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Abdominal obesity and risk of CVD: a dose–response meta-analysis of thirty-one prospective studies

Ran Xue[1], Qianwen Li[1], Yaping Geng[1], Hao Wang[1], Fudi Wang[1,2] and Shenshen Zhang[1]*

[1]*Department of Precision Nutrition Innovation Center, Department of Nutrition and Food Hygiene, College of Public Health, Zhengzhou University, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, People's Republic of China*
[2]*The First Affiliated Hospital, School of Public Health, Institute of Translational Medicine, Zhejiang University School of Medicine, Hangzhou, People's Republic of China*

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Abstract

This meta-analysis aimed to study the relationship between abdominal obesity and the risk of CVD by waist circumference (WC), waist:hip ratio (WHR) and waist:height ratio (WHtR). We systematically searched PubMed, Embase and Web of Science. Prospective studies that estimated cardiovascular events by WC, WHR and WHtR were included in this study. Pooled relative risks with 95 % CI were calculated using random effects models. A total of thirty-one studies were included in the meta-analysis, including 669 560 participants and 25 214 cases. Compared the highest with the lowest category of WC, WHR and WHtR, the summary risk ratios were 1·43 (95 % CI, 1·30, 1·56, $P < 0·001$), 1·43 (95 % CI, 1·33, 1·54, $P < 0·001$) and 1·57 (95 % CI, 1·37, 1·79, $P < 0·001$), respectively. The linear dose–response analysis revealed that the risk of CVD increased by 3·4 % for each 10 cm increase of WC, and by 3·5 and 6·0 % for each 0·1 unit increase of WHR and WHtR in women, respectively. In men, the risk of CVD increased by 4·0 % for each 10 cm increase of WC, and by 4·0 and 8·6 % for each 0·1 unit increase of WHR and WHtR, respectively. Collectively, abdominal obesity is associated with an increased risk of CVD. WC, WHR and WHtR are good indicators for the prediction of CVD.

Key words: Waist circumference: Waist:hip ratio: Waist:height ratio: Abdominal obesity: CVD: Systematic reviews: Meta-analyses

CVD is a severe public health threat around the world, which mainly includes CHD, cerebrovascular disease, peripheral arterial disease and rheumatic heart disease. According to the WHO, an estimated 17·9 million people died from CVD in 2016, accounting for 31 % of all deaths globally. The Global Burden of Disease Study also announced that the total deaths from CVD increased by 21 % between 2007 and 2017[1].

Obesity is an independent risk factor for CVD and associated with many co-morbidities of CVD such as hypertension, hyperlipidaemia and the metabolic syndrome[2]. As a serious public health issue worldwide, obesity had affected a total of 107·7 million children and 603·7 million adults from 195 countries in 2015, resulting in 4·0 million (2·7–5·3 million) deaths and 120 million (84–158 million) disability-adjusted life years among adults globally. CVD was the leading cause of deaths and disability-adjusted life years related to obesity[3]. It is generally known that BMI is a common indicator to define obesity, which is easy to perform. However, it does not reflect the location of fat distribution, and conclusions about the relationship between BMI and CVD are inconsistent. Some studies found a protective effect of BMI on CVD, which is called 'obesity paradox'[4,5]. Coutinho *et al.* found that the risk of death decreased with the increase of BMI in 15 923 patients with coronary artery disease, whereas abdominal obesity was positively associated with the mortality[6].

Some indices of abdominal obesity such as waist circumference (WC), waist:hip ratio (WHR) and waist:height ratio (WHtR) are considered to be good indicators for predicting CVD. These indicators can reflect fat distribution and visceral fat accumulation to some extent, which are more easily available than computed tomography and MRI. Many epidemiological studies have begun to use these indicators to assess the relationship between obesity and CVD accurately. The international day for the evaluation of abdominal obesity, a large epidemiological study, investigated the relationship between WC and risk of CVD in 168 000 primary care patients in sixty-three countries, which demonstrated a significant correlation between waistline expanding and increased risk of

Abbreviations: RR, risk ratio; WC, waist circumference; WHR, waist:hip ratio; WHtR, waist:height ratio.

* **Corresponding author:** Shenshen Zhang, email zsslb2005@163.com

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CVD[7]. Karin *et al.* found that WHtR is a useful indicator to estimate the risk of CVD in patients with diabetes[8]. The meta-analysis of Ashwell *et al.*[9], Lee *et al.* [10] and Savva *et al.*[11] also suggested that measures of abdominal obesity were superior to BMI in detecting cardiovascular risk. However, studies from different countries and ethnicities have different conclusions regarding the superiority of different obesity indicators. Therefore, we collected the related prospective studies and made a meta-analysis to estimate the relationship between abdominal obesity and CVD by WC, WHR and WHtR.

Methods

Search strategy

The meta-analysis was conducted by the Meta-analysis of Observational Studies in Epidemiology. We conducted a systematic search of the literature on prospective cohort studies from PubMed, Embase and Web of Science up to 28 September 2019, using the following keywords and their synonyms (combined unexploded version of the Medical Subject Headings): ('cardiovascular diseases' OR 'cerebrovascular disease' OR 'coronary heart disease' OR 'stroke' OR 'myocardial infarction' OR 'venous thromboembolism') AND ('waist circumference' OR 'waist to hip ratio' OR 'waist to height ratio') AND ('prospective cohort study' OR 'follow-up study'). The reference lists within the relevant publications were searched to identify other additional information. The corresponding author was contacted to request the required data if necessary.

Inclusion criteria

Studies were included in the meta-analysis if they met the following criteria: (1) participants were 18 years or older; (2) follow-up durations were more than 3 years; (3) at least one of the anthropometric measures was measured and reported, including WHR, WC or WHtR during the follow-up; (4) the outcome was the occurrence of CVD; (5) risk ratios (RR) or hazard ratios and their corresponding 95 % CI could be calculated and (6) studies were prospective study design.

Data abstraction and assessment for study quality

From each retrieved study, we extracted the following information: the first author's name, year of publication, specific outcomes, name of cohort, number of participants/cases, mean age or age range, follow-up duration, anthropometric measurement method, covariates adjusted in multivariate analysis, quintiles of WHR, WC and WHtR, and corresponding RR of CVD with 95 % CI. Quality of the included studies was evaluated according to the Newcastle–Ottawa scale for non-randomised studies. The score of 0–3, 4–6 or 7–9 was regarded as low, moderate or high quality, respectively. Data extraction process and study quality assessment were performed by two independent investigators (X. R. and G. Y.), and group discussion to solve disagreements.

Statistical analysis

We collected the RR with 95 % CI as the common measure of associations across studies, where necessary, the hazard ratios were used to approximate RR. For the comparison between the highest categories and lowest categories of WC, WHR and WHtR, the summarised RR or hazard ratios and their corresponding 95 % CI were calculated using a random effects model. The model with the greatest control in each study was used to eliminate potential confounding factors.

