Comparison of Body Mass Index, Waist Circumference, and Waist/Hip Ratio in Predicting Incident Diabetes: A Meta-Analysis

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Body mass index, waist circumference, and waist/hip ratio have been shown to be associated with type 2 diabetes. From the clinical perspective, central obesity (approximated by waist circumference or waist/hip ratio) is known to generate diabetogenic substances and should therefore be more informative than general obesity (body mass index). Because of their high correlation, from the statistical perspective, body mass index and waist circumference are unlikely to yield different answers. To compare associations of diabetes incidence with general and central obesity indicators, the authors conducted a meta-analysis based on published studies from 1966 to 2004 retrieved from a PubMed search. The analysis was performed with 32 studies out of 432 publications initially identified. Measures of association were transformed to log relative risks per standard deviation (pooled across all studies) increase in the obesity indicator and pooled using random effects models. The pooled relative risks for incident diabetes were 1.87 (95% confidence interval (CI): 1.67, 2.10), 1.87 (95% CI: 1.58, 2.20), and 1.88 (95% CI: 1.61, 2.19) per standard deviation of body mass index, waist circumference, and waist/hip ratio, respectively, demonstrating that these three obesity indicators have similar associations with incident diabetes. Although the clinical perspective focusing on central obesity is appealing, further research is needed to determine the usefulness of waist circumference or waist/hip ratio over body mass index.

body fat distribution; body mass index; diabetes mellitus, type 2; meta-analysis; obesity; waist-hip ratio

Abbreviations: BMI, body mass index; CI, confidence interval; RR, relative risk; SD, standard deviation; WC, waist circumference; WHR, waist/hip ratio.

INTRODUCTION

Obesity has become a major worldwide epidemic affecting more than 300 million people. It is an important risk factor for diabetes mellitus, type 2, a chronic disorder of carbohydrate, fat, and protein metabolism. From the clinical perspective, visceral adipose tissue is known to generate diabetogenic substances (1) and, as such, may be more informative than total fat for diagnostic evaluation. The standard epidemiologic translation of these important clinical facts uses anthropometric measures. Waist circumference and waist/hip ratio have been used as measures of central obesity (where visceral adipose tissue is stored), and body mass index (kg/m^2) has been used as a measure of general obesity (2).

Clinical evidence suggests that the association of diabetes with central obesity is stronger than the association with general fat. Studies using computed tomography and magnetic resonance imaging have provided further evidence to support that central obesity, visceral adipose tissue, and upper-body nonvisceral fat are the major contributors to the metabolic complications (3–6). Central obesity has been associated with decreased glucose tolerance, alterations in glucose insulin homeostasis, reduced metabolic clearance of insulin, and decreased insulin-stimulated glucose disposal.

In addition, studies that have analyzed the association of anthropometric measures and abdominal visceral fat have found waist circumference to be a better measure of central obesity because it is a better predictor of abdominal visceral fat obtained with computed tomography than is waist/hip

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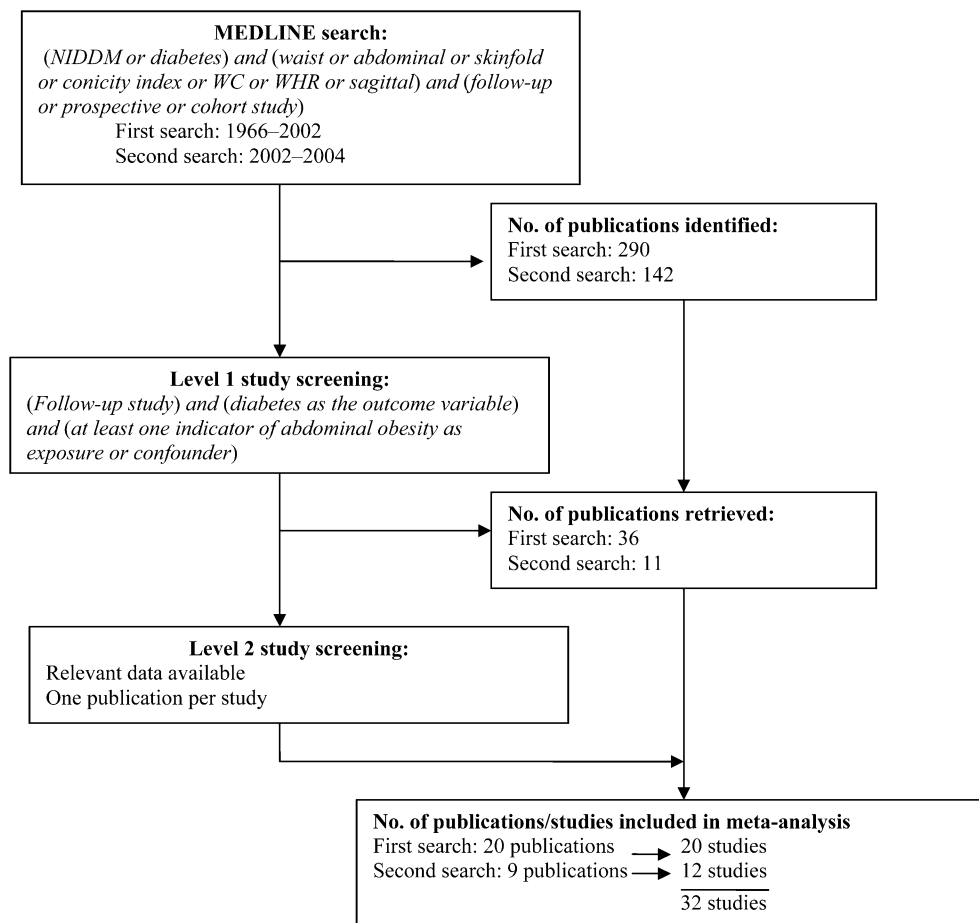
FIGURE 1. Study selection diagram for the meta-analysis of studies published from 1966 to 2004. NIDDM, non-insulin-dependent diabetes mellitus; WC, waist circumference; WHR, waist/hip ratio.

ratio, and it can be easily measured and interpreted (2, 7–10). However, waist circumference cannot distinguish abdominal subcutaneous fat, total abdominal fat, and total body fat, and it is strongly correlated with body mass index. Body mass index has been shown to be a good indicator of general fatness (fat areas in the arm, thigh, and waist using computed tomography scans), muscularity (muscle area in the thigh), and frame size (bone area in thighs) (11).

As expected, epidemiologic studies have demonstrated that these three obesity indicators are strong and consistent predictors of diabetes mellitus, type 2. However, despite the clear, clinical difference between visceral and other forms of fat, little epidemiologic difference would be expected in the relations of diabetes with body mass index versus waist circumference. From a statistical perspective, the two measures yield similar information, with the correlation coefficient typically about 0.8 (12). Several studies have shown that waist circumference is a better predictor of diabetes mellitus, type 2, than is body mass index, but these findings are inconclusive (13–15), while other studies provide evidence that waist/hip ratio has a positive effect independent of body mass index (16–18). In addition, the ability of these

obesity indicators to predict diabetes may differ by ethnicity, age, and sex (19–22). For example, among Asian populations, central obesity has been shown to be a more consistent predictor of diabetes than is total obesity (18, 23), while general obesity has been shown to be a better predictor among White US populations and Europeans (24, 25).

To study the magnitude of the association among different obesity indicators in multiethnic populations comprising studies worldwide, we performed a meta-analysis of published studies that reported the association between obesity and incident diabetes. Additionally, we explored if the associations differed by region and other population characteristics. Finally, we investigated if the study designs and model assumptions contributed to the heterogeneity of the reported results.

