Journal of the American Heart Association

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_{total}=1 137 044; n_{cases}=34 422). Summary relative risk (RR) per 5-kg/m^2 higher body mass index was 1.42 (95% CI, 1.40–1.42; ζ^2=0.02, I^2=94.4%), 1.28 (95% CI, 1.26–1.31; ζ^2=0.01, I^2=75.8%) per 10-cm higher waist circumference, and 1.33 (95% CI, 1.28–1.37; ζ^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.

JAHA is available at: www.ahajournals.org/journal/jaha

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/m^2) and overweight or obese ranges (BMI >25 kg/m^2) at higher risk than those in the normal range (18.5–25 kg/m^2).[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 heterogenous 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 CRD42020224584).[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 January19, 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-analysis[12] 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/m^2 higher BMI, 10-cm higher WC, 0.1-unit higher WHR, 1-unit higher body fat percent, 10-cm^3 higher pericardial fat, and 100-cm^3 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 glst 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 glst 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 Islas 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 22 884 records were identified from the initial literature search. After removal of duplicate records (934 records) and title and abstract screening (19 908 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 Study[30] 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 Study[68] excluded individuals at extremes of BMI (<15 kg/m^2 or >50 kg/m^2). Five publications from 3 studies[3–5,69,70] used imaging methods to measure body fat distribution, whereas 1 study[53] 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 Study[30] both reported a U-shaped association, whereas the 45 and Up Study[68] 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 ($P_{nonlinearity}$<0.001). There was no evidence of excess risk at lower BMI (<25 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 (ζ^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 (ζ^2=0.03 and I^2=93.2% in men versus ζ^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]; ζ^2=0.02, I^2=78%) than older individuals (1.30 [95% CI, 1.27–1.33]; ζ^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; ζ^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]; ζ^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]; ζ^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]; ζ^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]; ζ^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 al[55] 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

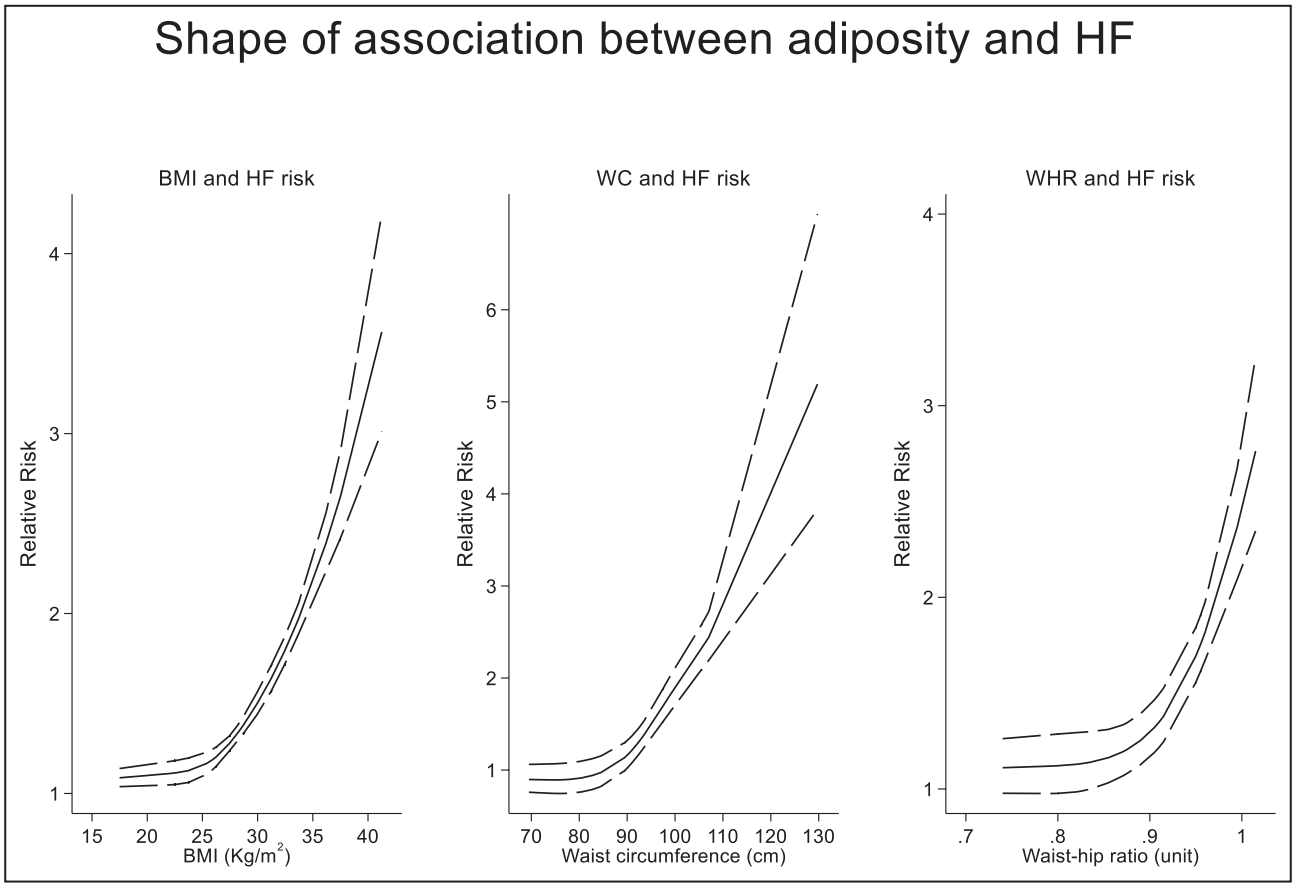

Figure 1. Shape of association between adiposity measures and HF risk.
BMI indicates body mass index; HF, heart failure; WC, waist circumference; and WHR, waist–hip ratio.

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 219 241 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 (ζ^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]; ζ^2=0.005, I^2=66.1%) than of women (1.24 [95% CI, 1.20–1.27]; ζ^2=0.004, I^2=77.2%). Associations were also stronger in younger individuals (1.37 [95% CI, 1.33–1.42]; ζ^2=0, I^2=0%) than older individuals (1.25 [95% CI, 1.29–1.53]; ζ^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]; ζ^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]; ζ^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]; ζ^2=0.01, I^2=57.3%), whereas exclusion of studies with estimated effect sizes (RR, 1.28 [95% CI, 1.25–1.30]; ζ^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]

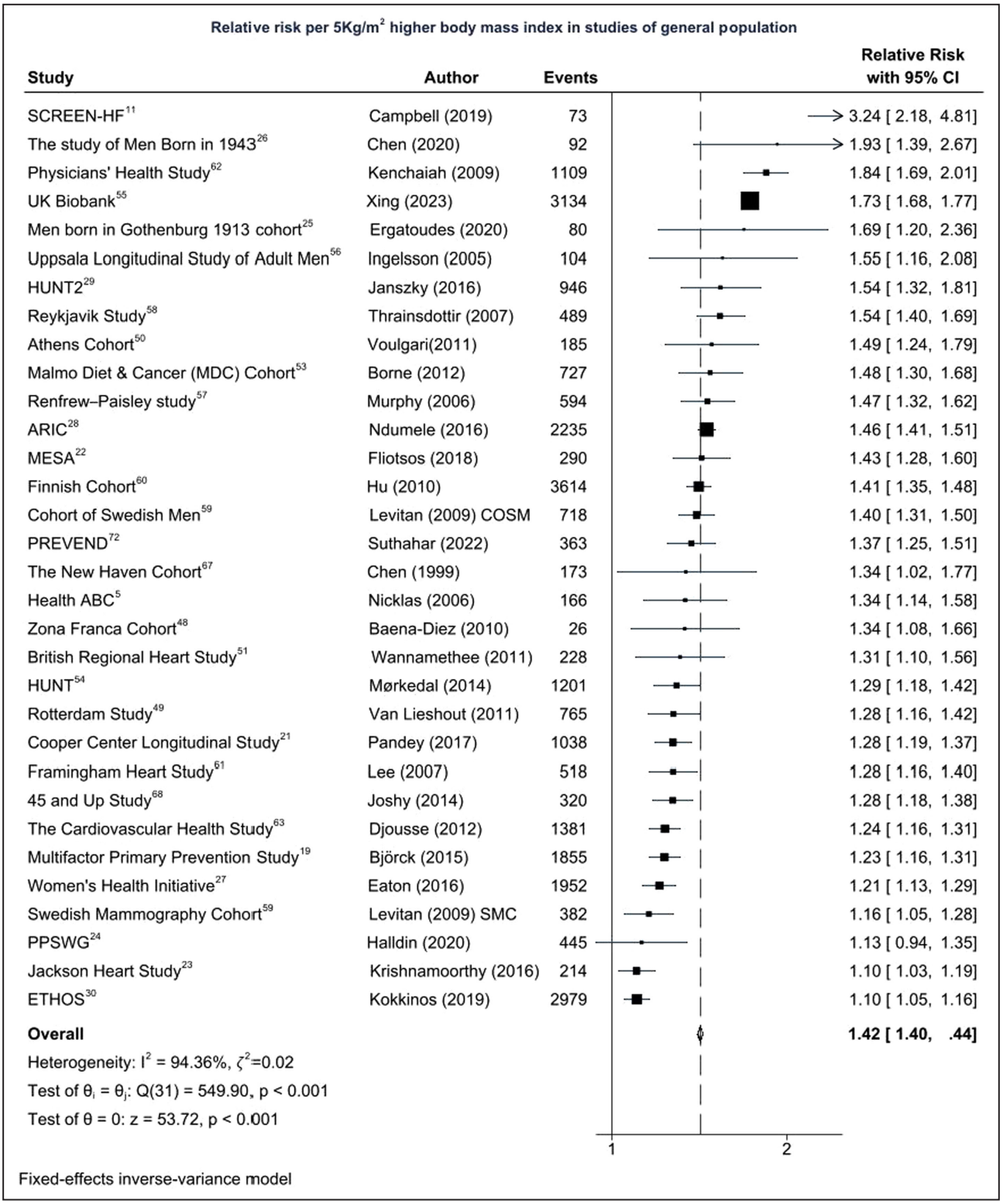

Figure 2. Body mass index and heart failure (HF) incidence: 28 396 HF incident events among 1 095 412 participants.
ARIC indicates Atherosclerosis Risk in the Community; ETHOS, Exercise Testing and Health Outcomes Study; Health ABC, Health, Aging and Body Composition Study; HUNT, The Nord-Trøndelag Health 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/m² higher					Waist circumference per 10 cm higher					Waist–hip ratio per 0.1-unit higher				
	N	RR (95% CI)	I^2, %	P_{het}* value	P_{het}† value	N	RR (95% CI)	I^2, %	P_{het}* value	P_{het}† value	N	RR (95% CI)	I^2, %	P_{het}* value	P_{het}† value
All studies	32	1.42 (1.40–1.44)	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	0.003/0.001§	4	1.34 (1.26–1.42)	94.6	<0.001	0.47/0.26§
Men	9	1.29 (1.25–1.32)	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)	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)	78.0	<0.001	<0.001/<0.001‖	3	1.37 (1.33–1.42)	0.0	0.94	<0.001/<0.001‖	4	1.48 (1.40–1.56)	96.6	<0.001	<0.001/<0.001‖
≥65 y	13	1.30 (1.27–1.33)	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)	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	…	…	…	0.21	0		…	…	<0.001
Hispanic or Chinese	0	…	…	…		0	…	…	…		0		…	…	
White	19	1.36 (1.33–1.39)	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)	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)	92.1	<0.001	0.09/<0.001#	9	1.26 (1.22–1.30)	29.9	0.18	0.02/0.35#	7	1.22 (1.18–1.27)	87.0	<0.001	<0.001
United States	11	1.31 (1.29–1.34)	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	132 (1.22–1.43)	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)	80.8	<0.001	<0.001	7	1.29 (1.24–1.34)	45.6	0.09	0.65	2	1.10 (1.03–1.17)	0.0	0.35	<0.001
≥10 y	12	1.45 (1.43–1.47)	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/m² higher					Waist circumference per 10 cm higher					Waist–hip ratio per 0.1-unit higher				
	N	RR (95% CI)	I^2, %	P_{het}* value	P_{het}† value	N	RR (95% CI)	I^2, %	P_{het}* value	P_{het}† value	N	RR (95% CI)	I^2, %	P_{het}* value	P_{het}† value
Baseline exclusion of CVD															
Yes	13	1.54 (1.51–1.56)	94.5	<0.001	<0.001	4	1.36 (1.32–1.40)	46.1	0.14	<0.001	3	1.30 (1.22–1.39)	78.7	0.009	0.45
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	<0.001/<0.001**	4	1.29 (1.21–1.37)	72.4	0.01	0.006/0.06**	2	1.35 (1.16–1.58)	0.0	0.49	0.89/0.99[3]
HFrEF	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	0.02	5	1.29 (1.26–1.33)	89.0	<0.001	0.28	3	1.54 (1.46–1.62)	97.1	<0.001	<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; HFrEF, 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 HFrEF.

