD mortality									
Metabolic syndrome									
No	243	133,629.1	1.8	Ref.		Ref.		Ref.	
Yes	193	55,729.5	3.5	1.47	1.22 – 1.78	1.51	1.25 – 1.83	1.48	1.22 – 1.79
General obesity phenotypes									
Metabolically healthy non-obese	72	90,864.1	0.8	Ref.		Ref.		Ref.	
Metabolically unhealthy non-obese	208	50,808.6	4.1	2.18	1.66 – 2.86	2.30	1.75 – 3.02	2.24	1.70 – 2.95
Metabolically healthy obese	23	13,135.3	1.8	1.96	1.22 – 3.14	2.16	1.34 – 3.48	2.06	1.28 – 3.33
Metabolically unhealthy obese	133	34,550.6	3.8	2.48	1.85 – 3.32	2.78	2.07 – 3.75	2.61	1.93 – 3.53
Abdominal obesity phenotypes									
Metabolically healthy non-abdominally obese	63	77,437.9	0.8	Ref.		Ref.		Ref.	
Metabolically unhealthy non-abdominally obese	185	55,204.6	3.4	1.84	1.37 – 2.45	1.95	1.46 – 2.61	1.90	1.42 – 2.54
Metabolically healthy abdominally obese	20	16,915.5	1.2	1.27	0.76 – 2.10	1.36	0.82 – 2.27	1.30	0.78 – 2.17
Metabolically unhealthy abdominally obese	168	39,800.6	4.2	2.50	1.85 – 3.36	2.74	2.03 – 3.71	2.58	1.90 – 3.51

HR = hazard ratio, CI = confidence interval, IR = crude incidence rate per 1000 person-years.

Adjustments were made for sex (model 1) plus smoking (model 2) plus leisure-time physical activity, education and alcohol consumption (model 3). All models were inherently adjusted for age by using attained age as the time-scale. In the all-cause mortality models, we applied stratified Cox models with separate baseline hazards for subgroups of smoking status to satisfy the proportional hazard assumption. In the CVD mortality models, we applied stratified Cox models with separate baseline hazards for subgroups of sex and smoking status to satisfy the proportional hazard assumption.



Supplementary Figure 1. The functional relationships between mortality (all-cause and CVD) and continuous obesity measures (body mass index, waist circumference and a body shape index) with corresponding hazard ratios with 95% confidence bands in women. The reference of all curves were women with a BMI of 26.7 kg/m², a waist circumference of 79 cm and a body shape index Z-score of 0 (median values). P-values originates from likelihood ratio tests comparing models with/without linear terms terms. Estimates are predicted for median values of confounders (smoking, leisure-time physical activity, education, alcohol consumption). All models were inherently adjusted for age by using attained age as the time-scale. The vertical, dotted lines represent the nadir of risk. ABSI = a body shape index, BMI = body mass index, WC = waist circumference.



Supplementary Figure 2. The functional relationships between mortality (all-cause and CVD) and continuous obesity measures (body mass index, waist circumference and a body shape index) with corresponding hazard ratios with 95% confidence bands in men. The reference of all curves were men with a BMI of 27.2, a waist circumference of 90 cm and a body shape index Z-score of 0 (median values). P-values originates from likelihood ratio tests comparing models with/without linear terms terms. Estimates are predicted for median values of confounders (smoking, leisure-time physical activity, education, alcohol consumption). All models were inherently adjusted for age by using attained age as the time-scale. The vertical, dotted lines represent the nadir of risk. ABSI = a body shape index, BMI = body mass index, WC = waist circumference.

Paper III

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ORIGINAL ARTICLE

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Relationships between metabolic markers and obesity measures in two populations that differ in stature—The SAMINOR Study

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Summary

Background: The relationships between metabolic markers and obesity measures may differ by ethnicity, sex, and height. Questions have been posed whether these relationships differ by ethnicity in the population in Northern Norway, but this has not been explored yet.

Objectives: Investigate the relationships between metabolic markers and obesity measures in Sami and non-Sami and explore the impact of stature.

Methods: In total, 13 921 men and women aged 30 and 36 to 79 years (22.0% Sami) from a population-based cross-sectional survey in Norway, the SAMINOR 1 Survey (2003-2004, 57.2% attendance), were included. Relationships between triglycerides, high-density lipoprotein cholesterol, glucose, systolic/diastolic blood pressure (BP), metabolic syndrome and diabetes mellitus as outcomes, and body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR), respectively, were modelled using fractional polynomial regression. Appropriate interaction analyses and adjustments were made.

Results: The non-Sami were approximately 6 cm taller than the Sami. No interactions were found between ethnicity and obesity. At the same levels of WC, BMI, or WHtR, levels of lipids and BP differed marginally between Sami and non-Sami, but these were eliminated by height adjustment, with one exception: At any given WC, BMI, or WHtR, Sami had approximately 1.4 mmHg (95% CI, −2.1 to −0.7) lower systolic BP than non-Sami (*P* values < .001).

Conclusions: Height explained the marginal ethnic differences in metabolic markers at the same level of obesity, except for systolic BP, which was lower in Sami than in non-Sami at any given BMI, WC, or WHtR.

KEYWORDS

body mass index, ethnicity, metabolic syndrome, waist circumference

1 | INTRODUCTION

The relationships between obesity measures, body fat, and metabolic markers in various populations are a research priority of several health organizations.[1,2] In Asian populations, the World Health Organization has recommended lower body mass index (BMI)/waist circumference (WC) cut-offs because they are predisposed to disease at low levels of obesity.[3] In other ethnically diverse populations, such as in New Zealand, Greenland, Canada, and in the United States, findings diverge and implications for clinical practice are uncertain.[4-7]

The Sami is an ethnic minority and indigenous people living mainly in the northern parts of Norway, Sweden, and Finland and on the Kola Peninsula in Russia. In the last four decades, research from Norway has shown variations in obesity levels between people with and without Sami affiliation.[8-11] Sami women have repeatedly been shown to have higher BMI and/or larger WC than non-Sami women.[8-11] Yet researchers have observed differences concerning diabetes mellitus (DM) prevalence comparing the two groups with lower risks of DM in Sami than in non-Sami women in 1974–1975,[9] similar in 2003–2004,[12] and higher in 2012–2014.[11] In contrast, Sami men have previously been shown to have a lower WC than non-Sami men,[11,12] although recent reports show that Sami men have a higher prevalence of DM[11] and a higher severity score of metabolic syndrome (MetS) than non-Sami men.[13] However, no studies have explicitly examined the relationships between metabolic markers and obesity measures in this population.

As cut-offs for obesity should be population specific,[1] researchers have questioned the need for ethnic-specific cut-offs in Northern Norway.[8,12] On average, Sami populations have lower statures than non-Sami Norwegian populations.[9,11] Short people with a given WC are likely to be relatively fatter and have higher metabolic risk than tall people with the same WC.[14] Therefore, the aim of this study was to evaluate whether the relationships between metabolic markers and various obesity measures differ between Sami and non-Sami and to investigate the impact of stature on these relationships.

2 | METHODS

Data from the first survey of the population-based study on health and living conditions in regions with Sami and Norwegian populations—the SAMINOR Study—were used. The SAMINOR Study is run by the Centre for Sami Health Research at UiT The Arctic University of Norway. The first SAMINOR Survey was carried out in collaboration with the National Institute of Public Health during 2003 to 2004 in 24 rural municipalities in Northern and Central Norway.[15] Everyone who was 30 or 36 to 79 years old and registered in the National Registry as residents in the predefined areas was invited (27 987 individuals). In total, 16 014 (57%) attended the clinical examination and gave informed consent to participate in medical research. Trained personnel performed all clinical measurements and blood sampling. If pathologic measures were found, participants were encouraged to visit their primary physician. Researchers/health workers who are either Sami or work in Sami core areas have been consulted in order to meet the needs of the Sami community. This study has been approved by the SAMINOR Project Board and The Regional Committee for Medical and Health Research Ethics.

2.1 | Metabolic markers

Triglycerides, high-density lipoprotein (HDL) cholesterol, glucose, and systolic and diastolic blood pressure (BP) were included as dependent variables. BP was measured with a Dinamap-R automatic device (Critikon, Tampa, Florida, USA). Following at least 2-minute seated rest, three BP measurements with 1-minute intervals were recorded; the average of the second and third measurements was used in the analyses. Blood samples, taken nonfasting due to examination throughout the day, were drawn by venipuncture in a seated position. Samples were centrifuged within 1.5 hours, and serum was sent by overnight post to the laboratory at Ullevål University Hospital, Oslo. Lipids and glucose were measured by an enzymatic method (Hitachi 917 autoanalyzer, Roche Diagnostic, Switzerland). DM was based on self-report or current use of glucose-lowering drug (further details below). MetS was defined as having two or more of the following four metabolic abnormalities: hypertension (systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg or use of BP-lowering drug), hypertriglyceridemia (triglycerides ≥ 1.7 mmol/L), reduced HDL cholesterol (HDL-C < 1.0 mmol/L in men and <1.3 mmol/L in women or use of cholesterol-lowering drug), or hyperglycaemia (glucose ≥ 11.1 mmol/L or DM). Although commonly included in the MetS definition,[2] WC was excluded from the criteria in order to avoid circular reasoning. Missing values in biochemical variables or BP measurements existed in less than 0.3% of cases.

2.2 | Obesity measures

WC was recorded to the nearest centimetre at the umbilicus with the participant breathing normally in a standing position. Height was measured to the nearest 0.1 cm, and weight was measured to the nearest 100 g, using an electronic height and weight scale with participants wearing light clothing and no shoes. BMI was calculated as weight in kilograms (kg) divided by height in metres raised to the second (kg/m^2), and waist-to-height ratio (WHtR) was calculated as WC divided by height measured in centimetres. Missing values in these measurements existed in less than 0.5% of cases.

2.3 | Lifestyle and drug use

Information on the following lifestyle factors were obtained from the questionnaire (answer options in parenthesis): education in years, alcohol consumption (never/not this year/a few times during this year/1 time per month/2-3 times per month/1 time per week/2-3

times per week/4-7 times per week), and smoking (currently/previously/never). Alcohol consumption was dichotomised into "weekly alcohol consumption" and "less than weekly alcohol consumption." Smoking was dichotomised into "current smoker" and "not current smoker."

Participants were asked about their leisure-time physical activity (PA) the last year through a question that has shown moderate validity.[16] One out of four categories were available: reading, watching television, or engaging in sedentary activities (sedentary); at least 4 hours a week of walking, bicycling, or other types of PA (light); at least 4 hours a week of participating in recreational athletics or heavy gardening (moderate); and regular, vigorous training or participating in competitive sports several times a week (hard). The latter two categories were merged into one, "medium/hard," because of low number in the "hard" category.

Participants were asked about DM (yes/no), use of BP-lowering drug (currently/previously, but not now/never), use of cholesterol-lowering drug (currently/previously, but not now/never), use of insulin (currently/previously, but not now/never), and use of glucose-lowering drug in tablet format (currently/previously, but not now/never). In addition to questions regarding specific medication, participants were asked to list any medication they had used within the last 4 weeks. These were later coded with ATC codes. Three drug variables were created—use of cholesterol-lowering drug, BP-lowering drug, and glucose-lowering drug—by combining responses to the drug-specific questions and the ATC codes that had cholesterol/BP/glucose-lowering (side) effects (see Supporting Information for details).

Responses were ad-hoc imputed by assuming that those who did not reply to questions concerning drug use (BP-lowering drug, n = 122; cholesterol-lowering drug, n = 288; glucose-lowering drug, n = 506) or DM (n = 477) were nonusers/did not have DM. Missing values existed for the following variables (percent missing in non-Sami men, Sami men, non-Sami women, and Sami women, respectively): leisure-time PA (7.3%, 9.1%, 10.4%, and 10.0%), alcohol consumption (2.0%, 3.4%, 3.5%, and 4.2%), and smoking (0.8%, 0.9%, 1.0%, and 0.7%).

2.4 | Ethnic categorisation

In Norway, it is by law illegal to register ethnicity in any registry or medical records, but for research purposes, it is permitted to ask about ethnic background. The questionnaire included three facets of ethnicity—language, ethnic background, and self-perceived ethnicity—making up in total eleven questions: *What language do/did you/your parents/your grandparents speak at home? What is your, your father's and your mother's ethnic background? What do you regard yourself as?* Alternatives were (more than one alternative was permitted) Norwegian, Sami, Kven (an ethnic minority of descendants of Finnish immigrants in the 1700s and 1800s), or other. Two criteria for Sami ethnicity were defined in this study. Participants had to answer Sami as

1. home language for at least one of their grandparents, parents, or themselves, and
2. their own ethnic background or self-perceived ethnicity.

All others were categorised as non-Sami.

2.5 | Final study sample

Participants were excluded if they failed to hand in the questionnaire (n = 213), did not answer any of the eleven ethnicity-related questions (n = 52) or questions regarding leisure-time PA (n = 1421), smoking (n = 80), or alcohol consumption (n = 240). Further, participants were excluded if they had missing information on any of the anthropometric measures (height, weight, or waist circumference, n = 59) or metabolic markers (triglycerides, HDL cholesterol, glucose, or systolic or diastolic BP, n = 28). A total of 13 921 subjects (7124 women and 6797 men, 50% of the invited population) were eligible for complete-case analysis (see Figure S1 for flow-chart).

2.6 | Statistical analyses

STATA version 15.1 (StataCorp, College Station, TX, USA) was used. Statistical code can be made available upon request. Sample characteristics are presented for each stratum of sex and ethnic group. Continuous variables are given as mean (standard deviation) or median (interquartile range) where appropriate; categorical variables are given as numbers (percentage). Because the relationships between metabolic markers and obesity may be non-linear, models were fitted using fractional polynomial regression, which is an extension of conventional polynomial regression.[17] It is implemented with the "fp" function in STATA and allows for m degrees of the continuous predictor X (the obesity measure in this case), with $p_1 \ldots p_m$ powers, which are chosen from {−2, −1, −0.5, 0, 0.5, 1, 2, 3}, where 0 means $\log(X)$.[17] In epidemiology, it is usually sufficient with $m = 2$.[18] Alpha (α) was set to.05 for selection of powers. In a closed selection procedure using maximum likelihood, models with different m are compared with a linear model; the linear fit is chosen unless a more complex model fits the data better.

Initially, interactions between sex and WC/BMI/WHtR and ethnicity and BMI/WC/WHtR were tested for using the "mfpigen" function.[19] Significant interactions ($P < .05$) were found between sex and obesity in models with HDL cholesterol and diastolic BP as outcomes; these models were therefore stratified by sex. No significant interactions were found between ethnicity and obesity. Ethnicity was therefore included as a covariate. All models were adjusted for age, age squared, smoking, alcohol consumption, leisure-time PA, and sex (except in sex-stratified models). In models with triglycerides and HDL cholesterol as dependent variables, additional adjustment was made for current use of cholesterol-lowering drugs. In models with glucose as dependent variable, adjustment was made for DM (including users of glucose-lowering drugs) and current use of cholesterol-lowering

drugs, because of its potential influence on glucose metabolism.[20] In models with systolic and diastolic BP, adjustment was made for current use of BP-lowering drugs.

Models were inspected visually for heteroscedasticity and nonnormality of residuals. All outcome variables were log-transformed because of nonnormality, and normality was confirmed. In models that still had heteroscedasticity, robust standard errors were computed. Results were back-transformed and plotted with the "marginscontplot2" function, which estimates average marginal effects with 95% confidence intervals by ethnic group (holding all other covariates constant). After plotting the models for visual presentation, all models were additionally adjusted for height.

2.7 | Sensitivity analyses

Several sensitivity analyses were conducted. First, the ethnicity variable was replaced with a variable indicating whether a subject was "short" or "tall," based on having a value below or above the sex-specific mean height in the sample (161 cm in women and 174 cm in men). Second, a three-level category of Sami ethnic markers was used. This was created by counting the number of "Sami answers": answered "Sami" on all 11 questions, 1 to 10 questions, or no questions. Third, the analyses were restricted to a presumably healthy sample, excluding individuals with DM (including those using glucose-lowering drugs), previous stroke, angina or myocardial infarction, and current use of cholesterol- or BP-lowering drugs. Fourth and finally, a multiply imputed data set was created, and all models were repeated using this data set. Multiple imputation is challenging when combined with fractional polynomials, mainly because of non-linearity in the models, and for not being able to use maximum likelihood in the model selection procedure.[21] Regarding the former, however, this was not viewed as an issue, as there was less than 0.5% missing in the fractional polynomial variables. Therefore, all missing data in the original sample, except the 52 individuals with missing ethnic information (N = 15 749), were imputed using multiple imputation chained equation. A total of 20 datasets were imputed using a "rich dataset" in order to make the missing-at-random assumption more likely. Fractional

TABLE 1 Sex- and ethnicity-stratified sample characteristics in the SAMINOR 1 Survey (2003-2004, N = 13 921)

	Women (N = 7124)		Men (N = 6979)	
	Sami (N = 1538)	Non-Sami (N = 5586)	Sami (N = 1494)	Non-Sami (N = 5303)
Age, y	52.5 (11.3)	53.2 (11.4)	54.1 (11.0)	54.0 (11.2)
Education, y	11.5 (4.6)	11.7 (3.8)	10.7 (4.1)	11.3 (3.7)
Current smoker	504 (32.8%)	1747 (31.3%)	490 (32.8%)	1638 (30.9%)
Weekly alcohol consumption	203 (13.2%)	1211 (21.7%)	389 (26.0%)	1748 (33.0%)
Leisure-time PA				
Sedentary	437 (28.4%)	1253 (22.4%)	371 (24.8%)	1229 (23.2%)
Light >4 h/w	933 (60.7%)	3686 (66.0%)	795 (53.2%)	2940 (55.4%)
Moderate-hard >4 h/w	168 (10.9%)	647 (11.6%)	328 (22.0%)	1134 (21.4%)
Diabetes mellitus	68 (4.4%)	258 (4.6%)	66 (4.4%)	225 (4.2%)
Metabolic syndrome	597 (38.8%)	2102 (37.6%)	681 (45.6%)	2460 (46.4%)
Cholesterol-lowering drug	188 (12.2%)	651 (11.7%)	252 (16.9%)	802 (15.1%)
BP-lowering drug	328 (21.3%)	1165 (20.9%)	327 (21.9%)	1179 (22.2%)
Glucose-lowering drug	53 (3.4%)	185 (3.3%)	53 (3.5%)	170 (3.2%)
Height, cm	156.7 (6.0)	162.4 (6.4)	169.4 (6.4)	175.4 (6.8)
Waist circumference, cm	85.5 (12.2)	85.2 (11.9)	92.6 (10.7)	94.6 (10.5)
Body mass index, kg/m^2	28.2 (5.0)	27.3 (4.8)	27.8 (4.0)	27.5 (3.8)
Waist-to-height ratio	0.547 (0.082)	0.525 (0.076)	0.547 (0.064)	0.540 (0.060)
Triglycerides, mmol/L	1.31 (0.97, 1.91)	1.29 (0.93, 1.81)	1.58 (1.10, 2.34)	1.56 (1.09, 2.24)
HDL cholesterol, mmol/L	1.45 (0.37)	1.49 (0.39)	1.26 (0.35)	1.26 (0.33)
Glucose, mmol/L	5.24 (4.81, 5.84)	5.27 (4.87, 5.82)	5.42 (4.99, 6.01)	5.40 (4.97, 6.00)
Systolic BP, mmHg	127.4 (20.2)	129.2 (20.9)	133.6 (19.5)	134.1 (18.1)
Diastolic BP, mmHg	71.8 (9.8)	72.5 (10.2)	77.5 (9.6)	78.0 (10.0)

Notes. Numerical variables are given in mean (standard deviation), except triglycerides and glucose, which are given in median (1st quartile, 3rd quartile). Categorical variables are given in frequency (percent).

Abbreviations: BP, blood pressure; HDL, high-density lipoprotein; PA = physical activity; h/w = hours per week.

polynomial models were then fitted on the multiply imputed data using the "mfpmi" command in STATA, which utilises log-likelihood type tests.[21]

All statistical tests had a two-sided significance level of.05. Because of a large sample size and multiple testing, strong emphasis was put on effect sizes in the interpretation of the results.

3 | RESULTS

3.1 | Sample characteristics

Table 1 shows sample characteristics by ethnic group (22.0% were categorised as Sami). Non-Sami of both sexes were on average approximately 6 cm taller than Sami.

3.2 | Relationships between metabolic markers and obesity measures

The relationships between metabolic markers and obesity measures were the same in Sami and non-Sami (no significant interactions), but there were some differences in the levels of metabolic markers between Sami and non-Sami at the same level of the obesity measure.

Visualisations of the *estimated* relationships concerning the three measures of obesity (WC, BMI, and WHtR), and triglycerides, glucose, systolic BP, MetS, and DM are found in Figure 1, and sex-stratified models for HDL cholesterol and diastolic BP are found in Figure 2.

There were no ethnic differences in glucose levels or probabilities of DM with respect to any obesity measure.

At any given WC, Sami had higher levels of triglycerides (+0.04 mmol/L, 95% confidence interval [CI], 0.01-0.07) and, in

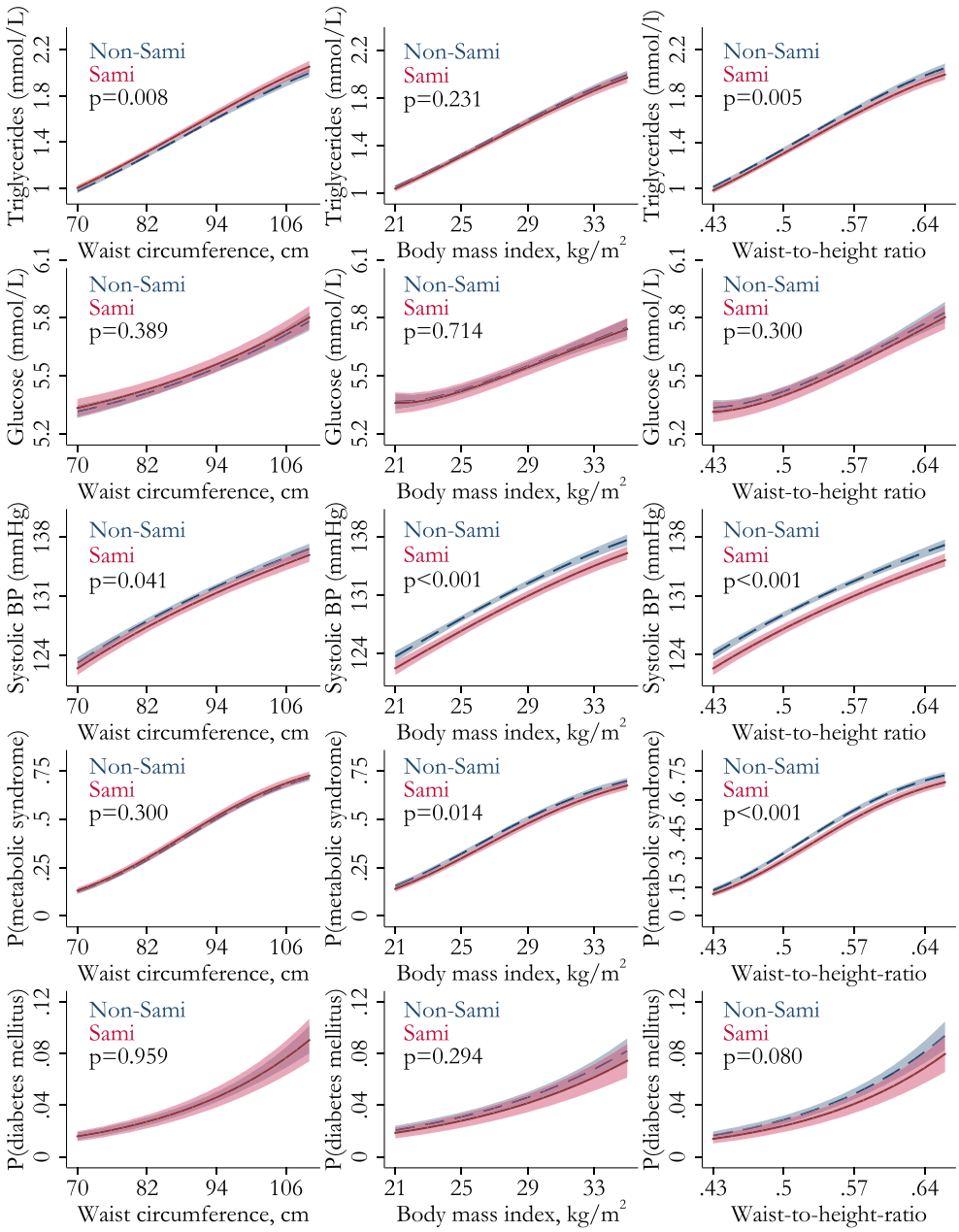

FIGURE 1 Estimated relationships between metabolic markers and obesity measures in Sami vs non-Sami. All models were fitted with fractional polynomial regression and adjusted for age, age squared, leisure-time PA, smoking, alcohol consumption, sex, and relevant use of medication. Curves are drawn separate for Sami (red, solid line) and non-Sami (blue, dashed line). *P* values are for Sami vs non-Sami. Average marginal effects for each ethnic group were estimated, holding all other variables in the model constant, for the 5th to the 95th percentile of the obesity measure. BP, blood pressure

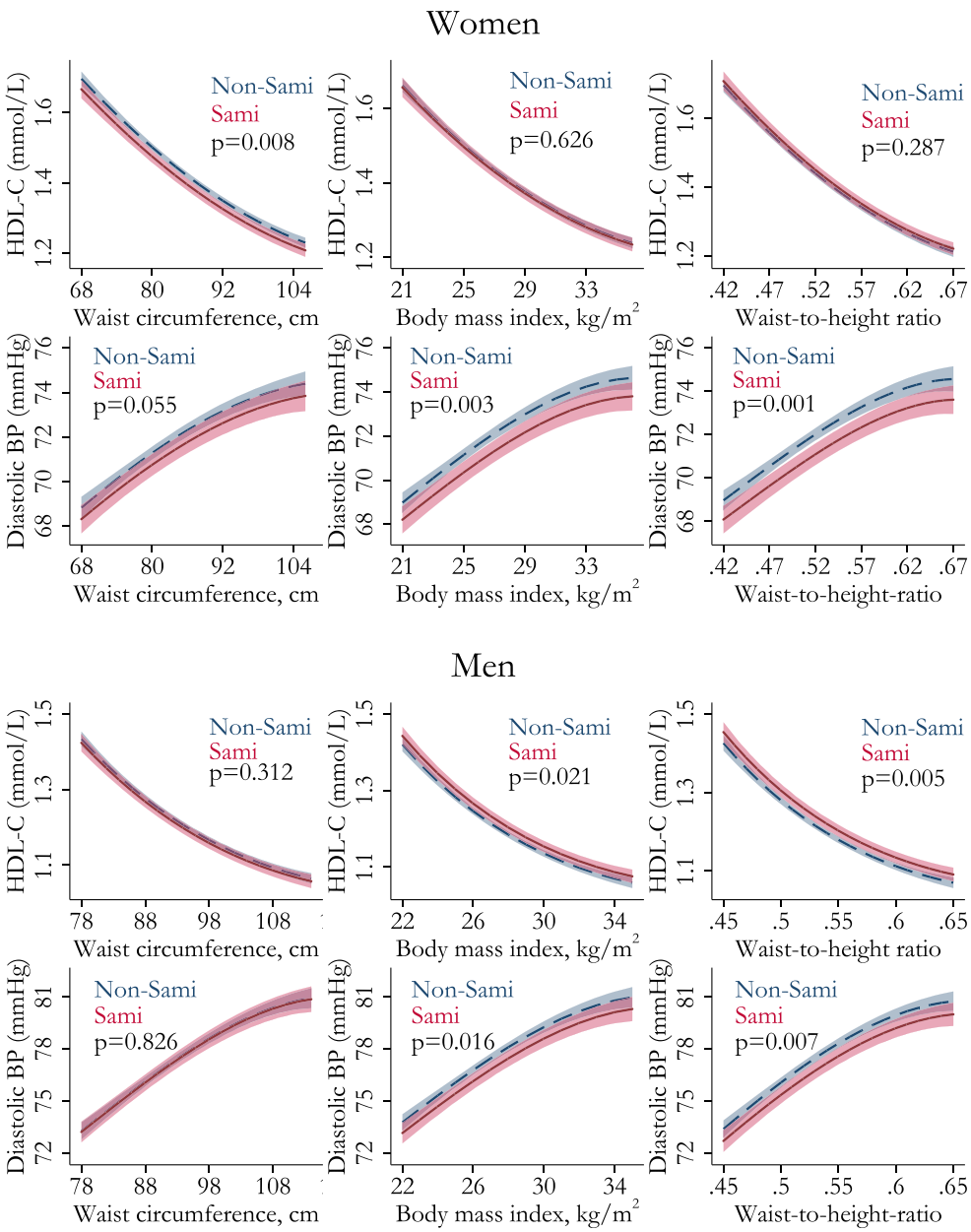

FIGURE 2 Estimated sex-stratified relationships between metabolic markers and obesity measures in Sami vs non-Sami. All models were fitted with fractional polynomial regression and adjusted for age, age squared, leisure-time PA, smoking, alcohol consumption, and relevant use of medication. Curves are drawn separate for Sami (red, solid line) and non-Sami (blue, dashed line). *P* values are for Sami vs non-Sami. Average marginal effects for each ethnic group were estimated, holding all other variables in the model constant, for the 5th to the 95th percentile of the obesity measure. HDL-C, high-density lipoprotein cholesterol. BP, blood pressure

women, lower levels of HDL cholesterol (−0.03 mmol/L, 95% CI, −0.04 to −0.01) than non-Sami. However, at any given WC, Sami had more favourable levels of systolic BP than non-Sami (−0.70 mmHg, 95% CI, −1.37 to −0.03) (Table 2).

