A Meta-Analysis of Effect of Dietary Salt Restriction on Blood Pressure in Chinese Adults

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ABSTRACT

The aim of this study was to estimate the effects of dietary salt reduction on blood pressure (BP) in Chinese adults and the effects of China-specific cooking salt-reduction strategies (the use of salt substitutes and salt-restriction spoons). The PubMed and China National Knowledge Infrastructure databases were searched for studies satisfying the search criteria. Outcomes extracted from each included study were 24-h urinary sodium excretion, salt (sodium chloride) intake, and BP before and after dietary salt lowering. A random-effects meta-analysis was performed, and results were evaluated for evidence of publication bias and heterogeneity. Because most studies aggregated results for hypertensive and normotensive participants, estimates were made for hypertensive participants only and for hypertensive and normotensive participants combined. Six salt-restriction experiment studies (3,153 participants), 4 cooking salt-restriction spoon studies (3,715 participants), and 4 cooking salt-substitute studies (1,730 participants) were analyzed. In salt-restriction experiment studies, the pooled estimate of mean change in 24-h urinary sodium excretion in hypertensive participants was −163.0 mmol/day (95% confidence interval [CI]: −233.5 to −92.5 mmol/day), which was associated with a mean reduction of −8.9 mm Hg (95% CI: −14.1 to −3.7 mm Hg) in systolic BP. Each 1.00-g dietary salt reduction in hypertensive participants was associated with a reduction of 0.94 mm Hg in systolic BP (95% CI: 0.69 to 1.03 mm Hg). These systolic BP reductions in hypertensive participants were 1.71 times greater compared with the mixed hypertensive and normotensive group. Salt-restriction spoon studies demonstrated a 1.46-g decrease in daily salt intake level. The effect of salt-substitute use on systolic BP control was substantial among the hypertensive participants (−4.2 mm Hg; 95% CI: −7.0 to −1.3 mm Hg), but the change did not reach statistical significance in hypertensive and normotensive participants combined (−2.31 mm Hg; 95% CI: −5.57 to 0.94 mm Hg). Salt restriction lowers mean BP in Chinese adults, with the strongest effect among hypertensive participants. Future studies of salt-restriction strategies should be report results stratified by hypertension status and adjust for medication use.

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Blood pressure (BP) is one of the most important modifiable risk factors for cardiovascular diseases in China [1]. Mean national consumption is more than 12 g/day of salt (sodium chloride), a level higher than in most other countries [2,3]. Dietary salt reduction may be an effective population-wide approach to reducing disease burden attributable to elevated BP in China.

Dietary salt-lowering programs have been launched in China, but the effect of salt reduction on BP in Chinese adults has not been reviewed and summarized. Past meta-analyses reported that salt restriction was consistently and linearly associated with BP reduction, with greater BP reductions in hypertensive patients [4−6]. These studies showed larger reductions in BP associated with the same reductions in dietary salt in adults of recent African ancestry compared with Caucasians, but few participants of East Asian ancestry were selected for the studies reviewed [5,7].

Unlike in Western countries, most dietary salt is added in home cooking in China [3]. Culturally tailored cooking salt-restriction strategies have been developed that target salt added in cooking in China, including the use of cooking salt-restriction spoons and cooking salt substitutes [8−10]. The purpose of this meta-analysis was to summarize the effects of sodium restriction and sodium substitution on BP in Chinese adults.

METHODS

Eligibility criteria

To explore the effects of salt change on BP change in ethnic Chinese adults, salt-restriction studies were considered for review if they satisfied the following criteria: (1) papers reported on intervention studies or randomized controlled trials conducted in Chinese participants; (2) change in BP was due only to the change in sodium, that is, without other dietary changes; (3) salt intake was estimated by 24-h urinary sodium testing; (4) pre- and post-intervention mean salt intake and standard deviation were reported; (5) pre- and post-intervention or change in mean BP and standard deviation were reported; (6) duration of salt-reduction intervention was at least 1 week; and (7) participants were ≥35 years of age.

Cooking salt-restriction spoon studies only measured change in salt. We therefore explored the effect of salt-restriction spoon use on change in salt intake level alone. The inclusion criterion for salt-restriction spoon studies was salt intake level estimated by 24-h urinary test or salt directly weighed before cooking. Otherwise, the aforementioned criteria (1, 2, 4, 6, and 7) for salt-restriction studies were met (Online Table 1).

Cooking salt-substitute studies used a formulation composed of 65% sodium chloride, 25% potassium chloride, and 10% magnesium sulfate. As a result, the effect of salt substitution on BP was due to the contributions of multiple components, and BP could decrease because of lower sodium intake, higher potassium intake, or both. Salt-substitute studies measured changes in BP, urinary sodium, and urinary potassium. In recent studies, sodium and potassium were estimated from the first morning urinary collection. Because this measurement was not the gold standard, we analyzed only change in BP due to the salt substitute. Salt-substitute studies had to fulfill criteria 1, 5, 6, and 7 for salt-restriction studies (Online Table 1).

Outcome measures

The outcomes extracted from each study were the changes in sodium, salt, systolic BP, and diastolic BP. Data on region of China (north or south), mean and range of participants' ages, sex, and hypertension status were also extracted from the papers for the purpose of potential stratified analyses. Because most studies did not report on effects in hypertensive and normotensive participants separately, we were only able to stratify into groups of hypertensive participants only and the combination of hypertensive and normotensive participants.

Search strategy

Electronic databases, international conference reports, reference lists of articles, and a prior Cochrane review were searched by one study investigator (M.W.). We searched the National Library of Medicine's MEDLINE database for English-language papers and the China National Knowledge Infrastructure's database for articles written in Chinese. There were no language limits in the 2 search strategies. The last search was run on July 1, 2014. The search terms used in this study are listed in Table 1. For the search for cooking salt-restriction or salt-substitute intervention studies in China, we added the term "salt-restriction spoon" or "salt substitute" in the title, abstract, and key words, then screened any additional studies not captured in the original electronic search.

Study selection and data extraction

Two investigators (W.M. and A.M.) reviewed the included studies once full-text reports were obtained and results were translated into English. A third reviewer (D.Z.) resolved disagreement between the 2 primary reviewers. A data extraction sheet was developed to collect key information, including characteristics of the study and participants (age, sex, region, sample size, published year, and hypertension status of the participants), methods of intervention (type and duration), methods of salt intake measurement, pre- and post-intervention salt, urinary sodium and potassium, and BP for data collection and risk for bias estimation. Each study was evaluated to find any additional reporting on subgroups (such as data stratified by sex or hypertension status; Online Tables 1–4) [8–21].