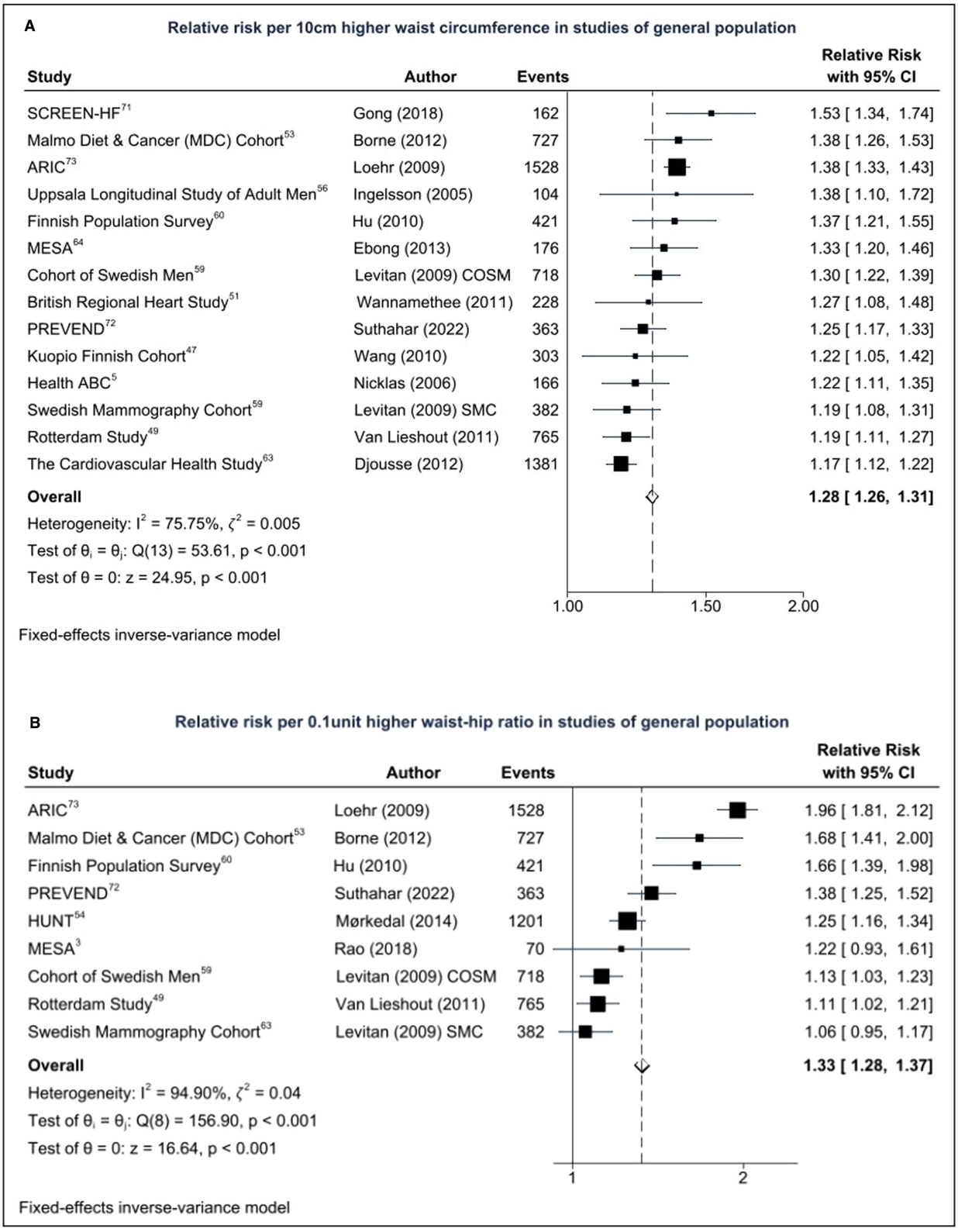

Figure 3. Central adiposity measures and incident heart failure (HF) risk.
A, Waist circumference and HF incidence: 7424 HF incident events among 219 241 participants. **B**, Waist–hip ratio and HF incidence: 6175 HF incident events among 258 100 participants. ARIC indicates Atherosclerosis Risk in the 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 (ζ^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]; ζ^2=0.06, I^2=96.6%), which were more heterogeneous than older individuals (1.10 [95% CI, 1.06–1.14]; ζ^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 al[73] 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 (ζ^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-cm^3 higher VAT (95% CI, 1.04–1.12), whereas SAT was not significantly associated with HF incidence (RR per 100 cm^3, 1.02 [95% CI, 1.04–1.12]). Pooled estimates from the MESA[70] and Jackson Heart Study[69] suggested similar 8% higher risk of HF per 10-cm^3 higher pericardial fat volume (95% CI, 1.06–1.10), with no difference between studies (ζ^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]; ζ^2=0.02, I^2=85.8%) than for HFrEF (RR, 1.13 [95% CI, 1.05–1.22]; ζ^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]; ζ^2=0.008, I^2=72.4%) than for HFrEF (RR, 1.13 [95% CI, 1.05–1.23]; ζ^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/m^2, 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-cm^3 higher VAT and per 10-cm^3 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

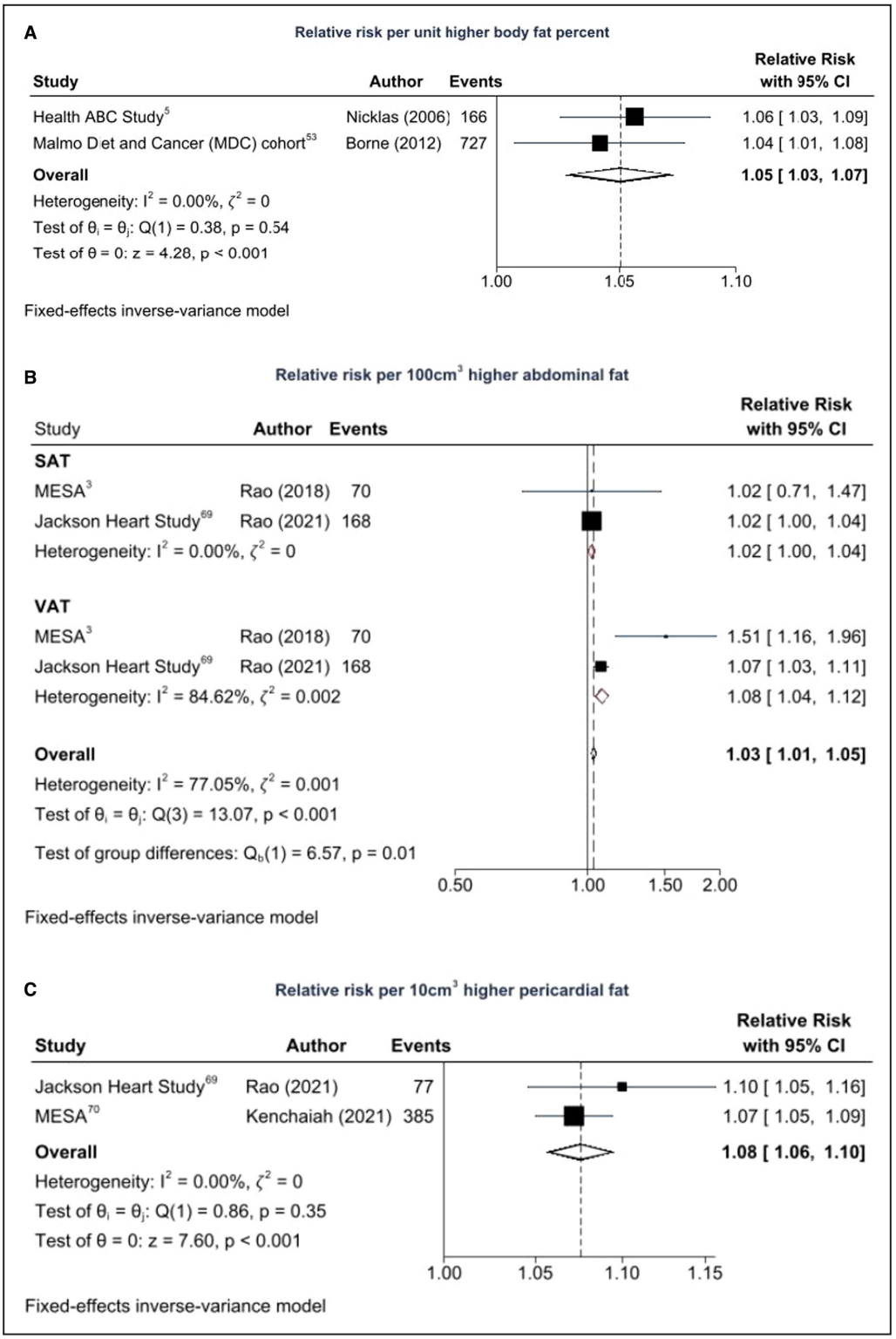

Figure 4. Regional fat measures and incident heart failure (HF) risk.
A, Body fat percent and HF incidence: 893 HF incident events among 29088 participants. **B**, Abdominal fat and HF incidence: 238 HF incident events among 4688 participants. **C**, Pericardial fat and HF incidence: 462 HF incident 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.

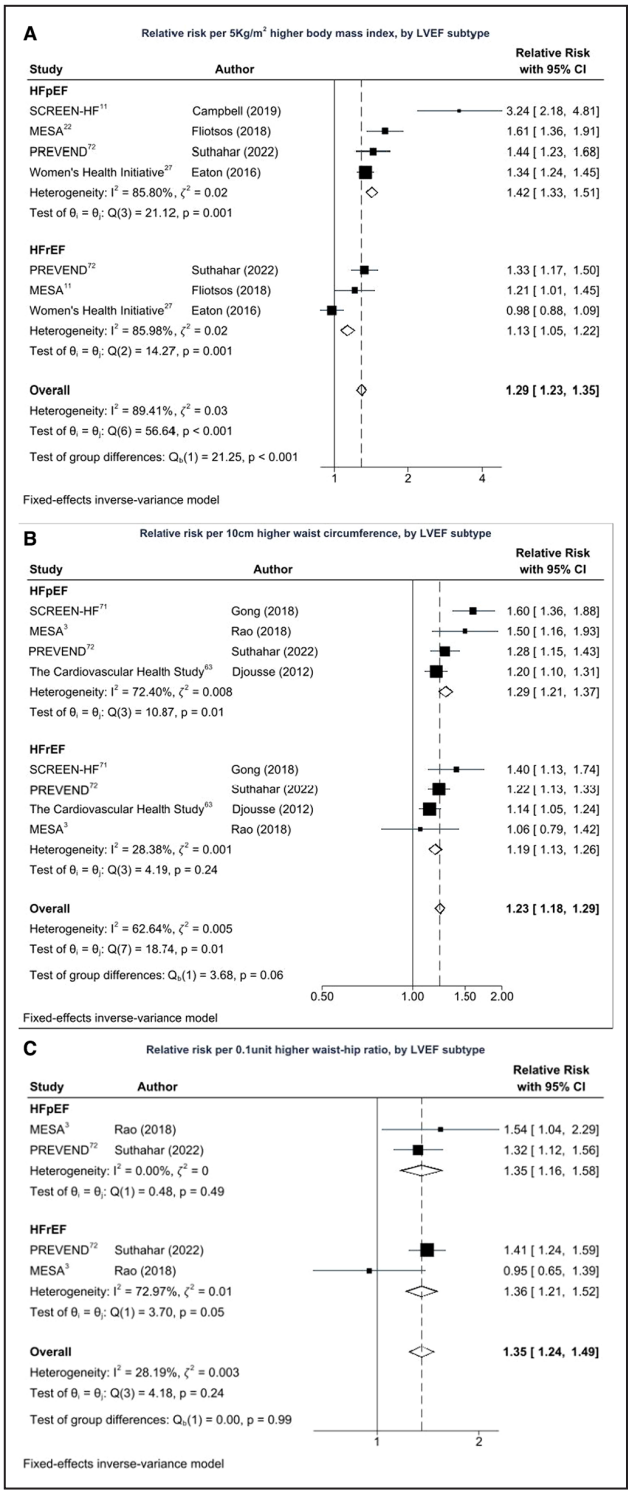

Figure 5. Dose–response meta-analysis of adiposity measures and incident HF subtypes.
A, Relative risk per 5-kg/m^2 higher body mass index, by left ventricular ejection fraction (LVEF) subtype. **B**, Relative risk per 10-cm higher waist circumference by LVEF subtype. **C**, Relative risk per 0.1-unit 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.

