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Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women

Short running title: Metabolically healthy obese and incident cardiovascular disease

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Abstract

Background: Previous studies have been unclear about the cardiovascular risks for metabolically healthy obese individuals.

Objectives: We aimed to examine the associations of metabolically healthy obese with 4 different presentations of incident cardiovascular disease in a contemporary population.

Methods: We used linked electronic health records (1995 to 2015) in The Health Improvement Network (THIN) to assemble a cohort of 3.5 million individuals, 18 years or older and initially free from cardiovascular disease. We created body size phenotypes defined by BMI categories (underweight, normal weight, overweight and obesity) and three metabolic abnormalities (diabetes, hypertension, and hyperlipidemia). The primary endpoints were the first record of one of 4 cardiovascular presentations [coronary heart disease (CHD), cerebrovascular disease, heart failure, and peripheral vascular disease (PVD)].

Results: During a mean follow-up period of 5.4 years, obese individuals with 0 metabolic abnormalities had a higher risk of CHD (multivariable-adjusted hazard ratio (HR) 1.49, 95% CI 1.45, 1.54), cerebrovascular disease (1.07, 95% CI 1.04, 1.11) and heart failure (1.96, 95% CI 1.86, 2.06) compared to normal weight individuals with 0 metabolic abnormalities. Risk of CHD, cerebrovascular disease and heart failure in normal weight, overweight and obese individuals increased with increasing number of metabolic abnormalities.

Conclusion: Individuals with obesity with no metabolic abnormalities had a higher risk of coronary heart disease, cerebrovascular disease and heart failure than normal weight metabolically healthy individuals. Even individuals who are normal weight can have metabolic abnormalities, and have similar risks for cardiovascular disease events.

Key words: Cardiovascular diseases, Metabolically healthy obesity, Phenotype

Condensed abstract

Whether individuals who are metabolically healthy obese (MHO) are associated with excess risk of cardiovascular disease remains a subject of debate. The present study of 3.5 million adults examines and compares associations between body size phenotypes with or without metabolic abnormalities and incident cardiovascular disease. Our results suggest that individuals who are MHO are at higher risk of coronary heart disease, cerebrovascular disease and heart failure than normal weight metabolically healthy individuals. Clinicians additionally need to be aware that individuals with a normal BMI can have metabolic abnormalities, and therefore be at high risk for cardiovascular disease events.

Abbreviations

MHO= metabolically healthy obese

PVD= peripheral vascular disease

THIN= the Health Improvement Network

BMI= body mass index

CVD= cardiovascular disease

HR= hazard ratio

CI= 95% confidence interval

CHD= coronary heart disease

Introduction

Obesity, an established risk factor for cardiovascular diseases (1), has been increasing globally over the past four decades (2). Metabolic abnormalities such as hypertension, dyslipidemia, and dysglycemia are known to mediate its effects, (3) however the clustering of obesity-related metabolic abnormalities varies widely among obese individuals. In fact, a subset of obese individuals without obesity-related metabolic abnormalities are referred to as “metabolically healthy obese” (MHO) (4-8).

Three meta-analyses (9-11), have demonstrated that compared with metabolically healthy normal-weight individuals, obese individuals are at increased risk for cardiovascular disease events. Whether MHO is associated with excess risk of cardiovascular disease remains a subject of debate, because of important limitations to the evidence base. The main limitation is the inconsistent definition of metabolic health across studies. Previous studies have also not compared the association of MHO and a wide range of cardiovascular disease events such as cerebrovascular disease, heart failure, and peripheral vascular disease (PVD). Potential confounders also have been inconsistently controlled for across studies, and there are also a limited numbers of studies that have examined other metabolically defined body size phenotypes.

We sought to address these limitations in a large contemporary cohort, based on linked electronic health records, which combine routine information about diagnoses, risk factors, and medication use with future cardiovascular disease events. Our objective was to examine associations between body size phenotypes (underweight, normal weight, overweight and obese) with or without metabolic abnormalities (diabetes, hypertension, hyperlipidaemia) and incident coronary heart disease (angina, ischaemic heart disease, myocardial infarction), cerebrovascular disease (transient ischemic attack, ischaemic stroke, haemorrhagic stroke), heart failure, and

peripheral vascular disease. We tested the hypothesis that compared with metabolically healthy (i.e. no metabolic abnormalities) normal weight individuals, metabolically healthy obese individuals are at increased risk for cardiovascular disease events.