Method of analysis

The meta-analysis was done using Stata 12 meta-analysis software (StataCorp LP, College Station, Texas) using random-effects models. The effect of salt intake change on BP was calculated by dividing the pooled change in BP (in millimeters of mercury) by the pooled change in reduced salt (1 g salt = 0.393 g sodium, 1 g sodium = 43.5 mmol sodium) from the meta-analysis. Only 1 study did not report the standard deviation of the post-intervention BP [19]. In this case, the standard deviation of pre-intervention BP was used as a proxy (Online Table 2). We qualitatively assessed the risk for bias in individual studies associated with the sampling strategy, study design, randomization, blinding, selection and use of control participants, intervention duration, and method of salt-intake estimation. Begg's and Egger's tests were also applied to quantify potential publication bias.

To assess for evidence of heterogeneity, we estimated the I^2 statistic. We also evaluated the data for effect measure modification by selected variables by conducting a meta–regression analysis with the change in systolic BP as the dependent variable and age (mean age of the participants in each study), sex, and hypertension status (hypertensive only or mixed hypertensive and normotensive) as the independent variables. A p value < 0.05 assigned to comparison of adjusted means was considered to indicate statistical significance.

RESULTS

Effect of salt restriction on BP

Six studies representing 3,153 participants were included in the meta-analysis of the effect of salt restriction on BP [16–21]. The summary changes in sodium (in millimoles per day) and BP are listed in Figures 1 to 3. In hypertensive participants, salt level decreased by 9.6 g (163.0 mmol sodium), which was associated with an 8.91 mm Hg systolic BP reduction and a 5.88 mm Hg diastolic BP reduction (Table 2). Each 1-g dietary salt reduction in hypertensive participants was associated with a reduction of 0.94 mm Hg (95% confidence interval [CI]: 0.69 to 1.03 mm Hg) in systolic BP and of 0.62 mm Hg (95% CI: 0.38 to 0.71 mm Hg) in diastolic BP. For the same dietary salt reduction, systolic BP change due to salt restriction was 1.71 times greater in the hypertensive-only group compared with the mixed hypertensive and normotensive group.

TABLE 1. Steps in selecting studies of the effect of salt intake reduction on blood pressure change in Chinese adults

Category		English-Language Papers	Chinese-Language Papers
Source		PubMed	CNKI
First step	Search strategy	Title/abstract: China or Chinese AND Title: salt or sodium AND Filters: human and adult ≥19 y	Title or keywords: salt or sodium AND Title or keywords: blood pressure AND Filters: core journals including SCI, EI, and CSSCI and extended search in Chinese and English
	Search result	147	139
Second step	Exclusion criteria	Did not report salt intake level OR Salt intake level was not estimated using 24-h urine test, and salt in condiments was not included OR Ages of participants all < 35 y	
	Number eligible	49	
Third step	Exclusion criteria	Did not report the mean and variance of blood pressure measured pre- and post-intervention OR Mean and variance of blood pressure change compared with pre-intervention	
	Number eligible	10	
Fourth step	Exclusion criteria	Data from the same study and population	
	Number eligible	8	
Fifth step	Exclusion criteria	With concomitant interventions, such as salt substitutes including potassium or magnesium	
	Number eligible	6	

CNKI, China National Knowledge Infrastructure; CSSCI, Chinese Social Sciences Citation Index; EI, Engineering Index; SCI, Science Citation Index.

Effects of cooking salt-restriction or salt-substitution interventions

Four cooking salt-restriction spoon studies represented 3,715 Chinese participants [8,13−15]. One study reported the resulting change in BP but did not report the standard deviation [8]. Other studies reported only change in dietary salt intake. The meta-analysis estimated that the use of salt-restriction spoons accompanied by educational materials could result in a reduction in salt of 1.46 g (95% CI: 0.52 to 2.40 g) after 3 to 12 months of follow-up (Fig. 4).

Four selected studies explored the effect of salt substitution on BP change in China [9−12]. Only 1 study reported the effect of salt substitution on BP in hypertensive participants alone (213 hypertensive participants) [9]. That study showed that the use of salt substitution was associated with a −4.2 mm Hg (95% CI: −7.0 to −1.3 mm Hg) change in systolic BP and a −0.6 mm Hg (95% CI: −2.6 to 1.4 mm Hg) change in diastolic BP in hypertensive patients [9]. Other studies enrolled 1,517 participants and evaluated the effect of salt substitution in a mix of normotensive and hypertensive participants. In those studies, salt substitution was associated with a nonsignificant −2.31 mm Hg (95% CI: −5.57 to 0.94 mm Hg) change in systolic BP compared with the control group (Fig. 5). All studies showed that the change in diastolic BP associated with salt substitution did not reach a statistically significant difference (Fig. 6).

Publication bias

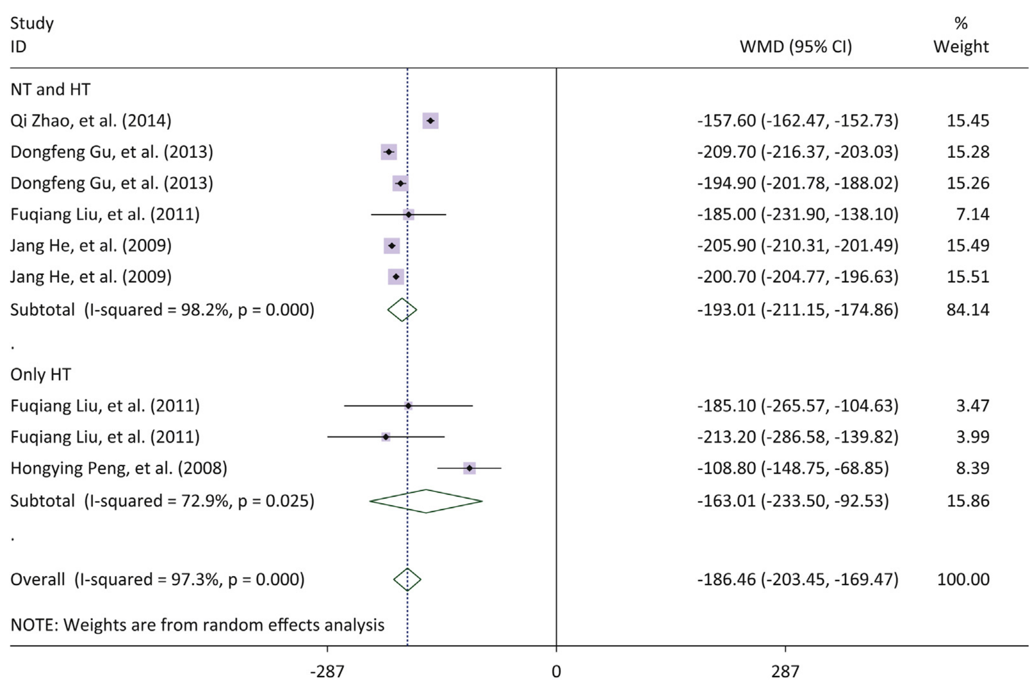
The results of Begg's and Egger's tests for systolic BP change among the studies suggested no evidence of publication bias ($z = 1.15$, $p = 0.251$) or a small study effect ($z = 1.15$, $p = 0.251$) (Online Figures 1 and 2). The same held true for sodium change ($z = 0.940$, $p = 0.348$) (Online Figures 3 and 4). Begg's and Egger's tests were not performed among the cooking salt-restriction intervention studies focused on salt-restriction spoon or salt-substitute use, because of the small number of studies included.