Dose–response analysis was conducted using the method described by Greenland & Longnecker[12] based on an increase of 10 cm for WC, 0·1 units for WHR and WHtR. We extracted the categories of WC, WHR and WHtR, the distributions of cases and number of subjects or person-years, and RR with 95 % CI. If studies reported results separately for different outcomes or other subgroups besides men and women, we combined the subgroup-specific estimates using a fixed effects model to generate an overall estimate so that each study was only conducted once in the main analysis. If the reference category was not the lowest in some studies, the RR were recalculated with the lowest category as a reference by the method provided by Hamling *et al.*[13]. The median point in each category of WC, WHR and WHtR was assigned to the corresponding RR for each study. If medians were not reported, we considered the midpoint of the upper and lower boundaries as the dose of each category. If the highest and/or lowest category was open-ended, the midpoint of that category was set by assuming that the categorical width was the same as the next adjacent category.

Heterogeneity of studies was estimated by the I^2 statistic, and the values of 25, 50 and 75 % were defined as low, moderate and high heterogeneity, respectively. We performed subgroup analysis to evaluate the potential sources of heterogeneity. The analyses were conducted in men and women, respectively, to rule out the potential effects of sex difference. Subgroups analysis was carried out according to outcomes, age, geographic location, follow-up durations, number of participants and quality of articles. Potential publication bias was assessed using Begg's test, Egger's linear regression test and funnel plot asymmetry. If publication bias existed, 'trim-and-fill' was applied to correct the bias[14]. We conducted sensitivity analysis in which a single study was excluded from the analysis at a time to verify the reliability of this study. All statistical analyses were performed using Stata statistical software version 12 (Stata Corp). $P < 0{\cdot}05$ was considered as significant.

Results

Literature search and study characteristics

We found 6580 potential articles through literature search, and 6399 articles were excluded by title and abstract, leaving 181 relevant articles for review of full text. Thirty articles were left after full-text review according to the exclusion criteria (details are shown in Fig. 1). One of the articles included two different cohorts was regarded as two independent studies[15]. Finally, thirty-one prospective cohort studies and

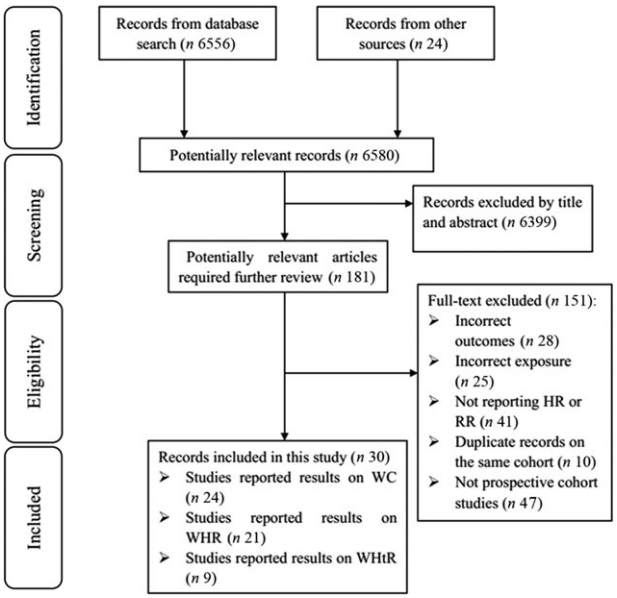

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. WC, waist circumference; WHR, waist:hip ratio; WHtR, waist:height ratio; HR, hazard ratio; RR, risk ratio.

a cross-sectional study with follow-up were included in this meta-analysis with a total of 669 560 participants and 25 214 cases. There were five studies for female participants[15–19], eleven studies for male participants[15, 20–29] and fifteen studies for both male and female participants[30–44]. Mean age ranged from 34 to 75 years old. The characteristics of included studies are presented in Table S1.

Waist circumference and CVD

Twenty-four studies examined associations between WC and risk of CVD, including 571 789 participants and 18 452 cases. Compared the highest category with the lowest category, the summary RR was 1·43 (95 % CI, 1·30, 1·56; $I^2 = 58·6$ %; $P < 0·001$). The pooled RR with 95 % CI was 1·42 (95 % CI 1·25, 1·61) and 1·46 (95 % CI 1·25, 1·72) in men and women with moderate heterogeneity, respectively (men: $I^2 = 55·3$ %, $P_{heterogeneity} < 0·05$; women: $I^2 = 61·4$ %, $P_{heterogeneity} < 0·05$) (Fig. 2). Eleven studies were available for inclusion in dose–response meta-analysis. Through sex-specific linear dose–response analysis, we found that each 10 cm increase of WC enhanced the risk of CVD by 4·0 % in men (RR 1·04; 95 % CI 1·02, 1·06; $P < 0·001$) and 3·4 % in women (RR 1·03; 95 % CI 1·01, 1·06; $P < 0·05$). The non-linear dose–response analysis also showed a significant relevance between WC and risk of CVD in both men and women ($P < 0·001$). In male participants, we observed that there was no change in the trend of the curve when WC was lower than 80 cm. When WC was about 80–90 cm, the incidence of CVD grew slowly. However, it was obvious that the risk of CVD increased with a steep slope when WC was over 90 cm. In women, the risk of CVD increased significantly when WC was over 80 cm (Fig. 3).

Waist:hip ratio and CVD

Twenty-one studies with 447 467 participants and 16 828 cases were included in the analysis of WHR and risk of CVD. The summary RR was 1·43 (95 % CI 1·33, 1·54; $I^2 = 30·6$ %; $P < 0·001$) compared the highest category with the lowest category. The pooled RR was 1·43 (95 % CI 1·31, 1·57) with a low heterogeneity ($I^2 = 17·0$ %; $P_{heterogeneity} = 0·259$) in men, and 1·48 (95 % CI 1·29, 1·70) with a moderate heterogeneity ($I^2 = 49·9$ %; $P_{heterogeneity} = 0·02$) in women (Fig. 4). Twelve studies provided enough information to carry on dose–response meta-analysis. The risk of CVD increased by 4·0 % in men (RR 1·04; 95 % CI 1·02, 1·06; $P < 0·001$) and 3·5 % in women (RR 1·03; 95 % CI 1·01, 1·06; $P < 0·05$) with each 0·1 unit increase of WHR by sex-specific linear dose–response analyses. When the non-linear dose–response analysis was used, a significant non-linear relationship was found ($P < 0·001$). The dose–response plot showed a slow slope when WHR increased to 0·9, and when WHR values were higher than 0·9, the risk of CVD rose more obvious in men. While in female participants, the curve with an inconspicuous inflexion point reminded that the risk of CVD enhanced continuously with the increase of WHR (Fig. 5).

Waist:height ratio and CVD

Nine studies involving 187 137 participants and 7557 cases reported sufficient information on WHtR and risk of CVD. Compared the highest category with the lowest category, the summary RR was 1·57 (95 % CI 1·37, 1·79; $I^2 = 37·6$ %; $P < 0·001$). In analysis of different sexes, the summary RR was 1·67 (95 % CI 1·40, 1·98; $P < 0·05$) with a low heterogeneity ($I^2 = 16·4$ %; $P_{heterogeneity} = 0·31$) in women and 1·56 (95 % CI 1·25, 1·95; $P < 0·05$) with a moderate heterogeneity ($I^2 = 38·2$ %; $P_{heterogeneity} = 0·152$) in men (Fig. 6). Four studies were available in dose–response analyses. The linear dose–response analysis revealed that the risk of CVD increased by 8·6 % in men (RR 1·08; 95 % CI 1·01, 1·16; $P < 0·05$) and 6·0 % in women (RR 1·06; 95 % CI 1·03, 1·09; $P < 0·001$) with each 0·1 unit increase of WHR. There was a non-linear relationship between WHtR and risk of CVD in men ($P < 0·05$) and women ($P < 0·001$) with the random effects dose–response analysis. The non-linear dose–response curve revealed that the risk of CVD would rise sharply both in men and women when WHtR over 0·5 (Fig. 7).

