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The effects of capsaicin intake on weight loss among overweight and obese subjects: a systematic review and meta-analysis of randomised controlled trials

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Abstract

Animal studies have shown that capsaicin plays a positive role in weight management. However, the results in human research are controversial. Therefore, the present systematic review and meta-analysis aimed to evaluate the effect of capsaicin on weight loss in adults. We searched PubMed, Embase, China Biomedical Literature Database (CBM), Cochrane library and clinical registration centre, identifying all randomised controlled trials (RCT) published in English and Chinese to 3 May 2022. A random-effect model was used to calculate the weighted mean difference (WMD) and 95 % CI. Heterogeneity between studies was assessed by the Cochran Q statistic and *I*-squared tests (I^2). Statistical analyses were performed using STATA version 15.1. *P*-values < 0·05 were considered as statistically significant. From 2377 retrieved studies, fifteen studies were finally included in the meta-analyses. Fifteen RCT with 762 individuals were included in our meta-analysis. Compared with the control group, the supplementation of capsaicin resulted in significant reduction on BMI (WMD: −0·25 kg/m^2, 95 % CI = –0·35, –0·15 kg/m^2, $P < 0·05$), body weight (BW) (WMD: −0·51 kg, 95 % CI = –0·86, –0·15 kg, $P < 0·05$) and waist circumference (WC) (WMD: −1·12 cm, 95 % CI = –2·00, –0·24 cm, $P < 0·05$). We found no detrimental effect of capsaicin on waist-to-hip ratio (WMD: −0·05, 95 % CI = –0·17, 0·06, $P > 0·05$). The current meta-analysis suggests that capsaicin supplementation may have rather modest effects in reducing BMI, BW and WC for overweight or obese individuals.

Key words: Capsaicin: Obesity: Overweight: Meta-analysis: Weight loss

Recent statistics indicate that overweight/obesity has now become a global public health issue. In 2016, the WHO reported more than 1·9 billion adults were overweight (BMI ≥ 25 kg/m^2), and over 650 million adults were obese (BMI ≥ 30 kg/m^2)[(1)]. Established evidence suggested that overweight and obesity were associated with multiple health problems, such as hypertension, type 2 diabetes mellitus, CHD and cancers, which brings heavy economic burden to family and society. Novel, individualised interventions may thus be necessary to effectively prevent and treat overweight and obesity, such as the phytochemicals extracted from plants. Dietary chili peppers supplementation or to be food additives, with ideal dosage, may be tentative methods for capsaicin to play its protective roles in metabolic health[(2)].

Capsaicin, as the most important compound of chili pepper[(4)], is the major pungent principle in various species of capsicum fruits such as hot chili peppers and has long been globally used as an ingredient of spices, preservatives and medicines[(5)]. Animal studies showed that dietary capsaicin may reduce the prevalence of obesity by suppressing inflammatory responses and enhancing fatty acid oxidation in adipose tissue and liver[(6–9)]. However, the results in human studies are controversial and uncertain. Some studies have shown that capsaicin supplementation has no significant effect on energy intake and appetite during the intervention period[(10–12)]. Some researches indicated that foods containing chili peppers can help control body weight (BW) and reduce the risk of developing overweight and obesity[(13–15)]. Some studies have demonstrated that capsaicin has a potential role in increasing the risk of developing overweight and obesity[(16–19)].

Furthermore, previous human studies involving capsaicin supplementation and weight loss are either observational studies or randomised controlled trials (RCT) with small sample size, resulting in the conflicting conclusions. Therefore, the purpose

Abbreviations: BW, body weight; RCT, randomised controlled trial; TRPV1, transient receptor potential vanilloid subtype 1; WC, waist circumference; WHR, waist-to-hip ratio; WMD, weighted mean difference.

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of this study was to conduct a systematic review and meta-analysis of RCT to clarify the effects of capsaicin supplementation on weight loss among overweight and obese subjects.

Methods

Research question

This study was conducted based on the preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement[20]. PICOS (participant, intervention, comparison, outcome, study design) criteria were followed to develop the research question[21]. In this study, the population was healthy adults aged 18 or older, the intervention was capsaicin supplementation, the comparison was matched placebo group or control group, the outcome was BMI, BW, waist-to-hip ratio (WHR), waist circumference (WC) and the study design was clinical trial.

Search strategy

The published studies involving capsicum and obesity were searched through PubMed, Embase, China Biomedical Literature Database (CBM), Cochrane library and clinical registration centre, from database inception to 3 May 2022. The search was limited to studies in human and published in English and Chinese. In addition, the literature traceability method and manual retrieval method were used to complete the search strategy. Studies retrieved that examined the association between supplementation with capsaicin and body composition, and metabolic profiles by using the following MeSH: ('capsicum' OR 'capsaicin'), and ('body mass index (BMI)' OR 'body weight (BW)' OR 'waist-to-hip ratio (WHR)'). The trials were initially selected on the basis of their summaries; then the whole content was reviewed to determine the final inclusion. The search strategy is developed by all researchers and executed by two persons (zws and zby).

The search strategy is as follows:

