Salt Reduction and Blood Pressure

Importance of Salt in Determining Blood Pressure in Children
Meta-Analysis of Controlled Trials

Feng J. He, Graham A. MacGregor

Abstract—To assess the effect of reducing salt intake on blood pressure in children, we carried out a meta-analysis of controlled trials. Trials were included if participants were children (≤18 years), and duration of salt reduction must have been for ≥2 weeks. Mean effect size was calculated using a fixed-effect model, because there was no significant heterogeneity. Ten trials of children and adolescents with 966 participants were included (median age: 13 years; range: 8 to 16 years; median duration: 4 weeks; range: 2 weeks to 3 years). Salt intake was reduced by 42% (interquartile range [IQR]: 7% to 58%). There were significant reductions in blood pressure: systolic: −1.17 mm Hg (95% CI: −1.78 to −0.56 mm Hg; P<0.001); diastolic: −1.29 mm Hg (95% CI: −1.94 to −0.65 mm Hg; P<0.0001). Three trials of infants with 551 participants were included (median duration: 20 weeks; range: 8 weeks to 6 months). Salt intake was reduced by 54% (IQR: 51% to 79%). There was a significant reduction in systolic blood pressure: −2.47 mm Hg (95% CI: −4.00 to −0.94 mm Hg; P<0.01). This is the first meta-analysis of salt reduction in children, and it demonstrates that a modest reduction in salt intake causes immediate falls in blood pressure and, if continued, may well lessen the subsequent rise in blood pressure with age. This would result in major reductions in cardiovascular disease. These results in conjunction with other evidence provide strong support for a reduction in salt intake in children. (Hypertension. 2006;48:861-869.)

Key Words: salt ■ blood pressure ■ children ■ meta-analysis

Raised blood pressure (BP) is the major cause of cardiovascular disease, accounting for 62% of strokes and 49% of coronary heart disease.1 A recent systematic analysis of population health data shows that raised BP is the biggest cause of death in the world and the second biggest cause of global burden of disease coming after underweight in children.2 In adults there is much evidence from different types of studies, including observational epidemiological studies,3 migration studies,4 population-based intervention studies,5 treatment trials,6 and animal7 and genetic studies8 that dietary salt (sodium chloride) is a causal factor for the raised BP and that our current high salt intake is largely responsible for the rise in BP with age.3

It has been shown that BP in children follows a tracking pattern that continues into the third and fourth decades of life.9–11 This suggests that BP in early life may be an indicator of the risk for adult hypertension and that the early introduction of intervention strategies may lead to a reduction in the high incidence of hypertension. Circumstantial evidence from epidemiological, clinical, and animal studies suggests that salt intake may play an important role in regulating BP in children.12–14 A number of controlled trials have studied the effect of reducing dietary salt intake on BP in children.15–27 However, many of the trials may be underpowered to detect a small change in BP with changing salt intake in children. We, therefore, carried out a meta-analysis of controlled trials to determine the effect of a reduction in salt intake on BP in children.

Methods

Literature Search
We developed a strategy (Table 1) to search for salt reduction trials in children from electronic databases: Medline (1966 to January 2006) and EMBASE (1980 to January 2006). We also searched the Cochrane Library with terms of “dietary sodium and children” or “dietary salt and children” in all fields. Furthermore, we reviewed the reference list of original and review articles to search for more trials. Only studies that were published as full articles and in English were considered.

Inclusion and Exclusion Criteria
For inclusion, trials needed to satisfy the following criteria: (1) participants were children aged ≤18 years; (2) the intervention aimed to reduce salt intake, and there was a control group or control period; and (3) duration of salt reduction must have been for ≥2 weeks. Trials were excluded if: (1) salt reduction was combined with other interventions; (2) participants were >18 years of age; (3) participants were taking antihypertensive drugs or other medications; or (4) there was no control group or control period.