Subgroup analysis, publication bias, sensitivity analysis

The subgroup analysis was conducted to explore the potential sources of heterogeneity. Subgroup analyses were carried out by outcome, age, geographic location, follow-up duration, number of participants and quality of articles in male and female (Tables 1–3). Most of the subgroups still kept relevant to CVD risk after subgroup analysis. When subgroup analysis was performed by outcomes, we found that the association is stronger in women than in men in relationship between CHD and WC and WHR. However, perhaps due to the limited studies, the same phenomenon has not been observed in WHtR. In the sensitivity analysis, one single study was removed at a time and the analysis

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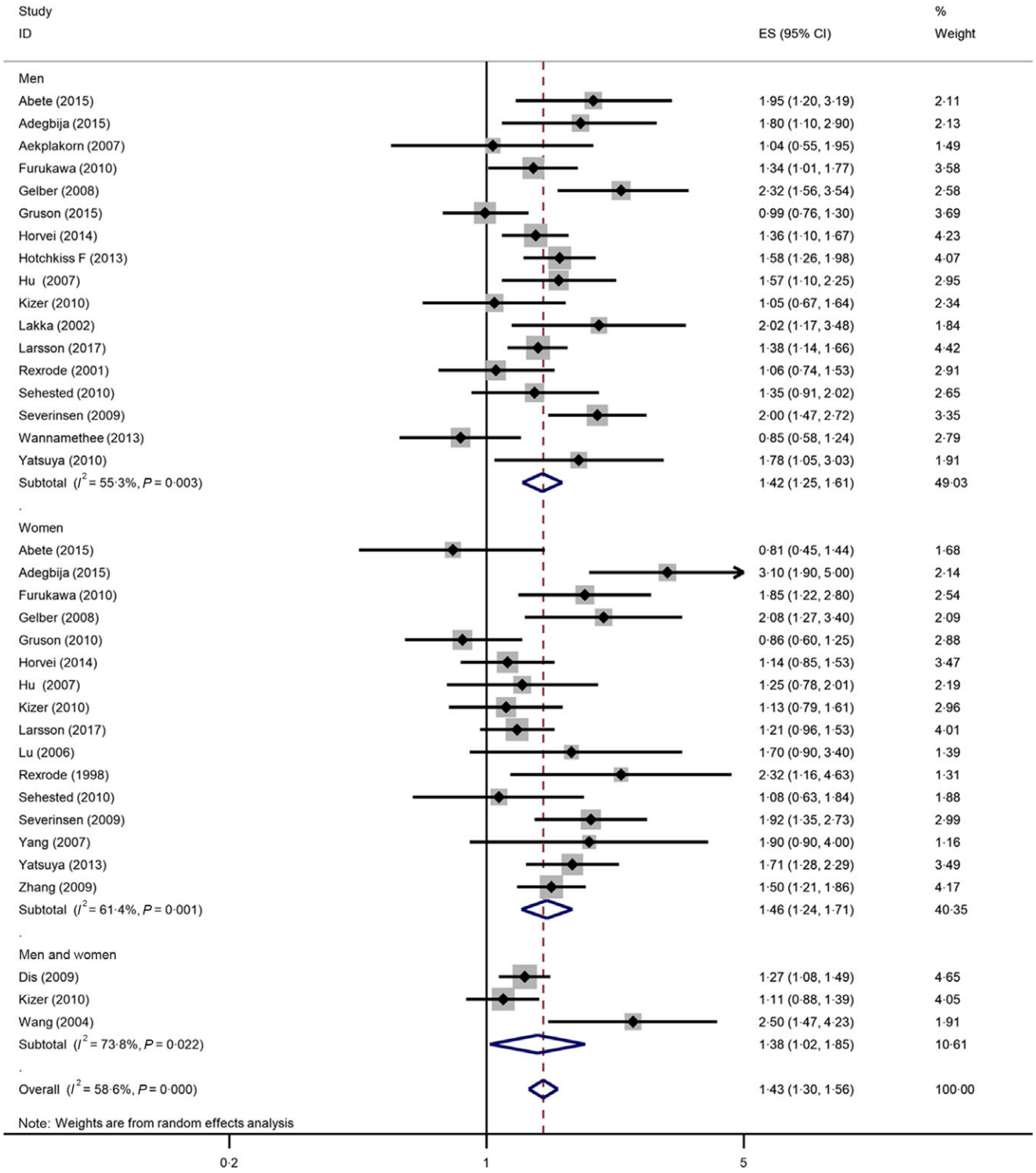

Fig. 2. Forest plot of association between waist circumference and risk of CVD. ES, effect size.

was conducted with the remaining studies to assess whether the result was affected by the excluded study. The result revealed that no individual study affected the pooled effect size (Figs. S1–S3). The funnel plot, Egger's test and Begg's test were used to analyse the publication bias. No evidence of publication bias was found in the relationship between CVD and WC and WHtR (Figs. S4 and S6). However, publication bias was observed in study of the relationship between CVD and WHR ($P < 0·05$), and the funnel plot seemed to be asymmetric (Figs. S5). After using the 'trim-and-fill' method to correct the publication bias,

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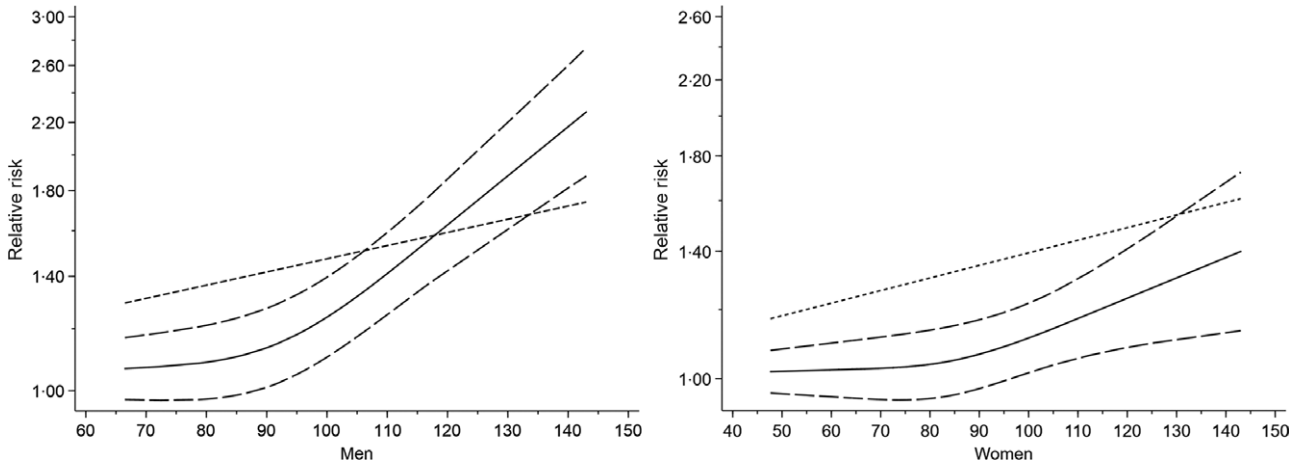

Fig. 3. Dose–response analysis between waist circumference (cm) and risk of CVD among men (left) and women (right). Solid line: non-linear dose response. Dotted line: 95 % CI. Straight dotted line: linear dose–response.

the result was still statistically significant (RR 1·36, 95 % CI 1·25, 1·47).

