REVIEW

Association between the Urinary Sodium to Potassium Ratio and Blood Pressure in Adults: A Systematic Review and Meta-Analysis

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ABSTRACT

While sodium and potassium are individually important for blood pressure (BP) regulation, the relative contribution of sodium to potassium intake has not been sufficiently investigated. This study aimed to evaluate the association between urinary sodium to potassium ratio (UNa: K) and systolic and diastolic BP in adults. A systematic review (PROSPERO; CRD42016035296) was conducted and was reported according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Three scientific databases (MEDLINE, Scopus, Web of Science) were searched to March 2020 while reference lists of included articles were further hand-searched. Randomized controlled trials (RCT), cohort and cross-sectional studies that assessed 24-h urinary excretion in adults were included. Data from eligible studies were extracted and summarized. Random effects meta-analysis was conducted on RCT data to assess standardized mean differences (SMD) in systolic and diastolic BP according to 24-h UNa: K. Thirty-nine studies were included. Meta-analysis of 5 RCTs found a lower UNa: K ratio to be associated with a significantly greater reduction in systolic and diastolic BP compared with a higher UNa: K ratio [SMD: −1.09 (95% CI: −1.91, −0.28) mmHg and −1.42 (95% CI: −2.24, −0.59) mmHg, respectively]. Heterogeneity between RCTs was observed in systolic and diastolic BP ($I^2 = 97\%$, $P < 0.0001$ and $I^2 = 98\%$, $P < 0.0001$, respectively). The current body of evidence demonstrates that a lower 24-h UNa: K ratio is associated with lower BP in adults. Dietary strategies to achieve an increase in potassium while at the same time lowering sodium would be beneficial in lowering BP. *Adv Nutr* 2021;12:1751–1767.

Keywords: hypertension, pre-hypertension, DASH diet, dietary patterns, sodium, potassium, public health, sodium-to-potassium ratio

Introduction

Hypertension and hypertension-related diseases such as stroke, renal dysfunction, and ischemic heart disease are major global health challenges. In addition, high blood pressure (BP) is one of the leading risk factors for cardiovascular disease globally (1). Despite the well-acknowledged relationship between a Western dietary pattern and lifestyle-related diseases (2), effective strategies to encourage the adoption of healthier dietary patterns have not been widely implemented. Dietary sodium and potassium intake are important in the etiology and pathogenesis of hypertension. Numerous studies, including the large ecological INTERSALT study, have demonstrated the influence and association of dietary sodium intake on BP (3). Two meta-analyses concluded that reduced dietary sodium intake resulted in reduced BP in both normotensive and hypertensive participants (4, 5) but there was a noticeably greater reduction in systolic BP (SBP) in hypertensive participants. Furthermore, 2 randomized double-blinded crossover clinical trials (RCTs) have demonstrated that restricting dietary sodium in pre-hypertensive individuals results in a gradual, significant decrease in BP (6, 7).

Conversely, an inverse association between BP and both dietary potassium intake and urinary potassium excretion has been shown in adults (3). Potassium supplementation has resulted in significant reductions in BP (8, 9); however, similar to sodium interventions, the benefits vary across the range of BP distribution.

The Dietary Approaches to Stop Hypertension (DASH) diet includes both low sodium and high potassium sources of food to collectively reduce SBP and diastolic BP (DBP) (10–12) within a whole-of-diet eating plan. The degree to

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Abbreviations used: ADA, American Dietetic Association; BP, blood pressure; DASH, Dietary Approaches to Stop Hypertension; DBP, diastolic blood pressure; NHMRC, National Health and Medical Research Council; RCT, randomized controlled trials; SBP, systolic blood pressure; SMD, standardized mean differences; UNa: K, urinary sodium to potassium ratio.

which the DASH diet beneficially lowers BP varies between normotensive, pre-hypertensive, and hypertensive adults (13). Two short-term RCTs showed that the DASH diet in participants with hypertension had a greater reduction in BP than in their normotensive counterparts (11, 12).

It has been suggested that the ratio of sodium to potassium intake could be more important than the intake of either of these minerals alone (14–16). An analysis of the Japanese Nagahama study cohort reported that spot urine samples of sodium and potassium concentrations ($n = 18{,}505$) were positively correlated with BP, but that this association was steeper in older groups (17).

Given a lack of synthesis of the evidence to date, we conducted a systematic literature review to identify the association between urinary sodium to potassium ratio (UNa: K) and BP in adults.

Methods

This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO), (http://www.crd.york.ac.uk/PROSPERO, registration number: CRD42016035296). The PICO (problem, intervention, comparison, outcome) question investigated was "Does a low versus high urinary sodium-to-potassium ratio result in BP reduction in adults?" Search terms and combinations relating to sodium to potassium ratio and hypertension were used, including: "sodium potassium ratio" OR "sodium to potassium ratio" OR "sodium-potassium ratio" OR "Na: K ratio" OR "sodium/potassium ratio" OR "Na/K ratio" OR "sodium: potassium ratio" AND "blood pressure" OR "hypertension." In addition, hand-searching of reference lists of retrieved articles was undertaken. Three databases were searched; Scopus, Web of Science, and MEDLINE (Ovid), and all years of publication included until 30 March, 2020.

Types of studies eligible for inclusion were RCTs, cohort studies, and cross-sectional studies. Inclusion criteria were: *1*) studies published in English; *2*) conducted in adults over 18 years; *3*) assessment of UNa: K using 24-h urine collections; and *4*) reporting a primary outcome of measured office or ambulatory 24-h SBP and DBP.

Exclusion criteria included: *1*) non-English articles; *2*) animal studies; and *3*) studies of potassium supplementation. All retrieved studies were exported to EndNote (EndNote X7, Thomson Reuters, 2014) and Excel (Microsoft Excel 2013, Redmont, WA) to identify any duplicates. Relevant studies were screened based on title and abstracts by 3 authors (RN; RI; RH), and full-text articles retrieved for further screening.

Assessment of level of evidence and quality rating

Data was extracted to summary tables, to include: the year of publishing; the country the study was conducted in; characteristics of study participants; urinary sodium and potassium; sodium to potassium ratio; study type; intervention method; change in SBP and DBP; regression coefficients for cross-sectional studies; quality rating and level of evidence. The level of evidence of all included studies was categorized according to Australian National Health and Medical Research Council (NHMRC) criteria, while the quality of the studies was assessed using the American Dietetic Association (ADA) Evidence Analysis Manual quality rating criteria checklist (18). The quality rating included questions relating to relevance and validity of the research studies in terms of study design, execution, statistical analysis, results, conclusions, and sponsorship. Data extraction and quality rating was conducted by two authors (RN, RI) and consensus reached with a third author (KC). In the case of missing data, of interest in the included studies, primary authors were contacted by email, with 1 follow-up email in the case of non-response.

Meta-analysis

Cochrane Review Manager Software, RevMan Version 5.3 (The Cochrane Collaboration, Copenhagen) was used to conduct a meta-analysis of identified RCTs. Random effects meta-analysis was conducted to calculate standardized mean differences (SMD) (with 95% CI) in change or final values for systolic and diastolic BP. Study groups were categorized as "lower sodium to potassium ratio" (experimental) and "higher sodium to potassium ratio" (control). In cases where there were more than 2 groups, study group data were pooled for analysis whereby data from groups that reduced Na: K ratio over the course of the study were compared with groups with increased Na: K ratio. Heterogeneity of the meta-analysis was determined using X^2 and I^2 tests with 75% considered as substantial heterogeneity (19).

Results

The literature search resulted in 734 articles after removal of duplicates, with 28 full papers included in this review (**Figure 1**). Articles included 6 RCTs (20–25) (only 5 of which were included in the meta-analysis since 1 was a quasi-experiment (24)), 2 cohort studies (14, 26), and 20 cross-sectional studies. All the 28 studies conducted 24-h urinary analysis at baseline, which is considered the "gold standard" measure for objectively assessing urinary sodium and potassium excretion (27) (**Tables 1** and **2**). Of these studies, 8 were conducted in China (15, 28–30, 29, 31, 32), 4 in the United States (21, 24, 25, 33), 2 in the United Kingdom (34, 35), and 3 in Australia (22, 36, 37, 38). One was a global study (39) while the remaining studies were from Indonesia (40), Switzerland (41), Iran (42), Korea (43), Mexico (44), South Africa (16), Canada (23), and Zaire (45).