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 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 al[12] 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 etiogenesis 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,

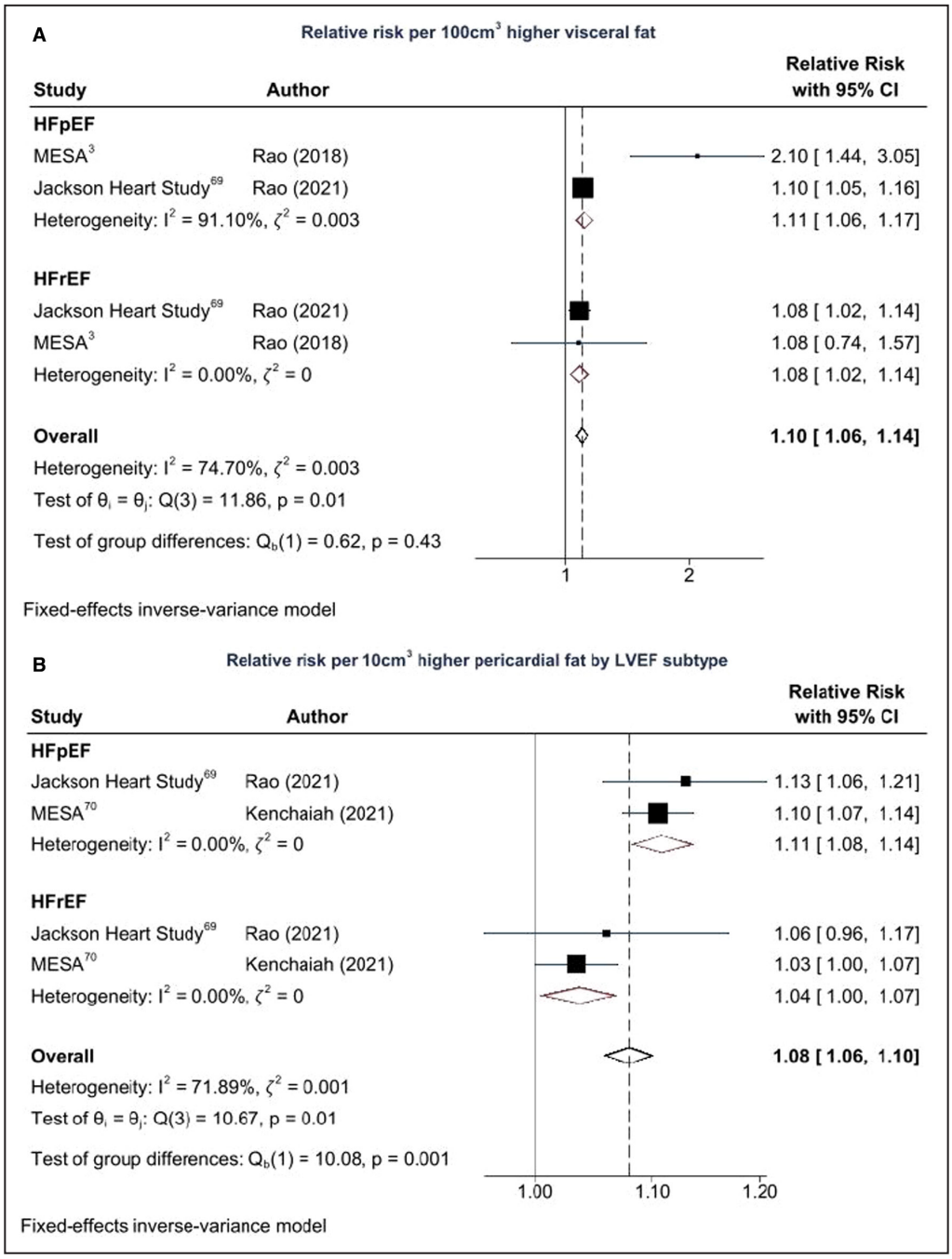

Figure 6. Regional fat and incident heart failure subtypes.
A, Relative risk per 100-cm^3 higher visceral fat by left ventricular ejection fraction (LVEF) subtype. **B**, Relative risk per 10-cm^3 higher pericardial fat by LVEF subtype. HFpEF indicates heart failure with preserved ejection fraction; 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]

REFERENCES

1. Lippi G, Sanchis-Gomar F. Global epidemiology and future trends of heart failure. *AME Med J*. 2020;5:1–6. doi: 10.21037/amj.2020.03.03
2. Taylor CJ, Ordóñez-Mena JM, Roalfe AK, Lay-Flurrie S, Jones NR, Marshall T, Hobbs FDR. Trends in survival after a diagnosis of heart failure in the United Kingdom 2000-2017: population based cohort study. *BMJ*. 2019;364:1–10. doi: 10.1136/bmj.l223
3. Rao VN, Zhao D, Allison MA, Guallar E, Sharma K, Criqui MH, Cushman M, Blumenthal RS, Michos ED. Adiposity and incident heart failure and its subtypes: MESA (Multi-Ethnic Study of Atherosclerosis). *JACC Heart Fail*. 2018;6:999–1007. doi: 10.1016/j.jchf.2018.07.009
4. Pandey A, Kondamudi N, Patel K, Ayers C, Simek S, Hall M, Musani SK, Blackshear C, Mentz RJ, Khan H, et al. Association between regional adipose tissue distribution and risk of heart failure among Blacks The Jackson Heart study. *Circ Heart Fail*. 2018;11:1–9. doi: 10.1161/CIRCHEARTFAILURE.118.005629
5. Nicklas BJ, Cesari M, Penninx BWJH, Kritchevsky SB, Ding J, Newman A, Kitzman DW, Kanaya AM, Pahor M, Harris TB. Abdominal obesity is an independent risk factor for chronic heart failure in older people. *J Am Geriatr Soc*. 2006;54:413–420. doi: 10.1111/j.1532-5415.2005.00624.x
6. Rahimi K, Bennett D, Conrad N, Williams TM, Basu J, Dwight J, Woodward M, Patel A, McMurray J, MacMahon S. Risk prediction in patients with heart failure a systematic review and analysis. *JACC Heart Fail*. 2014;2:440–446. doi: 10.1016/j.jchf.2014.04.008
7. Yang H, Negishi K, Otahal P, Marwick TH. Clinical prediction of incident heart failure risk: a systematic review and meta-analysis. *Open Heart*. 2015;2:1–8. doi: 10.1136/openhrt-2014-000222
8. Global BMI Mortality Collaboration, Di Angelantonio E, Bhupathiraju S, Wormser D, Gao P, Kaptoge S, Berrington de Gonzalez A, Cairns BJ, Huxley R, Jackson C, et al. Body-mass index and all-cause mortality: individual-participant-data meta-analysis of 239 prospective studies in four continents. *Lancet*. 2016;388:776–786. doi: 10.1016/S0140-6736(16)30175-1
9. Huang MY, Wang MY, Lin YS, Lin CJ, Lo K, Chang IJ, Cheng TY, Tsai SY, Chen HH, Lin CY, et al. The association between metabolically healthy obesity, cardiovascular disease, and all-cause mortality risk in Asia: a systematic review and meta-analysis. *Int J Environ Res Public Health*. 2020;17:1–11. doi: 10.3390/ijerph17041320
10. Mahajan R, Stokes M, Elliott A, Munawar DA, Khokhar KB, Thiyagarajah A, Hendriks J, Linz D, Gallagher C, Kaye D, et al. Complex interaction of obesity, intentional weight loss and heart failure: a systematic review and meta-analysis. *Heart*. 2020;106:58–68. doi: 10.1136/heartjnl-2019-314770
11. Campbell DJ, Gong FF, Jelinek MV, Castro JM, Coller JM, McGrady M, Boffa U, Shiel L, Liew D, Stewart S, et al. Threshold body mass index and sex-specific waist circumference for increased risk of heart failure with preserved ejection fraction. *Eur J Prev Cardiol*. 2019;26:1594–1602. doi: 10.1177/2047487319851298
12. Aune D, Sen A, Norat T, Janszky I, Romundstad P, Tonstad S, Vatten LJ. Body mass index, abdominal fatness, and heart failure incidence and mortality a systematic review and dose–response meta-analysis of prospective studies. *Circulation*. 2016;133:639–649. doi: 10.1161/CIRCULATIONAHA.115.016801
13. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, Burri H, Butler J, Celutkiene J, Chioncel O, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2021;42:3599–3726. doi: 10.1093/eurheartj/ehab368
14. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, et al. AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145:895–1032. doi: 10.1161/CIR.0000000000001073
15. Tsujimoto T, Kajio H. Abdominal obesity is associated with an increased risk of all-cause mortality in patients with HFpEF. *J Am Coll Cardiol*. 2017;70:2739–2749. doi: 10.1016/j.jacc.2017.09.1111
16. Oh A, Okazaki R, Sam F, Valero-Muñoz M. Heart failure with preserved ejection fraction and adipose tissue: a story of two tales. *Front Cardiovasc Med*. 2019;6:1–10. doi: 10.3389/fcvm.2019.00110
17. Lam CS, Chandramouli C. Fat, female, fatigued features of the obese HFpEF phenotype. *JACC Heart Fail*. 2018;6:710–713. doi: 10.1016/j.jchf.2018.06.006
18. Pandey A, LaMonte M, Klein L, Ayers C, Psaty BM, Eaton CB, Allen NB, de Lemos JA, Carnethon M, Greenland P, et al. Relationship between physical activity, body mass index, and risk of heart failure. *J Am Coll Cardiol*. 2017;69:1129–1142. doi: 10.1016/j.jacc.2016.11.081
19. Bjorck L, Novak M, Schaufelberger M, Giang KW, Rosengren A. Body weight in midlife and long-term risk of developing heart failure-a 35-year follow-up of the primary prevention study in Gothenburg. *Sweden BMC Cardiovasc Disord*. 2015;15:19. doi: 10.1186/s12872-015-0008-2
20. Del Gobbo LC, Kalantarian S, Imamura F, Lemaitre R, Siscovick DS, Psaty BM, Mozaffarian D. Contribution of major lifestyle risk factors for incident heart failure in older adults: the Cardiovascular Health Study. *JACC Heart Fail*. 2015;3:520–528. doi: 10.1016/j.jchf.2015.02.009
21. Pandey A, Cornwell WK, Willis B, Neeland IJ, Gao A, Leonard D, DeFina L, Berry JD. Body mass index and cardiorespiratory fitness in mid-life and risk of heart failure hospitalization in older age: findings from the Cooper Center Longitudinal Study. *JACC Heart Fail*. 2017;5:367–374. doi: 10.1016/j.jchf.2016.12.021
22. Fliotsos M, Zhao D, Rao VN, Ndumele CE, Guallar E, Burke GL, Vaidya D, Delaney JCA, Michos ED. Body mass index from early-, mid-, and older-adulthood and risk of heart failure and atherosclerotic cardiovascular disease: MESA. *J Am Heart Assoc*. 2018;7:e009599. doi: 10.1161/JAHA.118.009599
23. Kokkinos P, Faselis C, Franklin B, Lavie CJ, Sidossis L, Moore H, Karasik P, Myers J. Cardiorespiratory fitness, body mass index and heart failure incidence. *Eur J Heart Fail*. 2019;21:436–444. doi: 10.1002/ejhf.1433
24. Halldin AK, Lissner L, Lernfelt B, Bjorkelund C. Impact of changes in physical activity or BMI on risk of heart failure in women - the prospective population study of women in Gothenburg. *Scand J Prim Health Care*. 2020;38:56–65. doi: 10.1080/02813432.2020.1717083
25. Ergatoudes C, Hansson PO, Svärdsudd K, Rosengren A, Östgärd Thunström E, Caidahl K, Pivodic A, Fu M. Comparison of incidence rates and risk factors of heart failure between two male cohorts born 30 years apart. *Heart*. 2020;106:1672–1678. doi: 10.1136/heartjnl-2019-316059
26. Chen X, Thunström E, Hansson PO, Rosengren A, Mandalenakis Z, Zhong Y, Ergatoudes C, Caidahl K, Fu M. High prevalence of cardiac dysfunction or overt heart failure in 71-year-old men: a 21-year follow-up of "The study of men born in 1943". *Eur J Prev Cardiol*. 2020;27:717–725. doi: 10.1177/2047487319871644
27. Eaton CB, Pettinger M, Rossouw J, Martin LW, Foraker R, Quddus A, Liu S, Wampler NS, Hank Wu WC, Manson JE, et al. Risk factors