Discussion

CVD has been becoming a serious public health burden around the world. Obesity, especially abdominal obesity is closely related to CVD. WC, WHR and WHtR are precise indicators of abdominal obesity, which have advantage of easily available. Previous studies have demonstrated that indicators of abdominal obesity were better than BMI for prediction of many diseases[8–11]. Identifying the relationship between these regulable factors and CVD will help reduce the risk of CVD. However, many researchers explored the association between abdominal obesity indices and cardiovascular risk factors, such as hypertension, the metabolic syndrome and type 2 diabetes. A comprehensive meta-analysis to investigate the relationship between WC, WHR, WHtR and incidence of CVD is urgent to be done.

Our meta-analysis comprehensively evaluated the relationship between WC, WHR, WHtR and the risk of CVD in general population with linear and non-linear dose–response models incorporating the data from thirty-one prospective studies. These results showed significant correlations of WC, WHR, WHtR with cardiovascular risk. Compared with the lowest category of WC, WHR and WHtR, the CVD risk of highest group was increased by 43, 43 and 57 %, respectively. The linear dose–response analysis showed the risk of CVD increased by 4·0 and 3·4 % for each 10 cm increase of WC in men and women, respectively. When WHR and WHtR increase by 0·1 units, the incidence of CVD enhanced by 4·0 and 8·6 % in men, and increased by 3·5 and 6·0 % in women, respectively.

Non-linear analysis showed that the risk of CVD rose continuously when WC was over 90 cm, WHR was over 0·9, WHtR was over 0·5 in men, and when WC was over 80 cm, WHtR was over 0·5 in women. It was interesting to note the non-linear dose–response curve with inconspicuous inflexion point in women. This trend showed that the risk of CVD increased continuously with WHR in women. Some epidemiological studies have demonstrated that the risk estimates for WC without hip circumference adjustment would underestimate the risk of CVD[45,46], which reminded us that large hip circumference may be a protective factor for CVD in women.

The results of non-linear analysis can also help determine the boundary markers for prevention of CVD. Cut-off points recommended by WHO to define abdominal obesity are as follows: WC > 102 cm, WHR > 1·0 for men, and WC > 88 cm, WHR > 0·85 for women. According to our analysis, men should keep their WC below 90 cm and WHR below 0·9 to maintain cardiovascular fitness. As for women, they should keep their WC below 80 cm and WHR should be as small as possible within the normal range. WHtR below 0·5 applies to both men and women.

It is worth mentioning that the existing literature suggested that 0·5 was an appropriate boundary value for predicting abdominal adiposity, cardiovascular risk and all-cause mortality. Research from Jayedi *et al.* of seventy-two prospective cohort studies suggested that the risk of all-cause mortality increased sharply when WHtR was >0·5[47]. Browning *et al.*[48], Castanheira *et al.*'s research conducted in 9246 Brazilian adults[49] and Gibson *et al.*'s recent data from 4112 adults in England[50] had shown that 0·5 was a suitable cut-off point for predicting cardiovascular risk. Several other studies also supported this point of view[51,52]. Our research demonstrated that the risk of CVD increased sharply when WHtR was over 0·5 through analysis of 187 137 participants from different regions and races. This strongly supported the simple public health message: Keep your WC to less than half your height.

Many scientists have been studying how abdominal obesity up-regulates the risk of CVD. Some researchers believed that increased abdominal fat is a marker of more ectopic fat in some organs, including liver and heart[53]. Fat tissue can be divided into subcutaneous fat tissues and

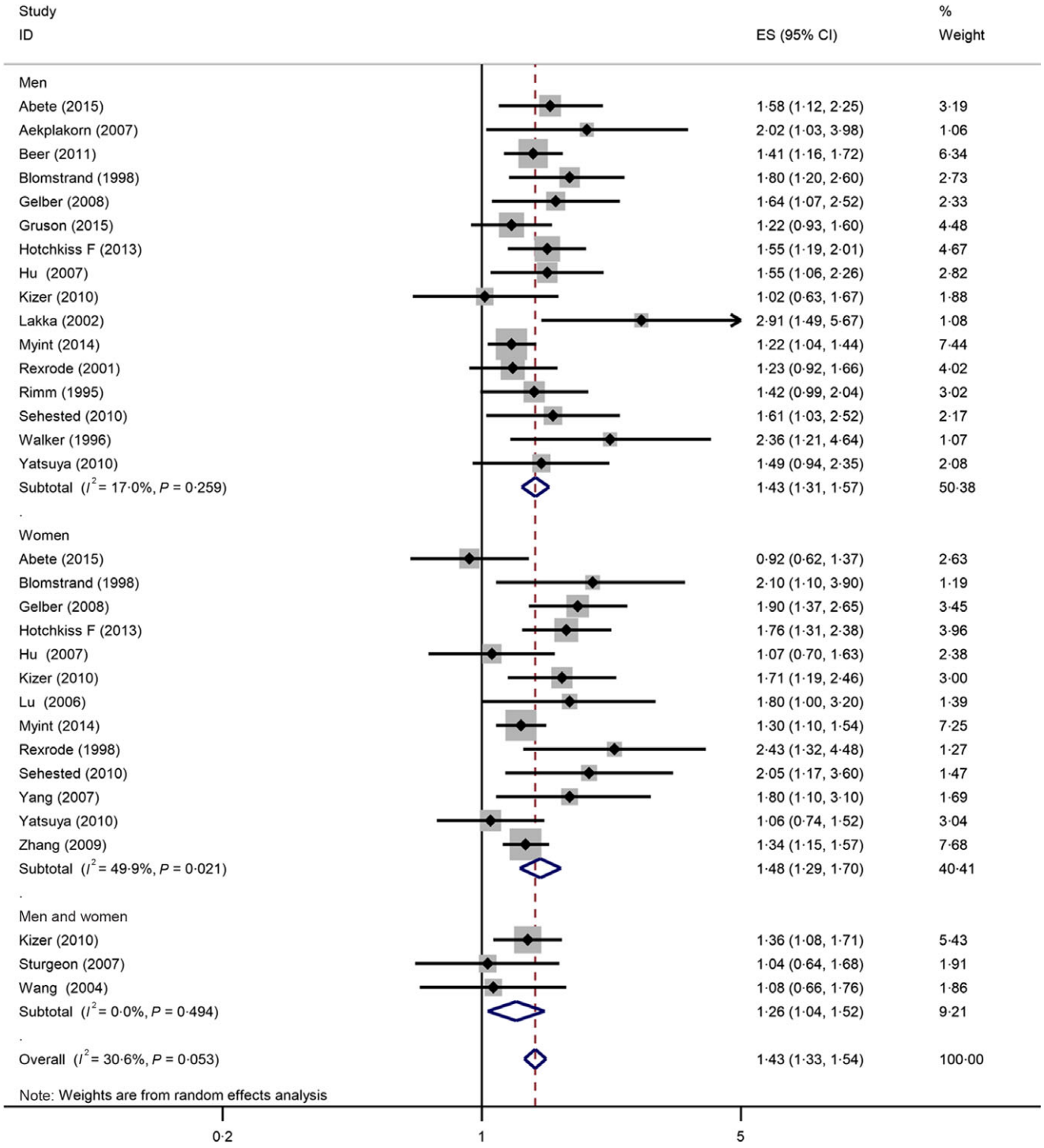

Fig. 4. Forest plot of association between waist:hip ratio and risk of CVD. ES, effect size.