Methods to assess urinary Na: K concentrations were either the ion-specific electrode method (28–30, 29, 31–33, 35–37, 40, 41, 43) or emission flame photometry (30, 31). In the 24-h urinary studies, collections were deemed to be incomplete if urinary volumes were low (i.e., less than 400 mL (30), 500 mL (30, 36, 40), or 1L (37, 43) per day) and/or

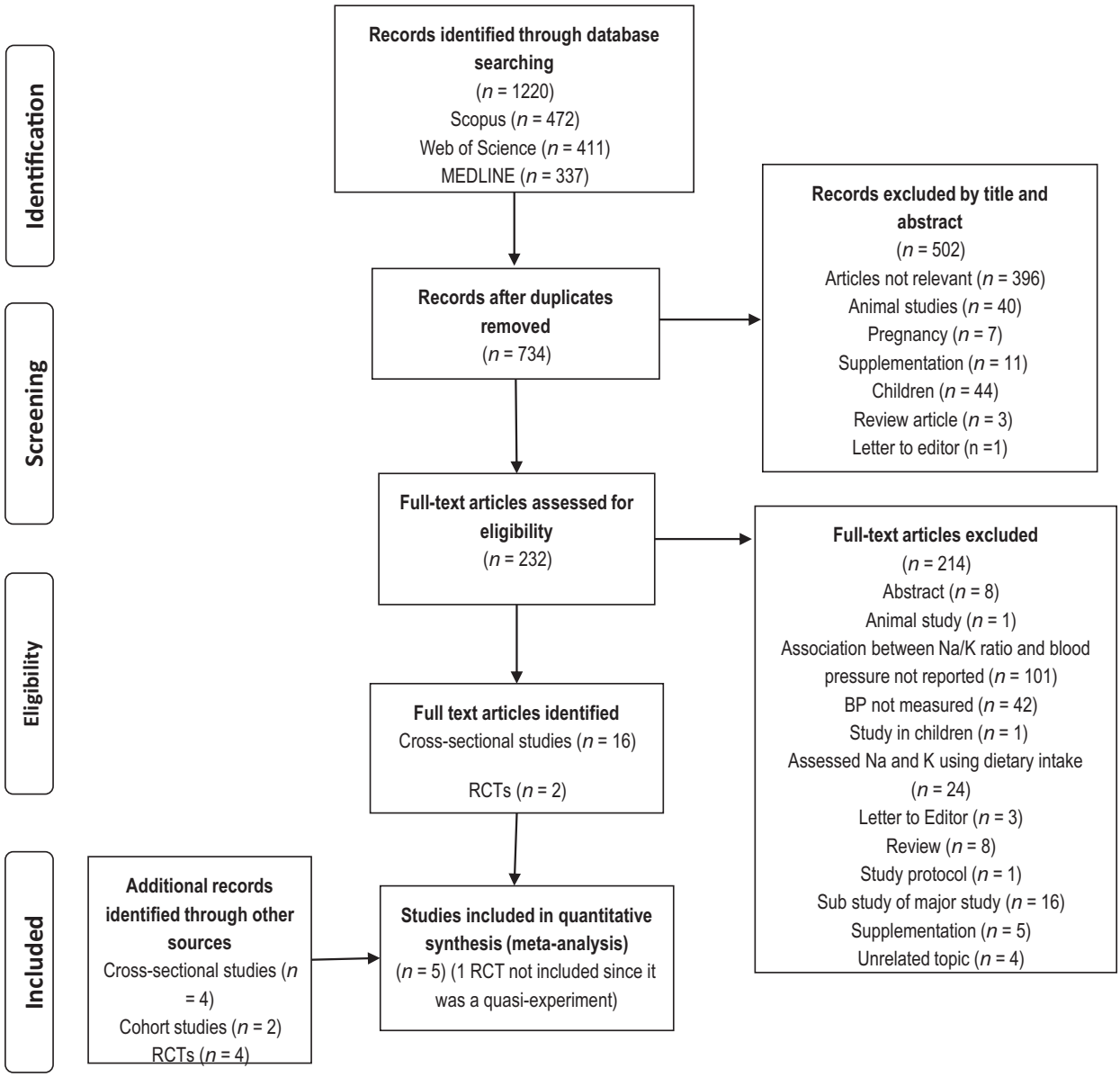

FIGURE 1 PRISMA flow chart for study selection process. RCT, randomized controlled trials.

if 24-h urinary creatinine concentration was greater than 2 to 3 standard deviations beyond the sex-specific means (28, 32, 36, 37, 40, 41, 43). To further validate the urinary analyses, some studies also included a verbal questionnaire to inquire about the completeness of the 24-h urine samples collected or also included a dietary questionnaire (36, 40, 42). Study participants were classified as either normotensive or hypertensive and BMIs ranged from normal to obese (mean BMI 19.3–29.6 kg/m^2).

The studies that performed 24-h urine collections specified measured brachial BP using a calibrated mercury or random zero sphygmomanometer (15, 20, 21, 24, 28–33, 40, 42, 46, 47) automated oscillometric device (14, 25, 26, 34, 36, 41) or a validated wrist-worn BP device (16). One study measured office BP, ambulatory BP, and aortic BP and reported all 3 (43).

All but 3 of the studies included in this review indicated that a higher Na: K ratio was associated with higher SBP and/or DBP as shown by regression coefficients, with a stronger correlation observed with SBP than with DBP. Three studies reported no association between Na: K ratio and SBP/DBP, even after the adjustments for covariates known to be associated with BP (32, 40, 44). One study that compared the use of 24-h, overnight and daytime urine collection with BP showed that 24-h urinary measures of Na: K ratio had stronger associations with BP compared with both overnight and daytime urine samples (35).

A summary of experimental studies (clinical trials) included in this review is shown in Table 1. Participants in these studies were aged 20 years or older and had BP indicative of pre-hypertension or were diagnosed as being hypertensive.

TABLE 1 Summary of experimental studies exploring the association between sodium to potassium ratio and blood pressure in adults, using 24-h urine collections[1]