At any given BMI, Sami had more favourable levels of several metabolic markers than non-Sami. Levels of HDL cholesterol in men were higher (+0.02 mmol/L, 95% CI, 0.00 to 0.04). Levels of systolic (−1.50 mmHg, 95% CI, −2.16 to −0.83) and diastolic BP (in women, −0.81 mmHg, 95% CI, −1.34 to −0.27; in men, −0.64 mmHg, 95% CI, −1.17 to −0.12) and probability of MetS (−0.02, 95% CI, −0.04 to −0.00) were lower in Sami than in non-Sami at any given BMI (Table 2).

Models with WHtR showed similar ethnic differences as in models with BMI. Compared with non-Sami, Sami had lower levels of triglycerides (−0.04 mmol/L, 95% CI, −0.07 to −0.01), higher levels of HDL cholesterol in men (+0.02 mmol/L, 95% CI, 0.01 to 0.04), lower levels of systolic (−1.73 mmHg, 95% CI, −2.40 to −1.07) and diastolic BP (in women, −0.92 mmHg, 95% CI, −1.46 to −0.38; in men, −0.72 mmHg, 95% CI, −1.25 to −0.20), and probability of MetS (−0.04, 95% CI, −0.05 to −0.02) at the any given WHtR (Table 2).

When adjusting the models for height, most of the ethnic differences in metabolic markers were attenuated and lost statistical significance except in models with systolic BP or MetS as dependent variables ($Model_{heightadj}$ in Tables 3–5). Effect sizes concerning MetS were small, whereas effect sizes concerning systolic BP were substantial, and all *P* values were <.001: Compared with non-Sami, Sami had 1.37 mmHg (95% CI, −2.09 to −0.66) lower systolic BP at any given WC, 1.45 mmHg (95% CI, −2.16 to −0.73) lower at any given BMI, and 1.38 mmHg (95% CI, −2.10 to −0.67) lower at any given WHtR (results not shown).

TABLE 2 Estimated average marginal effects with 95% confidence intervals (CI) for Sami vs non-Sami in main models

	Waist Circumference			Body Mass Index			Waist-to-Height Ratio		
Metabolic marker	AME	95% CI	N	AME	95% CI	N	AME	95% CI	N
Triglycerides, mmol/L	0.04	0.01, 0.07	13 921	−0.02	−0.05, 0.01	13 921	−0.04	−0.07, −0.01	13 921
HDL-C, women, mmol/L	−0.03	−0.04, −0.01	7124	−0.00	−0.02, 0.01	7124	0.01	−0.01, 0.03	7124
HDL-C, men, mmol/L	−0.01	−0.02, 0.01	6797	0.02	0.00, 0.04	6797	0.02	0.01, 0.04	6797
Glucose, mmol/L	0.02	−0.02, 0.06	13 921	−0.01	−0.05, 0.03	13 921	−0.02	−0.07, 0.02	13 921
Systolic BP, mmHg	−0.70	−1.37, −0.03	13 921	−1.50	−2.16, −0.83	13 921	−1.73	−2.40, −1.07	13 921
Diastolic BP, women, mmHg	−0.53	−1.07, 0.01	7124	−0.81	−1.34, −0.27	7124	−0.92	−1.46, −0.38	7124
Diastolic BP, men, mmHg	−0.06	−0.59, 0.47	6797	−0.64	−1.17, −0.12	6797	−0.72	−1.25, −0.20	6797
Metabolic syndrome (probability)	0.01	−0.01, 0.03	13 921	−0.02	−0.04, −0.00	13 921	−0.04	−0.05, −0.02	13 921
Diabetes mellitus (probability)	−0.00	−0.01, 0.01	13 921	−0.00	−0.01, 0.00	13 921	−0.01	−0.01, 0.00	13 921

Notes. The average marginal effects are estimated from the models, which were adjusted for age, age squared, smoking, alcohol consumption, leisure-time PA, relevant drug use, and sex (except in sex-stratified models). Average marginal effects are computed by fixing the value for ethnicity, but keeping the other variables in the models (those adjusted for) at their observed values in the sample. The probability/mean for each case is calculated, and then all estimates are averaged across the sample. This is done by fixing the ethnicity variable first at Sami, then at non-Sami. The average marginal effects for Sami and non-Sami are then compared. As all other variables except ethnicity are identical between the two hypothetical populations, the difference in the averaged mean/probability are attributed to the fixed variable: ethnicity.

Abbreviations: AME, average marginal effects; BP, blood pressure; CI, confidence interval; HDL, high-density lipoprotein cholesterol; N, sample size.

3.3 | Sensitivity analyses

Overall, sensitivity analyses agreed with the main analyses (Tables 3–5). In models evaluating stature, short people were found to have markedly less favourable levels of most markers at any given WC ($Model_{short/tall}$ in Table 3 and Figure 3), and somewhat better levels of most markers at any given WHtR ($Model_{short/tall}$ in Table 5), than tall people.

4 | DISCUSSION

In this population-based study from parts of rural Northern and Central Norway, the relationships between metabolic markers and WC, BMI, or WHtR were the same in Sami as in non-Sami. Sami and non-Sami had some differences in levels of metabolic markers, but these differences were only marginal in size. Adjusting the models for height eliminated practically all ethnic differences, but not regarding systolic BP, which was lower in Sami than in non-Sami at any given WC, BMI, or WHtR.

Two other findings with public health implications should be noted: First, short people had worse metabolic profile at any given WC compared with tall people; second, increases in obesity were associated with sharp increases in the probability of MetS.

Some results from studies on metabolic markers and obesity in other ethnically diverse Arctic populations are relevant for comparisons. At the same level of BMI, both the Greenlandic and Canadian Inuit had more favourable levels of BP and lipids, but not glucose and insulin, than their respective non-Inuit reference population.[22,23] On the other hand, the South Asian, Chinese, and Aboriginal descendant Canadians (from the Six Nation Reserve) had less favourable levels of cardiometabolic risk factors than European descendant Canadians at the same level of BMI.[24] An exception was for systolic BP, which was approximately 5 mmHg lower in Aboriginal than European descendant Canadians.[24] This resembles the findings in this study, although the effect sizes were much larger than in this study (approximately 5 vs 1.4 mmHg).

In a study comparing Pima Indians and White Americans, autonomic nervous system activation seemed to differ between the two groups, possibly explaining why Pima Indians have a lower prevalence of hypertension but a higher prevalence of obesity than Whites.[25] There is no reason to believe that the physiological response to obesity differ in Sami and non-Sami, but an intriguing question is whether they have different amounts/types of body fat at the same levels of obesity. For instance, a study found that Greenlandic Inuit and Kenyans had less adipose tissue at the same levels of obesity as Danes.[5] Currently, there are no such data available, but it is important to emphasise that throughout history, the Sami have lived side by side the majority Norwegian population and a large part of the population in Northern Norway have ethnically mixed ancestry. On the contrary, Pima Indians and Greenlandic Inuit have lived as isolated populations. Any physiologic difference in response to obesity or body composition between Norwegians with and without Sami affiliation therefore seems highly unlikely. The possibility of chance findings or residual confounding cannot be ruled out either.

The relationship between height and disease in a context with Sami ethnicity has previously been discussed: Ethnic differences in stroke were in general reduced when controlling for height,[26] and in women, height was inversely associated with both DM and myocardial infarction independently of ethnicity.[9] Height is largely determined by genetics, and whether individuals utilise their full genetic potential is considered to be influenced by environmental factors in utero[27] and in childhood.[28] Perhaps by being a marker of unfavourable environments, short stature is associated with an

TABLE 3 Analyses for waist circumference

	Triglycerides	HDL, Women	HDL, Men	Glucose	SBP	DBP, Women	DBP, Men	MetS	DM
$Model_{main}$									
Log-β/*OR	0.03	−0.02	−0.01	0.00	−0.01	−0.01	−0.00	1.05*	0.99*
95% CI	0.01, 0.05	−0.03, −0.00	−0.02, 0.01	−0.00, 0.01	−0.01, −0.00	−0.01, 0.00	−0.01, 0.01	0.96, 1.15	0.81, 1.22
P value	.008	.008	.312	.389	.041	.055	.826	.300	.959
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{heightadj}$									
Log-β/*OR	−0.02	−0.00	−0.00	−0.01	−0.01	−0.01	−0.00	0.89*	0.83*
95% CI	−0.04, 0.00	−0.01, 0.01	−0.02, 0.01	−0.01, 0.00	−0.02, −0.01	−0.02, 0.00	−0.01, 0.01	0.81, 0.98	0.67, 1.02
P value	.117	.891	.870	.201	<.001	.094	.648	.016	.081
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{short/tall}$									
Log-β/*OR	0.08	−0.03	−0.01	0.01	0.01	−0.00	0.00	1.35*	1.44*
95% CI	0.06, 0.09	−0.04, −0.02	−0.02, −0.00	0.01, 0.02	0.00, 0.01	−0.01, 0.01	−0.00, 0.01	1.25, 1.46	1.21, 1.71
P value	<.001	<.001	.039	<.001	.005	.655	.532	<.001	<.001
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{imputed}$									
Log-β/*OR	0.02	−0.02	−0.00	0.01	−0.00	−0.01	0.00	1.03*	1.10*
95% CI	0.00, 0.04	−0.03, −0.00	−0.02, 0.01	−0.00, 0.01	−0.01, 0.00	−0.01, −0.00	−0.00, 0.01	0.94, 1.12	0.92, 1.31
P value	.033	.011	.501	.131	.077	.045	.529	.545	.314
N	15 749	8233	7516	15 749	15 749	8233	7516	15 749	15 749
$Model_{healthy}$									
Log-β/*OR	0.04	−0.01	−0.01	0.00	−0.01	−0.00	−0.00	1.01*	
95% CI	0.01, 0.06	−0.03, 0.00	−0.02, 0.01	−0.01, 0.01	−0.01, −0.00	−0.01, 0.00	−0.01, 0.01	0.90, 1.13	
P value	.001	.082	.533	.872	.004	.392	.834	.886	
N	10 040	5212	4828	10 040	10 040	5212	4828	10 040	

(Continues)

TABLE 3 (Continued)

	Triglycerides	HDL, Women	HDL, Men	Glucose	SBP	DBP, Women	DBP, Men	MetS	DM
$Model_{altethnic}$									
1-10 Sami									
Log-β/*OR	0.02	−0.02	0.00	0.00	0.01	−0.01	0.00	1.14*	1.08*
95% CI	−0.00, 0.04	−0.03, −0.00	−0.01, 0.02	−0.00, 0.01	0.00, 0.01	−0.01, 0.00	−0.00, 0.01	1.04, 1.25	0.88, 1.32
P value	.096	.011	.800	.221	.047	.081	.526	.004	.454
11 Sami									
Log-β/*OR	0.04	−0.03	−0.01	0.00	−0.01	−0.01	−0.01	1.09*	1.12*
95% CI	0.01, 0.07	−0.05, −0.01	−0.03, 0.01	−0.01, 0.01	−0.02, −0.00	−0.02, −0.00	−0.02, 0.00	0.96, 1.23	0.86, 1.45
P value	.005	.001	.239	.692	.015	.041	.183	.195	.419
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921

Notes. Coefficient estimates are for Sami vs non-Sami ethnicity (short vs tall in $Model_{short/tall}$). The columns represent different dependent variables (indicated by the column names). The rows represent the different models (main models, height adjusted, short vs tall, imputed, healthy, and alternative ethnic categorisation). Models for HDL cholesterol and diastolic blood pressure were stratified by sex, hence the sex-specific columns for these variables.

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL, high-density lipoprotein cholesterol; MetS, metabolic syndrome; N, sample size; OR, odds ratio; SBP, systolic blood pressure.

*Odds ratio (OR).

TABLE 4 Analyses for body mass index

	Triglycerides	HDL, Women	HDL, Men	Glucose	SBP	DBP, Women	DBP, Men	MetS	DM
$Model_{main}$									
Log-β/*OR	−0.01	−0.00	0.02	−0.00	−0.01	−0.01	−0.01	0.89*	0.90*
95% CI	−0.03, 0.01	−0.02, 0.01	0.00, 0.03	−0.01, 0.01	−0.02, −0.01	−0.02, −0.00	−0.02, −0.00	0.82, 0.98	0.74, 1.10
P value	.231	.626	.021	.714	<.001	.003	.016	.014	.294
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{heightadj}$									
Log-β/*OR	−0.02	−0.00	0.00	−0.01	−0.01	−0.01	−0.00	0.88*	0.83*
95% CI	−0.04, 0.00	−0.02, 0.01	−0.01, 0.02	−0.01, 0.00	−0.02, −0.01	−0.02, 0.00	−0.01, 0.00	0.80, 0.97	0.67, 1.03
P value	.086	.685	.698	.188	<.001	.099	.400	.011	.091
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{short/tall}$									
Log-β/*OR	0.01	−0.00	0.02	0.00	−0.00	−0.01	−0.01	1.01*	1.19*
95% CI	−0.01, 0.03	−0.02, 0.01	0.01, 0.04	−0.00, 0.01	−0.01, 0.00	−0.02, −0.00	−0.02, −0.00	0.94, 1.09	1.00, 1.41
P value	.293	.414	<.001	.140	.054	.007	.001	.794	.052
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{imputed}$									
Log-β/*OR	−0.02	−0.00	0.02	0.00	−0.01	−0.01	−0.01	0.88*	0.99*
95% CI	−0.03, 0.00	−0.02, 0.01	0.00, 0.03	−0.01, 0.01	−0.02, −0.01	−0.02, −0.00	−0.01, 0.00	0.81, 0.96	0.83, 1.19
P value	.067	.679	.007	.770	<.001	.004	.112	.003	.937
N	15 749	8233	7516	15 749	15 749	8233	7516	15 749	15 749
$Model_{healthy}$									
Log-β/*OR	−0.00	0.00	0.02	−0.00	−0.02	−0.01	−0.01	0.86*	
95% CI	−0.02, 0.02	−0.01, 0.02	0.00, 0.03	−0.01, 0.00	−0.02, −0.01	−0.02, 0.00	−0.02, −0.00	0.77, 0.96	
P value	.924	.971	.026	.453	<.001	.067	.013	.009	
N	10 040	5212	4828	10 040	10 040	5212	4828	10 040	

(Continues)

TABLE 4 (Continued)

	Triglycerides	HDL, Women	HDL, Men	Glucose	SBP	DBP, Women	DBP, Men	MetS	DM
$Model_{altmarker}$									
1-10 Sami									
Log-β/*OR	−0.01	−0.01	0.02	0.00	0.00	−0.01	−0.00	1.00*	0.99*
95% CI	−0.03, 0.01	−0.02, 0.01	0.01, 0.03	−0.01, 0.01	−0.00, 0.01	−0.02, −0.00	−0.01, 0.00	0.92, 1.09	0.81, 1.20
P value	.167	.431	.004	.872	.930	.011	.318	.984	.885
11 Sami									
Log-β/*OR	−0.01	−0.01	0.02	−0.00	−0.02	−0.02	−0.02	0.87*	0.97*
95% CI	−0.04, 0.01	−0.03, 0.01	0.00, 0.04	−0.02, 0.01	−0.03, −0.01	−0.03, −0.01	−0.03, −0.01	0.77, 0.99	0.75, 1.27
P value	.317	.351	.041	.430	<.001	.002	<.001	.030	.833
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921

Notes. Coefficient estimates are for Sami vs non-Sami ethnicity (short vs tall in $Model_{short/tall}$). The columns represent different dependent variables (indicated by the column names). The rows represent the different models (main models, height adjusted, short vs tall, imputed, healthy, and alternative ethnic categorisation). Models for HDL cholesterol and diastolic blood pressure were stratified by sex, hence the sex-specific columns for these variables.

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL, high-density lipoprotein cholesterol; MetS, metabolic syndrome; N, sample size; OR, odds ratio; SBP, systolic blood pressure.

*Odds ratio (OR)

TABLE 5 Analyses for waist-to-height ratio

	Triglycerides	HDL, Women	HDL, Men	Glucose	SBP	DBP, Women	DBP, Men	MetS	DM
$Model_{main}$									
Log-β/*OR	−0.03	0.01	0.02	−0.00	−0.01	−0.01	−0.01	0.84*	0.84*
95% CI	−0.05, −0.01	−0.01, 0.02	0.01, 0.03	−0.01, 0.00	−0.02, −0.01	−0.02, −0.01	−0.02, −0.00	0.76, 0.92	0.68, 1.02
P value	.005	.287	.005	.300	<.001	.001	.007	<.001	.080
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{heightadj}$									
Log-β/*OR	−0.02	−0.00	−0.00	−0.01	−0.01	−0.01	−0.00	0.89*	0.82*
95% CI	−0.04, 0.00	−0.02, 0.01	−0.02, 0.01	−0.01, 0.00	−0.02, −0.01	−0.02, 0.00	−0.01, 0.01	0.81, 0.98	0.66, 1.02
P value	.123	.853	.871	.168	<.001	.106	.651	.016	.073
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{short/tall}$									
Log-β/*OR	−0.03	0.01	0.04	0.00	−0.01	−0.01	−0.01	0.88*	1.07*
95% CI	−0.04, −0.01	0.00, 0.02	0.03, 0.05	−0.01, 0.01	−0.01, −0.00	−0.02, −0.01	−0.02, −0.01	0.82, 0.95	0.90, 1.27
P value	.003	.028	<.001	.905	<.001	<.001	<.001	.001	.460
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921
$Model_{imputed}$									
Log-β/*OR	−0.03	0.01	0.02	−0.00	−0.01	−0.01	−0.01	0.82*	0.99*
95% CI	−0.05, −0.02	−0.00, 0.02	0.01, 0.03	−0.01, 0.01	−0.02, −0.01	−0.02, −0.01	−0.01, 0.00	0.76, 0.90	0.83, 1.19
P value	<.001	.183	.001	.657	<.001	.001	.062	<.001	.937
N	15 749	8233	7516	15 749	15 749	8233	7516	15 749	15 749
$Model_{healthy}$									
Log-β/*OR	−0.02	0.01	0.02	−0.01	−0.02	−0.01	−0.01	0.80*	
95% CI	−0.04, 0.00	−0.00, 0.03	0.01, 0.04	−0.01, 0.00	−0.02, −0.01	−0.02, −0.00	−0.02, −0.00	0.72, 0.90	
P value	.108	.181	.005	.180	<.001	.017	.003	<.001	
N	10 040	5212	4828	10 040	10 040	5212	4828	10 040	

(Continues)

TABLE 5 (Continued)

	Triglycerides	HDL, Women	HDL, Men	Glucose	SBP	DBP, Women	DBP, Men	MetS	DM
Model$_{altmarker}$									
1-10 Sami									
Log-β/*OR	−0.03	0.00	0.02	−0.00	−0.00	−0.01	−0.00	0.96*	0.95*
95% CI	−0.04, −0.01	−0.01, 0.02	0.01, 0.04	−0.01, 0.01	−0.01, 0.00	−0.02, −0.00	−0.01, 0.00	0.88, 1.05	0.77, 1.16
P value	.009	.767	.001	.811	.697	.004	.200	.357	.592
11 Sami									
Log-β/*OR	−0.03	0.00	0.02	−0.01	−0.02	−0.02	−0.02	0.81*	0.89*
95% CI	−0.06, −0.00	−0.02, 0.02	0.01, 0.04	−0.02, 0.00	−0.03, −0.01	−0.03, −0.01	−0.03, −0.01	0.71, 0.92	0.69, 1.17
P value	.020	.757	.013	.175	<.001	.001	<.001	.001	.413
N	13 921	7124	6797	13 921	13 921	7124	6797	13 921	13 921

Notes. Coefficient estimates are for Sami vs non-Sami ethnicity (short vs tall in Model$_{short/tall}$). The columns represent different dependent variables (indicated by the column names). The rows represent the different models (main models, height adjusted, short vs tall, imputed, healthy, and alternative ethnic categorisation). Models for HDL cholesterol and diastolic blood pressure were stratified by sex, hence the sex-specific columns for these variables.

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL, high-density lipoprotein cholesterol; MetS, metabolic syndrome; N, sample size; OR, odds ratio; SBP, systolic blood pressure.

*Odds ratio (OR)

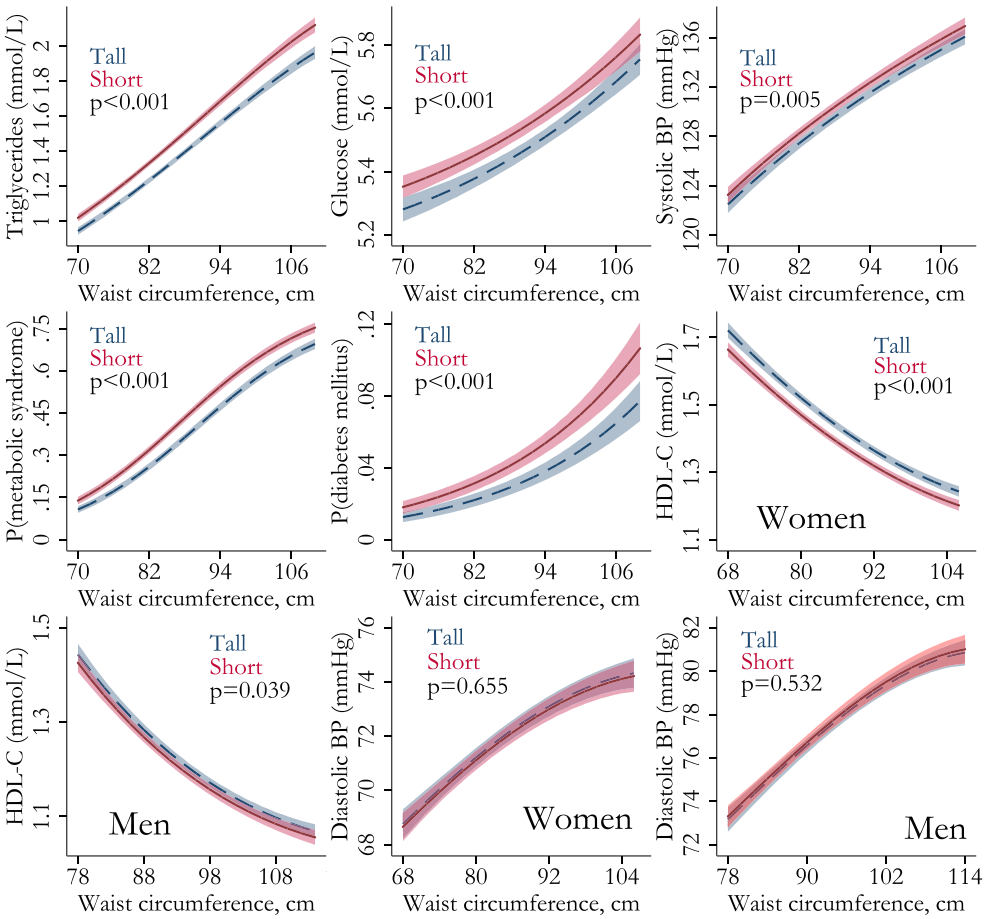

FIGURE 3 Estimated relationships between metabolic markers and waist circumference in short vs tall people. All models were fitted with fractional polynomial regression and adjusted for age, age squared, leisure-time PA, smoking, alcohol consumption, sex (not in models with HDL-C and diastolic BP as dependent variables; these were sex stratified) and relevant use of medication. Curves are drawn separate for short (red, solid line) and tall (blue, dashed line) people. *P* values are for short vs tall people. Average marginal effects for each group were estimated, holding all other variables in the model constant, for the 5th to the 95th percentile of the obesity measure. HDL-C, high-density lipoprotein cholesterol. BP, blood pressure

increased risk of DM, cardiovascular disease, and mortality.[29,30] On the contrary, genetically determined height has been linked to cardiovascular disease perhaps trough shared biological pathways.[31] However, in contrast to previous studies on height, Sami ethnicity, and disease,[9,26] this study has examined the clinical implications when using various obesity measures, not the implication of height in itself. Hence, this topic will not be further elaborated on.