visceral adipose tissue according to their distribution. When fat accumulates in vital organs such as liver and heart, it is likely to be closely associated with an increased CVD risk. Therefore, many researchers have put forward ideas that the essential role of visceral fat in the development of CVD should be taken into account[54]. The expansion of adipose tissue would induce the occurrence of adipokine secretion and function dysregulation, which play a fundamental role in development of inflammatory disorders, cardiometabolic disorders and vascular disorders, ultimately leading to a variety of cardiovascular events[55]. In addition, studies have found that pericardial fat and visceral adipose tissue were associated with CVD after age and sex adjustment for quantitative volume of adipose tissue by chest multidetector computed tomography[56].

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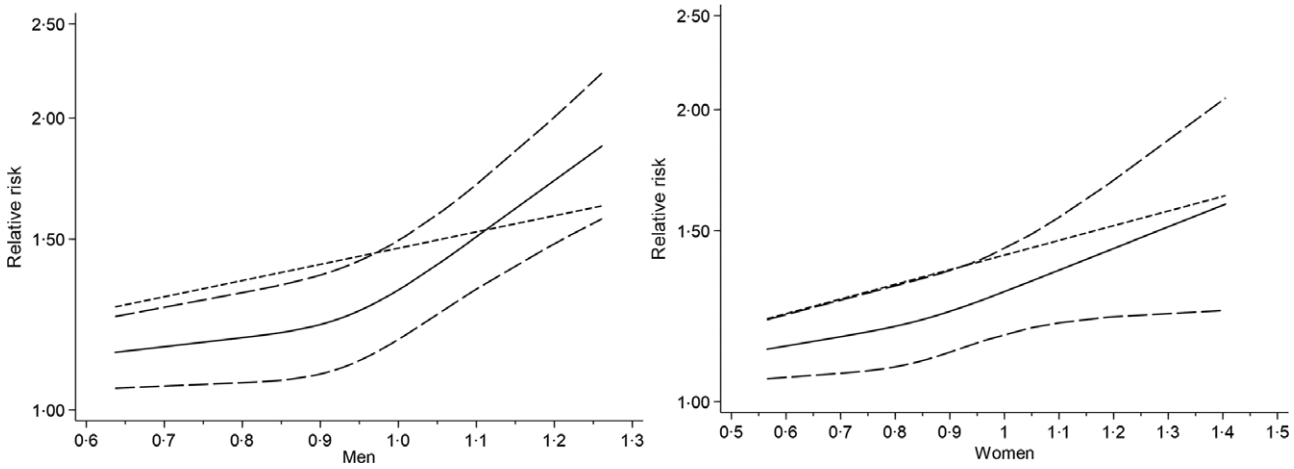

Fig. 5. Dose–response analysis between waist:hip ratio and risk of CVD men (left) and women (right). Solid line: non-linear dose response. Dotted line: 95 % CI. Straight dotted line: linear dose–response.

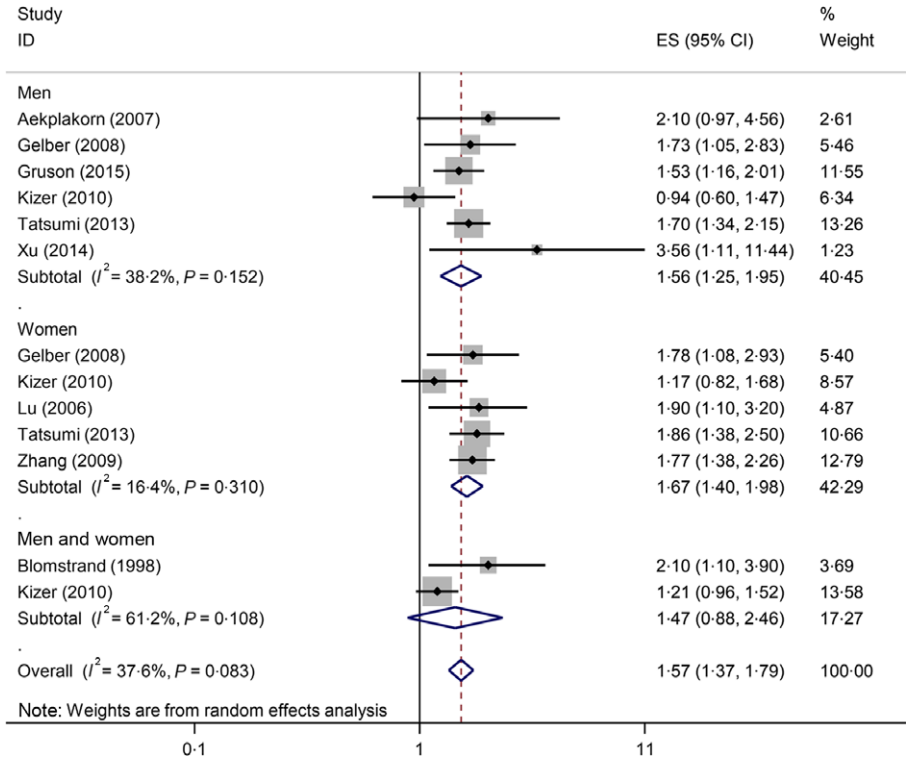

Fig. 6. Forest plot of association between waist:height ratio and risk of CVD. ES, effect size.

In addition, many researchers take WHtR as a preferable indicator in the prediction of CVD. The study of Castanheira *et al.*, a longitudinal study of Brazilian[49], revealed that WHtR was better than other adiposity for predicting CVD with good discriminatory power in Brazilian adults. Ashwell's meta-analysis also supported this conclusion, which was conducted in 123 231 men and 182 620 women with hypertension, type 2 diabetes, dyslipidaemia, the metabolic syndrome and general CVD[9]. Our study included a larger sample size of healthy adults which confirmed this conclusion to some extent.

In conclusion, our research showed that, as good indicators of abdominal obesity, WC, WHR and WHtR were significantly associated with the incidence of CVD. WHtR may be better than WC and WHR, and 0·5 could be an appropriate boundary value for the prediction of CVD.