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Intervention	Urinary Na[4] and K[4]	Na:K ratio[5]	Change SBP and DBP (mmHg)	Conclusions, quality rating[6], and level of evidence (NHMRC)[7]
Wing et al. (24) 1984 USA Quasi-experiment	Total $n = 41$, HT Weight intervention: $n = 19$ Age: 56.53 ± 6.08y SBP: 155.74 ± 14.40 mmHg DBP: 93.47 ± 6.28 mmHg Na:K intervention: $n = 22$ Age: 52.77 ± 9.84y SBP: 147.00 ± 20.24 mmHg DBP: 93.59 ± 8.86 mmHg	Weight control: 5% reduction in body weight No change in Na, K, or Na:K ratio Na:K intervention Decrease Na intake <70 mEq/day Increase K intake >100 mEq/day	Urinary Na: Weight intervention: Pre: 147.75 ± 69.27 mEq/day Post: 139.87 ± 107.62 mEq/day Change: −7.88 mEq/day Na:K intervention: Pre: 168.87 ± 96.01 mEq/day Post: 107.72 ± 48.09 mEq/day Change: −61.15 mEq/day Urinary K: Weight intervention: Pre: 59.09 ± 17.61 mEq/day Post: 52.49 ± 22.33 mEq/day Change: -6.60 mEq/day Na:K intervention: Pre: 76.11 ± 32.69 mEq/day Post: 82.34 ± 35.22 mEq/day Change: +6.23 mEq/day	Weight intervention: - Pre: 2.61 - Post: 2.69 - Change: +0.08 Na:K intervention: - Pre: 2.50 - Post: 1.52 - Change: −0.98	SBP: Weight intervention: -13.94 mmHg*** Na:K intervention:-6.20 mmHg** DBP: Weight intervention:-7.71 mmHg** Na:K intervention: -4.1 mmHg**	Weight reduction reduced BP more than dietary modification aimed to lower Na/K ratio Ø, II
Lin et al. (25) 2012 USA RCT	Total $n = 20$, HT Age: 44.3 ± 7.8y BMI: 33.9 ± 6.6 kg/m^2 SBP: 144.2 ± 9.38 mmHg DBP: 88.5 ± 6.03 mmHg	Intervention: DASH diet Control: American control diet	Urinary Na: Control: Baseline: 122.6 ± 40.82 mmol/day Change: 17.85 ± 65.93 mmol/day DASH: Baseline: 131.4 ± 42.83 mmol/day Change: -1.5 ± 64.40 mmol/day Urinary K: Control: Baseline: 46.6 ± 13.3 mmol/day Change: -7.9 ± 16.4 mmol/day DASH: Baseline: 42.2 ± 14.7 mmol/day Change: 25.3 ± 28.6 mmol/day	Control: Baseline: 2.76 ± 1.13 Change: 0.61 ± 1.20 DASH: Baseline: 3.20 ± 0.69 Change: −.06 ± 2.91	SBP: Control: -0.9 ± 16.4 mmHg DASH: -9.6 ± 11.2* mmHg DBP Control: 1.6 ± 11.6 mmHg DASH: -8.6 ± 9.1 * mmHg	Lower Na/K ratio associated with lowered BPP, II
Dodson (20) 1983 UK RCT	Total $n = 53$, HT Modified diet: Age: 53.6 ± 8.5y SBP: 173.8 ± 23.8 mmHg DBP: 98.4 ± 9.2 mmHg Control: Age: 55.3 ± 6.7y SBP: 169.7 ± 18.2 mmHg DBP: 94.4 ± 7.3 mmHg	Modified diet: High dietary fibre (35-40 g/day) High unrefined carbohydrate (65% E) Low fat (15% E) Low Na (40-450 mmol/day) Normal K (70-80 mmol/day) Control: Normal Western diet	Urinary Na: Modified diet: - Pre: 195 ± 78.1 mmol/day - Post: 136.7 ± 70.2 mmol/day Control: - Pre: 180.2 ± 58.2 mmol/day - Post: 162.6 ± 48.1 mmol/day Urinary K: Modified diet: - Pre: 83.5 ± 61.5 mmol/day - Post: 80.1 ± 25.5 mmol/day Control: - Pre: 66.9±20 mmol/day - Post: 68.2 ± 21.7 mmol/day	Modified diet: - Pre: 2.68 ± 1.08 - Post: 1.82 ± 1.09 Control: - Pre: 2.96 ± 1.39 - Post: 2.84 ± 1.33	SBP Modified diet: -5.3 mmHg Control: +4.4 mmHg DBP Modified diet: -6.7 mmHg*** Control: +2.3 mmHg	Lower Na/K ratio associated with lowered BP Ø, II

(*Continued*)

TABLE 1 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Intervention	Urinary Na[4] and K[4]	Na:K ratio[5]	Change SBP and DBP (mmHg)	Conclusions, quality rating[6], and level of evidence (NHMRC)[7]
Sacks FM et al. (21) 2001 USA RCT	Total *n* = 412, NT and HT DASH diet: Age: 47 ± 10y BMI: 29±5 kg/m^2 SBP: 134 ± 10 mmHg DBP: 86 ± 5 mmHg Control diet: Age: 49 ± 10y BMI: 30±5 kg/m^2 SBP: 135 ± 10 mmHg DBP: 86 ± 4 mmHg	Intervention: DASH diet Control: Usual American diet	Urinary Na: High sodium level: - DASH: 144±58 mmol/day - Control: 141 ± 55 mmol/day Intermediate sodium: - DASH: 107±52 mmol/day - Control: 106±44 mmol/day Low sodium level: - DASH: 67±46 mmol/day - Control: 64±37 mmol/day Urinary K: High sodium level: - DASH: 75±27 mmol/day - Control: 40 ± 14 mmol/day Intermediate sodium: - DASH: 81±31 mmol/day - Control: 41±14 mmol/day Low sodium level: - DASH: 81±29 mmol/day - Control: 42±14 mmol/day	High sodium level: - DASH: 1.92 - Control: 3.53 Intermediate sodium: - DASH: 1.32 - Control: 2.59 Low sodium level: - DASH: 0.83 - Control: 1.52	SBP net change (95% CI) High: -5.9 (−8.0 to -3.7) mmHg Intermediate: -5.0 (-7.6 to -2.5) mmHg Low: -2.2 (-4.4 to -0.1) mmHg DBP: (net change) High: -2.9 (-4.3 to -1.5) mmHg Intermediate: -2.5 (-4.1 to -0.8) mmHg Low: -1.0 (-2.5 to -0.4) mmHg	Lower Na/K ratio associated with lowered BP P, II
Nowson et al. (22) 1988 Australia RCT	Total *n* = 212, HT Age: NR BMI: NR SBP: NR DBP: Mean of 4 readings between 90 and 100 mmHg	A: Normal diet B: High potassium diet C: Low sodium diet D: Low sodium, high potassium diet	Urinary Na: A: Pre: 107 mmol/day Post: 107 mmol/day B: Pre: 92 mmol/day Post: 99 mmol/day C: Pre: 97 mmol/day Post: 50 mmol/day D: Pre: 93 mmol/day Post: 49 mmol/day Urinary K: A: Pre: 84 mmol/day Post: 75 mmol/day B: Pre: 82 mmol/day Post: 114 mmol/day C: Pre: 79 mmol/day Post: 72 mmol/day D: Pre: 81 mmol/day Post: 104 mmol/day	A: Pre: 1.4 Post: 1.5 B: Pre: 1.2 Post: 0.9 C: Pre: 1.3 Post: 0.7 D: Pre: 1.2 Post: 0.5	SBP: A: -3.8 ± 1.0 mmHg B: -7.7 ± 1.1 mmHg C: -8.9 ± 1.0 mmHg D: -7.9 ± 0.9 mmHg DBP: A: -1.6 ± 0.6 mmHg B: -4.7 ± 0.7 mmHg C: -5.8 ± 0.6 mmHg D: -4.2 ± 0.7 mmHg	Lower Na/K ratio associated with lowered BP P, II

(*Continued*)

TABLE 1 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Intervention	Urinary Na[4] and K[4]	NaK ratio[5]	Change SBP and DBP (mmHg)	Conclusions, quality rating[6], and level of evidence (NHMRC)[7]
Jenkins et al. (23) 2015 Canada RCT	Total *n* = 241 Age: > 20–85 y Portfolio diet: Mean (95% CI) BMI: 27 (95% CI: 26–27) SBP: 120 (95% CI: 118–122) mmHg DBP: 73 (95% CI: 72–75) mmHg Control DASH diet: Mean (95% CI) BMI: 27 (95% CI: 26–28) SBP: 118 (95% CI: 115–121) mmHg DBP: 72 (95% CI: 70–74) mmHg	Two diets: Portfolio diet per 1000 kcal diet 9.8g viscous fibres 22.5g soy protein 0.94g plant sterols Control (DASH diet)	Urinary Na: NR Urinary K: NR	Portfolio diet: Baseline: 2.1 (95% CI: 1.9, 2.3) Change: 0 (95% CI: −0.2, 0.2) Control DASH: Baseline: 2.1 (95% CI: 1.8, 2.3) Change: 0 (95% CI: −0.3, 0.2)	SBP: Portfolio diet: -0.11 mmHg DASH: -0.08 mmHg DBP: Portfolio diet: -0.18*** mmHg DASH: -0.03 mmHg	Lower Na/K ratio associated with lowered BP P, II

[1] * $P < 0.05$. ** $P < 0.01$. *** $P < 0.001$. [†]Not included in current meta-analysis because it is a quasi-experimental trial. BMI, body mass index; CI, 95% confidence interval; DBP, diastolic blood pressure; HT, hypertensive; Pre-HT, pre-hypertensive; NR: not reported; SBP, systolic blood pressure.
[2] Body mass index is Mean ± SD unless otherwise indicated.
[3] Blood pressure is Mean ± SD unless otherwise indicated.
[4] Mean ± SD (all such values).
[5] Mean ± SD values or changes.
[6] Quality rating: P = Positive, Ø = Neutral, − = Negative.
[7] NHMRC (National Health and Medical Research Council) rating is classified as I, III-1, III-2, III-3 or IV.