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TABLE 1. Search Strategy to Identify Salt Reduction Trials in Children

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<td>33</td>
<td>1 and 12 and 32</td>
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Data Extraction and Statistical Analyses

Relevant data recorded were first author’s name, year of publication, country of centers, details of participants and study design, intervention procedures, compliance assessment, and methods of BP measurements. The main outcome measures extracted were the net changes in systolic and diastolic BP. For the purpose of pooled analyses, statistics that could be used to estimate the SEs of the net change in systolic and diastolic BP were also recorded.

The net changes in outcome measures were calculated as the differences between the reduced salt and control group for mean change from baseline for parallel trials. For crossover trials, the net changes were the mean differences between the reduced salt and control period for mean change from the baseline of each treatment period. For trials in infants (all used parallel design), the net changes were the mean differences between the reduced salt and control group in outcome measures at the end of follow-up, because baseline measurements were not available. In infants, only systolic BP was included in the meta-analysis, because the measurements of diastolic BP might not be reliable.

Different methods were used to assess the compliance with different salt intakes in the trials included in the meta-analysis, for example, 24-hour urinary sodium, overnight urinary sodium, spot urinary sodium/creatinine ratio, and sodium from food diary. We, therefore, calculated the percentage change of these measurements as an index of the change in salt intake. Several studies used >1 method to assess the compliance, for example, urinary sodium and diet diary (Table 2), and the studies showed close agreement in compliance between the different assessment methods. In our meta-analysis, we used urinary measurements when both diet diary and urinary sodium were reported.

When the SEs of net change in BP were not reported in individual studies, they were derived from SDs, CIs, exact t or P values, or calculated from SDs or SEs of paired difference for parallel trials.6–8 In 2 studies,7,15 the SEs of paired difference were imputed by assuming a correlation coefficient of 0.5 between the initial and final BP.29

Mean effect sizes were calculated using both fixed and random effects models, and the 2 models yielded very similar estimates. We present the results based on the fixed-effect model in this article, because there was no significant heterogeneity between studies (ie, P>0.1). Heterogeneity was analyzed using the I² and Q statistics. I² describes the percentage of variation across studies that is a result of heterogeneity rather than chance.28 We used funnel plot asymmetry to detect whether there was publication bias and Egger’s regression test to measure funnel plot asymmetry.31,32 Statistical analyses were performed using Cochrane Collaboration Review Manager 4.2 software and the Statistical Package for the Social Sciences (SPSS).

Results

Figure 1 shows the number of studies assessed and excluded through the stages of the meta-analysis. A total of 13 trials were included. Among the 13 trials, 10 were in children and adolescents,15–24 and 3 were in infants.25–27 The data for these 2 groups were analyzed and reported separately. One trial enrolled both children and adults,21 and we included only the subgroup with age of <18 years in our meta-analysis. The characteristics of the included trials are summarized in Table 2.

Children and Adolescents

There were 966 participants in the 10 trials included. Median age was 13 years, ranging from 8 to 16 years. The median duration of salt reduction was 4 weeks, ranging from 2 weeks to 3 years. Of the 10 trials, 6 used crossover design,17–19,22–24, and 4 used parallel design comparisons.15,16,18,23 All but 1 was randomized (Table 2). Among the 10 trials, 1 was double blind,18 7 were BP observer blind,15–17,20–23 and 2 did not report any blinding procedure.19,24 The median BP at baseline was 111/64 mm Hg.

The changes in salt intake were assessed by 24-hour urinary sodium in 3 trials,21,23,24 overnight urinary sodium in 3 trials,15,17,19 spot urinary sodium/creatinine ratio in 1 trial,22 spot urinary sodium in 1 trial,18 and food diary in 1 trial.20 In 1 study by Trevisan et al,16 random 24-hour urinary sodium was measured, but the results were not reported; however, Trevisan et al16 reported a significant reduction in erythrocyte sodium concentration in the low-salt group and no significant change in the control group. For each individual study except the one by Trevisan et al,16 we calculated the percentage change in the above measurements and used the percentage change of these measurements as an index of the change in salt intake (Table 2). The median net change in salt intake for the 9 trials was a reduction of 42% (interquartile range: 7% to 58%).
## TABLE 2. Characteristics of the Included Studies