This study has several strengths, we systematically assessed the linear and non-linear dose–response relation between WC, WHR, WHtR and the risk of CVD, and then we found all of these three indicators were closely related to the risk of CVD. A total of approximately 670 000 participants and 25 000 cases were included in our study, which could help minimise potential bias

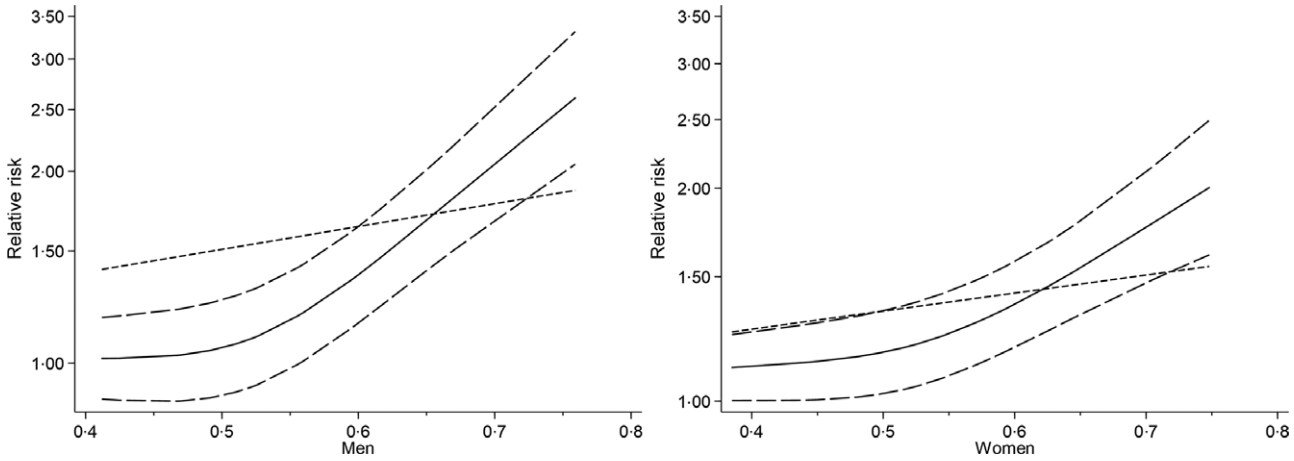

Fig. 7. Dose–response analysis between waist:height ratio and risk of CVD among men (left) and women (right). Solid line: non-linear dose response. Dotted line: 95 % CI. Straight dotted line: linear dose–response.

Table 1. Subgroup analyses of waist circumference (WC) and risk of CVD in men and women (Risk ratios (RR) and 95 % confidence intervals)

	Men					Women				
	n	RR	95 % CI	I^2 (%)	*P*	*n*	RR	95 % CI	I^2 (%)	*P*
All studies	17	1·42	1·25, 1·61	55·3	<0·001	15	1·46	1·24, 1·71	61·4	<0·001
Outcome										
CVD	4	1·64	1·26, 2·15	38·5	<0·001	4	1·92	1·24, 2·96	63·8	<0·05
CHD	4	1·27	0·97, 1·66	63·3	0·08	3	1·80	1·40, 2·32	0	<0·001
Stroke	6	1·36	1·06, 1·76	45·5	<0·05	7	1·21	0·97, 1·51	46·5	0·096
MI	2	1·22	0·98, 1·52	0	0·07	2	1·03	0·77, 1·38	0	0·854
VTE	2	2·06	1·59, 2·66	0	<0·001	2	2·07	1·46, 2·95	4·8	<0·001
Age (years)										
<60	10	1·45	1·26, 1·66	29·8	<0·001	10	1·42	1·13, 1·78	62·1	<0·05
≥60	5	1·32	0·98, 1·78	74·2	0·068	4	1·35	1·01, 1·78	62·5	<0·05
Geographic region										
Europe	10	1·44	1·23, 1·69	64·4	<0·001	9	1·38	1·13, 1·69	53·3	<0·05
USA	4	1·48	1·02, 2·14	62·5	<0·05	4	1·29	0·88, 1·88	65·0	0·192
Asia	2	1·28	0·99, 1·66	0	0·055	2	1·57	1·30, 1·90	0	<0·001
Australia	1	1·80	1·11, 2·92	–	–	1	3·10	1·91, 5·03	–	–
Follow-up duration										
<10 years	2	0·95	0·73, 1·24	0	0·725	2	1·64	1·25, 1·72	28·1	<0·05
≥10 years	15	1·49	1·33, 1·68	42·2	<0·001	14	1·44	1·20, 1·72	61·1	<0·001
Study quality										
0–3 stars	–	–		–	–	–	–		–	–
3–6 stars	3	1·56	1·23, 1·98	0	<0·001	2	1·17	0·82, 1·67	0	0·379
7–9 stars	14	1·41	1·23, 1·61	55·9	<0·001	14	1·50	1·27, 1·79	62·0	<0·001
Number of participants										
<5000	5	1·32	0·95, 1·84	58	0·096	2	1·84	0·66, 5·18	87·8	0·247
≥5000	12	1·46	1·28, 1·66	50·7	<0·001	14	1·42	1·22, 1·65	51·3	<0·001

MI, myocardial infarction; VTE, venous thromboembolism.

preferably. To eliminate the interference of sex, we conducted subgroup analyses of each sex based on the study and participant characteristics.

There are still some limitations in this study. Although the estimates in our analyses were derived from maximally adjusted models to reduce potential confounding factors, the adjusted factors for each study are not identical and some confounders still exist. This is a possible source of heterogeneity. Some of studies included in our analysis collected information via self-reporting questionnaires, which might produce errors in the measurement of WC, WHR and WHtR. The publication bias was found in the analysis of relationship between WHR and CVD risk, while the result was still statistically significant when 'trim-and-fill' was applied to correct the bias. Therefore, the results were basically reliable. Furthermore, most available studies have focused on the degree of adiposity as important risk factors in the development of CVD, but the effect of the duration of obesity was ignored. The consequences of exposure to higher levels and longer duration of obesity should be taken into account in future studies.

Table 2. Subgroup analyses of waist:hip ratio (WHR) and risk of CVD in men and women (Risk ratios (RR) and 95 % confidence intervals)

	Men					Women				
	n	RR	95 % CI	I^2 (%)	*P*	*n*	RR	95 % CI	I^2 (%)	*P*
All studies	16	1·43	1·31, 1·57	17·0	<0·001	13	1·48	1·29, 1·70	49·9	<0·001
Outcome					<0·001					
CVD	4	1·34	1·19, 1·50	1·1	<0·001	3	1·62	1·18, 2·22	64·6	<0·05
CHD	7	1·50	1·26, 1·78	35·5	<0·001	4	1·89	1·51, 2·36	0	<0·001
Stroke	5	1·50	1·20, 1·87	18·4	<0·001	6	1·26	1·05, 1·52	41·1	<0·001
MI		–		–		–	–		–	–
VTE		–		–		–	–		–	–
Age (years)										
<60	10	1·54	1·35, 1·75	5·8	<0·001	9	1·43	1·18, 1·72	53·4	<0·001
≥60	5	1·29	1·16, 1·44	0	<0·001	3	1·56	1·21, 2·01	59·9	<0·001
Geographic region										
Europe	7	1·44	1·24, 1·68	39·6	<0·001	7	1·40	1·19, 1·66	50·6	<0·001
USA	7	1·45	1·22, 1·73	18·7	<0·001	5	1·69	1·27, 2·24	53·7	<0·001
Asia	–	–		–	–	1	1·34	1·15, 1·57	–	–
Australia	2	1·45	1·20, 1·75	0·2	<0·001	–	–		–	–
Follow-up duration										
<10 years	6	1·38	1·20, 1·58	27·7	<0·001	4	1·44	1·19, 1·73	46·2	<0·001
≥10 years	10	1·50	1·31, 1·72	12·6	<0·001	9	1·48	1·21, 1·81	54·2	<0·001
Study quality										
0–3 stars	–	–		–	–	–	–		–	–
3–6 stars	3	1·77	1·29, 2·45	27·2	<0·001	2	1·44	0·76, 2·72	69·6	0·259
7–9 stars	13	1·39	1·27, 1·52	10·5	<0·001	11	1·49	1·29, 1·72	51·1	<0·001
Number of participants										
<5000	5	1·55	1·19, 2·04	45·6	<0·001	2	1·80	1·33, 2·45	49·9	<0·001
≥5000	11	1·40	1·27, 1·55	9·4	<0·001	11	1·44	1·24, 1·67	52·5	<0·001

MI, myocardial infarction; VTE, venous thromboembolism.