Only 3 of the studies reported the BMI of participants, and these ranged from overweight to obese (27.2–33.9 kg/m^2). Twenty-four-hour urine collection was included in all 5 of the RCTs. Most studies investigated the effect of decreasing sodium intake and/or increasing potassium intake on BP and reported the relationship according to the Na: K ratio. Common intervention diets used were either the DASH diet (20, 21, 25) or other diets (20, 22, 24, 34, 48) aimed to simultaneously reduce sodium intake and increase potassium intake, compared with a normal American or Western diet. For the purpose of our analyses, groups that had a lower Na: K ratio were compared with groups that had a higher Na: K ratio. For the cross-sectional studies shown in Table 2, participants' ages ranged from 45 to 52 y with a BMI of between 24 and 32. The studies had both normotensive and hypertensive participants.

Results of the meta-analysis of 5 RCTs demonstrated that a diet with a lower Na: K ratio was associated with a significantly greater reduction in SBP and DBP compared with a higher Na: K ratio (SMD: −1.09 mmHg; 95% CI: −1.91, −0.28 mmHg and SMD: −1.42 mmHg; 95% CI: −2.24, −0.59 mmHg, respectively). High heterogeneity was observed for both SBP and DBP ($I^2 = 97\%$ and $I^2 = 98\%$, $P < 0.001$, respectively). The forest plot of the meta-analysis for SBP and DBP is shown in **Figures 2** and **3**, respectively. As there were fewer than 10 studies included in the meta-analyses, funnel plots were not generated to investigate small study effects, in line with recommendations of the Cochrane Handbook (19).

Discussion

This systematic review and meta-analysis has confirmed a positive association between increasing sodium to potassium ratio and both systolic and diastolic BP in adults. For the purpose of the review, an optimal Na: K was considered to be 1:1 or lower, as recommended by the WHO as a target for optimal health outcomes (49, 50). A meta-analysis of 5 RCTs resulted in a magnitude of reduction of 1.09 mmHg and 1.42 mmHg associated with a more favorable Na: K ratio, for systolic and diastolic BP, respectively. This effect can be considered both statistically and clinically significant. Appel et al. (11) demonstrated that lowering systolic and diastolic BP by 5.0 mmHg and 3.0 mmHg, respectively, would decrease the incidence of coronary heart disease and stroke by approximately 15% and 27%, respectively, in the US population. The dietary modifications included in the RCT interventions were based on the principles of the DASH diet, and our meta-analysis is consistent with a previously reported meta-analysis that described a reduction of 6.74 mmHg for SBP and 3.59 mmHg for DBP associated with adherence to a DASH diet (10).

In the experimental studies included in the meta-analysis, we found evidence of a greater reduction in BP associated with a greater magnitude of reduction in the urinary Na: K in participants with hypertension, compared with those with pre-hypertension. These findings are consistent with the

TABLE 2 Summary of cross-sectional studies exploring associations between sodium to potassium ratio and blood pressure in adults using 24-h urinary collection[1]

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
Jackson et al. (35) 2018 USA Cross-sectional	Total *n*: 766 HT *n*: 235 Age: 52.3 ± 0.7y BMI: 32.6 ± 1.0 kg/m^2 Pre-HT *n*: 183 Age: 45.0 ± 1.2y BMI: 31.2 ± 0.8 kg/m^2 Optimal *n*: 348 Age: 37.0 ± 1.0y BMI: 27.5 ± 0.5 kg/m^2	Urinary Na HT: 162.60 ± 3.04 mmol/day Pre-HT: 154.51 ± 2.61 mmol/day Optimal: 159.04 ± 3.19 mmol/day Urinary K HT: 51.12 ± 1.10 mmol/day Pre-HT: 53.35 ± 1.29 mmol/day Optimal: 55.24 ± 1.37 mmol/day	HT: 3.18 Pre-HT: 2.90 Optimal: 2.90	SBP 1.72 [0.76-2.68]** DBP 0.30 [−0.53 - 1.12]	Urinary Na:K associated with SBP	P, IV
Stamler et al. (41) 2018 Global (Japan, China, UK, USA) Cross-sectional	Total including INTERMAP *n*: 4680; NT and HT Age: 49.17 ± 5.47y BMI: 26.37 ± 5.47 kg/m^2 SBP: 118.93 ± 14.69 mmHg DBP: 73.84 ± 10.03 mm Hg US participants *n*: 2195 Age: 49.14 ± 5.39y BMI: 28.90 ± 5.92 kg/m^2 SBP: 118.60 ± 13.89 mmHg DBP: 73.41 ± 9.68 mmHg	Urinary Na Total: 181.10 ± 72.42 mmol/day US participants: 162.58 ± 59.37 mmol/day Urinary K Total: 53.16 ± 20.02 mmol/day US participants: 57.65 ± 20.91 mmol/day	INTERMAP: 3.89 ± 2.11 US participants: 3.08 ± 1.23	SBP INTERMAP: 2.43 [1.50-3.37]**** US participants: 2.46 [1.35- 3.58]**** DBP INTERMAP: 0.92 [0.30- 1.54]** US participants: 1.20 (0.42-1.97)**	Urinary Na:K ratio associated with SBP and DBP	P, IV
Farapti et al. (42) 2017 Indonesia Cross-sectional	Total *n*: 51 Female subjects Age: 56.98 ± 5.7y BMI: 25.96 ± 4.85 kg/m^2 SBP:132.25 ± 17.78 mmHg DBP: 83.63 ± 10.3 mmHg NT *n*: 32 Age: 57.19 ± 6.85y BMI: 24.26 ± 5.24 kg/m^2 SBP: 121.09 ± 9.89 mmHg DBP: 77.03 ± 6.33 mmHg HT *n*: 19 Age: 57.16 ± 3.45y BMI: 28.82 ± 1.36 mmHg SBP: 151.05 ± 10.75 mmHg DBP: 94.74 ± 4.24 mmHg	Urinary Na Total: 104.85 ± 59.3 mmol/day NT: 94.6 ± 41.1 mmol/day HT: 120.5 ± 81.0 mmol/day Urinary K Total: 20.5 ± 9.7 mmol/day NT: 21.2 ± 10.18 mmol/day HT:19.50 ± 9.08 mmol/day	Total: 5.28 ± 1.68 NT: 4.74 ± 1.36 HT: 6.01 ± 1.89	SBP 3.89 [1.18-6.6]* Excluding participants taking antihypertensive drugs: 4.89 [1.93-7.84]* DBP 1.72 [−0.189-3.63]	Urinary Na:K ratio associated with SBP not DBP	Ø,IV

(*Continued*)

