Systematic Review and Meta-Analysis

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Associations of anthropometric adiposity indexes with hypertension risk

A systematic review and meta-analysis including PURE-China

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Abstract

Background and objective: The association between hypertension and obesity has been confirmed, while no agreement has been reached about which anthropometric adiposity index is the best. This meta-analysis aimed to perform a systematic review and meta-analysis on the associations of hypertension risk with body mass index (BMI), waist circumstance (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR), and a prospective urban and rural epidemiology study from China (PURE-China) was added into this meta-analysis as an individual study.

Methods: Systematic literature searching was conducted to identify relevant articles published up to September 2018 in CNKI, WANFANG Data, Web of Science, SinoMed, PubMed, MEDLINE, EMBASE, Cochrane Library and cross-referencing. Literature reporting the association of hypertension risk with BMI, WC, WHR, and WHtR were defined as eligible. PURE-China data were analyzed and included as 1 eligible study into meta-analyses. Summary odds ratio (OR) and area under receiver operating characteristic curve (AUC) were pooled using meta-analysis methods. Heterogeneity and publication bias were evaluated. Subgroups based on gender, country and study design were conducted as well.

Results: Thirty-eight original articles including PURE-China were included into meta-analyses, involving 309,585 subjects. WHtR had the strongest association with hypertension risk (OR, 1.68; 95% confidence interval, [CI]:1.29–2.19) and prediction ability (AUC, 70.9%; 95% CI: 67.8%–74.2%), which were also confirmed in subgroup analyses based on gender and country. However, BMI was found to have the highest prediction ability in adjusted models of PURE-China and followed WC, both of which were superior to WHtR (73.7% and 73.4% vs 73.2%).

Conclusions: Our overall meta-analysis further confirmed WHtR as a good indicator at discriminating those individuals at increased risk of hypertension, and in some cases, it is better than BMI, WC, and WHR.

Abbreviations: AAI = anthropometric adiposity indexes, AUC = area under receiver operating characteristic curve, BMI = body mass index, CI = confidence interval, OR = odds ratio, PURE= prospective urban and rural epidemiology study, WC = waist circumstance, WHR = waist-to-hip ratio, WHtR = waist-to-height ratio.

Keywords: body mass index, hypertension, meta-analysis, systematic review, waist circumstance, waist-to-height ratio, waist-to-hip ratio

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1. Introduction

Hypertension is not only a common disease itself, but also one of the main causes for risk of cerebrovascular and cardiovascular diseases, such as stroke, metabolic syndromes, and coronary artery diseases.[1–5] According to World Health Organization (WHO) Report in 2013, 1 billion individuals suffered from hypertension worldwide, and 9 million are deceased due to raised blood pressure annually.[6] Moderate numbers of studies provided strong evidence that hypertension contributes markedly to the global burden of diseases.[7–11] Although hypertension diagnosis seemed easier and cheaper than other cardiovascular diseases, no syndromes are reported by a number of people with high blood pressure. Additionally, some population is not engaged in annual physical examinations due to busy working, unlike to hospital, and self-feeling healthy and others. Therefore, the awareness, treatment, and control of hypertension are very low in some countries.[12–20]

Thus, applying some simple anthropometric adiposity indexes (AAI) in evaluating and predicting the risk groups of hypertension is valuable. Since obesity has a strong association with hypertension,[21–24] 4 AAI are common to be used as risk evaluation indexes in many epidemiological studies,[25–34] including body mass index (BMI), waist circumstance (WC), waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR), all of which can be self-measured. Two meta-analytic reviews were published in 2008 and provided more supports for centralized obesity, especially WHtR, while BMI was the poorest discriminator for detecting cardiovascular risk factors in both male and female.[35,36] Additionally, a robust association was observed among Asians compared to non-Asian populations.[36]

However, Lee et al[35] only searched MEDLINE database up to 2006, and another study[36] used the original data of 19 cross-sectional studies from 10 countries in the Asia-Pacific regions. A number of individual studies were reported in the last decade.[37–44] Thus, we conducted an updated systematic review and meta-analysis and summarize literature evidence of association of hypertension risk with BMI, WC, WHR, and WHtR, as well as further evaluate sex-based and country-based difference for these associations. Our data in a prospective urban and rural epidemiology study in China (PURE-China) was added into meta-analyses as an individual study.

2. Methods

2.1. Searching strategies

All procedures of this study followed the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[45] A systematic searching was conducted to identify the related articles in the following literature databases up to September 2018, including Cochrane Library (CENTRAL), PubMed, MEDLINE, EMBASE, Web of Science, WANFANG Data, China National Knowledge Infrastructure (CNKI), and SinoMed, and using the combinations of the following terms: (“body mass index” or “BMI”) and (“waist” or “waist circumference” or “WC”) and (“waist to hip ratio” or “waist-hip ratio” or “WHR” or “WHPR” or “waist; hip ratio”) and (“waist to height ratio” or “waist-height ratio” or “waist: height ratio” or “waist to stature ratio” or “waist-stature ratio” or “WHtR” or “WHTR” or “WSR” or “WHeiR”) and (“blood pressure” or “hypertension”). Corresponding Chinese terms with above-mentioned terms were used for searching in Chinese literature databases, such as CNKI, WANFANG Data, and SinoMed. All the bibliographical references found in target literature databases were imported into Endnote X8 for verifying eligibility checking. Each title and/or abstract was screened to evaluate its possible relevance after excluding duplicates. Full-text articles were downloaded for further review and eligibility determination if both titles and abstracts were not enough to make decision. All article-selecting were completed by 2 researchers (Deng GJ and Liu WD) independently, the senior researcher (Yin L) made final decision when any discrepancies were shown. Personal email contacts with authors were used to obtain data when needed data were not explicitly reported or not derived from data in the articles. Cross-referencing was also conducted to improve the study identification process.