Methods

Study design and setting

We undertook a cohort study with prospectively collected data from The Health Improvement Network database (THIN), which contains computerized primary care records from primary care physicians who use the Vision IT system and have agreed at the practice level to participate [covering 6.2% of the United Kingdom (UK) population]. THIN captures diagnoses, prescriptions, and tests from primary care, and referrals to specialists, hospital admissions, and diagnoses made in secondary care, which are typically reported back to the primary care physicians. They record lifestyle (e.g. smoking status) and anthropometric measurements (e.g. height, weight); these measurements could be recorded at patient registration, opportunistically during care, or as deemed clinically relevant by the primary care physicians. THIN data is representative of the UK population (12), and comparisons to external statistics and other independent studies have shown that both the clinical diagnostic and prescribing information is well recorded and accurate (12,13). Data collection began in January 1995, and we used all data to September, 2015. For this study, approval was obtained via THIN's independent Scientific Review Committee in August 2016 (SRC reference number: 16THIN078).

Participants

We included all persons in THIN aged 18 years older with BMI data. Patients were only eligible to take part once their general practices had implemented the VISION IT system. Study entry began 12 months after registration to minimize the chance that cardiovascular disease

events recorded after registration reflected pre-existing or historical disease. We assigned the first BMI record from the registration date or the first one recorded after the VISION IT system was initiated. Individuals with any record of cardiovascular disease events before study entry were excluded.

Exposure

BMI was defined as body weight (kilograms) divided by height (meters) squared, and expressed in kg/m^2 at study entry. We defined individuals as having diabetes and hypertension by coded diagnoses (READ codes) recorded in THIN at study entry (Online Table 1). We defined individuals as having hyperlipidemia on the basis of whether individuals had a specific prescription records of lipid-lowering agents. Individuals who developed diabetes, hypertension or hyperlipidemia during follow-up were analysed according to their baseline status of no diabetes, hypertension or hyperlipidemia.

Body size phenotypes were defined using WHO criteria as follows: underweight ($\text{BMI} < 18.5 \text{ kg}/\text{m}^2$), normal-weight ($18 \text{ kg}/\text{m}^2 > \text{BMI} < 25 \text{ kg}/\text{m}^2$), overweight ($25 \text{ kg}/\text{m}^2 \geq \text{BMI} < 30 \text{ kg}/\text{m}^2$) and obese ($\text{BMI} \geq 30 \text{ kg}/\text{m}^2$). The three metabolic abnormalities were summed to create a metabolic abnormalities score (0, 1, 2 and 3). Persons were categorized into 14 body size phenotypes: underweight with 0 metabolic abnormalities, underweight with 1 or more metabolic abnormalities, normal weight with 0 metabolic abnormalities, normal weight with 1 metabolic abnormality, normal weight with 2 metabolic abnormalities, normal weight with 3 metabolic abnormalities, overweight with 0 metabolic abnormalities, overweight with 1 metabolic abnormality, overweight with 2 metabolic abnormalities, overweight with 3 metabolic abnormalities, obese with 0 metabolic abnormalities, obese with 1 metabolic abnormality, obese with 2 metabolic abnormalities, and obese with 3 metabolic abnormalities.

Outcomes

The endpoints were the first record of one of the following 4 presentations of cardiovascular disease: coronary heart disease (angina, ischemic heart disease, myocardial infarction), cerebrovascular disease (transient ischemic attack, ischemic stroke, hemorrhagic stroke), heart failure, and peripheral vascular disease. Any events occurring after the first cardiovascular disease presentation were ignored. Endpoint definitions are described in Online Table 2.

Covariates

Participant's age, sex, self-reported smoking status, and social deprivation were included in models. Data recorded at study entry was used to classify participants as never smokers, ex-smokers, or current smokers at baseline. Social deprivation was included as quintiles of the index of multiple deprivation (14), a score calculated for each participant's neighborhood on the basis of social indices such as income, education, and employment.

Statistical analysis

Of the 4,091, 344 million individuals aged 18 years or older in THIN without a history of CVD, we excluded persons with missing sex (128,458/4.09 million[X]), BMI (161,699/4.09 million [4.1%]), smoking (53,262 /4.09 million [1.6%]) and social deprivation (252,148 /4.09 million [6.7%]). After these exclusions, there remained a final sample of 3,495,777 participants (88.2% of the eligible sample). Those excluded due to missing information were less likely to be male (41.4% vs. 43.1%; $p < 0.001$), younger (41.1 years vs. 44.7 years; $p < 0.001$), have a lower BMI (25.9 kg/m² vs. 26.4 kg/m²; $p < 0.001$), more likely to belong to the most deprived quintile (14.5% vs. 14.0%; $p < 0.001$) and more likely to be current smokers (25.1% vs. 24.6%; $p < 0.001$).