Effect modification by covariates

On the basis of the limited information available in the studies reviewed, we found that hypertensive status (compared with a mix of hypertensive and normotensive participants) was significantly associated with the magnitude of BP change with salt restriction ($p = 0.042$). No evidence of effect modification was found for the included studies' mean participant ages or proportions of female participants ($p > 0.05$ for all).

DISCUSSION

This meta-analysis is the first to summarize the effect of controlled salt restriction on BP change in Chinese participants and the effects of culturally tailored cooking salt-restriction spoons and a cooking salt substitute. The results suggest that Chinese adults can control elevated BP



NT, normotensive; HT, hypertensive; NT and HT, do not report the result by NT and HT status; WMD, weighted mean difference.
1g sodium chloride = 0.393g sodium, 1g sodium = 43.5 mmol sodium

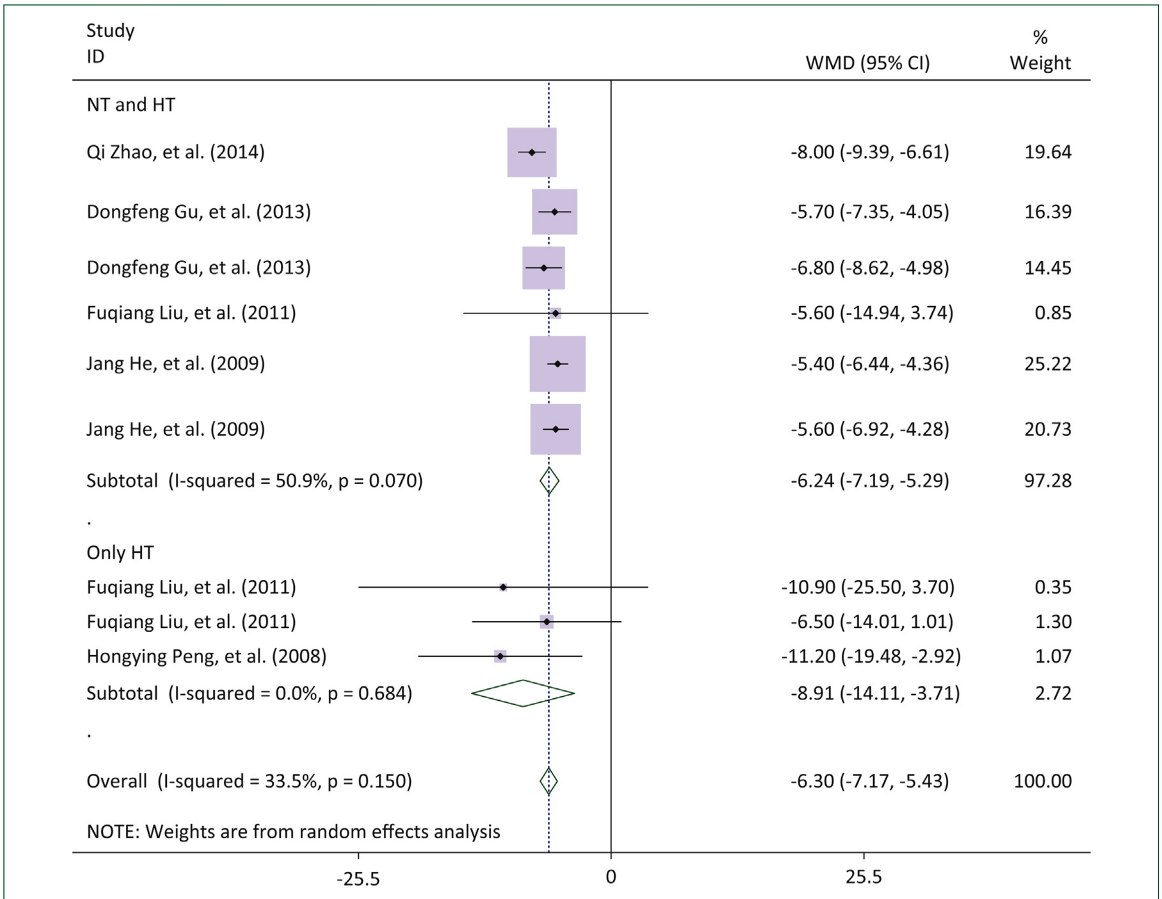
FIGURE 1. Meta-analysis of the change in sodium (mmol/day) after dietary salt reduction in Chinese adults. Conversions: 1 g sodium chloride = 0.393 g sodium, 1 g sodium = 43.5 mmol sodium. Some studies contributed more than 1 estimate, but each study participant's data was counted only once. "NT and HT" group: 6 participant groups from 4 studies were analyzed; normotensive and hypertensive were analyzed together because results were not reported stratified by hypertension status. In "only HT" group, 3 participant groups from 2 studies were analyzed. Details of the selected studies and participant groups are reported in Online Table 2. CI, confidence interval; HT, hypertensive; NT, normotensive; WMD, weighted mean difference.

by lowering dietary salt, most feasibly during home cooking. For the same dietary salt reduction, systolic BP change was much greater in the hypertensive-only group compared with the mixed hypertensive and normotensive group. Recent cooking salt-restriction spoon studies that reported only change in salt intake level showed that the intervention could achieve a 1.46-g (95% CI: 0.52 to 2.40 g) reduction in daily salt intake. The systolic BP change associated with the use of cooking salt substitutes was significant among the Chinese hypertensive participants but not in a mixture of normotensive and hypertensive participants.

Previous studies and meta-analyses found different BP responses to salt restriction among different ethnic groups [5–7]. A Cochrane systematic review and meta-analysis showed that the same salt reduction resulted in the largest BP reductions among hypertensive blacks, followed by, in order of diminishing BP reduction, hypertensive "Asians" (94% of 29 participants were South Asians living in London) [22], hypertensive whites, normotensive blacks, and normotensive whites [5]. The studies reviewed in that meta-analysis did not represent a substantial proportion of East Asian study participants. The NUTRICODE (Global Burden of Diseases Nutrition and Chronic Diseases Expert Group) explored the effect of salt change on BP by using metaregression in 160 salt-restriction trials, including 169 group comparisons [6]. Their results showed a significantly greater BP reduction for blacks compared with "nonblacks" (p for interaction < 0.001), but they did not make estimates for specific "nonblack" groups. Our comparison with the results for hypertensive and normotensive participants in other meta-analyses is limited, because only 2 of the 6 Chinese studies reported the effect of dietary salt restriction on the change in BP among hypertensive participants only [19,21], and only 1 study reported results in normotensive participants only [17]. In summary, past international meta-analyses demonstrated a diversity of BP responses to salt restriction among ethnic groups, but there has been limited evidence of the magnitude of BP effects among Chinese or other East Asian groups. Past meta-analyses have consistently shown greater BP reductions among hypertensive participants.