2.2. Inclusive criteria

The inclusive criteria of article selection were described as follows:

(1) only original articles were considered, and editorials, comments or reviews were excluded;
(2) hypertension risk was evaluated in epidemiological studies;
(3) only adults were included (age≥18-year-old), but studies with older adults (age≥60-year-old) were excluded;
(4) odds ratio (OR) for the associations of hypertension risk with BMI, WC, WHR, and WHtR, and/or area under receiver operating characteristic curve (AUC) for prediction abilities of hypertension risk had to be reported in 1 study. Studies with lack of any one of the indexes above-mentioned were excluded.

2.3. Data extraction

If articles were regarded as eligible, at least 2 co-authors extracted the following data independently in a standardized manner and any disagreement was discussed and resolved in our research group, including author’s name, publication year, country of study, study duration, study design, recruited participants (age, number, gender, BMI, WC, WHR, and WHtR), OR, and AUC with their 95% respective confidence interval (CI) for hypertension risk related to BMI, WC, WHR, and WHtR.

2.4. Literature quality assessment

The assessment for the quality and potential bias of the included articles were executed by 2 researchers independently using forms from Agency for Healthcare Research and Quality (AHRQ),[46] which consists of 11 items scored 0 or 1. One score was counted if any item was answered “Yes”, while the score was 0 when any item was answered “No” or “Unclear”. The total score was calculated by adding all the scores of 11 items, and the quality level was determined as low if the total score≤3, medium if the score ranged from 4 to 7, and high if total score≥8.

2.5. General information of PURE-China

Details of PURE-China have been reported elsewhere.[47,48] Based on 46,285 recruited participants, 1871 were excluded due to missing values of blood pressure, weight, height, WC, and hip circumference (HC) and 156 excluded due to implausible values for systolic blood pressure (SBP) (<70 or >260 mmHg), diastolic blood pressure (DBP) (<40 or >140 mmHg), weight (<30 or >130 kg), WC (>130 cm), and HC (<50 cm). Finally, 44,258 eligible subjects (18,174 male and 26,084 female) were included for the analyses.

Guided by 2010 Chinese guidelines of hypertension management,[49] hypertension is defined if 1 of the following 3 criteria is fulfilled:

(1) taking antihypertensive drugs regularly;
(2) history of hypertension diagnosis;
(3) SBP≥140 mmHg and/or DBP≥90 mmHg. BMI was calculated as weight (kg) divided by height square (m^2), WHR computed using WC (cm) divided by HC (cm), and WHtR using WC (cm) divided by height (cm).

2.6. Statistical analyses

Stata 12.0 was used for the meta-analyses. OR and AUC with their respective 95% CI for hypertension risk with 4 AAI (BMI, WC, WHR, WHtR) was defined as effect sizes. Heterogeneity was present if P value of Q test was typically ≤0.10. I^2 statistic was used to evaluate the heterogeneity across all included studies. If studies were homogeneity, the pooled OR and pooled AUC were calculated by using a random effects model with DerSimonian and Laird method. If not, the fixed effect models on the Mantel-Haenszel method were applied.[50–52] $P<.05$ with 2-sided will be considered as statistical significance regarding the pooled results of all outcomes. Subgroup analyses based on gender were performed to compare potential variations among females and males. The potential publication bias was examined by constructing a "funnel plot", and the Egger linear regression test was applied to test for asymmetry of funnel plots at 0.05 level for significance.[53] In order to test for the robustness of the results, sensitivity analyses were conducted by deleting 1 study each time, which was considered as having little influence on the overall effect size if the point estimate of its "deleted" analysis always lay inside the 95% CI of the pooled statistic. Meta-regressions were used to examine the impact of moderator variables (including gender and country) on study effect sizes using regression-based techniques.[54]

The Statistical Analysis System (SAS 9.4 for Windows; SAS Institute Inc., Cary, NC) software was used for the statistical analyses of PURE-China. Only baseline data were used for analyses. Continuous variables were shown as the mean± standard deviation (SD), and categorical variables as numbers (n) and percentages (%). The OR with 95% CI and AUC with 95% CI for hypertension risk in relation to BMI, WC, WHR, WHtR were computed using multivariate logistic regressions adjusted for age, sex (not for subgroup analyses by gender), education levels, alcohol use, smoking status, living location, levels of physical activities, as well as taking anti-diabetics drugs and lipid-lowering drugs. Subgroup analyses stratified by gender country and study design also were conducted.

3. Results

3.1. Systematic searching and article selection

The details of search strategy and included procedure were shown in Figure 1. Total of 1417 records was obtained from 8 above-mentioned literature databases and cross-referencing. PURE-China data were analyzed as an individual study. 505 duplicates were excluded. 912 titles and abstracts were screened for potential eligibility, among which 575 were deleted as irrelevant records with our topic, 14 were deleted as they were conference abstracts, and 9 were deleted as they were reviews. Furthermore, full-text reviewing of 314 records was performed, of which 216 were further excluded due to the following reasons: no hypertension risk reported (n=172), adolescent studies (n=60), at least 1 index not reported (n=41), only older adults included (n=2), only those with BMI <25 included (n=1). Finally, a total of 309,585 individuals from 38 articles were included in this meta-analysis, including our PURE-China data.