RESEARCH DESIGN AND METHODS

Data sources

A PubMed (http://www.ncbi.nlm.nih.gov/entrez/query. fcgi) search of published articles from 1966 to 2004

was performed during April 2002 (search 1) and updated in December 2004 (search 2) to select relevant publications. Refer to figure 1 for selection criteria.

Study selection

The search was limited to articles published in English. Study selection was performed with two levels of study screening. At the first level, abstracts were examined by two independent reviewers, using the following criteria: diabetes as the outcome, at least one indicator of abdominal obesity as the exposure or as a confounding factor, and follow-up study. Full manuscripts were then obtained for all publications accepted at level 1 screening. For level 2 screening, we verified that relevant data were available and that multiple publications describing the same study population were entered only once in the meta-analysis. When a study had multiple publications, the latest reference in which relevant data were available was used.

Data extraction

From each study, we retrieved study population characteristics (age range, gender, geographic area, ethnicity, inclusion criteria, incident diabetes rate, and mean and variability measure for each obesity indicator reported); study design characteristics (sampling design, follow-up time, number of visits, and sample size); diabetes assessment (epidemiologic criteria and collection instrument); and model assumptions (obesity indicator representation, parameter of association, level of covariate adjustment, and subgroup analysis). Estimates of magnitude of association and variability, that is, standard errors or 95 percent confidence intervals, were extracted over the entire study samples or by subgroups. Several publications reported associations with different levels of covariate adjustment, all of which were extracted.

Statistical analysis

The publications retrieved used different representations of the association of diabetes with the obesity indicator (continuous, categorical, and baseline means for diabetes cases and noncases). The measures were transformed to calculate a log-linear slope with diabetes risk per 1-standard deviation (pooled across all studies) increase of the obesity indicator. To transform measures based on categorical representations, the obesity indicators were assumed to be normally distributed, and all values in a category were assigned to the median value. This assumption was checked by repeating the analysis using a gamma distribution, revealing no differences in the individual study associations to the second decimal place. For studies with three or more categories of the obesity indicator, the slope was estimated with the method of Greenland and Longnecker (26) (using STATA's glst function; StataCorp LP, College Station, Texas), which calculates a weighted linear regression of the natural logarithm (log) of the relative risks across anthropometric categories, taking into account the correlation between estimates. For binary representation of the obesity indicator, classified according to the median value, the log relative risks were divided by the interquartile range. For studies with three or more categories reporting the association of only two categories, the log relative risks were divided by the distance between the median values of the reported categories. For studies with only baseline means and standard errors, the log relative risks were calculated from a simulation of cases and noncases assuming a normal distribution. Where the study measures of association were stratified by subgroups, stratum-specific estimates were pooled using a fixed-effects model, weighted by the inverse subgroup variance.

Studies were classified by region for comparative analysis. Degree of obesity and diabetes incidence were compared across populations. Region-specific means and standard deviations were pooled from individual studies to describe the degree of obesity measured by body mass index, waist circumference, and waist/hip ratio. Region-specific incident diabetes rates were calculated as geometric means.

To assess the association between the three measures of obesity and incident diabetes, we calculated pooled estimates across all studies for the relative risk using a random-effects model. Relative risks (RRs) were expressed per standard deviation (computed across all studies) of each indicator (body mass index (BMI), waist circumference (WC), waist/hip ratio (WHR)). The difference between RR_{BMI} and RR_{WC} (or RR_{BMI} and RR_{WHR}) was evaluated only in studies that included both of each pair of indicators. The analysis was performed using RR_{BMI} and RR_{WC} as repeated dependent variables within each study in SAS, version 9.1.3, PROC MIXED (27), following the method of van Houwelingen et al. (28). Within-study variances of the relative risks were fixed for each study using the PARMS (or parameter) statement, which declares the parameters and specifies their initial values. A similar analysis was done for RR_{BMI} and RR_{WHR}.

I^2 was used to describe the proportion of total variation among study-specific estimates that is due to heterogeneity (29). Heterogeneity was investigated ecologically by comparing pooled relative risks of subgroups defined by region, gender, mean body mass index, mean age, incident diabetes rate, and criteria used to define the target sample. Tests for differences between subgroups were performed unadjusted for other study level characteristics using meta-regression. Further exploration of the heterogeneity of the relative risk due to design characteristics and model assumptions was performed only for body mass index, including body mass index representation, reported parameter of association, outcome assessment, level of covariate adjustment, and follow-up time.

Additionally, funnel plots with pseudo 95 percent confidence intervals were used for visual assessment of publication bias, and the trim and fill method (30) was used to estimate any possible publication bias. All meta-analyses except the bivariate analyses were performed using the STATA, version 8.2, statistical package (31).

RESULTS

Figure 1 presents a flow diagram outlining the systematic review process. An initial search generated a list of 432 publications (290 in April 2002 and 142 in December 2004). After review of the abstracts, 47 publications

(36 from search 1 and 11 from search 2) met inclusion criteria. From those 47 publications, we included data from 29 publications, reporting on 32 distinct study populations (13, 16–18, 24, 32–56). Burke et al. (47) included a subset of Mexican origin subjects from the San Antonio Heart Study (13) to compare them with those from the Mexico City Diabetes Study. Although this study contained a subset of subjects already in our study sample, the study was retained because the majority of the sample targeted a different population. In addition, Edelstein et al. (56) reported the result of six studies, four not previously included. Only studies concerned with body mass index, waist circumference, and waist/hip ratio were included in the present analysis. Other anthropometric indicators reported in the publications were the subscapular/triceps skinfold thickness ratio, waist/thigh ratio, subscapular skinfold thickness, triceps skinfold thickness, skinfold thickness sum, hip circumference, and waist/height ratio.

Table 1 provides a summary of the characteristics of the included studies, and table 2 provides a detailed description of each study in the meta-analysis. Among the studies included, four targeted men, three targeted women, and 25 targeted both genders; the age range was 20–80 years. All studies analyzed the progression from nondiabetes to diabetes. However, several targeted more restricted populations; for example, the Mauritius study (40) targeted subjects with normal glucose tolerance, five studies targeted subjects with impaired glucose tolerance, and four studies included only participants free of chronic conditions. The studies were classified in three regions based on geographic proximity: Europe (nine studies), United States (12 studies), and Asia (four studies). Seven studies (36, 40, 44, 45, 47, 48, 55) were excluded from regional comparisons because they differed from the core population of each region or were located in other geographic areas. The study designs differed in sampling design, follow-up time, number of follow-up visits, and sample size. Diabetes assessment relied on different instruments and diagnostic criteria (57–60). In terms of the analysis, differences relied on the representation of the obesity–diabetes association, statistical approach, level of covariate adjustment, and level of stratification.

