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Prevalence of metabolic syndrome in mainland china: a meta-analysis of published studies

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Abstract

Background: Metabolic syndrome (MS) comprises a set of conditions that are risk factors for cardiovascular diseases and diabetes. Numerous epidemiological studies on MS have been conducted, but there has not been a systematic analysis of the prevalence of MS in the Chinese population. Therefore, the aim of this study was to estimate the pooled prevalence of MS among subjects in Mainland China.

Methods: We performed a systematic review by searching both English and Chinese literature databases. Random or fixed effects models were used to summarize the prevalence of MS according to statistical tests for heterogeneity. Subgroup, sensitivity, and meta-regression analyses were performed to address heterogeneity. Publication bias was evaluated using Egger's test.

Results: Thirty-five papers were included in the meta-analysis, with a total population of 226,653 Chinese subjects. Among subjects aged 15 years and older, the pooled prevalence was 24.5 % (95 % CI: 22.0–26.9 %). By sex, the prevalences were 19.2 % (95 % CI: 16.9–21.6 %) in males and 27.0 % (95 % CI: 23.5–30.5 %) in females. The pooled prevalence of MS increased with age (15–39 years: 13.9 %; 40–59 years: 26.4 %; and ≥60 years: 32.4 %). Individuals living in urban areas (24.9 %, 95 % CI: 18.5–31.3 %) were more likely to suffer from MS than those living in rural areas (19.2 %, 95 % CI: 14.8–23.7 %). Hypertension was the most prevalent component of MS in males (52.8 %), while the most prevalent component of MS for females was central obesity (46.1 %).

Conclusions: Our systematic review suggested a high prevalence of MS among subjects in Mainland China, indicating that MS is a serious public health problem. Therefore, more attention should be paid to the prevention and control of MS.

Keywords: Prevalence, Metabolic syndrome X, Meta-analysis

Background

Metabolic syndrome (MS) is characterized by a cluster of metabolic disorders, such as high blood pressure, hyperglycaemia, central adiposity, and dyslipidemia [1, 2]. MS is considered to be risk factor for coronary heart disease, other cardiovascular diseases (CVD), stroke, and type 2 diabetes mellitus [3, 4]. The prevalence of MS is increasing in both developed and developing countries and has become a serious public health problem worldwide [5–8].

China is the world's largest developing country and is experiencing an epidemic of MS [9]. The Nantong MS Study conducted between 2007 and 2008 in south China showed that the prevalence of MS was 15.2 % [10]. A study in north China revealed that the prevalence of MS was 21.6 % in males and 34.3 % in females [11]. The prevalence may vary due to the diverse populations of different regions, cultural behaviours, lifestyle habits, and the use of different diagnosis criteria [2, 9, 12].

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Although a number of epidemiological studies on MS were conducted in the Chinese population in recent years, very little nationwide information exists on the prevalence of MS. A nationwide estimate of MS prevalence in the China population would contribute to the planning and implementation of relevant public health strategies. Therefore, we performed a systematic review of epidemiological studies of MS to estimate the prevalence of MS among subjects in Mainland China.

Methods

Search strategy

We searched for epidemiological studies on MS from the several electronic databases, including Medline, Embase, the China National Knowledge Infrastructure (CNKI), and the Wanfang and Chongqing VIP. The following search strategy was used: ('Metabolic syndrome' OR 'MS' OR 'MetSyn') AND ('prevalence' OR 'epidemi*') AND ('Chinese' OR 'China' OR 'Mainland'). All studies published from January 1, 2005 to April 30, 2015 were searched. Unpublished studies were not retrieved. The search language was limited to English and Chinese.