Table 3. Subgroup analyses of waist:height ratio (WHtR) and risk of CVD in men and women (Risk ratios (RR) and 95 % confidence intervals)

	Men					Women				
	n	RR	95 % CI	I^2 (%)	*P*	*n*	RR	95 % CI	I^2 (%)	*P*
All studies	6	1·56	1·25, 1·95	38·2	<0·001	5	1·67	1·40, 1·98	16·4	<0·05
Outcome										
CVD	2	1·65	1·23, 2·21	0	<0·05	2	1·79	1·28, 2·50	0	<0·001
CHD	3	1·59	1·24, 2·03	0	<0·001	1	1·51	0·77, 2·96	–	–
Stroke	3	1·59	0·85, 3·00	72·7	<0·05	3	1·66	1·29, 2·13	42·1	<0·001
MI	–	–		–	–	–	–		–	–
VTE	–	–		–	–	–	–		–	–
Age (years)										
<60	3	1·73	1·23, 2·43	14·3	<0·05	2	1·79	1·43, 2·24	0	<0·001
≥60	3	1·33	0·95, 1·87	45·4	0·444	3	1·53	1·12, 2·09	39·7	<0·05
Geographic region										
Europe	1	1·53	1·16, 2·01	–	–	1	1·90	1·11, 3·24	–	–
USA	2	1·26	0·69, 2·30	68·8	0·444	2	1·39	0·93, 2·08	44·2	0·111
Asia	3	1·78	1·42, 2·22	0	<0·001	2	1·81	1·49, 2·18	0	<0·001
Australia	–	–		–	–	–	–		–	–
Follow-up duration										
<10 years	1	3·56	1·11, 11·43	–	–	1	1·77	1·38, 2·27	–	–
≥10 years	5	1·52	1·23, 1·88	35·1	<0·001	4	1·62	1·27, 2·07	32·9	<0·001
Study quality										
0–3 stars	–	–		–	–					
3–6 stars	1	3·56	1·11, 11·43	–	–	–	–		–	–
7–9 stars	5	1·52	1·23, 1·88	35·1	<0·05	5	1·67	1·40, 1·98	16·4	<0·05
Number of participants										
<5000	3	1·68	0·77, 3·67	68·5	0·19	1	1·17	0·82, 1·67	–	–
≥5000	3	1·64	1·38, 1·94	0	<0·001	4	1·81	1·53, 2·14	0	<0·001

MI, myocardial infarction; VTE, venous thromboembolism.

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Conclusion

According to the analysis of existing evidence, we found that the risk of CVD is related to abdominal obesity. The risk of CVD rose continually with the increase of WC, WHR and WHtR when they exceeded a certain range. Keep your WC to less than half your height could help reduce the risk of CVD. As sample and useful indicators of abdominal obesity, WC, WHR and WHtR, especially WHtR, are worth to popularise in future study and clinical application to help prevent CVD.

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R. X. designed the study, concept and performed the data analysis. R. X., Q. L. and Y. G. were involved in the data collection and analysis. R. X. wrote the first draft of the manuscript. All authors critically revised the manuscript and gave final approval and agreed to be accountable for all aspects of the work to ensure the integrity and accuracy. All the work was done under S. Z.'s direction.

The authors do not have any conflicts of interest to declare.

Supplementary material

For supplementary material referred to in this article, please visit https://doi.org/10.1017/S0007114521000064

References

1. Roth GA, Abate D, Abate KH, *et al.* (2018) Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* **392**, 1736–1788.
2. Ortega FB, Lavie CJ & Blair SN (2016) Obesity and cardiovascular disease. *Circ Res* **118**, 1752–1770.
3. Afshin A, Forouzanfar MH, Reitsma MB, *et al.* (2017) Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med* **377**, 13–27.
4. Romero-Corral A, Montori VM, Somers VK, *et al.* (2006) Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. *Lancet* **368**, 666–678.
5. Lavie CJ, Milani RV & Ventura HO (2009) Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol* **53**, 1925–1932.
6. Coutinho T, Goel K, Correa de Sa D, *et al.* (2011) Central obesity and survival in subjects with coronary artery disease: a systematic review of the literature and collaborative analysis with individual subject data. *J Am Coll Cardiol* **57**, 1877–1886.
7. Balkau B, Deanfield JE, Despres JP, *et al.* (2007) International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. *Circulation* **116**, 1942–1951.
8. Radholm K, Chalmers J, Ohkuma T, *et al.* (2018) Use of the waist-to-height ratio to predict cardiovascular risk in patients with diabetes: results from the ADVANCE-ON study. *Diabetes Obes Metab* **20**, 1903–1910.
9. Ashwell M, Gunn P & Gibson S (2012) Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev* **13**, 275–286.
10. Lee CM, Huxley RR, Wildman RP, *et al.* (2008) Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol* **61**, 646–653.
11. Savva SC, Lamnisos D & Kafatos AG (2013) Predicting cardiometabolic risk: waist-to-height ratio or BMI. A meta-analysis. *Diabetes Metab Syndr Obes* **6**, 403–419.
12. Phillips SG (1975) The community physician and atmospheric pollution. *J Soc Occup Med* **25**, 139–141.
13. Hamling J, Lee P, Weitkunat R, *et al.* (2008) Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. *Stat Med* **27**, 954–970.
14. Duval S & Tweedie R (2000) Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics* **56**, 455–463.
15. Gelber RP, Gaziano JM, Orav EJ, *et al.* (2008) Measures of obesity and cardiovascular risk among men and women. *J Am Coll Cardiol* **52**, 605–615.
16. Rexrode KM, Carey VJ, Hennekens CH, *et al.* (1998) Abdominal adiposity and coronary heart disease in women. *JAMA* **280**, 1843–1848.
17. Lu M, Ye W, Adami HO, *et al.* (2006) Prospective study of body size and risk for stroke amongst women below age 60. *J Intern Med* **260**, 442–450.
18. Yang L, Kuper H & Weiderpass E (2008) Anthropometric characteristics as predictors of coronary heart disease in women. *J Intern Med* **264**, 39–49.
19. Zhang X, Shu XO, Gao YT, *et al.* (2009) General and abdominal adiposity and risk of stroke in Chinese women. *Stroke* **40**, 1098–1104.
20. Rimm EB, Stampfer MJ, Giovannucci E, *et al.* (1995) Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *Am J Epidemiol* **141**, 1117–1127.
21. Walker SP, Rimm EB, Ascherio A, *et al.* (1996) Body size and fat distribution as predictors of stroke among US men. *Am J Epidemiol* **144**, 1143–1150.
22. Rexrode KM, Buring JE & Manson JE (2001) Abdominal and total adiposity and risk of coronary heart disease in men. *Int J Obes Relat Metab Disord* **25**, 1047–1056.
23. Lakka HM, Lakka TA, Tuomilehto J, *et al.* (2002) Abdominal obesity is associated with increased risk of acute coronary events in men. *Eur Heart J* **23**, 706–713.
24. Aekplakorn W, Pakpeankitwatana V, Lee CM, *et al.* (2007) Abdominal obesity and coronary heart disease in Thai men. *Obesity (Silver Spring)* **15**, 1036–1042.
25. Gruson E, Montaye M, Kee F, *et al.* (2010) Anthropometric assessment of abdominal obesity and coronary heart disease risk in men: the PRIME study. *Heart* **96**, 136–140.
26. Beer C, Alfonso H, Flicker L, *et al.* (2011) Traditional risk factors for incident cardiovascular events have limited importance in later life compared with the health in men study cardiovascular risk score. *Stroke* **42**, 952–959.
27. Wannamethee SG, Shaper AG, Whincup PH, *et al.* (2013) Adiposity, adipokines, and risk of incident stroke in older men. *Stroke* **44**, 3–8.