Table 3 provides descriptive information for body mass index (kg/m^2), waist circumference (cm), and waist/hip ratio by region. Information reported in publications was sometimes unadjusted and sometimes adjusted for age, sex, or other factors, and in two studies not reported. Pooled means for body mass index, waist circumference, and waist/hip ratio were 25.8 (standard deviation (SD): 4.3), 87.2 (SD: 11.6), and 0.84 (SD: 0.07), respectively. People from Asian studies were identified as being the leanest: 24.2 (SD: 3.1) kg/m^2 and 79.7 (SD: 8.6) cm for body mass index and waist circumference, respectively, while studies from Europe and the United States reported significantly higher values: 26.3 (SD: 3.4) kg/m^2 and 92.1 (SD: 9.9) cm for European studies and 26.6 (SD: 4.5) kg/m^2 and 88.2 (SD: 10.9) cm for studies in the United States. Body mass index and waist circumference, but not waist/hip ratio, reflected regional differences in degree of obesity between individuals from different regions (p values for geographic differences were 0.02 for both body mass index and waist circumference, using an F test for

TABLE 1. Summary of characteristics of studies between 1985 and 2004 included in the meta-analysis that reported the association of body mass index, waist circumference, or waist/hip ratio and incident diabetes

Concept	Characteristic
Population characteristics	
Sex	Men (*n* = 4); women (*n* = 3); both (*n* = 25)
Age range	20–80 years
Geographic regions	United States (*n* = 12); Europe (*n* = 9); Asia (*n* = 4); others (*n* = 7)
Baseline glycemic status	Nondiabetic (*n* = 22); nondiabetic and free of chronic conditions (*n* = 4); normoglycemic (*n* = 1); impaired glucose tolerance (*n* = 5)
Design characteristics	
Sampling design	Cohort (*n* = 31); nested-case control (*n* = 1)
Follow-up time	2–25 years
No. of visits	1–15 visits
Sample size	72–31,702 subjects
Incident diabetes assessments	
Assessment of event	Self-report only (*n* = 2); medical records only (*n* = 2); clinical measurement together with self-report and use of hypoglycemic medications (*n* = 28)
Epidemiologic criteria	WHO 85* (*n* = 15); WHO 99* (*n* = 6); ADA 97* (*n* = 4); 2-hour oral glucose tolerance test (*n* = 1); self-reported according to current clinical criteria (*n* = 6)
Obesity indicators	
Variable	Body mass index (*n* = 32); waist circumference (*n* = 18); waist/hip ratio (*n* = 25)
Exposure representation	Linear (*n* = 15); multiple categories (*n* = 6); binary (*n* = 5); baseline means (*n* = 6)
Model assumptions	
Association parameter	Odds ratio (*n* = 21); rate ratio (*n* = 11)
Level of covariate adjustment	Crude (*n* = 14); age and sex (*n* = 14); further adjustment using other risk factors (*n* = 1); adjustment that included body shape or total obesity (*n* = 3). Note: three studies presented more than one level of adjustment.
Stratified	Overall (*n* = 25); reported by sex, age group, or ethnic group (*n* = 7)

* WHO 85, World Health Organization 1985 criteria (fasting plasma glucose: ≥7.8 mmol/liter (140 mg/day/liter) or 2-hour post-plasma glucose: ≥11.1 mmol/liter (200 mg/day/liter)); WHO 99, World Health Organization 1999 criteria (fasting plasma glucose: ≥7 mmol/liter (126 mg/day/liter) or 2-hour post-plasma glucose: ≥11.1 mmol/liter (200 mg/day/liter)); ADA 97, American Diabetes Association 1997 criteria (fasting plasma glucose: ≥7 mmol/liter (126 mg/day/liter)).

overall difference). Correlations between obesity indicators at the study level were similar for those observed at the

individual level (13, 33): 0.88, 0.34, and 0.44 for body mass index–waist circumference, body mass index–waist/hip ratio, and waist circumference–waist/hip ratio, respectively.

Incident diabetes rates were highest for people from US studies (13.5 new cases per 1,000 person-years) and lowest for people from Asian studies (5.2 new cases per 1,000 person-years). They appear to vary according to differences in inclusion criteria and other individual characteristics of the study populations, including the level of obesity. However, diabetes rates should be interpreted with caution because they were reported at various levels of adjustment.

Figures 2, 3, and 4 and table 4 present the pooled and study-level relative risk for each of the obesity indicators. The pooled estimates of RR_{BMI} ($n = 32$) (SD: 4.3) were 1.92 (95 percent confidence interval (CI): 1.70, 2.17). Among the 18 studies that included both body mass index and waist circumference, RR_{BMI} was 1.72 (95 percent CI: 1.47, 2.02), and RR_{WC} (SD: 11.6) was 1.87 (95 percent CI: 1.62, 2.15). In the 25 studies that included both body mass index and waist/hip ratio, RR_{BMI} was 1.98 (95 percent CI: 1.70, 2.30) and RR_{WHR} (SD: 0.84) was 1.82 (95 percent CI: 1.55, 2.13). Neither comparison, body mass index and waist circumference ($p = 0.50$) or body mass index and waist/hip ratio ($p = 0.73$), revealed a significant difference in the magnitude of association. Heterogeneity was present for all obesity indicators: $I^2 > 0.90$.

Figures 5, 6, and 7 present the pooled RR_{BMI}, RR_{WC}, and RR_{WHR} stratified by study-level characteristics. Differences in the obesity–diabetes relative risks were marked between groups defined by study incident diabetes rate and inclusion criteria for all three obesity indicators. Those studies that targeted a sample of subjects with a higher diabetes rate or with impaired glucose tolerance presented a shallower obesity–diabetes relative risk. When pooled relative risks between obesity indicators were compared, some modest differences were found by region and age. RR_{BMI} and RR_{WC} were similar for the three regions but were shallower for RR_{WHR}-Asia (1.4 (95 percent CI: 1.1, 1.7)) compared with RR_{WHR}-Europe (1.9 (95 percent CI: 1.7, 2.2)) and RR_{WHR}-United States (1.7 (95 percent CI: 1.4, 2.2)). In addition, in studies where the mean age was less than 50 years, RR_{WHR} (2.1 (95 percent CI: 1.7, 2. 6)) was higher than RR_{BMI} (1.7 (95 percent CI: 1.4, 2.0)) and RR_{WC} (1.6 (95 percent CI: 1.4, 1.9)). For studies where the mean age was greater than or equal to 50 years, RR_{WHR} (1.7 (95 percent CI: 1.5, 2.0)) was weaker than RR_{BMI} (2.0 (95 percent CI: 1.7, 2.3)) and RR_{WC} (2.0 (95 percent CI: 1.6, 2.7)).

Figure 8 presents the pooled RR_{BMI} estimates by study design and model characteristic groups. Differences in study design, outcome assessment, and model assumption may explain some of the heterogeneity of the relative risks across studies. However, none of the characteristics alone seems to play an important role in the level of heterogeneity. In addition, it is not possible to differentiate the impact of each component with a multivariable approach because of the scarcity of studies in each category. Analysis was repeated for RR_{WC} and RR_{WHR}, and results were consistent with those found with RR_{BMI}.

The funnel plots and trim and fill method showed no publication bias for RR_{BMI} and RR_{WC} (figures not shown).

The filled RR_{WHR} was 1.7 (95 percent CI: 1.5, 2.0) after imputing three missing studies according to the trim and fill method compared with the observed RR_{WHR} (1.9 (95 percent CI: 1.6, 2.2)).

DISCUSSION

The association of body mass index, waist circumference, and waist/hip ratio with incident diabetes was confirmed in our study by the significant pooled estimates of the relative risk. When comparing the associations in the subset of studies with both body mass index and waist circumference, the pooled RR_{WC} was modestly stronger than the RR_{BMI}. When comparing the RR_{BMI} and RR_{WHR}, RR_{BMI} was modestly stronger. None of these differences was statistically significant.

