

ORIGINAL RESEARCH

Body Composition and Risk of Incident Heart Failure in 1 Million Adults: A Systematic Review and Dose–Response Meta-Analysis of Prospective Cohort Studies

Ayodipupo S. Oguntade , MBChB, MSc; Nazrul Islam , PhD; Reem Malouf, MD, MSc; Hannah Taylor , PhD; Danyao Jin, MSc; Sarah Lewington , DPhil; Ben Lacey , DPhil

BACKGROUND: The aim of this systematic review was to quantify the associations between body composition measures and risk of incident heart failure (HF) and its subtypes in the general population.

METHODS AND RESULTS: We searched Medline, Embase, and Global Health databases from each database inception to January 19, 2023 for prospective studies reporting on body composition and HF risk. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The Newcastle-Ottawa scale was used to assess the risk of bias of included studies. Fixed-effects models were used for meta-analysis. Thirty-five studies were included ($n_{\text{total}}=1\,137\,044$; $n_{\text{cases}}=34\,422$). Summary relative risk (RR) per 5-kg/m² higher body mass index was 1.42 (95% CI, 1.40–1.42; $\zeta^2=0.02$, $I^2=94.4\%$), 1.28 (95% CI, 1.26–1.31; $\zeta^2=0.01$, $I^2=75.8\%$) per 10-cm higher waist circumference, and 1.33 (95% CI, 1.28–1.37; $\zeta^2=0.04$, $I^2=94.9\%$) per 0.1-unit higher waist–hip ratio. Pooled estimates of the few studies that reported on regional fat suggested significant positive association between HF risk and both visceral fat (RR, 1.08 [95% CI, 1.04–1.12]) and pericardial fat (RR, 1.08 [95% CI, 1.06–1.10]). Among HF subtypes, associations were stronger for HF with preserved ejection fraction than HF with reduced ejection fraction. No study reported on lean mass.

CONCLUSIONS: Pooled data suggested strong associations between adiposity and HF. The association with adiposity is stronger for HF with preserved ejection fraction than HF with reduced ejection fraction, indicating that different mechanisms may be at play in etiopathogenesis of HF subtypes. Future studies are needed to investigate role of regional fat mass and lean mass in HF risk.

REGISTRATION INFORMATION: REGISTRATION: URL: www.crd.york.ac.uk/prospero/. Unique identifier: CRD42020224584.

Key Words: adiposity ■ body composition ■ body mass index ■ heart failure ■ systematic review

There are about 65 million new cases of heart failure (HF) globally, and 5-year mortality following diagnosis continues to exceed 50% in most settings.^{1,2} Higher adiposity has been associated with higher risk of HF. Body mass index (BMI) is the most widely used

measure of general adiposity. Although the relationship between HF risk and measures of central adiposity, such as waist circumference (WC) or waist–hip ratio (WHR), has been less well studied than for BMI, central adiposity has been shown in several studies to be a stronger risk

Correspondence to: Ayodipupo S. Oguntade, MBChB, MSc, Clinical Trials Service Unit & Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, UK. Email: ayodipupo.oguntade@wolfson.ox.ac.uk

This article was sent to Sula Mazimba, MD, MPH, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.122.029062>

For Sources of Funding and Disclosures, see page 15 and 16.

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CLINICAL PERSPECTIVE

What Is New?

- This large systematic review and meta-analysis of 34 422 heart failure (HF) events in >1 million individuals provides the most precise estimates to date of the shape and strength of the association of body composition (adiposity and body fat distribution) with incident HF.
- Excess adiposity, visceral fat, and pericardial fat were associated with increased HF risk, with no excess risk at lower adiposity levels, and the body composition measures showed stronger association with HF with preserved ejection fraction than HF with reduced ejection fraction. Overall general adiposity showed stronger association with HF with preserved ejection fraction than central adiposity measures, whereas central adiposity tended to be stronger in HF with reduced ejection fraction than general adiposity.

What Are the Clinical Implications?

- Public health guidance for the general population should emphasize weight reduction strategies to reduce the risk of HF even in individuals without cardiovascular disease, and there is a need for further population-based studies to clarify the role of imaging derived-body fat distribution over anthropometric adiposity measures in HF and its subtypes in different racial groups.

Nonstandard Abbreviations and Acronyms

ARIC	Atherosclerosis in the Community
HFpEF	heart failure with preserved ejection fraction
HFREF	heart failure with reduced ejection fraction
MESA	Multi-Ethnic Study of Atherosclerosis
SAT	subcutaneous adipose tissue
VAT	visceral adipose tissue
WC	waist circumference
WHR	waist-hip ratio

factor than general adiposity for HF.³⁻⁵ Furthermore, the value of fat imaging in HF risk evaluation remains unclear and, as yet, no systematic review has investigated its value over conventional anthropometry.

Some studies have shown a linear relationship between HF risk and BMI, whereas others have found a J-shaped association, with those in the underweight

(BMI <18.5 kg/m²) and overweight or obese ranges (BMI >25 kg/m²) at higher risk than those in the normal range (18.5–25 kg/m²).⁶⁻¹² However, difficulties with accurate assessment of body composition measures in studies that used routine data may have biased the reported associations. Moreover, many studies that reported on specific populations with diseases or studies that did not account for prevalent cardiovascular disease (CVD) at baseline among participants are prone to reverse causality (whereby HF may have affected adiposity) and may have underestimated the strength of observed associations.

HF is a heterogeneous condition with different phenotypes of different etiopathogenesis. It has been subtyped using left ventricular ejection fraction obtained from cardiac imaging into HF with preserved ejection fraction (HFpEF), HF with reduced ejection fraction (HFREF), and, more recently, HF with mildly reduced ejection fraction.^{13,14} Obesity has been shown to be a risk factor for HFpEF in some observational studies, but data on HFREF are scarce.^{3,15-18} Furthermore, previous reviews have tended not to assess the effect of body fat distribution on risk of different HF subtypes.^{10,12}

In summary, although there is strong evidence of an association of obesity with incident HF, previous systematic reviews may not have sufficiently accounted for reverse causality from prevalent cardiovascular disease in their assessment of the association of HF risk with body composition in the general population. Several prospective studies have been published since the last systematic review in this area, and there is a need for an updated systematic review including all the current evidence.^{3,11,19-30} Also, to the best of our knowledge, no meta-analyses have yet determined the associations between any of the measures of body composition and risk of HF subtypes. This is, in part, because such studies require measures of cardiac function that have not been feasible to include in large-scale studies until recently. We conducted this systematic review and meta-analysis of the current evidence from prospective cohort studies conducted in the general population to determine the associations between different measures of body composition and HF risk to address these uncertainties, and to inform efforts to prevent HF. Additionally, we investigated the extent to which the observed associations vary by HF subtypes.

Review Questions

1. What is the association between adiposity measures (as measured by BMI, WC, and WHR) and HF incidence?
2. What is the association between fat measures (as measured by total body fat, visceral adipose tissue [VAT], subcutaneous abdominal adipose tissue [SAT], and pericardial fat) and HF incidence?

3. To what extent do these associations between body composition and HF incidence vary by age, sex, race, and HF subtypes?

METHODS

The authors declare that all supporting data are available within the article (and its online supplementary files). This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, which is a standardized format for performing systematic reviews.³¹ Previously, we have published the protocol for this review (see S1).³² This review was registered on the International Prospective Register of Systematic Reviews-PROSPERO (number CRD420224584).³³ The review involved secondary analyses of previously published studies, and as such, separate institutional review board approval and informed consent were not required. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Search Strategy

A systematic search of Medline, Embase, and Global Health databases was performed by 2 reviewers (A.S.O. and D.J.) initially from each database inception to December 16, 2020 for articles that reported on the associations between body composition measures and HF risk; the search was updated to include articles published before January 19, 2023. The search strategy was developed in conjunction with an information specialist using Medical Subject Headings terms and text words associated with “body composition,” “adiposity,” “lean mass,” “obesity,” “sarcopenia,” “heart failure,” “cardiac dysfunction,” “ventricular dysfunction,” “cardiomyopathies,” “cohort studies,” and “adults.” A reference list of a previous meta-analysis¹² and reference lists of relevant studies were also screened for inclusion. The search strategy is shown in Table S1.

Study Selection and Eligibility Criteria

The titles and abstracts that were retrieved by the electronic searching of databases were imported into Rayyan review manager, a web page portal that allows article screening and selection for systematic reviews, for removing duplicated citations and screening by the reviewers.³⁴ Any disagreements about study selection were resolved through discussion between reviewers. Studies were included if they were prospective cohort studies, nested case-control studies, or randomized controlled trials that allowed for determination of the strength of associations between measures of body composition (BMI, WC, WHR, fat mass, lean mass, subcutaneous abdominal fat, and visceral fat)

and incident HF risk. Eligible studies were in adults aged ≥ 18 years and conducted in the general population. Studies were excluded if they were performed in cohorts with specific diseases only (eg, diabetes, hypertension, or coronary heart disease, or if they only recruited individuals with HF at baseline). Studies that did not provide effect sizes of associations between selected body composition measures and HF risk as well as studies with too few HF events (defined as 20 events or fewer) were also excluded. For the meta-analysis, eligible studies must have reported relative risk (RR) estimates (hazard ratios or risk ratio) with 95% CIs, and for the dose-response analysis, provided quantitative measure of body composition, number of incident cases, or person-years and noncases.

For cohorts with multiple publications, we included the publication with the largest number of HF events, except where the study with the largest number of events did not provide both categorical and continuous effect sizes for inclusion in both linear and nonlinear dose response analyses. In such cases, the article that reported both categorical and continuous effect sizes was included. Thus, each cohort was only represented once in the meta-analysis of each body composition measure.

Data Extraction

A predesigned data extraction form was used to extract the following data from each included publication: first author's last name, publication year, country of study, name of cohort, year of baseline survey, selection criteria for study participants, baseline characteristics (number of participants, mean age, percent men and women), body composition measures investigated (and mean or median, categories of each body composition where available), mean or median follow-up (years), number of incident events, HF subtype, shape of association, details of statistical analyses (including type of regression models, variables adjusted for, crude and adjusted RRs and 95% CIs), and main study findings.

Assessment of Bias

Risk of bias was assessed using the Newcastle-Ottawa Scale.³⁵ The Newcastle-Ottawa Scale uses 3 quality parameters (study selection, group comparability, and outcome assessment), which are divided into an 8-item list using a point-score system. The variables in the study selection domain were study representativeness (general adult population), detailed description of participants' selection and eligibility, use of standardized method for measuring body composition, and absence of HF at baseline. Group comparability domain included adjustment for key confounders. Outcome assessment domain included outcome ascertainment by

record linkage or adjudication method, follow-up period >5 years (to allow assessment of reverse causality), and adequacy of follow-up (complete follow-up or <10% lost to follow-up or nondifferential loss to follow-up). We assigned 1 point for each of the items if the criteria were met except for the item on adjustment for key confounders, which had a maximum score of 2 points (1 point if a study was adjusted for age and sex and an extra point if a study was adjusted for additional confounders).^{36,37} Studies were rated as high quality if they had at least 7 points, whereas studies with <7 points had a high risk of bias.^{36,37} Full details of risk of bias score of all included studies are shown in Table S2.

Statistical Analysis

For the dose-response meta-analyses, summary RR (95% CI) per 5-kg/m² higher BMI, 10-cm higher WC, 0.1-unit higher WHR, 1-unit higher body fat percent, 10-cm³ higher pericardial fat, and 100-cm³ higher abdominal fat were calculated using fixed-effects models. For each study, the risk estimate from the most fully adjusted model was used, except for when such a model adjusted for additional intermediate factors (eg, hypertension, blood pressure, diabetes). In such cases, the multivariable model without such adjustment was used. The average of the natural logarithm of the RR was calculated using the inverse variance weighting method.³⁸ In cases where studies provided RR (95% CI) per unit higher body composition measure, these estimates were scaled to the desired units by exponentiating the RR (95% CI) to the power of desired units. When studies reported RR separately for different subgroups (eg, age, sex, or race) instead of overall summary estimate, the subgroup estimates were combined using fixed-effects models to obtain an overall summary estimate. Each study was therefore only represented once in each main meta-analysis, but such subgroup-specific estimates are presented separately in subgroup analyses.

For the dose-response analysis, where studies reported estimates for categories of body composition measure or subgroups, such estimates were log-transformed and used to calculate study specific slopes and 95% CIs across categories of body composition measures as described by Greenland and Longnecker to generate overall study-specific RRs using the *gls* command in Stata.^{39–42} This method requires at least 3 categories of the categorical variable, and number of cases and noncases (or person-time) must not be missing in each category.⁴² Where studies only reported total cases and controls (or person-years), the total numbers were divided evenly across the categories.⁴² The mean or median of each category of each body composition measure was assigned to the corresponding RR for that category. For studies that did not report the mean or median body composition

measure in each category, the midpoint of the range of such category was used as the mean. A comparison of observed and predicted means of adiposity categories in relevant studies is shown in Table S3. When the lowest or highest category was open ended, the width of the interval was assumed to be the same as that of the adjacent category.⁴² Nonlinear dose-response relationship between each body composition measure and HF was determined using the *gls* package in Stata by fitting restricted cubic splines with 4 knots at 5th, 35th, 65th, and 95th of each body composition distribution.⁴³ A likelihood ratio test was used to test nonlinearity by assessing the difference between the linear and nonlinear models.

Heterogeneity between studies was determined using a Q test, whereas between-study variance was assessed using ζ^2 as described by Iolas and Rice.⁴⁴ The I^2 statistics was used to denote the percentage of total variability due to between-study heterogeneity. To investigate potential sources of heterogeneity, subgroup analyses were done based on sex, age group, race, study region, duration of follow-up, measured or self-reported body composition, study quality, and exclusion of CVD at baseline, and adjustment for confounders and potential intermediate factors. Few studies provided estimates for HF subtypes, but where available, these were presented in the meta-analyses.

To assess the robustness of the overall estimates, sensitivity analyses were done by removing 1 study at a time to determine whether results were influenced by large studies or studies with extreme results. We also assessed whether results were sensitive to quality of studies, estimation of data from presented results, and heterogeneity of study populations by excluding studies with poor-quality data and studies for which summary data were estimated. Publication bias and small-study effects were examined by inspecting funnel plots for asymmetry and with the Egger test. The trim and fill method of Duval and Tweedie was used when there was evidence of publication bias on statistical testing.^{12,45,46} All analyses were done in Stata/MP 17.0 (StataCorp, College Station, TX).

RESULTS

A total of 22884 records were identified from the initial literature search. After removal of duplicate records (934 records) and title and abstract screening (19908 records screened), 152 records were assessed for eligibility. We initially identified 35 publications that included 32 prospective cohorts. The updated search on January 19, 2023 yielded an additional 9 publications, including 3 new prospective cohorts. Thus, a total of 44 publications (35 studies) are included in this review (Figure S1).

Study Characteristics

The review included 35 prospective studies involving 1 137 044 individuals at baseline and 34 422 incident HF cases. There were 20 studies conducted in Europe,^{19,24–26,29,47–60} 13 in the United States,^{3,5,20–23,27,28,30,61–67} and 2 in Australia.^{11,68} Many of the studies recruited mainly White populations ($n=19$), 15 studies were multiracial, whereas only the Jackson Heart Study³⁰ in the United States recruited only Black participants. Many of the studies recruited middle-aged or older individuals, with 7 studies recruiting only elderly populations (aged ≥ 65 years). There were 3 studies that recruited only women, whereas 9 studies recruited only men (Table S4).

The majority of the studies reported on anthropometric measures; 33 studies reported on BMI, 14 studies reported on WC, and 9 studies reported on WHR. Nine studies excluded underweight individuals, whereas only the Australian 45 and Up Study⁶⁸ excluded individuals at extremes of BMI ($<15 \text{ kg/m}^2$ or $>50 \text{ kg/m}^2$). Five publications from 3 studies^{3–5,69,70} used imaging methods to measure body fat distribution, whereas 1 study⁵³ quantified body fat using bioimpedance. Importantly, no study reported on lean mass.

Studies' outcomes were reported as either first-ever incident HF events ($n=18$), or HF hospitalizations ($n=8$) or composite of hospitalizations or death from HF ($n=9$). HF events were ascertained by electronic record linkage to hospital data or national death registers in 19 cohorts, whereas 15 cohorts adjudicated outcomes using clinical criteria. Six studies provided information on HF left ventricular ejection subtypes.^{3,11,22,27,63,69–72} Follow-up ranged from 3.4 to 35 years. Overall, 15 cohorts were graded as low quality, whereas the remainder were high quality (Table S4).

Shape of Association and Nonlinear Dose Response Analyses

Most of the studies reported a linear association between BMI and HF risk. However, the Nord-Trøndelag Health Study 2 (HUNT2)²⁹ and Jackson Heart Study³⁰ both reported a U-shaped association, whereas the 45 and Up Study⁶⁸ reported a J-shaped association between BMI and HF risk. In dose–response analyses, there was a positive curvilinear association between BMI and HF risk ($P_{\text{nonlinearity}} < 0.001$). There was no evidence of excess risk at lower BMI ($<25 \text{ kg/m}^2$), and risk increased approximately linearly above this range. Associations were also curvilinear for both WC and WHR. There was approximate linear increase in risk above a threshold WC of 90 cm and threshold WHR of about 0.9 units (Figure 1). The shape was similar when restricted to studies that excluded CVD at baseline and when restricted to studies with low risk of bias.

BMI and HF Risk

Thirty-two cohorts were included in the dose–response meta-analysis of the association of BMI and incident HF (Figure 2).^{5,11,19,21–30,48–51,53,54,56–63,67,68,72} There were 28 396 HF incident events among 1 095 412 participants. The summary RR of HF for each 5-kg/m^2 higher BMI was 1.42 (95% CI, 1.40–1.44). Although there was substantial heterogeneity ($\zeta^2=0.02$, $I^2=94.4\%$, $Q=549.9$, $P<0.001$ for heterogeneity), all studies reported increased risk with higher BMI, but the strength of associations differed between the studies. As shown in the Table, there were significant sex and age differences between studies. Associations were stronger in men (1.29 [95% CI, 1.25–1.32]) than women (1.19 [95% CI, 1.13–1.25]), although studies reporting on men were more heterogeneous than women ($\zeta^2=0.03$ and $I^2=93.2\%$ in men versus $\zeta^2=0$ and $I^2=0\%$ in women), but pooled estimate for studies reporting on both sexes (1.48 [95% CI, 1.45–1.50]) were consistent with the overall RR estimates. Associations were also stronger for studies in younger individuals (1.45 [95% CI, 1.39–1.51]; $\zeta^2=0.02$, $I^2=78\%$) than older individuals (1.30 [95% CI, 1.27–1.33]; $\zeta^2=0.01$, $I^2=80.8\%$; $P<0.001$). The only study in Black individuals reported a weaker RR of 1.10 (95% CI, 1.03–1.19; $\zeta^2=0$, $I^2=0\%$; $P<0.001$), whereas multiracial studies reported higher risk than studies in White individuals. There was a temporal increase in strength of associations with longer duration of follow-up. When studies were stratified based on exclusion of CVD at baseline, there was some evidence of reverse causality. Studies that excluded CVD at baseline reported stronger associations (RR, 1.54 [95% CI, 1.51–1.56]; $\zeta^2=0.01$, $I^2=94.5\%$) than studies that did not exclude CVD at baseline (RR, 1.28 [95% CI, 1.25–1.30]; $\zeta^2=0.02$, $I^2=87.1\%$). There was some evidence that the strength of association varied according to adjustment for key confounders (age, sex, education, and smoking), when studies were grouped based on adjustment for these sets of confounders. Studies that adjusted for intermediate factors reported smaller estimates. Further subgroup analyses are shown in Table S5.