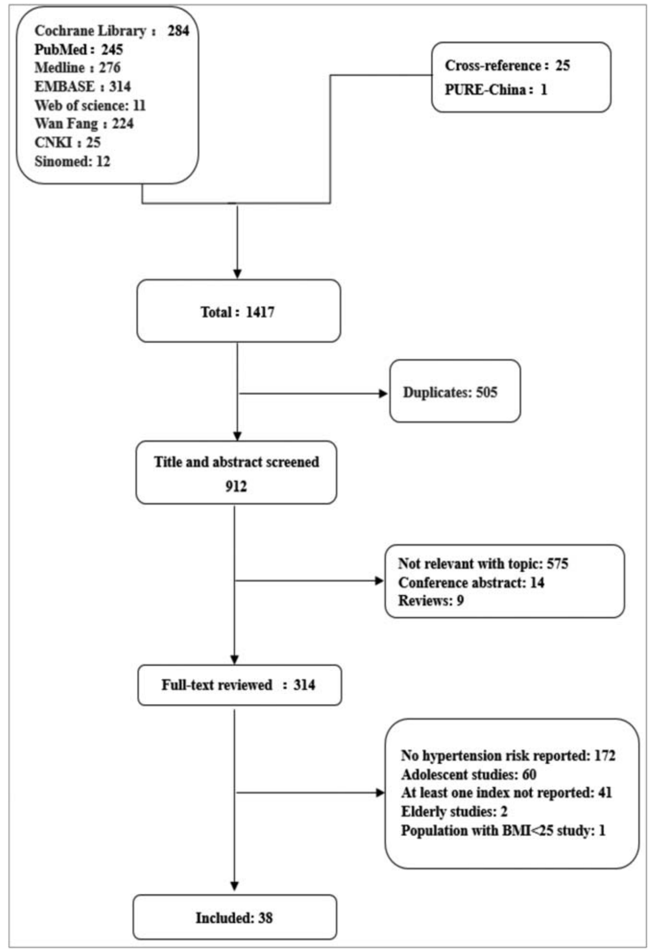

Figure 1. Flow diagram of the literature search process in meta-analysis. BMI=body mass index, PURE=prospective urban and rural epidemiology study.

The details of included studies were shown in Table 1. The included studies were published from 2002 to 2018, with sample size ranging from 180[54] to 55,563.[55] Only 6 studies had subjects less than 1000,[40,42,54,56–58] and there were 6 studies with more than 10 thousand subjects,[37,55,59–61] including PURE-China. According to AHRQ,[46] the overall quality of the included studies was good with the average score 9.1, ranged from 7 to 10. 15 studies were scored at 10,[39,41–43,62–71] including PURE-China, 13 studies at 9,[40,44,56,58–61,72–77] 9 studies at 8,[37,38,55,57,78–82] and 1 study at 7.[54]

3.2. Results of PURE-China

Baseline characteristics of eligible participants in PURE-China were shown in Table 2. Total of 44,258 Chinese including 18,174 males and 26,084 females were included in this study, among which 19,100 (43.2%) were identified as patients suffering from hypertension. Mean age was similar among females and males (51.0 vs 51.6 years), but those with hypertension were much older than those without hypertension (54.6 vs 48.7 years).

Table 1

Characteristic of eligible studies in meta-analysis.