Evidence from studies of cooking salt-restriction or salt-substitution studies

China is already promoting the use of dietary salt-restriction spoons accompanied by an education



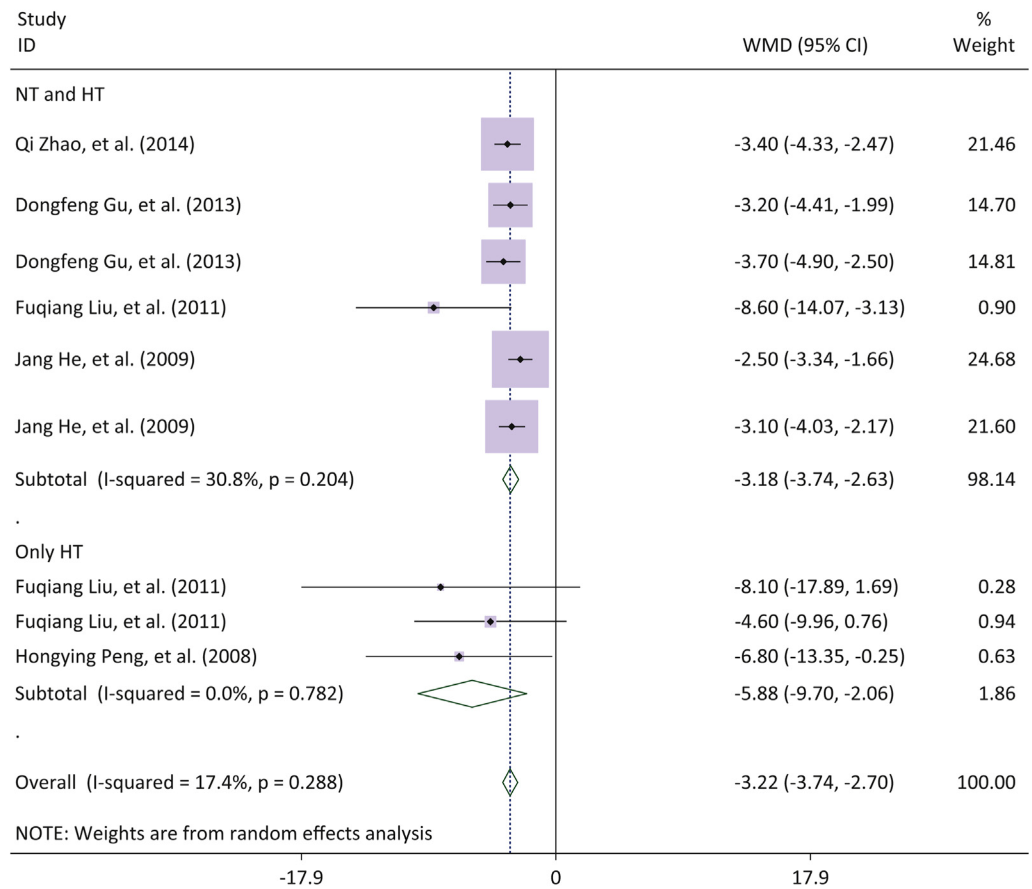
WMD, weighted mean difference.

FIGURE 2. Meta-analysis of the change in systolic blood pressure (mm Hg) after dietary salt reduction in Chinese adults. Some studies contributed more than 1 estimate, but each study participant's data was counted only once. "NT and HT" group: 6 participant groups from 4 studies were analyzed; normotensives and hypertensives were analyzed together because results were not reported stratified by hypertension status. In "only HT" group, 3 participant groups from 2 studies were analyzed. Details of the selected studies and participant groups are reported in Online Table 2. NT and HT, study does not report results by NT and HT status; other abbreviations as in Figure 1.

campaign that provides information about the harmful effects of high salt intake. Recent salt-restriction spoon studies in China only measured the effect of salt-restriction spoon use on salt intake and did not report change in BP. The results from the meta-analysis suggest that the use of salt-restriction spoons could result in a mean 1.46-g and a maximum 2.36-g decrease in daily salt intake among Chinese adults [15]. Only 4 studies reported enough data to evaluate the effect of salt-restriction spoon use on the change in salt intake level after 3 to 12 months of observation, and only 2 studies evaluated the salt intake change using the gold standard of a 24-h urinary test [8,14]. The other 2 studies evaluated salt intake level using the weighing method (direct weighing of crystalized salt and salt in condiments added before cooking) [13,15]. Another limitation of recent salt-restriction spoon studies was that no studies that enrolled both normotensive and hypertensive participants reported the effect of salt-restriction use stratified by hypertension status.

Effect of the potassium component of salt substitute on BP

A multinational meta-analysis showed that increased potassium intake would result in a 3.49 mm Hg reduction in systolic BP (95% CI: 1.82 to 5.15 mm Hg) [23]. The meta-analysis also showed that increased potassium intake seemed to significantly reduce BP only in adults with hypertension. For example, systolic BP among the hypertensive participants was associated with a 5.32 mm Hg (95% CI: 3.43 to 7.20 mm Hg) reduction after potassium-supplementation intervention, but among the normotensive participants, systolic BP was reduced by only 0.09 mm Hg (95% CI: −0.77 to 0.95 mm Hg) [23]. Chinese studies also showed the same pattern. In China, current use of salt



WMD, weighted mean difference.

FIGURE 3. Meta-analysis of the change in diastolic blood pressure (mm Hg) after dietary salt reduction in Chinese adults. Some studies contributed more than 1 estimate, but each study participant's data was counted only once. "NT and HT" group: 6 participant groups from 4 studies were analyzed; normotensives and hypertensives were analyzed together because results were not reported stratified by hypertension status. In "only HT" group, 3 participant groups from 2 studies were analyzed. Details of the selected studies and participant groups are reported in Online Table 2. Abbreviations as in Figures 1 and 2.