A recent meta-analysis of the association of body mass index and incident diabetes found similar results (61), although this study differed in some analytical aspects in estimating study-level relative risk, study selection, and target population. Because our meta-analysis focused on studies reporting an additional measure of central obesity, we have fewer studies included in our analyses.

Ford et al. (12) support the use of waist circumference as a measure of obesity to predict health risk. Among their arguments are that waist circumference has been shown to be a good or better predictor than body mass index of the metabolic syndrome, diabetes, cardiovascular disease, and all-cause mortality; it provides information about health risk in addition to body mass index; and it is conceptually easy to measure, although it does require some training and standardization. However, others have noted that substitution of body mass index by waist circumference as an indicator of risk for cardiovascular disease and diabetes may be an oversimplification (2, 11, 62). Some counterarguments are that waist circumference is strongly correlated to body mass index ($r \sim 0.8$) (12, 13, 33, 63); waist circumference does not differentiate between subcutaneous fat and visceral fat; it has not been shown that a consistent association exists between waist circumference with visceral fat after adjustment for age and body mass index; and body fat distribution is different across racial, sex, and age (2, 10, 62, 64, 65) strata.

Other indicators have been suggested to describe fat distribution associated with abdominal obesity (2). For example, the subscapular/triceps skinfold ratio has been used to describe central versus peripheral obesity. The waist/hip ratio and the waist/thigh ratio have been used to identify upper versus lower body obesity. In addition, other indices, such as waist/height ratio, conicity index, and abdominal to mid-thigh girth, have been developed on the basis of a variety of criteria. However, ratios are more difficult to interpret biologically, are less sensitive to weight gain, and have statistical limitations (66). Because relatively few studies have considered these indicators, we did not include them in our meta-analysis.

In our analysis, we included waist/hip ratio because it was the most common obesity-related predictor of diabetes after body mass index and it has a weaker correlation with body mass index ($r \sim 0.4$) (13, 33) than does waist circumference.

TABLE 2. Description of characteristics of studies between 1985 and 2004 included in the meta-analysis that reported the association of body mass index, waist circumference, or waist/hip ratio and incident diabetes

First author (reference no.)	Study name, location (acronym)	Baseline years	Mean years of follow-up or range	Follow-up (no.)	Population selection	Sample size (no.)	Mean age or range (years)	Men (%)	Diabetes rate/1,000 person-years	Anthropometric role	Assessment of event
Feskens (32)	Zutphen Study, Netherlands (Zutphen)	1960	25	15 visits	NDM*	841	40–59	100	3.8	Risk factor	Self-reported physician diagnosed or use of medications
Cassano (18)	Normative Aging Study, United States (NAS)	1963–1970	18	4 visits	NCHD* and NC*	1,972	20–80	100	6.4	Exposure	Clinical diagnosis with WHO 85* in study examination or diagnosed by a physician involved in the study
Ohlson (33)	Prospective Population Study of Men, Gothenburg, Sweden (Goteborg men)	1963	14	1 visit	NDM	766	50	100	4.5	Risk factor	Self-reported physician diagnosed, clinical diagnosis with WHO 85, or hospital and death register
Lundgren (17)	Prospective Population Study of Women, Gothenburg, Sweden (Goteborg women)	1968–1981	12	2 visits	NDM	1,318	38–60	0	2.5	Confounder	Self-reported physician diagnosed or clinical diagnosis with WHO 80*
Lipton (34)	First National Health and Nutrition Examination Survey, United States (NHANES I)	1971–1981	16	Registry	NDM	11,097	25–70	40	5.0	Risk factor	Self-reported physician diagnosed, hospital, nursing, or death register
Wei (13)	San Antonio Heart Study, United States (SAHS)	1971–1987	7.2	1 visit	NDM	721	25–64	37	20.2	Exposure	Clinical diagnosis with WHO 80, or self-reported physician diagnosed and use of medication
Folsom (35)	Iowa Women's Health Study, United States (IOWA)	1986	11–12	4 surveys	NDM, NCHD, and NC	31,702	55–69	0	4.3	Exposure	Self-reported physician diagnosed
Young (36)	Northern Native Canadian Cohort Study, Canada (N-NCCS)	1986	4–5	Registry	NDM	630	20–64	44	8.0	Risk factor	Medical records with diagnosis consistent with WHO 85
Mykkanen (37)	Finland study, Finland (FINRISK)	1986–1988	3.5	1 visit	NDM	892	65–74	36	22.1	Risk factor	Clinical diagnosis with WHO 85 criteria in study examination
Chan (24)	Male Health Professionals Study, United States (MHPS)	1986–1992	5	3 surveys	NDM, NCHD, and NC	27,983	40–75	100	1.9	Exposure	Self-report of any symptoms, clinical diagnosis with WHO 85 on two occasions, or medication
Carey (38)	Nurses' Health Study, United States (NHS)	1986–1992	7–8	4 surveys	NDM	43,581	30–55	0	2.2	Exposure	Self-reported physician diagnosed with further validation
Schmidt (39)	Atherosclerosis Risk in Communities Study, United States (ARIC)	1987	7	3 visits	NDM	11,880	45–64	46	16.1	Confounder	Self-reported physician diagnosed or use of medication, or clinical diagnosis with WHO 99*
Boyko (40)	Mauritius Noncommunicable Disease Study, Mauritius (Mauritius)	1987–1992	5	1 visit	NGT*	2,605	25–74	49	12.2	Risk factor	Self-reported physician diagnosed or use of medications, or clinical diagnosis with WHO 99
Snijder (41)	Hoorn Study, Netherlands (Hoorn)	1989–1996	6.4	1 visit	NDM	1,357	50–75	46	15.2	Exposure	Self-reported physician diagnosed or use of medication, or clinical diagnosis with WHO 99
Festa (42)	Insulin Resistance Atherosclerosis Study, United States (IRAS)	1992–1994	5.2	2 visits	NDM	1,047	55	32	26.4	Confounder	Clinical diagnosis with WHO 85
Shin (43)	Yonchon County Study, Korea (Yonchon)	1993–1995	2	1 visit	NDM	1,193	≥30	43		Risk factor	Clinical diagnosis with WHO 85
Sargeant (44)	Jamaica Study, Jamaica (Jamaica)	1993–1996	4	1 visit	NDM	728	25–74	40	1.84	Exposure	Self-reported physician diagnosed or use of medications, or clinical diagnosis with WHO 99