<table>
<thead>
<tr>
<th>Author and Adolescents</th>
<th>Participants</th>
<th>Study Design</th>
<th>Intervention Procedure</th>
<th>Compliance Assessment</th>
<th>BP Measurement</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Gillum et al, 1981 (United States)¹⁵</td>
<td>N=51 (15±36), Age: 6–9 y, 54% boys, High normal BP, ie, BP above the 95th percentile for age and sex, but &lt;130/90 mm Hg, Mean BP: 114±8 mm Hg</td>
<td>Randomized parallel, BP-observer blind. Duration: 1 year</td>
<td>Family intervention program. Both parents and children attended four biweekly intensive 90-min lecture demonstration sessions followed by bimonthly 90-min maintenance sessions over the intervention year. Materials, eg, low-salt cookbooks, were provided.</td>
<td>Overnight UNa was changed from 31 to 35 mmol/10 h in control group and from 26 to 29 mmol/10 h in low-salt group. Three-day food records were obtained at baseline and year 1 in low-salt group but at year 1 only in control group. Twenty-four–hour UNa was measured for children in the low-salt group only.</td>
<td>BP was measured at home using random-0 sphygmomanometer with appropriate cuff size.²⁴ Korotkoff sound 4 was taken for DBP.</td>
<td>ΔSalt intake: −1.36% (from overnight UNa); ΔSBP: 3.00±2.61 mm Hg; ΔDBP: 2.90±5.79 mm Hg</td>
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<tr>
<td>Trevisan et al, 1981 (United States)¹⁶</td>
<td>N=21 (12±9), Age: 11–15 y, Mean SBP: 109 mm Hg</td>
<td>Randomized parallel, BP-observer blind. Duration: 24 d</td>
<td>A special diet of similar composition as that for control group, except for a decrease in Na content of −70%, was made for low-salt group in boarding high school.</td>
<td>Random 24-h urine and random duplicate meals were collected for Na analysis, but no detailed results were reported. However, there was a significant reduction in erythrocyte Na concentration in low-salt group and no significant change in control group.</td>
<td>BP was measured with an automatic device (VITA-STAT). Mean of 2 readings, 1 min apart, after 5 min rest, was used in the analysis.</td>
<td>ΔSalt intake: NR; ΔSBP: −1.25±4.96; mm Hg ΔDBP: NA</td>
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<tr>
<td>Cooper et al, 1984 (United States)¹⁷</td>
<td>N=113. Mean age: 16 y, 47% boys, Mean SBP: 109±61 mm Hg</td>
<td>Randomized crossover with a 5-d washout in between, BP-observer blind. Duration: 24 d</td>
<td>During low-salt period, participants were served all meals with reduced salt content from 1 special serving line in the cafeteria in boarding high school. The diet was designed to approximate the control diet in nutrient content, except that salt was reduced from an anticipated level of ~200 to 60 mmol/d. Children were instructed not to add salt or other salt-containing condiments to their foods. Between-meal snacks were also provided.</td>
<td>Overnight UNa was collected in 42% (48/113) participants and changed from 31 to 13 mmol/8 h. Duplicate food samples were collected for 24-h period from a random sample of 3 participants per group per week. The food analysis was in very close agreement with UNa.</td>
<td>An initial BP was measured with a standard mercury sphygmomanometer after participants sat quietly without talking for 15 min. The second and third BP were measured with a random-0 device. Mean of the 2 random-0 readings was used for analysis. The observers were blind to the participants’ group assignment.</td>
<td>ΔSalt intake: −57.68% (from overnight UNa); ΔSBP: −0.60±0.70 mm Hg; ΔDBP: −1.40±1.00 mm Hg</td>
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<tr>
<td>Calabrese and Tuthill, 1985 (United States)¹⁸</td>
<td>N=153 (51±102), Mean age: 9 y, 51% boys, Mean BP: 99±57 mm Hg</td>
<td>Randomized parallel, double-blind. Duration: 12 wk</td>
<td>Bottled water with different salt concentration was provided for children’s family (drinking and water used in preparation of foods and beverages) and classrooms in school. Na concentration was 110 and 10 mg/L in control and low-salt group, respectively.</td>
<td>UNa from first-morning urine was changed from 141 to 128 mmol/L in low-salt group and from 121 to 124 mmol/L in control group.</td>
<td>BP was measured by nurses using a mercury sphygmomanometer in a quiet room after ≥10-min rest. Korotkoff 1 and 5 were taken for SBP and DBP, respectively. Mean of 3 readings was used in the analysis.</td>
<td>ΔSalt intake: −11.70% (from spot UNa); ΔSBP: −0.80±0.80 mm Hg; ΔDBP: −1.50±1.65 mm Hg</td>
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<td>Howe et al, 1985 (Australia)¹⁹</td>
<td>N=21. Age: 11–14 y, 52% boys, BP: &lt;90th percentile adjusted for age and height, Mean BP: 119±78 mm Hg</td>
<td>Randomized crossover. Duration: 3 weeks.</td>
<td>Parents and children were interviewed individually by a dietician who provided detailed instructions and advice on the foods and food preparation appropriate for each diet.</td>
<td>UNa derived from Na/creatinine ratio in overnight urine samples was changed from 179.1 to 101.7 mmol/24 h. Twenty-four–hour diet diary was also recorded and showed a reduction in salt intake.</td>
<td>BP was measured using a mercury sphygmomanometer with appropriate cuff size in supine position after lying supine for ≥15 min. Korotkoff sound 1 and 4 were taken for SBP and DBP, respectively.</td>
<td>ΔSalt intake: −43.25% (from overnight UNa); ΔSBP: 0±2.32 mm Hg; ΔDBP: −1.30±1.78 mm Hg</td>
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### TABLE 2. (Continued)