TABLE 2 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
Glatz et al. (43)☐ 2017 Switzerland Cross-sectional	Total *n*: 1336 German *n*: 709 Age: 48.8 ± 18y BMI: 25.3 ± 4.3 kg/m^2 SBP: 126.1 ± 15.9 mmHg DBP: 75.5 ± 10.2 mmHg French *n*: 428 Age: 47.8 ± 18.1y BMI: 25.5 ± 5.1 kg/m^2 SBP: 122.5 ± 14.9 mmHg DBP: 74.2 ± 9.8 mmHg Italian *n*: 199 Age: 45.3 ± 18.4 y BMI: 24.5 ± 4.2 kg/m^2 SBP: 120.5 ± 15 mmHg DBP: 69.9 ± 9.9 mmHg	Urinary Na German: 160 ±66 mmol/day French: 151 ± 71 mmol/day Italy: 158 ±72 mmol/day Urinary K German: 68.0 ± 24.8 mmol/day French: 65.7 ± 24.1 mmol/day Italy: 63.3 ± 27.3 mmol/day	NT: 2.35 (2.29; 2.62) HT: 2.52 (2.43; 2.62)	SBP (quintiles of BP) Q1 (*n* = 265) 2.32 (2.21; 2.44) Q2 (*n* = 262) 2.27 (2.16; 2.38) Q3 (*n* = 268) 2.36 (2.24; 2.47) Q4 (*n* = 269) 2.48 (2.38; 2.59) Q5 (*n* = 272) 2.53 (2.42; 2.65) DBP NR[8]	Urinary Na:K ratio associated with SBP	P, IV
Mohammadifard et al. (44) 2017 Iran Cross-sectional	Total *n*: 796 Males *n*: 349 Females *n*: 447 Age: 38.9 ± 11.4y BMI: 25.7 ± 4.4 kg/m^2 SBP: 112.0 ± 10.9 mmHg DBP: 70.8 ± 8.7 mmHg NT *n*: 309 Age: 37.8 ± 11.0y BMI: 25.4 ± 4.5 kg/m^2 SBP: 108.9 ± 8.5 mmHg DBP: 68.1 ± 6.5 mmHg Pre-HT *n*: 40 Age: 43.6 ± 11.7y BMI: 28.4 ± 4.5 kg/m^2 SBP: 126.2 ± 9.2 mmHg DBP: 83.5 ± 5.7 mmHg	Urinary Na Total: 176.94 ± 71.97 mmol/day NT: 177 ± 73 mmol/day Pre-HT: 176.8 ± 66.1 mmol/day Urinary K Total: 57.5 ±42 mmol/day NT: 56.5 ± 42.3 mmol/day Pre-HT: 54.5 ± 39.7 mmol/day	Total: 3.08 NT: 3.13 Pre-HT: 3.24	SBP Odds ratios (95% CI) of Pre-HT Q1 (Quartile of urinary Na:K ratio) 1.00 (0.45-2.21) Q2 1.31 (0.62-2.77) Q3 2.15 (1.08-4.55) *P* = 0.029 DBP N/A	Urinary Na:K ratio is significantly positively correlated with Pre-HT	P, IV
Ndanuko et al. (39) 2017 Australia Cross-sectional	Total *n*: 328 NT/HT Male *n*: 27 Females *n*: 73 Age: 43.6 ± 8y BMI: 32.4 ± 4.2 kg/m^2 SBP: 124.9 ± 14.5 mmHg DBP: 73.3 ± 9.9 mmHg	Urinary Na[6] [mean (95% CI)] 139 (99.2-180) mmol/day Urinary K [mean (95% CI) 74 (96.7-154.3)] mmol/day	1.9 (1.5-2.4)	SBP Correlation coefficient = 0.1, *P* = 0.02 DBP NR	Urinary Na:K ratio associated with SBP	P, IV

(*Continued*)

TABLE 2 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
Rhee et al. (45) 2017 Korea Cross-sectional	Total *n*: 524 Age: 48.1 ± 9.8 y BMI: 23.9 ± 3.3 kg/m^2 Casual SBP: 116.7 ± 12.9 mmHg Casual DBP: 75.0 ± 9.7 mmHg 24-h SBP: 116.6 ± 11.0 mmHg 24-h DBP: 75.9 ± 9.8 mmHg AoSBP: 110.7 ± 13.1 mmHg AoDBP: 76.6 ± 10.0 mmHg NTs *n*: 305 Age: 45.1 ± 9.6y BMI: 23.1 ± 3.1 kg/m^2 Casual SBP: 110.9 ± 10.0 mmHg Casual DBP: 70.4 ± 7.0 mmHg 24-h SBP: 110.8 ± 7.0 mmHg 24-h DBP: 70.3 ± 6.1 mmHg AoSBP: 104.8 ± 10.1 mmHg AoDBP: 72.0 ± 7.4 mmHg HTs *n*: 219 Age: 52.1 ± 8.5y BMI: 25.1 ± 3.2 kg/m^2 Casual SBP: 124.8 ± 12.3 mmHg Casual DBP: 81.5 ± 9.2 mmHg 24-h SBP: 124.6 ± 10.6 mmHg 24-h DBP: 83.7 ± 8.7 mmHg AoSBP: 118.8 ± 12.5 mmHg AoDBP: 83.1 ± 9.6 mmHg	Urinary Na Total: 159.8 ± 61.5 mmol/day NT: 154.8 ± 59.9 mmol/day HT: 166.8 ± 63.1 mmol/day Urinary K Total: 55.9 ± 20.7 mmol/day NT: 54.3 ± 18.8 mmol/day HT:58.3 ± 23.0 mmol/day	Total: 3.10 ± 1.22 NT: 3.05 ± 1.21 HT: 3.13 ± 1.25	SBP All subjects: β coefficient = 1.278 (P = 0.006) HTs: β coefficient = 1.446 (P = 0.047) DBP NR	Urinary Na:K ratio associated with SBP	Ø, IV
Vallejo et al. (46) 2017 Mexico Cross-sectional	Total *n*: 711 NTs Age: 37.4 ± 9.0y BMI: 27.1 ± 4.4 kg/m^2 SBP: 106.2 ± 10.2 mmHg DBP: 70.6 ± 7.9 mmHg Male *n*: 228 Age: 36.0 ± 8.9y BMI: 27.2 ± 4.3 kg/m^2 SBP: 110.5 ± 9.8 mmHg DBP: 73.4 ± 7.9 mmHg Female *n*: 483 Age: 38.1 ± 8.9y BMI: 27.1 ± 4.5 kg/m^2 SBP: 104.2 ± 9.7 mmHg DBP: 69.3 ± 7.6 mmHg	Urinary Na Male: 162±64 mmol/day Female: 125 ± 48.2 mmol/day Urinary K Male: 54 ± 18.5 mmol/day Female: 46.5 ± 16.4 mmol/day	Male: 3.2 ± 1.2 Female: 2.9 ± 1.1	SBP −0.2 [−0.7, 0.5] DBP 0.1 [−0.4, 0.6]	Urinary Na:K ratio not associated with SBP or DBP	P, IV
Ware et al. (16)[9] 2017 South Africa Cross-sectional	Total *n*: 2722 NTs/HTs Low salt *n*: 164 Data below are median (IQR) Age: 59 (18)y BMI: 28.0 (9.8) kg/m^2 SBP: 132 (25) mmHg DBP: 81 (17) mmHg Medium salt *n*: 195 Age: 57 (19)y BMI: 28.5 (8.1) kg/m^2 SBP: 127 (25) mmHg DBP: 78 (16) mmHg High salt *n*: 167 Age: 49 (26)y BMI: 30.4 (10.6) kg/m^2 SBP: 128 (24) mmHg DBP: 80 (16) mmHg	Urinary Na Median (IQR) Low salt: 62.7 (28.8) mmol/day Medium salt: 115.3 (37.3) mmol/day High salt: 217 (118.7) mmol/day Urinary K Median (IQR) Low salt: 22.2 (16.4) mmol/day Medium salt: 33.0 (24.2) mmol/day High salt: 67.0 (43.2) mmol/day	Low salt: 2.7 (2.3) Medium salt: 3.6 (2.1) High salt: 3.7 (2.4)	SBP NR SBP NR	Urinary Na:K ratio not associated with SBP and DBP	Ø,IV

(*Continued*)