("Capsicum"[MeSH Terms] OR ("bell pepper"[Title/Abstract] OR "bell peppers"[Title/Abstract] OR "pepper bell"[Title/Abstract] OR "peppers bell"[Title/Abstract] OR "sweet pepper"[Title/Abstract] OR "pepper sweet"[Title/Abstract] OR "peppers sweet"[Title/Abstract] OR "sweet peppers"[Title/Abstract] OR "red pepper"[Title/Abstract] OR "pepper red"[Title/Abstract] OR "peppers red"[Title/Abstract] OR "red peppers"[Title/Abstract] OR "green pepper"[Title/Abstract] OR "green peppers"[Title/Abstract] OR "pepper green"[Title/Abstract] OR "peppers green"[Title/Abstract] OR "cayenne pepper"[Title/Abstract] OR "cayenne peppers"[Title/Abstract] OR "pepper cayenne"[Title/Abstract] OR (("piper nigrum"[MeSH Terms] OR ("piper"[All Fields] AND "nigrum"[All Fields]) OR "piper nigrum"[All Fields] OR "Pepper"[All Fields] OR "Peppers"[All Fields]) AND "Cayenne"[Title/Abstract]) OR "Cayenne"[Title/Abstract] OR "Paprika"[Title/Abstract] OR "hot pepper"[Title/Abstract] OR "hot peppers"[Title/Abstract] OR "pepper hot"[Title/Abstract] OR "peppers hot"[Title/Abstract] OR "jalapeno pepper"[Title/Abstract] OR "jalapeno peppers"[Title/Abstract] OR (("piper nigrum"[MeSH Terms] OR ("piper"[All Fields] AND "nigrum"[All Fields]) OR "piper nigrum"[All Fields] OR "Pepper"[All Fields] OR "Peppers"[All Fields]) AND "Jalapeno"[Title/Abstract]) OR "peppers jalapeno"[Title/Abstract] OR "Pimiento"[Title/Abstract] OR "capsicum annuum"[Title/Abstract] OR "chilli pepper"[Title/Abstract] OR "chilli peppers"[Title/Abstract] OR "pepper chilli"[Title/Abstract] OR (("piper nigrum"[MeSH Terms] OR ("piper"[All Fields] AND "nigrum"[All Fields]) OR "piper nigrum"[All Fields] OR "Pepper"[All Fields] OR "Peppers"[All Fields]) AND "Chilli"[Title/Abstract]) OR "chile pepper"[Title/Abstract] OR "chile peppers"[Title/Abstract] OR (("piper nigrum"[MeSH Terms] OR ("piper"[All Fields] AND "nigrum"[All Fields]) OR "piper nigrum"[All Fields] OR "Pepper"[All Fields] OR "Peppers"[All Fields]) AND "Chile"[Title/Abstract]) OR (("piper nigrum"[MeSH Terms] OR ("piper"[All Fields] AND "nigrum"[All Fields]) OR "piper nigrum"[All Fields] OR "Pepper"[All Fields] OR "Peppers"[All Fields]) AND "Chile"[Title/Abstract]) OR "chili pepper"[Title/Abstract] OR "chili peppers"[Title/Abstract] OR "pepper chili"[Title/Abstract] OR "peppers chili"[Title/Abstract]) OR ("Capsaicin"[MeSH Terms] OR ("Capsaicine"[Title/Abstract] OR "8-Methyl-N-Vanillyl-6-Nonenamide"[Title/Abstract] OR "8-Methyl-N-Vanillyl-6-Nonenamide"[Title/Abstract] OR (("Antiphlogistine"[All Fields] AND "Rub"[All Fields] AND "A-535"[All Fields]) AND "Capsaicin"[Title/Abstract]) OR "Axsain"[Title/Abstract] OR "Zostrix"[Title/Abstract] OR "Capzasin"[Title/Abstract] OR "NGX-4010"[Title/Abstract] OR "NGX-4010"[Title/Abstract] OR "NGX4010"[Title/Abstract] OR "Capsin"[Title/Abstract]))) AND ("index body mass"[Title/Abstract] OR "quetelet index"[Title/Abstract] OR "index quetelet"[Title/Abstract] OR "quetelet s index"[Title/Abstract] OR "quetelets index"[Title/Abstract] OR "Body Mass Index"[MeSH Terms] OR ("body weights"[Title/Abstract] OR "weight body"[Title/Abstract] OR "weights body"[Title/Abstract] OR "Body Weight"[MeSH Terms]) OR ("ratio waist hip"[Title/Abstract] OR "ratios waist hip"[Title/Abstract] OR "Waist-Hip Ratio"[Title/Abstract] OR "waist hip ratios"[Title/Abstract] OR "waist to hip ratio"[Title/Abstract] OR "ratio waist to hip"[Title/Abstract] OR (("Ratio"[All Fields] OR "ratio s"[All Fields] OR "ratioes"[All Fields] OR "Ratios"[All Fields]) AND "Waist-to-Hip"[Title/Abstract]) OR "waist to hip ratio"[Title/Abstract] OR "waist to hip ratios"[Title/Abstract] OR "Waist-Hip Ratio"[MeSH Terms])).

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) enrolled subjects aged 18 or older, no disease, but includes overweight and obese participants and (2) studies that were RCT, which is divided into the intervention group and the control group. The intervention group was supplemented with capsaicin or red pepper, and the control group is given a regular diet. (3) Long-term trials (time of duration ≥ 4 weeks), (4) studies with detailed sample size and outcome observations, (5) studies include at least one of the required outcomes (BMI, BW, WHR, WC). And the exclusion criteria are as follows: (1) non-healthy adults, (2) repeatedly published papers, (3) lack of outcome variables needed for analysis, (4) review types of research literature and (5) studies with no

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control group. According to the inclusion and exclusion criteria, the two researchers screened the relevant literature independently, if there were different opinions on the inclusion and exclusion criteria, after discussion, it is decided whether the literature should be included or not.

Data extraction

The BMI of adults in the literature was collected as the outcome index. Eligible studies were reviewed and the following data were abstracted: name of the first author, year of publication, country, the sample size, duration of the intervention, intervention measures, intervention forms, BMI, BW, WHR and WC.

If the paper already provided the changes in mean and SD from the baseline, then these values were extracted. If the changes in mean and SD were not provided, then these values were calculated using the reported data. The changes in mean were calculated using the following formula:

$$\text{Mean}_{\text{change}} = \text{Mean}_{\text{postintervention}} - \text{Mean}_{\text{pre-intervention}}$$

The changes in SD were calculated using the method and formula provided in the online Cochrane handbook with the topic on imputing standard deviations for changes from baseline[22]. In brief, SD changes were calculated from CI if it was provided in the manuscript using the formula.

$$\text{SE} = (\text{upper limit} - \text{lower limit}) \div 3. \cdot 92$$

$$\text{SD} = \text{SE} \times \sqrt{n}$$

SD was calculated using a correlation coefficient of 0·99. Again, E is replaced by C when calculating the difference for the control group.

$$\text{SD}_{\text{E,change}} = \sqrt{\text{SD}^2_{\text{E,baseline}} + \text{SD}^2_{\text{E,final}} - (2 \times \text{Corr} \times \text{SD}_{\text{E,baseline}} \times \text{SD}_{\text{E,final}})}$$

The data extraction was carried out independently by two researchers (zws and zby).

Quality assessment

The Cochrane risk bias assessment tool was used to evaluate the quality of the included studies. The tool rates each study according to seven criteria (including whether the random allocation scheme generation method is correct, whether the allocation scheme is hidden, whether the blind method is used, the completeness of the resulting data, the selective reporting of research results and other sources of bias). The response to each criterion was classified as low bias risk, unclear or high bias risk[23]. The quality assessment was carried out independently by two researchers (zws and zby). When there was disagreement among them, differences were resolved by discussion with the senior researcher. Quality assessment was performed using Review Manager 5.3 software.