<table>
<thead>
<tr>
<th>Author</th>
<th>Participants</th>
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<th>Intervention Procedure</th>
<th>Compliance Assessment</th>
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<th>Outcome</th>
</tr>
</thead>
</table>
| Ellison et al, 1989 (United States)  
<sup>20</sup> | N—309 during intervention year and n—341 during control year. Mean age: 15 y, 49% boys, 77% white. Mean BP: 107/64 mm Hg | Nonrandomized crossover with a washout period of ~5 months. BP-observer blind. Duration: 6 mo | During the low-salt period, changes were made in food purchasing (certain meat products, cheese, potato chips, and other foods with a reduced salt content were obtained) and in preparation practices in the schools’ kitchens (foods were prepared with less added salt, using non-Na–containing spices and other flavorings) in boarding high school. | An average of 4.5 food diaries per subject was obtained during baseline and follow-up periods. Food diaries showed that average salt intake was reduced by 15% to 20%. | After appropriate training, students measured their own BP every week using Dinamap 845 devices connected to a computer. Three measurements were taken, and mean of last 2 was recorded. Students were not given their BP data until the end of the school year. Baseline BP was taken as the mean of all recordings obtained during 4 weeks at the beginning of the school year. Follow-up BP was taken as the mean of BP obtained during 6 weeks near the end of the school year. |                 |
| Myers, 1989 (Australia)  
<sup>21</sup> | N—23. Mean age: 11 y, 40% boys. Mean BP: 108/67 mm Hg | Randomized crossover. BP-observer blind. Duration: 2 wk | A dietitian advised individuals on their diet based on the previous dietary history and 24-h UNa. | Twenty-four–hour UNa was changed from 158 to 66 mmol/24 h. | A mercury sphygmomanometer was used with appropriate cuff size. BP was measured by trained observers who were not aware of the diet the participants were on. |                 |
| Howe et al, 1991 (Australia)  
<sup>22</sup> | N—100. Age: 11–14 y, 52% boys. Equal no. of children from top, middle, and bottom deciles of BP distribution. Mean BP: 115/60 mm Hg | Randomized crossover. BP-observer blind. Duration: 4 wk | Weekly individual dietary counseling for both children and parents, low-salt bread was provided for the low salt period and salt sachets were issued for control period. | Salt intake estimated from UNa/creatinine ratio of a midstream sample of the first morning void urine corrected for a factor which was derived from 24 hours urine collection in a subgroup of 77 children, was changed from 175.9 to 101.8 mmol/24 h. A subgroup completed diet diaries and showed a reduction in salt intake consistent with the change in UNa. | Supine BP was measured using Dinamap monitors with appropriate cuff sizes. An initial measurement was made to acclimatize children to the procedure and was not recorded. Two further readings were taken at least 15 min later and the mean was used for the analysis. |                 |
| Sinaiko et al, 1993 (United States)  
<sup>23</sup> | N—139 (70–69). Mean age: 13 years, 50% boy, 88% white. BP in the upper 15 percentiles of BP distribution. Mean BP: 114/64 mm Hg | Randomized parallel. BP-observer blind. Duration: 3 years | Trained nutritionists gave dietary counseling 7 times during the first 3 mo, and then every 3 mo. Phone calls between visits were also made to reinforce the instructions. | In control group, 24-h UNa was changed from 159 to 178 mmol in boys and from 150 to 128 mmol in girls. In low-salt group, 24-h UNa was changed from 142 to 162 mmol for boys and from 133 to 119 mmol in girls. However, only 59% of boys and 74% of girls had 24-h UNa measured at year 3, though all had 24-h UNa measured at baseline. | A random-0 sphygmomanometer was used to measure BP on the right arm with participants in a seated position. Means of 2 measures of SBP and fifth-phase DBP were used for analysis. |                 |
| Palacios et al, 2004 (United States)  
<sup>24</sup> | N—36. Age: 11–15 y, all girls, 39% white. Mean BP: 113/57 mm Hg | Randomized crossover with a 2-wk washout in between. Duration: 3 wk | All foods and drinks were provided. Children were strictly supervised at all times to ensure compliance and to avoid consumption of other foods. The 2 diets had the same composition except for a difference in Na (174 vs 43 mmol/d). | Twenty-four–hour UNa was reduced from 140.8 to 41.1 mmol. | Supine BP was measured using sphygmomanometer. Korotkoff sound 1 and 5 were taken for SBP and DBP, respectively. |                 |