Inclusion and exclusion criteria

To satisfy the analysis requirements and reduce selection deviation, the selected studies were required to meet the following criteria: 1) a population-based study conducted in Mainland China; 2) a cross-sectional study or data; 3) sufficient information of sample size and crude prevalence of MS; 4) a sample size > 500; 5) participants aged 15 years and older; and 6) the use MS diagnostic criteria proposed by the International Diabetes Federation (IDF) in 2005 [13]. According to the IDF criteria, the participants were classified as having MS if they had central obesity (waist circumference ≥ 90 cm for men and ≥ 80 cm for females) plus any two of the following four abnormalities: a) Hypertension: systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 85 mmHg, or treatment of previously diagnosed hypertension; b) Hypertriglyceridemia: ≥ 1.7 mmol/L triglycerides or specific medical treatment for lipid abnormalities; c) Hypo-HDL-cholesterol: < 1.03 mmol/L HDL cholesterol for men or < 1.29 mmol/L for females; and d) Raised fasting glucose: overnight ≥ 5.6 mmol/L plasma glucose or previously diagnosed diabetes. We excluded studies that investigated specific occupations, volunteers, and hospital-based populations. If there were multiple articles based on the same population, only the study that reported the most detailed data was included.

Data extraction and quality assessment

All searched articles from different electronic databases were combined in Endnote, and duplicates were removed. Two researchers independently screened the titles and abstracts and reviewed the full text of the eligible citations. If they were in disagreement, a third reviewer made the final decision. For each included study, two researchers independently extracted the following information: general information (e.g., first author, title, journal, and publication year); study characteristics (including study period, study area, study design, sample source, sample selection method, diagnostic criteria, and sample size); and all possible participant information(e.g., sex ratio, age, prevalence of MS, age-specific prevalence of MS, the prevalence of central obesity, hypertension, raised fasting glucose, hypertriglyceridaemia, and low high-density liprotein (HDL) cholesterol). Two researchers independently assessed the quality of each included study using observational study criteria that were recommended by the Agency of Healthcare Research and Quality [14]. Only when two reviewers agreed was the study included in the meta-analysis. The retained articles were required to have a quality score of at least 6 of 11.

Statistical analysis

We used a systematic analysis approach to calculate the pooled prevalence of MS from all eligible studies. A random or fixed effects model was selected to summarize the prevalence of MS, using statistical tests for heterogeneity. Heterogeneity among studies was assessed using Cochran's Q test and I^2 statistic, which shows the percentage of variation across studies (with values of 25, 50, and 75 % indicating low, moderate, and high degrees of heterogeneity, respectively) [15, 16]. If the data showed low or moderate heterogeneity ($I^2 < 50$ %), a fixed-effect model was used; otherwise, a random-effect model was used. Subgroup analyses by geographic region, age, sex, and the year of screening were performed to address heterogeneity. Additionally, a meta-regression was conducted to explore potential sources of heterogeneity. Variables such as the year of publication, year of screening, response rate, geographic area (e.g., northern vs. southern China), sex ratio (males vs. females), sample size, age range, and quality score were used to perform the meta-regression. Additionally, sensitivity analysis (i.e., recalculating the pooled estimate by omitting studies with low scores) was performed to assess the influence of any particular study on the pooled estimate.

Publication bias was evaluated using Egger's Test, and independent t-tests were performed as appropriate. The significance level was set at a P value of less than 0.05. All statistical analyses were performed using Stata version 12.0 (College Station, Texas) and SPSS version 20.0 (SPSS Inc., Chicago, USA).

Results

Search results and included subjects

A total of 1405 citations were searched. Of these, 510 duplicates were removed, and 358 citations were excluded

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after reading the titles and abstracts. Five hundred thirty-seven articles were further excluded after reviewing the full texts. In total, 35 eligible studies were included in the meta-analysis, which involved a total of 226,653 subjects. The flow diagram of the search process is shown in Fig. 1. Among the 35 published papers, 22 were written in Chinese and 13 were written in English. All of the included studies were cross-sectional surveys. Thirty-one studies reported data on males ($n = 94,241$) and 32 studies reported data on females ($n = 127,079$). Sixteen and 17 studies were conducted on the populations of south and north China, respectively, and two nationwide studies were conducted. Table 1 shows the detailed characteristics of the 35 studies selected. On a quality assessment scale, seven studies scored 6, and 28 articles scored between 6 and 10. Additional file 1 shows the score of each study.

Prevalence of metabolic syndrome

The pooled prevalence of MS among Chinese subjects was 24.5 % (95 % CI: 22.0–26.9 %), with a high-level between-study heterogeneity ($I^2 = 99.5$ %, $P < 0.0001$).