Results were comparable with overall estimates when studies with high risk of bias were excluded from the meta-analysis (RR, 1.46 [95% CI, 1.44–1.49]; $\zeta^2=0.02$, $I^2=95.6\%$) and when studies that did not directly report overall RRs were excluded from the meta-analysis (RR, 1.46 [95% CI, 1.44–1.49]; $\zeta^2=0.02$, $I^2=96.2\%$) as shown in Figures S2 and S3, respectively. The overall estimate was robust to 'leave one out analysis' and only slightly attenuated when the UK Biobank by Xing et al⁵⁵ was excluded (Figure S4). There was some evidence of publication bias for associations between BMI and HF risk (Egger $P<0.001$) and slight asymmetry of the funnel plot (Figure S5). A trim and fill funnel plot (Figure S5) added 11 studies, and the

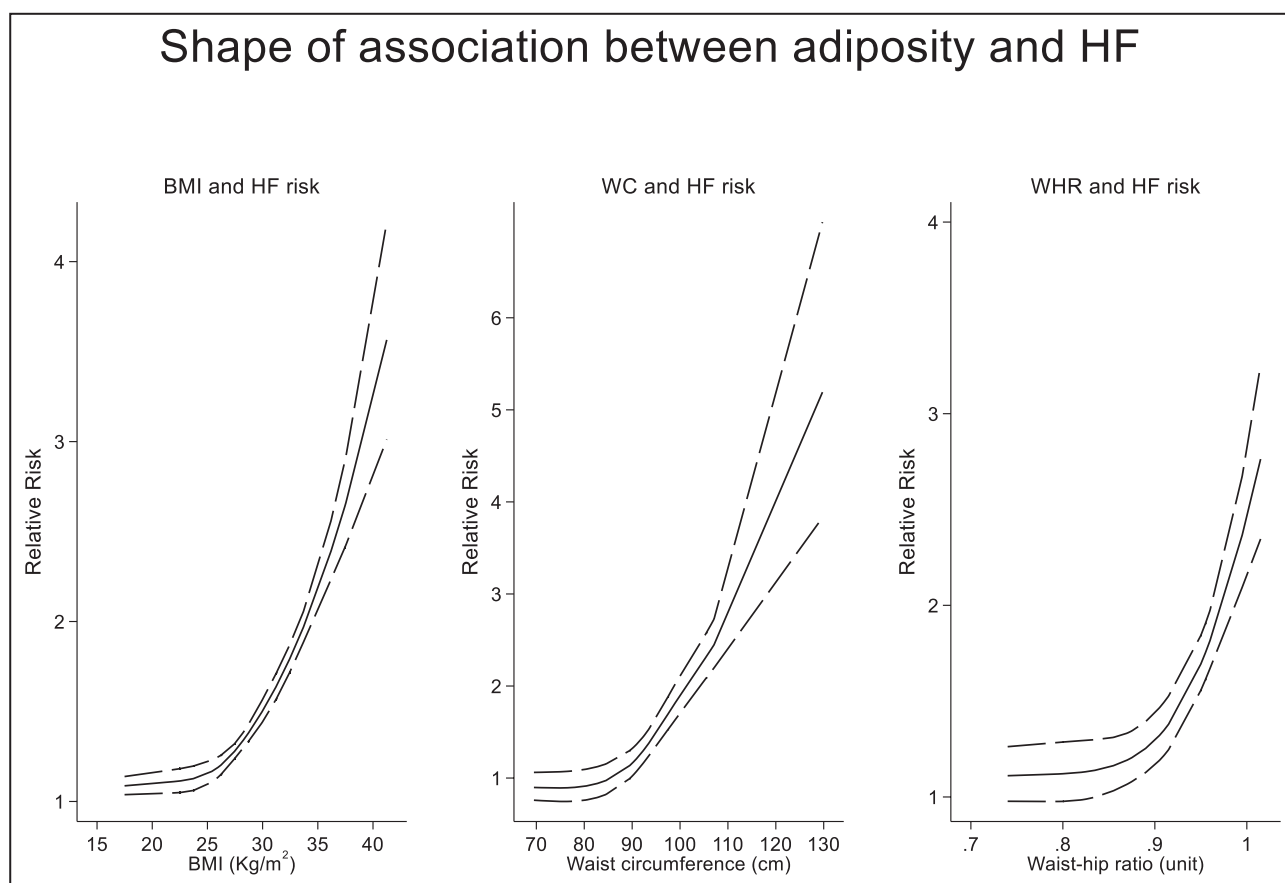


Figure 1. Shape of association between adiposity measures and HF risk.

BMI indicates body mass index; HF, heart failure; WC, waist circumference; and WHR, waist-hip ratio.

overall estimate (RR, 1.56 [95% CI, 1.54–1.57]) when these imputed studies were added was stronger than the observed meta-analysis estimate (RR, 1.42 [95% CI, 1.40–1.44]).

WC and HF Risk

Fourteen cohorts reported the association between WC and incident HF.^{5,47,49,51,53,56,59,60,63,64,71–73} There were 7424 HF incident events among 219241 participants. The summary RR of HF for each 10-cm higher WC was 1.28 (95% CI, 1.26–1.31). Although there was some heterogeneity ($I^2=75.8\%$, $Q=53.6$, $P<0.001$ for heterogeneity), the between-study variance was lower than for BMI ($\zeta^2=0.005$), and all studies reported higher risk with higher WC, but the strength of associations differed between the studies (Figure 3A). Associations were stronger in studies of men (1.33 [95% CI, 1.29–1.38]; $\zeta^2=0.005$, $I^2=66.1\%$) than of women (1.24 [95% CI, 1.20–1.27]; $\zeta^2=0.004$, $I^2=77.2\%$). Associations were also stronger in younger individuals (1.37 [95% CI, 1.33–1.42]; $\zeta^2=0$, $I^2=0\%$) than older individuals (1.25 [95% CI, 1.29–1.53]; $\zeta^2=0.001$, $I^2=52.4\%$). Studies that excluded CVD at baseline reported stronger associations (RR, 1.36 [95% CI, 1.32–1.40]; $\zeta^2=0.001$, $I^2=46.1\%$)

than studies that did not exclude CVD at baseline (RR, 1.23 [95% CI, 1.20–1.26]; $\zeta^2=0.004$, $I^2=62.9\%$).

When studies were grouped based on adjustment for the set of key confounders (age, sex, education, and smoking), the associations were not material changes, nor did studies differ by adjustment for intermediate factors (Table S5). There was no difference between subgroups based on exclusion of underweight, WC assessment method, and HF ascertainment method (Table S5). Exclusion of studies with a high risk of bias resulted in slight attenuation of the overall estimates (RR, 1.23 [95% CI, 1.20–1.27]; $\zeta^2=0.01$, $I^2=57.3\%$), whereas exclusion of studies with estimated effect sizes (RR, 1.28 [95% CI, 1.25–1.30]; $\zeta^2=0.00$, $I^2=79.8\%$) did not (see Figures S6 and S7, respectively). The overall estimate was robust to exclusion of influential studies in leave 1 out analysis (Figure S8). There was no evidence of publication bias for associations between WC and HF risk (Egger $P=0.75$), and no asymmetry of the funnel plot was observed (Figure S9).

WHR and HF Risk

As shown in Figure 3B, 9 cohorts reported on the association of WHR and incident HF.^{3,49,53,54,59,60,72,73}

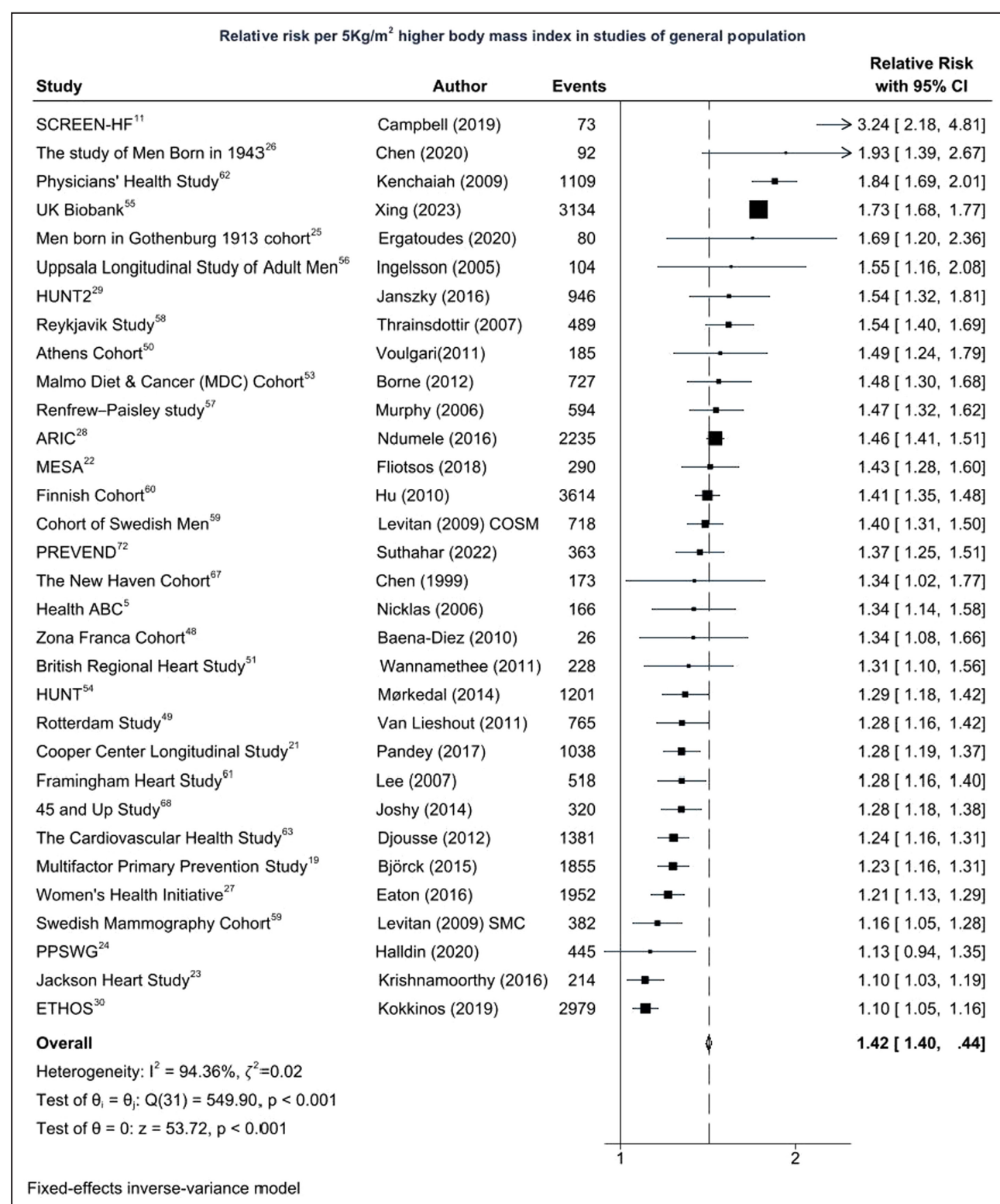


Figure 2. Body mass index and heart failure (HF) incidence: 28 396 HF incident events among 1 095 412 participants.

ARIC indicates Atherosclerosis Risk in the Community; ETHOS, Exercise Testing and Health Outcomes Study; Health ABC, Health, Aging and Body Composition Study; HUNT, The Nord-Trøndelag Health Study; HUNT2, The Nord-Trøndelag Health Study 2; MESA, Multi-Ethnic Study of Atherosclerosis; PPSWG, Prospective Population Study of Women in Gothenburg; PREVEND, Prevention of Renal and Vascular End-Stage Disease; and SCREEN-HF, Screening Evaluation of the Evolution of New Heart Failure.

Table. Subgroup Analyses of BMI, Waist Circumference, and Waist–Hip Ratio and Incident HF

Study characteristics	BMI, per 5 kg/m ² higher					Waist circumference per 10 cm higher					Waist–hip ratio per 0.1-unit higher				
	N	RR (95% CI)	P_{het}^*	I^2 , %	P_{het}^*	P_{het}^*	N	RR (95% CI)	I^2 , %	P_{het}^*	P_{het}^*	N	RR (95% CI)	I^2 , %	P_{het}^*
All studies	32	1.42 (1.40–1.44)	<0.001	94.4	<0.001		14	1.28 (1.26–1.31)	75.8	<0.001		9	1.33 (1.28–1.37)	94.9	<0.001
Sex															
Women	3	1.19 (1.13–1.25)	0	0.66	<0.001/0.01 [§]		6	1.24 (1.20–1.27)	77.2	0.001		4	1.34 (1.26–1.42)	94.6	<0.001
Men	9	1.29 (1.25–1.32)	<0.001	93.2	<0.001		8	1.33 (1.29–1.38)	66.1	0.004		4	1.27 (1.20–1.35)	97.3	<0.001
Men and women	20	1.48 (1.45–1.50)	<0.001	94.1	<0.001		5	1.27 (1.21–1.33)	12.4	0.34		4	1.32 (1.25–1.40)	71.3	0.02
Age group															
<65 y	11	1.45 (1.39–1.51)	<0.001	78.0	<0.001	<0.001/<0.001	3	1.37 (1.33–1.42)	0.0	0.94		4	1.48 (1.40–1.56)	96.6	<0.001
≥65 y	13	1.30 (1.27–1.33)	<0.001	80.8	<0.001		9	1.23 (1.20–1.25)	52.4	0.03		3	1.10 (1.06–1.14)	24.9	0.26
Unclassified	15	1.43 (1.41–1.46)	<0.001	96.8	<0.001		6	1.30 (1.24–1.37)	55.9	0.10		6	1.34 (1.27–1.41)	74.2	0.002
Race and ethnicity															
Black	1	1.10 (1.03–1.19)	0	...	<0.001/0.51		0		0	<0.001
Hispanic or Chinese	0		0		0
White	19	1.36 (1.33–1.39)	<0.001	65.7	<0.001		9	1.26 (1.22–1.30)	29.9	0.18		7	1.22 (1.18–1.27)	87.0	<0.001
Multiracial	12	1.47 (1.45–1.50)	<0.001	97.4	<0.001		5	1.30 (1.26–1.33)	90.2	<0.001		2	1.89 (1.75–2.04)	90.5	0.001
Region															
Europe	19	1.52 (1.49–1.55)	<0.001	92.1	<0.001	0.09/<0.001 [#]	9	1.26 (1.22–1.30)	29.9	0.18		7	1.22 (1.18–1.27)	87.0	<0.001
United States	11	1.31 (1.29–1.34)	<0.001	94.3	<0.001		4	1.29 (1.25–1.32)	91.3	<0.001		2	1.89 (1.75–2.04)	90.5	0.001
Australia	2	1.32 (1.22–1.43)	<0.001	95.1	<0.001		1	1.53 (1.34–1.74)	100.0	...		0
Follow-up time															
<10 y	11	1.27 (1.23–1.32)	<0.001	80.8	<0.001	<0.001	7	1.29 (1.24–1.34)	45.6	0.09		2	1.10 (1.03–1.17)	0.0	<0.001
≥10 y	12	1.45 (1.43–1.47)	<0.001	95.5	<0.001		7	1.28 (1.25–1.31)	85.8	<0.001		7	1.42 (1.36–1.47)	94.8	<0.001

(Continued)

Table. Continued

Study characteristics	BMI, per 5 kg/m ² higher				Waist circumference per 10 cm higher				Waist-hip ratio per 0.1-unit higher			
	N	RR (95% CI)	I ² , %	P _{het} [†] value	N	RR (95% CI)	I ² , %	P _{het} [†] value	N	RR (95% CI)	I ² , %	P _{het} [†] value
Baseline exclusion of CVD												
Yes	13	1.54 (1.51–1.56)	94.5	<0.001	4	1.36 (1.32–1.40)	46.1	0.14	3	1.30 (1.22–1.39)	78.7	0.009
No	19	1.28 (1.25–1.30)	87.1	<0.001	10	1.23 (1.20–1.26)	62.9	0.004	5	1.34 (1.29–1.39)	96.6	<0.001
HF type												
HFpEF	3	1.42 (1.33–1.51)	85.8	<0.001	4	1.29 (1.21–1.37)	72.4	0.01	2	1.35 (1.16–1.58)	0.0	0.49
HFrfEF	2	1.13 (1.05–1.22)	86.0	0.001	4	1.19 (1.13–1.26)	28.4	0.24	2	1.36 (1.21–1.52)	73.0	0.05
Unclassified	28	1.41 (1.39–1.43)	93.1	<0.001	11	1.31 (1.28–1.35)	61.3	0.004	7	1.32 (1.28–1.37)	96.2	<0.001
Adjustment for key confounders only [‡]												
Yes	7	1.39 (1.35–1.42)	81.1	<0.001	5	1.29 (1.26–1.33)	89.0	<0.001	3	1.54 (1.46–1.62)	97.1	<0.001
No	25	1.44 (1.41–1.46)	95.3	<0.001	9	1.26 (1.23–1.31)	50.4	0.04	6	1.19 (1.14–1.24)	84.1	<0.001

N=number of studies in subgroup meta-analysis (this is not always equal to the total number of studies in the overall analysis). BMI indicates body mass index; CVD, cardiovascular disease; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrfEF, heart failure with reduced ejection fraction; and RR, relative risk.

[†]P for heterogeneity within each subgroup.

[‡]P for heterogeneity between subgroups.

[§]Adequate adjustment is defined as adjusting for at least age, sex, education, and smoking.

^{||}P for heterogeneity between men and women (excluding men and women combined).

^{||}P for heterogeneity between age <65 y and age ≥65 y.

[¶]P for heterogeneity between Black and White.

[#]P for heterogeneity between Europe and United States.

^{**}P for heterogeneity between HFpEF and HFrfEF.

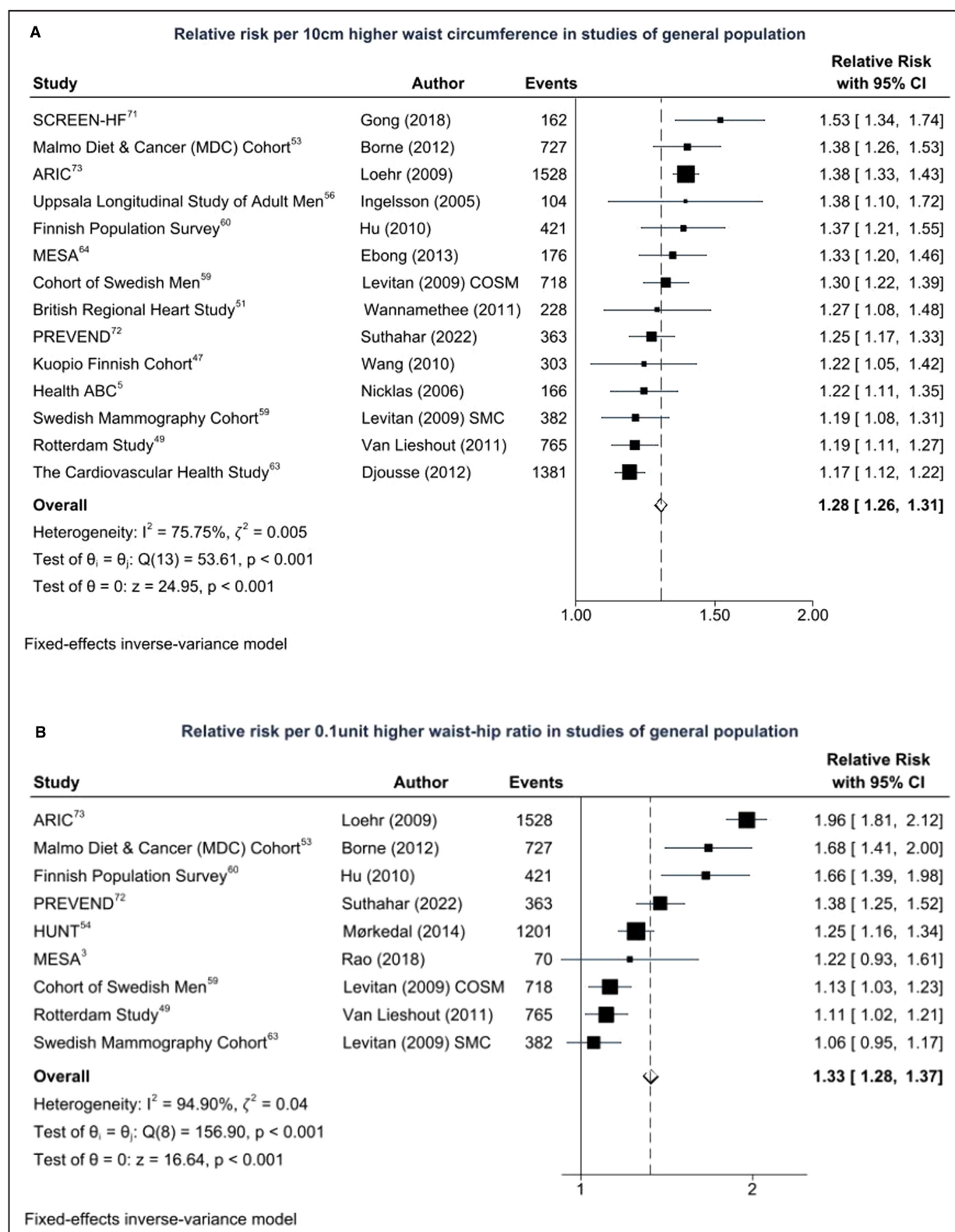


Figure 3. Central adiposity measures and incident heart failure (HF) risk.

A, Waist circumference and HF incidence: 7424 HF incident events among 219241 participants. **B**, Waist-hip ratio and HF incidence: 6175 HF incident events among 258100 participants. ARIC indicates Atherosclerosis Risk in the Community; Health ABC, Health, Aging and Body Composition Study; HUNT, The Nord-Trøndelag Health Study; PREVEND, Prevention of Renal and Vascular End-Stage Disease; and SCREEN-HF, Screening Evaluation of the Evolution of New Heart Failure.

There were 6175 HF incident events among 258 100 individuals. The summary RR of HF for each 0.1-unit higher WHR was 1.33 (95% CI, 1.28–1.37). There was substantial heterogeneity, and the between-studies variance was high ($\zeta^2=0.04$, $I^2=94.9\%$, $Q=156.9$, $P<0.001$ for heterogeneity), but all studies reported higher risk with higher WHR.