TABLE 2. Summary of the effect of salt restriction on salt intake or blood pressure change

	Number of Analysis Units*	NaCl Change (g)		SBP Change (mm Hg)		SBP Change/NaCl Change (mm Hg/g)†		DBP Change (mm Hg)		DBP Change/NaCl Change (mm Hg/g)†	
		Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Effect of salt change on BP											
Total	5 (9)	−10.9	(−11.9 to −9.9)	−6.30	(−7.17 to −5.43)	−0.58	(−0.60 to −0.55)	−3.22	(−3.74 to −2.70)	−0.30	(−0.31 to −0.27)
NT + HT‡	4 (6)	−11.3	(−12.4 to −10.2)	−6.24	(−7.19 to −5.29)	−0.55	(−0.58 to −0.52)	−3.18	(−3.74 to −2.63)	−0.28	(−0.30 to −0.26)
HT	2 (3)	−9.5	(−13.7 to −5.4)	−8.91	(−14.11 to −3.71)	−0.94	(−1.03 to −0.69)	−5.88	(−9.70 to −2.06)	−0.62	(−0.71 to −0.38)
Effect of salt-restriction spoon on NaCl change											
NT + HT‡	4 (4)	−1.46	(−2.40 to −0.52)	—	—	—	—	—	—	—	—
Effect of salt substitute on BP											
NT + HT‡	3 (3)	—	—	−2.31	(−5.57 to 0.94)	—	—	−0.85	(−1.76 to 0.05)	—	—
HT	1 (1)	—	—	−4.2	(−7.0 to −1.3)	—	—	−0.6	(−2.6 to 1.4)	—	—

Conversions: 1 g salt (sodium chloride) = 0.393 g sodium, 1 g sodium = 43.5 mmol sodium.
BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; HT, hypertensive; NaCl, sodium chloride; NT, normotensive; SBP, systolic blood pressure.
*Number of studies and study subgroups used in the meta-analysis. Some studies reported on more than 1 subgroup, but each subgroup was represented only once in the meta-analysis.
†BP change divided by the absolute value of salt intake change.
‡A mixture of hypertensive and normotensive; few studies reported results stratified on hypertension status.

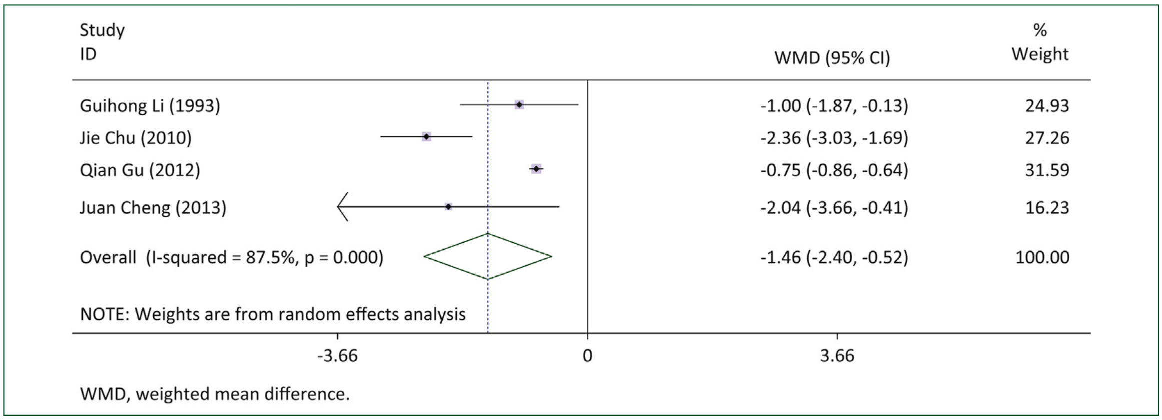


FIGURE 4. Effect of salt-restriction spoon use on sodium chloride consumption in Chinese adults. Except for Guihong Lin's study, in which 30 hypertensives were enrolled (1993), the other 3 studies enrolled both normotensives and hypertensives; results were not reported by hypertension status. Details in Online Table 3. Abbreviations as in Figure 1.

substitutes was composed of 65% sodium chloride, 25% potassium chloride, and 10% magnesium sulfate. Among the 4 studies, only 1 study explored the effect of salt-substitute use solely among hypertensive participants [9]. The other 3 potassium-supplementation studies explored the effect in a mixed group of hypertensive and normotensive participants and showed inconsistent results. So reporting on a mixture of normotensive and hypertensive participants may be the main reason why Chinese salt-substitute studies could not produce consistent results for salt-substitute use on BP control.

In this meta-analysis, we aimed to separate the effects of sodium change and potassium change on BP, but we lacked sufficient data to do so. First, the sodium and potassium changes in the 4 salt-substitute studies were all estimated by using the first morning urine collection. Then, we found among the 3 studies that showed changes in sodium and potassium levels that the change in urine sodium did not reach statistical significance (Online Table 4) [9,11,12]. Furthermore, sodium appeared to have in fact increased in 2 of the studies after intervention [11,12]. It may be that Chinese adults, accustomed to high sodium intake, might tend to add more salt substitute to satisfy their taste for sodium. The end result might be unchanged or increased total sodium intake coupled with increased potassium intake. So in recent Chinese salt-substitute studies, the effect of salt substitution on BP control might be more from potassium supplementation than from sodium restriction.

Limitations

This study is the first published meta-analysis of salt restriction and salt substitution studies in China, but conclusions to be drawn from the results are limited in several ways. Because of the limited number of Chinese studies, we estimated the effect of salt change on systolic BP by dividing mean systolic BP change by mean salt intake change. As a result, we were not able to demonstrate

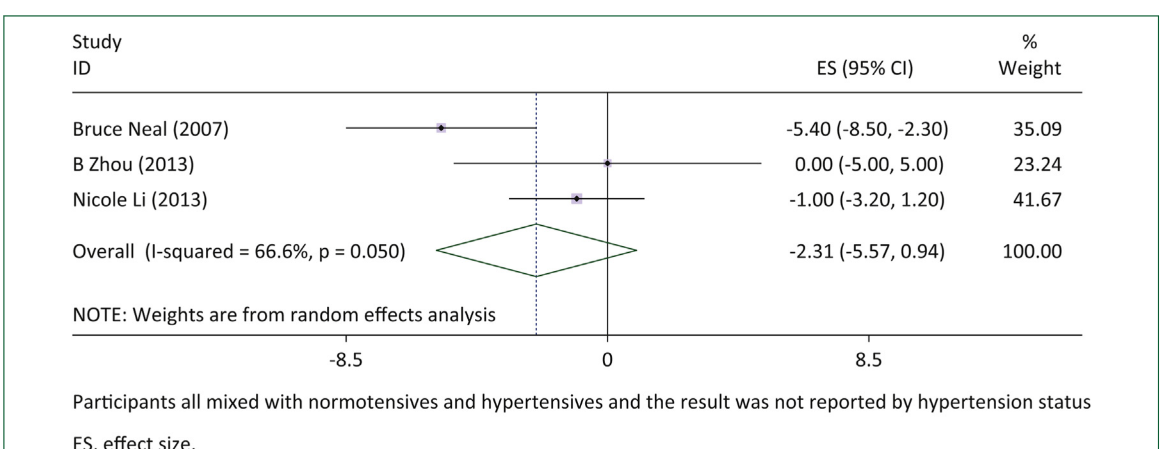
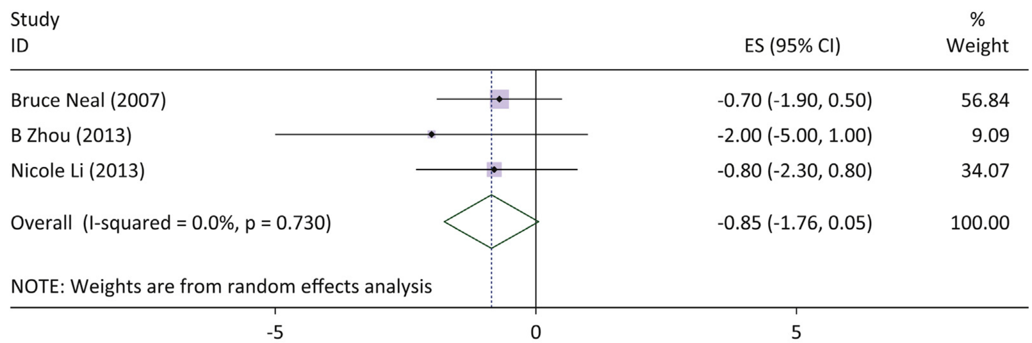