Author[ref.], year	Countries (baseline year)	N	Male (%)	Age	BMI	WC	WHR	WHtR	QA
Lin et al[55], 2002	China (1998–2000)	55,563	47.4	37.1±11.0	22.6±3.3	75.1±9.6	0.8±0.1	0.5±0.1	8
Ho et al[72], 2003	China (1995–1996)	2,895	48.8	45.8±13.0	24.1±3.6	79.1±10.3	0.8±0.1	0.5±0.1	9
Tran et al[73], 2004	Vietnam (2004)	1,488	48.2	N/A±NA	N/A±NA	N/A±NA	N/A±NA	N/A±NA	9
Pua et al [56], 2005	Singapore (2003)	566	0.0	38.0±1.6	23.4±1.0	74.3±3.1	0.8±0.0	0.5±0.02	9
Aekplakorn et al[78], 2006	Thailand (2000)	5,305	39.5	42.0±NA	24.0±NA	80.8±NA	0.9±NA	0.5±NA	8
Sakurai et al[79], 2006	Japan (1996)	4,557	64.4	45.4±6.5	23.1±3.0	77.5±8.9	0.8±0.1	0.5±0.1	8
Ghosh et al[54], 2007	India (NA)	180	100.0	35.7±9.4	22.4±3.7	80.7±10.0	0.9±0.1	0.5±0.1	7
Wang et al[80], 2007	Australia (1993–1997)	1186	N/A	43.0±0.6	28.9±0.4	96.6±1.4	0.9±0.1	0.6±0.01	8
Kaur et al[81], 2008	India (2003–2005)	2,148	100.0	40.5±11.1	25.0±3.6	90.0±10.1	0.9±0.1	0.5±0.1	8
Chei et al[74], 2008	Japan (1983–1998)	2,790	32.5	55.3±NA	22.9±NA	81.4±NA	0.5±NA	0.9±NA	9
Zhou et al[59], 2009	China (N/A)	29079	46.6	52.6±0.3	24.4±0.1	82.7±0.5	0.9±0.1	0.5±0.1	9
Can et al[62], 2009	Turkey (2003)	1692	33.7	45.4±13.1	29.6±5.0	95.1±12.3	0.9±0.1	0.6±0.1	10
Tuan et al[64], 2010	China (2004)	7336	48.3	43.9±0.5	23.1±0.3	80.5±10.9	0.9±0.1	0.5±0.1	10
Li et al[63], 2010	Australia (1999–2001)	2609	48.2	37.3±0.6	N/A±NA	95.1±1.4	0.9±0.1	0.6±0.1	10
Rodrigues et al[82], 2010	Brazil (1999–2001)	1,655	45.9	45.0±11.0	26.2±5.0	86.0±12.0	0.9±0.1	0.5±0.1	8
Lv et al[37], 2010	China (2006)	48,753	51.3	47.9±9.9	23.6±3.4	79.0±9.7	0.8±0.1	0.5±0.1	8
Wu et al[65], 2010	China (2008)	5,927	44.7	49.0±15.9	23.8±3.5	80.4±9.9	0.9±0.1	0.5±0.1	10
Tseng et al[75], 2010	China (2001)	4683	48.7	45.5±0.7	23.5±0.3	80.7±1.2	0.8±0.1	0.5±0.01	9
Qiu et al[38], 2011	China (2006)	6,830	43.6	51.1±15.7	25.0±3.5	83.0±9.4	0.9±0.1	0.5±0.1	8
Wang et al[39], 2013	China (2010)	5,817	49.6	42.8±13.6	24.2±3.5	82.4±10.6	0.9±0.1	0.5±0.1	10
Bhowmik et al[66], 2013	Bangladesh (2009–2012)	2,293	36.7	41.8±NA	22.6±NA	80.7±NA	0.9±NA	0.5±NA	10
Saeed et al[67], 2013	Saudi Arabia (2005)	4758	49.2	15~64	N/A±NA	N/A±NA	N/A±NA	N/A±NA	10
Lam et al[76], 2014	Singapore (2012)	1,891	22.0	35.7±12.1	23.2±4.2	77.9±11.2	0.8±0.1	0.5±0.1	9
Wang et al[60], 2015	China (1993–2012)	15,172	45.7	42.1±15.7	22.4±3.2	77.9±9.8	0.8±0.1	0.5±0.1	9
Lee et al[77], 2015	Korean (2001–2005)	4,454	47.8	50.3±8.3	24.2±3.0	81.1±8.4	0.9±0.1	0.5±0.1	9
Dou et al[40], 2015	China (NA)	155	N/A	47.1±NA	N/A±NA	N/A±NA	N/A±NA	N/A±NA	9
Haregu et al[68], 2016	Africa (2008–2009)	5,190	53.8	≥18	23.5±NA	83.2±NA	0.9±NA	0.5±NA	10
Vikram et al[57], 2016	India (NA)	509	54.6	39.4±8.9	24.7±4.4	86.5±12.1	0.9±0.1	0.5±0.1	8
Yu et al[61], 2016	China (2012)	16,766	45.9	47.8±13.2	N/A±NA	82.4±10.5	N/A±NA	N/A±NA	9
Padilha et al[70], 2017	Brazil (2008)	1,553	0.0	20-59	24.8±NA	80.5±NA	0.8±NA	0.5±NA	10
Janghorbani et al[41], 2017	Iran (2003–2005)	1,417	N/A	42.6±NA	N/A±NA	N/A±NA	N/A±NA	N/A±NA	10
Kidy et al[69], 2017	England (2004–2007)	6,268	N/A	56.1±10.7	28.0±5.0	93.0±13.0	0.9±0.1	0.6±0.1	10
Ononamadu et al[42], 2017	Nigeria (2012–2013)	912	47.8	17~79	N/A±NA	N/A±NA	N/A±NA	N/A±NA	10
Chua et al[58], 2017	Malaysia (N/A)	482	46.3	35.4±N/A	23.4±N/A	76.6±N/A	0.8±N/A	0.5±N/A	9
Chu et al[44], 2018	China (2002–2007)	1466	0	20~57	23.2±4.0	76.0±9.3	0.8±0.1	0.5±0.1	9
Choi et al[71], 2018	Korean (2005–2008)	1718	13.5	53.5±0.8	23.9±0.4	82.0±1.2	0.9±0.1	0.5±0.01	10
Castanheira et al[43], 2018	Brazil (2018)	9264	45.7	35~74	27.0±0.4	90.0±0.9	0.9±0.1	0.5±0.1	10
PURE-China	China (2005–2009)	44,258	41.1	51.3±9.4	24.6±3.6	81.1±10.5	0.9±0.1	0.5±0.3	10

N/A=not available, QA=quality assessment.

Additionally, 4 AAI were much higher among hypertension patients than normotensives, including BMI (25.6 vs 23.8 kg/m^2), WC (84.4 vs 78.6 cm), WHR (0.88 vs 0.85), and WHtR (0.53 vs 0.49).

OR and AUC and their respective 95% CI for hypertension risk according to various AAI in unadjusted and adjusted models were shown in Table 3. Significance was found for all associations of hypertension risk with 4 AAI in females, males, and both. The highest OR was observed for WHtR in both sexes (OR, 2.63; 95% CI, 2.54–2.71), women (OR, 2.76; 95% CI, 2.64–2.88), and men (OR, 2.51; 95% CI, 2.38–2.65) in unadjusted models. In adjusted models, the highest ORs were also observed for WHtR in both sexes (OR, 2.31; 95% CI, 2.23–2.40), as well as in women (OR, 2.15; 95% CI, 2.06–2.25) and in men (OR, 2.45; 95% CI, 2.31–2.60). The next was WHR (OR, 1.69; 95% CI, 1.64–1.75), and the 3rd was BMI (OR, 1.17; 95% CI, 1.16–1.18). WC was found to be the poorest one (OR, 1.05; 95% CI, 1.05–1.06).