As shown in the Table, there was no significant sex difference in association of WHR and HF risk ($P=0.47$). However, there was stronger association in studies of younger individuals (1.48 [95% CI, 1.40–1.56]; $\zeta^2=0.06$, $I^2=96.6\%$), which were more heterogeneous than older individuals (1.10 [95% CI, 1.06–1.14]; $\zeta^2=0.001$, $I^2=24.9\%$).

Similar to BMI, there was a temporal increase in strength of associations with longer duration of follow-up. When studies were grouped based on exclusion of CVD at baseline, there was no evidence of reverse causality ($P=0.45$). There was effect modification based on key confounders and adjustment for intermediate factors (eg, blood pressure accounted for between-studies variance). Details of other subgroup analyses are shown in Table S5. Unlike BMI and WC, there was no difference in the overall estimates when analyses were restricted to studies with low risk of bias or when studies with estimated effect sizes were excluded (Figures S10 and S11, respectively). The overall estimate was slightly attenuated when the ARIC (Atherosclerosis in the Community) study by Loehr et al⁷³ was excluded (Figure S12). There was no evidence of publication bias for associations between WHR and HF risk (Egger $P=0.28$) as shown in Figure S13.

Body Fat Distribution and HF Risk

Figure 4A through 4C show the association between fat measures and HF risk in the few studies that reported on these measures.^{3,5,53,69,70} Pooled estimates from the Health, Aging and Body Composition (Health ABC)⁵ and Malmö Diet and Cancer (MDC)⁵³ cohorts suggested a 5% higher risk of HF per unit higher body fat percent (95% CI, 1.03–1.07) with no difference between studies ($\zeta^2=0$, $I^2=0\%$, $Q=0.38$, $P=0.54$ for heterogeneity). Increased abdominal fat was significantly associated with HF principally due to VAT and not SAT.^{3,69} There was 8% higher HF risk per 100-cm³ higher VAT (95% CI, 1.04–1.12), whereas SAT was not significantly associated with HF incidence (RR per 100-cm³, 1.02 [95% CI, 1.04–1.12]). Pooled estimates from the MESA⁷⁰ and Jackson Heart Study⁶⁹ suggested similar 8% higher risk of HF per 10-cm³ higher pericardial fat volume (95% CI, 1.06–1.10), with no difference between studies ($\zeta^2=0$, $I^2=0\%$, $Q=0.86$, $P=0.35$ for heterogeneity).

Adiposity, Body Fat Distribution, and HF Subtypes

In analysis restricted to the studies that reported on HF subtypes,^{3,11,22,27,63,71,72} there was a stronger association between BMI and HFpEF (RR, 1.42 [95% CI, 1.33–1.51]; $\zeta^2=0.02$, $I^2=85.8\%$) than for HFrEF (RR, 1.13 [95% CI, 1.05–1.22]; $\zeta^2=0.02$, $I^2=86.0\%$) as shown in Figure 5A ($P<0.001$). There was also a trend of stronger association between WC and HFpEF (RR, 1.29 [95% CI, 1.21–1.37]; $\zeta^2=0.008$, $I^2=72.4\%$) than for HFrEF (RR, 1.13 [95% CI, 1.05–1.23]; $\zeta^2=0.001$, $I^2=28.4\%$) as shown in Figure 5B ($P=0.06$).^{3,63,71,72} The pooled estimate of the 2 studies that reported on WHR showed no differences between associations of WHR with HF subtypes ($P=0.99$) as shown in Figure 5C.^{3,72} Overall, general adiposity showed stronger association with HFpEF than central adiposity measures, whereas central adiposity tended to be stronger in HFrEF than general adiposity.

Figures 6A and 6B show the associations between regional fat and HF subtypes.^{3,69,70} The association between VAT and HF was similar for both HFpEF and HFrEF ($P=0.43$) in the 2 studies that reported on regional fat and HF subtypes. In addition, pericardial fat showed stronger association with HFpEF than HFrEF ($P<0.001$).

DISCUSSION

Our systematic review is the largest review of prospective cohorts in the general population, with >34 000 HF events in >1 million individuals, and provides the most precise estimates to date of the strength and shape of the associations of body composition measures and incident HF. We have shown that there is an increased risk of HF in association with a range of adiposity and regional fat measures. The reported associations were stronger in men than women for both BMI and WC, but similar in both sexes for WHR. Associations for all adiposity measures were stronger in individuals aged <65 years than older individuals. We have also shown that the risks conferred by different adiposity measures were approximately linear. Above a threshold BMI of 24 kg/m², 90 cm of WC, or 0.9 unit of WHR, HF risk increases log-linearly. We did not observe excess risk of HF at lower adiposity. In the few studies that reported on total body fat and regional fat, all the fat measures except SAT were associated with higher risk of HF. There was 8% higher HF risk per 100-cm³ higher VAT and per 10-cm³ higher pericardial adipose tissue. We found modest evidence for differences in risk between adiposity and fat measures and HF subtypes. In studies that reported on HF subtypes, we found a stronger positive association for HFpEF than HFrEF. Furthermore, general adiposity was stronger

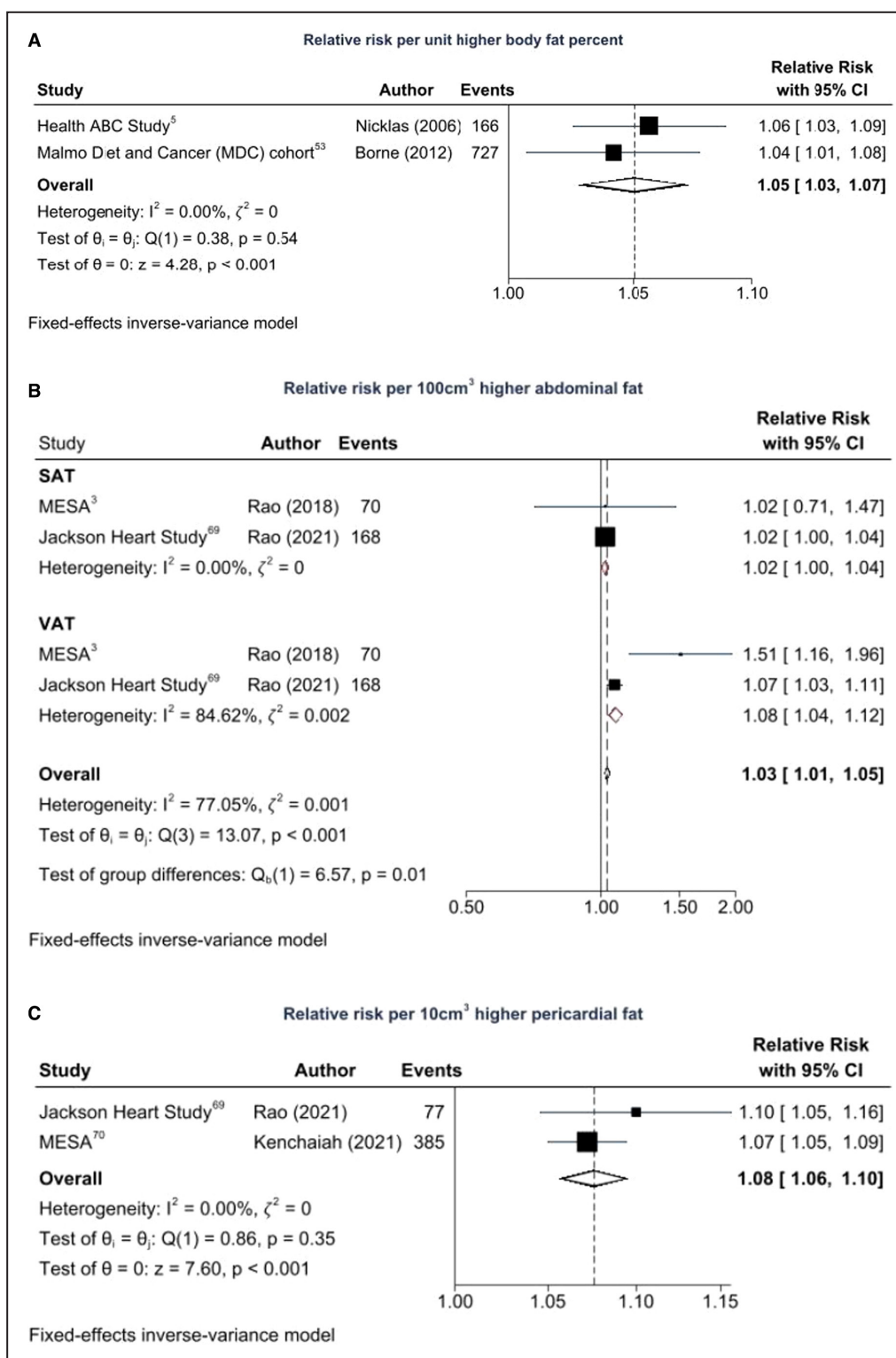


Figure 4. Regional fat measures and incident heart failure (HF) risk.

A. Body fat percent and HF incidence: 893 HF incident events among 29088 participants. **B.** Abdominal fat and HF incidence: 238 HF incident events among 4688 participants. **C.** Pericardial fat and HF incidence: 462 HF incident events among 9667 participants. Health ABC indicates Health, Aging and Body Composition Study; MESA, Multi-Ethnic Study of Atherosclerosis; SAT, subcutaneous abdominal adipose tissue; and VAT, visceral adipose tissue.

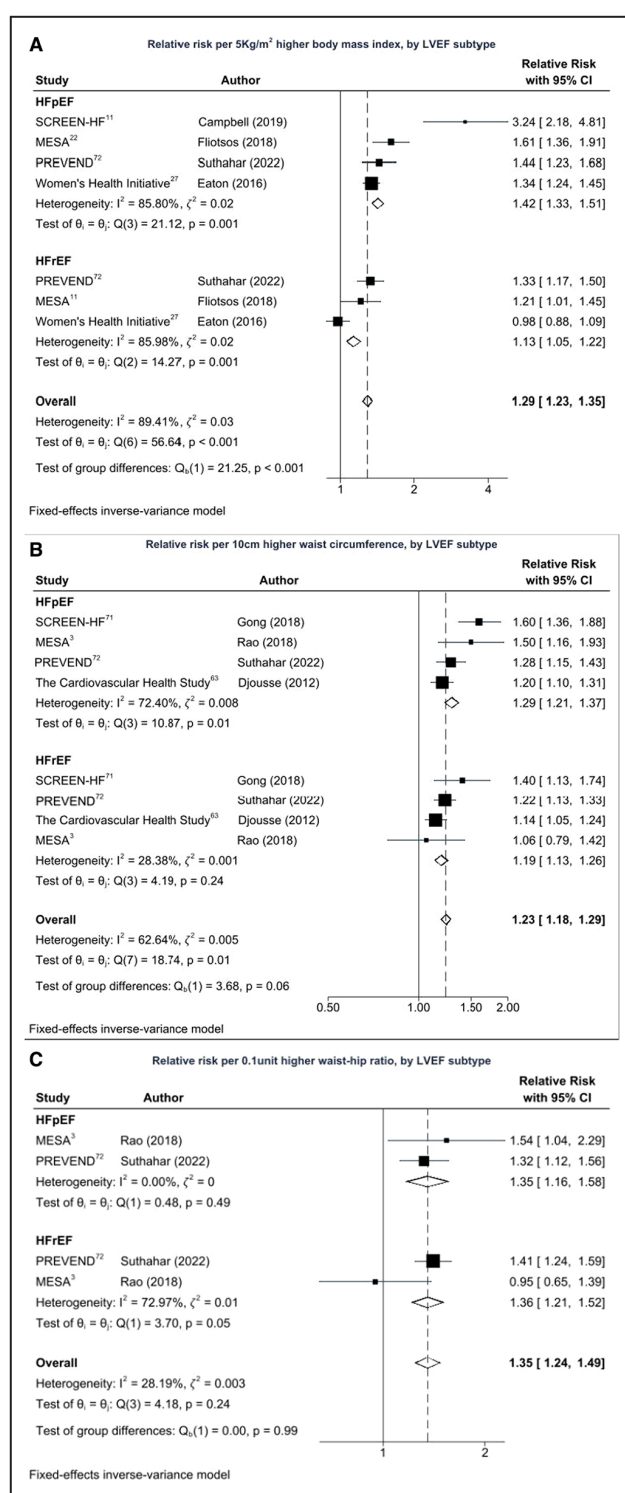


Figure 5. Dose-response meta-analysis of adiposity measures and incident HF subtypes.

A, Relative risk per 5-kg/m² higher body mass index, by left ventricular ejection fraction (LVEF) subtype. **B**, Relative risk per 10-cm higher waist circumference by LVEF subtype. **C**, Relative risk per 0.1-unit higher waist-hip ratio by LVEF subtype. HFpEF indicates heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; MESA, Multi-Ethnic Study of Atherosclerosis; PREVEND, Prevention of Renal and Vascular End-Stage Disease; and SCREEN-HF, Screening Evaluation of the Evolution of New Heart Failure.

risk conferred by higher adiposity is probably weaker in them due to weight loss and sarcopenia observed with old age.⁷⁹ It has previously been suggested that lower adiposity could be associated with increased cardiovascular events due to deleterious effects of sarcopenia, poor muscle oxygen uptake, and reduced cardiorespiratory fitness.⁸⁰ However, studies of bariatric surgery in individuals at high risk of HF have shown beneficial effects of weight loss in reducing HF incidence.^{80–82} Moreover, studies that have previously reported J-shaped association reported mainly on HF mortality. Reverse causation and residual confounding from other contributory factors to death, including severe disease, may have been the reason for the observed J-shaped phenomenon. A previous systematic review by Aune et al¹² also did not observe a J-shaped phenomenon for incident HF but rather observed the J-shaped association with studies reporting on HF mortality.

Few studies reported on HF subtypes, which indicates the likely different mechanisms of the etiology of these HF phenotypes. Increased adiposity has been associated with increased blood volume, higher blood pressure, elevated filling pressures, renin-angiotensin-aldosterone system activation, and arterial stiffness, which causes increased left ventricular mass, myocardial concentric remodeling, and hypertrophy, the hallmark of HFpEF.^{83–85} Until recently, the role of excess adiposity and body fat distribution in HFrEF was unclear. However, in this meta-analysis, we have shown that excess adiposity is also associated with higher HFrEF risk in the general population. This could be explained by the depressive effect of lipotoxicity on myocardial fibers and proarrhythmic properties of pericardial adipose tissue. Lipid accumulation in cardiomyocytes and epicardial tissue leads to mitochondrial dysfunction and apoptosis of myocardial cells. This lipotoxicity has been associated with left ventricular remodeling in the transition to HF.^{86–88} Accumulation of adipose tissue round the atria and conduction tissue has been linked to increased arrhythmogenesis and atrial fibrillation.^{86,88} There is a 3% to 8% increased risk of atrial fibrillation independent of other cardiovascular risk factors with each unit higher BMI.⁸³ Also,

for HFpEF, whereas central adiposity tended to be stronger for HFrEF.

The observed sex differences could be explained by the stronger clustering of cardiometabolic risk factors in men in epidemiologic studies.^{74–77} Elderly individuals have been shown to be at higher absolute risk of HF in population studies.⁷⁸ However, the relative

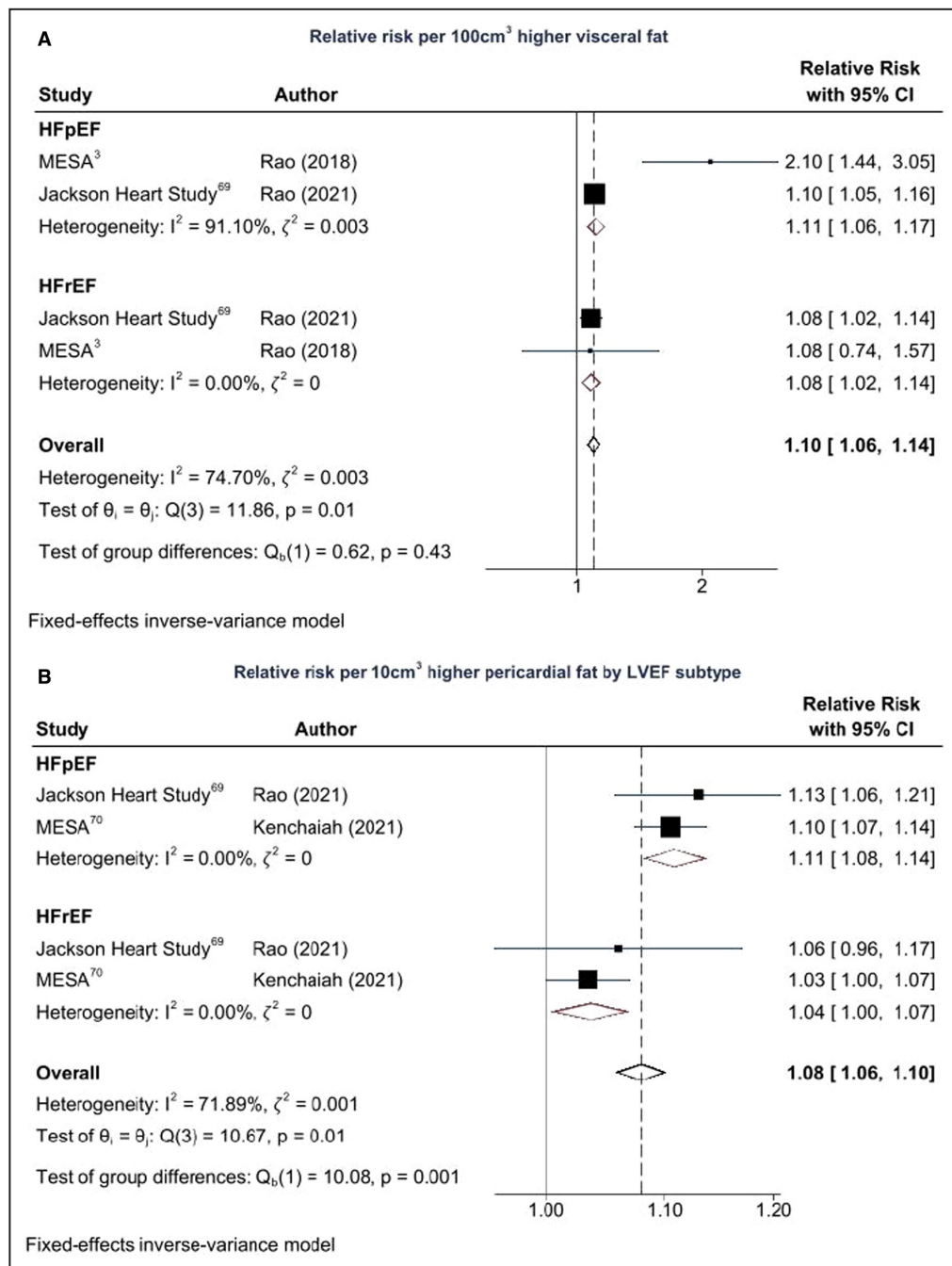


Figure 6. Regional fat and incident heart failure subtypes.

A, Relative risk per 100-cm³ higher visceral fat by left ventricular ejection fraction (LVEF) subtype. **B**, Relative risk per 10-cm³ higher pericardial fat by LVEF subtype. HFpEF indicates heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; and MESA, Multi-Ethnic Study of Atherosclerosis.

VAT, epicardial fat, and vascular tissue secrete proinflammatory cytokines (eg, TNF- α [tumor necrosis factor- α], IL-1 [interleukin-1], and IL-6 [interleukin-6]), which contribute to microvascular endothelial dysfunction and reduced vascular compliance.^{89,90} Reduced vascular compliance and rise in intracardiac pressures lead to further hypertrophy, eccentric remodeling,

and eventual myocardial burnout.^{85,91,92} Interestingly, in the Jackson Heart Study, higher BMI was associated with worse peak systolic circumferential strain on cardiac magnetic resonance, which may explain the role of adiposity in HFrEF.⁹³ Upregulation of systemic inflammation and blood volume expansion in obesity exacerbate cardiac dysfunction in the failing heart.

Myocardial inflammatory changes are also associated with profibrotic signals that contribute to impaired myocardial relaxation and diastolic dysfunction as seen in HFpEF.^{83,94} Although inflammatory biomarkers are elevated in HFpEF, this has not been well described in HFrEF, suggesting that this may not be a prominent pathway in HFrEF.^{95,96} There is a need for more studies to establish the role of adiposity and body fat distribution in HF subtypes, especially HFrEF.

Although there is emerging evidence of the role of lean mass in cardiovascular disease risk, none of the studies in this review reported on lean mass.^{97,98} Sarcopenia has been associated with adverse outcomes in HF, which may point to a possible protective role of muscle mass in HF.^{99–101} There is need for studies to investigate the role of muscle mass in HF risk. Moreover, it is still unclear if direct measurement of body fat or its distribution provides extra information above anthropometric measures in HF risk. These are areas of potential investigation for future population cohorts.

This meta-analysis is not without limitations. There was substantial heterogeneity in the included studies that persisted across different subgroup analyses of the adiposity measures. However, the direction of the observed association was consistent across studies and subgroups. Although 15 cohorts were of low quality, the heterogeneity did not appear to be due to differences in study quality, because the pooled estimates were similar in analyses restricted to studies with low risk of bias. Measurement errors in measurement of anthropometry could potentially explain some of the observed heterogeneity.