The findings regarding height, abdominal obesity, and metabolic markers support studies from Japan[14] and Germany[32]: Short people have worse metabolic profiles than tall people with the same WC but similar when having the same WHtR.[32] In a meta-analysis on a sample including a wide range of heights, WHtR was superior to WC with respect to cardiometabolic risk prediction.[33] In a recent review of anthropometric cut-offs and its impact on metabolic alterations, it was suggested that height differences could explain the different levels of metabolic markers at similar levels of obesity between various ethnic groups.[34] WHtR was suggested as a universal measure unaffected by ethnicity.[34] In our study, some metabolic markers were slightly more favourable at the same levels of BMI or WHtR in Sami than in non-Sami, despite height being integrated into both these measures. However, the differences were marginal and likely irrelevant clinically. Further, sensitivity analyses showed metabolic differences between short and tall people at the same level of WHtR, suggesting that WHtR does not capture the same level of metabolic markers along the entire range of height in this particular population.

Ethnicity is a complex concept and a challenging variable to define.[35] Depending on context, it can comprise language, culture, religion, skin colour, geography, diet, and genetics. In this study, an effort was made to tease the Sami ethnicity variable apart from other variables that may confound or mediate the relationships between metabolic markers and obesity, aiming to capture the "direct effect of ethnicity," whatever that entails.[36] The lack of such an effect is not surprising as Sami ethnicity is viewed first and foremost as a socio-cultural marker. Using various criteria for Sami ethnicity impacts both size and geographical distribution.[37] The residual "direct effect" of Sami ethnicity is—in this particular study—possibly a side-effect of dichotomising the sample into groups that differ substantially in height. Importantly, Sami ethnicity, defined in any way, is not deterministic with respect to short height. A person's stature seems to be a much more important predictor than a person's ethnic belonging, especially concerning WC.

The results do not support the need for ethnic-specific cut-offs of obesity to be used in rural Northern Norway. However, it may be suggested that researchers should evaluate whether some form of height adjustment is reasonable when studying obesity and its related disorders in two populations that differ in stature.

The large sample size is an obvious strength of the study. In addition, all measurements were performed by trained personnel and followed a protocol. Several markers of ethnicity were included such

that sensitivity (bias) analyses regarding the ethnic categorisation could be performed. Several factors comprising lifestyle and health status, such as leisure-time PA, smoking, and use of medication, were also possible to adjust for.

Limitations of the study include that it is cross-sectional, meaning that the temporality of the associations cannot be commented on. The response rate was moderately adequate: 57% overall attendance in the survey, but 50% in the final sample. Nonattendance with respect to ethnicity could not be evaluated, but it was more common in younger, unmarried men. The survey was conducted ~15 years ago, and extrapolation of the results beyond this sample is not advised. The results are exploratory and should be confirmed in other samples. Further limitations include nonfasting blood samples. Triglyceride levels have been found to vary around 20% between different fasting states,[38] but more importantly, random glucose is not a very valid measure of glucose metabolism nor diagnosing DM. Fasting blood samples on glucose, insulin, HbA1c, and an oral glucose tolerance test are necessary in order to evaluate the relationships between obesity and impaired glucose metabolism. Moreover, measurement error of self-reported variables cannot be excluded. However, if misclassification of these variables is of the same direction and magnitude in Sami and non-Sami, it is unlikely that it affects the confounding influence on the β-coefficient for ethnicity.

5 | CONCLUSION

The relationships between metabolic markers and obesity measures did not differ by ethnicity in Northern and Central Norway. The few marginal ethnic differences in levels of metabolic markers at the same levels of the obesity measure were eliminated by height adjustments. An exception was for systolic BP, which was lower in Sami than in non-Sami at any given level of obesity.

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CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

VLM conceived the idea behind the study, performed all statistical analyses, and wrote the manuscript. TB aided with technical assistance in the statistical analyses. TB, ARB, KK, and MM contributed with planning of the design and analyses, and the interpretation of the results. All authors critically revised the manuscript and accepted the final draft for publication.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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Paper IV

Sex-specific height-correction of weight in a population with ethnic groups that differ in stature—the SAMINOR 1 Survey: a cross-sectional study

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ABSTRACT

Background: Body mass index (BMI, weight/height^2) is a popular proxy for body fatness, but it is negatively correlated with height, particularly in women. In Norway, the ethnic Sami people have had higher BMI than their non-Sami peers, especially in women. However, Sami and non-Sami differ substantially in stature. The aim of this article was to examine if previous findings of obesity differences in Sami and non-Sami persist when applying a height-corrected weight index.

Methods: We estimated a sex-specific height-corrected weight index—the Benn index—that is, weight/height^p where p is estimated from log(weight)-log(height) regression. We used data on 15 717 men and women aging 30 and 36–79 years who participated in the SAMINOR 1 Survey (2003–2004). Correlations between height and weight and the indices BMI and Benn index were calculated using Pearson's correlation coefficient.

Results: Sami were on average 5.8 cm shorter than non-Sami. BMI and height had a modest, negative correlation that was stronger in women than in men. Analyses were stratified by sex due to an interaction between sex and log(height), $p<0.001$. There was no interaction with ethnicity. The p (95% confidence interval) in Benn index (weight/height^p) was estimated to 1.29 (1.21, 1.38) in women and 1.90 (1.83, 1.98) in men. Sami had higher BMI than non-Sami, in women particularly, but Benn index did not differ by ethnicity in either sex.

Conclusion: Previous findings of higher obesity in Sami than in non-Sami may be biased. Future studies should take into account the marked height differences between these groups when comparing obesity indices.

Introduction

Body weight is an indirect measure of body fatness. Because weight is expected to vary between people merely due to differences in height, height-corrected measures of weight has been developed. The most popular height-corrected weight index is known as the body mass index (BMI). However, the BMI is prone to many errors when used as a measure of body fatness (1).

In 1972, weight/height^2, with weight measured in kilograms and height in metres, was termed BMI by Keys et al. (2). The formula was already known as the Quetelet index, after its creation in the mid-1800s by the Belgian statistician Adolphe Quetelet. Premises of the BMI include being independent of height (i.e. no correlation) and being a measure of relative adiposity of which weight is a proxy for (i.e. strong correlation). In 1995, an Expert Committee of the World Health Organization promoted the BMI as a crude, but simple body fatness measure essentially independent of height (3). However, the Committee noted a modest negative correlation with height, and warned that the BMI biases individuals on either end of the height-spectrum. Already in 1971, Benn advised that p in weight/height^p, should be population-specific whenever possible as to avoid a negative correlation with height (4). The value of p typically falls between 1.07 and 2.35, with higher values in men than in women (5,6).

The Sami people populate northern parts of Norway, Sweden, Finland and the Kola Peninsula in the Russian Federation, and is acknowledged as indigenous by the Norwegian Government. Studies conducted in Northern Norway have repeatedly shown that Sami women have had higher mean BMI than non-Sami women, whereas Sami men have had slightly higher or similar BMI compared with non-Sami men (7–9). But on average, Sami are almost 6 cm shorter than non-Sami in Northern Norway (7,9,10). A recent study showed that at the same BMI value, Sami had slightly more favourable levels of some cardiometabolic risk factors (e.g. lipids, blood pressure) than non-Sami. However, this was eliminated by height adjustment, suggesting that BMI does not sufficiently correct for height in this ethnic group (10).

The aim of this article was to examine if previous findings of obesity differences in Sami and non-Sami persist when applying a height-corrected weight index. We used data from the SAMINOR 1 Survey, a population survey in Northern Norway, and aimed to 1) estimate the p in weight/height^p (Benn index) and test for interactions with ethnicity and sex, 2) estimate the correlation between height and weight and the indices BMI and Benn index, respectively, and 3) compare BMI and Benn index in Sami and non-Sami.

Materials and methods

Study sample

The SAMINOR 1 Survey is the first survey of the Population-based Study on Health and Living Conditions in Regions with Sami and Norwegian Populations—the SAMINOR Study, and was conducted in 2003–2004 as a collaboration between the Centre for Sami Health Research, UiT The Arctic University of Norway and the Norwegian Institute of Public Health. The survey comprised self-administered questionnaires and a clinical examination including blood samples. All inhabitants (27 987 individuals) aging 30 and 36–79 years in 24 municipalities mainly in northern, rural parts of Norway were invited and 16 865 (60.3%) participated and gave consent to participate in research. Details are found elsewhere (11).

We excluded 851 participants who did not attend the clinical examination. There were missing data for height and weight in 34 participants, whereas 263 participants failed to reply any ethnicity-related questions. These were excluded, leaving 15 717 participants to analyse.

The SAMINOR Project Board and the Regional Committee for Medical and Health Research Ethics approved this project (REC NORTH reference: 2017/1974). Written informed consent was obtained from all participants.

Height and weight

Height and weight were measured by trained personnel to the nearest 0.1 cm and 100 g, respectively, using an electronic scale with participants wearing light clothing and no shoes.

Ethnicity

Norwegian law states that it is illegal to register ethnicity in medical and population registries, but it is allowed to ask questions regarding ethnicity for research purposes. Eleven questions on ethnicity were posed in the self-administered questionnaire. These included the home language of grandparents, parents and oneself (seven questions), the ethnic background of parents and oneself (three questions) and the person's self-perceived ethnicity (one question). Multiple of the following answers were allowed: Norwegian, Sami, Kven and other. We categorised

Sami ethnicity according to a definition used frequently in studies using SAMINOR data, where both of the following criteria had to be fulfilled to be categorised as Sami: [1] answer Sami as home language of any relative or oneself, and [2] answer Sami as one's own ethnic background or self-perceived ethnicity. All others were categorised as non-Sami.

Statistical analysis

The distributions of weight and height were visualised using kernel density plots in strata of ethnicity and sex. All variables were normally distributed and presented as mean (standard deviation).

Let w denote weight in kilograms and h denote height in meters. Benn gave mathematical proof that a person's relative weight (the ratio of actual weight to a standard weight for height) can approximately be expressed as a power-type weight index, w/h^p (4). Benn proposed to estimate p as the gradient or slope in a regression of log(w) vs log(h), i.e. the coefficient β in the regression equation

$$\log(w) = \alpha + \beta \log(h) \qquad (1)$$

According to Benn, w/h^p is not only (approximately) independent of height, but it is also highly correlated relative weight.

All analyses were sex-stratified due to evidence of interaction between log(height) and sex (p-value <0.001) in the regression model. There was no interaction between log(height) and ethnicity. In strata of sex, we modelled log(w) on log(h) using linear regression and estimated p as the slope coefficient β. Next, we calculated BMI and the Benn index as weight in kg divided by height in metres raised to a power of 2 and p (the sex-specific β coefficient from log-log regression), respectively. The distributions of weight and height were visualised using kernel density plots in strata of ethnicity and sex.

We used two-sample t-tests to compare mean of weight, height, BMI and Benn index in Sami and non-Sami participants. We estimated correlations between BMI and height, BMI and weight, and between Benn index and height, and finally Benn index and weight, with Pearson's product-moment correlation coefficient, r, with 95% confidence intervals (CI).

We used the free software *R* version 4.0.0 in all analyses (12).

Results

A total of 3470 (22%) of the participants were categorised with Sami ethnicity. Table 1 displays sample characteristics and Figure 1 displays kernel density plots of the height and weight distributions in strata of sex and ethnicity. On average, Sami were shorter and weighed less than non-Sami.

Table 1. Ethnic- and sex-specific characteristics in the SAMINOR 1 Survey (2003–2004, N=15 717)

	Total	Sami	non-Sami	p-value
Women	N=8213	N=1777	N=6436	
Age, years	53.8 (11.7)	53.3 (11.7)	53.9 (11.7)	0.067
Height, cm	160.9 (6.8)	156.4 (6.1)	162.2 (6.4)	< 0.001
Weight, kg	71.3 (13.0)	69.0 (12.4)	71.9 (13.2)	< 0.001
Men	N=7504	N=1693	N=5811	
Age, years	54.4 (11.3)	54.6 (11.2)	54.3 (11.3)	0.409
Height, cm	173.8 (7.2)	169.3 (6.4)	175.1 (6.9)	< 0.001
Weight, kg	83.5 (13.5)	79.8 (13.3)	84.6 (13.4)	< 0.001

Mean (standard deviation) are given. P-values originate from two-sample t-tests.

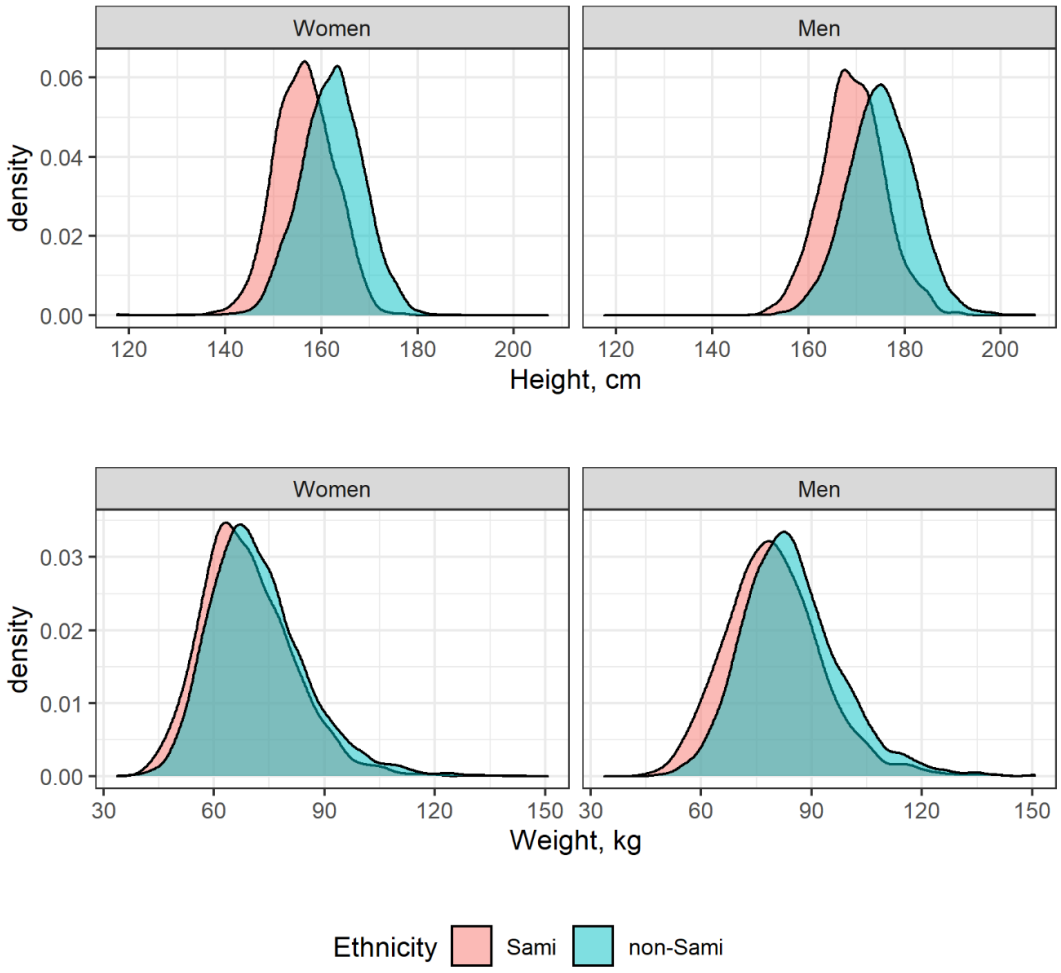

Figure 1. Kernel density plots of distributions of ethnic- and sex-specific height and weight in the SAMINOR 1 Survey (2003–2004, N=15 717).

The correlation coefficient r (95% CI) between weight and height was 0.30 (0.28, 0.32) in women and 0.49 (0.47, 0.50) in men. Hence, height explains 9% and 24% of the variance (r^2) in weight in women and men, respectively.

The slope of log(height) of the log-log-regression, p (95% CI), was 1.29 (1.21, 1.38) in women and 1.90 (1.83, 1.98) in men (p-value for interaction between sex and log(height) <0.001). Ethnicity-stratified analyses showed that p (95% CI) was estimated to 1.16 (0.95, 1.36) in Sami women and 1.36 (1.26, 1.47) in non-Sami women (p-value for interaction between ethnicity and log(height) = 0.07), and 2.01 (1.83, 2.2) in Sami men and 1.90 (1.81, 1.98) in non-Sami men (p-value for interaction = 0.24).

Table 2 shows sex-stratified comparisons of Sami and non-Sami with regard to BMI and the Benn index using p=1.29 and p=1.90 for women and men, respectively. For both men and women, BMI were slightly higher in Sami than non-Sami, while no differences were found for Benn index. Figure 2 displays kernel density plots of the distribution of BMI and Benn index in strata of sex and ethnicity.

Table 2. Ethnic- and sex-specific means (standard deviation) of Benn index and body mass index in the SAMINOR 1 Survey (2003–2004, N=15 717)

	Total	Sami	non-Sami	p-value
Women				
Body mass index, kg/m^2	27.5 (4.9)	28.2 (5.1)	27.4 (4.8)	< 0.001
Benn index, kg/m$^{1.29}$	38.5 (6.7)	38.7 (6.8)	38.4 (6.7)	0.164
Men				
Body mass index, kg/m^2	27.6 (3.9)	27.8 (4.1)	27.6 (3.9)	0.016
Benn index, kg/m$^{1.90}$	29.1 (4.1)	29.3 (4.3)	29.1 (4.1)	0.114

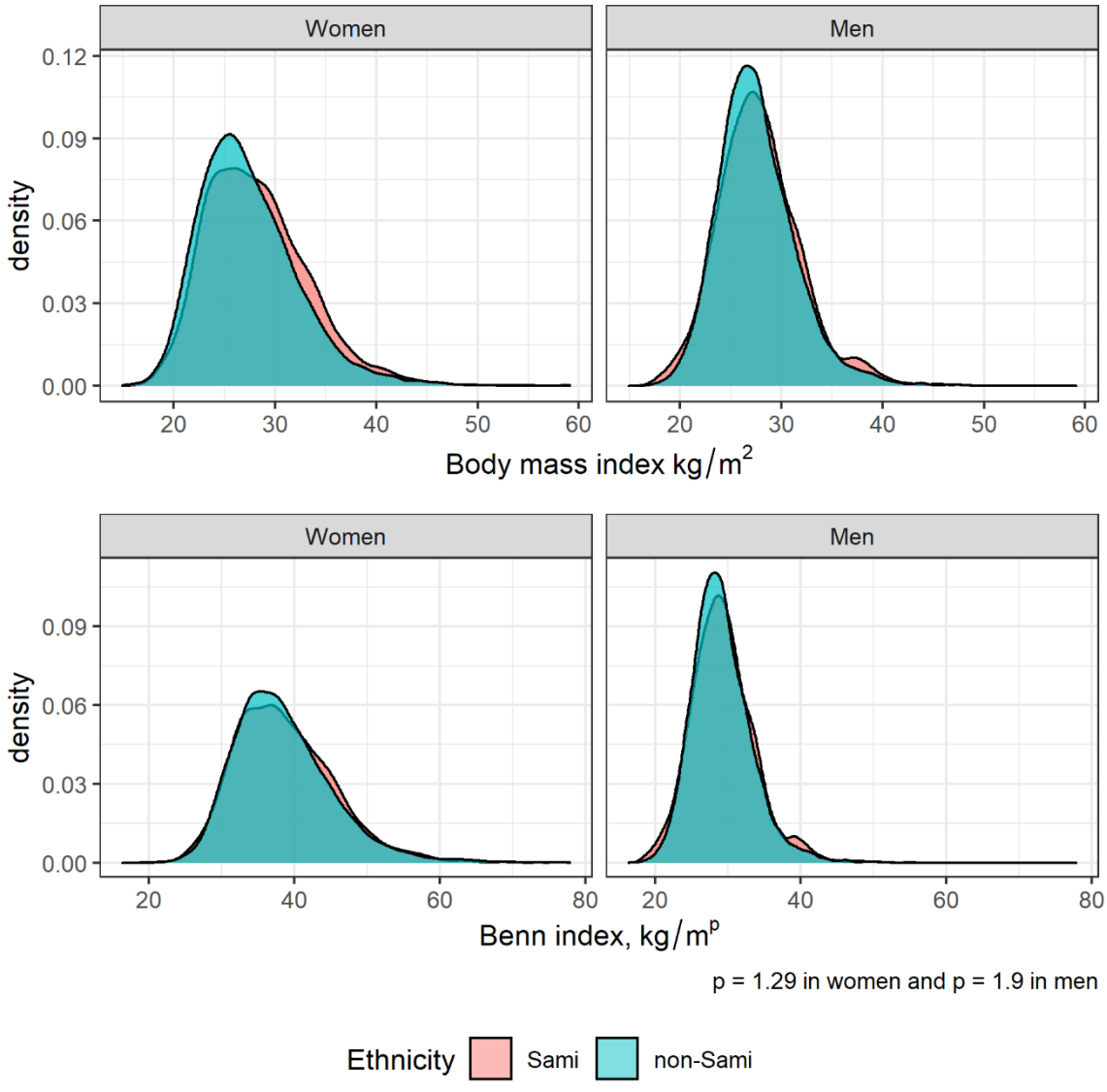

Figure 2. Kernel density plots of ethnic- and sex-specific distributions of body mass index and Benn index in the SAMINOR 1 Survey (2003–2004, N=15 717).

Table 3 and Figure 3 show correlation coefficients and scatterplots, respectively, of weight vs BMI, weight vs Benn index, height vs BMI and height vs Benn index. BMI and height had a negative correlation that was stronger in women than in men. By contrast, no correlation was found between Benn index and height. Both BMI and Benn index correlated highly with weight; estimates were somewhat higher for Benn index, in women particularly.

Table 3. Sex-specific correlations between height and BMI, height and Benn index, weight and BMI, and weight and Benn index in the SAMINOR 1 Survey (2003–2004, N=15 717)

	Height		Weight	
Women	r (95% CI)	p-value	r (95% CI)	p-value
Body mass index, kg/m^2	-0.17 (-0.19, -0.15)	< 0.001	0.89 (0.88, 0.89)	< 0.001
Benn index, kg/m$^{1.29}$	-0.00 (-0.02, 0.02)	0.753	0.95 (0.95, 0.96)	< 0.001
Men				
Body mass index, kg/m^2	-0.03 (-0.05, -0.01)	< 0.001	0.85 (0.85, 0.86)	< 0.001
Benn index, kg/m$^{1.90}$	0.00 (-0.02, 0.02)	0.689	0.87 (0.87, 0.88)	< 0.001

r = Pearson's correlation coefficient, CI = confidence interval

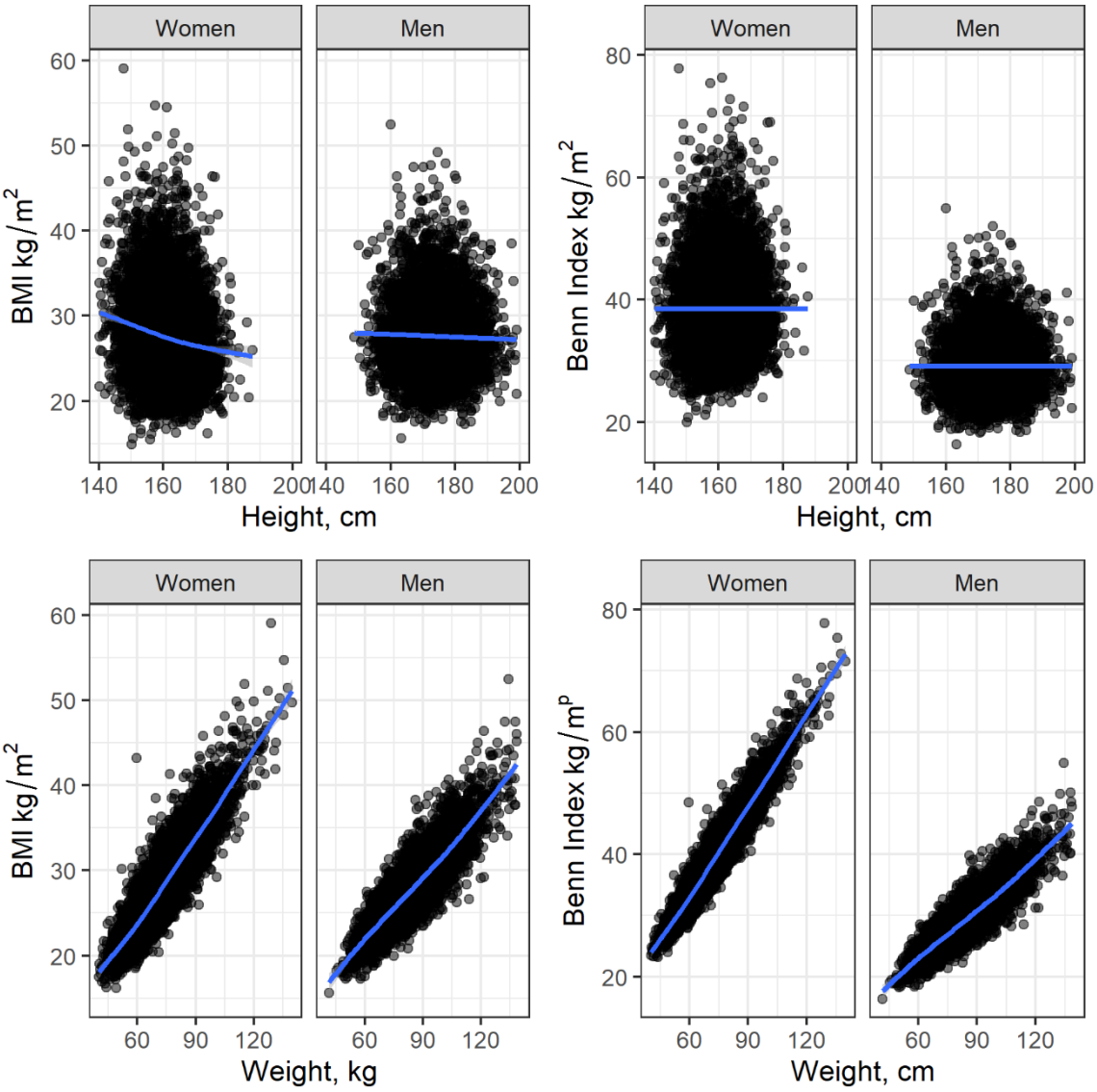

Figure 3. Sex-specific scatterplots of weight vs body mass index (BMI) and Benn index, respectively, and of height vs BMI and Benn index, respectively, with fitted lines in the SAMINOR 1 Survey (2003–2004, N=15 717).