Follow-up was censored at the occurrence of first cardiovascular disease endpoint, death, de-registration from the practice, or the last data collection for the practice, whichever occurred first. We used Cox proportional hazard models to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between each body size phenotype with or without metabolic abnormalities and cardiovascular disease event. We adjusted for age at BMI record, sex, self-reported smoking and social deprivation. We assessed the proportional hazards assumption by visually checking the Kaplan-Meier curves and tested it using Schoenfeld residuals. e In sensitivity analyses, we stratified associations by sex and age (<65 y, ≥ 65 y); defined metabolic status by diagnostic or prescription codes as well as laboratory or physical measurements; adjusted analyses for hormone replacement therapy (HRT) and oral contraceptives, respectively; and excluded patients with type 1 diabetes. The cut-off at 65 years was chosen as this is commonly used to designate an individual as an older person (15). Residual confounding by cigarette smoking has been suggested as a possible explanation for inconsistent associations between obesity and PVD (16). Therefore, we additionally examined the association between MHO and PVD only among individuals who reported never smoking cigarettes. Because excess risk for cardiovascular disease events associated with low BMI may be associated with smoking-related diseases [such as chronic obstructive pulmonary disease (COPD) and lung cancer] we examined the association between underweight and cardiovascular disease events among individuals who reported as never smoking cigarettes.

Results

Among 3,495,777 individuals, 2.7% were classified as underweight with no metabolic abnormalities, 37.7% were classified as normal weight with no metabolic abnormalities, 25.7% were classified as overweight with no metabolic abnormalities, and 14.8% were classified as

obese with no metabolic abnormalities (Online Table 3). The prevalence of 3 metabolic abnormalities was rare regardless of the weight category, with underweight individuals having the lowest (0%) (Online Table 3). Metabolically healthy obese individuals were more likely to be younger, male, current smokers and socioeconomically deprived and compared with metabolically unhealthy obese individuals (**Table 1**).

There were 154,051 (4.4%) deaths and 1,182,658 (33.8%) patients transferred out of their general practice. Over a mean 5.4 year follow-up, there were 165,302 initial cardiovascular disease presentations: 61,546(37.2%) developed CHD, 54,705 (33.1%) developed cerebrovascular disease, 25,254 (15.3%) developed heart failure and 23,797 (14.4%) developed PVD. Incidence rates of cardiovascular disease events by body size phenotype and metabolic status are shown in Online Tables 5-7. Among initially metabolically healthy overweight individuals, approximately 1.9% developed diabetes, 9.4% developed hyperlipidemia, and 7.2% developed hypertension. Among initially metabolically healthy obese individuals, approximately 5.6% developed diabetes, 11.5% developed hyperlipidemia, and 10.4% developed hypertension.

The **Central Illustration** depicts the associations between the 14 body size phenotypes with or without metabolic abnormalities/ and cardiovascular disease events (CHD, cerebrovascular disease, heart failure, and PVD) with the normal weight 0 metabolic abnormalities group as the reference.

Coronary heart disease

Individuals who were overweight with 0 metabolic abnormalities (HR 1.30, 95% CI 1.27, 1.34) and obese with 0 metabolic abnormalities (HR 1.49, 95% CI 1.45, 1.54), had an increased risk of coronary heart disease, compared to normal weight individuals with no metabolic

abnormalities after adjustment for potential confounders (central illustration). Risk of coronary heart disease in the normal weight, overweight and obese groups increased with increased number of metabolic abnormalities (**Central Illustration**).

Cerebrovascular disease

Individuals who were underweight (HR 1.31, 95% CI 1.23, 1.40) and obese with 0 metabolic abnormalities (HR 1.07, 95% CI 1.04, 1.11) had an increased risk of cerebrovascular disease, compared to normal weight individuals with no metabolic abnormalities after adjustment for potential confounders (central illustration). Risk of cerebrovascular disease in the normal weight, overweight and obese groups increased with the increasing number of metabolic abnormalities (**Central Illustration**).