TABLE 2 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
Xu et al. (28) 2017 China Cross-sectional	Total *n*: 2281 NTs/HTs Age: 42.1 ± 13.4y BMI classification: Normal *n*: 982 43.1% (95% CI: 41.0,45.1) Overweight *n*: 860 37.7% (95% CI: 35.7, 39.7) Obese: (*n* = 439) 19.2% (95% CI: 17.6, 20.9) SBP: 131.4 ± 19.9 mmHg DBP:83.6 ± 11.9 mmHg Male *n*: 1135 Age: 42.2 ± 13.5y BMI: Normal *n*: 480 42.3% (95% CI: 39.4, 45.2) Overweight *n*: 458 40.4% (95% CI: 37.5, 43.2) Obese *n*: 197 17.3% (95% CI: 15.2, 19.6) SBP:134.6 ± 18.0 mmHg DBP:85.9 ± 11.9 mmHg Female: (*n* = 1146) Age: 41.9 ± 13.4y BMI classification Normal *n* = 502 43.8% (95% CI: 40.9, 46.7) Overweight *n* = 402 35.1% (95% CI: 32.3, 37.8) Obese *n*: 242 21.1% (95% CI: 18.8, 23.5) SBP: 128.2 ± 21.1 mmHg DBP: 81.3 ± 11.5 mmHg	Urinary Na 166.9 ± 25.6 mmol/day Urinary K 25.3 ± 3.4 mmol/day	6.8 (1.5)	SBP β coefficient (95% CI): 0.97 [0.36 to 1.58]*** DBP β coefficient (95% CI): 0.65 [0.26 to 1.04]***	Urinary Na:Kratio associated with SBP and DBP	P, IV
Yan et al. (29) 2015 China Cross-sectional	Total *n*: 1948 HTs (23%) Age: 41.4 ± 13.9y BMI: NR SBP: NR DBP: NR	Urinary Na 235.7 (SD NR) mmol//day Urinary K 40.5 (SD NR) mmol/day	6.8 (SD NR)	SBP β coefficient (95% CI): 0.37 [0.26 to 0.49]*** DBP β coefficient (95% CI): 0.16 [0.03 to 0.29]*	Urinary Na:K ratio associated with increased of SBP and DBP	P, IV
Huggins et al. (40) 2011 Australia Cross-sectional	Total *n*: 738 HTs (43%) Age: 64.0 ± 6.3y Male *n*: 376 BMI: 28.4 ± 4.0 kg/m^2 SBP: 133.0 ± 13.1 mmHg DBP: 76.1 ± 9.2 mmHg Female *n*: 407 BMI: 28.0 ± 4.9 kg/m^2 SBP: 129.5 ± 16.8 mmHg DBP: 66.6 ± 10.4 mmHg	Urinary Na 155.1 ± 63.1 mmol/day Urinary K 82.3 ± 27.9 mmol/day	1.99 ± 0.83	SBP β coefficient (95% CI): 1.8 [0.2 to 3.4]* DBP β coefficient (95% CI): 0.40 [−0.69 to 1.48]	Urinary Na:K ratio associated with increased SBP	P, IV

(*Continued*)

TABLE 2 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
Zhao et al. (15) 2004 China Cross-sectional	Total *n*: 839 North *n*: 561 HTs = 22% Age: 48.9 ± 5.8y BMI: 23.8 ± 3.5 kg/m^2 SBP: 123.7 ± 18.4 mmHg DBP: 75.5 ± 10.4 mmHg South *n*: 278 HTs = 7% Age: 49.1 ± 5.7y BMI: 21.8 ± 2.6 kg/m^2 SBP: 116.3 ± 14.1 mmHg DBP: 68.6 ± 8.0 mmHg	Urinary Na North: 271±88 mmol/day South: 139±57 mmol/day Urinary K North: 37.1 ± 11.5 mmol/day South: 40.6 ± 14.7 mmol/day	North: 7.6 ± 2.4 South: 3.7 ± 1.5	SBP Coefficient for difference between North and South (95% CI NR) 3.30***	Urinary Na:K ratio associated with increased SBP and DBP	P, IV
Xie et al. (30) 2001 China Cross-sectional	Total *n*: 353 NTs/HTs Male *n*: 191 Age: 40.0 ± 16.5y BMI: 22.0 ± 2.3 kg/m^2 SBP: 116.9 ± 13.1 mmHg DBP: 74.3 ± 8.9 mmHg Female *n*: 162 Age: 36.7 ± 15.7y BMI: 22.7 ± 2.8 kg/m^2 SBP: 117.6 ± 17.5 mmHg DBP: 74.8 ± 11.1 mmHg	Urinary Na Male: 152.9 ± 62.5 mmol/day Female: 123.3 ± 59.3 mmol/day Urinary K Male: 28.7 ± 17.2 mmol/day Female: 23.7 ± 14.3 mmol/day	Male: 6.1 ± 2.3 Female: 6.1 ± 2.6	SBP β coefficient (95% CI NR): Male: 1.167** Female: 1.310** DBP β coefficient (95% CI NR): Male: 0.573* Female: NR	Urinary Na:K ratio associated with increased SBP and DBP	P, IV
Tian et al. (31) 1995 China Cross-sectional	Total *n*: 663 NTs/HTs Male *n*: 328 Age: 43.6 ± 13.6 y BMI: 23.4 ± 3.4 kg/m^2 SBP: 126 ± 18 mmHg DBP: 81 ± 11 mmHg Female *n*: 335 Age: 43.5 ± 13.3y BMI: 23.6 ± 4.4 kg/m^2 SBP: 121 ± 20 mmHg DBP: 78 ± 11 mmHg	Urinary Na Male: 257.8 ± 86.0 mmol/day Female: 249.2 ± 81.4 mmol/day Urinary K Male: 42.4 ± 17.0 mmol/day Female: 45.0 ± 18.2 mmol/day	Male: 6.6 ± 2.2 Female: 6.1 ± 2.4	SBP β coefficient ± SE Male: 0.735 ± 0.402 Female: 0.956 ± 0.380* Total: 0.795 ± 0.277** DBP β coefficient ± SE Male: 0.261 ± 0.253 Female: 0.561 ± 0.213** Total: 0.400 ± 0.164*	Urinary Na:K ratio associated with increased SBP and DBP in females and both sexes combined	P, IV

(*Continued*)

TABLE 2 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
He et al. (32) 1991 China Cross-sectional	Total *n*: 419 NTs High-mountain Yi Age: 30.9 ± 11.5y BMI: 19.3 ± 2.2 kg/m^2 SBP: 99.4 ± 7.8 mmHg DBP: 63.2 ± 7.4 mmHg Mountainside Yi Age: 36.4 ± 14.3y BMI: 19.4 ± 1.6 kg/m^2 SBP: 101.8 ± 9.1 mmHg DBP: 62.2 ± 8.2 mmHg Country Yi Age: 39.3 ± 12.7y BMI: 20.4 ± 2.1 kg/m^2 SBP: 108.6 ± 9.2 mmHg DBP: 71.3 ± 8.2 mmHg Country Han Age: 36.4 ± 12.1y BMI: 20.8 ± 2.7 kg/m^2 SBP: 107.3 ± 12.1 mmHg DBP: 69.6 ± 8.9 mmHg	Urinary Na High-mountain Yi: 73.9 ± 50.3 mmol/day Mountainside Yi: 117.9 ± 55.4 mmol/day Country Yi: 159.4 ± 62.6 mmol/day Country Han: 186.0 ± 73.0 mmol/day Urinary K High-mountain Yi: 58.6 ± 31.0 mmol/day Mountainside Yi: 48.5 ± 28.1 mmol/day Country Yi: 28.3 ± 13.6 mmol/day Country Han: 29.0 ± 10.4 mmol/day	High-mountain Yi: 1.45 ± 0.92 Mountainside Yi: 3.45 ± 2.50 Country Yi: 6.87 ± 3.79 Country Han: 7.00 ± 2.23	SBP β coefficient 0.928**** (95% CI NR): DBP β coefficient 0.645**** (95% CI NR):	Urinary Na:K ratio associated with increased SBP and DBP	Ø, IV
Staessen et al. (37) 1991 UK Cross-sectional	Total *n*: 301 Males NTs/HTs Age: 45 ± 6y BMI: 24.1 ± 2.8 kg/m^2 SBP: 126 ± 16 mmHg DBP: 78 ± 11 mmHg	Urinary Na Daytime: 120 ± 46 mmol/12h Nighttime: 54 ± 29 mmol/12h Whole day: 174 ± 557 mmol/day Urinary K Daytime: 56 ± 20 mmol/12 hr Nighttime: 18 ±11 mmol/12h Whole day: 73±22 mmol/day	Daytime: 2.4 ± 1.0 Nighttime: 3.5 ± 1.6 Whole day: 2.5 ± 10	SBP Whole day urine: β coefficient ± SE 2.110 ± 0.895* DBP Whole day urine: β coefficient ± SE 2.084 ± 0.653**	Urinary Na:K ratio associated with increased SBP and DBP	Ø, IV
Kesteloot et al. (33) 1987 China Cross-sectional	Total *n*: 2008 NTs/HTs Male *n*: 1002 North: Age: 40.4 ± 14.4 y SBP: 125.7 ± 17.6 mmHg DBP: 83.1 ± 12.1 mmHg South: Age: 40.4 ± 14.4y SBP: 118.1 ± 12.6 mmHg DBP: 77.6 ± 9.8 mmHg Female *n*: 1006 North: Age: 40.2 ± 14.4y SBP: 122.0 ± 21.7 mmHg DBP: 80.4 ± 14.7 mmHg South: Age: 40.5 ± 14.3y SBP: 112.3 ± 14.3 mmHg DBP: 75.0 ± 10.2 mmHg	Urinary Na M North: 226.9 ± 88.8 mmol/day M South: 179.4 ± 72.9 mmol/day F[11] North: 204.6 ± 82.1 mmol/day F South: 172.4 ± 70.6 mmol/day Urinary K M North: 37.5 ± 15.8 mmol/day M South: 28.8 ± 13.0 mmol/day F North: 37.5 ± 17.1 mmol/day F South: 29.7 ± 11.6 mmol/day	M[10] North: 6.56 ± 2.55 M South: 6.73 ± 2.41 F North: 5.92 ± 2.27 F South: 6.15 ± 2.28	SBP β coefficient range: 0.650 to 0.967* DBP β coefficient range: 0.402 to 0.751	Urinary Na:K ratio associated with increased SBP and DBP in northern China, while only with SBP in southern China	Ø, IV