for incident hospitalized heart failure with preserved versus reduced ejection fraction in a multiracial cohort of postmenopausal women. *Circ Heart Fail*. 2016;9:e002883. doi: 10.1161/CIRCHEARTFAILURE.115.002883
28. Ndumele CE, Matsushita K, Lazo M, Bello N, Blumenthal RS, Gerstenblith G, Nambi V, Ballantyne CM, Solomon SD, Selvin E, et al. Obesity and subtypes of incident cardiovascular disease. *J Am Heart Assoc*. 2016;5:1–10. doi: 10.1161/JAHA.116.003921
29. Janszky I, Romundstad P, Laugsand LE, Vatten LJ, Mukamal KJ, Morkedal B. Weight and weight change and risk of acute myocardial infarction and heart failure - the HUNT study. *J Intern Med*. 2016;280:312–322. doi: 10.1111/joim.12494
30. Krishnamoorthy A, Greiner MA, Bertoni AG, Eapen ZJ, O'Brien EC, Curtis LH, Hernandez AF, Mentz RJ. The obesity and heart failure epidemics among African Americans: insights from the Jackson Heart Study. *J Card Fail*. 2016;22:589–597. doi: 10.1016/j.cardfail.2016.03.004
31. Page MJ, Mckenzie JE, Bossuyt PM, Boutron I, Hoffmann C, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews systematic reviews and meta-analyses. *BMJ*. 2021;372:1–9.
32. Oguntade AS, Jin D, Islam N, Malouf R, Taylor H, Caleyachetty R, Lewington S, Lacey B. Body composition and risk of heart failure: protocol for a systematic review and meta-analysis. *Open Heart*. 2021;8:1–6. doi: 10.1136/openhrt-2021-001632
33. Oguntade A, Lacey B, Caleyachetty R, Islam N, Lewington S. Body composition and the prospective risk of heart failure: a systematic review. PROSPERO 2020 CRD42020224584 Accessed May 31, 2023. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42020224584
34. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5:210. doi: 10.1186/s13643-016-0384-4
35. Luchini C, Stubbs B, Solmi M, Veronese N. Assessing the quality of studies in meta-analyses: advantages and limitations of the Newcastle Ottawa Scale. *World J Meta-Anal*. 2017;5:80–84. doi: 10.13105/wjma.v5.i4.80
36. Noll L, Mitham K, Moran J, Mallows A. Identifying current uses of return to work screening tests and their effectiveness of reducing the risk of reinjury in athletic occupations – a systematic review. *Phys Ther Sport*. 2022;58:141–150. doi: 10.1016/j.ptsp.2022.10.010
37. Mengist B, Desta M, Tura AK, Habtewold TD, Abajobir A. Maternal near miss in Ethiopia: protective role of antenatal care and disparity in socioeconomic inequities: a systematic review and meta-analysis. *Int J Africa Nurs Sci*. 2021;15:100332. doi: 10.1016/j.ijans.2021.100332
38. Green J, Cairns BJ, Casabonne D, Wright FL, Reeves G, Beral V, Women M. Height and cancer incidence in the Million Women Study: prospective cohort, and meta-analysis of prospective studies of height and total cancer risk. *Lancet Oncol*. 2011;12:785–794. doi: 10.1016/S1470-2045(11)70154-1
39. Greenland S, Longnecker MP. Methods for trend estimation from summarized dose- response data, with applications to meta-analysis. *Am J Epidemiol*. 1992;135:1301–1309. doi: 10.1093/oxfordjournals.aje.a116237
40. Orsini N, Bellocco R, Greenland S. Generalized least squares for trend estimation of summarized dose–response data. *Stata J*. 2006;6:40–57. doi: 10.1177/1536867X0600600103
41. Orsini N. Weighted mixed-effects dose – response models for tables of correlated contrasts. *Stata J*. 2021;21:320–347. doi: 10.1177/1536867X211025798
42. Papier K, Knuppel A, Syam N, Jebb SA, Key TJ. Meat consumption and risk of ischemic heart disease: a systematic review and meta-analysis. *Crit Rev Food Sci Nutr*. 2023;63:426–437. doi: 10.1080/10408398.2021.1949575
43. Shim SR, Shin IS, Yoon BH, Bae JM. Dose-response meta-analysis using STATA software. *J Health Info Stat*. 2016;41:351–358. doi: 10.21032/jhis.2016.41.3.351
44. Domínguez Islas C, Rice KM. Addressing the estimation of standard errors in fixed effects meta-analysis. *Stat Med*. 2018;37:1788–1809. doi: 10.1002/sim.7625
45. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*. 2000;56:455–463. doi: 10.1111/j.0006-341X.2000.00455.x
46. Shi L, Lin L. The trim-and-fill method for publication bias: practical guidelines and recommendations based on a large database of meta-analyses. *Medicine (Baltimore)*. 2019;98:1–11. doi: 10.1097/MD.0000000000015987
47. Wang J, Sarnola K, Ruotsalainen S, Moilanen L, Lepistö P, Laakso M, Kuusisto J. The metabolic syndrome predicts incident congestive heart failure: a 20-year follow-up study of elderly Finns. *Atherosclerosis*. 2010;210:237–242. doi: 10.1016/j.atherosclerosis.2009.10.042
48. Baena-Diez JM, Byram AO, Claudia G, Vidal-Solsona M, Ledesma-Ulloa G, Gonz I, Vasquez-Lazo J. Obesity is an independent risk factor for heart failure: Zona Franca Cohort Study. *Clin Cardiol*. 2010;33:760–764. doi: 10.1002/clc.20837
49. Van Lieshout MAW, Verwoert GC, Mattace-Raso FUS, Zillikens MC, Sijbrands EJ, Deckers JW, Hofman A, Witteman JCM. Measures of body composition and risk of heart failure in the elderly: the Rotterdam Study. *J Nutr Health Aging*. 2011;15:393–397. doi: 10.1007/s12603-010-0288-2
50. Voulgari C, Tentolouris N, Dilaveris P, Tousoulis D, Katsilambros N, Stefanadis C. Increased heart failure risk in normal-weight people with metabolic syndrome compared with metabolically healthy obese individuals. *J Am Coll Cardiol*. 2011;58:1343–1350. doi: 10.1016/j.jacc.2011.04.047
51. Wannamethee SG, Shaper AG, Whincup PH, Lennon L, Sattar N. Obesity and risk of incident heart failure in older men with and without pre-existing coronary heart disease: does leptin have a role? *J Am Coll Cardiol*. 2011;58:1870–1877. doi: 10.1016/j.jacc.2011.06.057
52. Brouwers FP, De Boer RA, Van Der Harst P, Voors AA, Gansevoort RT, Bakker SJ, Hillege HL, Van Veldhuisen DJ, Van Gilst WH. Incidence and epidemiology of new onset heart failure with preserved vs. reduced ejection fraction in a community-based cohort: 11-year follow-up of PREVEND. *Eur Heart J*. 2013;34:1424–1431. doi: 10.1093/eurheartj/eht066
53. Borne Y, Hedblad B, Essen B, Engstrom G. Anthropometric measures in relation to risk of heart failure hospitalization: a Swedish population-based cohort study. *Eur J Pub Health*. 2014;24:215–220. doi: 10.1093/eurpub/cks161
54. Morkedal B, Vatten LJ, Romundstad PR, Laugsand LE, Janszky I. Risk of myocardial infarction and heart failure among metabolically healthy but obese individuals: HUNT (Nord-Trondelag Health Study). *Norway J Am Coll Cardiol*. 2014;63:1071–1078. doi: 10.1016/j.jacc.2013.11.035
55. Xing Z, Xiao B, Hu X, Chai X. Relationship between regional adiposity distribution and incident heart failure in general populations without cardiovascular disease. *Am J Med*. 2023;136:277–283.e2. doi: 10.1016/j.amjmed.2022.11.017
56. Ingelsson E, Sundstrom J, Arnlov J, Zethelius B, Lind L. Insulin resistance and risk of congestive heart failure. *JAMA*. 2005;294:334–341. doi: 10.1001/jama.294.3.334
57. Murphy NF, MacIntyre K, Stewart S, Hart CL, Hole D, McMurray JJV. Long-term cardiovascular consequences of obesity: 20-year follow-up of more than 15000 middle-aged men and women (the Renfrew-Paisley study). *Eur Heart J*. 2006;27:96–106. doi: 10.1093/eurheartj/ehi506
58. Thrainsdottir IS, Aspelund T, Gudnason V, Malmberg K, Sigurdsson G, Thorgeirsson G, Hardarson T, Rydén L. Increasing glucose levels and BMI predict future heart failure. Experience from the Reykjavík Study. *Eur J Heart Fail*. 2007;9:1051–1057. doi: 10.1016/j.ejheart.2007.07.017
59. Levitan EB, Yang AZ, Wolk A, Mittleman MA. Adiposity and incidence of heart failure hospitalization and mortality: a population-based prospective study. *Circ Heart Fail*. 2009;2:202–208. doi: 10.1161/CIRCHEARTFAILURE.108.794099
60. Hu G, Jousilahti P, Antikainen R, Katzmarzyk PT, Tuomilehto J. Joint effects of physical activity, body mass index, waist circumference, and waist-to-hip ratio on the risk of heart failure. *Circulation*. 2010;121:237–244. doi: 10.1161/CIRCULATIONAHA.109.887893
61. Lee DS, Massaro JM, Wang TJ, Kannel WB, Benjamin EJ, Kenchaiah S, Levy D, D'Agostino RBS, Vasan RS. Antecedent blood pressure, body mass index, and the risk of incident heart failure in later life. *Hypertension*. 2007;50:869–876. doi: 10.1161/HYPERTENSIONAHA.107.095380
62. Kenchaiah S, Sesso HD, Gaziano JM. Body mass index and vigorous physical activity and the risk of heart failure among men. *Circulation*. 2009;119:44–52. doi: 10.1161/CIRCULATIONAHA.108.807289
63. Djoussé L, Bartz TM, Ix JH, Zieman SJ, Delaney JA, Mukamal KJ, Gottdiener JS, Siscovick DS, Kizer JR. Adiposity and incident heart failure in older adults: the Cardiovascular Health Study. *Obesity*. 2012;20:1936–1941. doi: 10.1038/oby.2011.320