There were no studies from Africa and Asia in this meta-analysis. Body composition might differ between different racial groups and may explain the higher risk of cardiovascular events among South Asian and African individuals compared with European individuals in previous studies.¹⁰² It was difficult to adequately characterize racial differences in associations between adiposity and HF risk. In the only study that reported on African individuals, the observed associations were weaker than the association seen in White individuals and multiracial studies. There is need for population studies to investigate the racial differences in risk of HF due to adiposity.

Associations were stronger for studies with more events and longer follow-up, and weaker in studies with shorter follow-up. Although this could be due to insufficient power of studies with shorter follow-up to detect incident events, or weight gain over time being responsible for stronger association with time, these explanations do not fully explain this finding. It is well known that body fat distribution is dynamic and shows temporal variation. Studies that use baseline values of anthropometry are prone to underestimate the strength

of associations compared with long-term usual levels of these anthropometric measures. All the included studies used anthropometric measurements at baseline and did not correct for regression dilution bias. There is a need for future studies to explore this phenomenon.

Comparability of studies in meta-analysis is usually affected by differences in adjustment for confounders and intermediate factors. Several studies either under- or overadjusted their reported estimates. Studies that adjusted for intermediate factors and comorbidities reported shallower association. Our sensitivity analyses showed that the heterogeneity is largely explained by differences in handling of covariates and residual confounding.

We may have underestimated or overestimated the effect sizes in the trend estimation for studies that reported categories of anthropometry by assuming that adiposity measures are normally distributed in the general population. This is especially true for studies that did not provide distribution of cases, noncases, and means in each category. However, studies for which effect sizes were estimated had similar association to studies that directly reported effect sizes.

Contrary to our aims, we were unable to extensively investigate the associations between body fat distribution and lean mass with incident HF using imaging methods due to the dearth of studies in this area. Future studies are needed to investigate the independent and additive association of body fat distribution and lean mass in incident HF in the general population.

Our findings have important implications for clinical practice and preventive public health advice for the general population. Both general and central adiposity are associated with increased HF risk, and their routine measurement in the general practice clinics can be used as a predictive marker in individuals at increased risk of HF. We have also shown that VAT and pericardial adipose tissue, but not SAT, are associated with increased HF risk. The stronger association between adiposity and HFpEF than HFrEF points to different roles of adiposity in HF subtypes. Public health guidance for the general population should emphasize weight reduction strategies to reduce the risk of HF even in individuals without CVD. There is a need for larger studies to investigate the role of adiposity in HF subtypes, the added value of fat quantification over anthropometric measures in HF risk prediction, and the racial differences in association between adiposity and HF risk.

ARTICLE INFORMATION

Received December 1, 2022; accepted May 15, 2023.

Affiliations

Clinical Trial Service Unit & Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health (NDPH), University of Oxford, UK (A.S.O.,

N.I., H.T., D.J., S.L., B.L.); School of Primary Care, Population Sciences and Medical Education, Faculty of Medicine, University of Southampton, UK (N.I.); National Perinatal Epidemiological Unit, Nuffield Department of Population Health (R.M.) and MRC Population Health Research Unit, NDPH (S.L.), University of Oxford, UK; and UKM Medical Molecular Biology Institute (UMBI), Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia (S.L.).

Acknowledgments

The authors acknowledge N. Roberts for working with the authors to develop the search strategy for this work.

Sources of Funding

This work was funded by a doctoral scholarship to A.S.O. from the Nuffield Department of Population Health, University of Oxford (Oxford, United Kingdom). B.L. acknowledges support from UK Biobank, funded largely by the UK Medical Research Council and Wellcome.

Disclosures

S.L. reports grants from the Medical Research Council and research funding from the US Centers for Disease Control and Prevention Foundation (with support from Amgen) during the conduct of the study. N.I. reports grants from the Canadian Institutes of Health Research, Office for National Statistics, National Institute for Health and Care Research, and Health Data Research UK unrelated to this study. The remaining authors have no disclosures to report.

Supplemental Material

Tables S1–S5

Figures S1–S13

Reference [103]

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SUPPLEMENTAL MATERIAL

Table S1. Search strategy for the systematic review.

Search	Keywords	Thesaurus (MeSH)	Textwords
#1	Exposure	Body Composition/ Body Weights and Measures/ Adipose Tissue/ Obesity/ Obesity Hypoventilation Syndrome/ Obesity, Abdominal/ Obesity, Metabolically Benign/ Obesity, Morbid/ Obesity Management/ Bariatrics/ Metabolic Syndrome/ Adipocytes/ Adiposity/ Body Fat Distribution/ Anthropometry/ exp Subcutaneous Fat/ exp Subcutaneous Fat, Abdominal/ Body Mass Index/ Body Weight/ Body Height/ Waist Circumference/ Waist-Height Ratio/ Waist-Hip Ratio/ Body Constitution/ Somatotypes/ Body Size/ Overweight/ Abdominal Fat/ Body Weight Changes/ Sarcopenia/ Thinness/ Cachexia/ Intra-Abdominal Fat/	((body or abdom* or intraabdom* or central or truncal or trunk or appendicular or subcutaneous or sub- cutaneous or visceral or limb or arm or leg or peripheral or android or gynoid) adj fat?).mp body composition* body weight and measure* adipos* obes* metabolic syndrome* overweight* BMI* adipocyt* fat distribution* fat mass* anthropometr* quetelet* index* body weight* body height* waist circumference* waist-height ratio* hip circumference* waist-hip ratio* body constitution* Somatotypes* body size* body mass* sarcop?enia* thinness* muscle mass* muscle bulk* lean mass* fat-free mass* skeletal bulk* heart failure* cardiac failure* diastolic HF* systolic HF* pulmonary o?dema HFrEF* HFpEF* HFmEF* ventricular failure* biventricular failure* cardiac dysfunction* ventricular dysfunction* cardiomyopath* cardiorenal syndrome* cardiomegaly* ventricular* hypertrophy* cardia* hypertrophy* ventricular function ventricular remodeling* cardia* remodeling* BNP* NT-BNP* natriuretic peptide* cohort* longitudinal* prospective* follow-up* observational * incidence stud*
#2	Outcomes	exp Heart Failure/ Pulmonary Edema/ Ventricular Dysfunction/ Ventricular Dysfunction, Left/ Ventricular Dysfunction, Right/ exp Cardiomyopathies/ Cardiomegaly/ Hypertrophy, Left Ventricular/ Hypertrophy, Right Ventricular/ exp Ventricular Function/	
#3	Study type	exp Cohort Studies/ Observational Study/	
#4		#1 AND #2 AND #3	

Table S2. Quality grading of included studies.

S/No	Quality measure (met=1, not met=0)									
	First author (publication year)	Study selection				Group comparability	Outcome assessment			Total quality score (max. 9)
		Representative study ^a	Detailed description of participant selection and eligibility	Standardised or validated method of composition measurement	Absent HF at baseline		Record linkage or standardised adjudication used for outcome	Follow-up, >5 years	Adequate follow-up (complete follow-up or <10% loss to follow-up)	
1	Chen (1999) ⁶⁷ , USA, The New Haven Cohort	0	1	0	1	2	1	1	0	6
2	He (2001) ⁶⁶ , USA, NHANES 1 Epidemiologic follow-up Study	1	1	1	1	1	1	1	1	8
3	Kenchaiah (2002) ¹⁰³ , USA, Framingham Heart Study	1	1	1	1	1	1	1	1	8
4	Ingelsson (2005) ⁵⁶ , Sweden, The Uppsala Longitudinal Study of Adult Men cohort	1	1	0	1	0	1	1	1	6
5	Nicklas (2006) ⁵ , USA, The Health, Aging and Body Composition study	0	1	1	1	2	1	1	0	7
6	Murphy (2006) ⁵⁷ , Scotland UK, Renfrew–Paisley study	1	1	1	0	2	1	1	0	7
7	Thrainsdottir (2007) ⁵⁸ , Iceland, Reykjavík Study	1	1	0	1	0	1	1	0	5
8	Douglas Lee (2007) ⁶¹ , USA, Framingham Heart Study	1	1	1	1	1	1	1	0	7
9	Kenchaiah (2009) ⁶² , USA, Physicians' Health	0	1	0	1	2	1	1	0	6
10	Levitan (2009) ⁵⁹ , Sweden Swedish Mammography Cohort	1	1	0	1	2	1	1	0	7
11	Levitan (2009) ⁵⁹ , Sweden, Cohort of Swedish Men	1	1	0	1	2	1	1	0	7
12	Loehr (2009) ⁷³ , USA, Atherosclerosis Risk in Communities (ARIC)	1	1	1	1	2	0	1	0	7
13	Hu (2010) ⁶⁰ , Finland, Finnish Population Survey	1	1	1	1	2	1	1	0	8
14	Wang (2010) ⁴⁷ , Finland, Kuopio Finnish Cohort	1	1	1	1	2	0	1	0	7
15	Baena-Diez (2010) ⁴⁸ , Barcelona Spain, Zona Franca Cohort Study	1	1	1	1	1	0	1	0	6
16	Van Lieshout (2011) ⁴⁹ , Netherlands, Rotterdam Study	0	1	1	1	2	1	1	0	6
17	Voulgari (2011) ⁵⁰ , Greece, Athens Cohort	1	1	1	1	2	0	1	0	7
18	Wannamethee (2011) ⁵¹ , UK, The British Regional Heart Study	0	1	1	1	2	1	1	1	8
19	Djoussé (2012) ⁶³ , USA, The Cardiovascular Health Study (CHS)	0	1	1	1	2	1	1	0	7
20	Brouwers (2013) ⁵² , Groningen The Netherlands, PREVEND cohort	1	1	0	0	1	1	1	0	5
21	Ebong (2013) ⁶⁴ , USA, Multi-Ethnic Study of Atherosclerosis (MESA)	1	1	1	0	2	1	1	0	7

22	Borne (2014) ⁵³ Ahead of print 2012, Sweden, Malmo Diet and Cancer (MDC) cohort	1	1	1	1	2	1	1	0	8
23	Mørkedal (2014) ⁵⁴ , Norway, HUNT (Nord-Trøndelag Health Study)	1	1	1	1	1	1	1	0	7
24	Joshy (2014) ⁶⁸ , Australia, 45 and Up Study	1	1	0	1	2	1	0	0	6
25	Björck (2015) ¹⁹ , Gothenburg Sweden, Multifactor Primary Prevention Study	0	1	1	1	2	1	1	1	8
26	Del Gobbo (2015) ²⁰ , USA, Cardiovascular Health Study	1	1	1	1	2	1	1	0	8
27	Eaton (2016) ²⁷ , USA, Women's Health Initiative	0	1	0	1	2	1	1	0	6
28	Ndumele (2016) ²⁸ , USA, Atherosclerosis Risk in Communities (ARIC)	1	1	1	1	2	1	1	0	8
29	Janszky (2016) ²⁹ , Norway (HUNT2)	1	1	1	1	2	1	1	0	8
30	Krishnamoorthy (2016) ³⁰ , USA, Jackson Heart Study	1	1	1	1	2	1	1	0	8
31	Pandey (2017) ²¹ , USA, Cooper Center Longitudinal Study	1	1	1	0	1	1	1	0	6
32	Rao (2018) ³ , USA, Multi-Ethnic Study of Atherosclerosis (MESA)	1	1	1	1	2	1	1	0	8
33	Fliotsos (2018) ²² , USA, Multi-Ethnic Study of Atherosclerosis (MESA)	1	1	1	1	2	1	1	0	8
34	Gong (2018) ⁷¹ , Australia, SCREEN-HF study	0	1	1	1	0	1	0	0	4
35	Pandey (2018) ⁴ , USA, Jackson Heart Study	1	1	1	1	1	1	1	1	8
36	Kokkinos (2019) ²³ , USA, ETHOS Veteran cohort	0	1	1	1	2	1	1	0	7
37	Kubicki (2020) ⁶⁵ , USA, Southern Community Cohort Study (SCCS)	1	1	0	1	2	1	1	0	7
38	Campbell (2019) ¹¹ , Australia, SCREEN-HF	0	1	0	1	0	1	0	0	3
39	Halldin (2020) ²⁴ , Gothenburg Sweden, Prospective Population Study of Women in Gothenburg (PPSWG)	0	1	1	1	1	1	1	0	6
40	Ergatoudes (2020) ²⁵ , Gothenburg Sweden, Men born in Gothenburg 1913 cohort	0	1	1	1	2	1	1	0	7
41	Chen (2020) ²⁶ , Sweden, The Study of men born in 1943	0	1	1	1	2	1	1	0	7
42	Rao (2021) ⁶⁹ Jackson Heart Study	1	1	1	1	2	1	1	0	8
43	Kenchaiah (2021) ⁷⁰ , MESA	1	1	1	1	2	1	1	1	9
44	Suthahar (2022) ⁷² , The Netherlands, PREVEND	1	1	1	1	1	1	1	0	8
45	Xing (2023) ⁵⁵ , UK, The UK Biobank	1	1	1	1	2	1	1	1	9

^aRepresentative cohort defined as general adult population.

^bDefined as adjustment for at least age and sex (except for studies done in specific sexes or specific age group only). One extra point given for additional adjustment for other lifestyle confounders.

Table S3. Comparison of observed and predicted means of adiposity categories in relevant studies.

Author	Sex	BMI					WC					WHR				
		Categories	Minimum	Maximum	Reported mean	Calculated mean	Categories	Minimum	Maximum	Reported mean	Calculated mean	Categories	Minimum	Maximum	Reported mean	Calculated mean
Kenchiah (2002) ¹⁰³	women	normal	18.5	24.9	22.3	21.7										
	women	overweight	25	29.9	27.1	27.5										
	women	obese	30	34.9	34.1	32.5										
	men	normal	18.5	24.9	23.2	21.7										
	men	overweight	25	29.9	27.2	27.5										
	men	obese	30	34.9	32.7	32.5										
Murphy (2006) ⁵⁷	women	normal	18.5	24.9	22.5	21.7										
	women	overweight	25	29.9	27.1	27.5										
	women	obese	30	34.9	33.6	32.5										
	men	normal	18.5	24.9	22.8	21.7										
	men	overweight	25	29.9	27.1	27.5										
	men	obese	30	34.9	32.1	32.5										
	both sexes	normal	18.5	24.9	22.6	21.7										
	both sexes	overweight	25	29.9	27.1	27.5										
	both sexes	obese	30	34.9	33	32.5										
Kenchiah (2009) ⁶²	both sexes	lean	18.5	24.9	23	21.7										
	both sexes	overweight	25	29.9	26.6	27.5										
	both sexes	obese	30	34.9	32.4	32.5										
Loehr (2009) ⁷³ white women	white women	normal weight	18.5	25	22.2	21.7	first tertile	74	86.9	78.9	80.45	first tertile	0.79	0.85	0.8	0.82
	white women	overweight	25	29.9	27.2	27.5	second tertile	87	99.9	92.6	93.45	second tertile	0.86	0.92	0.89	0.89
	white women	obese	30	34.9	34.4	32.5	third tertile	100	112.9	111.2	106.45	third tertile	0.93	0.99	0.98	0.96
Loehr (2009) ⁷³ black women	black women	normal weight	18.5	25	22.7	21.7	first tertile	74	86.9	79.4	80.45	first tertile	0.79	0.85	0.8	0.82
	black women	overweight	25	29.9	27.5	27.5	second tertile	87	99.9	93.2	93.45	second tertile	0.86	0.92	0.89	0.89
	black women	obese	30	34.9	35.8	32.5	third tertile	100	112.9	113.4	106.45	third tertile	0.93	0.99	0.98	0.96
Loehr (2009) ⁷³ white men	white men	normal weight	18.5	25	23.1	21.7	first tertile	86.9	94.9	88.9	90.9	first tertile	0.9	0.93	0.91	0.915
	white men	overweight	25	29.9	27.3	27.5	second tertile	95	103	98.4	99	second tertile	0.94	0.97	0.96	0.955
	white men	obese	30	34.9	33	32.5	third tertile	103.1	111.1	110.4	107.1	third tertile	0.98	1.01	1.02	0.995

Table S4. Characteristics of studies included in the systematic review.

S/No	First author(Publication year), country, cohort name	Recruitment Year	Study size (% men or women), mean age- years (SD/IQR)	Mean/Median follow-up (years)	Exclusions	Body composition measure	Study outcome	Outcome ascertainment method	Count of incident HF	HF type/aetiologies	Adjustments	Shape of associations	Type of HR	Hazard/Risk Ratio (95%CI)	Study Quality score
1	Chen (1999) ⁶⁷ , USA, The New Haven Cohort	1982	1749 (59% women), 74.2 (6.8) years	7.9 years	Prevalent HF, or ischaemic heart disease	BMI	Incident heart failure	Electronic record linkage and review of hospital records	173	N/A	Age, sex, diabetes, pulse pressure, type of housing	N/A	Per strata	BMI categories BMI <24: ref BMI 24-27.9: 1.1 (0.7-1.6) BMI ≥28: 1.6 (1.0-2.4)	6
2	He (2001) ⁶⁶ , USA, NHANES 1 Epidemiologic Follow-up Study	1971-1975	13,643 (59.4% women) Men: 52.2 (15.2) years Women: 48.1 (15.4) years	9 years	Prevalent HF in the 6 months before recruitment, loss to follow-up	BMI	Incident HF	Participants/proxy interviews, review of hospital/nursing home records and death certificates	1382	N/A	Age, sex, race time-dependent history of coronary heart disease	N/A	Overweight (BMI ≥27.3 in women/ ≥27.8 in men) vs normal weight (BMI <27.3 in women/ <27.8 in men)	BMI categories Normal weight: ref Overweight women: 1.24 (1.01-1.51) Overweight men: 1.43 (1.19-1.72) Overweight overall: 1.35 (1.17-1.55)	8
3	Kenchaiah (2002) ¹⁰³ , Framingham Heart Study	1976-1979 and 1979-1983)	5881 (54.0% women),	14 years	Under-30 years old, underweight, prevalent HF, missing co-variables, lack of follow-up data	BMI	Incident HF	Adjudication by study panel physicians using Framingham criteria	496	N/A	Age, sex, alcohol, serum total cholesterol, cigarette smoking, valve disease, hypertension, diabetes, electrocardiographic Left ventricular hypertrophy and myocardial infarction	linear	per 1 kg/m ² increase of BMI and per strata of BMI	Per unit higher BMI Women: 1.07 (1.04-1.07) Men: 1.05 (1.02-1.09) Total: 1.06 (1.04-1.09) BMI categories Normal weight (18.5-24.9): ref Overweight (25.0-29.9): 1.34 (1.08-1.67) Obese (≥30.0): 2.04 (1.59-2.63)	8
4	Ingelsson (2005) ⁶⁸ , Sweden, The Uppsala Longitudinal Study of Adult Men cohort	1970-1974	1187 (100% men), ≥70 years	8.9 years (range, 0.01- 11.4 years)	Prevalent HF and valvular disease	BMI	Incident HF hospitalisation	Blinded adjudication of hospital discharge register	104	N/A	Diabetes plus prior acute MI, hypertension, electrocardiographic LVH, smoking, and serum cholesterol level	linear	per SD	BMI 1.35 (1.11-1.65); WC 1.36 (1.10-1.69)	6
5	Nicklas (2006) ⁵ , USA, The Health, Aging and Body Composition study	1997-1998	2435 (56% women), No HF: 74.1 (2.8) years HF: 74.6 (3.0) years	6.1 ± 1.4	Missing last contact date, prevalent adjudicated acute MI, coronary heart disease, heart failure or pacemaker	BMI, WC, waist-thigh ratio (WTR), TFM, BF%, VAT area, SAT area (DXA for fat quantification)	Incident adjudicated chronic HF	Adjudicated HF hospitalisations	166 (54 were diastolic HF)	N/A	age, sex, race, site, education, smoking, and chronic obstructive pulmonary disorder (COPD)	positive	per 4.88 kg/m ² increase of BMI, per 7.93% increase of BF%, per 8.76 kg increase of BFM, per 13.38 cm increase of WC, per 0.23 increase of WTR, per 66.37 cm ² increase of VAT area, per 124.19 cm ² increase of SAT area	BMI: 1.31 (1.13–1.52) WC: 1.33 (1.17–1.50) WTR: 1.19 (1.03–1.38) BF%: 1.55 (1.22–1.96) BFM: 1.31 (1.12–1.54) VAT area: 1.25 (1.08-1.45) SAT area: 1.27 (1.07–1.50)	7
6	Murphy (2006) ⁵⁷ , Scotland UK, Renfrew–Paisley study	1972-1976	15144 (53.8% women), 54(6) years	20	Underweight	BMI	Incident HF	Electronic health linkage	594	N/A	sex, age, adjusted FEV1, number of cigarettes smoked per day and social class.	linear	Per strata	Normal weight: Ref Overweight: 1.26 (1.05-1.50) Obese: 2.09 (1.68-2.59)	7
7	Thrairnisdottir (2007) ⁶⁹ , Iceland, Reykjavik Study	1967-1980	7060 (45% women), 33-84 years	13 ± 8 years	diabetes, abnormal glucose regulation or HF at first visit	BMI	Incident HF diagnosis	adjudicated	489	N/A	Sex, IHD, hypertension, cholesterol and smoking	positive	Per 1Kg/m ² increase	1.09 (1.07–1.11)	5
8	Douglas Lee (2007) ⁶¹ , USA, Framingham Heart Study	1968-1994	3362 (57% women), 62 years	20	Prevalent HF, less than 3 BP and BMI measurements in preceding (1970s) and remote (1960s) decades.	BMI	incident HF	Adjudication of medical histories, physical examinations at the heart study, hospitalization records, and communication with personal physicians using the Framingham criteria.	518	N/A	age, sex, serum cholesterol, systolic and diastolic BP, hypertension treatment, diabetes, smoking, valve disease, and previous myocardial infarction (all defined at the baseline examination) and for incidence of an interim myocardial infarction on follow-up.	linear increase	per Kg/m2	Baseline BMI: 1.05 (1.03-1.07)	6
9	Kenchaiah (2009) ⁶² , USA, Physicians' Health	1982	21094 (100% men), 53 years	20.5±5.4 years	Missing height, weight or physical activity at baseline, missing information on other covariates and HF before baseline examination	BMI	incident HF diagnoses	Adjudicated self-reported diagnoses and symptoms	1109	N/A	age,smoking, alcohol, parental history of myocardial infarction, trial group assignment	linear increase	per unit increase and per strata	BMI per unit increase 1.13 (1.11–1.15); BMI categories: Lean- reference overweight 1.62 (1.43–1.83) obese 3.38 (2.71–4.21)	5
10	Levitán (2009) ⁵⁹ , Sweden Swedish Mammography Cohort	1997-1998	36873 (100 % women), 48-83 years	7	Prevalent HF, underweight, HF hospitalisation or death in first 2 years of follow-up, absent or incorrect national identification numbers, implausible energy intakes, previous diagnosis of cancer (other than non-melanoma skin cancer)	BMI, WC, WHR, WHtR	incident HF admissions and deaths	Electronic record linkage to the Swedish inpatient and cause of-death registers.	382 women,	N/A	age, education, smoking, alcohol consumption, total physical activity, postmenopausal hormone therapy, living alone, and family history of myocardial infarction.	linear increase	per unit increase in BMI, per 10cm increase in WC, per IQR increase in WHR, per IQR increase in WHtR	BMI: 1.03 (1.01-1.05) WC: 1.19 (1.08-1.31), WHR: 1.05 (0.95-1.15), WHtR: 1.21 (1.06-1.38)	6
11	Levitán (2009) ⁵⁹ , Sweden, Cohort of Swedish Men	1997-1998	43487 (100% men), 45-79 years	7	Prevalent HF, underweight, HF hospitalisation or death in first 2 years of follow-up, absent or incorrect national identification numbers, implausible energy intakes, previous diagnosis of cancer (other than non-melanoma skin cancer)	BMI, WC, WHR, WHtR	incident HF admissions and deaths	Electronic record linkage to the Swedish inpatient and cause of-death registers.	718 men	N/A	age, education, smoking, alcohol consumption, total physical activity, marital status, and family history of myocardial infarction.	linear increase	per unit increase in BMI, per 10cm increase in WC, per IQR increase in WHR, per IQR increase in WHtR	BMI: 1.07 (1.05-1.08) WC: 1.30 (1.21-1.38), WHR: 1.10 (1.03-1.18), WHtR: 1.35 (1.25-1.46)	6
12	Loehr (2009) ⁷³ , USA, Atherosclerosis Risk in Communities (ARIC)	1987 and 1989	14641, 54% men with incident HF, 44% men without incident HF),	16	Non-White and non-Black ethnicities, Blacks outside Jackson or Forsyth County, missing anthropometry, prevalent HF, missing criteria to define prevalent HF	BMI, WC	Incident HF (hospitalised and fatal)	Review of participants' interviews, hospital discharges and death certificate files	1528	N/A	age, alcohol use, educational level, smoking status, and center	positive	per SD	BMI: Women 1.49 (1.39, 1.59) Men (1.39, 1.57) WC:	6