Heart failure

Individuals who were underweight (HR 1.36, 95% CI 1.23, 1.51), overweight with 0 metabolic abnormalities (HR 1.11, 95% CI 1.06, 1.16) and obese with 0 metabolic abnormalities (HR 1.96, 95% CI 1.86, 2.06) had an increased risk of heart failure, compared to normal weight individuals with no metabolic abnormalities after adjustment for potential confounders. (central illustration). Risk of heart failure in the normal weight, overweight and obese groups increased with increased number of metabolic abnormalities (**Central Illustration**).

Peripheral vascular disease

Individuals who were underweight had an increased risk of PVD (HR 1.49, 95% CI 1.36, 1.63), compared to normal weight individuals with no metabolic abnormalities after adjustment for potential confounders (central illustration). Individuals who were overweight with 0 metabolic abnormalities (adjusted HR 0.92, 95% CI 0.88, 0.96) and obese with 0 metabolic abnormalities (adjusted HR 0.91, 95% CI 0.86, 0.96) had a decreased risk of PVD compared to

normal weight individuals with no metabolic abnormalities (central illustration). Risk of PVD increased with the number of metabolic abnormalities in the normal weight, overweight and obese groups (central illustration).

Sensitivity analyses

We undertook several sensitivity analyses (Online Tables 8-15). There was some evidence that the risk of cerebrovascular disease in overweight and obese individuals without metabolic abnormalities, heart failure in overweight individuals without metabolic abnormalities, differed significantly by sex. Females had stronger positive associations with cerebrovascular disease and heart failure compared to males. There was some evidence that the risk of CHD, cerebrovascular disease, heart failure and PVD in overweight and obese individuals without metabolic abnormalities differed significantly by age. Individuals < 65 years had significantly stronger positive associations with CHD, cerebrovascular disease heart failure and PVD than individuals \geq 65 years. Among overweight and obese individuals without metabolic abnormalities, age-stratified analyses revealed significant positive associations with PVD. When metabolic status was derived from diagnostic codes or prescription records as well as laboratory/physical measurements, the magnitude of associations between the body size phenotypes and metabolic status with CHD, cerebrovascular disease, heart failure and PVD were generally larger (Online Tables 9, 11, 13, & 15). For metabolically healthy overweight or obese groups, the negative association with PVD became non-significant (Online Table 15). Further adjustment for HRT or oral contraceptives did not significantly change the estimates (Online Tables 9 & 11). Exclusion of participants with type 1 diabetes did not significantly alter the results (Online Tables 9, 11, 13, & 15). In analyses restricted to individuals who reported they never smoked cigarettes, individuals who were obese with no metabolic abnormalities obese, had

a significantly stronger positive association with PVD (Online Table 15). For individuals who were underweight, we repeated analyses only in those who reported they never smoked cigarettes. The results did not differ from the main results (Online Table 15).

Discussion

In this study of approximately 3.5 million individuals accruing 165,302 cardiovascular disease events during 5.4 years average follow-up, we showed that individuals who are obese and classified as metabolically healthy (either no metabolic abnormalities, 1 or 2) are still at an increased risk for CHD, cerebrovascular disease and heart failure compared with individuals who are normal weight with no metabolic risk factors. These associations were not dependent on participants' sex. Approximately, one in ten who were normal weight had metabolic abnormalities and had increased risks for CHD, cerebrovascular disease, heart failure and PVD compared to normal weight individuals without metabolic abnormalities.

Although three meta-analyses (9-11) have assessed the risks of cardiovascular disease for the MHO phenotype, these each had limitations. The meta-analysis of Kramer et al (10) demonstrated that MHO individuals had increased risk for cardiovascular disease events compared with metabolically healthy normal-weight individuals. However, their findings were controversial. The meta-analysis roughly merged cardiovascular disease events and all-cause mortality together to calculate the pooled risk estimates for MHO individuals. Another limitation of the meta-analysis was the fact that it did not adequately adjust for important baseline factors, including age, and sex. Similarly, in the meta-analysis of Fan et al (11), they did not differentiate cardiovascular disease events and all-cause death events separately, but merged them together to calculate the pooled risk estimate. Whereas, in our study we examined MHO with the incidence of specific cardiovascular disease events (i.e. CHD, cerebrovascular disease, heart failure and

PVD) based on validated electronic health records (17-19). We were also able to adjust for important baseline factors including age, sex, smoking status and socio-economic deprivation. Recently, Zheng et al (9) meta-analysis attempted to examine the association between MHO and cardiovascular disease events in only studies using the strictest definition for metabolic health (absence of all metabolic abnormalities). They found an insignificant association between MHO and cardiovascular disease events, however only 2 studies provided data and, as such, the statistical power was limited to detect significant associations. In our study, we had unprecedented statistical power to examine obese individuals classified by the number of metabolic abnormalities, potentially reflecting several definitions of the 'metabolically healthy' phenotype in relation to a range of cardiovascular disease events.