64. Ebong IA, Goff DC, Rodriguez CJ, Chen H, Bluemke DA, Szklo M, Bertoni AG. The relationship between measures of obesity and incident heart failure: the Multi-Ethnic Study of Atherosclerosis. *Obesity*. 2013;21:1915–1922. doi: 10.1002/oby.20298
65. Kubicki DM, Xu M, Akwo EA, Dixon D, Muñoz D, Blot WJ, Wang TJ, Lipworth L, Gupta DK. Race and sex differences in modifiable risk factors and incident heart failure. *JACC Heart Fail*. 2020;8:122–130. doi: 10.1016/j.jchf.2019.11.001
66. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk factors for congestive heart failure in US men and women NHANES I epidemiologic follow-up study. *Arch Intern Med*. 2001;161:996–1002. doi: 10.1001/archinte.161.7.996
67. Chen YT, Vaccarino V, Williams CS, Butler J, Berkman LF, Krumholz HM. Risk factors for heart failure in the elderly: a prospective community- based study. *Am J Med*. 1999;106:605–612. doi: 10.1016/S0002-9343(99)00126-6
68. Joshy G, Korda RJ, Attia J, Liu B, Bauman AE, Banks E. Body mass index and incident hospitalisation for cardiovascular disease in 158 546 participants from the 45 and Up Study. *Int J Obes*. 2014;38:848–856. doi: 10.1038/ijo.2013.192
69. Rao VN, Bush CG, Mongraw-Chaffin M, Hall ME, Clark D, Fudim M, Correa A, Hammill BG, O'Brien E, Min YI, et al. Regional adiposity and risk of heart failure and mortality: the Jackson Heart Study. *J Am Heart Assoc*. 2021;10:10. doi: 10.1161/JAHA.121.020920
70. Kenchaiah S, Ding J, Carr JJ, Allison MA, Budoff MJ, Tracy RP, Burke GL, McClelland RL, Arai AE, Bluemke DA. Pericardial fat and the risk of heart failure. *J Am Coll Cardiol*. 2021;77:2638–2652. doi: 10.1016/j.jacc.2021.04.003
71. Gong FF, Jelinek MV, Castro JM, Coller JM, McGrady M, Boffa U, Shiel L, Liew D, Wolfe R, Stewart S, et al. Risk factors for incident heart failure with preserved or reduced ejection fraction, and valvular heart failure, in a community-based cohort. *Open Heart*. 2018;5:1–12. doi: 10.1136/openhrt-2018-000782
72. Suthahar N, Meems LMG, Withaar C, Gorter TM, Kieneker LM, Gansevoort RT, Bakker SJL, van Veldhuisen DJ, de Boer RA. Relative fat mass, a new index of adiposity, is strongly associated with incident heart failure: data from PREVEND. *Sci Rep*. 2022;12:1–9. doi: 10.1038/s41598-021-02409-6
73. Loehr LR, Rosamond WD, Poole C, Mcneill AM, Chang PP, Folsom AR, Chambless LE, Heiss G. Association of multiple anthropometrics of overweight and obesity with incident heart failure: the Atherosclerosis Risk in Communities study. *Circ Heart Fail*. 2009;2:18–24. doi: 10.1161/CIRCHEARTFAILURE.108.813782
74. Walli-Attaei M, Joseph P, Rosengren A, Chow CK, Rangarajan S, Lear SA, Alhabib KF, Davletov K, Yusuf S. Variations between women and men in risk factors, treatments, cardiovascular disease incidence, and death countries (PURE): a prospective cohort study. *Lancet*. 2020;396:97–109. doi: 10.1016/S0140-6736(20)30543-2
75. Raitakari OT, Porkka KVK, Taimela S, Rasanen L, Viikari JSA. Characteristics of young men with clustering risk factors for coronary heart disease: the cardiovascular risk in young Finns study. *Am J Hum Biol*. 1997;571:565–571. doi: 10.1002/(SICI)1520-6300(1997)9:5<565::AID-AJHB4>3.0.CO;2-T
76. Wu J, Cheng X, Qiu L, Xu T, Zhu G, Han J, Xia L, Qin X, Cheng Q, Liu Q. Prevalence and clustering of major cardiovascular risk factors in China. *Medicine (Baltimore)*. 2016;95:1–10. doi: 10.1097/MD.0000000000002712
77. Gao Z, Chen Z, Sun A, Deng X. Gender differences in cardiovascular disease. *Med Nov Technol Devices*. 2019;4:100025. doi: 10.1016/j.medntd.2019.100025
78. Tromp J, Paniagua SMA, Lau ES, Allen NB, Blaha MJ, Gansevoort RT, Hillege HL, Lee DE, Levy D, Vasan RS, et al. Age dependent associations of risk factors with heart failure: pooled population-based cohort study. *BMJ*. 2021;372:1–9. doi: 10.1136/bmj.n461
79. Tyrovolas S, Panagiotakos D, Georgousopoulou E, Chrysohoou C, Tousoulis D, Haro JM, Pitsavos C. Skeletal muscle mass in relation to 10 year cardiovascular disease incidence among middle aged and older adults: the ATTICA study. *J Epidemiol Community Health*. 2020;74:26–31. doi: 10.1136/jech-2019-212268
80. Kuno T, Tanimoto E, Morita S, Shimada YJ. Effects of bariatric surgery on cardiovascular disease: a concise update of recent advances. *Front Cardiovasc Med*. 2019;6:1–10. doi: 10.3389/fcvm.2019.00094
81. Berger S, Meyre P, Blum S, Aeschbacher S, Ruegg M, Briel M, Conen D. Bariatric surgery among patients with heart failure: a systematic review and meta-analysis. *Open Heart*. 2018;5:1–9. doi: 10.1136/openhrt-2018-000910
82. Yang TWW, Johari Y, Burton PR, Earnest A, Shaw K, Hare JL, Brown WA. Bariatric surgery in patients with severe heart failure. *Obes Surg*. 2020;30:2863–2869. doi: 10.1007/s11695-020-04612-2
83. Ebong IA, Goff DC Jr, Rodriguez CJ, Chen H, Bertoni AG. Mechanisms of heart failure in obesity. *Obes Res Clin Pr*. 2014;8:e540–e548. doi: 10.1016/j.orcp.2013.12.005
84. Alpert MA, Lavie CJ, Agrawal H, Aggarwal KB, Kumar SA. Obesity and heart failure: epidemiology, pathophysiology, clinical manifestations, and management. *Transl Res*. 2014;164:345–356. doi: 10.1016/j.trsl.2014.04.010
85. Rider OJ, Lewis AJM, Neubauer S. Structural and metabolic effects of obesity on the myocardium and the aorta. *Obes Facts*. 2014;7:329–338. doi: 10.1159/000368429
86. Li C, Liu H, Xu F, Chen Y. The role of lipotoxicity in cardiovascular disease. *Emerg Crit Care Med*. 2022;2:214–218. doi: 10.1097/EC9.0000000000000024
87. Marín-Royo G, Ortega-Hernández A, Martínez-Martínez E, Jurado-López R, Luaces M, Islas F, Gómez-Garre D, Delgado-Valero B, Lagunas E, Ramchandani B, et al. The impact of cardiac lipotoxicity on cardiac function and miRNAs signature in obese and non-obese rats with myocardial infarction. *Sci Rep*. 2019;9:1–11. doi: 10.1038/s41598-018-36914-y
88. Sletten AC, Peterson LR, Schaffer JE. Manifestations and mechanisms of myocardial lipotoxicity in obesity. *J Intern Med*. 2018;284:478–491. doi: 10.1111/joim.12728
89. Makki K, Froguel P, Wolowczuk I. Adipose tissue in obesity-related inflammation and insulin resistance: cells, cytokines, and chemokines. *ISRN Inflamm*. 2013;2013:1–12. doi: 10.1155/2013/139239
90. Coppack SW. Pro-Inflammatory cytokines and adipose tissue. *Proc Nutr Soc*. 2001;60:349–356. doi: 10.1079/PNS2001110
91. Corden B, de Marvao A, Dawes TJ, Shi W, Rueckert D, Cook SA, O'Regan DP. Relationship between body composition and left ventricular geometry using three dimensional cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2016;18:32. doi: 10.1186/s12968-016-0251-4
92. Rayner JJ, Banerjee R, Holloway CJ, Lewis AJM, Peterzan MA, Francis JM, Neubauer S, Rider OJ. The relative contribution of metabolic and structural abnormalities to diastolic dysfunction in obesity. *Int J Obes*. 2018;42:441–447. doi: 10.1038/ijo.2017.239
93. Vivek G, Patel B, Gupta DK, Terry JG, Edmond K, Kabagambe TJW, Correa A, Griswold M, Taylor H, Carr JJ. Left ventricular function across the spectrum of body mass index in African Americans: the Jackson Heart Study. *JACC Heart Fail*. 2017;5:182–190. doi: 10.1016/j.jchf.2016.12.020
94. Nagueh SF. Heart failure with preserved ejection fraction: insights into diagnosis and pathophysiology. *Cardiovasc Res*. 2021;117:999–1014. doi: 10.1093/cvr/cvaa228
95. Kalogeropoulos A, Georgiopoulou V, Psaty BM, Rodondi N, Smith AL, Harrison DG, Liu Y, Hoffmann U, Bauer DC, Newman AB, et al. Biomarkers in heart failure inflammatory markers and incident heart failure risk in older adults the Health ABC (Health, Aging and Body Composition) study. *JACC*. 2010;55:2129–2137. doi: 10.1016/j.jacc.2009.12.045
96. Stone ML. *Biomarkers of inflammation in heart failure patients with reduced and preserved ejection fractions: Multi-Ethnic Study of Atherosclerosis*. University of North Florida; 2020.
97. Karas MG, Yee LM, Biggs ML, Djousse L, Mukamal KJ, Ix JH, Zieman SJ, Siscovick DS, Gottdiener JS, Rosenberg MA, et al. Measures of body size and composition and risk of incident atrial fibrillation in older people: the Cardiovascular Health Study. *Am J Epidemiol*. 2016;183:998–1007. doi: 10.1093/aje/kwv278
98. Tikkanen E, Gustafsson S, Knowles JW, Perez M, Burgess S, Ingelsson E. Body composition and atrial fibrillation: a Mendelian randomization study. *Eur Heart J*. 2019;40:1277–1282. doi: 10.1093/eurheartj/ehz003
99. Konishi M, Kagiyama N, Kamiya K, Saito H, Saito K, Ogasahara Y, Maekawa E, Misumi T, Kitai T, Iwata K, et al. Impact of sarcopenia on prognosis in patients with heart failure with reduced and preserved ejection fraction. *Eur J Prev Cardiol*. 2021;28:1022–1029. doi: 10.1093/eurjpc/zwaa117
100. Curcio F, Testa G, Liguori I, Papillo M, Flocco V, Panicara V, Galizia G, Della-Morte D, Gargiulo G, Cacciatore F, et al. Sarcopenia and heart failure. *Nutrients*. 2020;12:1–15. doi: 10.3390/nu12010211

101. Lena A, Anker MS, Springer J. Muscle wasting and sarcopenia in heart failure—the current state of science. *Int J Mol Sci*. 2020;21:1–27. doi: 10.3390/ijms21186549
102. Tillin T, Hughes AD, Mayet J, Whincup P, Sattar N, Forouhi NG, McKeigue PM, Chaturvedi N. The relationship between metabolic risk factors and incident cardiovascular disease in Europeans, South Asians, and African Caribbeans: SABRE (Southall and Brent Revisited) - a prospective population-based study. *J Am Coll Cardiol*. 2013;61:1777–1786. doi: 10.1016/j.jacc.2012.12.046
103. Kenchaiah S, Evans J, Levy D, Wilson PWF, Benjamin EJ, Larson MG, Kannel WB, Vasan RS. Obesity and the risk of heart failure. *N Engl J Med*. 2002;347:305–313. doi: 10.1056/NEJMoa020245

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*
#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/	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*
#3	Study type	exp Cohort Studies/ Observational Study/	cohort* longitudinal* prospective* follow-up* observational * incidence stud*
#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	Appropriate adjustment[b]	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	Djousse (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

[a]Representative cohort defined as general adult population.

[b]Defined 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
Kenchaiah (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										
Kenchaiah (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

Loehr (2009)[73] black men	black men	normal weight	18.5	25	22.4	21.7	first tertile	86.9	94.9	86.2	90.9	first tertile	0.9	0.93	0.9	0.915
	black men	overweight	25	29.9	27.4	27.5	second tertile	95	103	98.5	99	second tertile	0.94	0.97	0.96	0.955
	black men	obese	30	34.9	33.6	32.5	third tertile	103.1	111.1	111.8	107.1	third tertile	0.98	1.01	1.02	0.995
Baena-Diez (2010)[48]	both sexes	normal	18.5	25	24.2	21.7										
	both sexes	overweight	25	29.9	28.4	27.5										
	both sexes	obese	30	34.9	33.7	32.5										
Mørkedal (2014)[54]	both sexes	<25 metabolically healthy	20	24.9	22.6	22.45										
	both sexes	<25 metabolically unhealthy	20	24.9	23.9	22.45										
	both sexes	25-<30 metabolically healthy	25	29.9	26.9	27.45										
	both sexes	25-<30 metabolically unhealthy	25	29.9	27.7	27.45										
	both sexes	≥30 metabolically healthy	30	34.9	32.9	32.45										
	both sexes	≥30 metabolically unhealthy	30	34.9	33.3	32.45										
Ndumele (2016)[28]	both sexes	normal	18.5	25		21.7	sex specific WC Quintile 1	52	87	84.5	69.5					
	both sexes	overweight	25	29.9		27.5	sex specific WC Quintile 2	88	94.5	96.8	91.25					
	both sexes	obese	30	34.9		32.5	sex specific WC Quintile 3	95.5	103.5	107.1	99.5					
	both sexes	severely obese	35	39.9		37.5	sex specific WC Quintile 4	104.5	178	122	141.25					
Pandey (2017)[21]	both sexes	normal	18.5	25	22.7	21.7										
	both sexes	overweight	25	29.9	27	27.5										
	both sexes	obese	30	34.9	32.9	32.5										
Fliotsos (2018)[22]	both sexes	normal	18.5	25	22.6	21.7										
	both sexes	overweight	25	29.9	27.4	27.5										
	both sexes	obese	30	34.9	34.5	32.5										
Campbell (2019)[11]	both sexes		18.5	24.9	23.2	21.7										
	both sexes		25	27.4	26.3	26.2										
	both sexes		27.5	29.9	28.7	28.7										
	both sexes		30	32.4	32.7	31.2										

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-variates, 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)[56], 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	Thrainsdottir (2007)[58], Iceland, Reykjavík 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	Levitan (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	Levitan (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 Non-cases group: 53.8 (5.7) years											Women 1.54 (1.44, 1.66) 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	Djousse (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)[52], 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 hospitalisations, 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, hysterecetomy, 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	Fliotsos (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 5units 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	Insuin use, pregnancy, no consent, serious mental illness, life expectancy <1 year, treatment for malignancies (other than non-melanoma sin 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)[55], 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	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	/<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)

