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Modeling anthropometric indices in relation to 10-year (2002-2012) incidence of cardiovascular disease, among apparently healthy individuals: the ATTICA study

Short title: Anthropometric indices and CVD

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ABSTRACT

Aims: Body fat accumulation is implicated in the development of cardiovascular disease (CVD). Our objective was to explore potential associations between anthropometric indices and the 10-year CVD incidence in Greek adults without previous CVD.

Methods: During 2001-2, we enrolled 3042 adults without CVD from the general population of Attica, Greece. In 2011-2, the 10-year study follow-up was performed, recording the CVD incidence in 1958 participants with baseline body mass index (BMI) ≥18.5 kg/m^2.

Results: The study 10-year CVD incidence was 15.8%, exhibiting a gradual increase according to the baseline body mass index (BMI) category. Baseline BMI ≥30 kg/m^2 was related with significantly higher 10-year CVD risk compared to BMI <25 kg/m^2, even after adjustment for age and other known CVD risk factors. Baseline BMI, waist circumference, waist-to-hip ratio, waist-to-height ratio and waist-to-hip-to-height ratio were independently associated with the 10-year CVD risk in multi-adjusted models. Gender-specific analyses showed that these associations were more evident in men compared to women, with baseline BMI exhibiting an independent association with the 10-year CVD incidence in men.

Conclusions: Our results indicate that even simple anthropometric indices exhibit independent associations with CVD risk in a representative sample of the Greek general population without previous CVD.

Key words: anthropometric indices; cardiovascular disease; body mass index; waist circumference; obesity

1. INTRODUCTION

Obesity has reached epidemic proportions and is accompanied by a spectrum of deleterious health and socio-economic consequences[1]. More than one-third of the adults in the US is obese (body mass index, BMI ≥30 kg/m^2), with the annual medical costs per obese person being $1,429 higher than that of normal-weight individuals[2]. The ATTICA study cohort has also revealed increasing prevalence rates of overweight (53% and 31% in men and women, respectively) and obesity (20% and 15% in men and women, respectively) in the general population of Attica prefecture (Greece)[3,4].

In parallel to these obesity trends, cardiovascular disease (CVD) prevalence rates have been also increasing, posing a major public health problem with a serious economic impact. Indeed, CVD is the leading cause of death globally, accounting for more than 17.3 million deaths per year and producing a total cost greater than $316.6 billion[5]. Not surprisingly, obesity constitutes one of the key CVD risk factors, with adipose tissue distribution playing a vital pathogenetic role[6]. This strong pathogenetic association has raised the question about whether non-invasive, simple measures/indices of adiposity, which are easily obtained in everyday clinical practice (*e.g.* BMI, waist circumference and waist-to-hip ratio), can be used to reliably identify individuals with high long-term CVD risk. Such simple anthropometric indices have a well-established association with increased risk of insulin resistance, type 2 diabetes mellitus (T2DM), hyperlipidemia and hypertension[7]. Hence, anthropometric indices are generally considered as CVD risk indicators. However, BMI, which is a crude measure of total body adiposity, or other simple anthropometric indices are not included in traditional CVD risk models, such as the Framingham risk score (FRS)[8,9]. Moreover, even less evidence exists from large, prospective studies on the exact associations between simple anthropometric indices and the long-term CVD risk in Mediterranean (South European) populations.

The objective of the present work was to assess, in the context of the ATTICA study[10], the potential associations between anthropometric indices obtained at the entry/baseline study examination and the 10-year CVD incidence in the study cohort consisting of Greek adults from the general population without previous CVD.

SUBJECTS, MATERIALS AND METHODS

2.1 Study design

The "ATTICA" study is a population-based health and nutrition survey carried out in the province of Attica (including 78% urban and 22% rural areas), Greece, during 2001-02[10]. Briefly, the study sampling was designed to enroll only one participant per household through a random, multistage process based on the age and sex distribution of the Attica region (2001 Census). A total of 4056 adults (≥18 years) were randomly selected, of which 3042 (1514 men; 1528 women) consented to participate (75% participation rate). All participants were interviewed/examined by trained personnel (cardiologists, other physicians, dieticians and nurses), as per study protocol. Individuals with evidence/history of CVD or living in institutions were excluded, as previously described[10].