FIGURE 5. Effect of salt-substitute use on systolic blood pressure (millimeters of mercury) in Chinese adults. All studies enrolled a mixture of normotensives and hypertensives; results were not reported by hypertension status. Details in Online Table 4. CI, confidence interval; ES, effect size.



Participants all mixed with normotensives and hypertensives and the result was not reported by hypertension status

ES, effect size.

FIGURE 6. Effect of salt-substitute use on diastolic blood pressure (mm Hg) in Chinese adults. All studies enrolled a mixture of normotensives and hypertensives; results were not reported by hypertension status. Details in Online Table 4. Abbreviations as in Figure 5.

a linear, dose-response relationship between salt reduction and BP reduction in Chinese adults. The larger NUTRICODE analysis did find such a dose-response relationship (p for linearity < 0.001), so a similar linear effect should be expected among Chinese adults.

BP-lowering effects of certain antihypertensive drugs, such as loop or thiazide diuretics, are influenced by dietary sodium intake, and antihypertensive drugs initiated during follow-up might be the more important cause of BP lowering over time. Even on an international basis, salt-restriction studies have reported little information about the use of antihypertensive drugs among hypertensive participants. In a Cochrane systematic review and meta-analysis of 22 studies with hypertensive participants from different countries [5], though most studies (n = 19) considered the effect of antihypertensive drug use in their designs (enrolling untreated hypertensive participants or matching the antihypertensive drug use), only 32% of studies (7 of 22) clearly stated how they adjusted for antihypertensive medication use during the intervention or observation. The NUTRICODE meta-analysis found scant evidence about the potential confounding effects of antihypertensive drug use among hypertensive participants in the studies the investigators reviewed [6]. Among the 4 Chinese long-term salt-substitute studies, only 1 study clearly described adjustment for antihypertensive drug use both in the design and during the intervention [9], and 2 studies excluded potential participants using antihypertensive drugs at baseline but did not mention the approach to participants who initiated antihypertensive drug use during follow-up [11,12].

Hypertension status was a key factor influencing the observed changes in BP associated with salt restriction [5]. Among 13 Chinese salt-restriction experiment studies, only 3 studies showed results solely in hypertensive participants [9,19,21]. The effect of salt lowering on BP reduction among Chinese normotensive subjects is likely substantially less than that observed in the mixture of hypertensive and normotensive participants in the studies we found. Among the 6 studies that explored the effect of salt change on BP, 5 were short term (1 week in duration). The 4 included salt-substitute studies evaluated sodium and potassium intake through the first morning urinary test, but an overnight urine test may be much less accurate than the gold standard of a 24-h urinary test [24,25].

SUMMARY

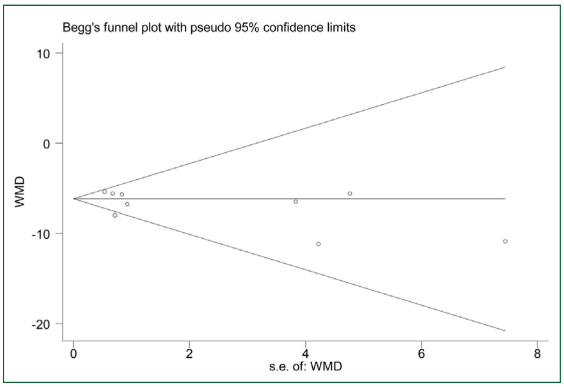
This meta-analysis estimated the magnitude of dietary salt intake and BP change that can be achieved in Chinese adults through salt restriction. For the same dietary salt reduction, systolic BP change was nearly 2-fold higher in hypertensive participants compared with a mixture of hypertensive and normotensive participants. Future studies of the effect of cooking salt-restriction strategies, such as salt-substitute or salt-restriction spoon interventions, should measure and report results by pre-intervention BP and adjust for antihypertensive drug use. This information is crucial, as one of the key questions for dietary salt programs is whether to apply the intervention to the whole population or restrict the intervention to adults with hypertension.

REFERENCES

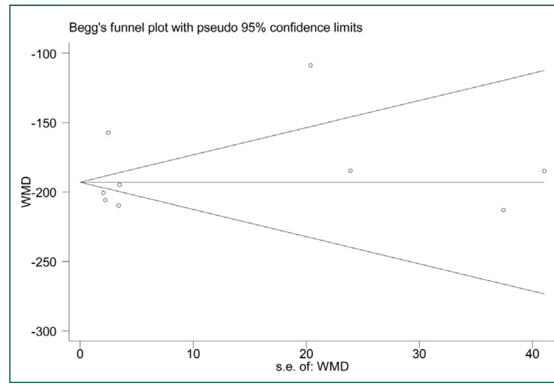
1. Wang Y, Liu J, Wang W, et al. Lifetime risk for cardiovascular disease in a Chinese population: the Chinese Multi-Provincial Cohort Study. Eur J Prev Cardiol 2014 May 12 [Epub ahead of print].
2. Anderson CA, Appel LJ, Okuda N, et al. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. J Am Diet Assoc 2010;110:736–45.
3. Xi B, Hao Y, Liu F. Salt reduction strategies in China. Lancet 2014;383:1128.
4. He FJ, MacGregor GA. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens 2002;16:761–70.
5. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ 2013;346:f1325.