			Incident HF group: 56.8 (5.4) years											Women 1.54 (1.44, 1.66)	
			Non-cases group: 53.8 (5.7) years											Men 1.52 (1.43, 1.62)	
														WHR:	
														Women 1.59 (1.46, 1.72)	
														Men 1.50 (1.41, 1.60)	
13	Hu (2010) ⁶⁰ , Finland, Finnish Population Survey	Surveys done in 1972, 1977, 1982, 1987, 1992, 1997, and 2002.	59178 (51.3% women), 45 (11) years	18.4	Prevalent HF, underweight, incomplete data	BMI, WC, WHR	Incident HF	Electronic record linkage to Finnish Hospital Discharge Register and the National Social Insurance Institution's Register and the Finnish Death Register	3614	N/A	age, study year, education, smoking, alcohol consumption, history of myocardial infarction, valvular heart disease, and diabetes mellitus, systolic blood pressure, total cholesterol, and physical activity.	N/A	Per strata	BMI: Men <25 ref, 25-29.9 1.25 (1.12-1.39) ≥30 1.99 (1.74-2.27) Women <25 ref, 25-29.9 1.33 (1.16-1.51) ≥30 1.99 (1.80-2.37) WC quartiles: Men Q1 1.06 (0.69-1.64) Q2 ref Q3 1.21 (0.84-1.76) Q4 1.85 (1.32-2.61) Women Q1 0.48 (0.21-1.13) Q2 ref Q3 1.18 (0.71-1.96) Q4 1.64 (1.02-2.64) WHR: Men Q1 0.88 (0.58-1.31) Q2 ref Q3 1.06 (0.74-1.50) Q4 1.71 (1.23-2.37) Women Q1 0.61 (0.31-1.19) Q2 ref Q3 0.98 (0.59-1.63) Q4 1.88 (1.17-3.01)	8
14	Wang (2010) ⁴⁷ , Finland, Kuopio Finnish Cohort	1986-1988	1032, 61.4% women with incident HF, 61.9% women without incident HF), Incident HF group: 69.1 (2.8) years Non-cases group: 68.8 (2.9) years	20	Prevalent HF	WC	Incident HF	Incident HF identified from medical records of the Kuopio University Hospital	303	N/A	age, gender, physical activity during leisure time, smoking, alcohol consumption, antihypertensive medications, total cholesterol and prevalent diabetes	N/A	Per strata	Waist circumference≥94cm (women:≥80 cm): 1.36 (1.03–1.79) Waist circumference≥102cm (women:≥88 cm) 1.40 (1.09–1.80) Waist-to-hip ratio > 0.90 (women: > 0.85) 1.29 (0.94–1.78) BMI≥30 kg/m² 1.55 (1.19–2.02)	7
15	Baena-Diez (2010) ⁴⁸ , Barcelona Spain, Zona Franca Cohort Study	1998	932 (BMI <25 61.2% women, BMI 25-29.9 51% women, BMI ≥30 64.4% women), 58 years	9.98	Prevalent HF	BMI	incident HF	Framingham criteria	26 (14 with systolic HF and 12 with non-systolic HF)	analyses presented as any incident HF	age, sex, hypertension, ischaemic heart disease, DM	linear	per unit and per strata	BMI per unit increase: 1.06 (1.01–1.10); BMI categories BMI <25: reference BMI 25-29.9: 0.79 (0.21–3.00) BMI ≥30:2.45 (1.02–5.61)	8
16	Van Lieshout (2011) ⁴⁹ , Netherlands, Rotterdam Study	1989-1993	5868	10.9 (4.4)	Prevalent HF	BMI, WC, WHR	incident HF	Adjudication of clinical symptoms and signs, hospital discharge letters and notes from general practitioners	765 (373 women, 392 men)	N/A	age, sex, cholesterol, DM, smoking, antihypertensive medications	linear	per SD	BMI 1.20 (1.11 – 1.29) WC 1.21 (1.12 – 1.30) WHR 1.11 (1.02-1.21) Association stronger in men than women; and in middle-aged than elderly	6
17	Voulgari (2011) ⁵⁰ , Greece, Athens Cohort	2003-2005	550	6	Cardiovascular disease, prevalent HF, valvular disease, CKD (eGFR <60ml/min), NSAIDs or corticosteroids in previous 3 months	BMI	Incident HF	Clinical assessment by study physician, LV systolic or diastolic dysfunction by echocardiography	185	N/A	age, sex, impaired glucose tolerance, dyslipidemia, hypertension, current cigarette smoking, physical inactivity, left ventricular hypertrophy and function	N/A	per strata	Normal No MetS Ref(1.00); Normal+MetS 2.33(1.25–4.36) Overweight NoMetS 1.12(0.35–1.33) Overweight+MetS 2.66 (1.73–4.13) Obese No MetS 0.41(0.10–1.31) Obese+MetS 2.13(1.29–3.17)	8
18	Wannamethee (2011) ⁵¹ , UK, The British Regional Heart Study	1998 -2000	4080 (720 pre-existing CHD 3360 no pre-existing CHD), 100% men, 60-79 years	9	Prevalent HF, underweight, missing BMI	BMI, WC	incident HF	Doctor confirmed diagnosis of HF from primary care records via electronic record linkage.	228 (80 CHD associated HF, 148 non CHD associated HF)	CHD associated HF, non CHD associated HF	age, smoking, physical activity, social class, antihypertensive treatment, prevalent diabetes, prevalent stroke, left ventricular hypertrophy, atrial fibrillation, use of beta-blockers, and FEV1	linear	per unit, per SD and per strata	Men without CHD: BMI per SD: 1.19 (1.04–1.37) BMI per unit 1.05 (1.01–1.10) WC per SD 1.17 (0.99–1.37) WC per unit 1.02 (0.99–1.03) Men with pre-existing CHD: BMI per SD: 1.32 (1.04–1.66) BMI per unit 1.07 (1.01–1.14) WC per SD 1.30 (1.06–1.59) WC per unit 1.03 (1.00–1.05)	8
19	Djoussé (2012) ⁶³ , USA, The Cardiovascular Health Study (CHS)	1989-1990; 1992-1993	4861 (42.5% men), mean age in men 73.0 (5.6) years, women (72.3 (5.4) years	11.3	Prevalent HF, missing BMI or WC, moderate/severe aortic or mitral regurgitation or stenosis on echocardiography, missing covariates	BMI, WC,	incident HF	Adjudication and review of self-reported physician diagnosed HF	1381	all HF, HFpEF, HFrEF	age, gender, clinic site, ethnicity,education, alcohol, smoking, physical activity, eGFR, vavular disease, atrial fibrillation, aspirin use, oestrogen use (for women)	linear	per SD	WC: all 1.23 (1.16–1.30) men 1.31 (1.19–1.45) women 1.20 (1.11–1.29) HFrEF 1.19 (1.07–1.33), HFpEF 1.27 (1.13–1.42) BMI all 1.22 (1.15–1.29), men 1.28 (1.16–1.42), women 1.19 (1.11–1.28) WHR All 1.89 (1.03-3.46)- additionally adjusted for BMI	7
20	Brouwers (2013) ⁶² , Groningen The Netherlands, PREVEND cohort	1997-1998	8592 (28-75 years old)	11.5 (range 10.8– 11.9)	Insulin dependent diabetes mellitus, pregnant women, and subjects unable or unwilling to participate	BMI used to define obesity as 30Kg/m2	New onset HF	Adjudication of clinical symptoms and signs, hospital records and echocardiographic records	374 subjects. 125 (34%) were classified as HFpEF and 241 (66%) as HFrEF	HFpEF, HFrEF	age and sex	not given	per strata (obesity vs no obesity)	All HF 1.93 (1.37–2.73) HRs of HFpEF, HFrEF not reported	6

21	Ebong (2013) ⁶⁴ , USA, Multi-Ethnic Study of Atherosclerosis (MESA)	2000-2002	6809, 45-84 years old	7.6	Participants without baseline measurements of obesity, and those for whom no follow-up was completed	BMI, WC	HF hospitalisation s, HF deaths or outpatient diagnosis of HF	Adjudication of hospital records	176	N/A	age, ethnicity, educational status, cigarette smoking, intentional exercise and center.	linear	Per SD	BMI Men: 1.33 (1.10-1.61) Women: 1.70 (1.33-2.17) WC Men: 1.38 (1.18-1.62) Women: 1.64 (1.29-2.08)	
22	Borne (2014) ⁵³ Ahead of print 2012, Sweden, Malmo Diet and Cancer (MDC) cohort	March 1991 to September 1996	26653 (61.6% women), 45-73 years old	14	history of cardiovascular events (MI or stroke), or HF before baseline exam, missing values of anthropometric measurements and covariates	BMI, WC, WHR, BF%	incident HF hospitalisation as primary diagnosis	Electronic record linkage to Swedish Hospital Discharge Register	727 individuals (398 men and 329 women)	N/A	age, sex, civil status, education level, immigrant status, smoking habits, alcohol consumption, physical activities, blood pressure-lowering medication, lipid-lowering medication, systolic blood pressure, leucocyte count and diabetes mellitus	N/A	per strata	BMI quintiles Q1 ref(1.00) Q2 0.98 (0.76–1.25) Q3 1.12 (0.88–1.42) Q4 1.80 (1.45–2.24) WC quintiles Q1 1.00 (ref) Q2 0.92 (0.71–1.19) Q3 1.15 (0.90–1.46) Q4 1.87 (1.50–2.34) WHR quintiles Q1 1.00 (ref) Q2 1.04 (0.82–1.32) Q3 1.13 (0.90–1.42) Q4 1.77 (1.43–2.19) BF% quintiles Q1 1.00(ref) Q2 0.98 (0.77–1.24) Q3 1.18 (0.95–1.47) Q4 1.35 (1.09–1.68)	7
23	Mørkedal (2014) ⁵⁴ , Norway, HUNT (Nord-Trøndelag Health Study)	August 1995 to June 1997	61299 (53.9% women), ≥20 years	12.3	missing information on BMI and individuals with a history of AMI, HF or cerebral stroke at baseline	BMI	first HF hospitalisation	Electronic record to medical records and national death registry. HF was diagnosed by cardiologists using European Society of Cardiology guidelines	1201	N/A	age and sex	N/A	per strata	BMI categories BMI <25 metabolically healthy reference BMI <25 metabolically unhealthy 1.3(0.9–1.8) BMI metabolically healthy 25-29.9 1.0(0.8–1.2) BMI 25-29.9 metabolically unhealthy 1.2(1.0–1.4) BMI >30 metabolically healthy 1.6(1.3–2.0) BMI >30 metabolically unhealthy 1.7(1.4–2.0)	8
24	Joshy (2014) ⁶⁸ , Australia, 45 and Up Study	1 January 2006 to 31 December 2008	158546, mean age 57.8 (13.9) years	3.4	invalid age and/or date of recruitment, extreme measures of BMI (<15 kg/m ² or >50 kg/m ²), cancer or CVD at baseline	BMI	HF hospitalisation	Electronic record linkage	320	N/A	age, sex, region of residence, household income, education, smoking, alcohol intake and health insurance.	J-shape	Per strata	BMI categories 15-19.99: 1.72 (1.09-2.72) 20.0-22.49: Ref 22.5-24.99: 0.91 (0.62-1.32) 25.0-27.49: 1.13 (0.78-1.64) 27.5-29.99: 0.96 (0.63-1.47) 30.0-32.49: 1.63 (1.06-2.51) 32.5-50: 3.52 (2.39-5.19)	6
25	Björck (2015) ¹⁹ , Gothenburg Sweden, Multifactor Primary Prevention Study	1970	7495 (100% men), 51.1 (2.3) years	35	Prevalent HF	BMI	Primary or secondary diagnosis of HF	Electronic record linkage to Swedish national Inpatient Register (IPR) and the Swedish Cause of Death register	1855 total, 851 non ischaemic, 1004 ischaemic	any HF, non-ischaemic HF, ischaemic HF	age, IHD, smoking, physical activity and occupational status	linear	per strata	BMI categories BMI <22.5 1.00 (ref) BMI 22.5-24.99 1.19 (1.02-1.39) BMI 25-27.49 1.30 (1.11-1.52) BMI 27.5-29.9 1.51 (1.28-1.79) BMI ≥30 1.61 (1.32-1.96) Risk higher in ischaemic than non-ischaemic HF	8
26	Del Gobbo (2015) ²⁰ , USA, Cardiovascular Health Study	1989-1990, also recruited 687 African Americans in 1992	4490 (61% women) mean age 72 years	21.5	prevalent HF or moderate and/or severe mitral or aortic regurgitation at baseline, missing information on lifestyle risk factors, or implausible energy intake	BMI and WC	incident HF	Adjudication of outpatient and inpatient medical records, diagnostic tests, clinical consultations, and interviews	1380 (336 in obese, 1044 in non-obese)	N/A	age, sex, race, enrolment site, education, annual income	N/A	per strata	BMI categories BMI ≥30: reference, BMI 30: 0.66 (0.62 to 0.82) WC categories WC < 88cm women, < 92cm men: 0.76 (0.68-0.86) WC ≥ 88cm women, ≥ 92cm men: 1.0 (ref)	7
27	Eaton (2016) ²⁷ , USA, Women's Health Initiative	1993-1998	42170 (100% women), 50-79 years old	13.2	Self-reported prevalent HF, chronic HF on first adjudication, self-reported race: Asian/Pacific islander, Native American, or unknown race/ethnicity	BMI	hospitalised HF	Adjudication of self-reported HF hospitalisation	1952 in total, 902(46.2%) HFpEF, 508 (26.0%) HFrEF, 533 (27.3%) HF unknown ejection fraction, and 9 HF with recovered HF	HFpEF and HFrEF	age, education, family income, history of MI, history of CHD, stroke ever, hypertension, treated diabetes mellitus, history of cancer, hysterectomy, oophorectomy, atrial fibrillation, chronic lung disease, anemia, comorbidity index, diuretic use, beta blocker use, aspirin use, current hormone therapy, any insurance, alcohol intake, total energy expenditure/week from physical activity, age at screening and heart rate	N/A	per strata	HFpEF BMI <25 reference BMI 25-<30 1.11 (0.88–1.40) BMI 30-<35 1.35 (1.06–1.72) BMI ≥35 2.36 (1.84–3.03) HFrEF BMI <25 reference, BMI 25-<30 0.91 (0.68–1.21) BMI 30-<35 1.00 (0.74–1.36) BMI ≥35 0.87 (0.61–1.24)	5