Discussion

In this population-based study of approximately 16 000 adult women and men from rural, Sami-core areas in Northern Norway, we show a negative correlation between BMI and height, but no correlation between Benn index and height. Whereas mean BMI differ between Sami and non-Sami, mean Benn index does not differ between the ethnic groups. The estimated power *p* is markedly lower in women than in men (1.28 vs 1.90, respectively), corresponding with findings from several previous large studies from a wide variety of geographical regions, ages, ethnic groups and periods (5,6,13,14). We found no evidence of effect modification by ethnicity. Therefore, we used the same sex-specific *p* in both ethnic groups, which is an advantage in order to compare figures between the groups.

Our findings from a multi-ethnic population-based sample correspond with a previous multi-ethnic study from the U.S. In 1981, Lee et al. compared several indices of weight corrected for height (weight/height, weight/height^2, weight/height^3, weight/height^p) and their correlation with weight and height in five ethnic groups in the US (White, Japanese, Chinese, Filipino and Hawaiian) (5). The p differed substantially between the sexes, but differed less between ethnic groups within the same sex (1.18–1.59 in women and 1.65–2.09 in men). When estimating p from the overall ethnic heterogeneous sample, weight/height^p was unbiased with respect to height. Consequently, the authors supported the same Benn index for height-unbiased weight comparisons across population groups that differ in height (5). However, the study by Lee et al. is four decades old.

In 2005, a research collaboration group analysed the weight-height relationship in 72 adult subgroups from 25 diverse countries from the US, Europe and Asia, including more than 380 000 individuals (and ethnicities) (6). A negative correlation between BMI and height was found in 31 of 40 samples of men and all 32 samples of women. The summary estimates of p from log-log regression was 1.92 (95% CI, 1.87–1.97) in men and 1.45 (95% CI, 1.39–1.51) in women. These correspond quite well with our findings (1.90 and 1.28 in men and women, respectively). In 2016, Sperrin et al. analysed height and weight data from 1992 to 2011 on more than 180 000 men and women from England (13). Based on their findings that BMI and height are negatively correlated and that p differ by sex, the authors suggested more sophisticated statistical modelling than simple mean BMI contrasts when comparing heterogeneous populations (13). These studies support the findings in our study, that is, the weak negative correlation between BMI and height may be a source of bias when comparing obesity within heterogeneous populations.

Ultimately, the goal is to find an index that is a good proxy of complications from having too much body fat. BMI or Benn index are not a direct measures of fat, but measures of relative weight. An increased waist circumference is a better predictor of adverse health outcomes than BMI (15–17). A meta-analysis concluded that both waist circumference and waist-to-height ratio were better than BMI in detection of cardiometabolic risk (17). Waist-to-height ratio was slightly superior to waist circumference, and the authors promoted it as a universal measure across various ethnic groups, sexes and ages (17). However, the correlation between height and waist circumference and waist-to-height ratio is positive and negative, respectively (18). Recognising that BMI and waist circumference is highly correlated (typically with a correlation coefficient ~0.9), Krakauer et al. quite recently created a body shape index (ABSI) from weight, height and waist circumference that is independent of BMI and predictive of mortality (19). Hence, there are several other body fatness and body composition indices that may be better epidemiological measures of obesity than the simple BMI.

The aim of this article was to examine whether a height-corrected weight index differed between Sami and non-Sami. We have shown that it does not. Previous findings of higher obesity prevalence in Sami than non-Sami may be biased. Future studies should aim for properly height-corrected measures when comparing obesity in Sami and non-Sami.

Strenghts and limitations

Strengths of this study include a large sample size, objectively measured height and weight by trained personnel, negligible missing data for height and weight, and several self-reported questions relating to various facets of ethnicity. Limitations include a moderate participation rate (~60%) that may have induced selection bias. Information about the ethnicity of the invitees is not available. Hence, it is impossible to know whether response rates differ between Sami and non-Sami. Further, there is no consensus on how to define Sami ethnicity. Some of those categorised as non-Sami in our analyses have Sami ancestors, but do not consider themselves Sami. Finally, it is a limitation that we were not able to include precise information on body fatness e.g. DXA in our analyses.

Conclusion

The frequently reported difference in BMI between Sami and non-Sami is biased due to a negative correlation between BMI and height. When the power p in weight/height^p is estimated through sex-specific linear regression of log(weight) on log(height) (Benn index), we find that mean levels of this index do not differ between Sami and non-Sami. However, no weight-for-height indices are direct measures of body fatness or distribution of body fat. The actual levels of body fatness in the Sami and non-Sami population remains unknown.

Acknowledgements

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Appendix A

The SAMINOR 1 Survey

- Information brochure
  - Design 1
  - Design 2
- Invitation letter, design 1
- Informed written consent form
- Remainder card
- Screening questionnaire (english translation), design 2

All listed items and their Norwegian versions are available at www.saminor.no.

med opplysninger om deg i andre registre for forskningsformål slik som *Kreftregisteret, Dødsårsaksregisteret* og folketellingene. I alle disse tilfellene vil navn og personnummer bli fjernet. Forsikringsselskaper får ikke tilgang til dataene.

4) At blodprøven din kan lagres og brukes til medisinsk forskning og genetiske analyser for å finne årsak til sykdom. All bruk av denne prøven vil bare skje i samsvar med godkjenning fra *Datatilsynet* og etter at *Regional komité for medisinsk forskningsetikk i Nord-Norge* har vurdert og tilrådd prosjektet.

Selv om du sier ja til dette nå, kan du senere ombestemme deg og be om å bli slettet fra undersøkelsen uten at du må oppgi noen grunn for det. Dette gjøres ved skriftlig beskjed til **Institutt for samfunnsmedisin, UiTø, 9037 Tromsø**. Blodprøven din vil da bli tilintetgjort.

Vi ønsker å følge alle som møter til helseundersøkelsen i lang tid framover med hensyn til hjerteinfarkt, hjerneslag og andre aktuelle sykdommer. Derfor ønsker vi å lagre opplysningene du har gitt, frem til fylte 100 år, for å sammenholde disse med opplysninger fra sentrale registre slik som *Kreftregisteret* og *Dødsårsaksregisteret.*

Velkommen til helseundersøkelsen

Selv om du nettopp har vært hos lege eller selv om du føler deg frisk, kan du likevel delta i undersøkelsen. Da hjelper du oss til bedre kunnskap og riktigere oversikt over helsen i kommunen og fylket ditt.

Dødsårsaksregistret ja olmmošlohkamat. Visot dáid oktavuođain sihkko namma ja personnummar. Dáhkádusfitnodagat eai beasa dáid dieđuid oaidnit.

4) Ahte du varraiskkus sáhttá ráddjot ja adnot medisiinnalaš dutkamii ja genetalaš analysaide gávnnahit dávddaid árttaid. Dán iskosa juohke geavaheapmi geavvá dušše *Datatilsynet* dohkkeheami mielde ja maŋŋil go *Regional komite for medisinsk forskningsetikk i Nord-Norge* lea árvvoštallan ja rávven prošeavtta.

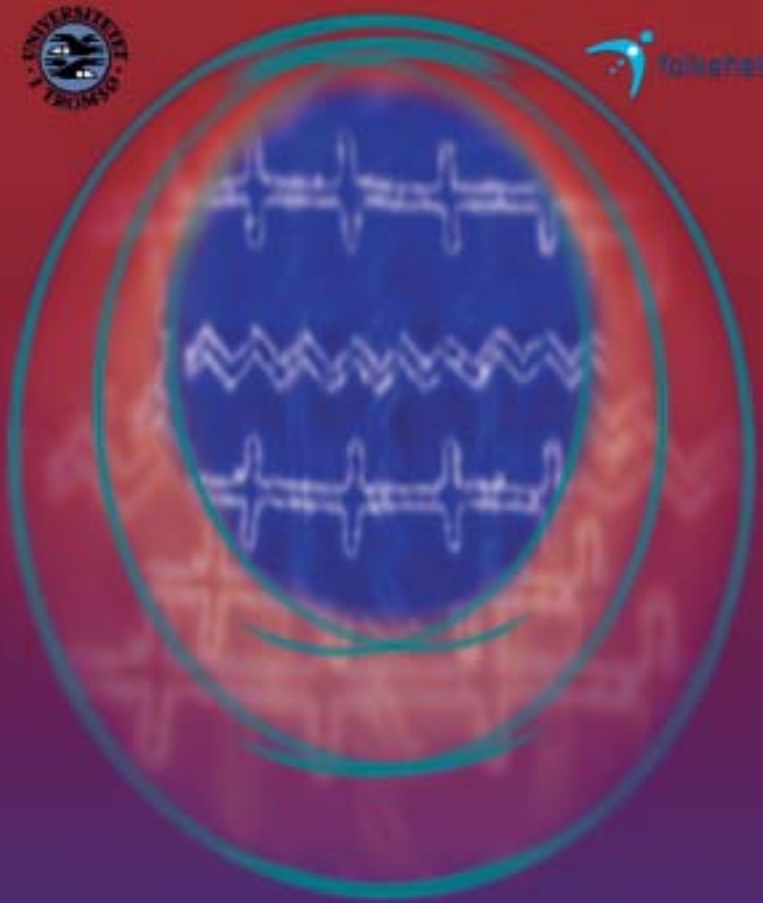
Vaikke dása dál mieđat, de sáhtát maŋŋil molsut oaivila ja bivdit sihkkot iskkadeamis dieđitkeahttá makkárge ákka dasa. Dán dagat čálalaččat Institutt for samfunnsmedisinii; **Institutt for samfunnsmedisin, UiTø, 9037 Tromsø**. Du varraiskkus dalle bálkestuvvo.

Mii dáhtošeimmet guhkit áiggi čuovvut juohkehačča gii boahtá dearvvasvuođaiskkadeapmái váibmodohppehaga, vuoiŋŋašgáldnanvigi ja eará vejolaš dávddaid hárrái. Danne dáhtošeimmet rádjat du addán dieđuid, gitta devdon 100 jahkái, vai daid beassá sulastahttit guovddáš registariid dieđuiguin, nugo *Kreftregistret* ja *Dødsårsaksregistret.*

Bures boahtin dearvvasvuođaiskkadeapmái

Vaikke leatge aiddo leamaš doaktára luhtte dahje dovddat iežat dearvvasin, de sáhtát liikká searvat iskkadeapmái. Dalle veahkehat min oažžut eanet máhtu ja riektasat dieđuid du gieldda ja fylkka dearvvasvuođas.

Gráfalaš barggus vástida/Grafisk utforming: Britt Hansen Biti – BHB Gráfalaš bálvalusat/Grafiske tjenester, Kárášjohka/Karasjok.
Deaddilan/Trykk: Bjørkmanns Trykkeri, Alaheadju/Alta.



Nå skal vi sette fokus på helsen i kommunen din.
Hvordan står det egentlig til? Hvordan fungerer helsetjenesten?
Er det store helseforskjeller i de ulike delene av fylket eller mellom de ulike etniske gruppene? Er kvinner friskere enn menn?
Hvorfor øker sukkersyke her i landet?

Dál áigut giddet fuomášumi dearvvasvuhtii din gielddas. Mo dat duođas lea?
Mo doaibmá dearvvasvuođabálvalus? Leatgo stuorra dearvvasvuođaerohusat fylkka iešguđet osiin dahje iešguđet čearddalaš joavkkuid gaskkas?
Leatgo nissonat dearvasat go albmát?
Manne lassána sohkardávda dán riikkas?

For mer informasjon, ring 78 46 89 04, Senter for samisk helseforskning, Karasjok.
E-post: helseus@fagmed.uit.no

Jus dárbbašat eambbo dieđuid, čuojahastte 78 46 89 04, Sámi dearvvašvuođadutkama guovddážii, Kárášjohka. E-poasta: helseus@fagmed.uit.no

Helseundersøkelsen har tre formål:

- Du som deltar i helseundersøkelsen får sjekket om du har bestemte sykdommer, eller om det er fare for at du kan få dem.
- Å få ny kunnskap om helse, sykdom og levekår i områder med samisk og norsk bosetting.
- Å lage en oversikt over folks helse – en «helseprofil» for fylket. Dette er viktig for å gi fylket og de enkelte kommunene et bedre grunnlag for å planlegge helsetjenesten i framtida.

Hvem kan delta?

Alle født 1925–1967 og i 1973 fra områder med samisk og norsk bosetting. Det er 9 kommuner i Finnmark, 6 i Troms, 4 i Nordland og 2 i Nord-Trøndelag med i undersøkelsen.

Hvordan får du time til helseundersøkelsen?

Dersom du ønsker å være med i helseundersøkelsen, krysser du av for det i vedlagte spørreskjema, besvarer det og sender det inn. Deretter får du time til helseundersøkelsen som vil foregå enten i buss eller i et fast lokale i kommunen. Hvis den oppsatte timen ikke passer, kan du møte når du vil innenfor åpningstiden vår som du finner i invitasjonsbrevet. Undersøkelsen er gratis. Du får tilsendt et spørreskjema sammen med innkallingen. Vi ber om at du fyller ut skjemaet hjemme og tar det med når du møter fram til helseundersøkelsen.

Dearvvasvuođaiskkadeami dieđuin leat golbma ulbmila:

- Dus gii searvvat iskkadeapmái iskat leatgo dus dihto dávddat, dahje leago dus várra daid oažžut.
- Oažžut ođđa máhtu dearvvasvuođa, dávddaid ja eallindili birra sámi ja dáža ássanguovlluin.
- Ráhkadit várdosa olbmuid dearvvasvuođas – fylkka «dearvvasvuođaprofiilla». Dát lea dehálaš vai fylkkas ja juohke gielddas lea buoret vuođđu plánet boahttevaš dearvvasvuođabálvalusa.

Gii sáhttá searvat?

Juohkehaš riegádan 1925–1967 ja 1973 guovlluin gos ásset sápmelaččat ja dážat. 9 gieldda Finnmárkkus, 6 Tromssas, 4 Nordlánddas ja 2 Davvi-Trøndelagas leat iskkadeamis mielde.

Mo oaččut diimmu dearvvasvuođaiskkadeapmái?

Jus dáhtut leat mielde dearvvasvuođaiskkadeamis, de russet dan čuovvu gažadanskovis, vástidat dan ja sáddet dan midjiide. Dasto oaččut diimmu iskadeapmái mii lea juogo busses dahje dihto lanjas gielddas. Jus biddjon áigi ii heive, de sáhtát boahtit vaikke goas min rahpanáiggis maid oainnát rávkanreivves. Iskkadeapmi lea nuvttá. Oaččut gažadanskovi oktan rávkamiin. Bivdit du deavdit skovi ruovttus ja váldit dan mielde go boađát iskkadeapmái.

Hvordan foregår helseundersøkelsen?

Det gjøres målinger av blodtrykk, høyde, vekt og livvidde, og det taes en blodprøve. Blodprøven kan senere bli analysert på fettstoffer i blodet, blodsukker, markører for betennelsesreaksjoner, kosthold, hormoner, lever- og nyrefunksjon samt beinmarkører. Genetiske analyser av blodet kan også bli aktuelt.

Omtrent fire uker etter helseundersøkelsen får du et brev i posten med opplysninger om ditt kolesterol, blodtrykk og blodsukker, og hvordan du ligger an i forhold til anbefalte verdier. De som har særlig høy risiko for å få hjerte- og kar sykdommer og sukkersyke, vil bli bedt om å ta kontakt med sin egen lege for videre oppfølging.

Alle som møter fram til helseundersøkelsen, får et tilleggsskjema, med spørsmål om blant annet kosthold og levekår.

Vi trenger din tillatelse

Når du møter fram til helseundersøkelsen, ber vi deg om å undertegne et samtykke der du sier deg enig i et eller flere av de fire punktene nedenfor. (Du vil få kopi av samtykke erklæringen).

1) At du kan bli kontaktet med anbefaling om oppfølging, behandling eller for å forebygge sykdom.

2) At opplysningene dine kan brukes til medisinsk forskning etter vurdering og tilråding fra *Regional komité for medisinsk forskningsetikk i Nord-Norge* og *Datatilsynet.*

3) At resultatene dine (etter godkjenning fra *Datatilsynet*) kan settes sammen

Mo iskkojuvvot?

Varradeaddu, allodat, lossodat ja seakkáš mihtiduvvojit, ja váldo varraiskkus. Varraiskosis sáhttá maŋŋil iskat vara buoideávdnasiid, varrasohkkara, infekšunreakšuvnnaid mearkkaid, biepmu, hormonaid, vuoivvas- ja monimušdoaimma ja dáktemearkkaid. Vara genetalaš analysat maid soitet šaddat áigeguovdilat.

Sullii njeallje vahku maŋŋil dearvvasvuođaiskkadeami oaččut poasttas reivve iežat kolestrola, varradeattu ja varrasohkkara birra, ja mo dat leat rávvejuvvon meriid ektui. Bivdit sin geain lea hui alla váibmo- ja suotnadávddavárra ja sohkardávda, váldit oktavuođa iežaset doaktáriin joatkka čuovvoleapmái.

Juohkehaš gii boahtá iskkadeapmái, ažžu lassiskovi, gažaldagaiguin ee. biepmu ja eallindili birra.

Mii dárbbašat du lobi

Go boađát iskkadeapmái, de bivdit du čállit vuollái miehtama, mas logat iežat leat ovttamielas ovtta dahje moatti dán njeallje čuoggás vulobealde (Miehtamis oaččut máŋgosa).

1) Ahte duinna sáhttá váldit oktavuođa go áigu rávvet čuovvoleami, dálkkodit dahje eastadit dávddaid.

2) Ahte visot du dieđut sáhttet adnot medisiinnalaš dutkamii *Regional komite for medisinsk forskningsetikk i Nord-Norge* ja *Datatilsynet* árvvoštallama ja rávvaga mielde.

3) Ahte du bohtosiid (*Datatilsynet* dohkkeheami mielde) sáhttá čohkket dieđuiguin du birra eará registariin dutkandoaimmaide nugo *Kreftregistret,*

Selv om du sier ja til dette nå, kan du senere ombestemme deg og be om å bli slettet fra undersøkelsen uten at du må oppgi noen grunn for det. Dette gjøres ved skriftlig beskjed til **Institutt for samfunnsmedisin, UiTø, 9037 Tromsø**. Blodprøven din vil da bli tilintetgjort.

Vi ønsker å følge alle som møter til helseundersøkelsen i lang tid framover med hensyn til hjerteinfarkt, hjerneslag og andre aktuelle sykdommer. Derfor ønsker vi å lagre opplysningene du har gitt, frem til fylte 100 år, for å sammenholde disse med opplysninger fra sentrale registre slik som *Kreft-* og *Dødsårsaksregisteret.*

Resultatene vil bli publisert i massemedia, og det utformes en rapport fra helse- og levekårsundersøkelsen når den er avsluttet.

Datatilsynet har gitt konsesjon for lagring av opplysninger fra undersøkelsen og forskningsprosjektet er tilrådd av *Regional komite for medisinsk forskningsetikk i Nord- Norge.*

Velkommen til helseundersøkelsen

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Bohtosiid almmuhat mediain, ja čállo raporta dearvvasvuođa- ja eallindilleiskkadeamis go dat lea loahpahuvvon.

Datatilsynet lea addán sierralobi rádjat iskkadeami dieđuid ja dutkanprošeavtta lea rávven *Regional komite for medisinsk forskningsetikk i Nord-Norge.*

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Dearvvuođaiguin / Med hilsen

Anne Kirsten Anti
Sámi dearvvašvuođadutkama guovddáš,
Senter for samisk helseforskning
Kárášjohka/Karasjok

Eiliv Lund
Institutt for samfunnsmedisin
Institutt for samfunnsmedisin
Romsa/Tromsø

Per G. Lund-Larsen
Nasjonalt folkehelseinstitutt/
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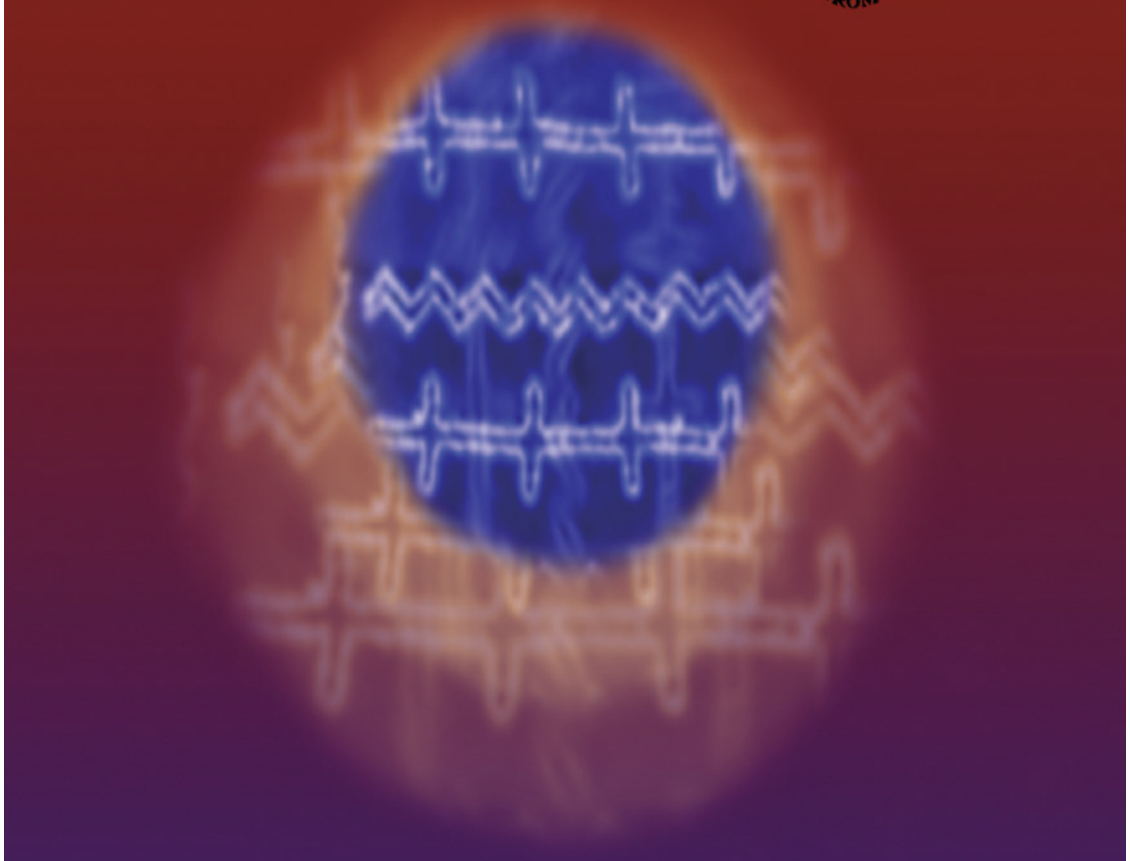

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Alle født 1925–1967 og i 1973 fra områder med samisk og norsk bosetting. Det er 9 kommuner i Finnmark, 6 i Troms, 4 i Nordland og 2 i Nord-Trøndelag med i undersøkelsen.

Hvordan får du time til helseundersøkelsen?

Du får tilsendt et spørreskjema sammen med innkallingen. Vi ber om at du fyller ut skjemaet hjemme og tar det med når du møter fram til helseundersøkelsen. Helseundersøkelsen vil foregå enten i buss eller i et fast lokale i kommunen. Hvis den oppsatte timen ikke passer, kan du møte når du vil innenfor åpningstiden vår. Undersøkelsen er gratis.

Hvordan foregår helseundersøkelsen?

Det gjøres målinger av blodtrykk, høyde, vekt og livvidde, og det taes en blodprøve. Blodprøven kan senere bli analysert på fettstoffer i blodet, blodsukker, markører for betennelsesreaksjoner, kosthold, hormoner, lever- og nyrefunksjon samt beinmarkører. Genetiske analyser av blodet kan også bli aktuelt.