Table 2 demonstrates the pooled prevalence of all subgroups stratified by sex, geographic area, study period, and age range. The pooled prevalence in males (19.2 %, 95 % CI: 16.9–21.6 %, Fig. 2) was lower than that of females (27.0 %, 95 % CI: 23.5–30.5 %, Fig. 3). The t-tests showed that the prevalence of MS was significantly different between males and females ($P = 0.002$). The prevalences of MS in the populations of north and south China were similar (24.4 and 24.6 %, respectively). The pooled prevalence of MS in the population living in rural areas (19.2 %, 95 % CI: 14.8–23.7 %) was lower than was observed in urban areas (24.9 %, 95 % CI: 18.5–31.3 %). The pooled prevalence of MS increased with time. The pooled prevalence was 23.8 % (95 % CI: 17.7–29.9 %) during 2000–2005, increasing to 22.3 % (95 % CI: 20.3–24.3 %) during 2005–2010 and 27.0 % (95 % CI: 22.2–31.8 %) during 2010–2015. Additionally, the summarized prevalence of MS increased with age. The pooled prevalences of MS for specific age ranges were 13.9 % (95 % CI: 9.5–18.2 %) for subjects aged 15–39 years, 26.4 % (95 % CI: 20.5–32.3 %) for subjects aged 40–59 years,
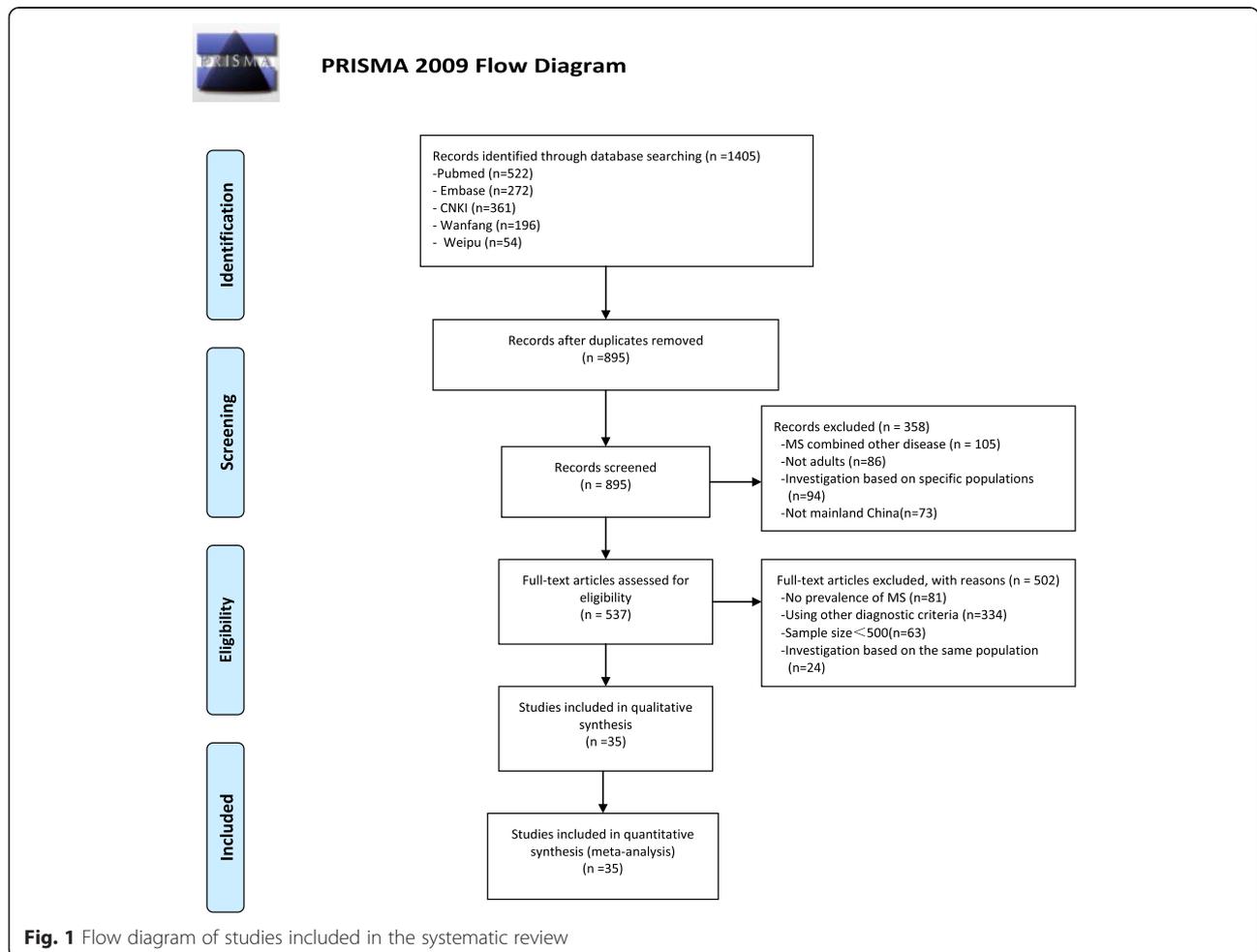
Fig. 1 Flow diagram of studies included in the systematic review