Regarding prediction abilities of hypertension risk, WHtR was the strongest in unadjusted model (both sexes: AUC, 66.5%; 95% CI: 66.0%–67.1%; females: AUC, 67.9%; 95% CI, 67.3%–68.6%; males: AUC, 64.9%; 95% CI, 64.1%–65.7%). However, BMI showed strongest prediction abilities in adjusted models (AUC, 73.7%; 95% CI, 73.2%, 74.2%) among both sexes, in males (AUC, 71.1%; 95% CI, 70.4%–71.9%) and females (AUC, 75.6%; 95% CI, 75.0%–76.2%).

3.3. Meta-analysis results

3.3.1. Overall ORs of meta-analyses. The summary ORs of 4 AAI for hypertension risk in China, non-China countries and global were shown in Figure 2. Together with PURE-China, 10 articles[40,54,61,67–69,76,80,81] reported ORs for the associations with hypertension risk, 8 articles[38,54,59,66,74,75,81] reported ORs in men, 6 articles[38,59,66,74,75] reported ORs in women. ORs from all countries were combined using meta-analysis methods and found WHtR was the highest OR (OR, 1.68; 95% CI, 1.29–2.19), followed WHR (OR, 1.44; 95% CI, 1.20–1. 72), the 3rd for BMI (OR, 1.38; 95% CI, 1.31–1.45), and the lowest for WC (OR, 1.16; 95% CI, 1.13–1.20), but large heterogeneity was observed across individual studies (all I^2 >95%). Publication bias was found for BMI (Egger test P=.003), WC (Egger test P=.001) and WHtR (Egger test P=.044), but not for WHR (Egger test

Table 2

Characteristics of eligible participants in PURE-China.

	Gender			Blood pressure		
Characteristics*	Male (n=18,174)	Female (n=26,084)	*P* value	Hypertension (-) (n=25,158)	Hypertension (+) (n=19,100)	*P* value
Age, years	51.6±9.6	51.0±9.3	<.001	48.7±9.0	54.6±8.9	<.001
BMI, kg/m^2	24.4±3.4	24.6±3.6	<.001	23.8±3.3	25.6±3.6	<.001
WC, cm	83.8±10.3	79.2±10.2	<.001	78.6±9.9	84.4±10.4	<.001
WHR	0.89±0.07	0.84±0.07	<.001	0.85±0.07	0.88±0.07	<.001
WHtR	0.50±0.06	0.51±0.07	<.001	0.49±0.06	0.53±0.06	<.001
SBP, mmHg	135.0±20.7	132.4±22.8	<.001	119.5±11.3	151.9±19.0	<.001
DBP, mmHg	84.0±12.4	82.0±12.1	<.001	75.8±7.6	92.0±11.1	<.001
PP, mmHg	51.0±13.5	50.5±15.4	<.001	43.7±8.7	59.8±15.8	<.001
Self-reported diabetes	4.2 (765)	4.7 (1222)	.02	2.7 (669)	6.9 (1318)	<.001
Self-reported stroke	2.3 (420)	1.6 (405)	<.001	0.7 (179)	3.4 (646)	<.001
Current smoking	50.0 (9083)	2.8 (742)	<.001	22.5 (5660)	21.8 (4165)	.08
Current drinking	44.3 (8055)	4.6 (1194)	<.001	20.2 (5088)	21.8 (4161)	<.001
Education levels			<.001			<.001
Primary or lower	27.0 (4,912)	38.5 (10,034)		29.9 (7,511)	38.9 (7,435)	
Middle school graduate	61.4 (11,165)	54.5 (14,227)		60.4 (15,200)	53.4 (10,192)	
College or higher	11.2 (2,029)	6.7 (1,753)		9.4 (2,368)	7.4 (1,414)	
Missing value	0.4 (68)	0.3 (70)		0.3 (79)	0.3 (59)	
MET of physical activities, min/week		.31			.05	
<600	12.1 (2,206)	11.7 (3,063)		11.9 (3,006)	11.8 (2,263)	
600–3000	42.1 (7,644)	41.9 (10,920)		42.2 (10,611)	41.6 (7,953)	
>3000	41.3 (7,498)	42 (10,957)		41.2 (10,376)	42.3 (8,079)	
Missing value	4.5 (826)	4.4 (1,144)		4.6 (1,165)	4.2 (805)	

BMI=body mass index, DBP=diastolic blood pressure, MET=Metabolic equivalent task, PP=pulse pressure, equal to SBP minus DBP, SBP=systolic blood pressure, WC=waist circumstance, WHR=waist-to-hip ratio, WHtR=waist-to-height ratio.

* Results are shown as mean±standard deviance for continuous variables or % (n) for categorical variables.