Omtrent fire uker etter helseundersøkelsen får du et brev i posten med opplysninger om ditt kolesterol, blodtrykk og blodsukker, og hvordan du ligger an i forhold til anbefalte verdier. De som har særlig høy risiko for å få hjerte- og kar sykdommer og sukkersyke, vil bli bedt om å ta kontakt med sin egen lege for videre oppfølging.

Alle som møter fram til helseundersøkelsen, får et tilleggsskjema, med spørsmål om blant annet kosthold og levekår.

De som fullfører hele helse- og levekårsundersøkelsen vil være med i trekningen av 3 reisegavekort hver verdt kr. 10000,–. Vi regner med en deltakelse på ca. 15000 personer.

Dearvvasvuođaiskkadeami dieđuin leat golbma ulbmila:

- Dus gii searvvat iskkadeapmái iskat leatgo dus dihto dávddat, dahje leago dus várra daid oažžut.
- Oažžut ođđa máhtu dearvvasvuođa, dávddaid ja eallindili birra sámi ja dáža ássanguovlluin.
- Ráhkadit várdosa olbmuid dearvvasvuođas – fylkka «dearvvasvuođaprofiilla». Dát lea dehálaš vai fylkkas ja juohke gielddas lea buoret vuođđu plánet boahttevaš dearvvasvuođabálvalusa.

Gii sáhttá searvat?

Juohkehaš riegádan 1925–1967 ja 1973 guovlluin gos ásset sápmelaččat ja dážat. 9 gieldda Finnmárkkus, 6 Tromssas, 4 Nordlánddas ja 2 Davvi-Trøndelagas leat iskkadeamis mielde.

Mo oaččut diimmu dearvvasvuođaiskkadeapmái?

Oaččut gažadanskovi oktan rávkamiin. Bivdit du deavdit skovi ruovttus ja váldit dan mielde go boađát iskkadeapmái. Iskadeapmi lea juogo busses dahje dihto lanjas gielddas. Jus biddjon áigi ii heive, de sáhtát boahtit vaikke goas min rahpanáiggis. Iskkadeapmi lea nuvttá.

Mo iskkojuvvot?

Varradeaddu, allodat, lossodat ja seakkáš mihtiduvvojit, ja váldo varraiskkus. Varraiskosis sáhttá maŋŋil iskat vara buoideávdnasiid, varrasohkkara, infekšunreakšuvnnaid mearkkaid, biepmu, hormonaid, vuoivvas- ja monimušdoaimma ja dáktemearkkaid. Vara genetalaš analysat maid soitet šaddat áigeguovdilat.

Sullii njeallje vahku maŋŋil dearvvasvuođaiskkadeami oaččut poasttas reivve iežat kolestrola, varradeattu ja varrasohkkara birra, ja mo dat leat rávvejuvvon meriid ektui.

Bivdit sin geain lea hui alla váibmo- ja suotnadávddavárra ja sohkardávda, váldit oktavuođa iežaset doaktáriin joatkka čuovvoleapmái.

Juohkehaš gii boahtá iskkadeapmái, oažžu lassiskovi, gažaldagaiguin ee. biepmu ja eallindili birra.

Sii geat čađahit olles dearvvasvuođa- ja eallindilleiskkadeami leat mielde vuorbádeamen 3 mátkeskeaŋkakoartta man árvu lea 10000,– ru. guđesge. Doaivut ahte su. 15000 olbmo servet.

Vi trenger din tillatelse

Når du møter fram til helseundersøkelsen, ber vi deg om å undertegne et samtykke der du sier deg enig i et eller flere av de fire punktene nedenfor. (Du vil få kopi av samtykke erklæringen).

1) At du kan bli kontaktet med anbefaling om oppfølging, behandling eller for å forebygge sykdom.

2) At opplysningene dine kan brukes til medisinsk forskning etter vurdering og tilråding fra *Regional komité for medisinsk forskningsetikk i Nord-Norge* og *Datatilsynet*.

3) At resultatene dine (etter godkjenning fra *Datatilsynet*) kan settes sammen med opplysninger om deg i andre registre for forskningsformål slik som *Kreftregisteret, Dødsårsaksregisteret* og folketellingene. I alle disse tilfellene vil navn og personnummer bli fjernet. Forsikringsselskaper får ikke tilgang til dataene.

4) At blodprøven din kan lagres og brukes til medisinsk forskning og genetiske analyser for å finne årsak til sykdom. All bruk av denne prøven vil bare skje i samsvar med godkjenning fra *Datatilsynet* og etter at *Regional komité for medisinsk forskningsetikk i Nord-Norge* har vurdert og tilrådd prosjektet.

Mii dárbbašat du lobi

Go boađát iskkadeapmái, de bivdit du čállit vuollái miehtama, mas logat iežat leat ovttamielas ovtta dahje moatti dán njeallje čuoggás vulobealde (Miehtamis oaččut máŋgosa).

1) Ahte duinna sáhttá váldit oktavuođa go áigu rávvet čuovvoleami, dálkkodit dahje eastadit dávddaid.

2) Ahte visot du dieđut sáhttet adnot medisiinnalaš dutkamii *Regional komite for medisinsk forskningsetikk i Nord-Norge* ja *Datatilsynet* árvvoštallama ja rávvaga mielde.

3) Ahte du bohtosiid (*Datatilsynet* dohkkeheami mielde) sáhttá čohkket dieđuiguin du birra eará registariin dutkandoaimmaide nugo *Kreftregistret, Dødsårsaksregistret* ja olmmošlohkamat. Visot dáid oktavuođain sihkko namma ja personnummar. Dáhkádusfitnodagat eai beasa dáid dieđuid oaidnit.

4) Ahte du varraiskkus sáhttá ráddjot ja adnot medisiinnalaš dutkamii ja genetalaš analysaide gávnnahit dávddaid árttaid. Dán iskosa juohke geavaheapmi geavvá dušše *Datatilsynet* dohkkeheami mielde ja maŋŋil go *Regional komite for medisinsk forskningsetikk i Nord-Norge* lea árvvoštallan ja rávven prošeavtta.

Helse- og levekårsundersøkelse

– et forskningsprosjekt

Helsedepartementet har bedt oss undersøke helse- og levekårsforhold hos alle født i 1925–1967 og i 1973 i utvalgte kommuner med samisk og norsk bosetting i Nord-Norge og Nord-Trøndelag. Formålet er å innhente opplysninger om hjerte- og karsykdommer, kreft, allergier, smerter og andre lidelser samt ulykker for å kunne forebygge dem. Videre er målet å få et bilde av folks oppfatning av helsetjenestetilbudet, deres levesett slik som kosthold og røyking, levekår og tilhørighet. De som ønsker å delta, blir med i et forskningsprosjekt som består av spørreskjemaer og helseundersøkelse. Alle opplysninger fra undersøkelsen vil bli behandlet konfidensielt.

Helse- og levekårsundersøkelsen er nærmere beskrevet i brosjyren, som ligger vedlagt. Dersom du er i tvil om noe, kan du kontakte oss på tlf. 78 46 89 04 eller på e-post: helseus@fagmed.uit.no

Du kan delta på følgende måter: (kryss av øverst på spørreskjema under «samtykke til deltakelse»)

A Dersom du ønsker å delta i helseundersøkelsen og forskningsprosjektet, krysser du av punkt **A**, fyller ut spørreskjemaet og returnerer det til oss i vedlagte konvolutt. Du vil senere få et brev med tid og sted for fremmøte sammen med et nytt spørreskjema.

B Dersom du bare ønsker å delta i en innledende del av forskningsprosjektet uten helseundersøkelse, krysser du av punkt **B** , fyller ut spørreskjemaet og returnerer det til oss i vedlagte konvolutt.

C Du kan unngå purring fra oss ved å krysse av punkt **C** og returnere spørreskjemaet til oss. Purring vil skje skriftlig.

Datatilsynet har gitt konsesjon for lagring av opplysninger fra undersøkelsen og forskningsprosjektet er tilrådd av *Regional komite for medisinsk forskningsetikk i Nord- Norge.*

For forskningen sin del vil det være av stor interesse at vi får inn så mange opplysninger som mulig. Du deltar frivillig og kan, etter å ha sagt ja til deltakelse, senere trekke deg uten å begrunne hvorfor og uten at det vil ha noen konsekvenser for deg. Det samme gjelder dersom man i utgangspunktet ikke ønsker å delta. Opplysninger du har gitt kan du be om å få slettet.

Resultatene vil bli publisert i massemedia, og det utformes en rapport fra helse- og levekårsundersøkelsen når den er avsluttet.

De som fullfører hele helse- og levekårsundersøkelsen vil være med i trekningen av 3 reisegavekort til en verdi av á kr. 10 000,–. Vi regner med en deltakelse på ca. 15000 personer.

Med hilsen

Anne Kirsten Anti
Senter for samisk helseforskning
Karasjok

Eiliv Lund
Institutt for samfunnsmedisin
Tromsø

Per G. Lund-Larsen
Nasjonalt folkehelseinstitutt
Oslo

Dearvvasvuođa ja eallindilleiskkadeapmi

– dutkanprošeakta

Dearvvasvuođadepartementa lea min bivdán iskat dearvvasvuođa- ja eallindili juohkehaččas riegádan 1925–1967 ja 1973 dihto gielddain sámi ja dáža ássamiin Davvi-Norggas ja Davvi-Trøndelágas. Ulbmilin lea viežžat dieđuid váibmo- ja suotnadávddaid, borasdávdda, allergiaid, bákčasiid ja eará gillámušaid ja lihkohisvuođaid birra vai daid sáhtášii eastadit. Dasto lea ulbmilin diehtit olbmuid oaivila dearvvasvuođabálvalusa birra, sin eallinvuogi nugo biepmu ja borgguheami, eallindili ja gullevašvuođa birra. Geat háliidit searvat, leat mielde dutkanprošeavttas mas leat gažadanskovit ja dearvvasvuođaiskkadeapmi. Iskkadeami visot dieđut meannuduvvojit čiegusvuođas.

Dearvvasvuođa- ja eallindilleiskkadeapmi lea dárkilat válddahallon gihppagis mii čuovvu mielde. Jus eahpidat maidege, sáhtát gulahallat minguin tlf. 78 46 89 04 dahje e-poasta: helseus@fagmed.uit.no

Dán láhkai sáhtát searvat: (russe bajimučča gažadanskovis «mieđan searvamii» buohta)

A. Jus háliidat searvat dearvvasvuođaiskkadeapmái ja dutkanprošektii, de russet **A** čuoggá, deavddát gažadanskovi ja máhcahat dan midjiide čuovvu konfaluhtas. Maŋŋil oačču reivve mas čuožžu goas ja gosa boađát oktan ođđa gažadanskoviin.

B. Jus háliidat searvat dušše dutkanprošeavtta álgooasis almmá dearvvasvuođaiskkadeami haga, de russet **B** čuoggá, deavddát gažadanskovi ja máhcahat dan midjiide čuovvu konfaluhtas.

C. Eat rása jus russet **C** čuoggá ja máhcahat gažadanskovi midjiide. Rássan lea čálalaččat.

Datatilsynet lea addán sierralobi rádjat iskkadeami dieđuid ja dutkanprošeavtta lea rávven *Regional komite for medisinsk forskningsetikk i Nord-Norge.*

Dutkama dáfus lea hui miellagiddevaš ahte oažžut nu olu dieđuid go vejolaš. Don searvvat eaktodáhtolaččat ja sáhtát, maŋŋil go leat miehtan searvamii, geassádit vuođuškeahttá ja dutnje čuozakeahttá. Seamma guoská jus álggus juo ii hálit searvat. Dieđuid maid leat almmuhan sáhtát bivdit sihkkut.

Bohtosiid almmuhat mediain, ja čállo raporta dearvvasvuođa- ja eallindilleiskkadeamis go dat lea loahpahuvvon.

Sii geat čađahit olles dearvvasvuođa- ja eallindilleiskkadeami leat mielde vuorbádeamen 3 mátkeskeaŋkakoartta man árvu lea 10 000,– ru. guđesge. Doaivut ahte su. 15000 olbmo servet.

Dearvvuođaiguin

Anne Kirsten Anti
Sámi dearvvašvuođadutkama guovddáš, Kárášjohka

Eiliv Lund
Institutt for samfunnsmedisin
Romsa

Per G. Lund-Larsen
Nasjonalt folkehelseinstitutt
Oslo

INFORMERT SAMTYKKE

Jeg har lest informasjonen om undersøkelsen og samtykker i at (stryk det / de avsnitt du reserverer deg mot):

1. Jeg kan bli kontaktet med anbefaling om oppfølging, behandling eller for å forebygge sykdom.

2. Opplysningene mine kan brukes i medisinsk forskning til å kartlegge og finne årsaker til helse, sykdom og levekår. All bruk av opplysningene i eventuell framtidig medisinsk forskning vil bare bli brukt dersom Regional komité for medisinsk forskningsetikk og Datatilsynet ikke har noen innvendinger mot dette.

3. Etter godkjenning fra Datatilsynet kan opplysningene mine settes sammen med opplysninger om meg i andre registre for forskningsformål. I alle disse tilfellene blir navnet og personnummeret mitt fjernet. Det kan være registre om trygd, sykdom, inntekt, utdanning, yrke, og opplysninger fra de tidligere hjerte- og kar undersøkelsene. Eksempler på slike registre er Kreftregistret, Dødsårsaksregistret og folketellingene. Forsikringsselskaper vil ikke få tilgang til dataene.

4. Blodprøven min kan lagres og brukes til medisinsk forskning og genetiske analyser for å finne årsak til sykdom. All bruk av denne prøven vil bare skje i samsvar med godkjenning fra Datatilsynet og etter at Regional komite for medisinsk forskningsetikk i Nord- Norge har vurdert de etiske sidene ved gjennomføring av prosjektet.

....

sted og dato underskrift

DIEĐIHUVVON MIEHTAN

Lean lohkan dieđuid iskkadeami birra ja mieđan ahte (sihko dan / daid osiid maidda várašat):

1. Sáhttá muinna váldit oktavuođa go áigu rávvet čuovvoleami, dálkkodit dahje eastadit dávddaid.

2. Mu dieđuid sáhttá atnit medisiinnalaš dutkamii kártet ja gávdnat dearvvasvuođa, dávddaid ja eallindili árttaid. Visot dieđuid geavaheapmi soaiti boahttevaš medisiinnalaš dutkamii, adno dušše jus Regional komite for medisinsk forskningsetikk ja Datatilsynet eai vuosttal dan.

3. Datatilsynet dohkkeheami vuođul, sáhttá mu dieđuid čohkket mu dieđuiguin eará registariin dutkandoaimmaide. Visot dáid oktavuođain sihkko mu namma ja personnummar. Sáhttet leat oaju, dávddaid, sisaboađu, oahpu ja fidnu birra registarat ja dieđut ovddeš váibmo- ja suotnaiskkademiin. Dákkár registariid ovdamearkkat leat Kreftregistret, Dødsårsaksregistret ja olmmošlohkamat. Dáhkádusfitnodagat eai beasa dáid dieđuid oaidnit.

4. Mu varraiskkus sáhttá ráddjot ja adnot medisiinnalaš dutkamii ja genetalaš analysaide gávnnahit dávddaid árttaid. Dán iskosa juohke geavaheapmi geavvá dušše Datatilsynet dohkkeheami mielde ja maŋŋil go Regional komite for medisinsk forskningsetikk i Nord- Norge lea árvvoštallan prošeavtta čađaheami ehtalaš beliid.

....

báiki ja beaivi vuolláičála

IN-25132027-3 3000 11.2002 e.s.trykk-Oslo

Muittuhus – Påminnelse

Dál leat mannan čađa dearvvasvuođa- ja eallindilleiskkadeami boahtán vástádusaid guovlluin gos ásset sámit ja dážat.

Váldit dál duinna oktavuođa gullan dihtii ahte leatgo muitán sáddet gažadanskovi maid mis ožžot duvle.

Jus gieskat leat máhcahan skovi, de it galgga dán muittuhusas beroštit.

Ii leat vel menddo maŋŋit sáddet skovi. Bija veaháš áiggi vástidit gažaldagaid. Gii diđeš, soaittát leat nu lihkoš ahte vuoittát 10000,– ru. árvosaš mátkeskeaŋkakoartta. Jus dus ii šat leat gažadanskovvi, de sáhtát oažžut ođđa go jearat: Institutt for samfunnsmedisin, Universitetet i Tromsø, 9037 TROMSØ, tlf. 77 64 66 38, Bente A. Augdalas.

Vi har nå gått igjennom innkomne svar fra helse- og levekårsundersøkelsen fra områder med samisk og norsk bosetting.

Vi tar kontakt med deg nå for å høre om du har glemt å sende inn spørreskjemaet som du mottok fra oss for en stund siden.

Dersom du nylig har returnert skjemaet, ber vi deg se bort fra denne henvendelsen.

Det er fremdeles ikke for sent å sende inn skjemaet. Sett av litt tid til å besvare spørsmålene. Hvem vet, kanskje blir du den heldige vinner av et reisegavekort til en verdi av kr. 10000,–. Dersom du ikke lenger har spørreskjemaet, kan du få et nytt ved å kontakte: Institutt for samfunnsmedisin, Universitetet i Tromsø, 9037 TROMSØ, tlf. 77 64 66 38 v/ Bente A. Augdal.

Ustitlaš dearvvuođaiguin / Med vennlig hilsen

Institutt for samfunnsmedisin, Universitetet i Tromsø
Sámi dearvvašvuođadutkama guovddáš /Senter for samisk helseforskning
Nasjonalt folkehelseinstitutt

Porto betalt.

UNIVERSITETET I TROMSØ

folkehelseinstituttet

1. YOUR OWN HEALTH

What is your current state of health? *(Mark only one)*
☐ Poor ☐ Not so good ☐ Good ☐ Very good

Do you have or have you had the following?	Yes	No	Age first time
Asthma	☐	☐	
Chronic bronchitis, emphysema, COPD	☐	☐	
Diabetes	☐	☐	
Fibromyalgia/chronic pain syndrome	☐	☐	
Psychological problems for which you have sought help	☐	☐	
Myocardial infarction (heart attack)	☐	☐	
Angina pectoris (heart cramp)	☐	☐	
Cerebral stroke/brain haemorrhage	☐	☐	
Multiple sclerosis	☐	☐	
Ulcerative colitis	☐	☐	

	Yes	No
Do you get chest pain or discomfort when walking up hills or stairs, or walking fast on level ground?	☐	☐
Do you get such pain or discomfort even if you are resting?	☐	☐

2. MUSCULAR AND SKELETAL PAIN

	Yes	No
Have you *during the last year* **suffered from pain and/or stiffness in muscles or joints that has lasted for** *at least 3 months***?**	☐	☐

Have you ever had the following?	Yes	No	Age last time
A wrist/forearm fracture?	☐	☐	
A hip fracture?	☐	☐	

3. STOMACH AND INTESTINAL SYMPTOMS

	Yes	No
Have you experienced pyrosis/heartburn almost daily for at least a week?	☐	☐
Have you ever had stomach pains/aches lasting for at least 2 weeks?	☐	☐

If yes, where in the stomach are the pains situated? *(Mark only one)*
☐ Upper part ☐ Lower part ☐ The whole stomach

Normally, for how long are the stomach pains present? *(Mark one)*
For periods of weeks in length ☐
For periods of months in length ☐
Always ☐

	Yes	No
Do you often suffer from flatulence, a rumbling stomach or much wind?	☐	☐

What consistency is your stool usually? *(Tick one or more boxes)*
☐ Normal ☐ Loose ☐ Hard and lumpy
☐ Alternating hard and loose ☐ Smelly

	Yes	No
Do you sometimes have three stools per day or more?	☐	☐
Have you had stomach/intestinal problems after consuming milk?	☐	☐

Are there others in your family with similar stomach symptoms?
☐ Mother ☐ Father ☐ Siblings ☐ Child ☐ None

4. OTHER PAINS/PROBLEMS

Listed below are some symptoms or problems. Have you experienced any of these *during the last week* **(including today)?**
(Tick one box for each item)

	Not affected	Slightly affected	Affected quite a lot	Severely affected
Suddenly scared for no reason	☐	☐	☐	☐
Feeling fearful or anxious	☐	☐	☐	☐
Faintness or dizziness	☐	☐	☐	☐
Feeling tense or keyed up	☐	☐	☐	☐
Blaming yourself for things	☐	☐	☐	☐
Insomnia/sleeplessness	☐	☐	☐	☐
Feeling blue/melancholic	☐	☐	☐	☐
Feeling of worthlessness/of little value	☐	☐	☐	☐
Feeling everything is an effort	☐	☐	☐	☐
Feeling hopeless about future	☐	☐	☐	☐
Thinking of ending your life	☐	☐	☐	☐

5. ILLNESS IN THE FAMILY

	Yes	No	Don't know
Have one or more of your parents or siblings had a heart attack or angina (heart cramp)?	☐	☐	☐

Tick off relatives who have, or have ever had, any of the following conditions, and report the age of when they got the illnesses.
(If several siblings were affected by a condition, report the one who got the illness at the youngest age)

	Mother	Father	Sister	Brother	Child	None	Age first time
Myocardial infarction before age 60	☐	☐	☐	☐	☐	☐	
Myocardial infarction after age 60	☐	☐	☐	☐		☐	
Diabetes	☐	☐	☐	☐	☐	☐	
Cerebral stroke or brain hemorrhage	☐	☐	☐	☐	☐	☐	
Asthma	☐	☐	☐	☐	☐	☐	
Colon cancer	☐	☐	☐	☐	☐	☐	
Breast cancer	☐		☐		☐	☐	
Ovarian cancer	☐		☐		☐	☐	

	Brothers	Sisters
How many siblings do you have?		

6. USE OF MEDICATION

Medicines, in this context, means medicines bought at a pharmacy. Food supplements and vitamins are not included here.

Do you take any of the following?	Currently	Previously, but not now	Never used
Medications for high blood pressure	☐	☐	☐
Cholesterol reducing medication	☐	☐	☐
Insulin	☐	☐	☐
Tablets for diabetes	☐	☐	☐

How often during the last 4 weeks have you used the following medications? *(Tick one box for each line)*

	Not used for the last 4 weeks	Less frequently than every week	Every week, but not daily	Daily
Painkillers without prescription	☐	☐	☐	☐
Painkillers with prescription	☐	☐	☐	☐
Sleeping pills	☐	☐	☐	☐
Tranquilizers	☐	☐	☐	☐
Antidepressants	☐	☐	☐	☐
Other prescribed medicines	☐	☐	☐	☐

For those medicines you have ticked off in the last two questions, and you have taken *during the last 4 weeks*:

State the name of the medicines and your reason for taking/ having taken them (disease, symptom): *(Tick one box on each line)*

Brand name of medicine *(one name per line)*	Reason for use of medicine	For how long? Up to one year	For how long? One year or more
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐

If there is not enough space here, continue on a separate page and enclose it with the form.

7. FOOD AND BEVERAGES

How often do you usually eat the following foods?

	Rarely/ never	1–3 per month	1–3 per week	4–6 per week	1–2 per day	3 or more per day
Fruit	☐	☐	☐	☐	☐	☐
Berries	☐	☐	☐	☐	☐	☐
Cheese (all types)	☐	☐	☐	☐	☐	☐
Potatoes	☐	☐	☐	☐	☐	☐
Boiled vegetables	☐	☐	☐	☐	☐	☐
Fresh vegetables/salad	☐	☐	☐	☐	☐	☐

What type of fat do you usually use? *(Tick one box for each line)*

	Do not use	Butter	Hard margarine	Soft/light margarine	Oils	Other
On bread	☐	☐	☐	☐	☐	☐
For cooking	☐	☐	☐	☐	☐	☐

Do you use the following food supplements?

	Yes, daily	Sometimes	No
Cod liver oil or cod liver oil capsules	☐	☐	☐
Fish oil capsules (omega 3)	☐	☐	☐
Vitamins and/or mineral supplements	☐	☐	☐

How much do you normally drink of the following?

(Tick one box on each line)

	Rarely/ never	1–6 glasses per week	1 glass per day	2–3 glasses per day	4 glasses a day or more
Full-fat milk, full-fat curdled milk or yoghurt	☐	☐	☐	☐	☐
Semi-skimmed milk, semi-skimmed curdled milk or low-fat yoghurt	☐	☐	☐	☐	☐
Skimmed milk or skimmed curdled milk	☐	☐	☐	☐	☐
Semi-skimmed milk	☐	☐	☐	☐	☐
Fruitjuice	☐	☐	☐	☐	☐
Water	☐	☐	☐	☐	☐
Soft drinks/cola drinks with sugar	☐	☐	☐	☐	☐
Soft drinks/cola drinks without sugar	☐	☐	☐	☐	☐

How many cups of coffee and tea do you usually drink per day?

(Write 0 for the types you do not drink daily)

	Number of cups
Filtered coffee	☐☐
Boiled coffee (coarsely ground coffee for brewing)	☐☐
Other coffee	☐☐
Tea	☐☐

How often during the last year have you consumed alcohol?

(Low-alcohol beer and non-alcoholic beer are not included)

- Never consumed alcohol ☐
- Not during the last year ☐
- A few times during the last year ☐
- 1 time per month ☐
- 2–3 times per month ☐
- 1 time per week ☐
- 2–3 times per week ☐
- 4–7 times per week ☐

To those who have consumed alcohol during the past year:

When you drink alcohol, how many glasses or drinks do you normally drink? *Number of glasses or drinks* ☐☐

Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? *Number of times* ☐☐

Which of the following types of alcohol do you normally drink?

(Tick one or more boxes)

☐ Beer ☐ Wine ☐ Spirits

8. SMOKING AND SNUFF USE

How many hours a day do you normally spend in smoke-filled rooms? *(Number of whole hours)* ☐☐

Did any adults living at home with you while you were growing up smoke?	Yes	No
	☐	☐

Do you currently, or did you previously live with a daily smoker after your 20th birthday? ☐ Yes ☐ No

Are you currently, or were you previously a daily smoker? ☐ Yes, currently ☐ Yes, previously ☐ Never

If you are current a daily smoker, do you smoke the following?