Being metabolically unhealthy, regardless of BMI, generally conferred increased risk for cardiovascular disease events and that normal weight status did not necessarily indicate metabolic health. Some individuals with normal weight have previously been reported to have elevated metabolic abnormalities (20,21). In the United States, the Preventive Services Task Force currently recommends that clinicians in primary care settings use overweight and obesity as the main criteria to screen adults for abnormal blood glucose as part of cardiovascular risk assessment (22). This could result in failure to identify metabolic abnormalities in many patients. Early detection and management of normal weight individuals with metabolic abnormalities may therefore be beneficial in the prevention of cardiovascular disease events. We found that underweight individuals had an increased risk of cerebrovascular disease, heart failure, and PVD. The impact of underweight on cardiovascular disease events has been understudied, with most previous research not evaluating the underweight individuals separately from normal weight individuals. (3,23) Excess risk for cardiovascular disease events associated with low BMI may

be related to smoking-related diseases such as chronic obstructive pulmonary disease (COPD) and lung cancer. To minimize this possibility, in a separate analyses we only examined the association between underweight with no metabolic abnormalities and cardiovascular disease events restricted to individuals who never reported smoking cigarettes. Underweight individuals with no metabolic abnormalities only had a significant risk for heart failure and PVD.

Our finding that obesity was associated with a lower risk of PVD was surprising, considering that it may influence the atherosclerotic process (24). Previous studies on the association between obesity and PVD have been inconsistent (16). In the Israeli Ischemic Heart Disease Project (25), those with new-onset intermittent claudication had a higher BMI than those who remained symptom free. Other large population-based studies however have failed to demonstrate that obesity increases risk for PVD (26-28), with some studies even reporting a reduction in risk for PVD (29-31). In the Framingham Study Cohort, relative weight was found to be inversely associated with intermittent claudication (30). One potential explanation for this is residual confounding by cigarette smoking (cigarette smoking is strongly associated with both PVD and lower BMI) (16). In sensitivity analyses, restricted to individuals who were obese with no metabolic abnormalities and reported never smoking cigarettes, risk for PVD was increased, compared to normal weight individuals with no metabolic abnormalities.

To the best of our knowledge, this is the largest prospective study of the association between body size phenotypes with or without metabolic abnormalities (including MHO) and a range of incident cardiovascular disease events, with unprecedented precision and power. Dividing our participants into four BMI groups according to the classification provided by World Health Organization, gave us the possibility of a more granular analysis of the CVD risk in the different body size phenotypes. Several limitations of our study however require careful

consideration. BMI has many advantages as a surrogate of body fat, such as simplicity and reproducibility (32) however we are unable to distinguish differences between high percentage of body fat and preserved or increased lean mass, particularly in participants with a BMI <30 kg/m². Even though patients registered in THIN are representative of the general UK adult population (12), persons with a BMI measurement might not necessarily be representative of the general population. BMI data if not recorded at registration, tends to be opportunistically recorded (i.e. recorded when the patient is attending for other reasons or when the matter is of direct clinical importance). We limited this possibility by only using the first BMI recorded from the registration date (because they would have probably been recorded for administrative and not health reasons). Our findings are drawn from baseline measurements of BMI and metabolic abnormalities. Considering the difficulty in losing weight, it is more likely that individuals transition to higher weight (i.e. normal weight/overweight to obese) categories than transition to lower weight categories (i.e. obese to overweight/normal weight) (10). Thus, the potential misclassification effect of changes in weight over time was probably conservative. In our study, a small proportion of individuals who were initially metabolically healthy overweight or obese did progress to metabolically unhealthy overweight or obesity. Therefore, due to changes in metabolic abnormalities, a degree of misclassification, did occur. We did not have access to appropriate data on diet or physical activity, and therefore could not examine for example, whether physical activity could modify the association between metabolically healthy obese and incident cardiovascular disease. Patients were defined as having diabetes or hypertension utilizing diagnostic codes and hyperlipidemia was defined utilizing prescription codes. Given that a proportion of individuals with metabolic abnormalities may be undiagnosed in the UK (33,34) we used available measures of HbA1c, blood pressure and serum lipids to minimize

misclassification error. Additionally, given that improvement of glycemic, blood pressure, or lipid control obtained through treatment can prevent cardiovascular disease events in the long term, we may therefore expect that optimally treated/controlled patients would have a reduced risk of developing a cardiovascular disease events compared to those who are uncontrolled, and therefore our HR estimates would be conservative.