Statistical analysis

In the current study, we computed weighted mean difference (WMD)[24] and 95 % CI to estimate the effect sizes. Heterogeneity between studies was evaluated by I^2 and Cochran's Q test statistics[25]. Heterogeneity in body composition and metabolic profiles was assessed by conducting stratified meta-analysis. Subgroup analyses were conducted to assess the source of heterogeneity between studies. Predefined subgroups were created based on regions (Asia or other regions), intervention forms (capsaicin or capsaicin-containing bioactive supplements), duration of intervention (4 weeks or 6–12 weeks) and body type (overweight ($25\ \text{kg/m}^2 \leq \text{BMI} < 30\ \text{kg/m}^2$) or obese ($\text{BMI} \geq 30\ \text{kg/m}^2$)). Comparative types (control group or placebo group) used random-effect models to explore potential sources of heterogeneity. In addition, sensitivity analyses were performed to examine the contribution of a particular study to the pooled WMD. Egger's test was used to detect the existence of potential publication bias for the primary outcome measure. Statistical analyses were performed using STATA 15.1. *P*-values < 0·05 were considered as statistically significant.

Results

Literature search

A total of 2377 articles were identified in the study. After removing the duplicated records, 1817 articles were left for screening. First, 1751 studies were excluded after checking titles and abstracts. Then, we excluded sixty-six studies through full-text evaluation because of unavailable to get full text, incomplete data, non-RCT, acute test and article out of line. Finally, fifteen articles with 762 participants were remained for this systematic review and meta-analysis (Fig. 1).

Study characteristics

The articles included in this study were published between 1998 and 2021, spanning five continents in ten different countries, including Asia[26–32], Europe[33,34], Australia/Oceania[10], North America[35–38] and South America[36], with the sample size ranging from 20 to 123. The detailed characteristics of the included studies are demonstrated in Table 1. All of the included studies used parallel designs. One study was conducted in female only[31], another was conducted in the male participants only[26] and the rest of the studies were completed in both sexes. Nine studies were carried out in overweight individuals[10,26–30,32,33,38], while one study did not report BMI data and the rest were carried out in obese individuals. The intervention time of capsaicin supplementation ranged from 4 to 12 weeks, nine of which took capsaicin, and the rest took active supplements containing capsaicin (Table 1).

Study quality

The quality of the included literatures was evaluated by the Cochrane Collaboration's tool, and the results of risk of bias are summarised in Fig. 2.

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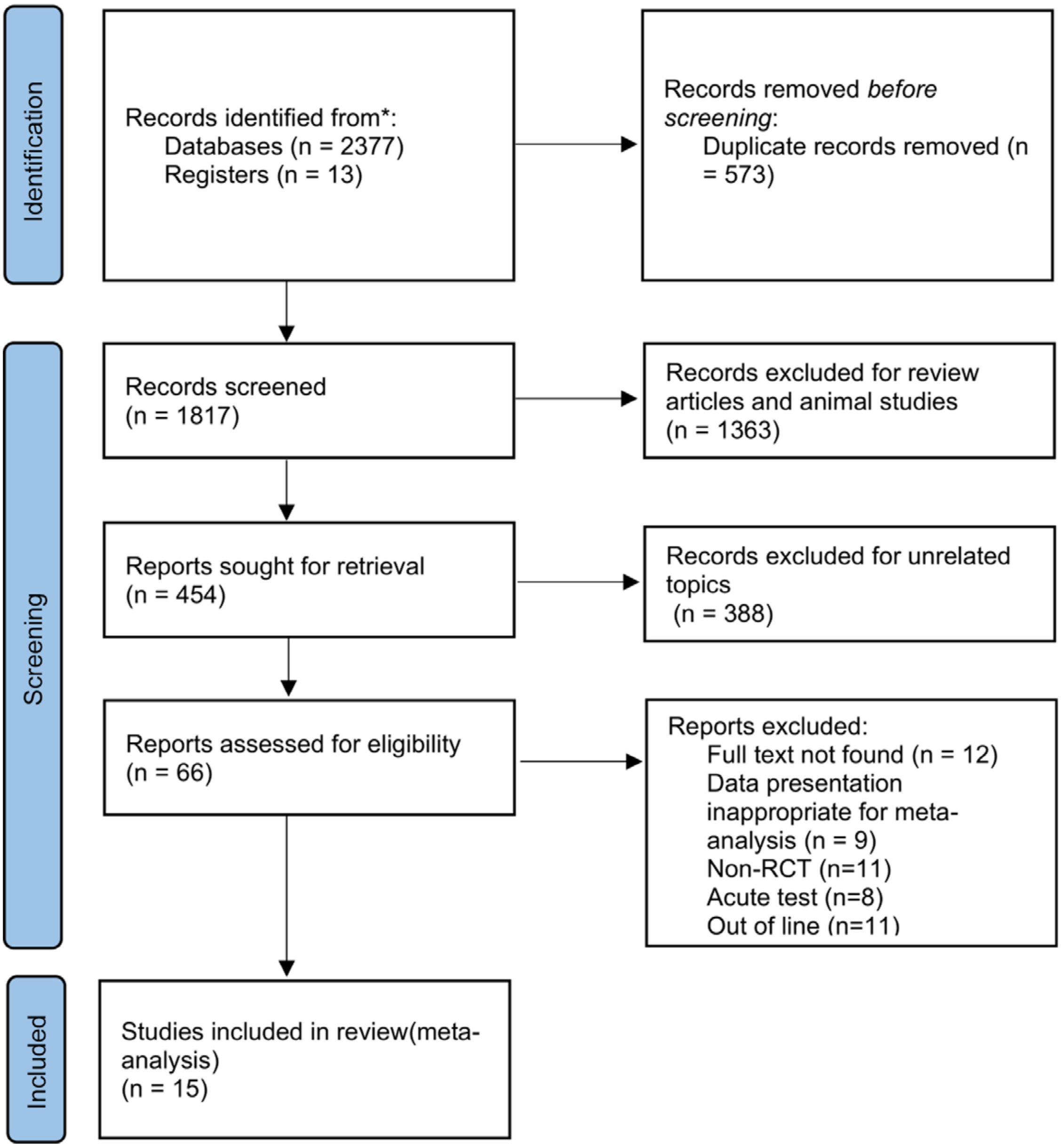

Fig. 1. A schematic diagram of the study inclusion process.