28	Ndumele (2016) ²⁸ , USA, Atherosclerosis Risk in Communities (ARIC)	1987 to 1989	13730	23	Prevalent HF or cardiovascular disease, missing BMI, underweight (BMI <18.5Kg/m ²), not of either black or white race	BMI and WC	incident first hospitalization or death related to HF	Adjudication of discharge codes from hospitalizations and death certificates	2235	N/A	age, race, sex, alcohol use, smoking status, physical activity, occupation, and education level	linear increase	per strata	BMI categories normal weight Reference; overweight 1.38 (1.23–1.54); obese 2.10 (1.85–2.38); severely obese 3.74 (3.24–4.31) Sex-specific WC quartiles Q1 1.0 (Ref); Q2 1.43 (1.23–1.67); Q3 1.74 (1.50–2.00) Q4 3.01 (2.63–3.44)	8
29	Janszky (2016) ²⁹ , Norway (HUNT2)	August 1995 to June 1997	26097 (56.3% women), 61.0 (12.2) years	11.4	Underweight BMI, missing information on BMI and individuals with a history of AMI, HF or stroke at baseline.	BMI	incident HF	Electronic record linkage to the two hospitals of Nord-Trøndelag County	946	N/A	sex, age, smoking status, level of education, marital status, physical activity, and alcohol consumption	U shaped for average BMI and HF risk	per strata	BMI <24.9 Reference BMI 25.0-27.4: 1.07 (0.84-1.36) BMI 27.5-29.9: 1.26 (0.98-1.61) BMI 30.0-32.4: 1.26 (0.93-1.70) BMI 32.5-34.9: 1.84 (1.30-2.59) BMI ≥35: 2.65 (1.86-3.77)	8
30	Krishnamoorthy (2016) ³⁰ , USA, Jackson Heart Study	September 2000 and January 2013	5184	7	HF at baseline	BMI categorised into normal (<25 kg/m2), overweight (25 to<30 kg/m2),obese (30 to<35 kg/m2), and morbidly obese (≥35 kg/m2)	HF hospitalisation	Adjudication of HF hospitalisations using modified Gothenburg criteria	214	N/A	age, sex, prior myocardial infarction, hypertension, prior stroke, diabetes mellitus, chronic lung disease, smoking status, systolic blood pressure, pulse, sodium, estimated glomerular filtration rate, haemoglobin, glucose, high-sensitivity C-reactive protein, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, left ventricular ejection fraction, left ventricular hypertrophy, left ventricular diameter, beta-blocker, angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker, statin, antiplatelet agent, missing medication status and prevalent HF at examination 1	U shaped	per Kg/m2 increase and per strata	BMI per unit increase: crude 1.03 (1.01-1.04), adjusted 1.02 (1.01-1.04); BMI categories (adjusted) normal 1.00 [Reference] overweight 0.79 (0.54–1.14), obese 0.68 (0.46–1.02), morbidly obese 0.97 (0.66–1.44)	6
31	Pandey (2017) ²¹ , USA, Cooper Center Longitudinal Study	1970-2009	19485, individuals ≥65 years old	6.67	self-reported history of myocardial infarction or stroke at study entry, <65 years of age (due to Medicare coverage for disability, endstage renal disease, and other factors), Individuals lacking both Part A and B Medicare coverage and those with Health Maintenance Organization exclusions	BMI	HF hospitalisation	Electronic record linkage to Medicare heart failure billing codes	1038	N/A	age and sex	linear	per 3Kg/m2	BMI per 3Kg/m2 increase: 1.25 (1.17 to 1.32)	6
32	Rao (2018) ³ , USA, Multi-Ethnic Study of Atherosclerosis (MESA)	2002-2004, and between 2004-2005	1806 (48.4% men), 64.5 (9.6) years	10.5	Cardiovascular disease at baseline, HF event before the abdominal CT scan date, missing subcutaneous fat and visceral fat for all slices, missing ejection fraction at time of HF diagnosis, or missing other covariates in main analysis	BMI, WC, WHR, subcutaneous fat, visceral fat	incident HF	Adjudication of medical records	Total HF=70 (34 HFpEF, 36 HFrEF)	HFpEF, HFrEF	age, sex, race/ethnicity, smoking, and physical activity	linear increase	per SD	All HF: BMI 1.43 (1.11, 1.84) WC 1.40 (1.08, 1.81) WHR 1.22 (0.93, 1.61) SAT at L2-L3 1.22 (0.92, 1.63) SAT sum of 6 pcs 1.02 (0.73, 1.42) VAT at L2-L3 1.50 (1.16, 1.93) VAT sum of 6 pcs 1.46 (1.15, 1.86) HFpEF: BMI 1.73 (1.23–2.42) WC 1.74 (1.23–2.46) WHR 1.54 (1.04–2.30) SAT at L2-L3 1.31 (0.89–1.93) SAT sum of 6 pcs 1.23 (0.79–1.90) VAT at L2-L3 2.06 (1.44–2.95) VAT sum of 6 pcs 1.98 (1.40–2.79) HFrEF: BMI 1.14 (0.77–1.68) WC 1.08 (0.74–1.58) WHR 0.95 (0.65–1.39) SAT at L2-L3 1.12 (0.73–1.70) SAT sum of 6 pcs 0.80 (0.47–1.35) VAT at L2-L3 1.08 (0.75–1.55) VAT sum of 6 pcs 1.07 (0.76–1.52)	7
33	Flotsos (2018) ²² , USA, Multi-Ethnic Study of Atherosclerosis (MESA)	2000-2002	6437 (47.4% men), 62.2 (10.2) years	13	missing self-reported weight at age 20 or 40 years, had no follow-up information for atherosclerotic cardiovascular disease or HF, or were missing key covariates	baseline BMI	definite or probable HF (hospitalized)	Adjudication of medical records, telephone interviews every 9 to 12 months regarding interim hospital admissions, outpatient cardiovascular diagnoses	290	all HF, HFpEF, HFrEF	adjusted for age at baseline, sex, race/ethnicity, center, and education	curvilinear	per Sunits change	All HF: 1.43 (1.28, 1.60) BMI categories normal: reference overweight 1.24 (0.90, 1.71) obese 1.86 (1.34, 2.60), HFpEF: 1.61 (1.36, 1.91) BMI categories	8

								and procedures, and deaths;							normal: reference overweight 1.27 (0.77, 2.10) obese 1.862.09 (1.24, 3.52), HFrEF : 1.21 (1.01, 1.46) BMI categories normal: reference overweight 0.96 (0.59, 1.57 obese 1.39 (0.84, 2.30)	
34	Gong (2018) ⁷¹ , Australia, SCREEN-HF study	May 2007-January 2010	3847 (56.6% men) ≥60 years	4.5	Prevalent HF, LVEF < 50%, significant valve abnormality	Baseline BMI and waist circumference	Incident HF	Adjudication of HF events using ESC criteria of 2012	162 (73 HFpEF, 53 HFrEF, 36 Vavular HF)	All, HFpEF, HFrEF and valvular HF	univariate	N/A	log BMI per doubling per 10cm higher waist circumference	HFpEF BMI: 15 (6-35) WC: 1.6 (1.3-1.8) HFrEF BMI: 2.0 (0.7-5.4) WC: 1.4 (1.1-1.7) Valvular HF BMI: 0.5 (0.1-2.0) WC: 0.9 (0.7-1.2)	4	
35	Pandey (2018) ⁴ , USA, Jackson Heart Study	2005-2009 (visit 2)	2602 (35% men), 59 years	7.1	Weight >350pounds, pregnancy/unknown pregnancy status, age <40 years in women or <35 years in men, prevalent HFand loss to follow up	BMI, visceral fat (VAT) and abdominal subcutaneous fat (SAT)	Incident HF	Adjudication of HF events	122	N/A	Age and sex	linear	per strata per SD of VAT and SAT per 1kg/m² BMI	VAT: 1.29 (1.09-1.52) Tertile 1: ref Tertile 2: 1.40 (0.84-2.32) Tertile 3: 1.82 (1.14-2.92) SAT: 1.21 (0.99-1.48) Tertile 1: ref Tertile 2: 0.81 (0.49-1.32) Tertile 3 1.69 (1.07-2.67) BMI: 1.05 (1.02-1.08)		
36	Kokkinos (2019) ²³ , USA, ETHOS Veteran cohort	veterans who underwent treadmill tes between 1987 and 2017	20 254 (100% men), 58 (11.3) years	mean 3.6 ± 7.7 years, with a median of 13.4 years,	existing HF at the time of exercise testing or developed HF within 3months after the exercise test, BMI <18.5Kg/m², unstable or required emergent intervention or were unable to complete the test for orthopaedic, neurologic, or other reasons, exercise capacity <2METs, implanted pacemaker,lost to follow-up or missing data	BMI	Incident HF	Review of VA Computerized Patient Record System (CPRS) using ICD codes for HF	2979	N/A	age, BMI, ethnic origin, beta-blockers, calcium channel block-ers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers,diuretics, lipid-lowering agents, hypoglycaemic agents, smoking status, type 2 diabetes, dyslipidaemia, and hypertension	linear	per Kg/m2	1.02 (1.01 –1.03)	7	
37	Campbell (2019) ¹¹ , Australia, SCREEN-HF		3842 (55% men), 70 (65-75) years	Total 5.6 (IQR: 4.5–6.3); HFpEF 4.5 (interquartile range: 2.9–5.5)	known heart failure, ejection fraction <50% or more than mild valve abnormality	BMI, WC	Incident HF (ambulatory and hospital diagnosed)	Adjudication by 2 HF specialists according to European Society of Cardiology (ESC) criteria of 2012	162 (73 with HFpEF, 53 with HFrEF and 36 with VHF)	HFpEF	age, hypertension, diabetes, myocardial infarction, atrial fibrillation, serum amino-terminal pro-B-type natriuretic peptide (NT-proBNP) quintile, haemoglobin, and calcium channel blocker therapy	positive increase across categories	per strata	BMI BMI <25 (ref), BMI 25-27.4 : 2.5 (0.9-6.8) BMI 27.5-29.9: 5.4 (2.1-13.8) BMI ≥30: 7.6 (3.3-17.8); WC quintiles Q1. 66–94 in men; 57–83 in women: 1(ref) Q2. 95–100 in men; 84–90 in women: 2.8 (0.8-9.7) Q3. 101–105 in men; 91–96 in women: 5.0 (1.6-15.5) Q4. 106–112 in men; 97–104 in women: 4.4 (1.4-13.7) Q5. 113–155 in men; 105–146 in women: 10.2 (3.5-29.6)	6	
38	Kubicki (2020) ⁶⁵ , USA, Southern Community Cohort Study (SCCS)	2002-2009	27,078 (62.6% women), 69% black, 54 (47-65) years	5.2 (3.1, 6.7) years	Prevalent HF	BMI	Incident HF	Electronic health record linkage	4341	N/A	Age, sex, race, history of myocardial infarction or coronary artery bypass graft, stroke, transient iscahemic attack, education, annual household income, marital status, enrolment source, diabtes, hypertension, underactivity, smoking, poor diet and serum cholesterol	N/A	BMI ≥25 kg/m² vs normal BMI <25 kg/m²	BMI <25 kg/m²: ref BMI ≥25 kg/m² :1.12 (1.03-1.22)	7	
39	Halldin (2020) ²⁴ , Gothenburg Sweden, Prospective Population Study of Women in Gothenburg (PPSWG)	PPSWG (1968-1969); PPSWG (1980-1981)	1968-1980 cohort 1132; 1980-1992 cohort 932 (100% women)	1968 to 1980 cohort: 44 years; 1980 to 1992: 32 years	previous history, sign or diagnosis of HF	BMI	hospitalisation or mortality for HF	Electronic record linkage to Swedish Hospital Discharge Registry and Swedish National Board of Health and Welfare register of causes of death	1968-1980 cohort 271, 1980-1992 cohort 174	N/A	age	N/A	per strata	1968-1980 cohort BMI <25: reference BMI 25- <30: 1.26 (0.90–1.72) BMI ≥30: 1.21 (0.73–1.99) 1980-1992 cohort BMI <25: reference BMI 25- <30: 1.01 (0.66–1.54) BMI ≥30: 1.27 (0.72–2.21)	6	
40	Ergatoudes (2020) ²⁵ , Gothenburg Sweden, Men born in Gothenburg 1913 cohort	1963	855 (100% men), 50 years old	21	Not mentioned	BMI	Incident HF hospitalisation or HF death	Electronic record linkage to National Hospital Discharge Register or National Cause of Death Register	80	N/A	hypertension, SBP, smoking, cholesterol, physical activity, alcohol, diabetes, AF and IHD	linear	Per unit BMI	HR per unit: 1.11 (1.04-1.19) Obese vs non-obse BMI: HR 2.25 (1.13-4.51)	6	

41	Chen (2020) ²⁶ , Sweden, The Study of men born in 1943	1993	798 (100% men),	21	Not mentioned	BMI	HF hospitalisation or HF death or cardiac dysfunction at age 71 years	Electronic record linkage to National Hospital Discharge Register or National Cause of Death Register	92	N/A	smoking, BMI, systolic BP, hyperlipidemia, sedentary lifestyle, and diabetes	linear	Per unit BMI	HR per unit: 1.14 (1.07–1.22)	8
42	Rao (2021) ⁶⁹ , USA, Jackson Heart Study	Exam 2 (2005–2008)	2882 (35% men), 59.4 years	10.6 years	Prevalent HF at exam 2, missing measures for BMI, waist, or hip circumference	Visceral fat (VAT), subcutaneous fat (SAT), pericardial fat (PAT)	All-cause death, HF hospitalisation	Adjudication of HF events	168 HF hospitalisations (in VAT and SAT analyses) and 77 HF hospitalisations in PAT analyses	HFpEF, HFrEF	age, sex, education, and smoking status	linear	VAT- per 100 cm ³ SAT- per 100 cm ³ PAT- per 10 cm ³	HF VAT: 1.07 (1.03–1.11) SAT: 1.02 (1.00–1.04) PAT: 1.10 (1.04–1.15) HFpEF VAT: 1.10 (1.04–1.15) PAT: 1.13 (1.06–1.21) HFrEF VAT: 1.08 (1.01–1.13) PAT: 1.06 (0.96–1.17)	8
43	Kenchaiah (2021) ⁷⁰ , USA, MESA	July 17, 2000, and August 31, 2002,	6,785 participants (3,584 women and 3,201 men), ages 45 to 84	mean: 13.4 (4.6) years; median: 15.7 years; interquartile range: 11.7 to 16.5 years; maximum: 17.5 years	Clinical cardiovascular disease at baseline, no cardiac CT at baseline, participants with suboptimal image quality for pericardial fat volume (PFV) measurement, missing information on newly diagnosed HF during follow-up.	Pericardial fat volume (PFV)	Incident HF	Independent adjudication of HF events	385 participants (5.7%; 164 women and 221 men)	HFpEF, HFrEF, HFmEF, HFuEF	age (for every 1-year increase), sex, race (White [referent], Black, Hispanic, Chinese), cigarette smoking (no [referent], past, current), alcohol consumption (no or past [referent], mild-to-moderate, heavy), and vigorous physical activity at baseline	linear	PFV per SD (1 SD = 42 cm ³) higher	HF Men: 1.24 (1.12–1.37) Women: 1.68 (1.42–1.98) Both sexes: 1.34 (1.23–1.46) HFpEF : 1.52 (1.35–1.72) HFrEF : 1.15 (1.00–1.33) HFmEF : 1.44 (1.12–1.85) HFuEF : 1.23 (0.89–1.70)	9
44	Suthahar (2022) ⁷² , Groningen, The Netherlands, PREVEND	1997–1998	8295 participants (4134 women), 49.8% women, 50 (13) years	11.3 ± 3.1 years	Insulin use, pregnancy, no consent, serious mental illness, life expectancy <1 year, treatment for malignancies (other than non-melanoma skin cancer), HF at baseline, underweight, waist circumference <40cm, missing covariates	BMI, WC, WHR, body shape index (BSI), weight-adjusted-waist index (WWI), body roundness index (BRI) and relative fat mass (RFM)	Incident HF	Independent adjudication of HF events using ESC guidelines	363 incident HF	HFpEF, HFrEF	age, sex	linear	HRs per SD higher adiposity measures	HF BMI: 1.39 (1.26, 1.54) WC: 1.49 (1.32, 1.68) WHR: 1.57 (1.37, 1.80) BSI: 1.25 (1.10, 1.43) WWI 1.44 (1.27, 1.63) BRI: 1.46 (1.32, 1.62) RFM: 1.93 (1.60, 2.33) HFpEF BMI: 1.46 (1.24, 1.72) WC: 1.56 (1.28, 1.90) WHR: 1.48 (1.17, 1.86) BSI: 1.20 (0.97, 1.48) WWI: 1.38 (1.13, 1.69) BRI: 1.48 (1.25, 1.75) RFM: 2.04 (1.48, 2.81) HFrEF BMI: 1.34 (1.18, 1.52) WC: 1.44 (1.24, 1.67) WHR: 1.61 (1.36, 1.91) BSI: 1.29 (1.10, 1.52) WWI: 1.46 (1.25, 1.71) BRI: 1.43 (1.26, 1.63) RFM: 1.84 (1.46, 2.32)	8
45	Xing (2023) ³⁵ , UK, The UK Biobank,	2006–2010	483,316 participants, 55.4% women, 56.3 years	12.1 years (IQR 11.6–13.1 years)	Prevalent HF, prevalent cardiovascular diseases, lack of bioimpedance analysis data, and loss of follow-up	BMI, Arm fat index (AFI), Trunk fat index (TFI), leg fat index (LFI)	Incident HF	Electronic health record linkage	3134	-	Age, race, sex, BMI	J-shaped	HRs per SD higher adiposity measures	BMI: 1.67 (1.63–1.71) AFI: 1.00 (0.96–1.05) TFI: 1.00 (0.93–1.07) LFI: 0.78 (0.72–0.84)	9

Table S5. Other subgroup analyses of BMI, waist circumference, and waist-hip ratio and incident heart failure.

Study characteristics	BMI, per 5 Kg/m ² higher					Waist circumference per 10cm higher					Waist-hip ratio per 0.1unit higher				
	N	RR (95% CI)	I ² , %	P _{het} [*]	P _{het} [†]	N	RR (95% CI)	I ² , %	P _{het} [*]	P _{het} [†]	N	RR (95% CI)	I ² , %	P _{het} [*]	P _{het} [†]
All studies	32	1.42 (1.40-1.44)	94.4	<0.001		13	1.28 (1.26-1.31)	75.8	<0.001		9	1.33 (1.28-1.37)	94.9	<0.001	
Underweight excluded															
Yes	9	1.39 (1.36-1.42)	87.3	<0.001	0.005	5	1.27 (1.22-1.32)	0.0	0.41	0.57	3	1.16 (1.09-1.23)	89.6	<0.001	<0.001
No	23	1.44 (1.42-1.47)	95.4	<0.001		9	1.29 (1.26-1.32)	83.8	<0.001		6	1.40 (1.35-1.46)	95.5	<0.001	
Assessment of measures															
Measured	27	1.43 (1.41-1.45)	94.7	<0.001	0.45	12	1.28 (1.26-.131)	78.5	<0.001	0.60	7	1.42 (1.36-1.47)	94.8	<0.001	<0.001
Self-reported	5	1.40 (1.35-1.46)	92.9	<0.001		2	1.26 (1.20-1.34)	54.6	0.14		2	1.10 (1.03-1.17)	0.0	0.35	
Events, n															
< 500	16	1.31 (1.26-1.35)	80.3	<0.001	<0.001	8	1.27 (1.22-1.32)	40.7	0.11	0.67	3	1.22 (1.14-1.31)	89.4	0.001	<0.001
500-1000	6	1.38 (1.33-1.44)	46.0	0.10		3	1.27 (1.22-1.32)	72.7	0.03		3	1.17 (1.10-1.24)	89.1	<0.001	
>1000	10	1.46 (1.43-1.48)	97.9	<0.001		3	1.29 (1.26-1.33)	94.1	<0.001		3	1.54 (1.46-1.62)	97.1	<0.001	
HF ascertainment															
Adjudicated	13	1.35 (1.32-1.38)	88.0	<0.001	<0.001 /<0.001 [§]	8	1.28 (1.25-1.31)	85.1	<0.001	0.41	4	1.46 (1.39-1.54)	96.8	<0.001	<0.001
Record linkage	17	1.45 (1.43-1.48)	95.6	<0.001		6	1.30 (1.25-1.36)	14.8	0.32		5	1.22 (1.17-1.28)	88.6	<0.001	
Self-reported	1	1.84 (1.69-2.01)	100.0	-		-	-	-	-		-	-	-	-	
Study quality score															
0-6	15	1.31 (1.28-1.35)	89.5	<0.001	<0.001	6	1.32 (1.29-1.36)	79.7	<0.001	<0.001	4	1.31 (1.26-1.37)	97.9	<0.001	0.41
7-9	17	1.46 (1.44-1.49)	95.6	<0.001		8	1.23 (1.20-1.27)	57.3	0.02		5	1.35 (1.28-1.42)	75.2	0.003	
Effect size reported or estimated															
Directly reported	18	1.46 (1.44-1.49)	96.2	<0.001	<0.001	11	1.28 (1.25-1.30)	79.8	<0.001	0.15	6	1.32 (1.27-1.37)	96.5	<0.001	0.65
Estimated	14	1.37 (1.34-1.40)	83.2	<0.001		3	1.35 (1.26-1.44)	0.0	0.38		3	1.34 (1.26-1.43)	87.0	<0.001	
Adjustment for confounders															
Age															-
Yes	28	1.42 (1.40-1.44)	95.0	<0.001	0.02	12	1.28 (1.25-1.30)	76.2	<0.001	0.01	9	1.33 (1.28-1.37)	94.9	<0.001	
No	4	1.57 (1.45-1.71)	0.0	0.61		2	1.49 (1.33-1.66)	0.0	0.44		0		-	-	
Sex															
Yes	19	1.48 (1.46-1.51)	93.9	<0.001	<0.001	8	1.28 (1.25-1.30)	83.5	<0.001	0.29	6	1.40 (1.35-1.46)	95.5	<0.001	<0.001
No	13	1.30 (1.27-1.33)	92.7	<0.001		6	1.31 (1.25-1.37)	49.9	0.08		3	1.16 (1.09-1.23)	89.6	<0.001	
Ethnicity															
Yes	6	1.49 (1.46-1.52)	98.6	<0.001	<0.001	3	1.28 (1.25-1.32)	94.1	<0.001	0.87	2	1.89 (1.75-2.04)	90.5	0.001	<0.001
No	26	1.38 (1.35-1.40)	85.1	<0.001		11	1.28 (1.24-1.32)	49.3	0.03		7	1.22 (1.18-1.27)	87.0	<0.001	
Education															
Yes	12	1.37 (1.34-1.39)	81.9	<0.001	<0.001	8	1.29 (1.26-1.32)	82.5	<0.001	0.22	6	1.37 (1.32-1.43)	96.3	<0.001	0.002
No	20	1.47 (1.44-1.49)	95.9	<0.001		6	1.25 (1.20-1.31)	58.6	0.03		3	1.22 (1.15-1.30)	81.6	0.004	
Smoking															
Yes	22	1.33 (1.31-1.35)	90.7	<0.001	<0.001	11	1.28 (1.25-1.31)	78.3	<0.001	0.65	8	1.32 (1.27-1.37)	95.5	<0.001	0.40
No	10	1.62 (1.59-1.66)	92.5	<0.001		3	1.30 (1.23-1.37)	72.7	0.03		1	1.38 (1.25-1.52)	0.0	-	
Alcohol															
Yes	11	1.39 (1.36-1.41)	90.2	<0.001	<0.001	7	1.29 (1.26-1.32)	84.6	<0.001	0.28	6	1.37 (1.32-1.43)	96.3	<0.001	0.002
No	21	1.45 (1.43-1.48)	95.4	<0.001		7	1.26 (1.22-1.31)	55.5	0.04		3	1.22 (1.15-1.30)	0.0	0.004	
Physical activity															