28. Xu J, Xu T, Bu X, *et al.* (2014) The predictive value of waist-to-height ratio for ischemic stroke in a population-based prospective cohort study among Mongolian men in China. *PLOS ONE* **9**, e110245.
29. Myint PK, Kwok CS, Luben RN, *et al.* (2014) Body fat percentage, body mass index and waist-to-hip ratio as predictors of mortality and cardiovascular disease. *Heart* **100**, 1613–1619.
30. Abete I, Arriola L, Etxezarreta N, *et al.* (2015) Association between different obesity measures and the risk of stroke in the EPIC Spanish cohort. *Eur J Nutr* **54**, 365–375.
31. Kizer JR, Biggs ML, Ix JH, *et al.* (2011) Measures of adiposity and future risk of ischemic stroke and coronary heart disease in older men and women. *Am J Epidemiol* **173**, 10–25.
32. Hotchkiss JW, Davies CA & Leyland AH (2013) Adiposity has differing associations with incident coronary heart disease and mortality in the Scottish population: cross-sectional surveys with follow-up. *Int J Obes (Lond)* **37**, 732–739.
33. Folsom AR, Stevens J, Schreiner PJ, *et al.* (1998) Body mass index, waist/hip ratio, and coronary heart disease incidence in African Americans and whites. Atherosclerosis Risk in Communities Study Investigators. *Am J Epidemiol* **148**, 1187–1194.
34. Yatsuya H, Folsom AR, Yamagishi K, *et al.* (2010) Race- and sex-specific associations of obesity measures with ischemic stroke incidence in the Atherosclerosis Risk in Communities (ARIC) study. *Stroke* **41**, 417–425.
35. Van Dis I, Kromhout D, Geleijnse JM, *et al.* (2009) Body mass index and waist circumference predict both 10-year nonfatal and fatal cardiovascular disease risk: study conducted in 20,000 Dutch men and women aged 20–65 years. *Eur J Cardiovasc Prev Rehabil* **16**, 729–734.
36. Furukawa Y, Kokubo Y, Okamura T, *et al.* (2010) The relationship between waist circumference and the risk of stroke and myocardial infarction in a Japanese urban cohort: the Suita study. *Stroke* **41**, 550–553.
37. Tatsumi Y, Watanabe M, Kokubo Y, *et al.* (2013) Effect of age on the association between waist-to-height ratio and incidence of cardiovascular disease: the Suita study. *J Epidemiol* **23**, 351–359.
38. Hu G, Tuomilehto J, Silventoinen K, *et al.* (2007) Body mass index, waist circumference, and waist-hip ratio on the risk of total and type-specific stroke. *Arch Intern Med* **167**, 1420–1427.
39. Horvei LD, Braekkan SK, Mathiesen EB, *et al.* (2014) Obesity measures and risk of venous thromboembolism and myocardial infarction. *Eur J Epidemiol* **29**, 821–830.
40. Severinsen MT, Kristensen SR, Johnsen SP, *et al.* (2009) Anthropometry, body fat, and venous thromboembolism: a Danish follow-up study. *Circulation* **120**, 1850–1857.
41. Sehested TS, Hansen TW, Olsen MH, *et al.* (2010) Measures of overweight and obesity and risk of cardiovascular disease: a population-based study. *Eur J Cardiovasc Prev Rehabil* **17**, 486–490.
42. Wang Z & Hoy WE (2004) Waist circumference, body mass index, hip circumference and waist-to-hip ratio as predictors of cardiovascular disease in Aboriginal people. *Eur J Clin Nutr* **58**, 888–893.
43. Adegbija O, Hoy W & Wang Z (2015) Prediction of cardiovascular disease risk using waist circumference among Aboriginals in a remote Australian community. *BMC Public Health* **15**, 57.
44. Larsson SC, Wolk A, Hakansson N, *et al.* (2017) Overall and abdominal obesity and incident aortic valve stenosis: two prospective cohort studies. *Eur Heart J* **38**, 2192–2197.
45. Yusuf S, Hawken S, Ounpuu S, *et al.* (2005) Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case–control study. *Lancet* **366**, 1640–1649.
46. Canoy D, Boekholdt SM, Wareham N, *et al.* (2007) Body fat distribution and risk of coronary heart disease in men and women in the European Prospective Investigation Into Cancer and Nutrition in Norfolk cohort: a population-based prospective study. *Circulation* **116**, 2933–2943.
47. Jayedi A, Soltani S, Zargar MS, *et al.* (2020) Central fatness and risk of all cause mortality: systematic review and dose-response meta-analysis of 72 prospective cohort studies. *BMJ* **370**, m3324.
48. Browning LM, Hsieh SD & Ashwell M (2010) A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev* **23**, 247–269.
49. Castanheira M, Chor D, Braga JU, *et al.* (2018) Predicting cardiometabolic disturbances from waist-to-height ratio: findings from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) baseline. *Public Health Nutr* **21**, 1028–1035.
50. Gibson S & Ashwell M (2020) A simple cut-off for waist-to-height ratio (0.5) can act as an indicator for cardiometabolic risk: recent data from adults in the Health Survey for England. *Br J Nutr* **123**, 681–690.
51. Garnett SP, Baur LA & Cowell CT (2008) Waist-to-height ratio: a simple option for determining excess central adiposity in young people. *Int J Obes (Lond)* **32**, 1028–1030.
52. Ashwell M & Gibson S (2014) A proposal for a primary screening tool: 'Keep your waist circumference to less than half your height'. *BMC Med* **12**, 207.
53. Smith U (2015) Abdominal obesity: a marker of ectopic fat accumulation. *J Clin Invest* **125**, 1790–1792.
54. Shimabukuro M (2009) Cardiac adiposity and global cardiometabolic risk: new concept and clinical implication. *Circ J* **73**, 27–34.
55. Harwood HJ Jr. (2012) The adipocyte as an endocrine organ in the regulation of metabolic homeostasis. *Neuropharmacology* **63**, 57–75.
56. Mahabadi AA, Massaro JM, Rosito GA, *et al.* (2009) Association of pericardial fat, intrathoracic fat, and visceral abdominal fat with cardiovascular disease burden: the Framingham Heart Study. *Eur Heart J* **30**, 850–856.

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