Effect of capsaicin supplementation on BMI

Figure 3 shows the effect of capsaicin supplementation on BMI was estimated in eleven studies. Compared with the control group, the study showed that capsaicin supplementation could significantly decreased BMI (WMD: −0·25 kg/m^2, 95 % CI = −0·35, −0·15 kg/m^2, $P < 0{\cdot}05$) with high heterogeneity ($I^2 = 77{\cdot}1$ %) among studies.

Effect of capsaicin supplementation on reduction of BMI levels was greater among the others (–0·259 kg/m^2, 95 % CI = –0·464, –0·054 kg/m^2; $I^2 = 0$ %), compared with Asia (–0·253 kg/m^2, 95 % CI = –0·371, –0·136 kg/m^2; $I^2 = 85{\cdot}7$ %).

Effect of capsaicin supplementation on reduction of BMI levels was greater among active supplement (–0·284 kg/m^2, 95 % CI = –0·412, –0·157 kg/m^2; $I^2 = 73{\cdot}4$ %), compared with capsaicin alone (–0·226 kg/m^2, 95 % CI = –0·414, –0·038 kg/m^2; $I^2 = 78{\cdot}1$ %).

In stratified analysis by the duration of study (4 weeks *v.* 6–12 weeks), capsaicin supplementation only had a significant effect on BMI reduction in 6–12 weeks category (–0·281 kg/m^2, 95 % CI = –0·401, –0·162 kg/m^2; $I^2 = 88{\cdot}8$ %) (Table 2).

In stratified analysis by body type, capsaicin supplementation had a better effect on BMI in obese individuals, with overweight (–0·176 kg/m^2, 95 % CI = –0·266, –0·087 kg/m^2; $I^2 = 69{\cdot}5$ %) and

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Table 1. Main characteristics of the included studies

First author	Publication year	Country	Sample size	intervention/ control	Duration(week)	Intervention/control	Ingestion form	BMI (kg/m^2) (intervention/ control)
A Belza[28]	2007	Denmark	80	57/23	8	Daily intake of bioactive supplement/ the placebo tablets contained 50/50 microcrystalline cellulose	Active supplement	28·8 ± 2·6/ 29·2 ± 2·4
Sayuri Fuse[27]	2020	Japan	38	19/19	6	Take capsaicin capsule/take placebo capsule	Capsaicin	25·2 ± 1·4/ 25·7 ± 1·3
Werner W. K. Hoeger[35]	1998	America	123	56/67	4	Take an over-the-counter dietary supplement/take placebo supplement	Capsaicin	35·3 ± 6·0/ 32·8 ± 5·5
Ashil Joseph[26]	2021	India	21	11/10	4	Take capsaicin capsule/take placebo capsule	Capsaicin	29·9 ± 1·9/ 29·8 ± 1·7
Wang Jing[33]	2016	China	20	10/10	4	Take capsaicin capsule/take placebo capsule	Capsaicin	27·84 ± 1·95/ 26·99 ± 2·-31
KDK Ahuja[10]	2007	Australia	36	20/16	4	Add chilli to the food after cooking/add placebo to the food	Active supplement	26·4 ± 4·8
Naohiko INOUE[29]	2007	Japan	30	15/15	4	Daily intake of capsinoids/daily intake of placebo	Capsaicin	26·10 ± 0·87/ 26·18 ± 0·-76
Yunkyoung Lee[30]	2017	Korea	53	26/27	12	Take Korean fermented soyabean chili sauce/take placebo without Kochujang's principal ingredients	Active supplement	26·5 ± 0·7/ 27·4 ± 0·7
Mariangela Rondanelli[34]	2013	Italy	96	41/45	8	Take capsaicin capsule/take placebo capsule	Active supplement	30·4 ± 3·6/ 30·0 ± 2·8
Mohsen Taghizadeh[31]	2017	Iran	50	25/25	8	Take capsule of dietary supplements/ take placebo capsule	Active supplement	32·3 ± 4·2/ 32·4 ± 5·9
TszYing Amy Lee[36]	2010	America	31	16/15	4	Take capsaicin capsule/take placebo capsule	Capsaicin	31·3 ± 0·7/ 30·9 ± 0·9
Vilton Emanoel Lopes de Moura e Silva[55]	2021	Brazil	20	11/9	6	Take capsaicin capsule/take placebo capsule	Capsaicin	Only body weight data
Soren Snitker[37]	2009	America	75	37/38	12	Take capsaicin capsule/take placebo capsule	Capsaicin	30·6 ± 2·4/ 30·3 ± 2·4
Roxanne M. Vogel[38]	2015	America	23	9/14	4	Take capsaicin capsule/take placebo capsule	Capsaicin	26·4 ± 6·4/ 25·6 ± 3
Youn-Soo Cha[32]	2013	Korea	53	26/27	12	Take Korean fermented soyabean chili sauce/take placebo without Kochujang's principal ingredients	Active supplement	26·5 ± 0·4/ 27·4 ± 0·8

obese (WMD: −0·509 kg/m^2, 95 % CI = −0·846, −0·172 kg/m^2; I^2 = 68·8 %) (Table 2).

Effect of capsaicin supplementation on body weight

Figure 4 shows the effect of capsaicin supplementation on BW was estimated in twelve studies. Compared with the control group, the study showed that capsaicin supplementation could significantly decrease BW (WMD: −0·51 kg, 95 % CI = −0·86, −0·15 kg, $P < 0·05$) with high heterogeneity (I^2 = 67·8 %) among studies.

In stratified analysis by region, capsaicin supplementation had a significant effect on BW reduction in Asia category (WMD: −0·709 kg, 95 % CI = −1·209, −0·210 kg; I^2 = 83·1 %), compared with the others category (WMD: −0·230 kg, 95 % CI = −0·746, 0·286 kg; I^2 = 31·0 %).

In stratified analysis by ingestion form, capsaicin supplementation neither had a significant effect on BW reduction in active supplement category (WMD: −0·946 kg, 95 % CI = −1·988, 0·095 kg; I^2 = 87·9 %) or capsaicin category (WMD: −0·271 kg, 95 % CI = −0·591, 0·049 kg; I^2 = 20·0 %).

In stratified analysis by the duration of study, capsaicin supplementation had a significant effect on BW reduction in 6–12 weeks category (WMD: −0·681 kg, 95 % CI = −1·278, −0·085 kg; I^2 = 76·3 %) compared with 4 weeks category (WMD: −0·265 kg, 95 % CI = −0·789, 0·260 kg; I^2 = 52·7 %).

In stratified analysis by the body type (overweight *v.* obese), capsaicin supplementation only had a significant effect on BW reduction in overweight category (WMD: −0·329 kg, 95 % CI = −0·465, −0·193 kg; I^2 = 0 %) (Table 2).