Yes	12	1.36 (1.33-1.39)	84.8	<0.001	<0.001	7	1.24 (1.20-1.28)	68.4	0.004	0.002	6	1.22 (1.17-1.28)	85.8	<0.001	<0.001
No	20	1.47 (1.45-1.50)	95.7	<0.001		7	1.32 (1.28-1.35)	76.4	<0.001		3	1.47 (1.40-1.55)	97.8	<0.001	
Adjustment for potential mediators															
Hypertension															
Yes	9	1.21 (1.17-1.24)	89.9	<0.001	<0.001	1	1.38 (1.10-1.72)	0.0	-	0.53	0	-	-	-	-
No	23	1.48 (1.46-1.50)	93.2	<0.001		13	1.28 (1.26-1.31)	77.5	<0.001		8	1.33 (1.28-1.37)	94.9	<0.001	
Blood pressure															
Yes	5	1.33 (1.28-1.37)	89.9	<0.001	<0.001	2	1.38 (1.28-1.49)	0.0	0.89	0.05	2	1.67 (1.47-1.89)	0.0	0.93	<0.001
No	27	1.44 (1.42-1.46)	94.7	<0.001		12	1.28 (1.25-1.30)	77.5	<0.001		7	1.30 (1.26-1.35)	95.8	<0.001	
Diabetes															
Yes	14	1.26 91.23-1.29)	87.6	<0.001	<0.001	6	1.27 (1.21-1.33)	44.9	0.11	0.59	3	1.26 (1.18-1.36)	92.8	<0.001	0.13
No	18	1.49 (1.47-1.52)	94.5	<0.001		8	1.29 (1.26-1.31)	84.2	<0.001		6	1.35 (1.30-1.40)	96.1	<0.001	
Ischaemic heart disease															
Yes	10	1.30 (1.27-1.34) 1.46 (1.44-1.48)	87.8	<0.001	<0.001	2	1.37 (1.23-1.53)	0.0	0.96	0.21	1	1.66 (1.39-1.98)	95.4	-	0.01
No	22		95.0	<0.001		12	1.28 (1.25-1.30)	78.9	<0.001		8	1.32 (1.27-1.36)	100.0	<0.001	
Atrial fibrillation															
Yes	3	1.24 (1.18-1.29)	91.4	<0.001	0.001	1	1.17 (1.12-1.22)	100	-	<0.001	0	-	-	-	-
No	29	1.44 (1.42-1.46)	94.2	<0.001		13	1.31 (1.28-1.34)	62.5	0.001		9	1.33 (1.28-1.37)	94.9	<0.001	
Valvular heart disease															
Yes	3	1.33 (1.29-1.38)	84.2	0.002	<0.001	2	1.19 (1.14-1.24)	82.5	0.02	<0.001	1	1.66 (1.39-1.98)	100.0	-	0.01
No	29	1.44 (1.42-1.46)	94.6	<0.001		12	1.31 (1.28-1.34)	65.1	0.001		8	1.32 (1.27-1.36)	95.4	<0.001	
Left ventricular hypertrophy															
Yes															
No	4	1.19 (1.11-1.26)	78.8	<0.001	<0.001	2	1.30 (1.15-1.48)	0.0	0.55	0.80	0	-	-	-	-
	28	1.44 (1.42-1.45)	94.6	0.003		12	1.28 (1.26-1.31)	79.3	<0.001		9	1.33 (1.28-1.37)	94.9	<0.001	
Cholesterol															
Yes	9	1.27 (1.23-1.30)	91.4	<0.001	<0.001	4	1.24 (1.17-1.30)	40.3	0.17	0.14	2	1.20 (1.11-1.29)	93.8	<0.001	0.004
No	23	1.47 (1.45-1.50)	93.9	<0.001		10	1.29 (1.26-1.32)	80.6	<0.001		7	1.36 (1.31-1.41)	95.5	<0.001	
Lipid lowering drugs															
Yes	3	1.14 (1.09-1.18)	89.4	<0.001	<0.001	1	1.39 (1.26-1.53)	0.0	-	0.12	1	1.68 (1.41-2.00)	100.0	-	0.008
No	29	1.46 (1.44-1.48)	92.7	<0.001		13	1.28 (1.25-1.30)	76.5	<0.001		8	1.32 (1.27-1.36)	95.3	<0.001	
Adjustment for key intermediate factors [‡]															
Yes	7	1.30 (1.26-1.34)	89.7	<0.001	<0.001	2	1.37 (1.23-1.53)	0.0	0.96	0.21	1	1.66 (1.39-1.98)	100.0	-	0.01
No	25	1.45 (1.43-1.47)	94.7	<0.001		12	1.28 (1.25-1.30)	78.9	<0.001		8	1.32 (1.27-1.36)	95.4	<0.001	

N= number of studies in subgroup meta-analysis (this is not always equal to the total number of studies in the overall analysis). BMI indicates body mass index; CI, confidence interval; and RR, relative risk.

*P for heterogeneity within each subgroup.

†P for heterogeneity between subgroups.

‡Adjustment for key intermediate factors (BP/hypertension, diabetes and ischaemic heart disease)

§P for heterogeneity between adjudicated and record linkage (excluding self-reported HF events)

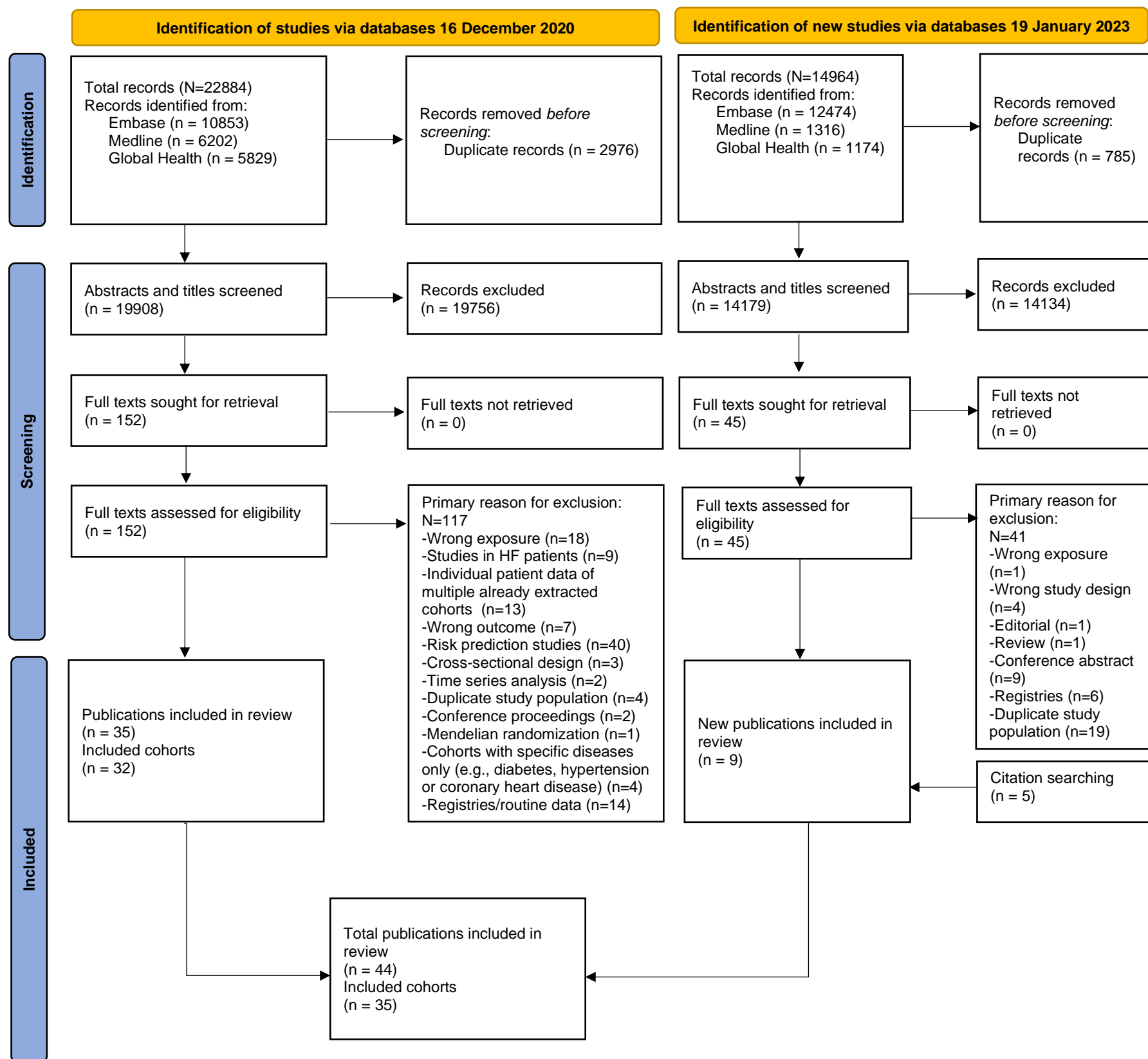
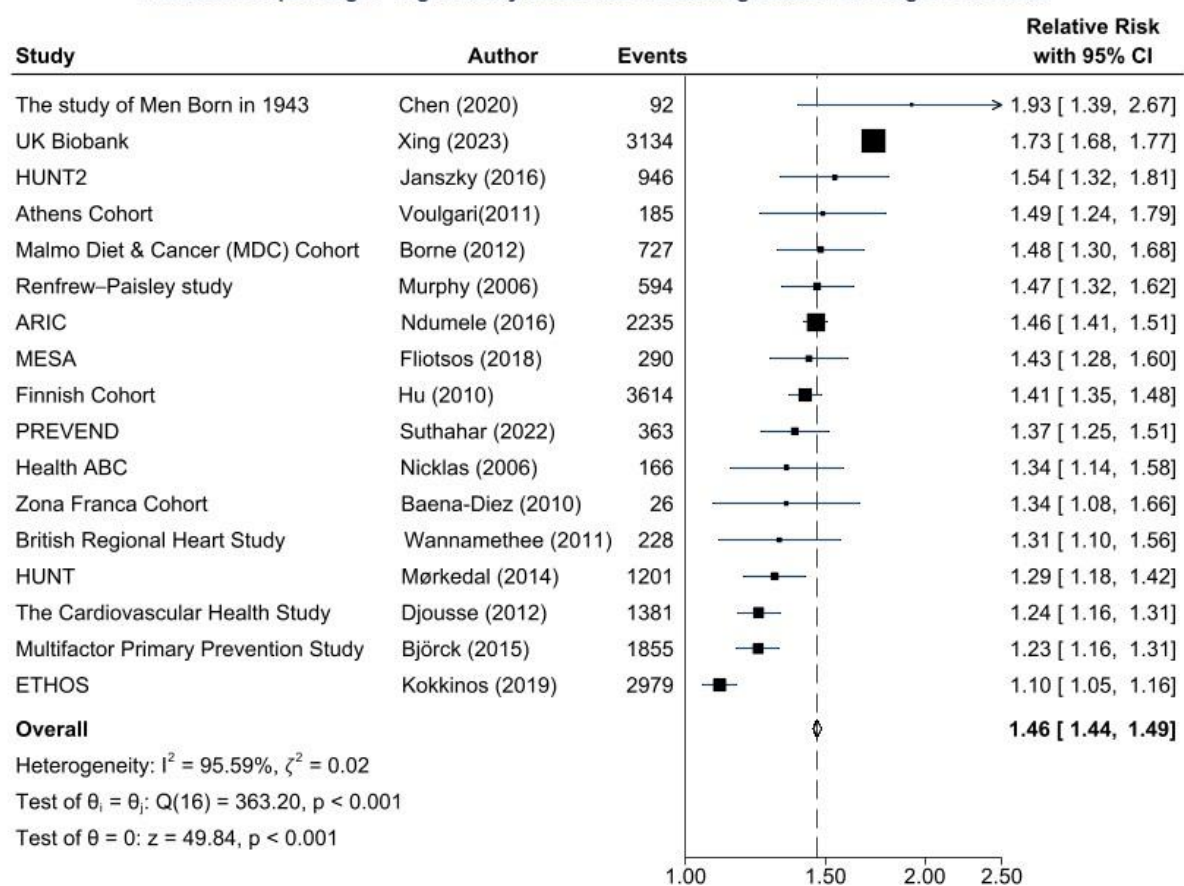


Figure S1: PRISMA flowchart of study selection

Relative risk per 5Kg/m² higher body mass index excluding studies with high risk of bias



Fixed-effects inverse-variance model

Figure S2: Dose-response meta-analysis of BMI and HF incidence excluding studies with high risk of bias

Relative risk per 5Kg/m² higher body mass index in studies that directly reported effect sizes

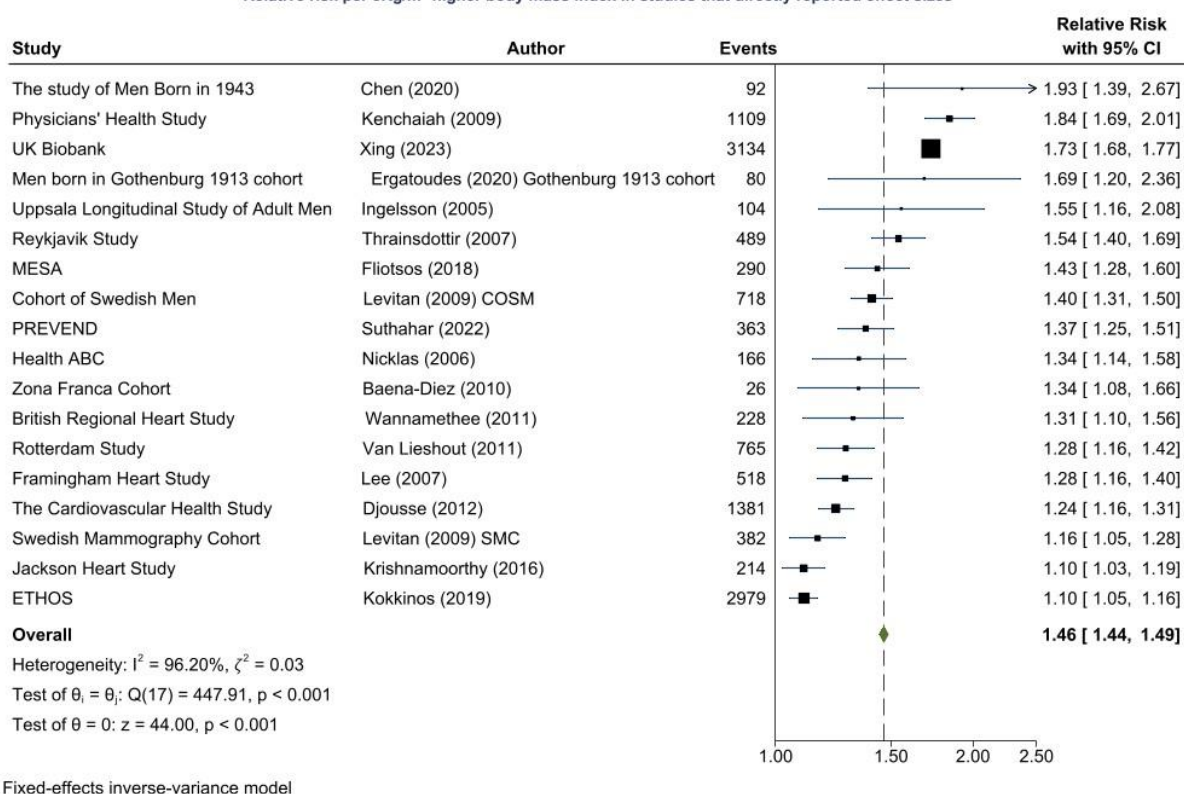
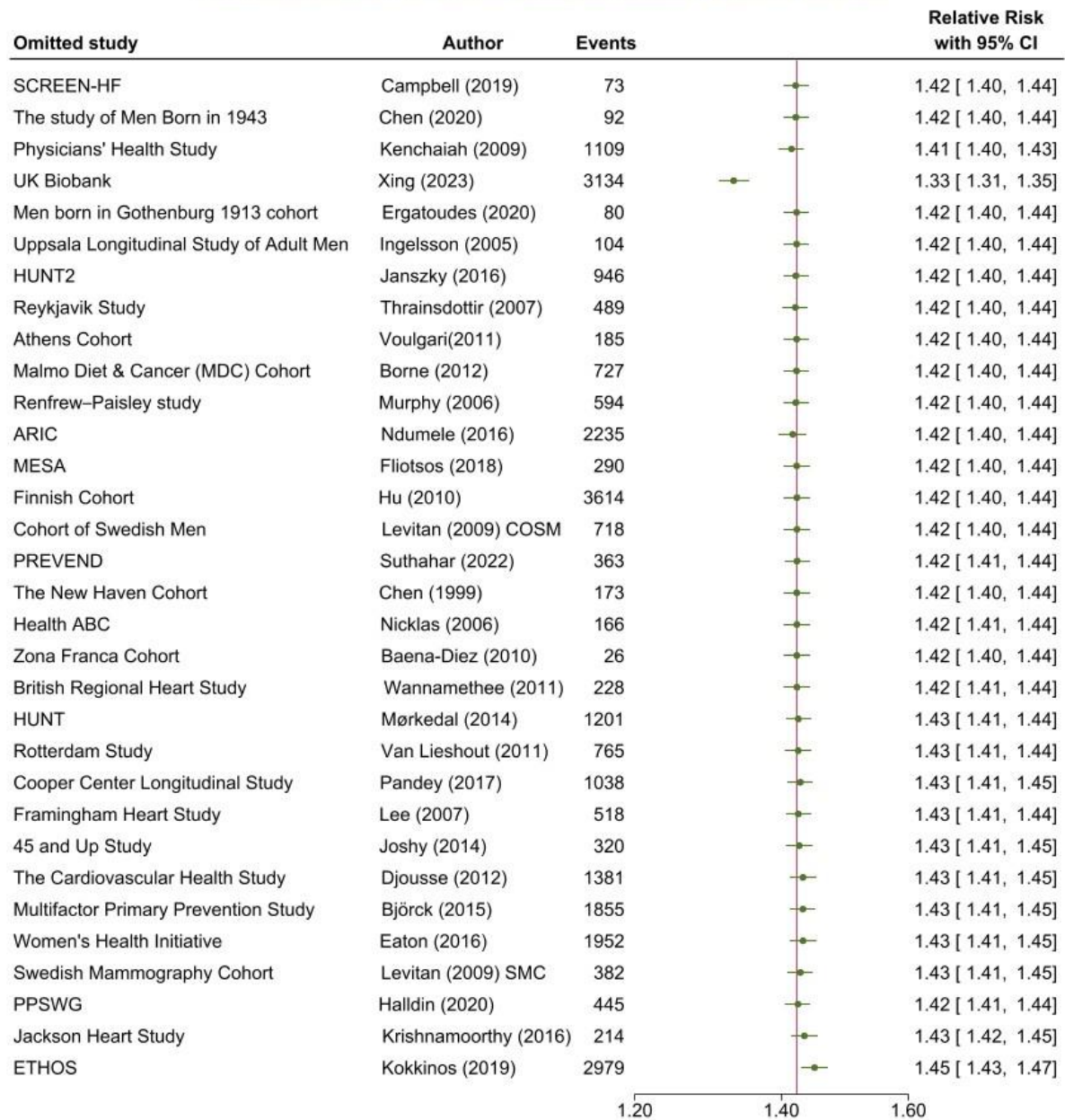


Figure S3: Dose-response meta-analysis of BMI and HF incidence in studies that directly reported effect sizes