P=.093). Further trim and fill analyses were conducted to obtain filled ORs for BMI (OR, 1.26; 95% CI, 1.19–1.33), WC (OR, 1.11; 95% CI, 1.07–1.15) and WHtR (OR, 1.68; 95% CI, 1.29–2.19), which still reached statistical significance. Sensitivity analyses were conducted to evaluate the stability of overall effect size, and no outliers were detected for overall effect sizes for WHR and WHtR. However, the study by Kaur 2008,[81] Yu 2016[61] and PURE-China were identified as outliers for BMI and WC. After deleting these 2 studies, larger OR were observed for both BMI (OR, 1.74; 95% CI, 1.46–2.06) and WC (OR, 1.61; 95% CI, 1.32–1.97).

Subgroup analyses were performed to evaluate the associations between 4 AAI and hypertension risk in China and non-China countries, as well as females and males, all of which were illustrated in Figure 2. These association strengths seemed similar in China and non-China countries (*P* for meta-regression=.59 for WHtR; .52 for WHR; .75 for WC; .95 for BMI). Additionally, no significant difference was observed for meta-regression based

Table 3

OR and AUC and their 95% CI for hypertension risk per various AAI.

	OR and 95% CI		AUC and 95% CI	
No.	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Total				
BMI	1.16 (1.16, 1.17)	1.17 (1.16, 1.18)	0.647 (0.642, 0.652)	0.737 (0.732, 0.742)
WC	1.06 (1.06, 1.06)	1.05 (1.05, 1.06)	0.660 (0.655, 0.665)	0.734 (0.729, 0.739)
WHR	1.85 (1.80, 1.91)	1.69 (1.64, 1.75)	0.630 (0.624, 0.635)	0.714 (0.710, 0.719)
WHtR	2.63 (2.54, 2.71)	2.31 (2.23, 2.40)	0.665 (0.660, 0.671)	0.732 (0.727, 0.737)
Male				
BMI	1.16 (1.15, 1.17)	1.18 (1.16, 1.19)	0.637 (0.629, 0.645)	0.711 (0.704, 0.719)
WC	1.05 (1.05, 1.06)	1.06 (1.05, 1.06)	0.643 (0.635, 0.651)	0.711 (0.704, 0.719)
WHR	1.78 (1.69, 1.87)	1.76 (1.67, 1.85)	0.612 (0.604, 0.620)	0.689 (0.682, 0.697)
WHtR	2.51 (2.38, 2.65)	2.45 (2.31, 2.60)	0.649 (0.641, 0.657)	0.708 (0.701, 0.716)
Female				
BMI	1.17 (1.16, 1.18)	1.16 (1.16, 1.17)	0.656 (0.649, 0.662)	0.756 (0.750, 0.762)
WC	1.06 (1.06, 1.07)	1.05 (1.05, 1.05)	0.669 (0.662, 0.676)	0.750 (0.744, 0.756)
WHR	2.00 (1.92, 2.08)	1.58 (1.51, 1.64)	0.641 (0.634, 0.648)	0.733 (0.727, 0.739)
WHtR	2.76 (2.64, 2.88)	2.15 (2.06, 2.25)	0.679 (0.673, 0.686)	0.749 (0.743, 0.755)

AAI=anthropometric adiposity indexes, AUC=receiver operating characteristic curve, BMI=body mass index, CI=confidence interval, OR=odds ratio, WC=waist circumstance, WHR=waist-to-hip ratio, WHtR=waist-to-height ratio.

* Adjusted for age, sex (not for female and male subgroup analysis), education, alcohol, smoke, location, physical activities, self-reported use of anti-diabetic drugs, and lipid-lowering drugs.