Effect of capsaicin supplementation on waist-to-hip ratio

Figure 5 shows the effect of capsaicin supplementation on WHR was estimated in five studies. The difference between the control group and the intervention group was found to be statistically insignificantly (WMD: −0·05, 95 % CI = −0·17, 0·06, $P > 0·05$) with high heterogeneity (I^2 = 100 %) among studies.

In stratified analyses by region (Asia *v.* others), ingestion form (capsaicin *v.* active supplement), duration of study (4 weeks *v.* 6–12 weeks) or body type (overweight *v.* obese), capsaicin supplementation had none significant decrease on WHR (Table 2).

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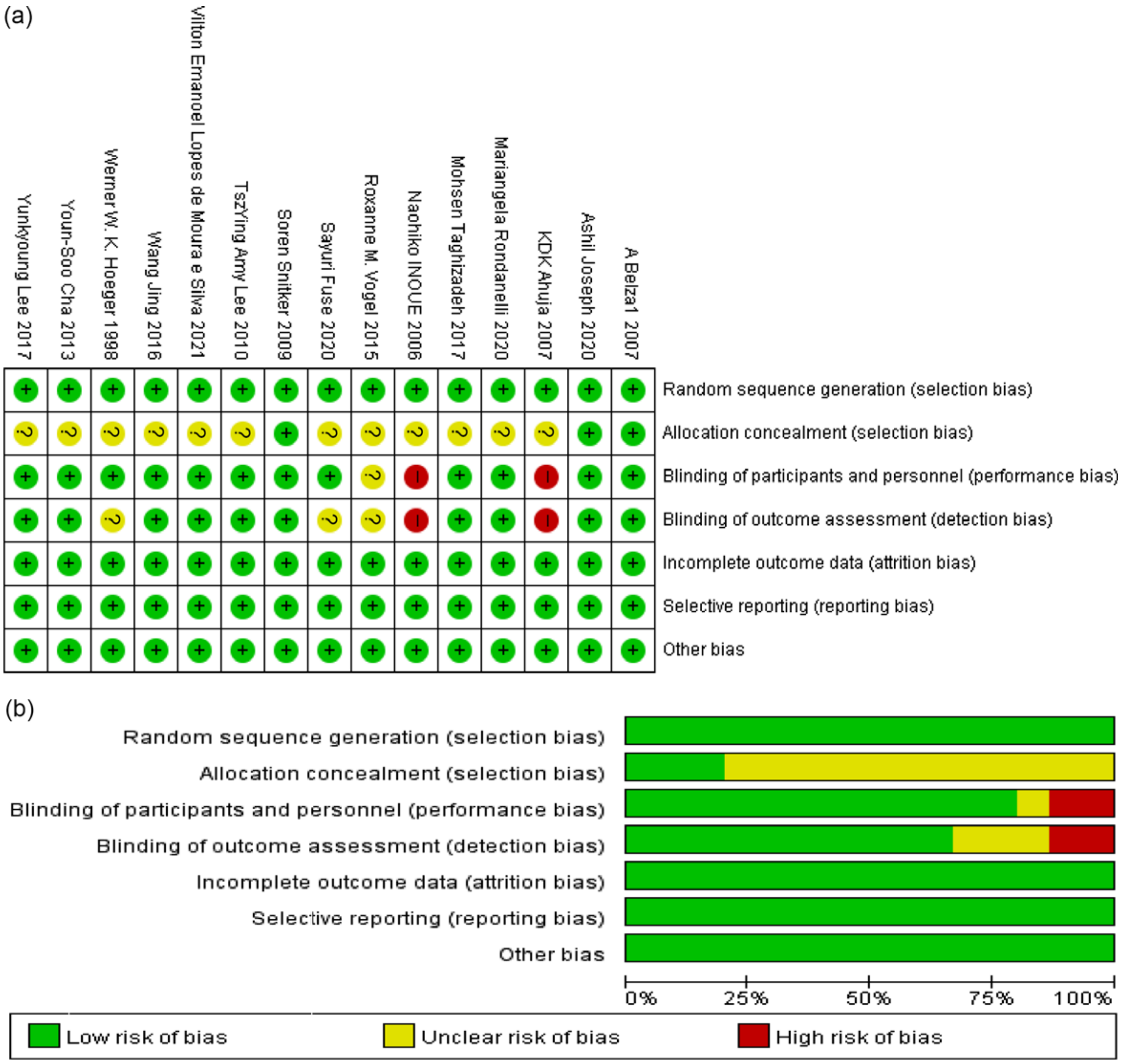

Fig. 2. The methodological quality of included trials on effect of capsaicin on body composition and metabolic profiles based on review authors' judgements about each risk of bias item presented as percentages across all included studies (a) and each risk of bias item for each included study (b).

Effect of capsaicin supplementation on waist circumference

Figure 6 shows the effect of capsaicin supplementation on WC was estimated in four studies. Compared with the control group, the study showed that capsaicin supplementation could significantly decrease WC (WMD: −1·12 cm, 95 % CI = −2·00, −0·24 cm, $P < 0{\cdot}05$) with high heterogeneity ($I^2 = 64{\cdot}4$ %) among studies.

In stratified analyses by the region (Asia *v.* others), capsaicin supplementation only had a significant decrease on WC in Asia category (WMD: −1·509 cm, 95 % CI = −2·335, −0664 cm; $I^2 = 64{\cdot}0$ %).

In stratified analyses by the body type (overweight *v.* obese), capsaicin supplementation only had a significant decrease on WC in overweight category (WMD: −1·121 cm, 95 % CI = −2·153, −0·088 cm; $I^2 = 73{\cdot}8$ %) (Table 2).

In stratified analyses by ingestion form (capsaicin *v.* active supplement) or duration of study (4 weeks *v.* 6–12 weeks), capsaicin supplementation had none significant decrease on WC (Table 2).

Sensitivity analysis

To estimate the reliability of the main result, sensitivity analysis was conducted by removing studies one by one to estimate the effect of each study on the combined data. Taking BMI as the outcome index to do sensitivity analysis of forest map, the results show that the deletion of each study has little impact on the combined effect, indicating that the difference between the included research literature is small, the research results are stable and the analysis results are more reliable. In sensitivity analysis, the results showed no significant differences between pre- and post-sensitivity pooled WMD for results (Table 3).