Relative risk per 5Kg/m² higher body mass index excluding one study at a time



Fixed-effects inverse-variance model

Figure S4: Meta-analysis of BMI and HF risk excluding one study at a time

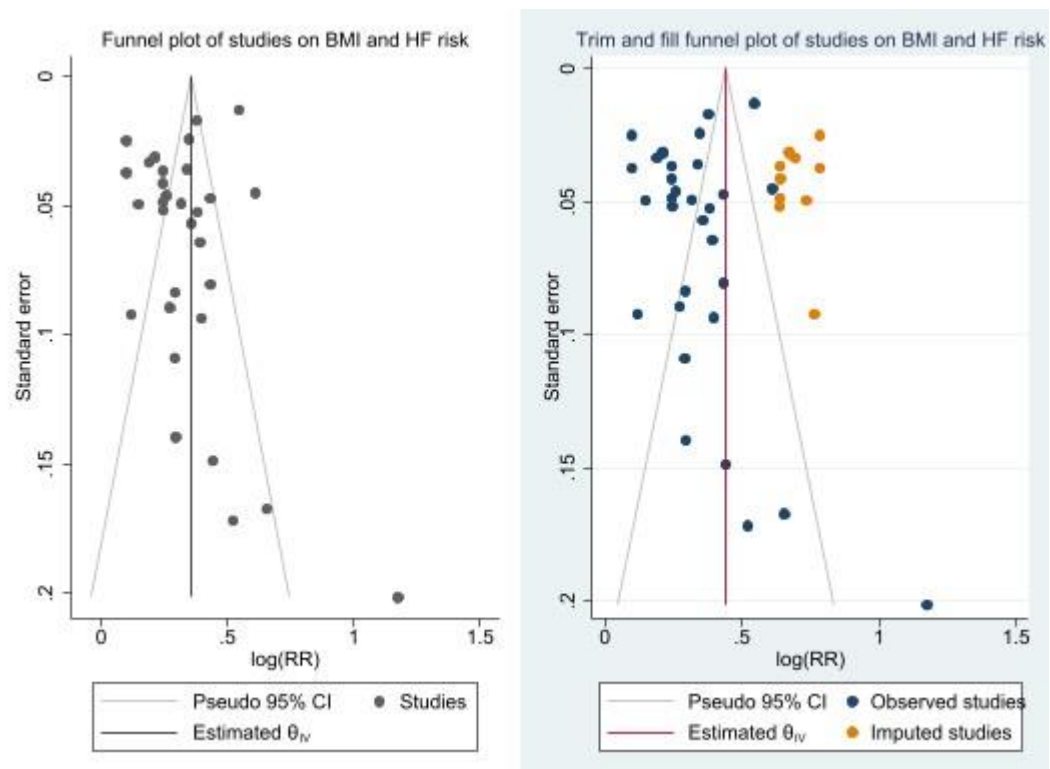
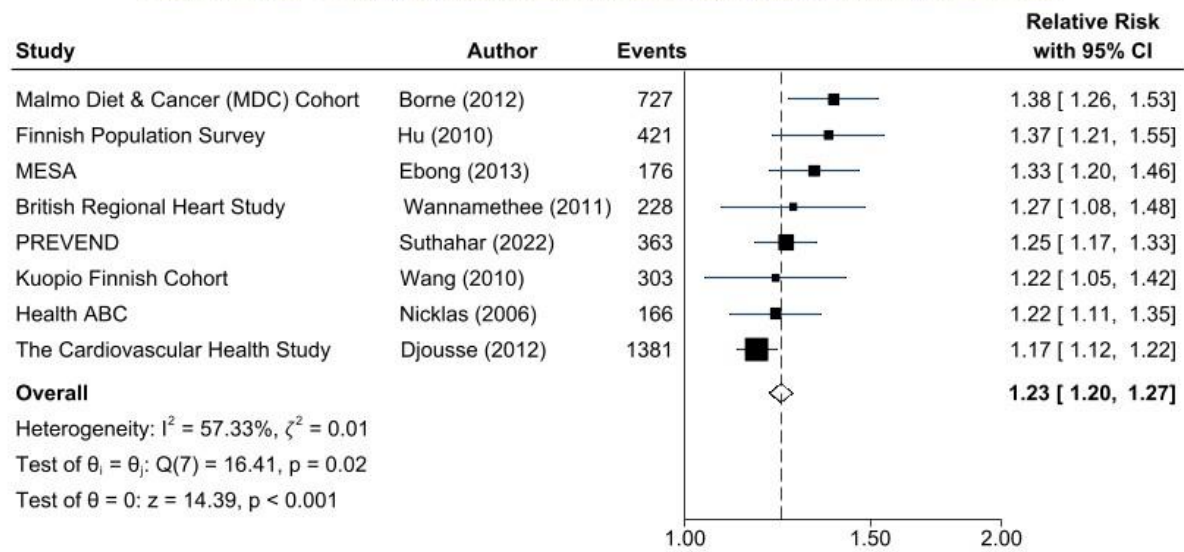


Figure S5: Funnel plot and Trim and fill plot of studies on BMI and HF risk

Relative risk per 10cm higher waist circumference excluding studies with high risk of bias



Fixed-effects inverse-variance model

Figure S6: Dose-response meta-analysis of waist circumference and HF incidence excluding studies with high risk of bias

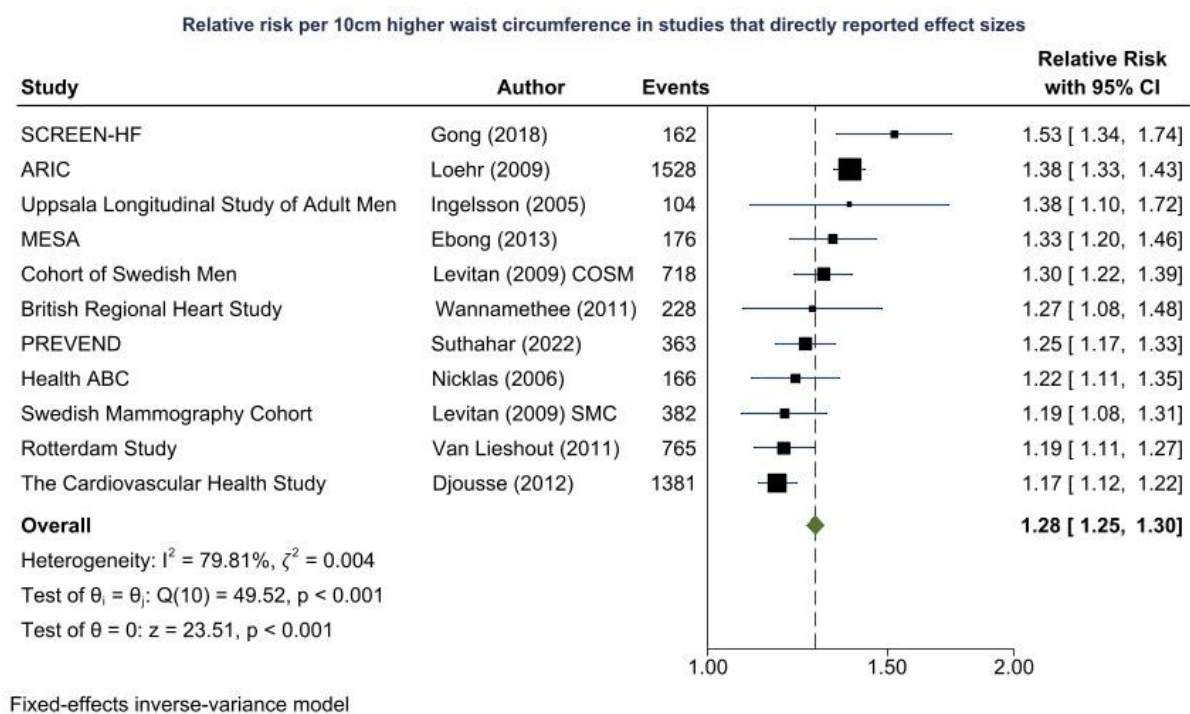


Figure S7: Dose-response meta-analysis of waist circumference and HF incidence in studies that directly reported effect sizes

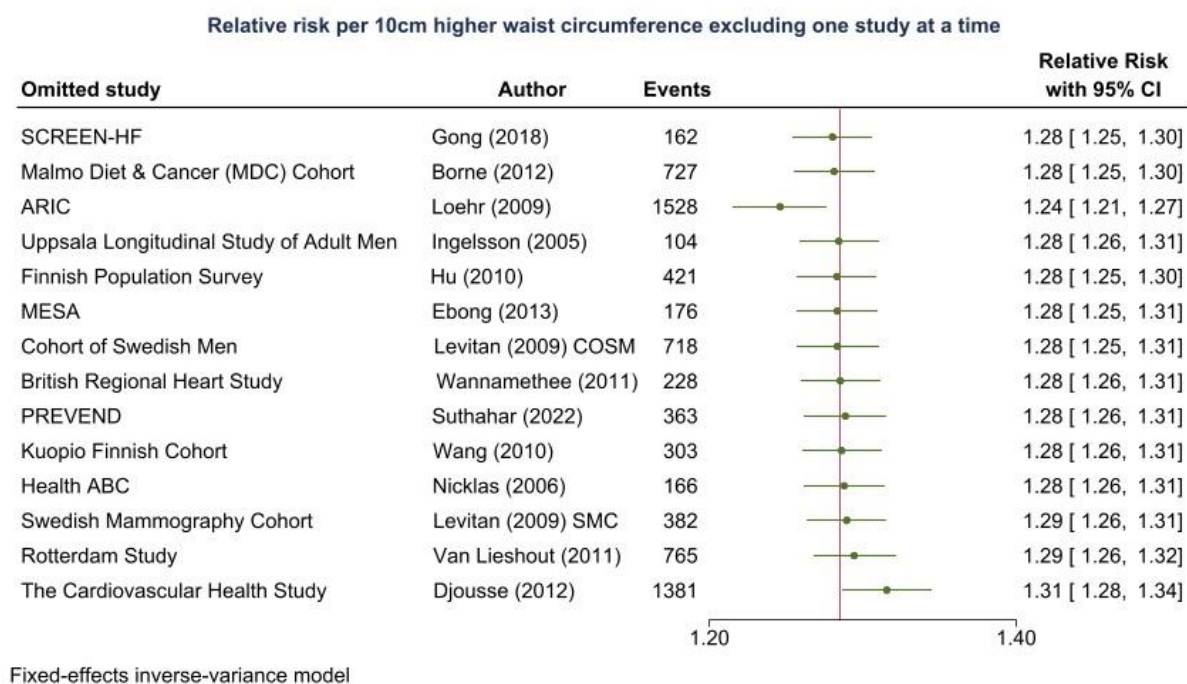


Figure S8: Meta-analysis of waist circumference and HF risk excluding one study at a time

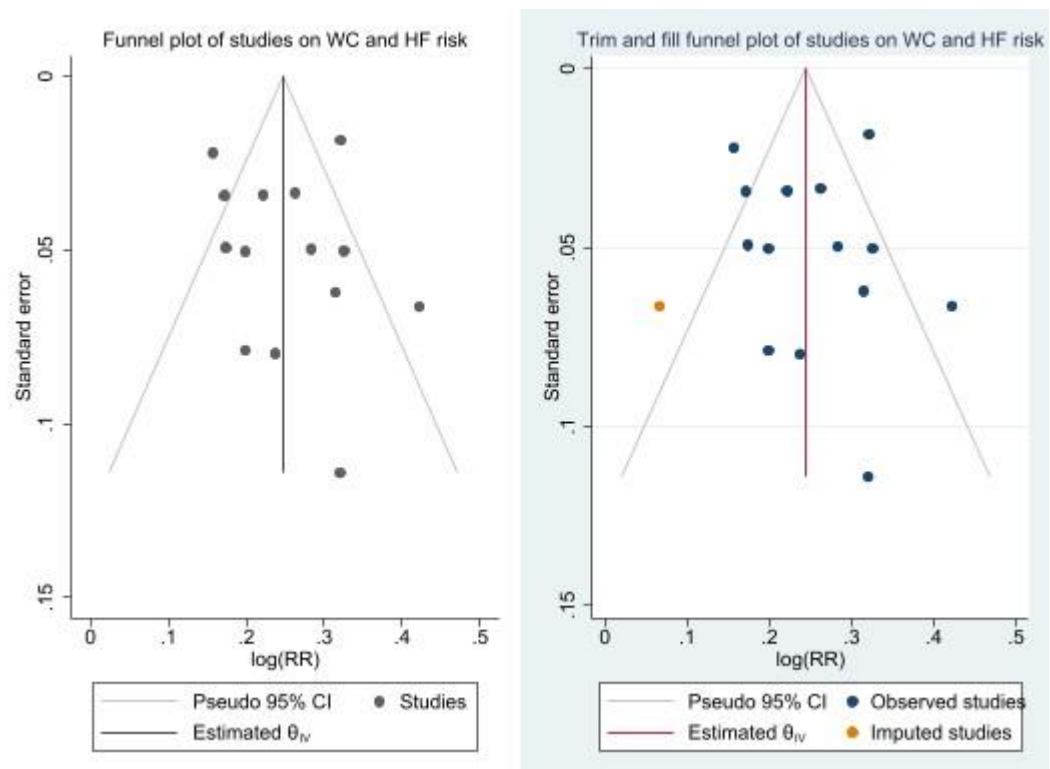


Figure S9: Funnel plot and Trim and fill plot of studies on waist circumference and HF risk

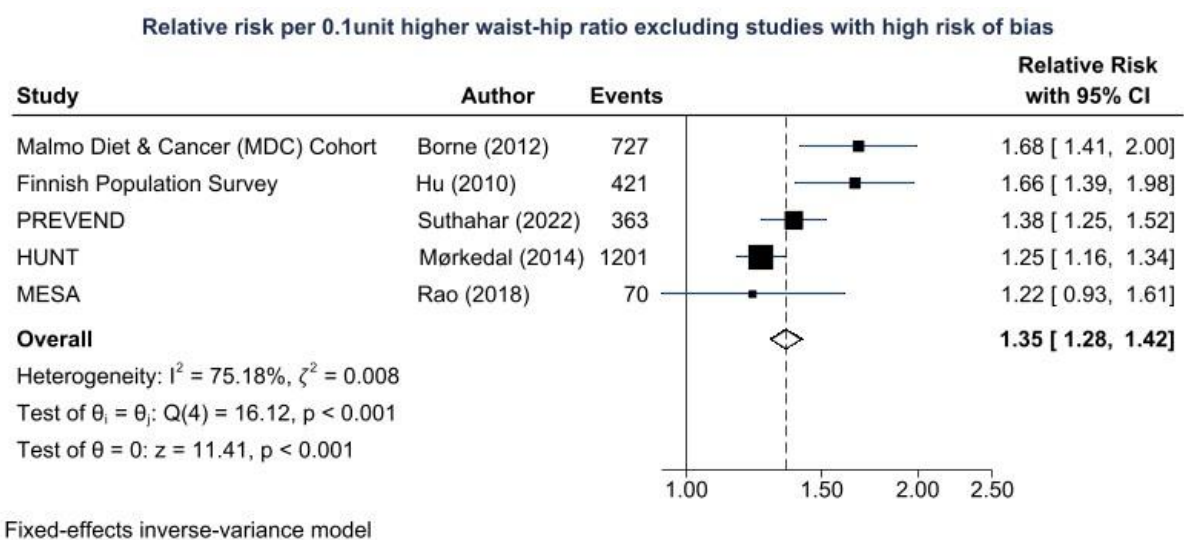


Figure S10: Dose-response meta-analysis of waist-hip ratio and HF excluding studies with high risk of bias

Relative risk per 0.1unit higher waist-hip ratio in studies that directly reported effect sizes

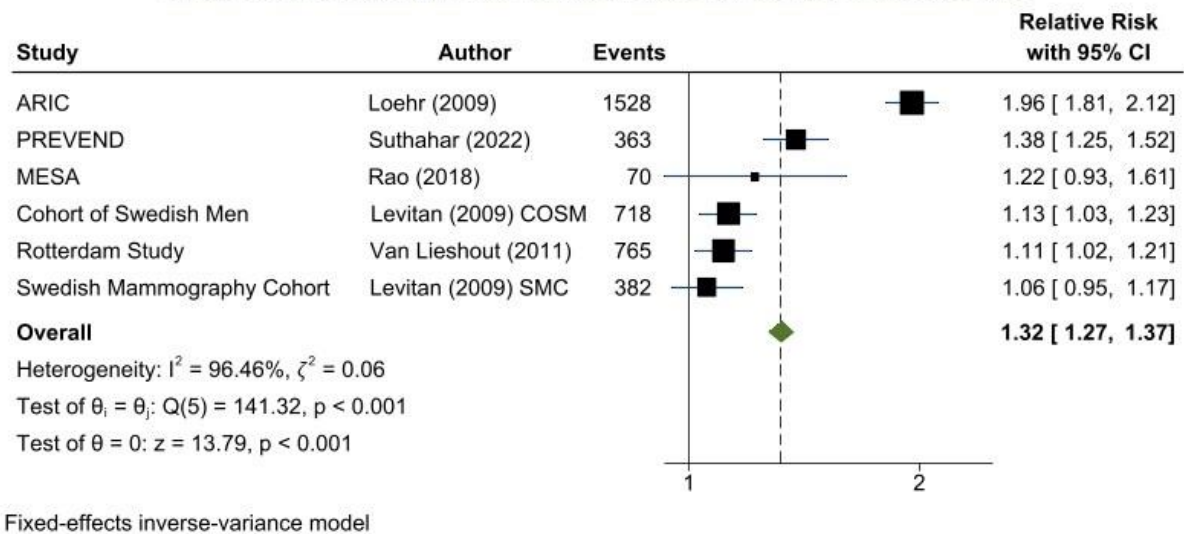


Figure S11: Dose-response meta-analysis of waist-hip ratio and HF incidence in studies that directly reported effect sizes

Relative risk per 0.1unit higher waist-hip ratio excluding one study at a time

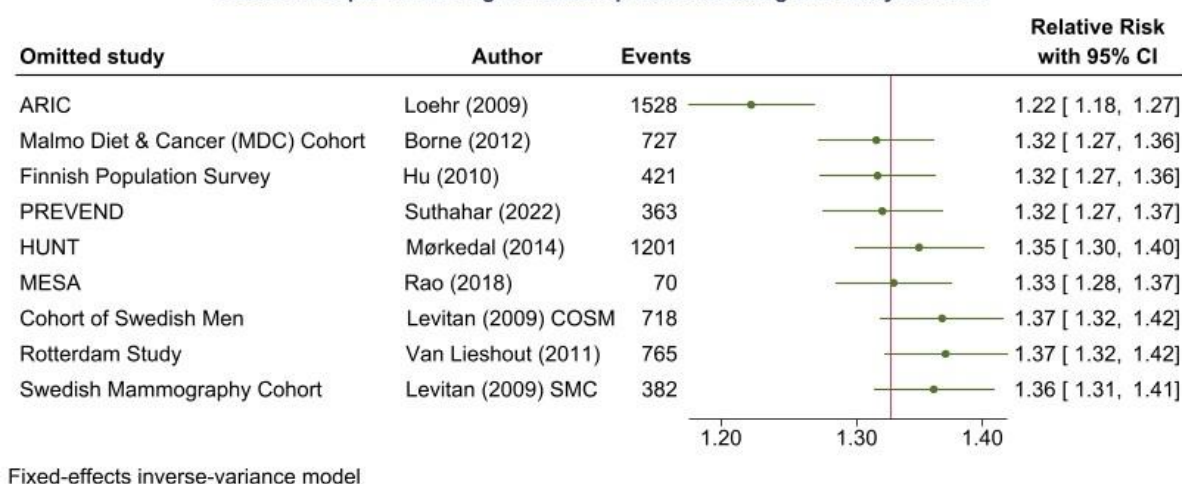


Figure S12: Meta-analysis of waist-hip ratio and HF risk excluding one study at a time

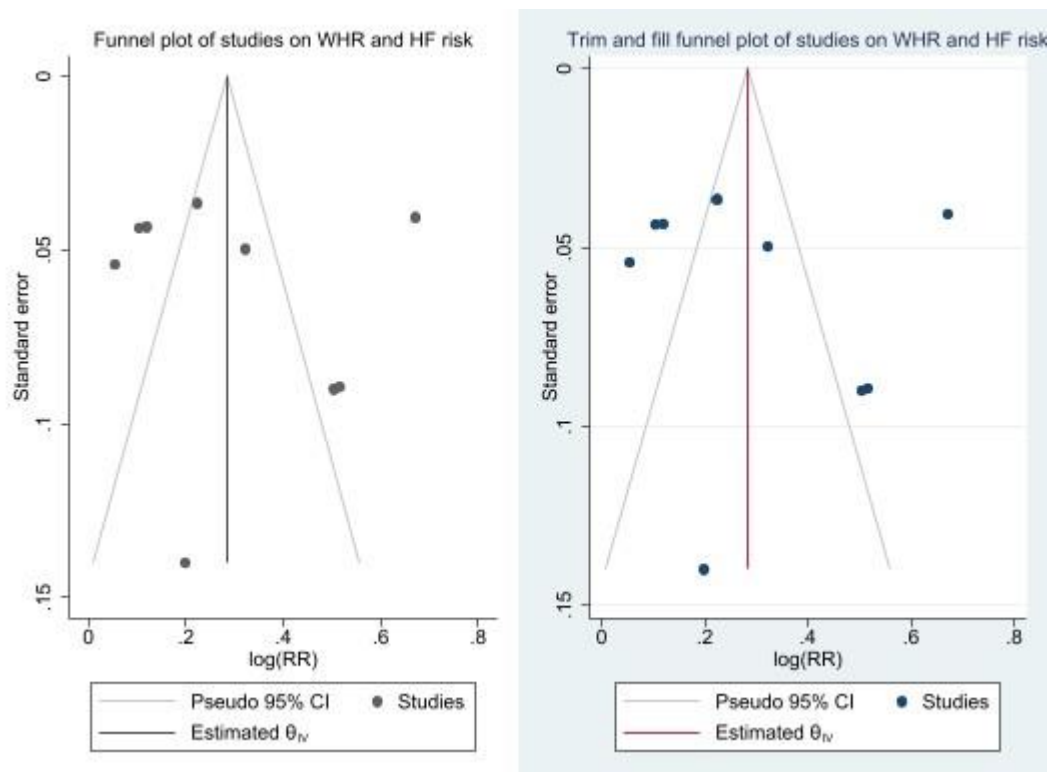


Figure S13: Funnel plot and Trim and fill plot of studies on waist-hip ratio and HF risk