McNeely (45)	Japanese-American Community Diabetes Study, United States (JACDS)	1983–1988	5	1 visit	NDM	466	34–75	52	21.0	Exposure	Clinical diagnosis with WHO 99 or use of medications
Wang (46)	Cardiovascular Disease Risk Factor Two-Township Study, Taiwan (Taiwan)	1990–1993	5	1 visit	NDM	2,190	35–74	45	2.6	Risk factor	Self-reported physician diagnosed or use of medications, or clinical diagnosis with WHO 85 (only FPG*)
Warne (48)	Pima Study, United States (Pima)	1988	1–6	1 visit	NDM	733	≥18	40	35.0	Exposure	Clinical diagnosis with WHO 85
Burke (47)	Mexico City Diabetes Study, Mexico (MCDS)	1984	6	1 visit	NDM	1,754	35–64	24	12.1–22.9	Confounder	Clinical diagnosis with WHO 85, or self-reported physician diagnosed and use of medications
	San Antonio Heart Study, United States (SAHS)		7			466		27			
Daimon (49)	Funagata Study, Japan (Funagata)	1995–1997	5	1 visit	NDM	978	59	79	3.7	Confounder	Clinical diagnosis with WHO 85
Nauck (50)	Gottingen's first-degree relatives, Germany (Gottingen)	1967	25	1 visit, 1 survey	NDM and first-degree family history	135	64	54	12.4	Risk factor	Clinical diagnosis with WHO 85
Chen (51)	Penghu Study, Taiwan (Penghu)	1995	3	1 visit	NDM	600	60	52	14.4	Confounder	Clinical diagnosis with ADA 97*
Spranger (52)	European Prospective Investigation into Cancer and Nutrition-Potsdam Study, Europe (EPIC-Potsdam)	1994–1998	4	1 visit	NDM	565	35–65	59		Confounder	Self-reported physician diagnosed, current use of medications, dietary treatment with physician confirmation
Laaksonen (53)	Kuopio Ischemic Heart Disease Risk Factor Study, Finland (KIHDRF)	1988–1989	4	1 visit	NDM	907	42–62	100	14.1	Risk factor	Clinical diagnosis with ADA 97 or use of medications
Harding (54)	European Prospective Investigation into Cancer and Nutrition-Norfolk Study, Europe (EPIC-Norfolk)	1993–1997	3–7	1 survey, 1 visit	NDM, NCHD, and NC	21,472	40–74	45	Men: 4.1 Women: 2.4	Confounder	Self-reported physician diagnosed with no insulin prescribed within the first year following diagnosis and/or an HbA1c* level greater than 7% at baseline or follow-up visit, general practice diabetes register, hospital diabetes register, death certificates
Rodríguez-Moran (55)	Durango, Mexico (Durango)	1997	2	1 visit	NDM	72	≥30	43	48.6	Confounder	Clinical diagnosis with ADA 97
Edelstein (56)	Baltimore Longitudinal Study of Aging, United States (BLSA)	1964	1–9	2–8 visits	IGT*	675	59 23–92	74	35.8	Risk factor	Clinical diagnosis with WHO 85, use of medications, physician diagnosis (RBS* only)
	Rancho Bernardo Study, United States (RBS)	1984–1987	7–9	1 visit	IGT	186	68 52–82	35	40		
	Nauru Study, Nauru (Nauru)	1987	5–12	2–4 visits	IGT	305	37 2–75	46	62.8		
	San Luis Valley Diabetes Study, United States (SLVDS)	1984–1988	1–3	2–4 visits	IGT	177	60 31–75	40	72.9		

* NDM, non-diabetes mellitus; NCHD, non-coronary heart disease; WHO 85, World Health Organization 1985 criteria (59); NC, noncancer; WHO 80, World Health Organization 1980 criteria (58); WHO 99, World Health Organization 1999 criteria (60); NGT, normal glucose tolerance; FPG, fasting plasma glucose; ADA 97, American Diabetes Association 1997 criteria (57); HbA1c, hemoglobin A1c; IGT, impaired glucose tolerance; RBS, Rancho Bernardo Study.

TABLE 3. Incident diabetes rate, mean and standard deviation of body mass index, waist circumference, and waist/hip ratio by region and overall for studies between 1985 and 2004 included in the meta-analysis

Region	Incident diabetes rate/1,000 person-years (geometric mean)	Body mass index (kg/m²)		Waist circumference (cm)		Waist/hip ratio	
		Mean	Standard deviation	Mean	Standard deviation	Mean	Standard deviation
Asia	5.2	24.2	3.1	79.7	8.6	0.92	0.06
Europe	7.2	26.3	3.4	92.1	9.9	0.85	0.08
United States	13.5	26.6	4.5	88.2	10.9	0.83	0.08
Overall		25.8	4.3	87.2	11.6	0.84	0.07

However, some have argued against the use of waist/hip ratio as a measure of obesity because of its ambiguous biologic interpretation, its lesser sensitivity to weight gain, its greater variability across age, sex, and ethnic groups, and its greater computational complexity and interpretation in a public health context (2).
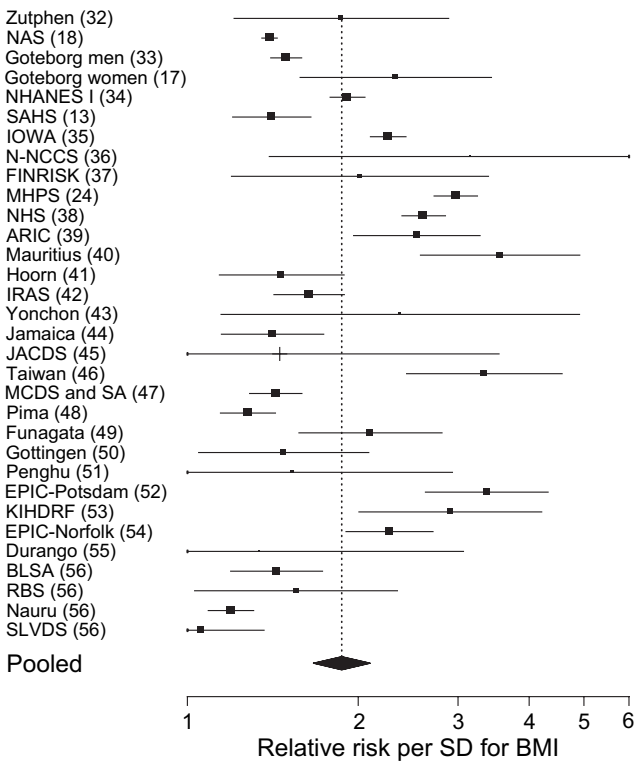

FIGURE 2. Forest plot of the association between body mass index (BMI) and incident diabetes (95% confidence interval) for 32 studies published between 1985 and 2004. The pooled relative risk per standard deviation (SD: 4.3) (plotted as diamond) is 1.87 (95% confidence interval: 1.67, 2.10). NAS, Normative Aging Study; NHANES I, First National Health and Nutrition Examination Survey; SAHS, San Antonio Heart Study; IOWA, Iowa Women's Health Study; N-NCCS, Northern Native Canadian Cohort Study; FINRISK, Finland study; MHPS, Male Health Professionals Study; NHS, Nurses' Health Study; ARIC, Atherosclerosis Risk in Communities Study; IRAS, Insulin Resistance Atherosclerosis Study; JACDS, Japanese-American Community Diabetes Study; MCDS, Mexico City Diabetes Study; SA, San Antonio; EPIC, European Prospective Investigation into Cancer and Nutrition; KIHDRF, Kuopio Ischemic Heart Disease Risk Factor Study; BLSA, Baltimore Longitudinal Study of Aging; RBS, Rancho Bernardo Study; SLVDS, San Luis Valley Diabetes Study.