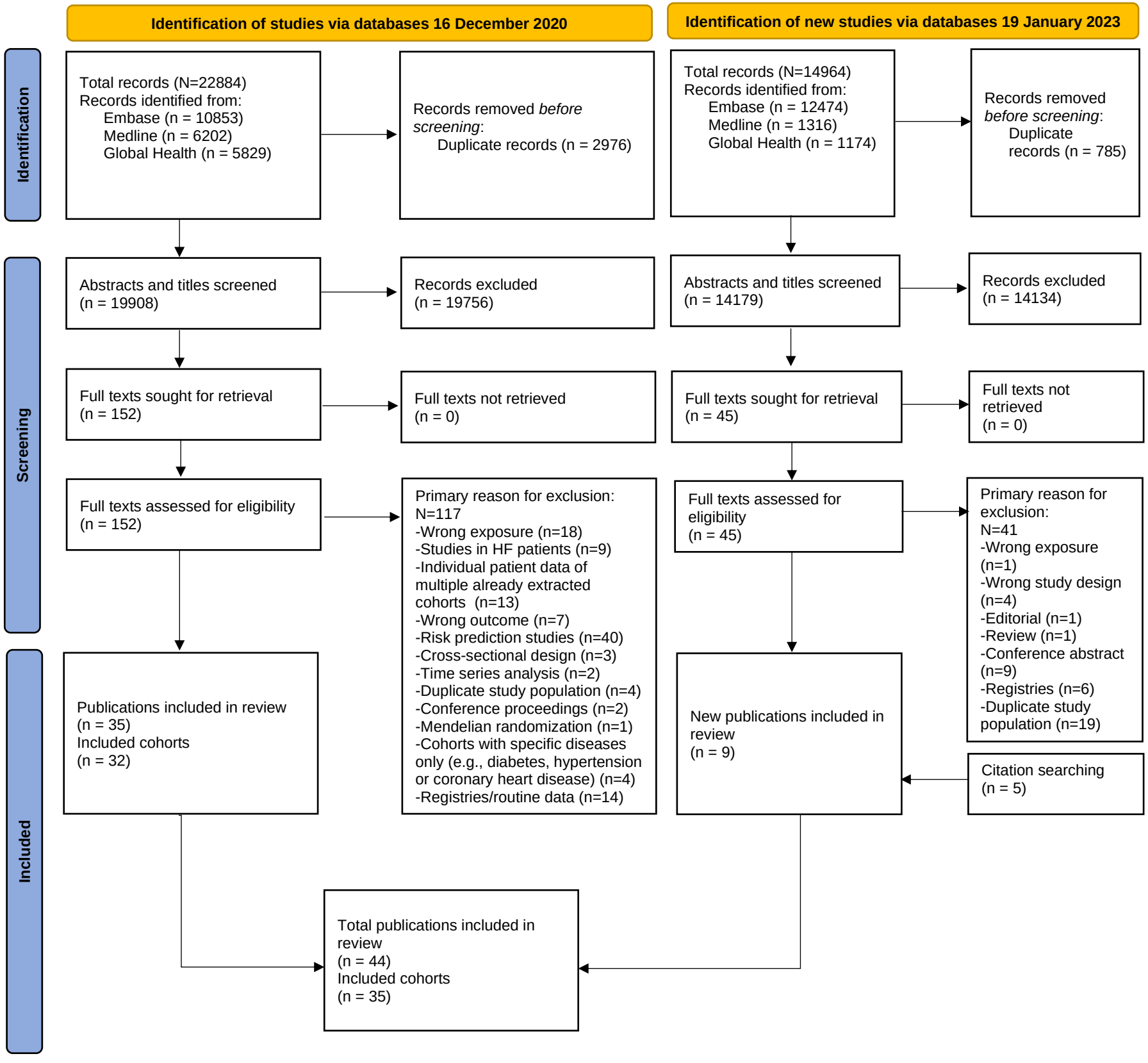

Figure S1: PRISMA flowchart of study selection

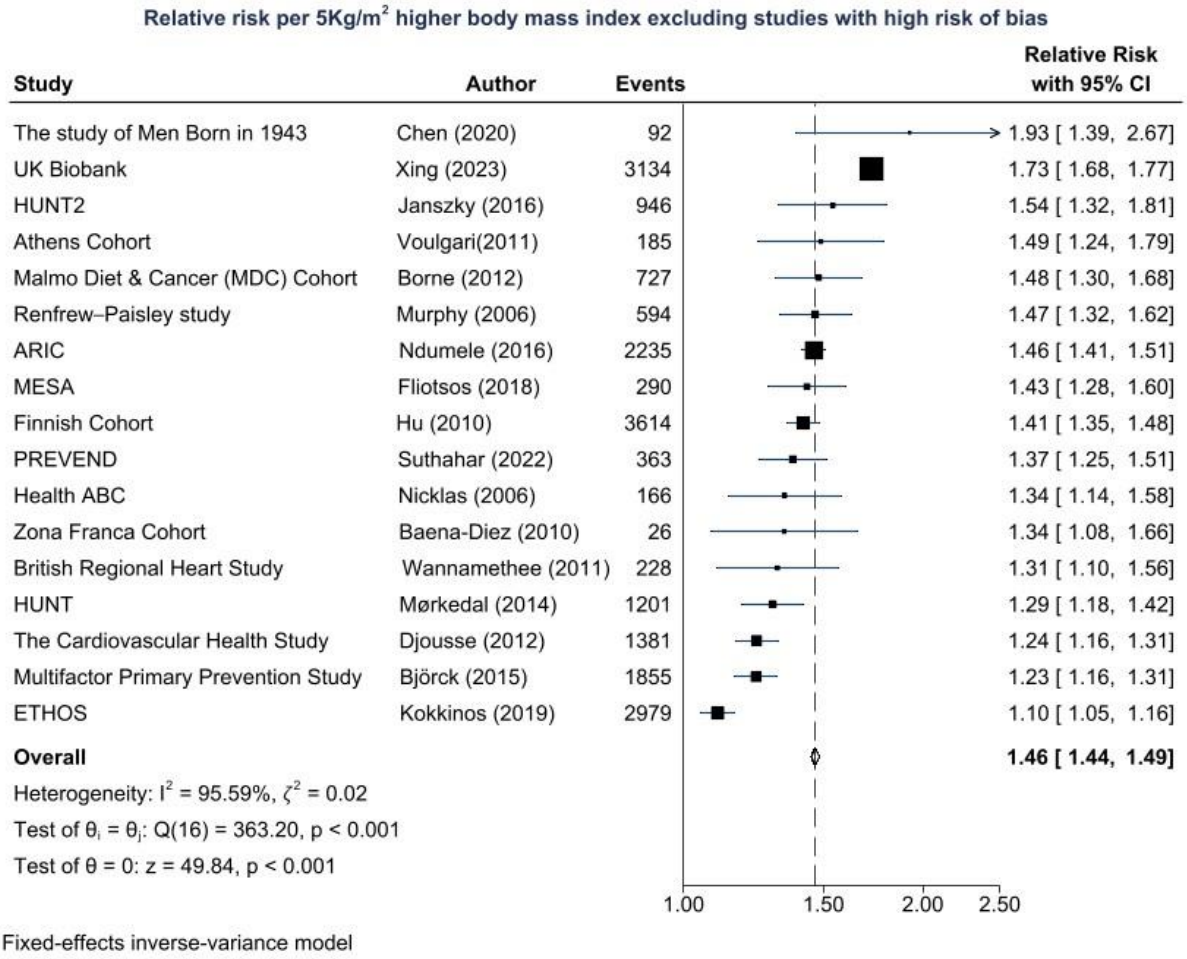

Figure S2: Dose-response meta-analysis of BMI and HF incidence excluding studies with high risk of bias

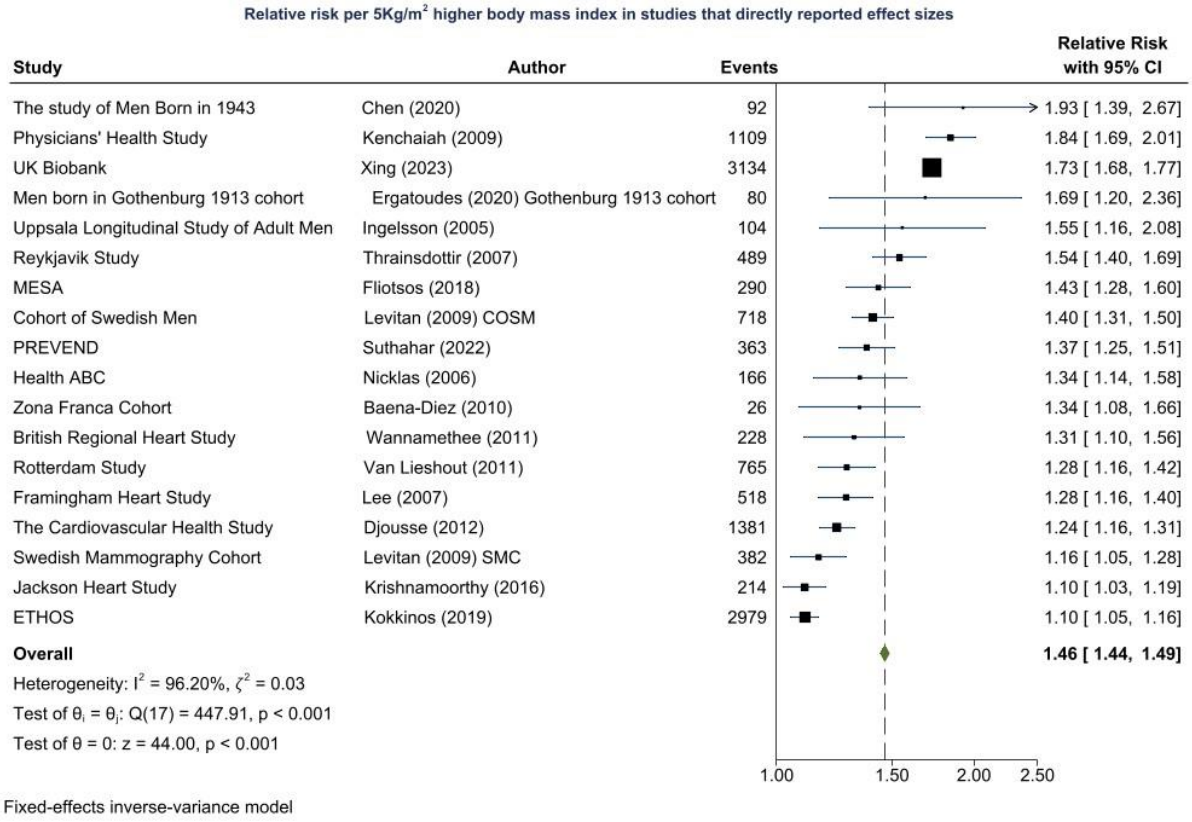

Figure S3: Dose-response meta-analysis of BMI and HF incidence in studies that directly reported effect sizes