(*Continued*)

TABLE 2 (*Continued*)

Reference, year, country, study type	Subjects (*n*, age, sex, BMI[2], BP[3])	Urinary Na and K[4]	Na:K ratio	Regression coefficient (95% CI) (SBP and DBP)[5]	Conclusions	Quality rating[6] and level of evidence (NHMRC)[7]
Chan et al. (34) 1998 China Cross-sectional	Total *n*: 126 NTs/HTs Males *n*: 42 Age: 41.8 ± 16.4y SBP: 113.4 ± 14.7 mmHg DBP: 113.4 ± 14.7 mmHg Female *n*: 84 Age: 41.6 ± 10.9y SBP: 106.0 ± 16.4 mmHg DBP: 106.0 ± 16.4 mmHg	Urinary Na Male: 145.2 ± 48.7 mmol/day Female: 135.3 ± 45.8 mmol/day Urinary K Male: 40.4 ± 15.1 mmol/day Female: 41.3 ± 14.3 mmol/day	Males: 4.0 ± 1.7 Female: 3.5 ± 1.4	SBP NR DBP NR	Non-significant association between urinary Na:K ratio with SBP and DBP (data not shown)	Ø, IV
Kim et al. (51)[9] 2019 South Korea Cross-sectional Cross-sectional	Total *n*: 740 HTs = 40% Data below is median (25th, 75th percentile) Age: 48 (41, 56) y BMI: 23.5 (21.5, 25.6) kg/m^2 HT *n*: 299 SBP: 115.3 (107.9, 122.8) mmHg DBP: 75.5 (68.4, 82.2) mmHg	Urinary Na (median, 25th, 75th percentile) 153.9 (116.3, 197.5) mmol/day Urinary K (median, 25th, 75th percentile) 54.9 (43.0, 69. 8) mmol/day	2.9 (2.2, 3.7)	SBP β coefficient (95% CI) 0.0364 [−0.0308 to 0.1035] Older group (≥55 years) 0.1325 [0.0031 to 0.2620]* DBP β coefficient (95% CI) 0.0317 [−0.0322 to 0.0955] Older group (≥55 years) 0.1234 [0.0025 to 0.2444]*	Urinary Na:K associated with BP in older population	P, IV
Libianto et al. (38) 2017 Australia Cross-sectional	Total *n*: 116 NTs/HTs Age: 65 ± 12y BMI: 31±5 kg/m^2 SBP: 130 ± 14 mHg DBP: NR	Urinary Na 169±77 mmol/day Urinary K 70±25 mmol/day	2.5 ± 1.1	SBP β coefficient (95% CI): −2.373 [−4.447 to −0.299]* DBP β coefficient (95% CI): N/A	Urinary Na:K associated with SBP	P, IV
M'buyamba-Kabangu et al. (47)[9] 1986 Zaire Cross-sectional	Total *n*: 416 NTs/HTs Age: 32 ± 12y SBP: 124 ± 20 mmHg DBP: 72 ± 14 mmHg	Urinary Na Mean 87 (range minimum- maximum 8 to 312) mmol/day Urinary K Mean 33 (range minimum- maximum 3 to 132) mmol/day	3.1 (0.3-13.3)	SBP 1.02* (95% CI NR) DBP 0.68* (95% CI NR)	Urinary Na:K associated with both SBP and DBP	P, IV

[1] *$P < 0.05$. **$P < 0.01$.***$P < 0.001$. ****$P < 0.0001$. Electrolytes: ☐ Na: K ratio reported as adjusted (for age, BMI, sex and linguistic region) means (95% confidence limits); association of Na: K ratio with SBP reported by sex-specific quintile (Q) of systolic blood pressure P value < 0.001. Quartiles (Q) based on urinary sodium to potassium ratio, SBP: $P < 0.001$, DBP: $P = 0.003$. AoSBP, aortic systolic blood pressure; AoDBP, aortic diastolic blood pressure; BMI, body mass index; DBP, diastolic blood pressure; HT, hypertensive; NR, not reported; NT, normotensive; Pre-HT, pre-hypertensive; SBP, systolic blood pressure.

[2] Body mass index is Mean ± SD unless otherwise indicated;

[3] Blood pressure is Mean ± SD unless otherwise indicated;

[4] Mean ± SD in mmol/day;

[5] β coefficient (95% CI) unless specified;

[6] Quality rating: P = Positive, Ø = Neutral, − = Negative;

[7] NHMRC (National Health and Medical Research Council) rating is classified as I, III-1, III-2, III-3 OR IV;

[8] NR: Not reported;

[9] Subjects data and Na, K, Na: K ratio presented as median (IQR, interquartile range);

[10] M: Male

[11] F: Female

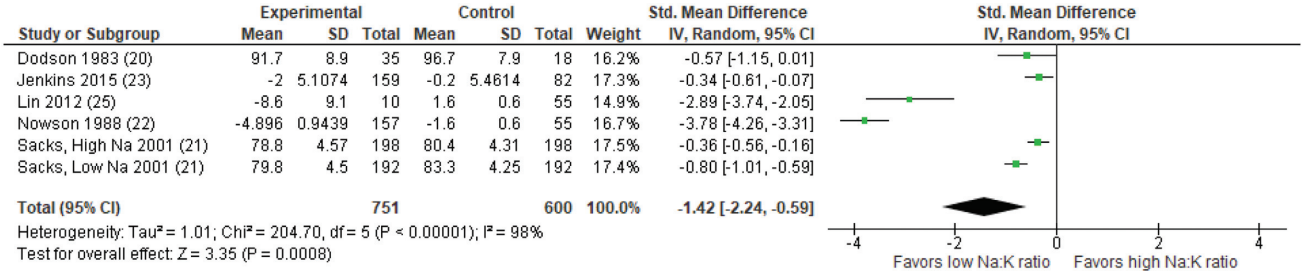

FIGURE 2 Forest plot of the association between different sodium to potassium ratios and systolic blood pressure (mmHg) in adults in 5 RCTs. Diamonds indicate weighted mean difference with 95% confidence intervals. RCT, randomized controlled trials.

study of Parfrey et al. (52), which found a larger reduction in BP in hypertensive groups, compared with normotensive counterparts following dietary modifications that lowered sodium and simultaneously increased potassium intake. A similar positive association was also observed in the cross-sectional studies included in this review. For example, Zhao et al. (15) concluded that lowering sodium to potassium ratio reduced BP in both pre-hypertensive and hypertensive individuals. However, Mohammadifard et al. (42) was able to show that the incidence of pre-hypertension had a greater association with UNa: K ratio than with either urinary sodium or urinary potassium alone. It is noteworthy that 4 other cross-sectional studies included in this review (30, 31, 53, 54) also reported a positive association between a higher sodium to potassium ratio and increased BP in normotensive populations. Finally, 1 study from China (30) reported that achieving an optimal sodium to potassium ratio could decrease systolic and diastolic BP by 6 mmHg and 3 mmHg, respectively, in normotensive individuals. Similarly, a study of normotensive individuals reported that a combination of low dietary sodium with high dietary potassium intake over a 2-wk period resulted in BP reduction (55). The evidence summarized in our current review indicates that a lowered UNa: K ratio is beneficial in both hypertensive and normotensive populations.