FIGURE 3. Forest plot of the association between waist circumference (WC) and incident diabetes (95% confidence interval) for 18 studies published between 1985 and 2004. The pooled relative risk per standard deviation (SD: 11.6) (plotted as diamond) is 1.87 (95% confidence interval: 1.58, 2.20). NAS, Normative Aging Study; SAHS, San Antonio Heart Study; IOWA, Iowa Women's Health Study; MHPS, Male Health Professionals Study; NHS, Nurses' Health Study; IRAS, Insulin Resistance Atherosclerosis Study; JACDS, Japanese-American Community Diabetes Study; MCDS, Mexico City Diabetes Study; SA, San Antonio; KIHDRF, Kuopio Ischemic Heart Disease Risk Factor Study; BLSA, Baltimore Longitudinal Study of Aging; RBS, Rancho Bernardo Study; SLVDS, San Luis Valley Diabetes Study.
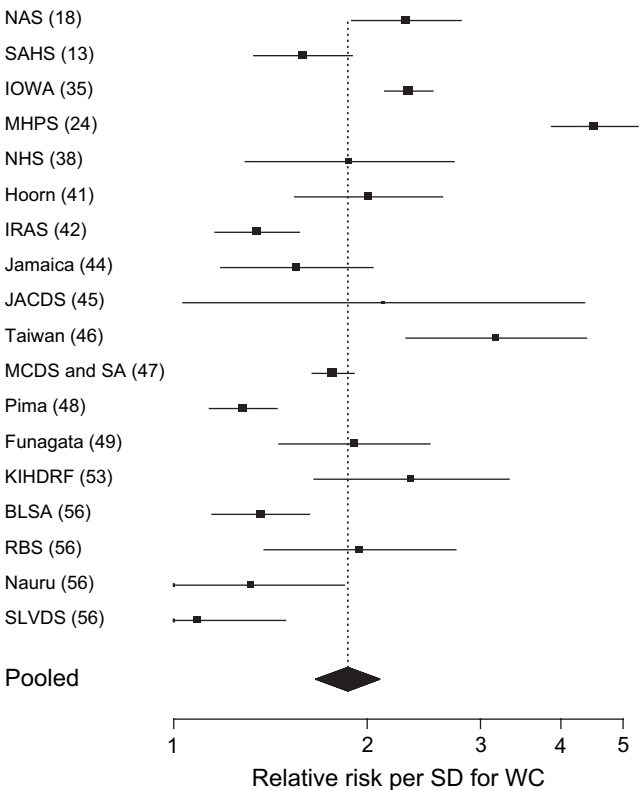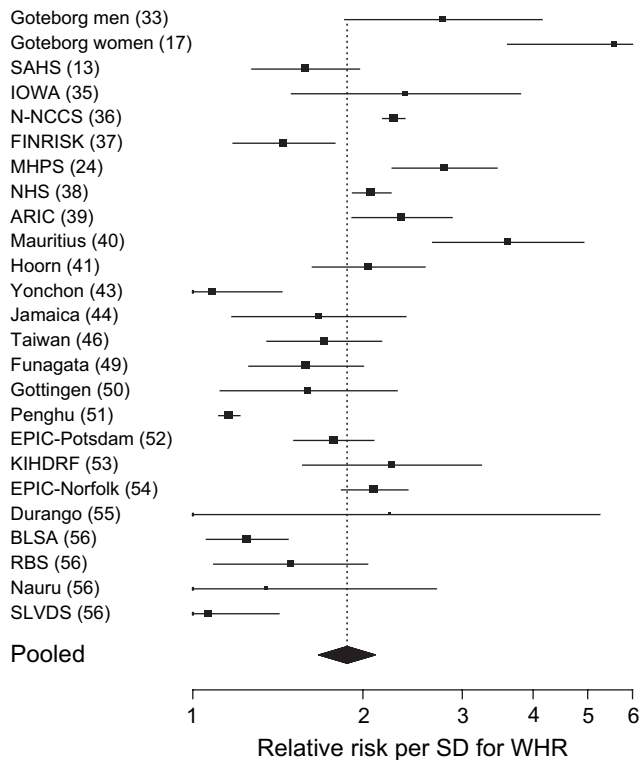
FIGURE 4. Forest plot of the association between waist/hip ratio (WHR) and incident diabetes (95% confidence interval) for 25 studies published between 1985 and 2004. The pooled relative risk per standard deviation (SD: 0.07) (plotted as diamond) is 1.88 (95% confidence interval: 1.61, 2.19). SAHS, San Antonio Heart Study; IOWA, Iowa Women's Health Study; N-NCCS, Northern Native Canadian Cohort Study; FINRISK, Finland study; MHPS, Male Health Professionals Study; NHS, Nurses' Health Study; ARIC, Atherosclerosis Risk in Communities Study; EPIC, European Prospective Investigation into Cancer and Nutrition; KIHDRF, Kuopio Ischemic Heart Disease Risk Factor Study; BLSA, Baltimore Longitudinal Study of Aging; RBS, Rancho Bernardo Study; SLVDS, San Luis Valley Diabetes Study.

ence between risk ratios. Several other strategies are possible to compare the performance of disease markers, such as measures of predictive power (likelihood measures) or measures of discriminatory performance, such as the area under the receiver-operating characteristic curve. For example, Stevens et al. (15) found that waist circumference had better discriminatory performance for diabetes than did body mass index or waist/hip ratio.

A potential problem that arises in meta-analyses of observational data, such as this one, is that the findings may appear to be very precise but are simply reinforcing biases present in individual studies. In addition, although an individual study may report an "un-confounded" estimate of an association, associations may differ between studies because of different distributions of the obesity indicator and the confounding variables or because of differences in the mechanism in biologic action across populations (67).

The necessity to investigate heterogeneity in meta-analyses of observational studies is well recognized (68). We investigated the role of study-level characteristics and found only two characteristics that affected the strength of the association: incident diabetes rate and study inclusion criteria. A smaller relative risk in studies with a higher incident diabetes rate or higher baseline glucose levels may be explained by study-level confounding or a different mechanism of biologic action between obesity and diabetes in those populations where diabetes is more prevalent. We found few differences in the relative risk of the three obesity indicators for each population group. Only for Asia do body mass index and waist circumference seem to have a stronger association than does waist/hip ratio with incident diabetes. We hypothesized that associations may be heterogeneous, reflecting different underlying causes of overweight, genetic predisposition, and obesity distribution.

When comparing differences between obesity indicators across study-level characteristics, we found that the present analysis had several limitations. Comparisons of waist circumference and body mass index or of waist/hip ratio and body mass index were not based on the same set of studies. In the case of body mass index, the estimated relative risk for the full set of studies was different from the estimated relative risk based on the subset of studies used for the pairwise comparisons with waist circumference and

In the present analysis, we have compared the associations across the obesity indicators by focusing on the differ-

TABLE 4. Pooled incident diabetes relative risk per standard deviation in the obesity indicator and measure of between-study heterogeneity for studies between 1985 and 2004 included in the meta-analysis

Obesity indicator	No. of studies	Pooled relative risk	95% confidence interval	Standard deviation	Between-study heterogeneity (I^2)
All studies					
Body mass index	32	1.87	1.67, 2.10	4.3	95.5
Studies with waist circumference					
Waist circumference	18	1.87	1.58, 2.20	11.6	93.3
Body mass index		1.72	1.47, 2.02		
Studies with waist/hip ratio					
Waist/hip ratio	25	1.88	1.61, 2.19	0.07	96.2
Body mass index		1.98	1.70, 2.30		

Women 2.4 (2.1, 2.7), *n* = 3
Men 2.0 (1.4, 2.8), *n* = 4

DM rate ≥20 1.4 (1.2, 1.5), *n* = 10
DM rate <20 2.1 (1.9, 2.4), *n* = 21

NDM & NCHD 2.1 (1.4, 3.2), *n* = 4
IGT 1.3 (1.1, 1.4), *n* = 5
NGT 3.6 (2.6, 4.9), *n* = 1
NDM 1.9 (1.7, 2.2), *n* = 22