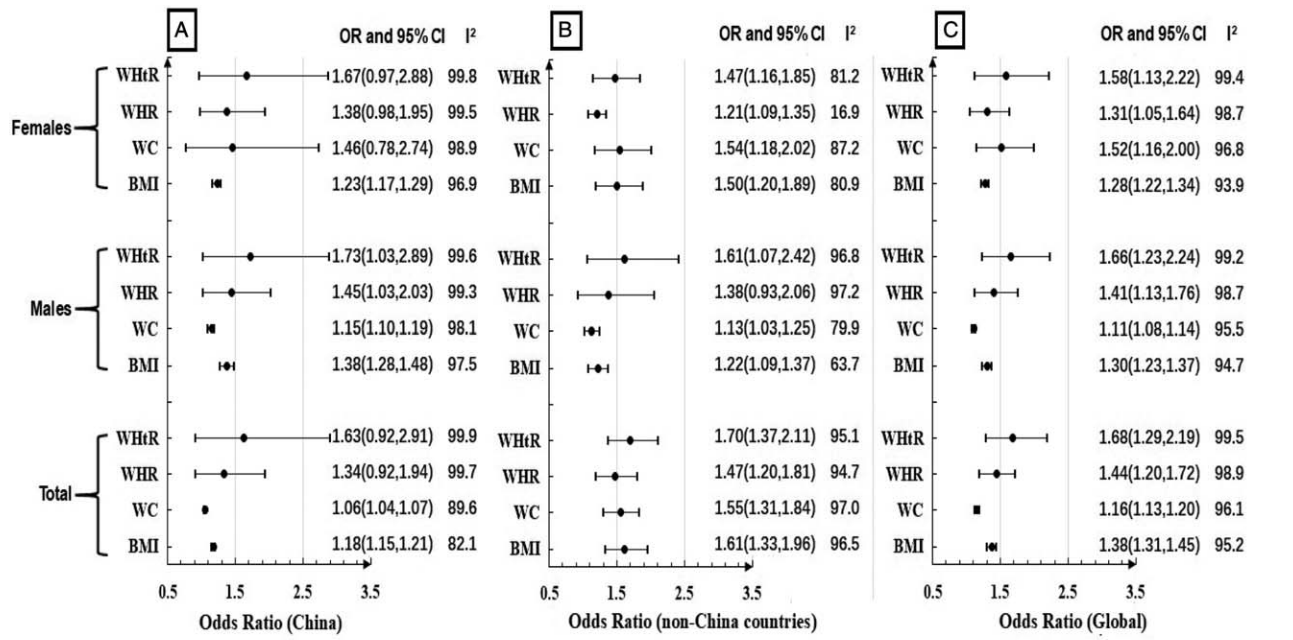

Figure 2. Summary ORs of BMI, WC, WHR, WHtR for hypertension risk in China (2A), non-China countries (2B) and global (2C). BMI = body mass index, CI = confidence interval, OR = odds ratio, WC = waist circumference, WHR = waist-to-hip ratio, WHtR = waist-to-height ratio.

on gender among both China and non-China countries (*P* for meta-regression ≥.4 for the 4 indexes).

Further subgroup analyses were conducted to evaluate the associations between cross-sectional, retrospective cohort study and prospective cohort study. And found that BMI was the highest OR among prospective cohort study (OR, 1.24; 95% CI, 1.12–1.39) and retrospective cohort study (OR, 1.29; 95% CI, 1.21–1.37) respectively. However, it was WHtR with the highest OR among cross-sectional study (OR, 1.75; 95% CI, 1.41–2.17). Significant difference was observed for meta-regression based on study design (*P* for meta-regression<0.01 for the 4 indexes).

3.3.2. Overall AUCs of meta-analyses. Summary AUCs of 4 AAI for hypertension risk was illustrated in Figure 3. Together with PURE-China study, a total of 31 articles[37–39,41–44,55–66,69–73,75–79,82] reported AUCs, including 13 articles[37–39,44,55,59–61,64,65,72,75] from China, and 18 articles[41–43,56–58,62,63,66,69–71,73,76–79,82] from other countries outside of China. In random effects models of meta-analysis, WHtR had the strongest prediction abilities of hypertension risk in both sexes (AUC, 70.9%; 95% CI: 67.8%–74.2%), whatever males (AUC, 68.9%; 95% CI: 67.1%–70.6%) and females (AUC, 72.6%; 95% CI: 70.9%–74.4%). Prediction abilities were higher among China

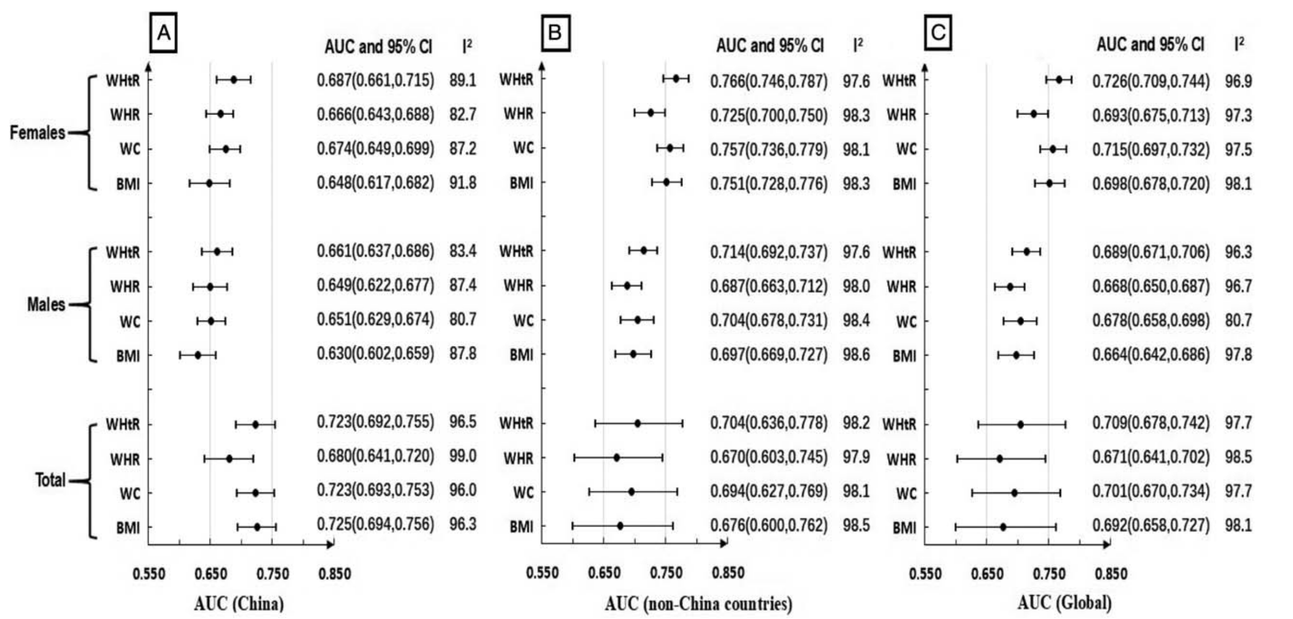

Figure 3. Summary AUCs of BMI, WC, WHR, WHtR for hypertension risk in China (3A), non-China countries (3B) and global (3C). AUC = receiver operating characteristic curve, BMI = body mass index, CI = confidence interval, WC = waist circumference, WHR = waist-to-hip ratio, WHtR = waist-to-height ratio.

studies than other countries (P for meta-regression <.01 for the 4 indexes). Large heterogeneity was observed for all meta-analyses for AUCs (all I^2>80%). No outliers were identified in sensitivity analyses for WHtR, WHR, WC, and BMI, and no publication bias was found (all Egger test P >.10). Trim and fill analyses were conducted to evaluate prediction abilities after filling "missing studies", filled AUC continued to show original prediction abilities for all 4 AAI.