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<tbody>
<tr>
<td>Infants</td>
<td>N=27 (13 + 14).</td>
<td>Parallel, BP-observer blind. Duration: 5 mo</td>
<td>All infant foods were provided, and the parents agreed to restrict feeding to the foods provided. Na intake was 9.25 and 1.93 mmol/100 kcal for control and low-salt group, respectively. These were within the range of Na content normally consumed in 1969.</td>
<td>At the end of the study, 3-day 24-h urine was collected via metabolic frames. UNa was 54.8 and 11.3 mmol/24 h in control and low-salt group, respectively. Dietary records showed a difference in salt intake between the 2 groups consistent with that from 24-h UNa.</td>
<td>An Air Shield BP Monitor was attached to the right arm, which automatically inflated the cuff every 5 min. Readings were recorded 6 to 12 times during the 3-d stay in hospital. Only readings made while the infants were asleep and —1 h after feeding were used for the analysis.</td>
<td>∆Salt intake: 79.38% (from 24-h UNa); ∆SBP: 2.00: 2.13 mm Hg</td>
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<td>Whitten et al, 1980 (United States)25</td>
<td>Age: 3 mo, all black boys</td>
<td>Duration: 6 mo</td>
<td>Spot UNa (average of wk 5, 13, and 21) was 22.7 mmol/L and 11.1 mmol/L in control and low-salt group, respectively. Average amount of Na consumed during the first 6 mo was calculated from the amount of baby food delivered with allowance for breastfeeding and was estimated to be 2.5 vs 0.89 mol of Na in control and low-salt group, respectively.</td>
<td>BP was measured on the right arm using a Doppler ultrasound device connected to a random-0 sphygmomanometer. The mean of 3 readings was used in the analysis. The readings were taken while the infants were awake and not crying except for a few infants in the first 2 mo whose BPs were measured while sleeping.</td>
<td>BP was measured using the Dianamap 8100 Vital Signs Monitor, which detects BP and pulse by the Doppler technique. BP measurements were made at the infants’ home during sleep, with an appropriate cuff size on the right arm.</td>
<td>∆Salt intake: 51.10% (from spot UNa); ∆SBP: 2.00: 0.92 mm Hg</td>
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<td>Hofman et al, 1983 (The Netherlands)26</td>
<td>N=466 (225 + 241). Newborn, 51% boys</td>
<td>Randomized, double-blind. Duration: 6 mo</td>
<td>All formula milk and solid foods were provided. The normal Na formula contained Na that was regular for Dutch formula milk commercially available during the study period. The low Na formula had one third of Na as that in the normal Na formula. The mothers were allowed to breastfeed their babies; however, there was no significant difference between the 2 groups in the proportion of infants receiving breastfeeding.</td>
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<tr>
<td>Pomeranz et al, 2002 (Israel)27</td>
<td>N=58 (25 + 33). Newborn</td>
<td>Randomized, parallel, BP-observer blind. Duration: 8 wk</td>
<td>The same milk powder formula was given to the 2 groups of infants, but in low-salt group the formula was diluted with low-Na mineral water, and in control group it was diluted with high-Na tap water. The Na concentration was 9.5 and 16.6 mmol/L for the 2 groups, respectively. Only infants whose mothers refused to breastfeed were included in the study.</td>
<td>Spot UNa/creatinine ratio was 2.6 and 1.2 in control and low-salt group, respectively. An analysis of milk imbibed by infants showed a difference in Na concentration consistent with that from urine analysis.</td>
<td>BP was measured using the Dianamap 8100 Vital Signs Monitor, which detects BP and pulse by the Doppler technique. BP measurements were made at the infants’ home during sleep, with an appropriate cuff size on the right arm.</td>
<td>∆Salt intake: 53.85% (from spot UNa/creatinine ratio); ∆SBP: 5.30: 2.06 mm Hg</td>
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N indicates number of participants, and the number in bracket represents the number of participants in low-salt and control group, respectively; UNa, urinary sodium; ∆salt intake, net change in salt intake; ∆SBP, net change in systolic BP; ∆DBP: net change in diastolic BP; NR: not reported.