Table 1 Characteristic of studies on the prevalence of metabolic syndrome

NO.	First author	Publication year	Screening year	Region	Area	Age range	Sex (M/F)	Case (n)	Sample size	Prevalence (%)	Score
1	Zhang YH et al. [a][37]	2014	2008	Beijing	Northern	≥18y	0.94	161	724	22.2	7
	Zhang YH et al. [b][37]	2014	2011	Beijing	Northern	≥18y	0.67	279	864	32.3	7
2	Cao YL et al. [38]	2015	2013	Hunan	Southern	≥18y	1.16	826	3108	26.58	7
3	Chen QY et al. [39]	2007	2003–2005	Guangxi	Southern	≥15y	1.28	3582	27,240	13.15	6
4	Li H et al. [40]	2013	2011	Guizhou	Southern	40–79y	0.37	4063	10,016	40.57	7
5	Fu SY et al. [41]	2010	2007	Heilongjiang	Northern	35–91y	0.802	1472	5984	24.6	8
6	Tao R et al. [42]	2015	2010	Jiangsu	Southern	18–95y	0.901	2472	8380	29.5	8
7	Xu DM et al. [43]	2010	2007–2008	Henan	Northern	18–88y	0	89	579	15.3	7
8	Lu W et al. [44]	2006	2002–2003	Shanghai	Southern	15–74y	0.745	2509	14,327	17.51	10
9	Hu Y et al. [45]	2008	2007	Liaoning	Northern	65–94y	1.96	633	2730	23.19	7
10	Wang WC et al. [46]	2014	2011	Hebei	Northern	≥45y	0.543	307	1447	21.2	8
11	Du YH et al. [47]	2007	2005–2006	Shanxi	Northern	20–93y	0.488	979	3869	25.3	9
12	Yu H et al. [48]	2012	2010	Tianjin	Northern	30–60y	1.02	546	2993	18.24	8
13	Yu L et al. [49]	2008	2003–2004	Neimonggu	Northern	≥20y	0.693	530	2536	20.9	8
14	Zhang SQ et al. [50]	2007	2002	Zhejiang	Southern	≥50y	0.672	288	1187	24.26	6
15	Zhao FC et al. [51]	2009	2007	Xinjiang	Northern	20–74y	0.69	823	3293	24.99	7
16	Li SJ et al. [52]	2012	2010	Zhejiang	Southern	≥18y	0.775	179	600	29.83	7
17	Deng M et al. [53]	2014	2011–2012	Chongqing	Southern	≥35y	0.713	1092	5384	20.28	6
18	Ye QY et al. [54]	2012	2010	Zhejiang	Southern	≥18y	0.88	339	1248	27.16	7
19	Ta JGL et al. [55]	2013	2010	Xinjiang	Northern	≥20y	0.457	817	2138	38.2	7
20	Li CH et al. [56]	2012	2010	Xinjiang	Northern	≥18y	0.97	730	3442	21.2	8
21	Li YQ et al. [57]	2014	2012	Guangdong	Southern	18–75y	0.595	383	1724	22.22	6
22	Zhao Y et al. [33]	2010	2008–2009	Ningxia	Northern	≥25y	null	355	1612	22	8
23	Sun M et al. [58]	2014	2011	Jiangsu	Southern	≥40y	0.6	2973	7489	39.7	9
24	Lao XQ et al. [9]	2014	2010	Guangdong	Southern	≥20y	0.82	872	3561	24.5	8
25	Yu M et al. [59]	2014	2009	Zhejiang	Southern	19–79y	1	1242	8169	15.2	6
26	He Yao et al. [60]	2006	2001–2002	Beijing	Northern	60–95y	0.67	1081	2334	46.3	8
27	Zhou HC et al. [61]	2014	2007–2008	14 provinces	National	≥20y	0.66	11,244	45,157	24.9	8
28	Xi B et al. [34]	2013	2009	9 provinces	National	≥18y	0.871	1767	7488	23.6	7
29	Peng X et al. [62]	2009	2007	Hunan	Southern	≥18y	0.99	260	1709	15.2	7
30	Cai H et al. [2]	2012	2007–2008	Jiangsu	Southern	18–74y	0	2965	13,505	22	6
31	Zhao J et al. [11]	2011	2006	Shandong	Northern	35–74y	0.688	1082	5355	20.2	7
32	Tan XU et al. [63]	2009	2002–2003	Neimonggu	Northern	≥20y	0.693	530	2536	20.9	7
33	Li G et al. [64]	2010	2005	Beijing	Northern	≥18y	0.652	4587	16,442	27.9	6
34	Zhao YL et al. [65]	2014	2010	Shanxi	Northern	18–80y	0.529	407	2990	13.6	8
35	Xu F et al. [66]	2011	2009–2010	Jiangsu	Southern	18–74y	0.878	1213	4493	27	7