Subgroup analyses based on gender and China and non-China countries were also conducted, which were illustrated in Figure 3. Significant difference was observed for meta-regression between China and non-China countries (P<.01 for the 4 indexes). Significant difference was observed for meta-regression between males and females in China for BMI (P=.03), WC (P=.04) and WHtR (P=.02). However, no significant difference was observed for meta-regression between males and females among non-China countries (P>.2 for the 4 indexes).

Further subgroup analyses were conducted to evaluate the associations between cross-sectional, retrospective cohort study, and prospective cohort study. WHtR had the strongest prediction abilities of hypertension risk among prospective cohort study (AUC, 64.4%; 95% CI, 60.3%–68.7%), cross-sectional study (AUC, 70.4%; 95% CI, 68.8%–72.1%) and retrospective cohort study (AUC, 74.5%; 95% CI, 69.0%–71.9%) respectively. Significant difference was observed for meta-regression based on study design (P for meta-regression <.01 for the 4 indexes).

4. Discussions

Together with PURE-China study, 38 articles involving 309,585 participants were identified to evaluate the associations of hypertension risk with 4 AAI, including BMI, WC, WHR, and WHtR using systematic review and meta-analysis strategies. Our results further confirmed the positive associations between hypertension risk and these AAI. Among the 4 AAI, WHtR has the strongest prediction ability for hypertension risk, irrespective of the gender, though large heterogeneity and publication bias were observed across the included studies. Further sensitivity analyses and trim and fill analyses did not alter the respective prediction abilities.

Our meta-analyses updated the results of 2 previous meta-analytic reviews[35,36] and further confirmed that WHtR had the highest pooled AUC and OR among the global countries. WHO report also recommended that WC, WHR, WHtR were superior to BMI in predicting CVD risk respectively.[83] Most studies provided more supports for central adiposity in predicting CVD risk including hypertension risk, especially WHtR;[22,84–86] however, some studies suggested that WC is the best indicator for reflecting the associations between obesity and hypertension risk.[24,87] Adjusted results from PURE-China showed that WHtR had the strongest association with hypertension risk, while BMI had the strongest prediction ability for hypertension, which might be related to other valuable confounders, such as alcohol use, smoking status, physical activities, and medication use, though AUC of WHtR was the best in unadjusted models. Nonetheless, several studies[37–44,54–58,60,62–65,67,70–73,77–79,82] did not report adjusted ORs and AUCs. We combined the effect sizes from 10 studies[59,61,66,68,69,74–76,80,81] with adjusted ORs, and found both BMI and WHtR (both OR, 1.41) were superior to WC (OR, 1.20) and WHR (OR, 1.28). We also combined effect sizes from 4 studies[59,61,69,76] with adjusted AUCs and found that the prediction ability of BMI, WC, and WHtR were almost the same (all AUC, 74%–75%), which little superior to WHR (AUC, 72.2%). Hence, more studies are needed to confirm this variation, and hitherto, BMI and WC are not excluded while predicting the risk of hypertension.

Similar to previous studies,[35–37] significant heterogeneity among females and males was observed when discriminating hypertension risk, and higher combined AUCs were found among females than males, which indicated that the hypertension risk was estimated rather precisely in women. Furthermore, except for WC, the association of hypertension risk was stronger in men than women, although this correlation variation was not confirmed in meta-regression with respect to sex. Additionally, the difference in discrimination abilities for hypertension risk in China and other countries are notable. According to OR, WHtR is the best predictor for both Chinese population and other ethnic groups. When considering about AUC, while the best predictors are BMI and WHtR for China and non-China countries respectively. And current evidence indicated that the strength of the association between the anthropometric measures with hypertension risk is higher in other countries than China, irrespective of indexes. Central adiposity has been emphasized by a number of studies, particularly for Asian populations who may have a 'normal' BMI along with disproportionately large WC.[36,37] However, BMI showed the strongest prediction abilities in adjusted models in our PURE-China study, in either females or males, or both sexes.

Our study has specific strengths and limitations. A major strength is the application of systematic review strategies and comprehensive evaluation of the associations between adiposity measures and hypertension risk from available data, despite large heterogeneity and publication bias were observed. First, major limitations are related to limitations of the data provided by the individual studies. As a result, the risk estimation may be less accurate if individual-level data were not been available. Some studies were excluded due to no complete data used for meta-analyses, even if we contacted with authors via emails.[88–91] Second, most of studies included in our meta-analyses were observational studies, which have potential methodological limitations to detect causality between exposure and outcome. Third, 3 studies including our PURE-China were defined as outliers when assessing the stability of effect sizes of BMI and WC. Additionally, potential publication bias was detected using Egger tests, though Begg and Mazumdar rank correlation test not. Finally, although 8 databases were searched for the reviews and extensive checks for completeness by cross-referencing were employed, we cannot promise that a relevant study might be missed.

5. Conclusions

Despite these limitations, our systematic review and meta-analyses summarize the available studies so far and provide a comprehensive picture for the associations between hypertension risk and 4 anthropometric measures. The magnitude of these association was partly similar among Chinese and non-Chinese populations. WHtR was confirmed as a good indicator at discriminating those individuals at increased risk of hypertension.

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