Biological plausibility exists regarding the combined effect of lowered sodium intake and increased potassium intake. The human body has developed numerous homeostatic mechanisms to maintain a tight sodium to potassium balance for fluid regulation and normal neuronal and muscular activity (56). Excessive dietary sodium intake resulting in deviations from the normal physiological range for prolonged periods leads to many pathophysiological conditions, including hypertension and cardiovascular disease (57). Conversely, the regulation of BP is affected by several physiological factors including blood volume, cardiac output, and peripheral resistance. Peripheral resistance is further influenced by the constant need to maintain blood viscosity homeostasis using sodium and potassium ions. Thus, changes to sodium intake will affect the renin-angiotensin-aldosterone system, which will consequently result in changes in plasma renin and aldosterone concentrations (4, 50, 58, 59). Maintaining a constantly high plasma sodium concentration due to high renin activity results in a prolonged high BP. However, a previous meta-analysis by Rhee et al. (59) found that while there was no significant correlation between plasma renin activity and 24-h urinary sodium, a longer duration of decreased sodium intake could reduce renin levels, thereby resulting in lowered BP.

Equally important, a deficit in plasma potassium results in sodium retention in the kidneys and a cellular potassium deficit, which affects vascular smooth muscle contraction and peripheral vascular resistance. This indirectly results in higher BP through the sodium–calcium exchanger type 1 mechanism (60). Conversely, an increased potassium intake could have antihypertensive effects by promoting endothelium vasodilation through stimulating the sodium pump and opening potassium channels. It is puzzling, therefore,

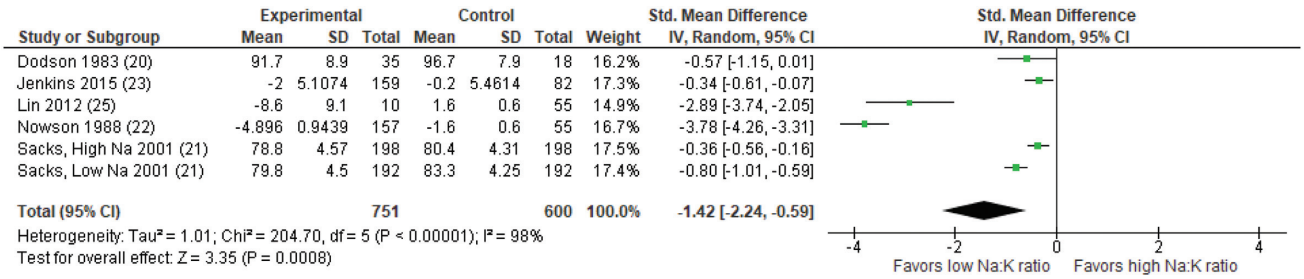

FIGURE 3 Forest plot of the association between different sodium to potassium ratios and diastolic blood pressure (mmHg) in adults in 5 RCTs. Diamonds indicate weighted mean difference with 95% confidence intervals. RCT, randomized controlled trials.

why the majority of investigations on the effect of sodium reduction on blood pressure have focused on measuring and reporting urinary sodium excretion without considering its relative excretion to urinary potassium. Our systematic review of cross-sectional and cohort studies indicate that 24-h UNa: K ratio was more significantly associated with the changes of blood pressure than either urinary sodium or urinary potassium alone (26, 30, 37, 40, 41), as well as with either reported dietary sodium or dietary potassium alone (40, 42).

Practical ways to reduce sodium intake while increasing potassium intake include increasing intake of fruits, vegetables, low-fat dairy, whole grains, poultry, fish, and nuts (prepared with little or no salt) (10, 61) as well as reducing intake of processed foods high in sodium. These are characteristics of the DASH diet, known to be effective in lowering systolic and diastolic BP (10). However, the DASH diet is not the only food-based strategy to obtain BP reductions (62). Other beneficial dietary patterns include the Nordic and Mediterranean diets (62).

In the current review there were many differences between studies, such as the number of participants, gender, age, study intervention, and duration of the intervention. Four cross-sectional studies in our review found different results for males and females (30, 29, 54, 63), which could be related to confounding effects of higher alcohol consumption in males and higher BMI in females. In comparison to cited studies that investigated 24-h urinary collections (30, 29), results between genders were inconsistent with results from those studies that collected spot urinary collections (54, 63). For example, 2 studies found a stronger association between blood pressure and UNa: K ratio in males, using casual urinary collections (54, 63) whereas a stronger association was found in females by Tian et al. (29) in their study, which collected 24-h urinary samples. Although 24-h urine was estimated in studies using casual urinary collections, all studies found an association and/or a correlation between UNa: K ratio and BP.

BMI is a factor known to affect BP, and Jackson et al. found a significant association between UNa: K ratio and BP only in obese participants with BMI $\geq$ 30 (2.28; 95% CI 0.60, 3.96, $P < 0.05$), but not in participants with a BMI <25 (0.66; −1.89, 3.20) (29). A cross-sectional study from China included in this review that compared normal weight and overweight/obese participants found a stronger association between higher sodium to potassium ratio and hypertension in the overweight/obese subjects (29). Conversely, other large-scale studies such as INTERSALT and INTERMAP samples found no mediating effect of BMI on the association between urinary sodium, potassium, and BP in Chinese sub-groups (3, 31).

The impact of UNa: K ratio in the context of low salt intakes warrants further exploration. For example, if populations shift their salt intakes to meet the WHO global target of <5g/d, but dietary potassium intake remains low, this may blunt the predicted BP reductions. The study by Farapti et al. (40) suggested that normotensive and hypertensive participants included in their study had low sodium concentrations, accompanied by even lower potassium intakes than recommended resulting in a positive association between UNa: K ratio and BP. A South African study by Ware et al. (16) reported a greater regression slope between age and SBP and DBP observed in those with a UNa: K ratio above 2, while associations were only evident with BP for sodium excretion at levels equivalent to ≥9g/d of salt.

A number of limitations need to be considered in the interpretation of this review. First, only 5 studies were included in the meta-analysis. The results of the meta-analysis indicated considerable heterogeneity. This may have been in part the result of variation between study characteristics, such as sample size and the dietary interventions used. Due to the small number of studies eligible for inclusion in the meta-analysis, it was not considered appropriate to further explore heterogeneity via sub-group analyses or meta-regression. There is an identified need for further RCTs on this topic. Second, other factors that affect BP measurements may not have been adequately controlled for in all studies. These include the use of diuretics, having a full bladder when taking BP readings, caffeine intake, exercise intensity, and alcohol consumption. It is important to note that causality cannot be inferred from data obtained from the included cross-sectional studies, and these were included in the review to indicate totality of evidence rather than draw firm conclusions from the studies. Additionally, many high-quality studies that have reported both 24-h urinary sodium and potassium excretion concentrations would not have been included in this review if the ratio of Na: K was not reported. Finally, the search strategy was restricted to published articles, which may have resulted in a publication bias. However, due to the small number of studies in the meta-analysis, we were unable to explore this formally using tests of funnel plot asymmetry.

Conclusions

This systematic review and meta-analysis has identified an association between lower sodium to potassium ratio and reduced BP in adults. This effect is evident for individuals with BP levels indicative of pre-hypertension and in those that are hypertensive. The quality of evidence for normotensives is too low to draw conclusions. The ratio of urinary sodium to potassium excretion appears to be a better predictor of BP than measurement of sodium or potassium excretion alone. However, further well-designed studies are required to identify the optimal sodium to potassium ratio in populations that have varying cuisines and to investigate the effect of different dietary patterns that contribute to the intake of these two cations.

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