The study was approved by our Institutional Review Board and was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. All participants were informed about the study aims/procedures and provided their consent before any study procedures.

2.2 Baseline measurements

At baseline, socio-demographic characteristics (age, sex, mean annual income and years of education), detailed medical history, dietary and other lifestyle habits, (*e.g.* smoking and physical activities) were recorded. Smoking was defined as smoking of at least one cigarette per day during the past year or recent discontinuation (during the previous year). Moreover, height, without shoes, was measured to the nearest 0.5 cm and body weight to the nearest 100 g, without shoes and with light clothing. BMI was calculated as weight (in kilograms, *Kg*) divided by the height (in meters, *m*) squared. According to the World Health Organization (WHO) obesity classification, normal weight, overweight and obesity were defined based on BMI as: BMI: 18.5-24.9 kg/m^2; 25-29.9 kg/m^2; and ≥30 kg/m^2, respectively[11]. Waist circumference was also measured on bare skin during mid-respiration between the 10th rib and the iliac crest, whilst hip girth was measured at the maximal circumference of the buttocks[10]. Waist-to-hip ratio (WHR), waist-to-height ratio (WHtR) and waist-to-hip-to-height ratio (WHHR) was calculated as waist circumference divided by hip circumference, or height, or both, respectively.

Arterial blood pressure was measured three times at the end of the physical examination with the participants at the sitting position for at least 30 minutes. Patients with average blood pressure levels ≥140/90 mmHg were classified as having hypertension, as those on antihypertensive drugs. Hypercholesterolemia was defined as total serum cholesterol levels >200 mg/dl or the use of lipid-lowering agents. Diagnosis of T2DM was based on the American Diabetes Association (ADA) criteria, *i.e.*, fasting blood glucose >125 mg/dL or the use of antidiabetic medication[12].

2.3 10-year follow-up

During 2011-12, the 10-year follow-up of the ATTICA study was performed (median follow-up time 8.41 years), as previously described[13]. Briefly, of the 3042 participants at baseline, 2583 were found in the follow-up (85% participation rate). For the participants who died during the follow-up, the relevant data were obtained from their relatives and medical notes/death certificates. The definition of the study outcomes was based on the International Classification of Diseases (ICD) 10th revision, and CVD data were collected for the development of: (a) myocardial infarction, angina pectoris, other identified forms of ischemia; coronary revascularization (*i.e.*, coronary artery bypass surgery and percutaneous coronary intervention); (b) heart failure of different types and chronic arrhythmias; and (c) stroke. Regarding CVD evaluation at follow-up, complete data were obtained from 2020 participants, of whom 62 participants with baseline BMI <18.5 kg/m^2 were excluded to avoid reverse causality, yielding a study sample of *n*=1958 participants (men/women: 985/973; 45.4±13.8 years; with no differences regarding the age-sex distribution of this follow-up sample and the baseline; p's >0.80).

2.4 Statistical analysis

Continuous variables are presented as mean values ± standard deviation (SD) and categorical variables as frequencies. The likelihood for CVD development (dependent outcome) during the 10-year period, according to the participants' baseline anthropometric indices and the baseline socio-demographic, lifestyle and clinical characteristics (independent factors), was estimated using the odds ratio and their corresponding 95% confidence intervals (CIs) through multi-adjusted logistic regression models. Similarly, the likelihood for CVD development (dependent

outcome) during the 10-year period, according to the participants' baseline body weight category and the baseline socio-demographic, lifestyle and clinical characteristics (independent factors), was estimated using the odds ratio and their corresponding 95% CIs through multiple logistic regression analysis. Moreover, survival analyses using Cox Proportional Hazard models were also applied showing similar results (data not shown, as the results from the logistic models showed better goodness-of-fit). The predictive abilities of the anthropometric indices were ranked by calculating the -2log-likelihood of each model (i.e., the lower the better). All reported *p*-values are based on two-sided tests. The SPSS version 21 (Statistical Package for Social Sciences, SPSS Inc, Chicago, IL, U.S.A.) software was used for all statistical calculations.