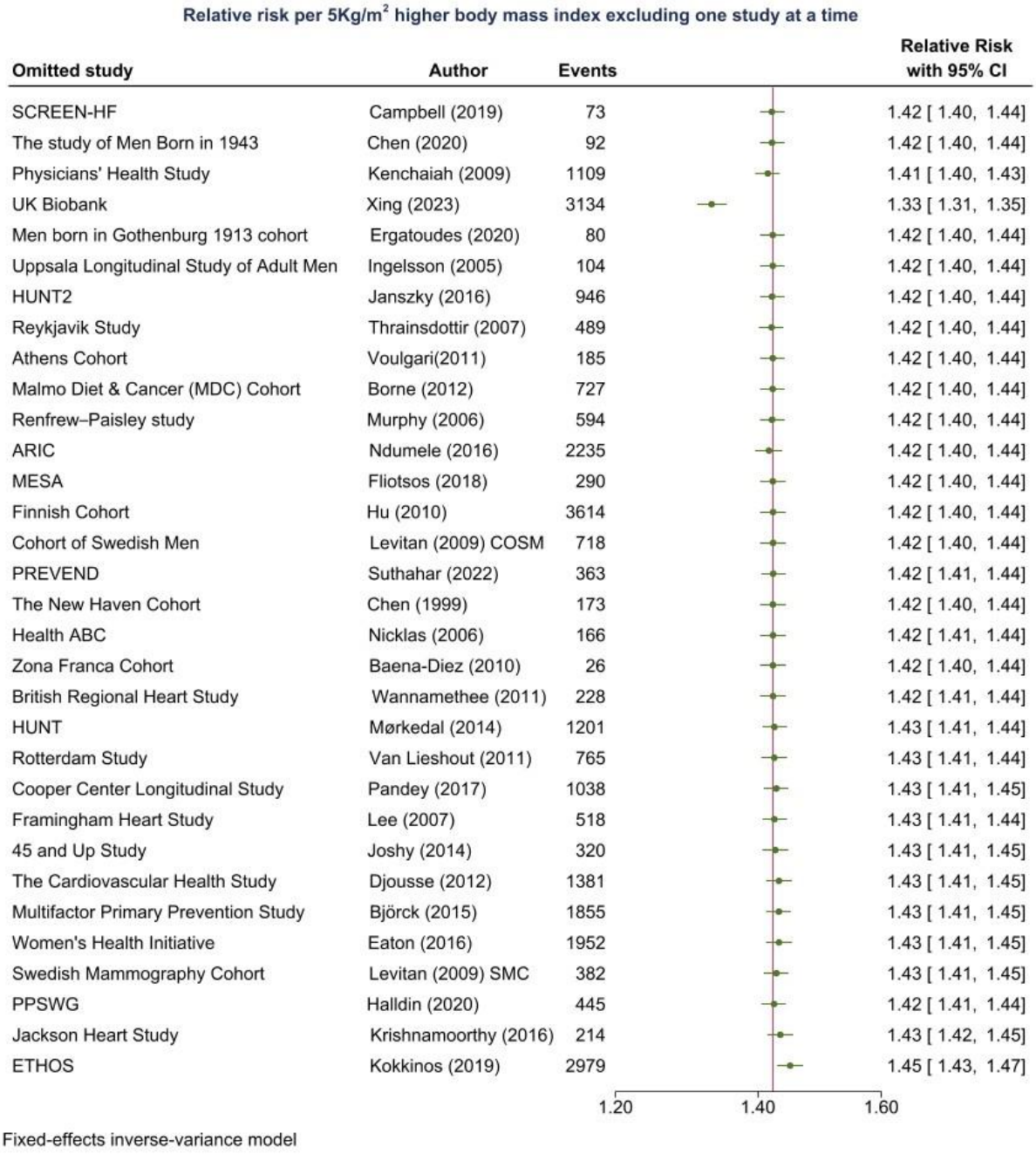

Figure S4: Meta-analysis of BMI and HF risk excluding one study at a time

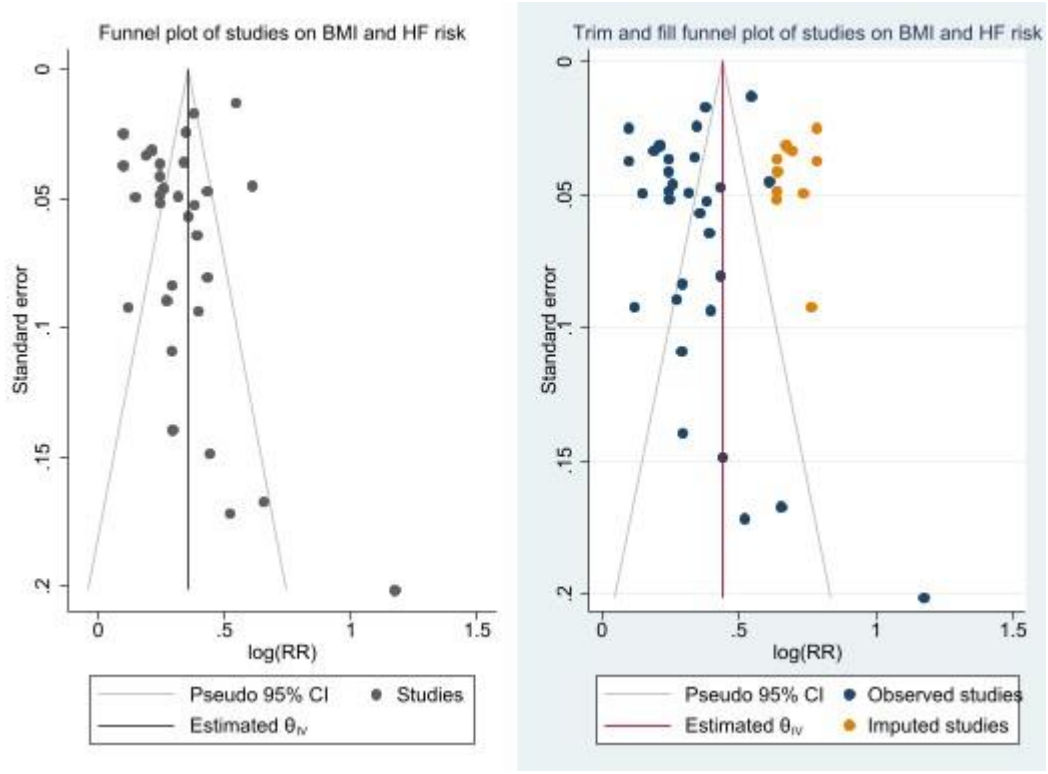

Figure S5: Funnel plot and Trim and fill plot of studies on BMI and HF risk

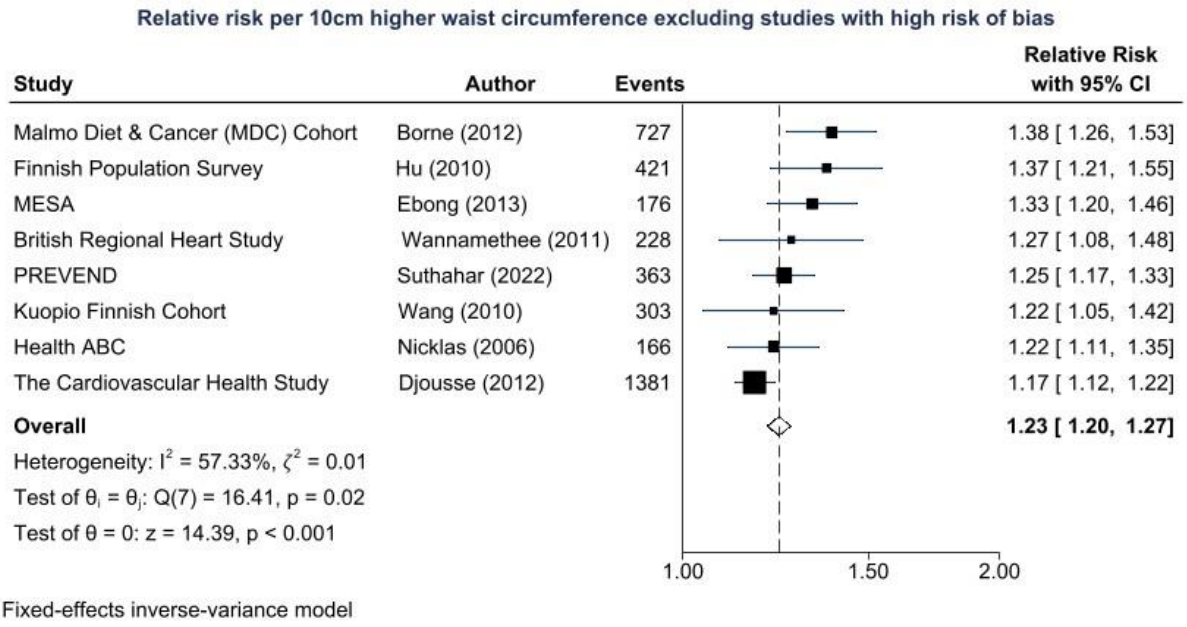

Figure S6: Dose-response meta-analysis of waist circumference and HF incidence excluding studies with high risk of bias

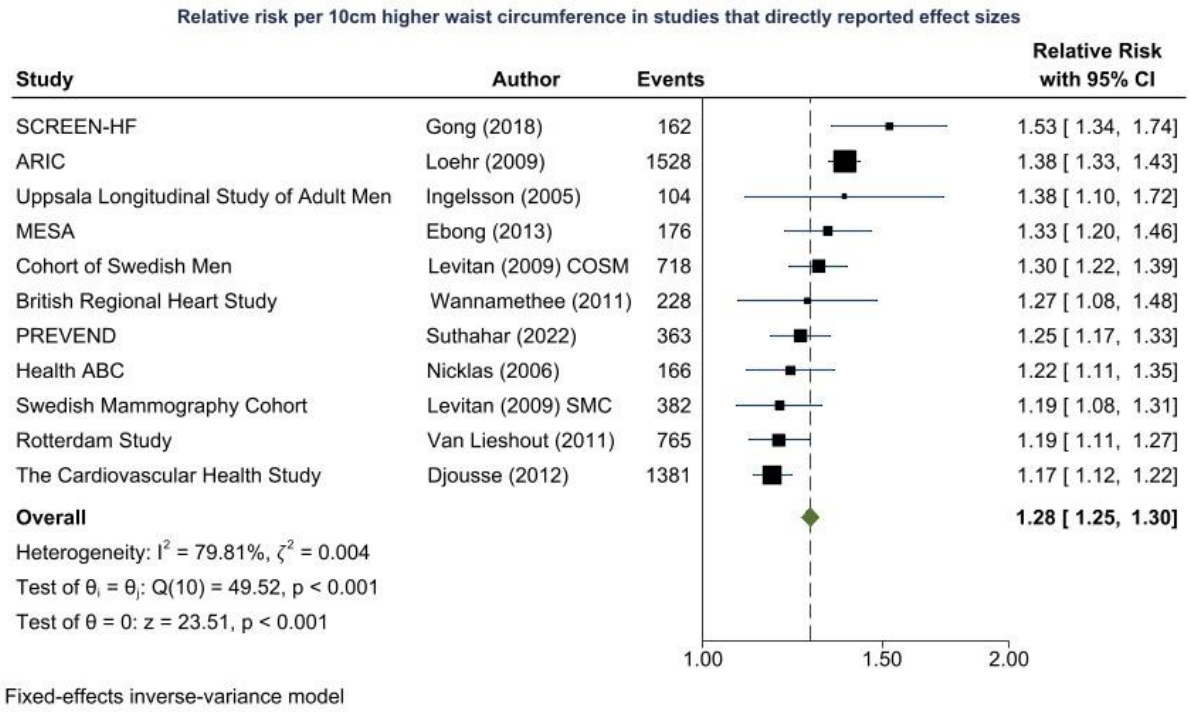

Figure S7: Dose-response meta-analysis of waist circumference and HF incidence in studies that directly reported effect sizes

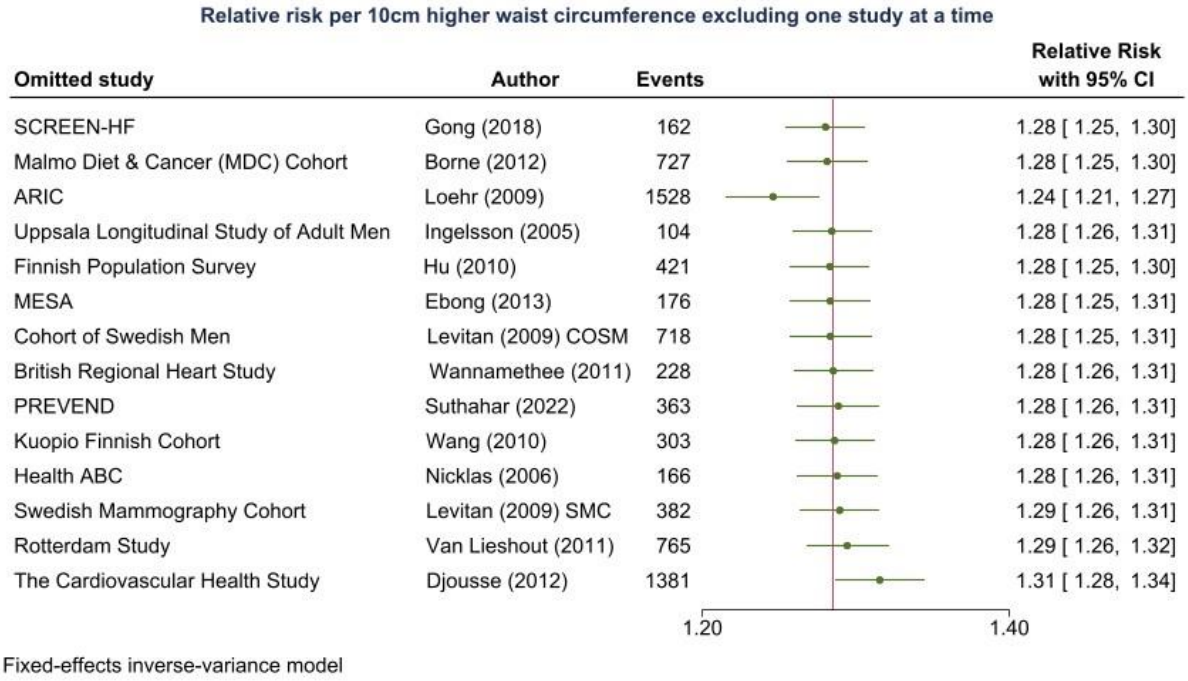

Figure S8: Meta-analysis of waist circumference and HF risk excluding one study at a time