Mean age ≥50 2.0 (1.7, 2.3), *n* = 21
Mean age <50 1.7 (1.4, 2.0), *n* = 11

Mean BMI ≥27 1.6 (1.3, 2.0), *n* = 12
Mean BMI <27 2.0 (1.7, 2.3), *n* = 19

Asia 2.4 (1.7, 3.3), *n* = 4
United States 1.7 (1.4, 2.1), *n* = 12
Europe 2.0 (1.6, 2.6), *n* = 9
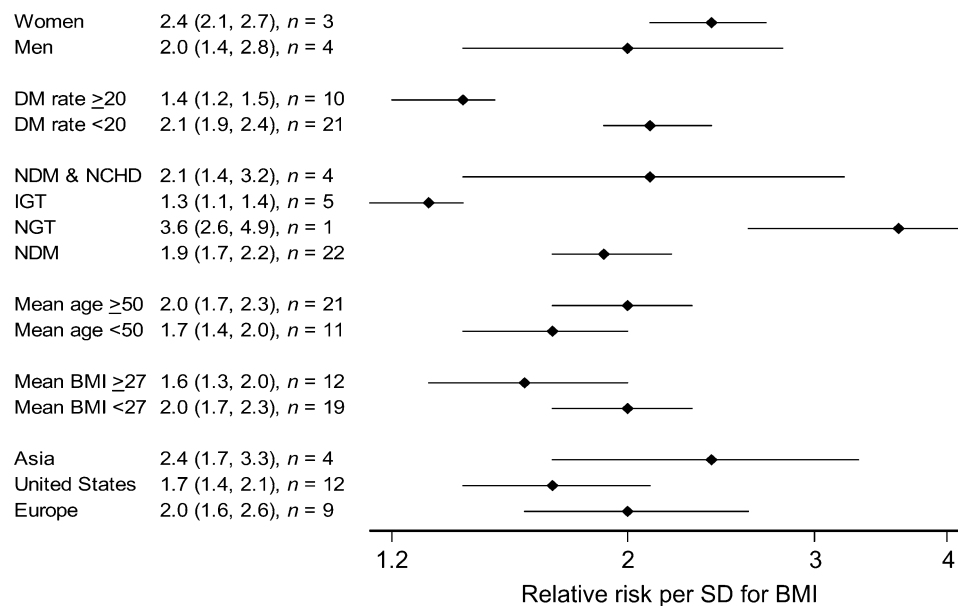
1.2 2 3 4

Relative risk per SD for BMI

FIGURE 5. Pooled relative risk (95% confidence interval) for body mass index (BMI) with incident diabetes from the meta-analysis of studies published between 1985 and 2004, stratified by study-level population characteristic: gender, diabetes rate, inclusion criteria, age, general obesity, and region. DM, diabetes mellitus; NDM, non-diabetes mellitus; NCHD, non-coronary heart disease; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; SD, standard deviation.

waist/hip ratio. The differences seen in the estimated relative risk between subsets may be due to differences in the study characteristics (study-level confounding) and random variation. When we performed ecologic comparisons, studies included in the analysis were not the same for all three obesity indicators, potentially introducing study-level confounding. Sparseness of studies in each category did not allow us to further analyze the heterogeneity with
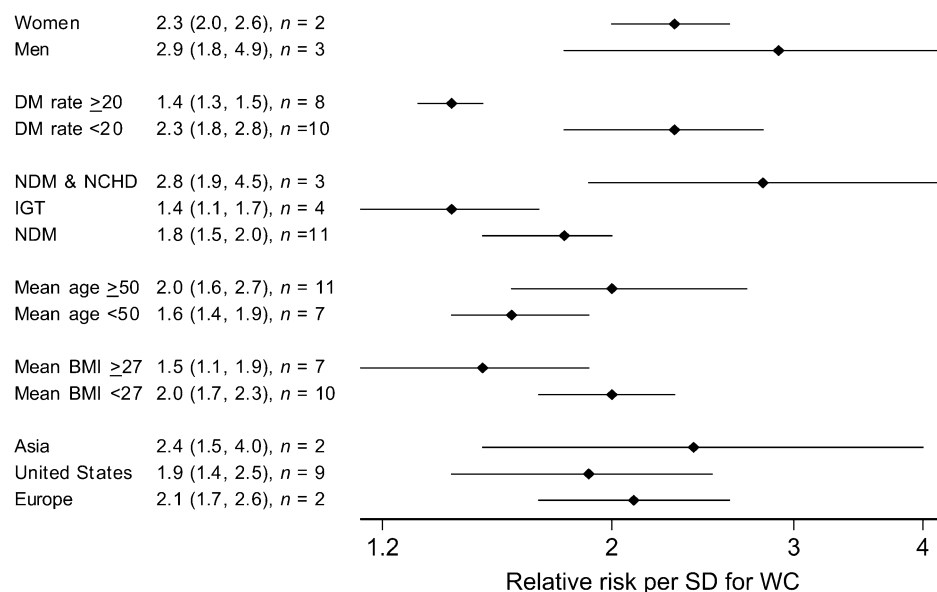
Women 2.3 (2.0, 2.6), *n* = 2
Men 2.9 (1.8, 4.9), *n* = 3

DM rate ≥20 1.4 (1.3, 1.5), *n* = 8
DM rate <20 2.3 (1.8, 2.8), *n* =10

NDM & NCHD 2.8 (1.9, 4.5), *n* = 3
IGT 1.4 (1.1, 1.7), *n* = 4
NDM 1.8 (1.5, 2.0), *n* =11

Mean age ≥50 2.0 (1.6, 2.7), *n* = 11
Mean age <50 1.6 (1.4, 1.9), *n* = 7

Mean BMI ≥27 1.5 (1.1, 1.9), *n* = 7
Mean BMI <27 2.0 (1.7, 2.3), *n* = 10

Asia 2.4 (1.5, 4.0), *n* = 2
United States 1.9 (1.4, 2.5), *n* = 9
Europe 2.1 (1.7, 2.6), *n* = 2