2. RESULTS

2.1 Baseline anthropometric indices and 10-year CVD incidence

The key baseline characteristics of the study sample (*n*=1958) are presented in Table 1. The overall CVD incidence during the 10-year follow-up period was 15.8% (*n*=310), being significantly higher in men [19.7% (*n*=194)] than women [11.9% (*n*=116)] (*p* for gender difference <0.001).

In the total study sample (*n*=1958), BMI, waist circumference, WHR, WHtR and WHHR were associated with the 10-year CVD incidence in an age-adjusted model (Table 2, *Model 1*), as well as in a model that included age, established CVD risk factors (smoking, diabetes, hypertension and hypercholesterolemia), educational status (years of school) and physical activity status (Table 2, *Model 2*). Then, the anthropometric indices were analyzed separately for men and women. An independent of age association between the 10-year CVD incidence and BMI, waist circumference, WHR, WHtR and WHHR was observed in men (Table 2, *Model 1*). In men, the independent association between BMI and the 10-year CVD incidence remained even after further adjustment for other known CVD risk factors (*i.e.,* smoking, hypertension, hypercholesterolemia, diabetes, educational and physical activity status) (Table 2 *Model 2*). Contrary, in women, while the odds ratios were indicative of a positive association, no significant independent associations between the baseline anthropometric indices and the 10-year CVD incidence was observed (Table 2). Between all investigated anthropometric indices, WHR, WHHR and waist circumference had the greater predictive ability (as evaluated with the lower -Log

likelihood (L) values) regarding the 10-year CVD risk in the total sample, as well as in men and women (Tables 2).

2.2 Baseline BMI categories and 10-year incidence of CVD

A progressive increase of the 10-year CVD incidence according to the baseline body weight status (9.7%, 18.5% and 23.7% for BMI in the normal-weight, overweight and obese range, respectively) was observed in the study sample (p for trend <0.001). This progressive increase was evident in both men and women (Figure 1).

In the total sample, obesity (BMI ≥30 kg/m^2) compared to non-obese status (BMI <30 kg/m^2) or to normal BMI status (BMI: 18.5-24.9 kg/m^2), as well as overweight (BMI 25-29.9 kg/m^2) compared to normal BMI status, were associated with significantly increased 10-year CVD incidence independently of age (Table 3, *Model 1*). Additionally, in the total sample the baseline obesity status (BMI ≥30 kg/m^2) compared to normal BMI (18.5-24.9 kg/m^2) or to non-obese status (BMI <30 kg/m^2) was independently associated with increased incidence of 10-year CVD events in a multivariate model that included age, smoking, hypertension, hypercholesterolemia, diabetes, educational and physical activity status (Table 3, *Model 2*). The independent of age increased incidence of 10-year CVD incidence with baseline obesity status (BMI ≥30 kg/m^2) compared to normal baseline BMI (18.5-24.9 kg/m^2) was evident in men (Table 3, *Model 1*). In multivariate models, the odds ratios of overweight and obesity status compared to normal BMI were indicative of a positive association with the 10-year CVD incidence, but without reaching statistical significance in either genders (Table 3, *Model 2*).

3. DISCUSSION

Herein, we present novel prospective data from the ATTICA study regarding the associations between anthropometric indices at the study baseline and the 10-year CVD incidence in a representative sample of the Greek general population without known CVD. As expected, we observed a gradual increase of the documented 10-year CVD incidence according to the baseline BMI class in both genders, Importantly, BMI, waist circumference, WHR, WHtR and WHHR were independently associated with the 10-year CVD incidence even in multivariate models including other known CVD risk factors.

These findings are in accord with the reported results from previous cohorts, showing an independent association between baseline BMI and long-term CVD incidence[14]. In the Framingham cohort study, which followed patients aged 28-62 years for a mean of 26 years, the group with increased body weight had higher coronary heart disease (CHD) risk compared with the leanest group, independently of age, cholesterol, systolic blood pressure, smoking, left ventricular hypertrophy and glucose intolerance[15]. Moreover, our findings are further supported by meta-analysis data. Indeed, a meta-analysis that included over one million participants and 37488 incident CHD cases showed that higher BMI was significantly associated with the age-adjusted CHD risk [age-adjusted hazard ratio (HR) in the overweight group 1.20 (95% CI 1.12–1.29) in women, and 1.22 (95% CI 1.12-1.32) in men; and in the obese group: 1.61 (95% CI 1.42-1.82) in women, and 1.60 (95% CI 1.43-1.79) in men, compared to the normal weight group][16]. Notably, a recent meta-analysis, including participants from 189 studies (n=3,951,455) who were never-smokers, did not have chronic diseases at recruitment and have survived 5 years, showed that a BMI >25 kg/m^2 is associated with increased CHD mortality [HR 1.42 (95% CI: 1.35-1.49) per 5 kg/m^2 higher BMI][17].