Study[37] has two parts; [a]the screening year of one part is 2008, [b]the screening year of the other part is 2011

and 32.4 % (95 % CI: 26.1–38.8 %) for subjects aged ≥ 60 years. The prevalence of MS increased with age in males, peaking in the 40–59 year age group and decreasing thereafter. The prevalence of MS also increased with age in females, peaking in the ≥ 60 years group.

Prevalence of components of metabolic syndrome

In terms of the different components of MS, the pooled prevalence estimates of central obesity, hypertension, high fasting plasma glucose, hypertriglyceridaemia, and low HDL cholesterol in males were 33.4, 52.8, 31.5, 32.9, and 27.4 %, respectively. For females, these estimates

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Table 2 Prevalence of MS according to a different category

Category	Subgroup	NO.of study	Prevalence (95 % CI)(%)	Sample	I^2(%)	P	P(Egger's Test)
Total		36	24.5(22.0–26.9)	226,653	99.5	<0.001	0.072
Geographic region	Northern	17	24.4(21.4–27.3)	61,868	98.7	<0.001	0.976
	Southern	16	24.6(20.2–29.1)	112,140	99.7	<0.001	0.036
	Urban	7	24.9(18.5–31.3)	24,560	99.3	<0.001	0.060
	Rural	16	19.2(14.8–23.7)	53,268	99.5	<0.001	0.048