	Yes	No
Cigarettes	☐	☐
Cigars/cigarillos/pipe	☐	☐
Rolling tobacco	☐	☐

If you previously smoked daily, how many years is it since you stopped smoking? ☐☐ *(Number of years)*

If you currently smoke, or have smoked before, how many cigarettes do/did you smoke per day? ☐☐ *(Number of cigarettes)*

If you currently smoke, or have smoked before, how old were you when you began smoking daily? ☐☐ *(Age in years)*

If you currently smoke, or have smoked before, how many years in all have you smoked daily? ☐☐ *(Number of years)*

Do you take or have you been taking snuff daily? ☐ Yes, currently ☐ Yes, previously ☐ Never

If you have been taking snuff, for how many years in total have you been taking snuff? ☐☐ *(Number of years)*

9. EXERCISE AND PHYSICAL ACTIVITY

How has your physical activity *in leisure time* **been** *during this last year***?** *(Think of your weekly average for the year. Time spent going to work counts as leisure time. Answer both questions)*

	Hours per week			
	None	Less than 1 hour	1–2 hours	3 hours or more
Light activity (not sweating or out of breath)	☐	☐	☐	☐
Hard physical activity (sweating/out of breath)	☐	☐	☐	☐

Describe your exercise and physical exertion *in leisure time***. If your activity varies much, for example between summer and winter, then give an average. The question refers** *only to the last twelve months***.** *(Tick the box that is most appropriate)*

Reading, watching TV, or other sedentary activity ☐

Walking, cycling, or other forms of exercise *at least 4 hours a week* *(This should include walking or cycling to work, Sunday stroll/walk, etc.)* ☐

Participation in recreational sports, heavy gardening, etc. *(Note: duration of activity at least 4 hours a week)* ☐

Participation in hard training or sports competitions regularly and *several times a week* ☐

10. EDUCATION AND WORK

How many years of schooling/education have you completed? *(Count all years you have attended school or been studying)* ☐☐ *(Number of years)*

How content are you with your job?
☐ Very content ☐ Content ☐ Discontent ☐ Very discontent

Do you believe that you are in danger of losing your current work or income within the next 2 years? ☐ Yes ☐ No

Do you receive any of the following benefits?

	Yes	No
Sickness benefit/Sick pay	☐	☐
Rehabilitation benefit	☐	☐
Social welfare benefits	☐	☐
Transition benefit for single parents	☐	☐

11. THE REST OF THE QUESTIONNAIRE IS TO BE ANSWERED BY WOMEN ONLY

How old were you when you started menstruating? ☐☐ (Age in years)

If you no longer menstruate, how old were you when you stopped menstruating? ☐☐ (Age in years)

Are you pregnant at the moment?
☐ Yes ☐ No ☐ Uncertain ☐ Past fertile age

How many children have you given birth to? ☐☐ *(Number of children)*

If you have given birth, enter what year each child was born and how many months you did breastfeed after the birth?
(If you didn't breastfeed, write 0)

Children	Year of birth	Breastfed number of months
1st child	☐☐☐☐	☐☐
2nd child	☐☐☐☐	☐☐
3rd child	☐☐☐☐	☐☐
4th child	☐☐☐☐	☐☐
5th child	☐☐☐☐	☐☐

(If you have had more children, use an extra sheet of paper)

Do you use or have you ever used the following? *(Tick one box on each line)*

	Currently	Previously, but not now	Never used
Contraceptive pills/minipill/ contraceptive injection	☐	☐	☐
Hormonal intrauterine device	☐	☐	☐
Estrogen (tablets or patches)	☐	☐	☐
Estrogen (cream or suppositories)	☐	☐	☐

If you use/have used prescribed estrogen, for how many years have you used it? ☐☐ *(Number of years)*

If you use contraceptive pills, a hormonal intrauterine device, or estrogen, what brand do you currently use? *(Specify)*

USE OF HEALTH SERVICES

How many times *during the past year* **have you personally used the following?** *(Tick one box on each line)*

	None	1–3 times	4+
GP (general practitioner)	☐	☐	☐
Medical specialist	☐	☐	☐
Emergency GP	☐	☐	☐
Admission to a hospital	☐	☐	☐
Home nursing care	☐	☐	☐

	None	1–3 times	4+
Home aid, organized by the municipality	☐	☐	☐
Physiotherapist	☐	☐	☐
Chiropractor	☐	☐	☐
Dentist	☐	☐	☐
Alternative medical practitioner	☐	☐	☐

How many doctors have you seen in the last 12 months? ☐☐ *(Number)*

Have you been given a regular GP, whose name you know? ☐ Yes ☐ No

When you are being examined, which language do you and your doctor communicate in? *(Tick one or more boxes)*

☐ Norwegian ☐ Sami ☐ Use an interpreter
☐ Other language

Do you and your doctor sometimes misunderstand each other due to linguistic problems?

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Not sure

If an interpreter is needed, is your doctor good enough to request one?

☐ Yes, always ☐ Yes, most of the time ☐ No, not always
☐ No, never ☐ Don't like to use interpreter

How satisfied/dissatisfied are you with the following aspects of the municipal health service in your municipality?
(Tick one box on each line)

	Very satisfied	Satisfied	Dis-satisfied	Don't know
The distance to your doctor	☐	☐	☐	☐
Your doctor's availability by telephone	☐	☐	☐	☐
How soon you can get an appointment with your doctor	☐	☐	☐	☐
How long you are allowed with your doctor	☐	☐	☐	☐
The chance you get to describe your pains and problems	☐	☐	☐	☐
Your doctor's understanding of your cultural background	☐	☐	☐	☐
The information your doctor gives about your health and the examination and treatment you get	☐	☐	☐	☐
Your doctor's language skills (Sami or Norwegian)	☐	☐	☐	☐
The local health services in your municipality as a whole	☐	☐	☐	☐
On the whole, how satisfied/ dissatisfied are you with the local health services in your municipality	☐	☐	☐	☐

How long is it since you last went to see a doctor? *(Report whole numbers)* Years ☐☐ Months ☐☐

If you have ever used an alternative practitioner, which did you use? *(Tick one or more boxes)*

A traditional healer *(guvllar, reader, "blåser", laying on of hands)* ☐
A (modern) healer ☐
An acupuncture practitioner ☐
A zone therapist, homeopath, kinesiologist etc. ☐

How long is it since you last used an alternative practitioner? *(Report whole numbers)* Years ☐☐ Months ☐☐

Suppose you need help/assistance from the local health- and social services *(home nursing care, home assistance services, social services, physiotherapy, etc.)***:**

	Yes	No	Uncertain
Do you know where to go (who to contact)?	☐	☐	☐
Do you feel confident you will receive help if you need it?	☐	☐	☐
If you already receive help from local health and social services, are you satisfied with the help they offer?	☐	☐	☐

INJURIES/ACCIDENTS

Have you been in accidents that resulted in treatment by a doctor and/or hospital admission?

	Yes	No	Number of times
Doctor	☐	☐	☐☐
Hospital admission	☐	☐	☐☐

If yes, what kind of accidents have you been treated for?

	At work	At home	During leisure time	No
Car accident	☐	☐	☐	☐
Motor cycle accident	☐	☐	☐	☐
Snowmobile accident	☐	☐	☐	☐
Quadbike accident	☐	☐	☐	☐
Tractor accident	☐	☐	☐	☐
Accident caused by falling	☐	☐	☐	☐
Cutting injury	☐	☐	☐	☐
Other	☐	☐	☐	☐

Has/have the accident(s) led to reduced ability to work?

☐ Completely ☐ Partly ☐ Not at all

FAMILY AND LINGUISTIC BACKGROUND

People of different ethnic backgrounds live in Northern Norway. That is, they speak different languages and have different cultures. Examples of ethnic background, or ethnic group, are Norwegian, Sami and Kven.

Which language did/do you, your parents, and your grand parents speak at home? *(Tick one or more boxes)*

	Norwegian	Sami	Kven	Other, specify
Mother's father	☐	☐	☐	☐
Mother's mother	☐	☐	☐	☐
Father's father	☐	☐	☐	☐
Father's mother	☐	☐	☐	☐

	Norwegian	Sami	Kven	Other, specify
Father.....	☐	☐	☐	☐
Mother.....	☐	☐	☐	☐
Myself.....	☐	☐	☐	☐

What are your, your father's, and your mother's ethnic backgrounds? *(Tick one or more boxes)*

	Norwegian	Sami	Kven	Other, specify
My ethnic background ...	☐	☐	☐	☐
My father's ethnic background ...	☐	☐	☐	☐
My mother's ethnic background ...	☐	☐	☐	☐

What do you consider yourself to be? *(Tick one or more boxes)*

☐ Norwegian ☐ Sami ☐ Kven
☐ Other, specify:

EMPLOYMENT/ECONOMY

What type of work/livelihood do you have? *(Tick one or more boxes)*

☐ Full time job with a fixed salary
☐ Part time job with a fixed salary
☐ Seasonal work ☐ Self-employed
☐ Unemployed ☐ Homemaker (fulltime housework)
☐ Old-age pension ☐ Disability pension
☐ Other, specify:

Would you be willing to move if you were offered work somewhere else?

☐ Yes ☐ No ☐ Parts of the year ☐ Uncertain

If you are out of work, for how long have you been seeking employment? *(Report whole numbers)*

Years ☐☐ Months ☐☐

If you are self-employed, what work do you do?

(Tick one or more boxes)

☐ Reindeer herding ☐ Fishing ☐ Farming
☐ Forestry ☐ Business
☐ Other, specify:

How many persons are living in your household?..... *(Number of persons)* ☐☐

What is your family's/household's gross income each year?

☐ Less than 150 000 NOK ☐ 150 000–300 000 NOK
☐ 301 000–450 000 NOK ☐ 451 000–600 000 NOK
☐ 601 000–750 000 NOK ☐ More than 750 000 NOK

How often do you participate in gambling (national lottery, football betting, gambling machines, etc.)?

☐ Never/rarely ☐ 1–3 times a month ☐ Once a week
☐ 2–6 times a week ☐ Daily

For how much money do you gamble per week on average?

☐ Less than 100 NOK ☐ 100–500 NOK
☐ 501–1000 NOK ☐ More than 1000 NOK

BULLYING

By bullying we mean when one or more persons *systematically and over time* **say or do bad things against you, and you have difficulty in defending yourself against them.**

Have you experienced bullying?

☐ Yes, in the last 12 months ☐ Yes, previously ☐ No

If you have been bullied, what kind of bullying did you experience?

(Tick one or more boxes)

☐ Talking behind your back/gossip ☐ Being ignored
☐ Discriminating remarks
☐ Other, specify:

Can you state where the bullying takes/took place?

☐ At school ☐ At boarding school/dormitory
☐ At work ☐ In local community
☐ Other, specify:

Appendix B

The SAMINOR 2 Clinical Survey

- Pamphlet
- Information brochure
- Invitation letter (example from the municipality of Evenes)
- Informed written consent form
- Questionnaires (english translation):
    - 40–69 years
    - 70–79 years

All listed items and their Norwegian versions are available at www.saminor.no.

Foto: Bjørn-Kåre Iversen, helsefak. uit.no

VI KOMMER NÅ TIL DIN KOMMUNE

Du vil i løpet av noen uker motta en forespørsel i posten fra Universitetet i Tromsø om å delta i en helseundersøkelse. Resultatene vil kunne bidra til å fremme folkehelse og forbedre velferdstilbud i nord.

HVORFOR SPØR VI DEG?

Alle mellom 40 – 79 år i din kommune vil bli invitert. Hver deltaker er like viktig, enten du er ung eller gammel, kvinne eller mann, frisk eller syk. Godt oppmøte er viktig for gode forskningsresultater.

UNDERSØKELSER AV DEG

- Høyde og vekt
- Liv- og hoftevidde
- Blodtrykk og puls
- Blodprøve

Vi ber deg også om å fylle ut et spørreskjema.

TILBAKEMELDING PÅ RESULTATER

Dersom du ønsker det, vil du ved undersøkelsen få dine egne resultater på høyde, vekt, liv- og hoftemål, blodtrykk, puls, blodprosent og langtidsblodsukker.

DIN SIKKERHET

Det er frivillig å delta.

Din sikkerhet er høyt ivaretatt. All behandling av helseopplysninger eller prøvemateriale skjer i tråd med helseforskningsloven. Alle opplysninger og prøver anonymiseres og blir da behandlet uten navn og fødselsnummer eller andre direkte gjenkjennbare opplysninger.

Undersøkelsen er godkjent av Datatilsynet og REK Nord – Regional komite for medisinsk og helsefaglig forskningsetikk.

Foto: Bjørn Erik Rygg Lunde/ Nordlandssykehuset

VI VIL HA ØKT KUNNSKAP OM

- Kosthold
- Diabetes
- Hjerte-karsykdommer
- Miljøgifter
- Tannhelse
- Søvn

REISEGAVEKORT

Alle som deltar vil være med i trekning av to reisegavekort verdt kr 10 000,- hver. I tillegg vil det trekkes to ekstra reisegavekort i den kommunen som har best deltagelse. Ut over dette gis det ingen økonomisk kompensasjon for deltakelse i studien.

VI KOMMER NÅ TIL DIN KOMMUNE

Du vi i løpet av noen uker motta et brev om sted og tid for undersøkelsen. Ved å delta, bidrar du til spennende og samfunnsnyttig forskning på helse og livsstil i nord.

DERSOM DU HAR SPØRSMÅL

ta gjerne kontakt med oss på telefon eller via e-post.

Senter for samisk helseforskning
Institutt for samfunnsmedisin
Universitetet i Tromsø
9037 Tromsø
http://site.uit.no/helseoglivsstil/
E-post: saminor@ism.uit.no
Telefon: 404 90 467

SAMINOR 2

UNIVERSITETET I TROMSØ UIT
DET HELSEVITENSKAPELIGE FAKULTET
uit.no/helsefak

GRAFISK FORM: BJØRN-KÅRE IVERSEN, FORMIDLINGSTJENESTEN, UIT.NO/HELSEFAK

UNIVERSITETET I TROMSØ UIT
DET HELSEVITENSKAPELIGE FAKULTET

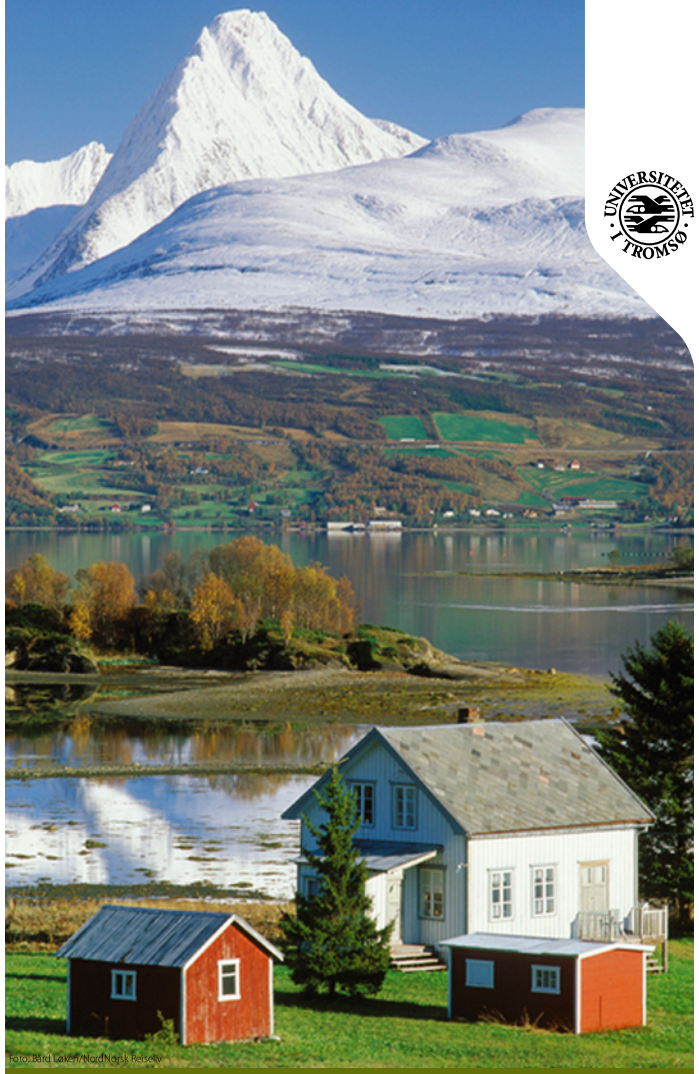


Foto: Bård Løken/NordNorsk Reiseliv

Helse- og livsstils-undersøkelse

BAKGRUNN OG HENSIKT

Dette er et spørsmål til deg om å delta i et forskningsprosjekt for å få mer kunnskap om helse, sykdom og levekår i områder med samisk og norsk bosetting. Du som deltar i denne undersøkelsen får sjekket om du har bestemte såkalte livsstilssykdommer eller om det er fare for at du kan få dem.

Du er invitert til å være med i denne studien fordi du er i alderen 40-79 år og tilhører en av de utvalgte kommuner. Studien utføres av Senter for samisk helseforskning, Institutt for samfunnsmedisin ved Universitetet i Tromsø.

HVA INNEBÆRER STUDIEN?

Du inviteres til å svare på vedlagte spørreskjema og ta det med når du møter opp på anvist forskningsstasjon i din kommune. Her vil det gjøres målinger av blodtrykk, puls, høyde, vekt og liv-hoftevidde, og det blir også tatt blodprøve.

Blodprøvene kan senere bli analysert for næringsstoffer, miljøgifter, fettstoffer og markører som kan knyttes til livsstilssykdommer eller tilstander som for eksempel diabetes (sukkersyke), hjerte-karsykdommer og søvnforstyrrelser. Genetiske analyser av blodet for å finne mulige årsaker til nevnte livsstilssykdommer/tilstander kan også bli aktuelt.

All bruk av blodprøvene krever godkjenning av Regional komité for medisinsk og helsefaglig forskningsetikk – REK nord.

Vedlagt følger informasjon om tid og sted for undersøkelsen. Hvis den foreslåtte tiden ikke passer, kan du møte opp uten å melde fra på forhånd.

MULIGE FORDELER OG ULEMPER

Det forventes ingen risiko forbundet med deltagelse i denne undersøkelsen. Blodprøven blir tatt ved stikk i blodåre i underarmen. Selve undersøkelsen vil ta om lag en halv time. Du vil på stedet få tilbud om resultater på egne målinger som blodtrykk, puls, høyde, vekt og liv-hoftevidde, blodprosent og HbA1c (gjennomsnittlig blodsukker de siste 6-8 ukene). Du kan reservere deg mot å få vite resultatene av prøvene dine. Men hvis et av disse prøveresultatene er slik at det er nødvendig med rask legebehandling, vil du uansett umiddelbart få tilbakemelding. Deltagelse i denne studien erstatter ingen legeundersøkelse. Dersom du har mistanke om noe galt med din helse, må du derfor i tillegg oppsøke din egen fastlege.

Foto: Bjørn-Kåre Iversen, helsefak. uit.no

HVA SKJER MED PRØVENE OG INFORMASJONEN OM DEG?

Prøvene tatt av deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Videre behandling av helseopplysninger eller prøvemateriale skjer i tråd med helseforskningsloven og eventuell annen aktuell lovgivning. Alle opplysninger og prøver vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Det betyr at opplysningene er avidentifisert. Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg. Det vil heller ikke være mulig å identifisere deg i resultatene av studien når disse publiseres. Du kan seinere bli kontaktet med forespørsel om du vil svare på tilleggsspørreskjema.

Opplysninger som registreres om deg er basert på spørreskjemaopplysninger, mål fra helseundersøkelsen og blodprøveanalyser. Etter godkjenning fra Datatilsynet og/eller REK kan opplysningene dine settes sammen med opplysninger om deg i andre registre for forskningsformål. Dette kan være registre om trygd, sykdom, inntekt, utdanning, yrke og opplysninger fra andre helseundersøkelser som du har deltatt i. Aktuelle registre er Kreftregisteret, Dødsårsaksregisteret, Folkeregisteret, Reseptregisteret, Medisinsk fødselsregister, Hjerte- og karregisteret og andre nasjonale registre over sykdommer som det forskes på i denne undersøkelsen samt registre i Statistisk sentralbyrå og folketellinger. I alle disse tilfellene blir navnet og personnummeret fjernet. Forsikringsselskaper eller andre kommersielle institusjoner vil ikke få tilgang til dataene.

Prosjektslutt er satt til 31. desember 2067. Etter dette anonymiseres alle dataene.

BIOBANK

Blodprøvene vil bli lagret i en såkalt forskningsbiobank ved Universitetet i Tromsø eller eventuelt ved et annet nasjonalt lager for biobank med høyeste grad av sikkerhet i forhold til prøvens kvalitet og personvern som er godkjent av aktuelle instanser. Hvis du sier ja til å delta i studien, gir du også samtykke til at blodprøvene inngår i denne biobanken. Universitetet i Tromsø er ansvarshavende for forskningsbiobanken.

BEHANDLINGSANSVARLIG

Universitetet i Tromsø ved administrerende direktør er databehandlingsansvarlig.

RETT TIL INNSYN OG SLETTING AV OPPLYSNINGER OG PRØVER

Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

KOMPENSASJON

Det gis ingen økonomisk kompensasjon for deltakelse i studien bortsett fra at alle som deltar vil være med i trekning av to reisegavekort hver verdt kr 10 000,-.
I tillegg vil det trekkes to ekstra reisegavekort i den kommunen som har best deltagelse.

ØKONOMI

Studien og biobanken er finansiert gjennom forskningsmidler fra det Regionale forskningsfond Nord-Norge, de tre nordligste fylkeskommunene, Helse Nord, Sametinget, Universitetet i Tromsø og Helse og omsorgsdepartementet. Ingen av disse instansene har interessekonflikter i undersøkelsen.

FORSIKRING

Deltakerne er dekket gjennom pasientskadeerstatningsloven.

HELSE OG LIVSSTIL

Kosthold – diabetes – hjerte-karsykdommer – miljøgifter – tannhelse – søvn

INFORMASJON OM UTFALLET AV STUDIEN

Resultater av undersøkelsen vil publiseres i internasjonale og nasjonale vitenskapelige tidsskrifter i tillegg til ulike populærvitenskapelige kanaler og media.

FRIVILLIG DELTAKELSE

Det er frivillig å delta i studien. Dersom du ønsker å delta, møter du opp til angitt sted og tidspunkt. Her vil du bli bedt om å signere et samtykke på deltakelse. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien.

Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte oss på vår prosjektelefon: **404 90 467** eller på e-post: saminor@ism.uit.no

Du finner ytterligere informasjon om studien på vår nettside
http://site.uit.no/helseoglivsstil/

VELKOMMEN TIL UNDERSØKELSEN

Magritt Brustad
Prosjektleder
Professor

Ann Ragnhild Broderstad
Forsker
Overlege Dr. med.

SAMINOR 2

UNIVERSITETET I TROMSØ UIT
DET HELSEVITENSKAPELIGE FAKULTET
uit.no/helsefak

GRAFISK FORM: BJØRN-KÅRE IVERSEN, FORMIDLINGSTJENESTEN, UIT HSV/HELSEFAK

UNIVERSITETET I TROMSØ UIT
DET HELSEVITENSKAPELIGE FAKULTET

FORESPØRSEL OM DELTAKELSE I HELSE- OG LIVSSTILS-UNDERSØKELSE

Foto: Bård Løken/NordNorsk Reiseliv

UNIVERSITETET I TROMSØ UiT

Helse og livsstil

Kosthold – diabetes – hjerte-karsykdommer – miljøgifter – tannhelse – søvn

Forespørsel om deltakelse i forskingsprosjekt

Vi spør deg om å delta i en helse- og livsstilsundersøkelse som Universitetet i Tromsø nå gjennomfører. Hele befolkningen i alderen 40-79 år i utvalgte distriktskommuner i Nord-Norge får tilbud om undersøkelsen. Skånland og Evenes kommune er først ut.

Vi inviterer deg til å møte opp på denne undersøkelsen som vil finne sted i tidsrommet **17. september til 25. oktober 2012** ved:

Helse- og sosialsenteret på Evenskjer, inngang v/NAV.

For å avvikle undersøkelsen raskest mulig, setter vi opp et visst antall personer i timen.

Du har fått tildelt frammøtetid:

Dato:
Tid:

Om du ikke kan møte opp til avtalt time, er du velkommen til å møte opp når som helst i åpningstiden for drop-in som skissert under. Merk at åpningsdagen åpner vi klokken **12:30**, og vi har lunsj i tidsrommet **12:00 -12:30**.

	Mandag	Tirsdag	Onsdag	Torsdag	Fredag	Lørdag 29.sept og 20.okt
Uke 38, 40, 42	09:30-15:45	09:30-19:30	09:30-15:45	09:30-19:30	09:30-15:15	10:15-14:30
Uke 39, 41, 43	09:30-19:30	09:30-15:45	09:30-19:30	09:30-15:45	09:30-15:15	

Senter for samisk helseforskning / Sámi dearvvašvuođadutkama guovddáš
Det helsevitenskapelige fakultet, Institutt for samfunnsmedisin,
Universitetet i Tromsø, NO-9037 Tromsø
http://saminor.uit.no • E-post: saminor@ism.uit.no
Sentralbord: 77 64 40 00 • Faks: 77 64 48 31• Mobil: 404 90 467

Hva undersøkes?

På stedet undersøker vi ditt blodtrykk, din puls, høyde, vekt og liv-hoftevidde, samt at vi tar en blodprøve av deg.

Ta med ditt utfylte spørreskjema til undersøkelsen

Vi ber deg om å svare på vedlagte spørreskjema og ta dette med for levering på undersøkelsesdagen. Her kan du også få hjelp til utfylling av skjemaet om du trenger det. Du kan la være å svare på enkelte spørsmål. Spørreskjemaet omhandler i hovedsak spørsmål vedrørende hjerte-karsykdommer, diabetes og kosthold. For å kunne beregne næringsinntak (kalorier, næringsstoffer o.l.) er det nødvendig med en grundig kartlegging av hva du normalt spiser.