It is well-established that obesity increases CVD risk indirectly through the development of diabetes, hypertension, hyperlipidemia, and metabolic syndrome[18]. Indeed, the prevalence of hypertension is increased in both men and women with BMI ≥30 kg/m^2 compared to normal weight individuals, due to multiple factors, including increased systemic vascular resistance, low-grade inflammation, insulin resistance, hyperinsulinemia, sympathetic nervous system overactivity and disordered sleep[19-21]. Similarly, dyslipidemia is more frequent among patients with increased body weight, with increased fasting triglycerides and low-density lipoprotein cholesterol levels, as well as low high-density lipoprotein cholesterol levels. Of note, obesity is further associated with the development of the small dense LDL phenotype and postprandial hyperlipidemia, leading to accumulation of atherogenic remnants and hepatic overproduction of apolipoprotein B-containing lipoproteins[22]. Moreover, increased body weight is associated with the development of insulin resistance, promoting an enhanced hepatic flux of free fatty acids to the liver, a mechanism that also links obesity, to dyslipidemia and other metabolic syndrome manifestations[23]. Finally, the association of increased body weight with T2DM has also been well-documented, with data from the prospective Secondary Manifestations of ARTerial disease

(SMART) cohort study showing that patients with increased BMI have higher T2DM risk compared to normal-weight subjects, even in the absence of concurrent metabolic dysfunction [HR: 2.5 (95% CI 1.5-4.2) for overweight and HR 4.3 (95% CI 2.2-8.6) for patients with obesity][24].

The results of our multi-adjusted analyses, that included other known CVD risk factors such as hypertension, hypercholesterolemia, smoking and diabetes, further highlight the independent role of increased BMI and other anthropometric indices in CVD development. Increased body weight, in addition to the aforementioned indirect effects, also affects directly the cardiovascular system. This is potentially mediated via structural/functional changes of the heart, ectopic adipose tissue deposition and other less well-known obesity-related mechanisms (*e.g.* detrimental CVD effects of various adipokines)[6,25,26]. Notably, obesity-related heart changes include left ventricular chamber dilation, concentric remodeling and concentric left ventricular hypertrophy and left atrial enlargement[27]. These abnormalities have adverse effects on diastolic and systolic function, and increase the risk of both heart failure and of atrial fibrillation and ventricular arrhythmias[28-30]. Moreover, obesity accelerates the atherosclerotic process, even from a young age. Indeed, autopsy data in young subjects (15-34 years) who died from accidental causes have shown that the extent of plaques and ulceration in the coronary arteries and abdominal aorta correlates with BMI and abdominal fat [Pathobiological Determinants of Atherosclerosis in Youth (PDAY) study][31]. Furthermore, obesity is the strongest factor linked to non-ST elevation myocardial infarction (NSTEMI) events in younger patients[32], with data showing that as BMI increases NSTEMI and ST-elevation myocardial infarction (STEMI) events are presented in patients with lower mean age[32,33]. Finally, obesity is also linked to increased incidence of ischemic stroke, as well as to arrhythmias and sudden cardiac death[28,34]. These effects could also be mediated by the prothrombotic (higher levels of plasminogen activator inhibitor-1 antigen and activity, fibrinogen, von Willebrand factor, and factor VII) and the proinflammatory state (increased levels of C-reactive protein and adipokines/cytokines) observed in obese patients[35,36].