Publication bias

Egger's regression tests indicated no significant publication bias for meta-analyses of assessing capsaicin effect on BMI ($t = -1{\cdot}04$, $P = 0{\cdot}326$), BW ($t = -0{\cdot}79$, $P = 0{\cdot}445$), WHR ($t = -0{\cdot}63$, $P = 0{\cdot}575$) and WC ($t = 4{\cdot}04$, $P = 0{\cdot}056$).

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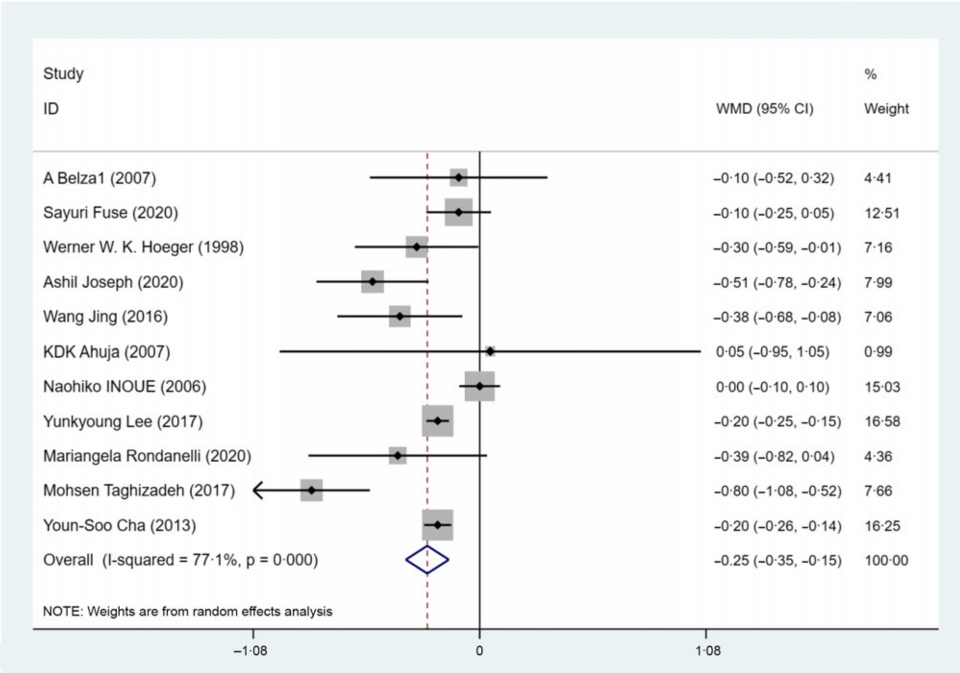

Fig. 3. Forest plot of the effect of capsaicin supplementation on BMI.

Table 2. The results of subgroup analyses (95 % confidence intervals)

Variable		Subgroups	Number of trials	Pooled effect estimate	95 % CI	I^2(%)	Overall I^2(%)
BMI	Region	Asia	7	−0·253	−0·371, −0·136	85·7	77·1
		Others	4	−0·259	−0·464, −0·054	0	
	Ingestion form	Capsaicin	5	−0·226	−0·414, −0·038	78·1	
		Active supplement	6	−0·284	−0·412, −0·157	73·4	
	Duration	4 weeks	5	−0·260	−0·521, 0·002	78·2	
		6–12 weeks	6	−0·251	−0·364, −0·137	75·6	
	Body type	Overweight	8	−0·176	−0·266, −0·087	69·5	
		Obese	3	−0·509	−0·846, −0·172	68·8	
BW	Region	Asia	5	−0·709	−1·209, −0·210	83·1	67·8
		Others	7	−0·230	−0·746, −0·286	31·0	
	Ingestion form	Capsaicin	8	−0·271	−0·591, 0·049	21·0	
		Active supplement	4	−0·946	−1·988, 0·095	87·9	
	Duration	4 weeks	5	−0·265	−0·789, 0·260	52·7	
		6–12 weeks	7	−0·681	−1·278, −0·085	76·3	
	Body type	Overweight	6	−0·329	−0·465, −0·193	0	
		Obese	5	−0·815	−1·957, 0·327	86·9	
WHR	Region	Asia	4	−0·060	−0·189, 0·068	100	100
		Others	1	−0·010	−0·026, 0·006	–	
	Ingestion form	Capsaicin	2	−0·015	−0·046, 0·015	93·6	
		Active supplement	3	−0·073	−0·215, 0·078	100	
	Duration	4 weeks	2	−0·015	−0·046, 0·015	93·6	
		6–12 weeks	3	−0·073	−0·215, 0·078	100	
	Body type	Overweight	4	−0·060	−0·189, 0·068	100	
		Obese	1	−0·010	−0·026, 0·006	–	
WC	Region	Asia	2	−1·509	−2·335, −0·664	64·0	64·4
		Others	2	−0·363	−1·591, 0·865	0	
	Ingestion form	Capsaicin	2	−0·892	−1·829, 0·045	0	
		Active supplement	2	−1·085	−2·824, 0·653	79·7	
	Duration	4 weeks	1	−0·890	−1·961, 0·181	–	
		6–12 weeks	3	−1·117	−2·326, 0·092	65·3	
	Body type	Overweight	3	−1·121	−2·153, −0·088	73·8	
		Obese	1	−0·900	−2·832, 1·032	–	

BW, body weight; WHR, waist-to-hip ratio; WC, waist circumference.
Overweight: 25 kg/m^2 ≤ BMI < 30 kg/m^2, obese: BMI ≥ 30 kg/m^2.

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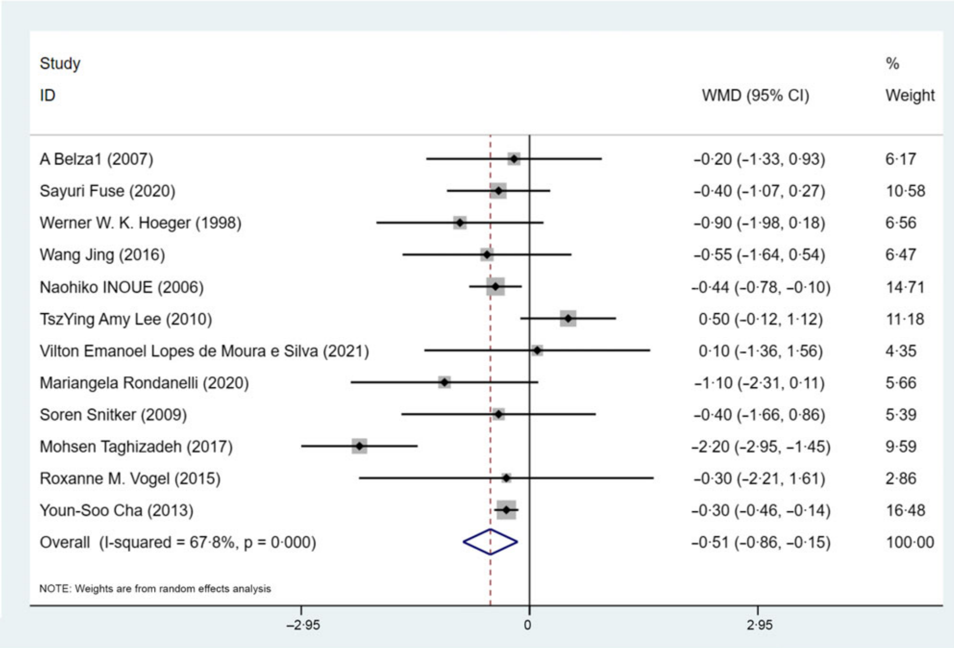