1.2 2 3 4

Relative risk per SD for WC

FIGURE 6. Pooled relative risk (95% confidence interval) for waist circumference (WC) with incident diabetes from the meta-analysis of studies published between 1985 and 2004, stratified by study-level population characteristic: gender, diabetes rate, inclusion criteria, age, general obesity, and region. DM, diabetes mellitus; NDM, non-diabetes mellitus; NCHD, non-coronary heart disease; IGT, impaired glucose tolerance; BMI, body mass index; SD, standard deviation.
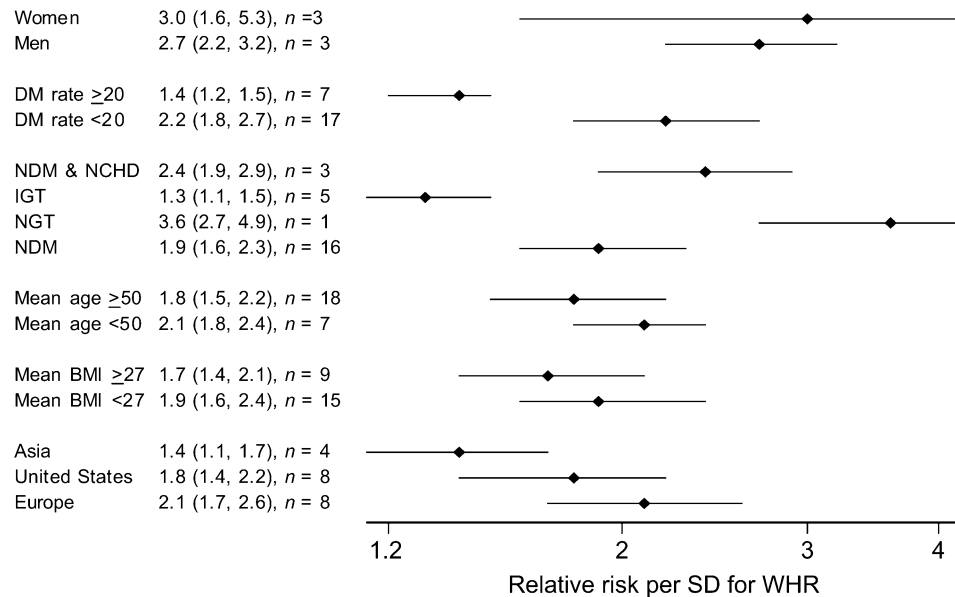
Women	3.0 (1.6, 5.3), *n* =3	
Men	2.7 (2.2, 3.2), *n* = 3	
DM rate ≥20	1.4 (1.2, 1.5), *n* = 7	
DM rate <20	2.2 (1.8, 2.7), *n* = 17	
NDM & NCHD	2.4 (1.9, 2.9), *n* = 3	
IGT	1.3 (1.1, 1.5), *n* = 5	
NGT	3.6 (2.7, 4.9), *n* = 1	
NDM	1.9 (1.6, 2.3), *n* = 16	
Mean age ≥50	1.8 (1.5, 2.2), *n* = 18	
Mean age <50	2.1 (1.8, 2.4), *n* = 7	
Mean BMI ≥27	1.7 (1.4, 2.1), *n* = 9	
Mean BMI <27	1.9 (1.6, 2.4), *n* = 15	
Asia	1.4 (1.1, 1.7), *n* = 4	
United States	1.8 (1.4, 2.2), *n* = 8	
Europe	2.1 (1.7, 2.6), *n* = 8	

Relative risk per SD for WHR

FIGURE 7. Pooled relative risk (95% confidence interval) for waist/hip ratio (WHR) with incident diabetes from the meta-analysis of studies published between 1985 and 2004, stratified by study-level population characteristic: gender, diabetes rate, inclusion criteria, age, general obesity, and region. DM, diabetes mellitus; NDM, non-diabetes mellitus; NCHD, non-coronary heart disease; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; BMI, body mass index; SD, standard deviation.

a multivariable approach. Additional heterogeneity may be derived from diversity of design features, clinical characteristics, and model assumptions. Importantly, study-level characteristics are ecologic and may not reflect the relative risks between subgroups formed across individuals within a study.

Although it is important to summarize the existing literature, the present meta-analysis suffers from having to work with the data as they were reported. In addition, for the relative risk to be obtained, assumptions had to be made regarding the distribution of the three anthropometric indicators and the correlation of the estimates across
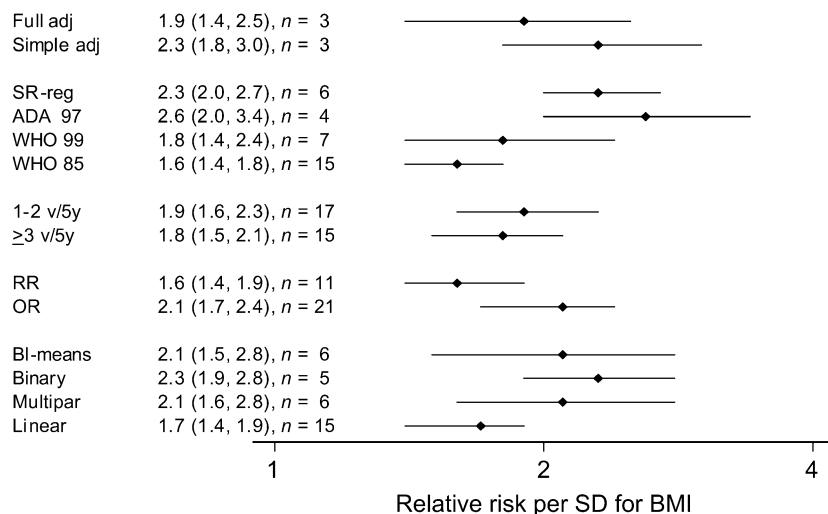
Full adj	1.9 (1.4, 2.5), *n* = 3	
Simple adj	2.3 (1.8, 3.0), *n* = 3	
SR-reg	2.3 (2.0, 2.7), *n* = 6	
ADA 97	2.6 (2.0, 3.4), *n* = 4	
WHO 99	1.8 (1.4, 2.4), *n* = 7	
WHO 85	1.6 (1.4, 1.8), *n* = 15	
1-2 v/5y	1.9 (1.6, 2.3), *n* = 17	
≥3 v/5y	1.8 (1.5, 2.1), *n* = 15	
RR	1.6 (1.4, 1.9), *n* = 11	
OR	2.1 (1.7, 2.4), *n* = 21	
Bl-means	2.1 (1.5, 2.8), *n* = 6	
Binary	2.3 (1.9, 2.8), *n* = 5	
Multipar	2.1 (1.6, 2.8), *n* = 6	
Linear	1.7 (1.4, 1.9), *n* = 15	

Relative risk per SD for BMI

FIGURE 8. Pooled relative risk (RR) (95% confidence interval) for body mass index (BMI)-incident diabetes from the meta-analysis of studies published between 1985 and 2004, stratified by study design features: level of adjustment, diagnostic criteria, frequency of diagnosis assessment, statistical model, and exposure representation. Full adj, adjustment for additional confounders; Simple adj, age and sex adjusted; SR-reg, self-reported or hospital registry; ADA 97, American Diabetes Association 1997 criteria; WHO 99, World Health Organization 1999 criteria; WHO 85, World Health Organization 1985 criteria; 1–2 v/5y, 1–2 visits within 5 years; ≥3 v/5y, three or more visits within 5 years; OR, odds ratio; Bl-means, baseline means; Multipar, multiparameter model; SD, standard deviation.

anthropometric categories. A more detailed approach can be performed with meta-analysis of data on individual participants.

The Collaborative Study of Obesity and Diabetes in Adults (CODA) project has been established to answer some of these questions. This project has collected data on individual participants from 37 studies worldwide (69). Preliminary results presented at the American Diabetes Association's 64th Scientific Sessions (63) were similar to those found in the present literature-based meta-analysis, that waist circumference is a slightly better predictor of diabetes than is body mass index: $RR_{WC} = 2.1$, 95 percent CI: 1.9, 2.3; $RR_{BMI} = 1.9$, 95 percent CI: 1.7, 2.0. The estimated relative risks from the data on individual participants were slightly higher than those observed in this literature-based meta-analysis. We hypothesize that the difference in the estimated relative risk may be explained because different sets of studies were analyzed in each project, producing random variation and study-level confounding, in addition to any bias introduced by our analytical approach.

In conclusion, despite the largely unexplained heterogeneity of relative risk, the present study demonstrated consistently strong associations of body mass index, waist circumference, and waist/hip ratio with incident diabetes. Although the clinical appeal of use of a measure of visceral fat is undeniable, the statistical reality is that waist circumference and body mass index are very highly correlated and likely to behave similarly in diabetes prediction. Waist/hip ratio, despite lower correlation with body mass index and waist circumference, appears to have the same ability to predict diabetes as do both body mass index and waist circumference. Additional insight into these issues will be gained by a meta-analysis of data on individual participants, such as the Collaborative Study of Obesity and Diabetes in Adults project is currently undertaking.

ACKNOWLEDGMENTS

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