6. Mozaffarian D, Fahimi S, Singh GM, et al. Global sodium consumption and death from cardiovascular causes. N Engl J Med 2014;371:624–34.
7. Bray GA, Vollmer WM, Sacks FM, et al. A further subgroup analysis of the effects of the DASH diet and three dietary sodium levels on blood pressure: results of the DASH-Sodium Trial. Am J Cardiol 2004;94:222–7.
8. Chen J, Tian Y, Liao Y, et al. Salt-restriction-spoon improved the salt intake among residents in China. PLoS One 2013;8:e78963.
9. Hu J, Zhao L, Li X, et al. Effects of salt substitution on blood pressure using home measurements in essential hypertensive patients. Chinese J Hypertens 2014;22:42–6.
10. Li N, Yan LL, Niu W, et al. A large-scale cluster randomized trial to determine the effects of community-based dietary sodium reduction-the China Rural Health Initiative Sodium Reduction Study. Am Heart J 2013;166:815–22.
11. China Salt Substitute Study Collaborative Group. Salt substitution: a low-cost strategy for blood pressure control among rural Chinese. A randomized, controlled trial. J Hypertens 2007;25:2011–8.
12. Zhou B, Wang HL, Wang WL, et al. Long-term effects of salt substitution on blood pressure in a rural north Chinese population. J Hum Hypertens 2013;27:427–33.
13. Gu Q, Lu W. The project of salt intake intervention in Shanghai. Shanghai, China: Fudan University; 2012.
14. Lin G, Gong Q, Yao C, et al. The evaluation of salt-restriction spoon use with education in population. Chinese J Health Educ 1993;9:24–6.
15. Chu J, Ma J, Guo X, et al. Study on intervention effect of salt measuring spoons and scaled oil pots for rural residents in Shandong province. Chinese Prev Med 2010;11:1104–7.
16. Gu D, Zhao Q, Chen J, et al. Reproducibility of blood pressure responses to dietary sodium and potassium interventions: the GenSalt study. Hypertension 2013;62:499–505.
17. Liu F, Mu J, Yuan Z, et al. Potassium supplement ameliorates salt-induced haemostatic abnormalities in normotensive subjects. Acta Cardiol 2011;66:635–9.
18. He J, Gu D, Chen J, et al. Gender difference in blood pressure responses to dietary sodium intervention in the GenSalt study. J Hypertens 2009;27:48–54.
19. Liu F, Mu J, Yuan Z, et al. Involvement of the lymphatic system in salt-sensitive hypertension in humans. Med Sci Mon 2011;17:CR542–6.
20. Zhao Q, Gu D, Chen J, et al. Blood pressure responses to dietary sodium and potassium interventions and the cold pressor test: the GenSalt replication study in rural North China. Am J Hypertens 2014;27:72–80.
21. Peng H, Wang Y, Mei X. Effect of dietary salt restriction on blood pressure of hypertensive patients with chronic kidney disease. Chinese J Pract Intern Med 2008;28:280–2.
22. He FJ, Marciniak M, Visagie E, et al. Effect of modest salt reduction on blood pressure, urinary albumin, and pulse wave velocity in white, black, and Asian mild hypertensives. Hypertension 2009;54:482–8.
23. Aburto NJ, Hanson S, Gutierrez H, et al. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. BMJ 2013;346:f1378.
24. Ji C, Sykes L, Paul C, et al. Systematic review of studies comparing 24-hour and spot urine collections for estimating population salt intake. Rev Panam Salud Publica 2012;32:307–15.
25. Mente A, O'Donnell MJ, Dagenais G, et al. Validation and comparison of three formulae to estimate sodium and potassium excretion from a single morning fasting urine compared to 24-h measures in 11 countries. J Hypertens 2014;32:1005–14.

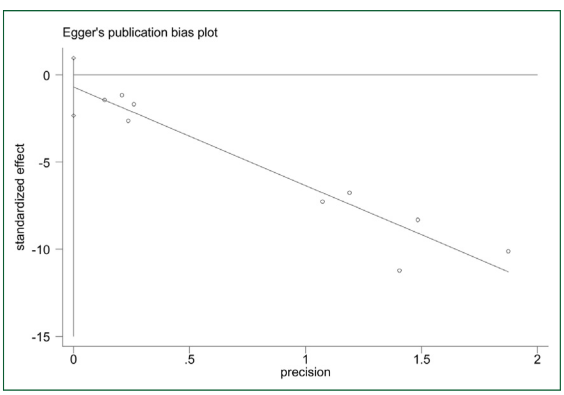
APPENDIX



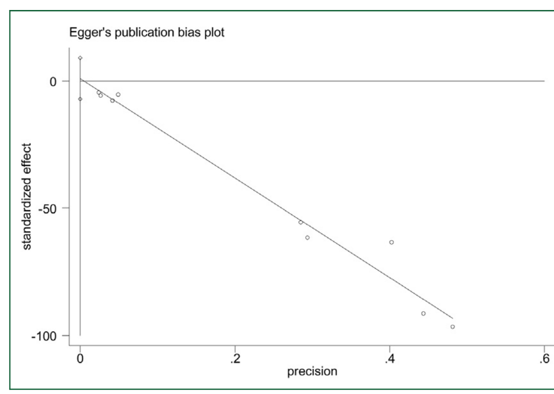
ONLINE FIGURE 1. Begg's test of systolic blood pressure change. s.e., standard error; WMD, weighted mean difference.



ONLINE FIGURE 3. Begg's test of sodium intake change. s.e., standard error; WMD, weighted mean difference.



ONLINE FIGURE 2. Egger's test of systolic blood pressure change.



ONLINE FIGURE 4. Egger's test of sodium intake change.

ONLINE TABLE 1. Inclusion criteria of salt-restriction and salt-substitute studies

Inclusion Criterion	Salt Reduction	Cooking Salt-Restriction Spoon	Cooking Salt Substitute
Papers reported on intervention studies or randomized controlled trials conducted in Chinese participants	√	√	√
Change in BP was due only to the change in sodium, that is, without other dietary changes	√	√	
Salt intake was estimated by 24-h urinary sodium testing	√		
Pre- and post-intervention mean levels of salt intake and standard deviations were reported	√	√	
Pre- and post-intervention mean BP and standard deviation were reported	√		√
Duration of salt-reduction intervention was at least 1 wk	√	√	√
Participants were ≥35 y of age	√	√	√
Salt intake level was estimated by 24-h urinary test or if NaCl was directly weighed		√	

BP, blood pressure; NaCl, sodium chloride.