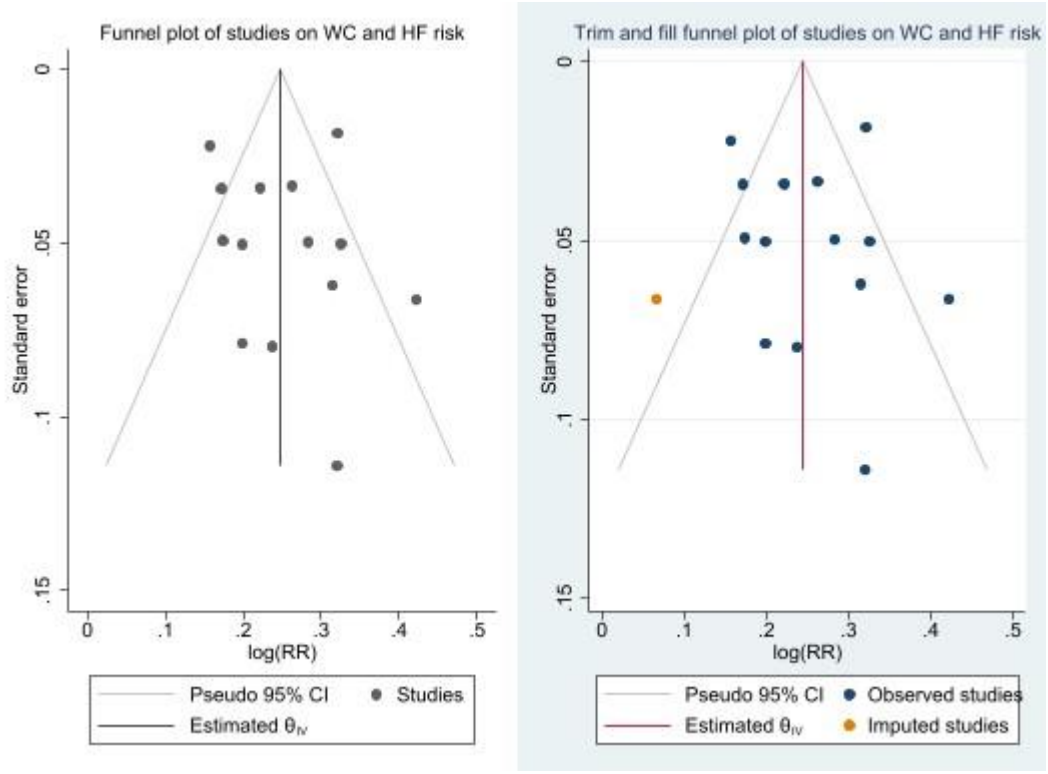

Figure S9: Funnel plot and Trim and fill plot of studies on waist circumference and HF risk

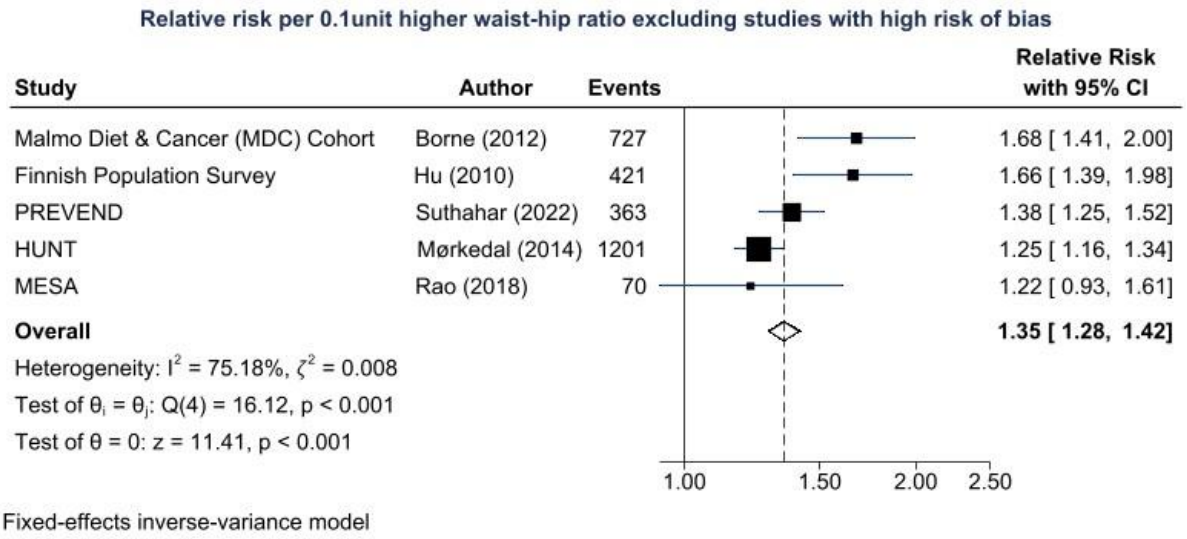

Figure S10: Dose-response meta-analysis of waist-hip ratio and HF excluding studies with high risk of bias

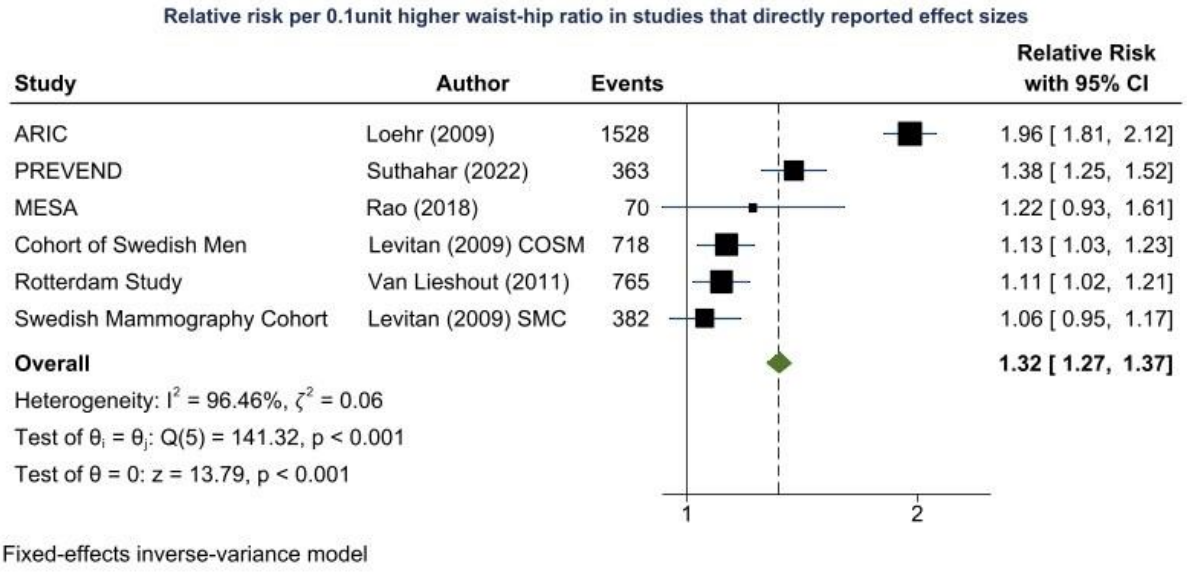

Figure S11: Dose-response meta-analysis of waist-hip ratio and HF incidence in studies that directly reported effect sizes

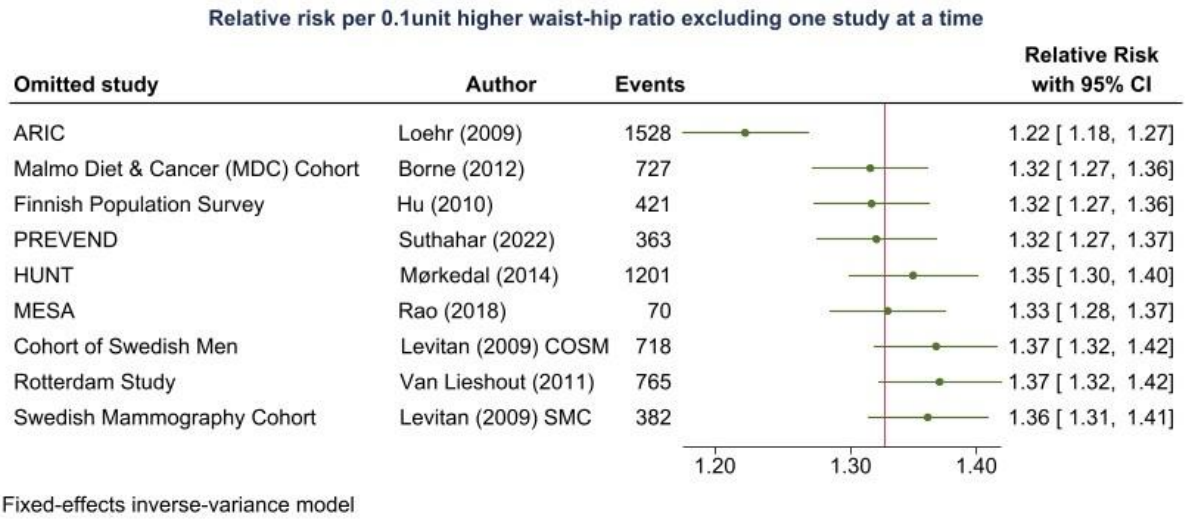

Figure S12: Meta-analysis of waist-hip ratio and HF risk excluding one study at a time

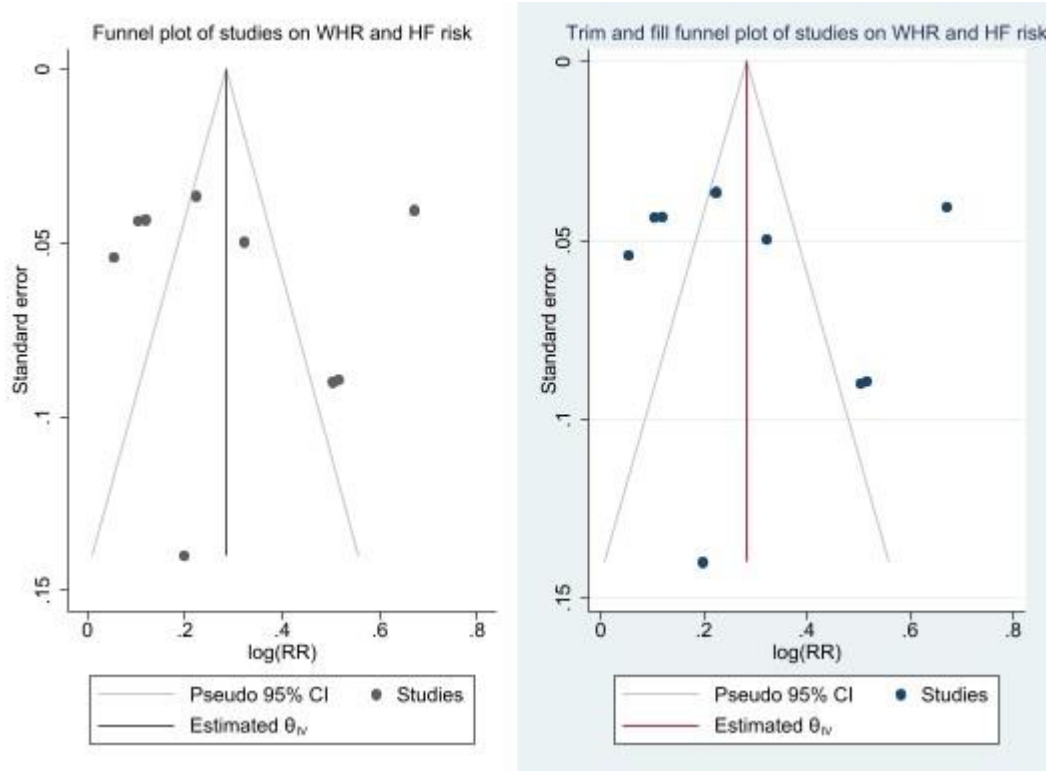

Figure S13: Funnel plot and Trim and fill plot of studies on waist-hip ratio and HF risk