Our analyses showed that WHR, WHHR, and waist circumference had the greater predictive ability between anthropometric indices regarding the 10-year CVD risk. These anthropometric indices indicate more precisely the fat distribution (visceral vs. subcutaneous) than body weight and BMI. Visceral fat accumulation is associated with accumulation of atherosclerotic risk factors, such as hyperlipidemia,

hypertension and metabolic syndrome as well as increased risk of T2DM[37-40]. Notably, the measures of fat distribution had similar odds ratios, a finding indicating that in clinical practice the measurement of waist circumference, which is easily obtained and followed, is not inferior than other more sophisticated measures (WHHR or WHtR). Moreover, in the whole sample the measures of fat distribution had comparable odds ratios with BMI (a crude measure of adiposity), but in men they were not independently associated with CVD risk compared to BMI. This difference may indicate that the association of measures of fat distribution with CVD may be mediated mainly through the development of comorbidities and accumulation of CVD risk factors, whereas total adiposity indices may indicate the presence of additional mechanisms that increase CVD risk (discussed above).

It is important to highlight that we observed stronger correlations of anthropometric indices with the 10-year CVD incidence in men compared with women. This observation may reflect the effects of abdominal fat distribution, since females have a higher proportion of subcutaneous fat and lower visceral fat compared to males, leading to different associations with cardiovascular risk factors[41]. Additionally, it may also be in part attributed to the significantly lower CVD events that we noted in women, making more difficult any differences in this sample to reach statistical significance. Generally, CVD events in women are observed in an older age compared with men and this effect may play a role in our study findings. This delayed CVD risk in women is at least partly attributed to the protective effects of exposure to endogenous oestrogens during the pre-menopausal period of life which appears to delay the atherosclerotic process[42].

Overall, the fact that simple anthropometric indices, such as BMI or waist circumference, are associated with long-term CVD incidence in our study cohort supports the notion that the clinical practice should utilize available indices of total and central adiposity as useful markers of increased CVD risk in the general population from Mediterranean (South Europe) countries, particularly in men. As such, despite their shortcomings as obesity indexes, simple anthropometric indices can be easily obtained/followed and, hence, could be useful for CVD risk estimation in the general population. Of note, traditional models such as the Framingham risk score (FRS) or the Systematic COronary Risk Evaluation (SCORE) risk charts include multiple parameters (*e.g.* cholesterol) but not BMI or waist circumference in their equations[8,9]. Interestingly, a recent analysis of 17791 men and women who

participated in the National Research Program 1A (NRP1A) and the Swiss Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) population survey showed that compared to cholesterol, the use of BMI in the study models revealed higher CVD risk at all ages, and could better discriminate persons at high and low CVD risk[43]. Moreover, other authors using electronic health records reported that using BMI instead of cholesterol resulted in at least equivalent CVD risk estimation[44]. Thus, the use of simple anthropometric indices as CVD risk indicators may aid clinicians to readily and reliably identify subjects at higher risk and reduce laboratory testing.

STRENGTHS AND LIMITATIONS OF THE STUDY

The present work is the first prospective study assessing the effect of simple anthropometric indices on the long-term (10-year) CVD incidence in a large sample of the Greek population without previous CVD (reflecting approximately 70% of the total Greek population; a population considered, at least to a certain extent, similar to those of other Southern/Mediterranean European countries). In addition, the design and extended protocol of the ATTICA study allowed the detailed capture of multiple factors associated with CVD (socio-demographic, lifestyle, clinical and biological) and permitted the analytical evaluation of baseline anthropometric indices on multivariate models that included most of the known CVD risk factors.

Our study has also certain limitations. The baseline anthropometric indices were measured once, thus a measurement error may exist. Additionally, anthropometric indices may change over time and this cannot be incorporated in the presented analyses. However, the study protocol was designed to enrol at baseline subjects with rather stable dietary habits and without significant recent body weight changes, thus the captured baseline anthropometric indices in this study represent in a significant degree the participants' usual values. The study sample consisted only of adults living in the greater Athens metropolitan area, which is mainly an urban region and, therefore, cannot entirely represent the Greek population living in more rural regions.

4. CONCLUSION

Simple anthropometric indices at the baseline/entry ATTICA study examination are positively and independently associated with the 10-year CVD incidence in a cohort of adults from the general population without previous CVD.

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CONFLICTS OF INTEREST: None to declare.