Forberedelser til undersøkelsen

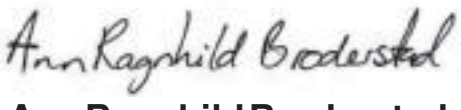
Ha gjerne på et kortermet plagg innerst som ikke strammer da det letter blodtrykksmålingen. Vekt og liv-hoftevidde måles også med lett påkledning og vekt uten sko. Ingen andre forberedelser som fasting o.l. er nødvendig.

Det er frivillig å delta. For mer informasjon om undersøkelsen, vennligst se vedlagte informasjonsfolder. Vi viser også til vår nettside http://site.uit.no/helseoglivsstil/

Har du spørsmål om undersøkelsen, kan du ringe Institutt for samfunnsmedisin ved Universitetet i Tromsø på telefon 77 64 48 36 eller mobil 404 90 467.

Med vennlig hilsen

Magritt Brustad
Prosjektleder
Professor



Ann Ragnhild Broderstad
Forsker
Overlege Dr. med.

Senter for samisk helseforskning / Sámi dearvvašvuođadutkama guovddáš
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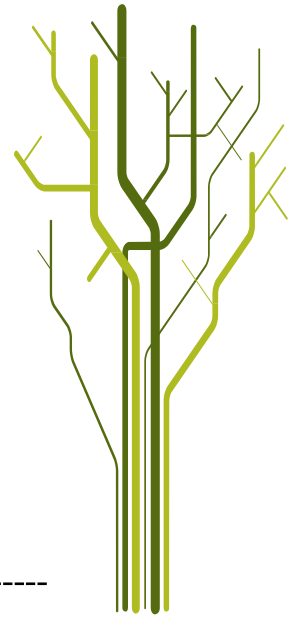
UNIVERSITETET I TROMSØ UiT

Helse- og livsstilsundersøkelse



Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

(Signert av prosjektdeltaker, dato)

☐ **Jeg ønsker ikke tilbakemelding på utvalgte prøvesvar**

Senter for samisk helseforskning / Sámi dearvvašvuođadutkama guovddáš
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Survey on health and lifestyle

We kindly request that you fill in the form as thoroughly and accurately as possible, and bring it with you to your scheduled physical examination. The form will be optically scanned. Please use blue or black ink. Use capital letters. Do not use decimals; for example, "0.5" should be rounded off to "1".

1. **In what year were you born?** ..... Year

2. **What is your gender?** ..... Female ☐ Male ☐

3. **What is your marital status?**

☐ Married ☐ Cohabiting ☐ Divorced
☐ Unmarried ☐ Widow/widower

4. **How many people live in your household?** ..... Number of persons

5. **How many years of education have you completed?** ..... Number of years
(Include all years you have attended school or studied)

6. **What is your family's/household's gross income per year?**

☐ Less than NOK 150,000 ☐ NOK 150,000–300,000
☐ NOK 301,000–450,000 ☐ NOK 451,000–600,000
☐ NOK 601,000–750,000 ☐ NOK 751,000–900,000
☐ More than NOK 900,000

Cardiovascular disease

7. **Are you taking medication for high blood pressure?** ..... Yes, currently ☐ Previously, but not now ☐ Never used ☐

8. **If you are taking high blood pressure medication, or have taken high blood pressure medication in the past, at what age did you start taking this type of medicine?** Age

9. **Have you ever had one or more heart attacks?**

☐ No, never ☐ One heart attack ☐ Two heart attacks ☐ Three or more heart attacks

10. **If yes, at what age did you have your first heart attack?** ..... Age

11. **Do you suffer from angina pectoris (heart cramp)?** ..... ☐ Yes ☐ No

12. **If yes, at what age did your symptoms of angina pectoris first emerge?** ..... Age

13. **If yes, how often have you experienced such pain in the past month?**

Rarely ☐ Once a week ☐ 2-3 times a week ☐ 4-6 times a week ☐ 7 times a week or more ☐

14. **Have you had heart (bypass) surgery?** ☐ Yes ☐ No

15. **Have you had your arteries unblocked/ had stent(s) placed** ☐ Yes ☐ No

16. **Has your doctor told you that you have atrial fibrillation?** ☐ Yes ☐ No

Physical activity

17. **We will now ask you to state your physical activity at the ages of 14, 30 and at your current age, on a scale from very low to very high.** The scale below runs from 1 to 10. Physical activity includes both housework and activity at work, as well as exercise and other physical activities such as walking/hiking, etc. Mark the number that best matches your level of activity:

	Very low									Very high
Age	1	2	3	4	5	6	7	8	9	10
14 years	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
30 years	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Current age	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Diabetes

18. **Have you ever been diagnosed with diabetes (elevated blood sugar levels)?** ..... ☐ Yes ☐ No
If no, please skip to question 28 regarding eating habits

19. **If yes, please specify your diabetes diagnosis:**
(chose one or more options)

Gestational diabetes ..... ☐
Type 1 diabetes ..... ☐
Type 2 diabetes ..... ☐

20. **How was your diabetes discovered?**

I consulted my doctor/physician because of symptoms ..... ☐ Yes ☐ No

It was discovered without the appearance of symptoms (medical certificate, work-related medical examination, pregnancy health examination, medical consultation for illness other than diabetes, etc.) ☐ Yes ☐ No

21. **At what age was your diabetes discovered/ diagnosed?** ..... Age

INSULIN

22. **Are you taking insulin for your diabetes?** ..... Yes, currently ☐ Previously, but not now ☐ Never used ☐

If you are taking (or have taken) insulin:

23. **At what age did you start your insulin treatment?** ..... Age ☐☐

24. **How many times per day do you/did you usually take insulin?** ..... ☐☐ times

25. **In total, how many units of insulin do you/did you take on an average day?** ..... ☐☐ units (E)

ORAL MEDICATION

26. **Are you taking oral medication for diabetes?** ..... Yes, currently ☐ Previously, but not now ☐ Never used ☐

If you are taking or have taken oral medication:

27. **At what age did you start taking oral medication for diabetes?** ..... Age ☐☐

Eating habits

Mark the square below the number that best describes your eating habits, taking the past four weeks into consideration:

28. **How satisfied are you with your eating habits?** (Choose only one option)

	1	2	3	4	5	6	7	
Very dissatisfied	☐	☐	☐	☐	☐	☐	☐	Very satisfied

29. **Have you resorted to 'comfort food' or excessive eating due to sadness or feelings of discontentment?** (Choose only one option)

	1	2	3	4	5	6	7	
Never	☐	☐	☐	☐	☐	☐	☐	Every day

30. **Have you ever felt guilty about eating/food?** (Choose only one option)

	1	2	3	4	5	6	7	
Never	☐	☐	☐	☐	☐	☐	☐	Every day

31. **Have you felt that strict diets (or other food-related rituals) are necessary for controlling the amount of food that you eat?** (Choose only one option)

	1	2	3	4	5	6	7	
Never	☐	☐	☐	☐	☐	☐	☐	Every day

32. **Have you felt that you are too fat?** (Choose only one option)

	1	2	3	4	5	6	7	
Never	☐	☐	☐	☐	☐	☐	☐	Every day

Smoking habits

33. **Have you ever smoked daily?** ..... ☐ Yes ☐ No

If you have **never smoked daily**, please skip to question 38.

34. **Are you currently a daily smoker?** ..... ☐ Yes ☐ No

35. **If you are no longer a daily smoker, at what age did you quit?** ..... Age ☐☐

36. **In total, for how many years have you smoked daily?** ..... Years ☐☐

37. **Considering all the years in which you smoked regularly (daily), how many cigarettes/rolling tobacco did you smoke per day, on average?** ..... ☐☐

38. **Do you live with someone who smokes?** ..... ☐ Yes ☐ No

Chronic pain

39. **Are you experiencing pain that has lasted three months or longer?** ..... ☐ Yes ☐ No

40. **If yes, please indicate the intensity of your pain in the past week:** (Choose only one option)

No pain										Most severe pain
0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

41. **Please indicate where your pain is most severe:** (Choose only one option)

☐ Neck ☐ Lower back ☐ Other

Diet

We would like to know more about your **usual** diet. For each of the following foods and beverages, please indicate **how often (the number of times)** you have consumed the food item in question **on average in the past year**, and the amount you usually eat/drink each time.

BEVERAGES

42. **How many glasses of milk do you normally drink?** (Choose only one option for each variety)

	Never/ rarely	1–4 per week	5–6 per week	1 per day	2–3 per day	4+ per day
Whole/full fat milk ("*Hel*") *(regular, sour/fermented)*	☐	☐	☐	☐	☐	☐
Semi-skimmed milk ("*Lett*") *(regular/sour/fermented)*	☐	☐	☐	☐	☐	☐
Low fat milk ("*Extra lett*")	☐	☐	☐	☐	☐	☐
Skimmed *(regular, sour/fermented)*	☐	☐	☐	☐	☐	☐

43. **How many cups of coffee/tea do you normally drink?** Choose only one option for each variety

	Never/ rarely	1–6 per week	1 per day	2–3 per day	4–5 per day	6–7 per day	8+ per day
Unfiltered or plunger/ steeped coffee	☐	☐	☐	☐	☐	☐	☐
Filtered coffee	☐	☐	☐	☐	☐	☐	☐
Espresso	☐	☐	☐	☐	☐	☐	☐
Latte	☐	☐	☐	☐	☐	☐	☐
Instant coffee	☐	☐	☐	☐	☐	☐	☐
Black tea	☐	☐	☐	☐	☐	☐	☐
Green tea	☐	☐	☐	☐	☐	☐	☐

44. **Do you take any of the following in your coffee?**

Sugar *(not including artificial sweeteners)* ..... ☐ Yes ☐ No

Milk or cream ..... ☐ Yes ☐ No

45. **Do you take any of the following in your tea?**

Sugar *(not including artificial sweeteners)* ..... ☐ Yes ☐ No

Milk or cream ..... ☐ Yes ☐ No

46. How many glasses of water do you drink on average?
(Choose only one option for each line)

	Never/ rarely	1–6 per week	1 per day	2–3 per day	4–5 per day	6–7 per day	8+ per day
Tap water	☐	☐	☐	☐	☐	☐	☐
Bottled water	☐	☐	☐	☐	☐	☐	☐

47. How many glasses of juice, squash/lemonade, and carbonated/soft drinks do you drink on a typical day?

(Choose only one option for each line)	Never/ rarely	1–3 per week	4–6 per week	1 per day	2–3 per day	4+ per day
Orange juice	☐	☐	☐	☐	☐	☐
Other juice	☐	☐	☐	☐	☐	☐
Squash/lemonade/soft drink containing sugar	☐	☐	☐	☐	☐	☐
Squash/lemonade/soft drink without sugar	☐	☐	☐	☐	☐	☐

YOGHURT/CEREAL

48. How often do you eat yoghurt (1 tub)? (Choose only one option)

☐ Never/rarely ☐ 1-3 per week
☐ 4-6 per week ☐ 1 or more per day

49. How often do you eat (breakfast) cereal, oatmeal or muesli?
(Choose only one option)

☐ Never/rarely ☐ 1-3 per week
☐ 4-6 per week ☐ 1 or more per day

BREAD/SANDWICHES

50. How many slices of bread (or equivalent; bread rolls, buns, crispbread, rye bread) do you normally eat? (1/2 bread roll = 1 slice of bread) (Choose only one option for each variety listed)

	Never/ rarely	1–4 per week	5–7 per week	2–3 per day	4–5 per day	6+ per day
Whole grain bread	☐	☐	☐	☐	☐	☐
Semi-whole grain bread	☐	☐	☐	☐	☐	☐
White bread (baguette)	☐	☐	☐	☐	☐	☐
Crispbread, etc.	☐	☐	☐	☐	☐	☐

The following questions are in regards to various sandwich spreads/ fillings. For each of the following sandwich spreads, we would like to know how many slices of bread/crispbread you normally eat with these spreads/fillings. If you regularly eat the given sandwich spreads with items other than bread (i.e., waffles, breakfast cereal, porridge) please include such use when answering the questions.

51. Please indicate how many slices of bread/crispbread you normally eat with the following sandwich spreads?

(Choose only one option for each line)	Never/ rarely	1–3 per week	4–6 per week	1 per day	2–3 per day	4+ per day
Jam	☐	☐	☐	☐	☐	☐
Brown (charamelised) whey cheese *(full fat)*	☐	☐	☐	☐	☐	☐
Brown cheese *(reduced fat)*	☐	☐	☐	☐	☐	☐
Cheese *(full fat)*	☐	☐	☐	☐	☐	☐
Cheese *(reduced fat)*	☐	☐	☐	☐	☐	☐
Mayonnaise based salads (*prawn salad, italian salad, etc.*)	☐	☐	☐	☐	☐	☐
Liver pâté	☐	☐	☐	☐	☐	☐
Preserved meats, low fat *(boiled ham, etc.)*	☐	☐	☐	☐	☐	☐
Preserved meats, high fat *(salami, cured mutton, etc.)*	☐	☐	☐	☐	☐	☐

52. Please indicate how many slices of bread/crispbread you have eaten on average per week in the past year with: (Choose one option for each line)

	Never/ rarely	1 per week	2–3 per week	4–6 per week	7–9 per week	10+ per week
Mackerel in tomato sauce; smoked mackerel	☐	☐	☐	☐	☐	☐
Caviar	☐	☐	☐	☐	☐	☐
Herring/anchovies	☐	☐	☐	☐	☐	☐
Salmon *(gravlax/smoked)*	☐	☐	☐	☐	☐	☐
Other types of fish	☐	☐	☐	☐	☐	☐

53. If you use butter/margarine on your sandwich/bread, how thick a layer do you normally spread onto it? (A single portion packet weighs 12 grams) (Choose only one option)

☐ Extra thin layer *(3 grams)* ☐ Thin layer *(5 grams)*
☐ Thick layer *(8 grams)* ☐ Extra thick layer *(12 grams)*

54. What type of butter/margarine do you normally put on your bread? (You may choose several options)

☐ I do not use butter/margarine on bread
☐ Butter
☐ Hard margarine *(e.g. Melange)*
☐ Soft margarine *(e.g. Soft, Vita)*
☐ Butter and margarine blends *(e.g. Bremyk)*
☐ *Brelett* (*fat reduced butter and margarine blend*)
☐ Reduced fat margarine *(e.g. Soft light, Vita Lett)*
☐ Olive oil margarine *(e.g. Brelett oliven, Soft oliven)*

FRUITS AND VEGETABLES

55. How often do you eat fruit? (Choose only one option for each line)

	Never/ rarely	1–3 per month	1 per week	2–4 per week	5–6 per week	1 per day	2+ per day
Apple/pear	☐	☐	☐	☐	☐	☐	☐
Orange/citrus fruit	☐	☐	☐	☐	☐	☐	☐
Banana	☐	☐	☐	☐	☐	☐	☐
Other fruit	☐	☐	☐	☐	☐	☐	☐

56. How often do you eat potatoes? (Choose only one option for each line)

	1-4 times per month	2-4 times per week	5-6 times per week	Once daily	Twice daily
Boiled	☐	☐	☐	☐	☐
Mashed	☐	☐	☐	☐	☐
Pan-fried/fried	☐	☐	☐	☐	☐

57. How often do you eat the following types of vegetables?
(Choose only one option for each line)

	Never/ rarely	1–3 per month	1 per week	2 per week	3 per week	4–5 per week	6–7 per week
Carrot	☐	☐	☐	☐	☐	☐	☐
Cabbage	☐	☐	☐	☐	☐	☐	☐
Swede	☐	☐	☐	☐	☐	☐	☐
Broccoli/cauliflower	☐	☐	☐	☐	☐	☐	☐

	Never/ rarely	1–3 per month	1 per week	2 per week	3 per week	4–5 per week	6–7 per week
Mixed salad	☐	☐	☐	☐	☐	☐	☐
Tomato	☐	☐	☐	☐	☐	☐	☐
Mixed vegetables (*frozen*)	☐	☐	☐	☐	☐	☐	☐
Onion	☐	☐	☐	☐	☐	☐	☐
Beans	☐	☐	☐	☐	☐	☐	☐
Peas	☐	☐	☐	☐	☐	☐	☐
Other vegetables	☐	☐	☐	☐	☐	☐	☐

58. **For the following vegetables in your diet, please indicate how much you typically eat each time:** (Choose only one option for each vegetable type)

Carrot ☐ 1/2 a carrot ☐ 1 carrot ☐ 1 1/2 carrot ☐ 2+ carrots

Potato ☐ 1-2 potatoes ☐ 3-4 potatoes ☐ 5-6 potatoes ☐ 7+ potatoes

Cabbage ☐ 1/2 dl ☐ 1 dl ☐ 1 1/2 dl ☐ 2+ dl

Swede ☐ 1/2 dl ☐ 1 dl ☐ 1 1/2 dl ☐ 2+ dl

Broccoli/cauliflower ☐ 1–2 pieces (bouquets) ☐ 3–4 pieces ☐ 5 + pieces

Mixed salad ☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

Tomato ☐ 1/4 of a tomato ☐ 1/2 a tomato ☐ 1 tomato ☐ 2+ tomatoes

Mixed vegetables (frozen) ☐ 1/2 dl ☐ 1 dl ☐ 2 dl ☐ 3+ dl

Beans ☐ 1–2 tbsp ☐ 3–4 tbsp ☐ 5–6 tbsp ☐ 7+ tbsp

Peas ☐ 1–2 tbsp ☐ 3–4 tbsp ☐ 5–6 tbsp ☐ 7+ tbsp

RICE, PASTA, PORRIDGE AND SOUP

59. **How often do you eat rice and pasta (spaghetti, macaroni)?** Choose only one option for each food)

	Never/ rarely	1-3 times per month	Once a week	Twice a week	3+ times per week
Rice	☐	☐	☐	☐	☐
Pasta (*spaghetti, macaroni, noodles*)	☐	☐	☐	☐	☐

60. **How often do you eat porridge?** (Choose only one option for each porridge type)

	Never/ rarely	Once a month	2-3 times per month	Once a week	2-6 times per week	1+ per day
Rice porridge	☐	☐	☐	☐	☐	☐
Other porridge *(oatmeal, etc.)*	☐	☐	☐	☐	☐	☐

61. **How often do you eat soup?** (Choose only one option per line)

	Never/ rarely	1-3 times per month	Once a week	Twice a week	3+ times per week
As a main course	☐	☐	☐	☐	☐
As appetizer, lunch or supper	☐	☐	☐	☐	☐

FISH

62. **We would like to know how often you eat fish, and kindly ask you to indicate your fish consumption below, as accurately as possible.** The availability of fish products may be seasonal; please indicate at which season you eat the various types of fish listed.

	Never/ rarely	Same amount all year	Winter	Spring	Summer	Autumn
Cod, saithe/coalfish, haddock, pollack	☐	☐	☐	☐	☐	☐
(Atlantic) wolf fish, flounder, redfish	☐	☐	☐	☐	☐	☐
Salmon, sea trout	☐	☐	☐	☐	☐	☐
Halibut	☐	☐	☐	☐	☐	☐
Mackerel	☐	☐	☐	☐	☐	☐
Herring	☐	☐	☐	☐	☐	☐
Freshwater fish (*perch, pike, grayling, charr, lavaret and trout)*	☐	☐	☐	☐	☐	☐
Other fish	☐	☐	☐	☐	☐	☐

63. **Considering the season(s) in which you eat fish, how often do you normally eat the following for dinner (main meal/course)?** (Choose only one option per line)

	Never/ rarely	Once a month	2–3 times per month	Once a week	2+ times per week
Boiled cod, saithe, pollack, haddock	☐	☐	☐	☐	☐
Pan-fried cod, saithe, pollack, haddocktorsk, sei, hyse, lyr	☐	☐	☐	☐	☐
Wolf fish, founder, redfish	☐	☐	☐	☐	☐
Salmon, sea trout	☐	☐	☐	☐	☐
Halibut	☐	☐	☐	☐	☐
Mackerel	☐	☐	☐	☐	☐
Herring	☐	☐	☐	☐	☐
Freshwater fish *(perch, pike, grayling, charr, lavaret, trout)*	☐	☐	☐	☐	☐
Other fish	☐	☐	☐	☐	☐

64. **If you eat fish, how much do you normally eat each time?** (1 piece/serving = 150 grams)

Boiled fish *(piece(s)/servings)* ☐ 1 ☐ 1 ½ ☐ 2 ☐ 3+

Pan-fried/oven-baked *(piece(s)/servings)* ☐ 1 ☐ 1 ½ ☐ 2 ☐ 3+

65. **How many times per year do you eat fish roe and fish liver?** (Choose only one option for each food)

	0	1–3	4–6	7–9	10+
Fish roe	☐	☐	☐	☐	☐
Fish liver	☐	☐	☐	☐	☐

66. **If you eat fish liver, how many tablespoons do you eat each time?** (Choose only one option)

☐ 1 ☐ 2 ☐ 3–4 ☐ 5–6 ☐ 7+

67. **How often do you eat the following fish products?** (Choose only one option per line)

	Never/ rarely	Once a month	2–3 times per month	Once a week	2+ times per week
Fishcakes/fish pudding/fish balls	☐	☐	☐	☐	☐
Fish stew/fish gratin	☐	☐	☐	☐	☐
Fried fish/fish fingers	☐	☐	☐	☐	☐
Other fish products/dishes	☐	☐	☐	☐	☐

68. **In which amounts do you normally eat the various following dishes?** (Choose only one option per line)

Fishcakes/fish pudding/fish balls *(pcs) (2 fish balls=1 fishcake)* ☐ 1 ☐ 2 ☐ 3 ☐ 4+

Fish stew, fish gratin *(dl)* ☐ 1–2 ☐ 3–4 ☐ 5+

Fried fish/fish fingers *(pcs)* ☐ 1–2 ☐ 3–4 ☐ 5–6 ☐ 7+

In addition to information regarding fish consumption, it is important to detail the sauces/fat that accompany fish meals.

69. How often do you eat the following as part of fish meals/ dishes?

	Never/ rarely	Once a month	2–3 times per month	Once a week	2+ times per week
Melted/solid butter	☐	☐	☐	☐	☐
Melted/solid margarine	☐	☐	☐	☐	☐
Sour cream, full fat *(35% fat)*	☐	☐	☐	☐	☐
Sour cream, reduced fat *(20% fat)*	☐	☐	☐	☐	☐
Sauce, high fat *(white/brown)*	☐	☐	☐	☐	☐
Sauce, fat free *(white/brown)*	☐	☐	☐	☐	☐

70. For the various types of fat/sauces that you regularly eat <u>with your fish</u>, please indicate how much you normally eat:

Melted/solid butter *(tbsp)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Melted/solid margarine *(tbsp)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Sour cream full fat *(tbsp)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Sour cream, red. fat *(tbsp)*	☐ ½	☐ 1	☐ 2	☐ 3	☐ 4+
Sauce, high fat *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Sauce, fat free *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+

71. How often do you eat shellfish? (i.e., prawns/shrimp, crabs, molluscs) (Choose only one option)

☐ Never/rarely ☐ Once a month
☐ 2-3 times per month ☐ Once a week or more

72. How many seagull eggs or eggs of other seabirds do you eat during the course of one year? (Choose only one option)

Never	1-3	4-6	7-9	10-15	16+
☐	☐	☐	☐	☐	☐

73. How often have you eaten freshwater fish? (perch, pike, grayling, charr, lavaret, trout) (Choose only one option per line)

	Never/ rarely	Once a month	2-3 times per month	Once a week	2-3 times per week	4+ per week
Childhood	☐	☐	☐	☐	☐	☐
Adolescence (13-19 yrs)	☐	☐	☐	☐	☐	☐
Adulthood (past year excl.)	☐	☐	☐	☐	☐	☐

MEATS

74. How often do you eat the following meat dishes? (Choose only one option for each meat type)

	Never/ rarely	1-2 times per month	3-4 times per month	2-3 times per week	4-6 times per week	7+ times per week
Reindeer meat	☐	☐	☐	☐	☐	☐
Moose/elk meat	☐	☐	☐	☐	☐	☐

75. How often do you eat the following meat and poultry dishes? (Choose only one option for each dish)

	Never/ rarely	Once a month	2–3 times per month	Once a week	2+ times per week
Roast *(beef, pork, mutton)*	☐	☐	☐	☐	☐
Cutlets *(beef, pork, mutton)*	☐	☐	☐	☐	☐
Steak *(beef, pork, mutton)*	☐	☐	☐	☐	☐
Hamburger/meat patties	☐	☐	☐	☐	☐
Sausages/hot dogs	☐	☐	☐	☐	☐
Grouse, other game birds	☐	☐	☐	☐	☐
Meat casserole, stew	☐	☐	☐	☐	☐
Pizza with meat toppings	☐	☐	☐	☐	☐
Chicken, unskinned	☐	☐	☐	☐	☐
Chicken, skinned	☐	☐	☐	☐	☐
Bacon	☐	☐	☐	☐	☐
Other meat dishes	☐	☐	☐	☐	☐
Blood-based dishes *(lamb/sheep, cattle, reindeer, moose)*	☐	☐	☐	☐	☐

76. If any of the following dishes are in your diet, please indicate your typical serving sizes: (Choose only one option for each dish)

Roast *(slices)*	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5+
Cutlets *(pcs)*	☐ ½	☐ 1	☐ 1½	☐ 2+	
Hamburgers, meat patties *(pcs)*	☐ 1	☐ 2	☐ 3	☐ 4+	
Sausages *(pcs; 1=150g)*	☐ ½	☐ 1	☐ 1½	☐ 2+	
Casserole/stew *(dl)*	☐ 1–2	☐ 3	☐ 4	☐ 5+	
Pizza with meat toppings *(slices of 100 grams each)*	☐ 1	☐ 2	☐ 3	☐ 4+	

77. Which of the following sauces do you have with your meat and pasta dishes? (Choose only one option for each sauce variety)

	Never/ rarely	Once a month	2–3 times per month	Once a week	2+ times per week
Brown sauce	☐	☐	☐	☐	☐
Gravy	☐	☐	☐	☐	☐
Tomato-based sauce	☐	☐	☐	☐	☐
Sauce with cream/sour cream	☐	☐	☐	☐	☐

78. For the various sauces listed, what amounts do you normally apply to your meals?

Brown sauce *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Gravy *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Tomato-based sauce *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+
Sauce with cream/sour cream *(dl)*	☐ ¼	☐ ½	☐ ¾	☐ 1	☐ 2+

OTHER FOODS

79. How many eggs do you normally eat in the course of <u>one week</u>? (pan-fried, boiled, scrambled, omelette) (Choose only one option)

☐ 0 ☐ 1 ☐ 2 ☐ 3–4 ☐ 5–7 ☐ 8-14 ☐ 15+

80. How often do you eat ice cream? (for dessert, Cornetto, etc.) (Choose one option for your ice cream consumption in summer, and one for the remainder of the calendar year)

	Never/ rarely	Once a month	2–3 times per month	Once a week	2+ times per week
In the summer	☐	☐	☐	☐	☐
The rest of the year	☐	☐	☐	☐	☐

81. How much ice cream do you normally eat each time? (Choose only one option)

☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

82. How often do you eat bakery goods, such as buns, cakes, danishes/pastries and cookies? (Choose only one option for each line)

	Never/ rarely	1–3 per month	1 per week	2–3 per week	4–6 per week	1+ per day
Yeasted bakery goods *(buns, etc.)*	☐	☐	☐	☐	☐	☐
Danish pastries	☐	☐	☐	☐	☐	☐
Cakes	☐	☐	☐	☐	☐	☐

	Never/ rarely	1–3 per month	1 per week	2–3 per week	4–6 per week	1+ per day
Pancakes	☐	☐	☐	☐	☐	☐
Waffles	☐	☐	☐	☐	☐	☐
Cookies, biscuits	☐	☐	☐	☐	☐	☐
Lefse, potato pancake	☐	☐	☐	☐	☐	☐

83. **How often do you have dessert?** (Choose only one option for each food)

	Never/ rarely	1 per month	2–3 per month	1 per week	2–3 per week	4+ per week
Pudding *(eg. chocolate/ caramel pudding)*	☐	☐	☐	☐	☐	☐
Creamed rice, mousse/ fromage	☐	☐	☐	☐	☐	☐
Compote, stewed fruit, canned fruit	☐	☐	☐	☐	☐	☐
Strawberries *(fresh, frozen)*	☐	☐	☐	☐	☐	☐
Other berries *(fresh, frozen)*	☐	☐	☐	☐	☐	☐

84. **How often do you eat chocolate?** (Sett ett kryss pr. linje)

	Never/ rarely	1–3 times per month	Once a week	2–3 times per week	4–6 times per week	Once a day or more
Dark chocolate	☐	☐	☐	☐	☐	☐
Milk chocolate	☐	☐	☐	☐	☐	☐

85. **If you eat chocolate, how much do you normally eat each time?** Imagine the size of a Kvikk Lunsj chocolate bar (47g), and indicate your serving size according to that.