ONLINE TABLE 2. Extracted data from studies exploring the effect of salt change on BP level

First Author [Ref. #]	Year	Mean Age	Male (%)	Sample Size	BP Category	Intervention Duration (wk)	Sodium Before Intervention (mmol)		Sodium After Intervention (mmol)		Mean of Sodium Change (mmol)	Category	BP Before Intervention (mm Hg)		BP After Intervention (mm Hg)		Risk of Bias Estimation			
							Mean	SD	Mean	SD			Mean	SD	Mean	SD	Population	Blinding	Control	Method
Qi Zhao [20]	2014	48	56	695	HT and NT	1	220.4	59.3	62.8	27.8	−157.6	SBP	124.5	14.5	116.5	11.9	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	80.4	9.3	77.0	8.4				
Dongfeng Gu [16]	2013	40	49	487	HT and NT	1	258.8	73.2	49.1	16.7	−209.7	SBP	118.1	13.5	112.4	12.7	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	74.3	9.8	71.1	9.4				
Dongfeng Gu [16]	2013	44	49	487	HT and NT	1	249	75.1	54.1	18.8	−194.9	SBP	123.3	15.4	116.5	13.6	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	80.4	9.9	76.7	9.2				
Fuqiang Liu [17]	2011	49	55	20	NT	1	225.1	105.8	40.1	16.1	−185.0	SBP	118.1	18.2	112.5	11.1	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	81.9	9.4	73.3	8.2				
Fuqiang Liu [19]	2011	43	67	9	HT	1	235.1	121	50	23	−185.1	SBP	129.4	15.8	118.5	15.8*	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	83.7	10.6	75.6	10.6*				
Fuqiang Liu [19]	2011	45	61	18	HT	1	267.2	158.3	54	13	−213.2	SBP	120.1	11.5	113.6	11.5*	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	80.8	8.2	76.2	8.2*				
Jiang He [18]	2009	39	100	1,010	HT and NT	1	251.1	69.8	45.2	15.9	−205.9	SBP	118.7	12.8	113.3	11.1	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	75.6	9.9	73.1	9.3				
Jiang He [18]	2009	38	0	896	HT and NT	1	232.7	61.6	32	8	−200.7	SBP	114.9	15.4	109.3	13	Community based; low risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	71.7	10.5	68.6	9.5				
Hongying Peng [21]	2008	46.5	56	18	HT	8	243.8	71.2	135	49.1	−108.8	SBP	142.3	13.5	131.1	11.8	Hospital based; high risk	Not mentioned; unclear	Self-control study; low risk	24-h urinary test; low risk
												DBP	91.5	9.3	84.7	10.7				

Conversions: 1 g sodium chloride = 0.393 g sodium, 1 g sodium = 43.5 mmol sodium.

BP, blood pressure; DBP, diastolic blood pressure; HT, hypertensive, NT, normotensive; SBP, systolic blood pressure; SD, standard deviation.

*The study did not show the standard deviation of the post-intervention blood pressure level, so use the pre-intervention standard deviation instead.

ONLINE TABLE 3. Extracted data from the effect of salt-restriction spoon studies

First Author [Ref. #]	Year	Mean Age	Male (%)	Sample Size	BP Category	Intervention Duration (mo)	NaCl Before Intervention (g)		NaCl After Intervention (g)		Risk for Bias Estimation			
							Mean	SD	Mean	SD	Population	Blinding	Control	Method
Juan Cheng [8]	2013	T: 54.7 C: 51.9	—	99	HT and NT	6	11.94	6.19	9.91	5.43	Community based; low risk	Blind to allocation, low risk	Control from same community, high risk	24-h urinary test; low risk
Qian Gu [13]	2012	45.4	48	2,736	HT and NT	12	7.13	2.08	6.38	1.93	Community based; low risk	Not applicable	Self-control study; low risk	Weighing method including condiments; low risk
Jie Chu [15]	2010	54.1	40	850	HT and NT	12	13.56	7.36	11.2	6.76	Community based; low risk	Not applicable	Self-control study; low risk	Weighing method including condiments; low risk
Guihong Lin [14]	1993	T: 59.2 C: 61.1	—	30	HT	3	6.3	1.81	5.3	1.61	Hospital based; high risk	Not mentioned; unclear	Control from clinical patients, low risk	24-h urinary test; low risk

Conversions: 1 g sodium chloride = 0.393 g sodium, 1 g sodium = 43.5 mmol sodium.
C, control group; NaCl, sodium chloride; T, treatment group; other abbreviations as in Online Table 2.

ONLINE TABLE 4. Extracted data from the effect of salt-substitute studies

First Author [Ref. #]	Year	Mean Age	Male (%)	Sample Size	Participants	Time Point	Intervention Group (mmol/L)		Control Group (mmol/L)
							Na*	K*	Na*
Jihong Hu [9]	2014	T: 57 C: 58	T: 34 C: 40	T: 110 C: 110	HT	Baseline 12 mo	125.5 (80.4 to 150.3) 122.5 (83.9 to 160.3)	20.7 (13.6 to 32.4) 40.5 (24.7 to 70.5)	126.9 (97.1 to 152.0) 124.2 (80.0 to 160.6)
Nicole Li [10]	2013	T: 66 C: 66	T: 50 C: 50	T: 2,521 C: 2,529	HT and NT	Baseline 18 mo	— —	— —	— —
B Zhou [12]	2013	T: 47 C:46	T: 50 C: 49	T: 224 C: 238	HT and NT	Baseline 24 mo	175 (139 to 201) 177 (137 to 261)	26 (17 to 42) 29 (18 to 45)	170 (134 to 233) 184 (108 to 228)
Bruce Neal [11]	2007	T: 59 C: 61	T: 48 C: 42	T: 319 C: 300	HT and NT	Baseline 12 mo	151 (92 to 201) —	20 (12 to 31) —	154 (94 to 200) —

Conversion: 1 g sodium chloride = 0.393 g sodium, 1 g sodium = 43.5 mmol sodium.

CI, confidence interval; K, potassium; Na, sodium; other abbreviations as in Online Tables 2 and 3.

*Mean and interquartile range, estimated by using first morning urinary test.

ONLINE TABLE 4. Continued

Control Group (mmol/L)	Change Compared With Control (mmol/L)		Change in BP (mm Hg)			Risk for Bias Estimation		
K*	Na*	K*	Category	Mean	95% CI	Population	Blinding	Control
24.3 (13.7 to 24.3) 28.6 (17.8 to 55.6)	—	—	SBP DBP	−4.2 0.6	(−7.0 to −1.3) (−2.6 to 1.4)	Community based; low risk	Blind to treatment; low risk	Control from same region; unclear
— —	—	—	SBP DBP	−1.0 −0.8	(−3.2 to 1.2) (−2.3 to 0.8)	Community based; low risk	Not mentioned; unclear	Control from other community; low risk
25 (16 to 42) 29 (18 to 51)	—	—	SBP DBP	0 −2.0	(−5.0 to 5.0) (−5.0 to 1.0)	Community based; low risk	Blind to treatment; low risk	Control from other family; low risk
20 (14 to 31) —	8 (−3.3 to 19.2)	7.2 (2.2 to 12.3)	SBP DBP	−5.4 −0.7	(−8.5 to −2.3) (−1.9 to 0.5)	Community based; low risk	Blinded to study investigators and participants; low risk	Control from same region; unclear