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FIGURE LEGENDS

Figure 1. The 10-year cardiovascular disease (CVD) incidence in the ATTICA study (2001-2 to 2011-2; Attica, Greece) according to the baseline body mass index [BMI (kg/m^2)] category.

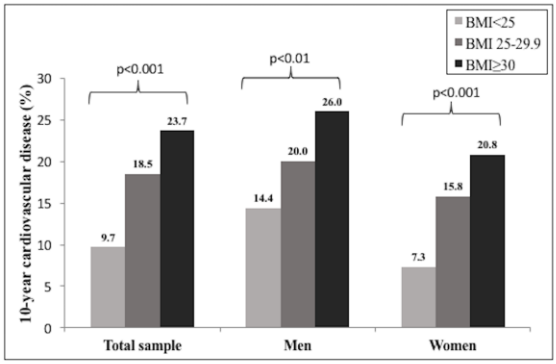

Table 1. Anthropometric and clinical characteristics of the study sample (*n*=1958) at the baseline/entry examination of the ATTICA study (Attica, Greece).

Age (years)	45.4±13.8
Gender (men/women)	985/973
Smoking [n (%)]	1077 (55)
Education (years of school)	12.2±3.8
Body weight (kg)	75.9±15.2
Body mass index (kg/m^2)	26.5±4.4
Waist circumference (cm)	90.8±14.4
Waist-to-hip ratio (cm/cm)	0.87±0.10
Waist-to-height ratio (cm/cm)	0.54±0.08
Waist-to-hip-to-height ratio (cm/cm/m)	0.51±0.06
Diabetes [n (%)]	144 (7.4)
Hypertension [n (%)]	590 (30.1)
Hypercholesterolemia [n (%)]	843 (40.1)

Table 2. Results from multiple logistic regression models*, evaluating the effect of anthropometric (per 1 unit or per 1 SD) indices at baseline in relation to the 10-year incidence of cardiovascular disease.