☐ ¼ ☐ ½ ☐ ¾ ☐ 1 ☐ 1½ ☐ 2+

86. **How often do you eat other sweets/candy?** (Choose only one option)

Never/ rarely	1–3 times per month	Once a week	2–3 times per week	4–6 times per week	Once a day or more
☐	☐	☐	☐	☐	☐

87. **How often do you eat salty snacks?** (Choose only one option for each line)

	Never/ rarely	1–3 times per month	Once a week	2–3 times per week	4–6 times per week	Once a day or more
Potato crisps	☐	☐	☐	☐	☐	☐
Peanuts	☐	☐	☐	☐	☐	☐
Other nuts	☐	☐	☐	☐	☐	☐
Other snacks	☐	☐	☐	☐	☐	☐

COD LIVER OIL AND FISH OIL CAPSULES

88. **Do you take bottled cod liver oil supplements?** ☐ Yes ☐ No

89. **If yes, how often do you take bottled cod liver oil?** (Choose only one option per line)

	Never/ rarely	1–3 times per month	Once a week	2–6 times per week	Daily
In the winter	☐	☐	☐	☐	☐
Other seasons	☐	☐	☐	☐	☐

90. **If you take bottled cod liver oil, what amounts do you take each time?**

☐1 teaspoon ☐½ tablespoon ☐1+ tablespoons

91. **Do you take cod liver oil capsules/fish oil capsules?**

☐ Yes ☐ No

92. **If yes, how often do you take cod liver oil capsules/fish oil capsules?** (Choose only one option for each line)

	Never/ rarely	1–3 times per month	Once a week	2–6 times per week	Daily
In the winter	☐	☐	☐	☐	☐
Other seasons	☐	☐	☐	☐	☐

93. **What brand/type of cod liver oil/fish oil capsules do you take, and how many capsules do you take each time?**

Product/brand name:_____

Number of capsules: ☐ 1 ☐ 2 ☐ 3+

Other dietary supplements

94. **Do you take other dietary supplements?** (vitamins/minerals) ☐ Yes ☐ No

Alcohol

95. **Do you practice total alcohol abstinence?** ☐ Yes ☐ No

96. **If no, how often and how much did you drink, on average, in the past year?** (Choose only one option for each line)

	Never/ rarely	1 per month	2-3 per month	1 per week	2-4 per week	5-6 per week	1 per day	2+ per day
Beer/alcopops *(½ l)*	☐	☐	☐	☐	☐	☐	☐	☐
Wine *(glass)*	☐	☐	☐	☐	☐	☐	☐	☐
Liquor/distilled spirits *(drink/shot)*	☐	☐	☐	☐	☐	☐	☐	☐
Liqueur/fortified wine *(glass)*	☐	☐	☐	☐	☐	☐	☐	☐

Dental health

97. **In your most recent visit to the dentist, did you see a dentist/ dental hygienist in private practice or a dentist/dental hygienist employed in the public dental health service?** (Mark with an "X")

☐ Dentist in private practice
☐ Dental specialist in private practice
☐ Dental hygienist in private practice
☐ Dentist employed in public dental health service
☐ Dental specialist employed in public dental health service
☐ Dental hygienist employed in public dental health service
☐ Dentist abroad (outside of Norway)

98. **When did you last see a dentist or dental nurse?**(Choose only one option)

☐ Less than a year ago ☐ 1-2 years ago
☐ 3-5 years ago ☐ More than 5 years ago

99. **If your most recent dental appointment was more than two years ago, please supply the reason for not going more frequently to the dentist:** (Choose only one option)

☐ I have not been scheduled for a regular appointment
☐ Long waiting time for appointment
☐ I have not had the time
☐ Economic/financial reasons
☐ I have not required dental care
☐ I am afraid or anxious about seeing the dentist
☐ Other reasons: _____

100. **In the past 12 months, how much money have you spent on dental care (dentist, dental specialist, dental hygienist)?** (Choose only one option)

- ☐ Nothing (I have not had dental appointments)
- ☐ Nothing (I have had my costs covered)
- ☐ Less than NOK 1000
- ☐ NOK 1000-5000
- ☐ NOK 5001-10,000
- ☐ NOK 10,001-20,000
- ☐ More than NOK 20,000

101. **Please mark the two aspects that are most important to you in regards to your teeth/oral health:**

- That my teeth are nice-looking when I talk and smile ☐
- That my teeth are pain-free (do not hurt) ☐
- That I can chew/eat without any trouble ☐
- That I have fresh breath ☐
- That I keep my teeth for the rest of my life ☐

102. **How would you rate your dental health?** (Choose only one option)

☐ Poor ☐ Not so good ☐ Good ☐ Very good

103. **Do you have dentures/a dental bridge?** ☐ Yes ☐ No

Sunlight exposure/Tanning

104. **Have you been on holiday in southern countries or other beach/sunbathing holiday in the past month?** ☐ Yes ☐ No

105. **Please estimate the total number of hours during which you have been outside (during daylight hours) in the past seven days?** ☐☐ hours

106. **Have you used a solarium in the past month?**

☐ No ☐ 1 - 2 times ☐ 3+ times

Skin care products/Cosmetics

107. **How often (number of times) do you use the following cosmetic products?** (Choose only one option per product)

	Never/ rarely	1–3 per month	1 per week	2–4 per week	5–6 per week	1 per day	2+ per day
Face cream	☐	☐	☐	☐	☐	☐	☐
Hand cream	☐	☐	☐	☐	☐	☐	☐
Body lotion	☐	☐	☐	☐	☐	☐	☐
Perfume/aftershave	☐	☐	☐	☐	☐	☐	☐
Deodorant	☐	☐	☐	☐	☐	☐	☐
Hair products *(not incl. shampoo/conditioner)*	☐	☐	☐	☐	☐	☐	☐

Children and breastfeeding

108. **This question applies to mothers only: What is the birth year of your child(ren), and what was the approximate number of months during which the child(ren) was/were breastfed?**

	Birth year	Number of months during which the child was breastfed	Not breastfed
Firstborn	☐☐☐☐	☐☐	☐
Second child	☐☐☐☐	☐☐	☐
Third child	☐☐☐☐	☐☐	☐
Fourth child	☐☐☐☐	☐☐	☐
Fifth child	☐☐☐☐	☐☐	☐

If you had more than five children, please continue on a separate sheet.

Family and linguistic background

109. **How would you describe your family's financial situation when you were growing up?** (Choose only one option)

☐ Very good ☐ Good ☐ Challenging ☐ Extremely challenging

People of different ethnic backgrounds live in Northern Norway. That is, they have different languages and cultures. Examples of ethnic backgrounds, or ethnic groups, are Norwegian, Sami and Kven.

110. **What language(s) do/did you, your parents and your grandparents speak at home?** (Put one or more crosses for each line)

	Norwegian	Sami	Kven	Other, describe:
Mother's father	☐	☐	☐	☐ .....
Mother's mother	☐	☐	☐	☐ .....
Father's father	☐	☐	☐	☐ .....
Father's mother	☐	☐	☐	☐ .....
Father	☐	☐	☐	☐ .....
Mother	☐	☐	☐	☐ .....
Myself	☐	☐	☐	☐ .....

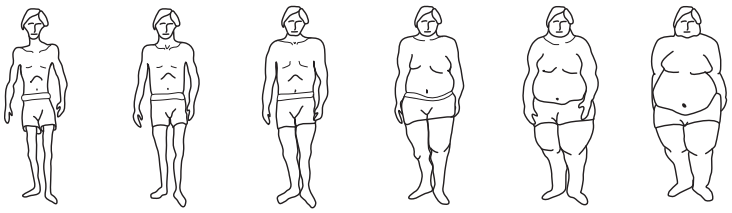
111. **What is your, your father's and your mother's ethnic backgrounds?** (Put one or more crosses for each line)

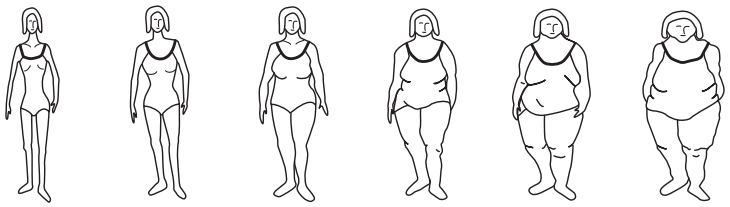
	Norwegian	Sami	Kven	Other, describe:
My ethnic background is	☐	☐	☐	☐ .....
My father's ethnic background is	☐	☐	☐	☐ .....
My mother's ethnic background is	☐	☐	☐	☐ .....

112. **What do you consider yourself to be?** (Put one or more crosses)

Norwegian	Sami	Kven	Other, describe:
☐	☐	☐	☐ .....

Body type/size





113. **Which of the above figures/illustrations most closely resembles your own body type/size?** ..... Figure number ☐

	Male figure number	Female figure number
114. **In your opinion, which figure corresponds to a healthy body type/size ?**	☐	☐
115. **Which figure is the first (in ascending numerical order) that you think of as representing a fat person?**	☐	☐
116. **Which figure/illustration is the first (in descending numerical order) that you think of as representing a skinny person?**	☐	☐

117. **How would you describe yourself?** (Choose only one response)

Extremely fat	Too fat	Average/Just right	Too thin/skinny	Extremely skinny
☐	☐	☐	☐	☐

118. **Have you attempted to lose weight (diet) in the past six months?** ..... ☐ Yes ☐ No

119. **If yes, how many kilograms have you lost in the past six months ?** ..... ☐☐ Kg

120. **Please indicate the methods used in order to lose weight?**
(You may choose one or more alternatives)

- ☐ Eating less
- ☐ Healthier diet
- ☐ Other dietary changes
- ☐ Exercise
- ☐ Weightloss drugs prescribed by doctor/physician
- ☐ Weightloss shakes/ powders
- ☐ Other, please describe: .....

Other health issues

121. **Below you will find a number of common health issues. Please consider each one carefully and individually, and then indicate the extent to which each individual health issue has affected you in the past four weeks.** (Choose only one option for each health issue)

	Not affected	Slightly affected	Affected quite a lot	Severely affected
Nervousness or shakiness inside	☐	☐	☐	☐
Feeling fearful	☐	☐	☐	☐
Feeling hopeless about the future	☐	☐	☐	☐
Worrying too much about things	☐	☐	☐	☐
Feeling blue/melancholic	☐	☐	☐	☐

Sleep/Sleeping habits

We would like to ask some questions concerning your sleeping habits. Please use the 24-hour time format, in which 11:00 corresponds to eleven o'clock in the morning and 23:00 corresponds to eleven o'clock at night.

122. **Have you taken part in shift work (worked night/evening shifts) in the past three months ?** ..... ☐ Yes ☐ No

123. **Please indicate the number of days a week in which you do not have the opportunity to choose freely when to go to sleep and when to get out of bed?** (This may apply, for instance, to any days in which you have to go to work, attend school, etc.) (Choose only one option)

0	1	2	3	4	5	6	7
☐	☐	☐	☐	☐	☐	☐	☐

124. **On the days that I do not have the opportunity to choose freely when to go to sleep/get out of bed,**

	Hours	Minutes
I go to bed at	☐☐	☐☐
I get ready to fall asleep at	☐☐	☐☐
Number of minutes that it normally takes before I fall asleep (fully):		☐☐
I wake up at	☐☐	☐☐

I wake up due to/using:

- ☐ Alarm clock
- ☐ External circumstances (i.e., noise caused by family members or others)
- ☐ I wake up naturally

Number of minutes normally passing from I wake up till I get out of bed: ..... ☐☐

On such days, do you sleep in other hours of the day? (i.e., afternoon nap) ..... ☐ Yes ☐ No

	Hours	Minutes
When (what hour) does this normally occur?	☐☐	☐☐
Provide the number of minutes of daytime sleeping:		☐☐

125. **On days in which I can freely choose my rising/waking/ sleeping hours:**

	Hours	Minutes
I go to bed at	☐☐	☐☐
I get ready to sleep at	☐☐	☐☐
Number of minutes that it normally takes before I fall asleep (fully):		☐☐
I wake up at	☐☐	☐☐

I wake up due to/using:

- ☐ Alarm clock
- ☐ External circumstances (i.e., noise caused by family members or others)
- ☐ I wake up naturally

Number of minutes normally passing from I wake up till I get out of bed: ..... ☐☐

On such days, do you sleep in other hours of the day (i.e., afternoon nap) ..... ☐ Yes ☐ No

Thank you for participating in the survey!

LUNDBLAD MEDIA AS – SVANEGODKJENT TRYKKSAK – 241 762 | 0-122027 – NORSK

Survey on health and lifestyle

We kindly request that you fill in the form as thoroughly and accurately as possible, and bring it with you to your scheduled physical examination. The form will be optically scanned. Please use blue or black ink. Use capital letters. Do not use decimals; for example, "0.5" should be rounded off to "1".

1. **In what year were you born?** ..... Year ☐☐☐☐

2. **What is your gender?** ..... Female ☐ Male ☐

3. **What is your marital status?**
☐ Married ☐ Cohabiting ☐ Divorced
☐ Unmarried ☐ Widow/widower

4. **How many years of education have you completed?** (Include any and all years in which you attended school or studied) ..... Number of years ☐☐

5. **If you are a woman: How many children have you given birth to?** ..... Number of children ☐☐

6. **If you are a woman: How many children have you breastfed?** ..... Number of children ☐☐

Personal health

7. **How is you state of health?** (Put one cross only)
☐ Poor ☐ Good
☐ Not so good ☐ Very good

8. **How is your dental health?** (Put one cross only)
☐ Poor ☐ Good
☐ Not so good ☐ Very good

9. **Do you have dentures/ a dental bridge?** ..... ☐ Yes ☐ No

10. **When did you last see a dentist or dental nurse?**
☐ Less than a year ago ☐ 1–2 years ago
☐ 3–5 years ago ☐ More than 5 years ago

11. **How satisfied are you with the dental health care offered in your municipality?** (Put one cross only)
Very dissatisfied ☐ ☐ ☐ ☐ ☐ ☐ Very satisfied ☐ Don't know

Cardiovascular disease

12. **Do you have, or have you ever had, high blood pressure?** ..... ☐ Yes ☐ No

13. **If yes, how old were you when you developed high blood pressure?** ..... Age ☐☐

14. **Are you taking medication for high blood pressure?** Yes, currently ☐ Previously, but not now ☐ Never ☐

15. **If you are taking high blood pressure medication, or have taken high blood pressure medication in the past, at what age did you start taking this type of medicine?** ..... Age ☐☐

16. **Have you ever had one or more heart attacks?**
☐ No, never ☐ One heart attack ☐ Two heart attacks ☐ Three or more heart attacks

17. **If yes, at what age did you have your first heart attack?** ..... Age ☐☐

18. **Do you suffer from angina pectoris (heart cramp)?** ..... ☐ Yes ☐ No

19. **If yes, how often have you experienced such pain in the past month?** .....
Rarely ☐ Once a week ☐ 2-3 times a week ☐ 4-6 times a week ☐ 7 times a week or more ☐

20. **How old were you when you had your first attack of angina pectoris?** ..... Age ☐☐

21. **Have you had heart (bypass) surgery?** ..... ☐ Yes ☐ No

22. **Have you had your arteries unblocked/had stent(s) placed?** ..... ☐ Yes ☐ No

23. **Has your doctor told you that you have atrial fibrillation?** ..... ☐ Yes ☐ No

24. **How old were you when you first experienced atrial fibrillation?** ..... Age ☐☐

Diabetes

25. **Have you ever been diagnosed with diabetes (elevated blood sugar levels)?** ☐ Yes ☐ No

If no, please skip to question 35.

26. **If yes, please specify your diabetes diagnosis:** (chose one or more options)

Gestational diabetes ☐

Type 1 diabetes ☐

Type 2 diabetes ☐

27. **How was your diabetes discovered?**

I consulted my doctor/physician because of symptoms ☐ Yes ☐ No

It was discovered without the appearance of symptoms (medical certificate, work-related medical examination, pregnancy health examination, medical consultation for illness other than diabetes, etc.) ☐ Yes ☐ No

28. **At what age was your diabetes discovered/diagnosed?** Age ☐☐

INSULIN

29. **Are you taking insulin for your diabetes?**	Yes, currently	Previously, but not now	Never used
	☐	☐	☐

If you are taking (or have taken) insulin:

30. **At what age did you start your insulin treatment?** Age ☐☐

31. **How many times per day do you/ did you usually take insulin?** ☐☐ times

32. **In total, how many units of insulin do you/did you take on an average day?** ☐☐ units (E)

ORAL MEDICATION

33. **Are you taking oral medication for diabetes?**	Yes, currently	Previously, but not now	Never used
	☐	☐	☐

If you are taking or have taken oral medication:

34. **At what age did you start taking oral medication for diabetes?** Age ☐☐

Other illnesses

35. **Do you have, or have you ever had, any of the following?**

	Yes	No	Age at onset
Asthma	☐	☐	☐☐
Eczema	☐	☐	☐☐
Chronic bronchitis, emphysema, COPD	☐	☐	☐☐
Multiple sclerosis (MS)	☐	☐	☐☐
Psoriasis	☐	☐	☐☐
Bechterew's disease	☐	☐	☐☐

Chronic pain

36. **Are you experiencing pain that has lasted three months or longer?** ☐ Yes ☐ No

37. **If yes, please indicate the intensity of your pain in the past week:** (Choose only one option)

No pain										Most severe pain
0	1	2	3	4	5	6	7	8	9	10
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

38. **Please indicate where your pain is most severe:** (Choose only one option)

☐ Neck ☐ Lower back ☐ Other

Physical activity

39. **We will now ask you to state your physical activity at the ages of 14, 30 and at your current age, on a scale from very low to very high.** The scale below runs from 1 to 10. Physical activity includes both housework and activity at work, as well as exercise and other physical activities such as walking/hiking, etc. Mark the number that best matches your level of activity:

	Very low									Very high
Age	1	2	3	4	5	6	7	8	9	10
14 years	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
30 years	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Current age	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Alcohol

40. **Do you practice total alcohol abstinence?** ☐ Yes ☐ No

41. **If no, how often and how much did you drink, on average, in the past year?** (Put one cross per line)

	Never/ rarely	1 per month	2–3 per month	1 per week	2–4 per week	5–6 per week	1 per day	2+ per day
Beer/alcopops *(½ l.)*	☐	☐	☐	☐	☐	☐	☐	☐
Wine *(glass)*	☐	☐	☐	☐	☐	☐	☐	☐
Liquor/distilled spirits *(drink/shot)*	☐	☐	☐	☐	☐	☐	☐	☐
Liqueur/fortified wine *(glass)*	☐	☐	☐	☐	☐	☐	☐	☐

Smoking habits

42. **Have you ever smoked daily?** ☐ Yes ☐ No

If you have never smoked daily, please skip to question 47.

43. **Are you currently a daily smoker?** ☐ Yes ☐ No

44. **If you are no longer a daily smoker, at which age did you quit?** Age ☐☐

45. **In total, for how many years have you smoked daily?** Years ☐☐

46. **Considering all the years in which you smoked regularly (daily), how many cigarettes/rolling tobacco did you smoke per day, on average?** Number of cigarettes ☐☐

47. **Do you live with someone who smokes?** ☐ Yes ☐ No

Language and use of interpreter

48. **In what language(s) do you primarily want to talk to health personnel?** (Put one or more crosses)

Norwegian	Sami	Other, describe:
☐	☐	☐ .....

49. **If you have answered "Sami" but were not offered a Sami-speaking doctor at your last doctors visit, did they offer you an interpreter?**

With your general practitioner:

☐ Yes ☐ No
☐ I do not want an interpreter ☐ Not relevant

In the hospital/with a specialist:

☐ Yes ☐ No
☐ I do not want an interpreter ☐ Not relevant

Family and linguistic background

50. **How would you describe your family's financial situation when you were growing up?** (Choose only one option)

☐ Very good ☐ Good ☐ Challenging ☐ Extremely challenging

People of different ethnic backgrounds live in Northern Norway. That is, they have different languages and cultures. Examples of ethnic backgrounds, or ethnic groups, are Norwegian, Sami and Kven.

51. **What language(s) do/did you, your parents and your grandparents speak at home?** (Put one or more crosses)

	Norwegian	Sami	Kven	Other, describe:
Mother's father	☐	☐	☐	☐ .....
Mother's mother	☐	☐	☐	☐ .....
Father's father	☐	☐	☐	☐ .....
Father's mother	☐	☐	☐	☐ .....
Father	☐	☐	☐	☐ .....
Mother	☐	☐	☐	☐ .....
Myself	☐	☐	☐	☐ .....

52. **What is your, your father's and your mother's ethnic backgrounds?** (Put one or more crosses)

	Norwegian	Sami	Kven	Other, describe:
My ethnic background is	☐	☐	☐	☐ .....
My father's ethnic background is	☐	☐	☐	☐ .....
My mother's ethnic background is	☐	☐	☐	☐ .....

53. **What do you consider yourself to be?** (Put one or more crosses)

Norwegian	Sami	Kven	Other, describe:
☐	☐	☐	☐ .....

Experience and use of health services

54. **Who is the doctor you normally use?**

☐ Your GP ☐ Another doctor

55. **How long have you had your current GP?**

☐ Less than 6 months ☐ 6 to 11 months

☐ 12 to 24 months ☐ More than two years

56. **In the last 12 months, have you contacted your doctor for help or advice for yourself?** ☐ Yes ☐ No

If yes, did you get the help you asked for?

☐ Never ☐ Sometimes ☐ Usually ☐ Always

57. **How satisfied are you with the following aspects of the doctor's service (regular GP scheme)?**
(Put one cross only)

	Very satisfied	Satisfied	Dissatisfied	Very dissatisfied	Don't know
The doctor's accessibility on the phone	☐	☐	☐	☐	☐
The waiting time for an appointment	☐	☐	☐	☐	☐
Time with the doctor	☐	☐	☐	☐	☐
The doctor's understanding of your problems	☐	☐	☐	☐	☐
Their information about your health issues, examination and treatment plan	☐	☐	☐	☐	☐
In total, how satisfied are you with the municipal health service?	☐	☐	☐	☐	☐

The next questions are about the specialized health service.

Specialized health service refers to hospitals, district psychiatric centers (DPS), specialized doctors services and individual specialists.

58. **In the last 12 months, have you been for examination or treatment for *physical problems* to the following?**

☐ The hospital ☐ Specialist medical center

☐ Private specialist ☐ None of these

59. **In the last 12 months, have you been for examination or treatment for *psychological problems* to the following?**

☐ Psychiatric hospital ☐ District psychiatric center

☐ Private specialist ☐ None of these

60. **If you have been for treatment with a specialist for physical or psychological problems in the last 12 months, answer the following questions:**
(Put one cross only) Answer on a scale from 0 to 10, where 0 = to a small extent, 10 = to a large extent.

Did you get a chance to say what you felt was important about your condition?

	0	1	2	3	4	5	6	7	8	9	10	Not relevant
Physical issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Psychological issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Did the doctors speak to you in a way you understood?

	0	1	2	3	4	5	6	7	8	9	10	Not relevant
Physical issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Psychological issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

All in all, do you trust the hospital or specialist who saw you?

	0	1	2	3	4	5	6	7	8	9	10	Not relevant
Physical issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Psychological issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

All in all, how satisfied are you with the care and treatment you eventually received?

	0	1	2	3	4	5	6	7	8	9	10	Not relevant
Physical issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Psychological issues	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Thank you for participating in the survey!