Figure 2 shows the net changes in systolic and diastolic BP in individual trials. The pooled analysis showed a significant reduction in both systolic and diastolic BP with a reduction in salt intake. The net change in systolic BP was 1.17 mm Hg (95% CI: −1.78 to −0.56; P<0.001), and it was −1.29 mm Hg (−1.94 to −0.65; P<0.0001) for diastolic BP. The test for heterogeneity showed that there was no significant heterogeneity between studies (P for heterogeneity=0.64, I²=0% for systolic BP; P for heterogeneity=0.54, I²=0% for diastolic BP).

In 2 of the included studies,15,23 the compliance with different salt intakes seemed to be poor, that is, the net change in salt intake was <5%. However, in 1 of these studies, only 59% of boys and 74% of girls had 24-hour urinary sodium measured at the end of follow-up (Table 2).23 Reanalyzing the data by excluding these 2 trials showed that the net change in BP was −1.18 mm Hg (95% CI: −1.82 to −0.55; P=0.0003) for systolic and −1.20 mm Hg (95% CI: −1.86 to −0.54; P=0.0003) for diastolic BP. There was no significant heterogeneity between studies (P for heterogeneity=0.78, I²=0% for systolic BP; P for heterogeneity=0.85, I²=0% for diastolic BP).
To examine whether there was a publication bias, we plotted the net change in BP against the reciprocal of the SE of the net change in BP. The funnel plot was symmetrical visually for both systolic and diastolic BP (Figure 3). Egger’s regression test suggested no significant asymmetry of the funnel plot ($P=0.841$ for systolic and $P=0.861$ for diastolic BP). This would indicate that there was no evidence of publication bias.