Fig. 4. Forest plot of the effect of capsaicin supplementation on body weight.

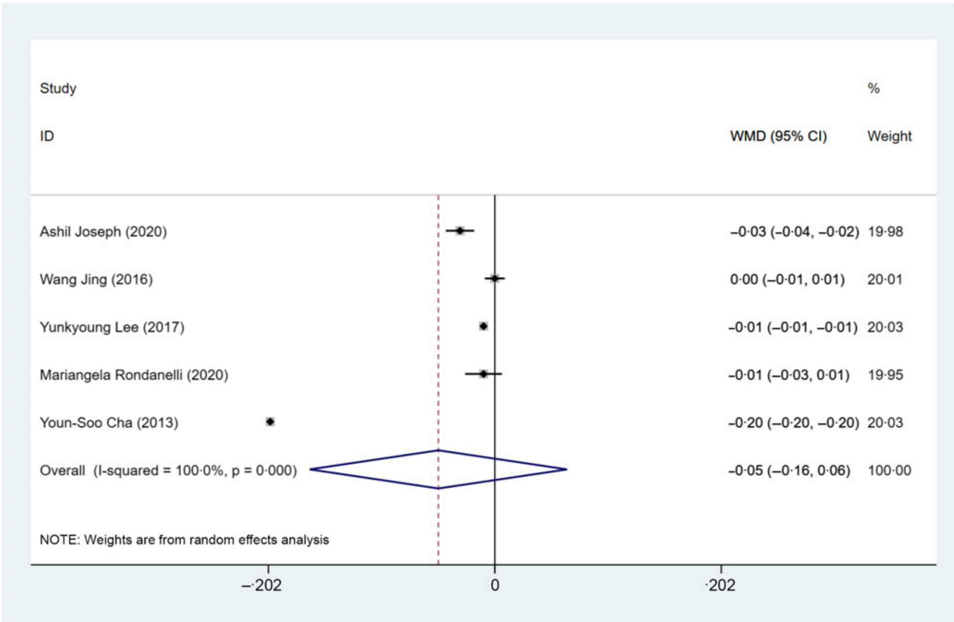

Fig. 5. Forest plot of the effect of capsaicin supplementation on waist to hip.

Discussion

In the present meta-analysis, with fifteen articles that totalled 762 participants, we found that capsaicin intervention consistently showed significant positive correlations with BMI, BW and WC, but did not affect WHR. It must be kept in mind that differences in regions, types of intervention, time of duration and body type, for example, overweight or obese, are important for interpreting the findings. The intervention included in the literature was to take capsaicin or capsaicin-containing active supplements. Evidence suggests that capsaicin compounds may play an important role in weight control, and the actual situation may be that it takes longer to intervene to produce more meaningful results. Controversial findings of individual studies investigating the effect of capsaicin on weight loss raise the possibility that some determining factors have not been considered yet.

The results of the current study were consistent with Stephen *et al.* which suggested that capsaicin and their sister compounds,

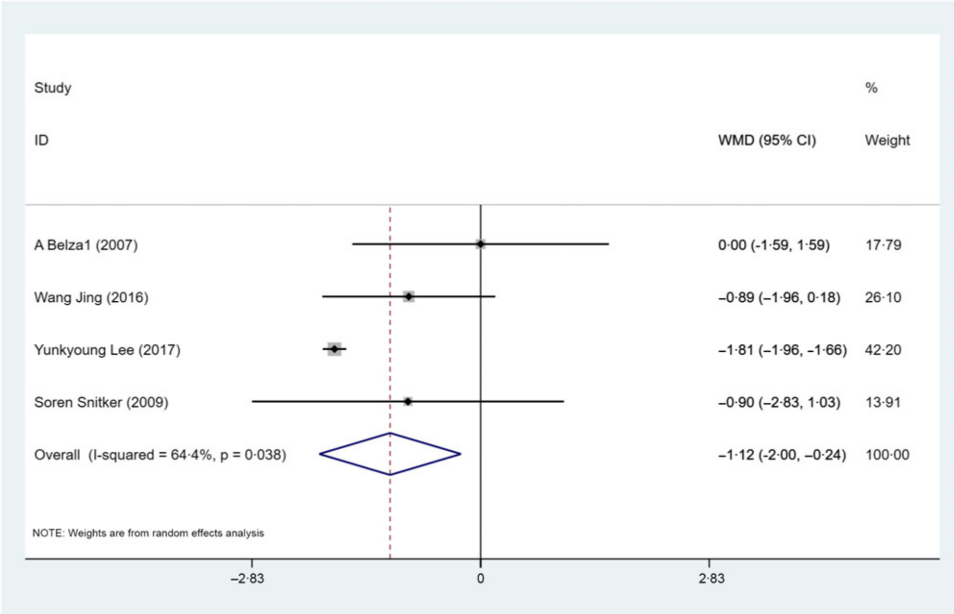

Fig. 6. Forest plot of the effect of capsaicin supplementation on waist circumference.