Sex	Male	31	19.2(16.9–21.6)	94,241	98.9	<0.001	0.150
	Female	32	27.0(23.5–30.5)	127,079	99.8	<0.001	0.141
Screening year	2000–2005	6	23.8(17.7–29.9)	50,160	99.6	<0.001	0.051
	2005–2010	15	22.3(20.3–24.3)	121,109	98.4	<0.001	0.322
	2010–2015	15	27.0(22.2–31.8)	55,384	99.4	<0.001	0.571
Age-specific group(y)	15–39	10	13.9(9.5–18.2)	20,273	98.8	<0.001	0.017
	40–59	12	26.4(20.5–32.3)	38,484	99.4	<0.001	0.258
	≥60	12	32.4(26.1–38.8)	18,652	98.8	<0.001	0.955
Male	15–39	5	14.9(6.8–23.0)	8585	99.0	<0.001	0.100
	40–59	7	23.4(16.3–30.5)	14,845	98.8	<0.001	0.279
	≥60	7	23.0(18.0–28.0)	7850	96.2	<0.001	0.292
Female	15–39	5	9.5(5.3–13.7)	9536	98.2	<0.001	0.069
	40–59	7	27.2(19.3–35.2)	19,586	99.3	<0.001	0.550
	≥60	7	42.9(34.5–51.3)	8800	98.4	<0.001	0.273
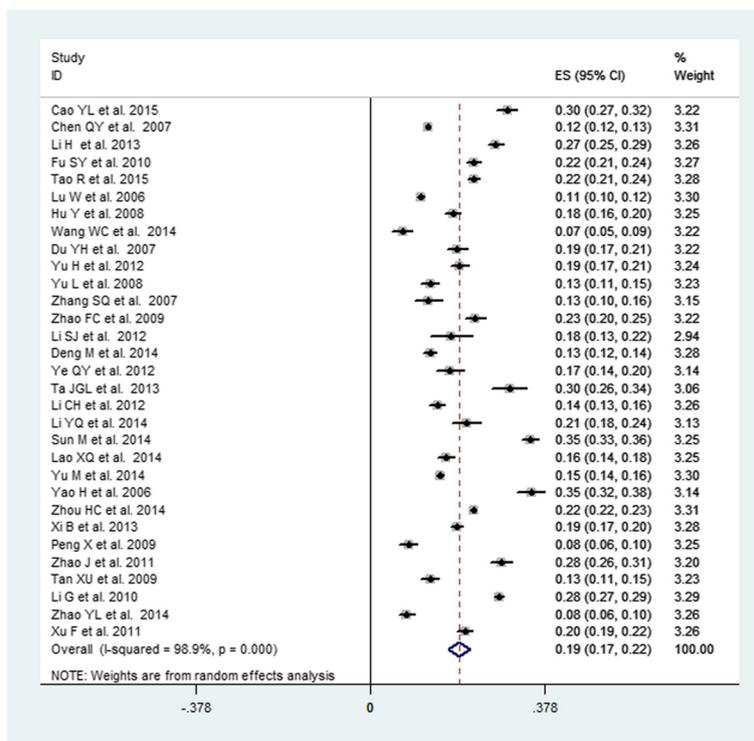
Fig. 2 Forest plot of the studies of males

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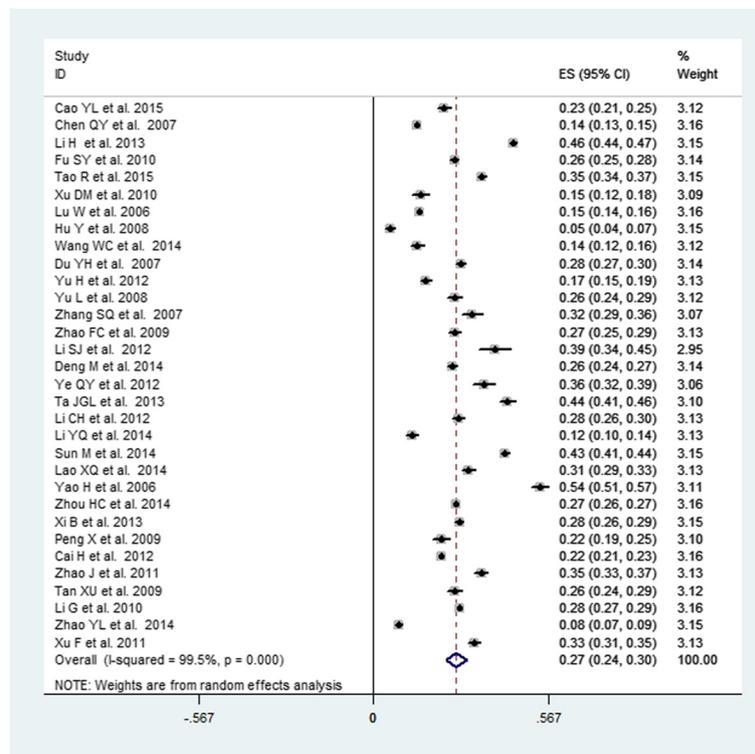
Fig. 3 Forest plot of the studies of females

were 46.1, 40.1, 26.3, 27.7, and 40.4 %, respectively. The prevalence of hypertension in males was significantly higher than in females ($P = 0.049$). Table 3 shows the pooled prevalences of different the components of MS.