Variable	**Model (-2logL)**	**Odds ratio (95% CI)** all subjects (*n*=1958)		**Model (-2logL)**	**Odds ratio (95% CI)** men (*n*=985)		**Model (-2logL)**	**Odds ratio (95% CI)** women (*n*=985)	
Body weight	Model 1	Per 1 kg 1.02 (1.01-1.03)	Per 1 SD 1.44 (1.24-1.67)	Model 1	Per 1 kg 1.02 (1.00-1.03)	Per 1 SD 1.25 (1.04-1.50)	Model 1	Per 1 kg 1.02 (0.99-1.03)	Per 1 SD 1.22 (0.98-1.52)
	Model 2 (1252)	Per 1 kg 1.02 (1.01-1.03)	Per 1 SD 1.35 (1.16-1.58)	Model 2 (726)	Per 1 kg 1.01 (1.00-1.03)	Per 1 SD 1.20 (1.00-1.44)	Model 2 (510)	Per 1 kg 1.02 (0.99-1.03)	Per 1 SD 1.20 (0.96-1.50)
Body mass index	Model 1	Per 1 kg/m^2 1.06 (1.03-1.09)	Per 1 SD 1.29 (1.13-1.47)	Model 1	Per 1 kg/m^2 1.06 (1.02-1.11)	Per 1 SD 1.25 (1.06-1.49)	Model 1	Per 1 kg/m^2 1.04 (0.99-1.09)	Per 1 SD 1.20 (0.97-1.49)
	Model 2 (1260)	Per 1 kg/m^2 1.05 (1.02-1.09)	Per 1 SD 1.24 (1.08-1.43)	Model 2 (725)	Per 1 kg/m^2 1.05 (1.00-1.10)	Per 1 SD 1.21 (1.00-1.45)	Model 2 (511)	Per 1 kg/m^2 1.03 (0.98-1.08)	Per 1 SD 1.16 (0.92-1.47)
Waist circumference	Model 1	Per 1 cm 1.03 (1.02-1.04)	Per 1 SD 1.43 (1.24-1.66)	Model 1	Per 1 cm 1.02 (1.00-1.04)	Per 1 SD 1.27 (1.05-1.54)	Model 1	Per 1 cm 1.01 (0.99-1.03)	Per 1 SD 1.17 (0.93-1.48)
	Model 2 (1221)	Per 1 cm 1.02 (1.00-1.03)	Per 1 SD 1.30 (1.09-1.54)	Model 2 (711)	Per 1 cm 1.01 (0.99-1.03)	Per 1 SD 1.11 (0.90-1.38)	Model 2 (489)	Per 1 cm 1.01 (0.99-1.03)	Per 1 SD 1.14 (0.88-1.48)
Waist-to-hip ratio	Model 1	*Not applicable*	Per 1 SD 1.46 (1.27-1.69)	Model 1	*Not applicable*	Per 1 SD 1.27 (1.05-1.54)	Model 1	*Not applicable*	Per 1 SD 1.13 (0.91-1.40)
	Model 2 (1213)	*Not applicable*	Per 1 SD 1.33 (1.14-1.55)	Model 2 (709)	*Not applicable*	Per 1 SD 1.15 (0.94-1.41)	Model 2 (485)	*Not applicable*	Per 1 SD 1.07 (0.85-1.36)
Waist-to-height ratio	Model 1	*Not applicable*	Per 1 SD 1.34 (1.15-1.55)	Model 1	*Not applicable*	Per 1 SD 1.26 (1.04-1.53)	Model 1	*Not applicable*	Per 1 SD 1.18 (0.92-1.49)
	Model 2 (1225)	*Not applicable*	Per 1 SD 1.21 (1.03-1.43)	Model 2 (711)	*Not applicable*	Per 1 SD 1.11 (0.89-1.37)	Model 2 (489)	*Not applicable*	Per 1 SD 1.13 (0.87-1.46)
Waist-to-hip-to-height ratio	Model 1	*Not applicable*	Per 1 SD 1.36 (1.17-1.59)	Model 1	*Not applicable*	Per 1 SD 1.26 (1.03-1.54)	Model 1	*Not applicable*	Per 1 SD 1.13 (0.89-1.44)
	Model 2 (1219)	*Not applicable*	Per 1 SD 1.24 (1.05-1.46)	Model 2 (710)	*Not applicable*	Per 1 SD 1.14 (0.92-1.41)	Model 2 (485)	*Not applicable*	Per 1 SD 1.05 (0.80-1.37)

Model 1: Adjusted for age, and sex. Model 2: Adjusted for age, cardiovascular disease risk factors (smoking, diabetes, hypertension and hypercholesterolemia), educational status (years of school) and physical activity status. SD: standard deviation. *Results of logistic regression models are presented as odds ratios and the corresponding confidence interval.

Table 3. Results from multiple logistic regression models*, evaluating the associations of the body mass index (BMI) category at baseline in relation to the 10-year incidence of cardiovascular disease in all subjects (*n*=1958).

		BMI <30 kg/m^2	BMI ≥30 kg/m^2	BMI <25 kg/m^2	BMI 25-29.9 kg/m^2	BMI ≥30 kg/m^2
All subjects (*n*=1958)	*Model 1*	Ref	1.48 (1.09-2.01)	Ref	1.49 (1.08-2.06)	1.89 (1.31-2.72)
	Model 2	Ref	1.42 (1.03-1.97)	Ref	1.29 (0.92-1.81)	1.68 (1.14-2.49)
Men (*n*=985)	*Model 1*	Ref	1.46 (0.99-2.17)	Ref	1.24 (0.79-1.94)	1.70 (1.03-2.82)
	Model 2	Ref	1.37 (0.90-2.09)	Ref	1.11 (0.69-1.79)	1.48 (0.86-2.53)
Women (*n*=973)	*Model 1*	Ref	1.40 (0.84-2.31)	Ref	1.28 (0.77-2.13)	1.60 (0.91-2.80)
	Model 2	Ref	1.36 (0.80-2.31)	Ref	1.16 (0.67-2.00)	1.49 (0.81-2.73)

Model 1: Adjusted for age. Model 2: Adjusted for age, cardiovascular disease risk factors (smoking, diabetes, hypertension and hypercholesterolemia), educational status (years of school) and physical activity status. SD: standard deviation. *Results of logistic regression models are presented as odds ratios and the corresponding confidence interval.