Table 3. The results of sensitivity analysis (95 % confidence intervals)

	Pre-sensitivity analysis				Post-sensitivity analysis		
Variable	No. of studies included	Pooled WMD (random effect)	95 % CI	Upper and lower of effect size	Pooled WMD (random effect)	95 % CI	Excluded studies
BMI	11	−0·25	−0·35, −0·15	Upper	−0·28	−0·42, −0·14	Yunkyoung Lee
				Lower	−0·25	−0·36, −0·14	Werner W. K. Hoeger
BW	12	−0·51	−0·86, −0·15	Upper	−0·31	−0·47, −0·15	Mohsen Taghizadeh
				Lower	−0·63	−98, −0·28	TszYing Amy Lee
WHR	5	−0·05	−0·17, −0·06	Upper	−0·06	−0·19,0·07	Yunkyoung Lee
				Lower	−0·06	−0·19, 0·07	Mariangela Rondanelli
WC	4	−1·12	−2·00, −0·24	Upper	−0·66	−1·47, 0·15	Yunkyoung Lee
				Lower	−1·48	−2·17, −0·79	A Belza1

WMD, weighted mean difference; BW, body weight; WHR, waist-to-hip ratio; WC, waist circumference.

capsaicin, could play a beneficial role in weight management[39]. In addition, data analysis of Csaba *et al.* showed that after ingestion of capsaicin or capsaicin the energy expenditure increased (245 kJ/d, $P = 0{\cdot}030$) and the RQ decreased ($P = 0{\cdot}031$) indicating a rise in fat oxidation[40]. Moreover, the study of Masayuki Saito and Takeshi Yoneshiro showed that a prolonged ingestion of capsaicin would recruit active brown adipose tissue and thereby increase energy expenditure and decrease body fat[41]. The potential mechanisms underlying this association were demonstrated by several studies. Evidence showed dietary chili has the potential to promote lipid oxidation[42], reduce appetite[43] and accelerate energy metabolism[44], which may have a certain impact on weight loss. The mechanism of increasing lipid oxidation and energy consumption is due to the activation of transient receptor potential vanilloid subtype 1 (TRPV1) channels[45]. Preclinical experiments have shown that capsaicin is a potent agonist of TRPV1. It is well accepted that the mechanism of action for this effect is caused by activation of the TRPV1 Ca channel, of which capsaicin is a potent antagonist[45]. A 2009 study found that capsaicin increased the energy metabolism in wild-type mice but not in TRPV1 knockout mice[46]. It seems TRPV1 activation causes the release of catecholamines, which stimulates the sympathetic nervous system via β-adrenoceptors[47]. In another trial, the use of β-adrenergic blocker propranolol abolished the increase in thermogenesis in human subjects[48]. There are also suggestions capsaicin may have an effect on other intestinal receptors[49]. It has been found that the TRPV1 channel of adipose tissue is damaged when human body is obese, but animal experiments show that long-term dietary capsaicin can significantly up-regulate the TRPV1 channel of adipose tissue and enhance its function, inhibit the related molecules of adipogenesis and thus inhibit the occurrence of obese induced by high fat in mice[50]. Interestingly, the effect on appetite, contrary to our perception that eating

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spicy food increases appetite, reduces appetite and increases satiety, but the mechanism of its effect on appetite is unclear. Acute lunches containing capsaicin have been shown to increase GLP-1 and tend to decrease auxin-releasing peptide, which may affect hunger[12]. It is also possible that the release of catecholamines caused by capsaicin affects appetite. Stimulating norepinephrine receptors to produce a sense of satiety is the pathway of most appetite suppressants[51].

In contrast to the abovementioned medical benefits of capsaicin consumption, some studies demonstrated possible negative effects of capsaicin. It is worth noting that a large population study in China (included 434 556 adults) recorded the relationship between spicy food consumption and anthropometric variables[16]. The results showed that there was a significant positive correlation between spicy food intake and anthropometric indicators in both men and women. The results of these studies contradict the results of the above meta-analysis, and the most likely is the difference between 'spicy food' with 'capsaicin'. In China, spicy foods often go hand in hand with oils and fats, such as the most common chili oil and chili sauce. Observational studies have not been able to separate the effects of capsaicin and oil, but RCT can. RCT requires the diet of the control group and the intervention group to be as consistent as possible except for capsaicin. That is, neither of these seemingly contradictory results actually looked at the same substance, and there is no way to compare them side by side.

Stratified analysis results showed that differences of region, body type of participants, as well as the duration of intervention and type of intervention all have some degree of influence on weight loss. This may have some reasons. One possible explanation may be Asian consumers prefer a 'sharp' heat in their chile peppers with 'more irritating' dihydrocapsaicin or 'irritating, harsh and very sharp' homodihydrocapsaicin, while the New Mexican pod-type, a favourite chile pepper for the southwestern USA, has mostly a 'flat' heat with 'least irritating' nordihydrocapsaicin[52]. Moreover, the effect of capsaicin intake on weight management of obese people was better than that of overweight people. Evidence also suggests that capsaicin has beneficial effects on lipid oxidation and centrally stored adipose tissue, with effects being more pronounced in obesity individuals. High body fat levels are associated with adverse health outcomes including CVD and the metabolic syndrome[53]. Regular consumption could therefore have major health benefits for takers, even without major weight change. An effect on central adipose tissue could offer particular health benefits, as it plays an important role in the development of CVD, as well as insulin resistance and type II diabetes[54].

There were several strengths in this study. First, the type of literature included in this study is the best evidence integration for evaluating interventions – RCT. Second, the indicators used in this study included BMI, BW, WHR and WC, and the changes of these indicators can clearly demonstrate the role of capsaicin in weight management. Moreover, a systematic and comprehensive search strategy was used to identify studies for this review to ensure relevant studies were captured and PRISMA guidelines were followed. Finally, subgroup analyses were undertaken to explore the potential sources of heterogeneity, and sensitivity analyses were performed to validate the current results.

However, our study also has several limitations. First, because there were few human-related RCT, the number of literatures that can be included in this study was limited. Second, the study did not include normal-weight or low-weight participants. Therefore, there are limits to the effect of capsaicin supplementation on weight management when generalised to all people. Third, some of the included literature did not provide data on the amount of change and standard deviation, so some parts needed to be manually calculated, which increased the possibility of error. However, we took great care to ensure the accuracy of the manual calculations and provided the formulas and raw data for readers to review. Fourth, because of the limited sample size and the difference of intervention measures taken of the included studies, larger samples and high-quality studies are therefore needed to obtain more reliable results. If the description of different sexes in RCT can be more detailed, it is expected to make a breakthrough in the analysis of sex differences in the future.

Conclusion

In summary, this systematic review and meta-analysis demonstrated that capsaicin intake has the potential to reduce BMI, BW and WC but did not affect WHR. The results suggest that dietary capsaicin supplementation could be considered as part of the weight management programme for overweight or obese individuals. Additional prospective studies investigating the effect of capsaicin supplementation on BMI, BW and WC are necessary.

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