Sensitivity analysis and meta-regression

Seven citations had a quality score of 6, the lowest among the included studies. In the sensitivity analysis, we noticed a slight change in the pooled MS prevalence estimate (from 24.5 to 25.4 %) when we omitted these seven studies. Egger's linear regression test ($P = 0.072$) suggested no significant publication bias.

A high level of heterogeneity between studies and subgroups was observed ($P < 0.001$, $I^2 = 96.2–99.8$ %). We performed a meta-regression to take this heterogeneity into account. In the univariate meta-regression and multivariable analyses, only the variable of age was significantly associated with heterogeneity ($P = 0.01$, $P = 0.02$, respectively) (Table 4).

Table 3 Prevalence of different components of MS

Types	Sex	NO. of study	Sample	Pooled prevalence(95 % CI)(%)	Median(%)	Minimum(%)	Maximum(%)	t	P
Central obesity	Male	14	38,434	33.4(25.3–41.5)	26	18	68.8	−2.034	0.052
	Female	15	44,646	46.1(37.0–55.2)	47.2	6.8	77.5		
Hypertension	Male	14	38,434	52.8(45.3–60.4)	30.3	52	79	2.066	0.049
	Female	15	44,646	40.1(32.2–48.0)	41.3	15	75.9		
High Fasting Plasma Glucose	Male	14	38,434	31.5(25.3–37.8)	31	10.2	52.3	0.981	0.335
	Female	15	44,646	26.3(19.0–33.6)	24	3.4	52.5		
Hypertriglyceridaemia (TG)	Male	14	38,434	32.9(27.5–38.3)	32.9	11.6	53.8	1.189	0.245
	Female	15	44,646	27.7(22.0–33.4)	27.1	7.3	56.3		
Low HDL-C	Male	14	38,434	27.4(22.2–32.5)	27.2	5	55.5	−1.991	0.057
	Female	15	44,646	40.4(30.6–50.2)	36.3	1.4	70.4		

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Table 4 Results of meta-regression for the prevalence of metabolic syndrome

Covariate	Meta-regression coefficient	95 % confidence interval	P value	Variance explained (%)
Univariate analyses				
Sex ratio(male *vs.* female)	0.846	0.6195–1.155	0.283	1.83
Area(northern *vs.* southern)	1.0104	0.8486–1.2031	0.904	−3.14
Quality score	1.0044	0.9370–1.1641	0.421	−0.96
Year of screening	1.1046	0.9617–1.2687	0.153	3.62
Sample size, continuous	1.0000	0.9999–1.0001	0.519	−1.65
Age group(15 ~ =1, 40 ~ =2, 60 ~ =3)	1.2625	1.0615–1.5017	0.010	17.63
Year of publication	1.0988	0.8671–1.3924	0.424	−0.90
Multivariable analyses				26.74
Sex ratio(male *vs.* female)	−0.2331	−0.5318–0.6585	0.121	
Area(northern *vs.* southern)	0.0095	−0.1543–0.1734	0.906	
Quality score	0.0285	−0.0746–0.1315	0.576	
Year of screening	0.0906	−0.9722–0.2785	0.331	
Sample size, continuous	$3.28e^{-7}$	−0.0000–0.0001	0.952	
Age group(15 ~ =1, 40 ~ =2, 60 ~ =3)	0.3035	0.1187–0.4884	0.002	
Year of publication	0.9168	−0.2391–0.4225	0.574	

Discussion

Our systematic review of observational studies conducted in the last decade included 35 studies that involved a total of 226,653 participants in Mainland China and covered most regions of the country. The definitions of IDF and the US National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) are widely used in China [9]. The IDF criteria recognize and emphasize differences in waist circumference for Chinese populations [17]. Thus, the IDF criteria were adopted in our meta-analysis.