Taking into consideration the genetic heterogeneity related to obesity (35), it is not implausible to assume that a distinct, benign phenotype in terms of CVD risk may be present. Of the body size phenotypes, MHO has been the most commonly examined phenotype (36), and it has been suggested that the concept of metabolically healthy obesity might be important in the stratification of individuals in the clinical treatment of obesity (36). Some researchers have called for a shift in the public health focus away from markers of adiposity such as BMI (37) and suggest that health providers prescribing weight loss interventions may be misusing time and resources. (38) Our study robustly challenges the assertion that MHO is a benign condition and adds to the evidence base that MHO is a high-risk state for future cardiovascular disease events.

Conclusions

Individuals who are obese with no metabolic abnormalities are at higher risk of coronary heart disease, cerebrovascular disease and heart failure than normal weight metabolically healthy persons Clinicians need to be aware that individuals who would otherwise be considered non-obese, based on a normal BMI, can have metabolic abnormalities, and therefore also be at high risk for cardiovascular disease events.

Perspectives

Competency in patient care and medical knowledge: Metabolically healthy obesity is a unique body size phenotype that apparently protects people from the metabolic complications of obesity including cardiovascular disease. However, whether these individuals are truly at less risk of cardiovascular disease has remained controversial. Our study of 3.5 million electronic primary care records suggest individuals who are obese and classified as metabolically healthy (either no metabolic abnormalities, 1 or 2) are still at an increased risk for coronary heart disease, cerebrovascular disease and heart failure compared with individuals who are normal weight with no metabolic risk factors. Individuals who are normal weight can also have metabolic abnormalities, and be at high risk for cardiovascular disease events.

Translational Outlook: Large and long-term cohort trials are still required to determine the effect of weight loss on risk of developing cardiovascular disease events among metabolically healthy obese individuals.

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Figure Legend

Central Illustration: Association of body size phenotypes and metabolic status with cardiovascular disease events in 3.5 million UK adults. Analyses adjusted for age, sex, smoking status and social deprivation. The reference category is normal weight, 0 metabolic abnormalities.

Table 1 Baseline characteristics of the study population, by body size phenotypes and metabolic health status

	Underweight	Normal weight	Overweight	Metabolically healthy and obese*	Metabolically unhealthy and obese[†]
Mean age (SD), (years)	38.0 (20.3)	41.3 (17.6)	47.7 (16.6)	42.6 (13.8)	58.6 (12.6)
Sex					
Male	24,753 (26.3)	547,600 (37.0)	603,492 (52.1)	301,974 (58.4)	114,196 (46.6)
Female	69,276 (73.7)	932,626 (63.0)	555,324 (47.9)	215,470 (41.6)	131,066 (53.4)
Smoking status					
Never smoker	51,614 (54.9)	842,573 (56.9)	637,442 (55.0)	284,510 (55.0)	133,878 (54.6)
Ex- smoker	10,075 (10.7)	235,766 (15.9)	257,903 (22.3)	109,051 (21.1)	73,015 (29.8)
Current smoker	32,340 (34.4)	401,887 (27.2)	263,471 (22.7)	123,883 (23.9)	38,369 (15.6)
Social deprivation quintile					
1 (least deprived)	16,736 (17.8)	352,906 (23.8)	295,984 (25.5)	110,089 (21.3)	54,712 (22.3)
2	16,119 (17.1)	303,729 (20.5)	256,192 (22.1)	104,285 (20.2)	52,844 (21.6)
3	20,083 (21.4)	318,076 (21.5)	248,836 (21.5)	114,512 (22.1)	53,628 (21.9)
4	22,583 (24.0)	293,845 (19.9)	212,177 (18.3)	108,679 (21.0)	49,278 (20.1)
5 (most deprived)	18,508 (19.7)	211,670 (14.3)	145,627 (12.6)	79,879 (15.4)	34,800 (14.2)
Mean BMI (SD), kg/m ²	17.4 (1.0)	22.3 (1.7)	27.2 (1.4)	34.4 (4.5)	34.9 (4.8)

BMI= body mass index

* Obese with 0 metabolic abnormalities

[†]Obese with 1 or more metabolic abnormalities