Our meta-analysis revealed that the pooled estimate of MS prevalence among subjects in Mainland China was 24.5 %. This estimate was higher than the prevalence of 16.5 % observed in China in 2000 and approached the worldwide prevalence of 20–25 % [5, 18]. The prevalence of MS has recently increased in developing countries. Several studies have reported a high prevalence of MS in Malaysia (27.5 %), India (28.2 %), Philippines (19.7 %), Nigeria (28.1 %), Brazil (29.6 %), Turkey (44.0 %), and Iran (36.9 %) [19–25]. As the largest developing country, China is experiencing an emerging epidemic of MS, which might be related to rapid economic development and urbanization [9]. Rapid industrialization and urbanization can lead to accelerating changes in lifestyle and nutrition. The prevalences of obesity and overweight have increased dramatically in China due to the changes in the lifestyle of the population, and some of these changes are independent factors that contribute to MS. Data from the China Health and Nutrition Survey shows that the age-adjusted prevalence of obesity increased from 3.75 % in 1991 to 11.3 % in 2011, and the

prevalence of overweight was up to 42.3 % in 2011 [26]. In addition, another major factor driving MS growth is likely the ageing of the Chinese population. Studies have shown an increased prevalence of MS with age [19, 27]. Data from the National Bureau of Statistics in 2011 showed that people aged 60 and older accounted for 13.26 % of the Chinese population, with those 65 years and older representing 8.87 % of the population. These data show that China is now an ageing society [28].

Our systematic review showed that MS was more common in females than in males (27.0 vs. 19.2 %), a result that is in line with previous findings [19, 27, 29]. Menopause may have effects on the high prevalence of MS among females. Post-menopausal status is associated with an increased risk of central obesity and insulin resistance [30]. Our meta-analysis discovered that central obesity was the most prevalent component of MS in females. Moreover, a relationship was observed between the prevalence of MS and age in both males and females, which is consistent with other studies [31, 32]. The increased prevalence of MS with age can be attributed to similar age-related trends in all components of MS [9, 33]. Additionally, individuals living in urban areas were more likely to suffer from MS than those living in rural areas. Unhealthy lifestyles in urban area, including decreased physical activity, excessive intake of animal fat and salt, and low intake of fruits and vegetables might explain the difference in MS prevalence between the two regions [34].

There is an emerging MS epidemic in Mainland China, and it has become a serious public health problem. MS increases the risk for morbidity and mortality

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of cardiovascular disease and is associated with an increased risk of diabetes [5]. Studies have shown that the components of the syndrome tend to aggregate in individuals, and this clustering effect is associated with a worse prognosis than exhibiting a single component [35, 36]. Our results showed that MS was highly prevalent, especially in female, elderly participants and those living in urban areas. These data may be useful for the Chinese government in its formulation of guidelines to prevent, screen for and treat MS.

Strengths and limitations

The overall quality of the studies included in our systematic review was good; therefore, the sensitivity analysis did not show major differences in the meta-analysis results when studies with the lowest quality scores were omitted. Our meta-analysis included 35 published studies with a large sample size. Nevertheless, our study had some limitations. First, we used the IDF criteria as our diagnosis criteria, and studies based on other diagnosis criteria were not included in our meta-analysis. Second, although most of the included studies had a large sample size that could generate an accurate estimation, the overall analysis revealed a high heterogeneity. Additionally, meta-regression and subgroup analyses did not indicate enough factors to explain the observed heterogeneity. We propose that other factors, such as cigarette smoking, alcohol consumption, stress, and physical inactivity may influence MS heterogeneity. Because of the limited information on these aspects, we could not perform further analyses. Third, the distribution of healthcare resources in Mainland China is unbalanced, with more economically developed areas having better access to health care facilities. This factor may have contributed to more diagnoses and, therefore, a higher reported prevalence in certain studies of different regions in Mainland China.

Conclusion

To the best of our knowledge, this was the first systematic review to estimate the pooled prevalence of MS among subjects in Mainland China. Our systematic review indicates a high prevalence of MS among subjects in Mainland China. Information on how MS and its components are distributed could provide a great deal of insight into MS and assist in the planning and implementation of future prevention and control programmes.

Additional file

Additional file 1: Table S1. Quality assessment scores of the included studies. (XLS 37 kb)

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Designed the experiments: LR LWC LYW CY. Performed the experiments: LR LWC LZJ. Analysed the data: LR LWC. Contributed reagents/materials/analysis tools: LYW CY. Wrote the paper: LR LWC. Revised the language/article: ZHP LYW Joseph Sam Kanu QS SZ. All of the authors read and approved the final manuscript.

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