**Infants**

There were 551 infants in the 3 trials included. Two trials started in newborn babies,$^{26,27}$ and 1 started in those 3 month of age.$^{25}$ Median duration of salt reduction was 20 weeks, ranging from 8 weeks to 6 months. All of the trials used paralledle comparisons. Two of the 3 trials were randomized,$^{26,27}$ and the other did not report whether the trial was randomized or not.$^{25}$ One was double blind,$^{26}$ 1 was BP observer blind,$^{27}$ and 1 did not report any blinding procedure (Table 2).$^{25}$ The median systolic BP at the end of follow-up was 91 mm Hg in the control group and 88 mm Hg in the low-salt group.

The changes in salt intake were assessed by 24-hour urinary sodium in 1 trial,$^{25}$ spot urinary sodium in 1 trial,$^{26}$ and spot urinary sodium/creatinine ratio in 1 trial.$^{27}$ The median reduction in salt intake was 54% (interquartile range: 51% to 79%). The pooled analysis showed a significant decrease in systolic BP ($-2.47$ mm Hg; 95% CI: $-4.00$ to $-0.94$; $P<0.01$). The test for heterogeneity showed no significant heterogeneity between studies ($P$ for heterogeneity = 0.33, $I^2$ = 8.7%).

**Discussion**

This is the first meta-analysis of salt reduction in children and demonstrates that a modest reduction in salt intake does have a significant effect on BP. From a population viewpoint, a reduction in BP of 1/1 mm Hg in children and adolescents observed in our study would have major public health implications in terms of preventing cardiovascular disease in the future.
Our meta-analysis in infants also showed a significant effect of salt reduction on BP. Two of the 3 trials included in our meta-analysis were carried out in the early 1970s and 1980s, and at that time, salt concentrations in formula milk were 3 times higher than in human milk. Currently, in most developed countries, salt is no longer added to baby foods, and salt concentrations in formula milk are very similar to those in human milk. However, salt intake in infants and toddlers is dramatically increased when solid foods are introduced, which usually begins at 6 to 9 months of age. The introduction of cow’s milk at 12 months of age increases salt intake further. A recent survey of the dietary intakes (the 2002 Feeding Infants and Toddlers Study) in the United States showed that almost all 12- to 24-month-old toddlers had salt intake exceeding the “adequate level” of the Dietary Reference Intake established by the Food and Nutrition Board of the Institute of Medicine, and the mean salt intake was 4.1 g per day.33 A recent study in infants in Israel showed that the high salt concentration in tap water, which was used to dilute milk powder formula, was related to an increased BP in infants.

How Much Salt Do Children and Adolescents Eat?
Several different methods have been used to estimate salt intake in the trials included in our meta-analysis, for example, 24-hour urinary sodium, overnight urinary sodium, spot urinary sodium/creatinine ratio, and food diary. These methods are useful in assessing the compliance with the different salt intakes, particularly because the same method was used in all of the participants throughout the whole study, but most of these methods are unreliable in assessing the amount of dietary intake of salt. Twenty-four-hour urinary sodium is the only accurate way to assess dietary salt intake. Only 3 trials included in our meta-analysis measured 24-hour urinary sodium in children and adolescents.21,23,24 Among these 3 trials, 1 was carried out in the Metabolic Unit, and all of the foods and drinks were provided during the study.24 Therefore, the salt intake in this study may not reflect the children’s usual intake. The other 2 studies were carried out in free-living individuals who agreed to take part in the trial, and the usual salt intake was 133 mmol per day (7.8 g per day of salt) for children with an average age of 11 years in 1 study and 150 and 142 mmol per day (8.8 and 8.4 g per day of salt) for 13-year-old boys and girls, respectively, in the other study.23 de Courcy et al,34 in 1986, measured 24-hour urinary sodium in 17 pupils aged 4 to 6 years who were randomly selected from 2 primary schools. All of the children collected 2 consecutive 24-hour urine samples. The results showed that the average urinary sodium was 64 mmol per 24 hours (3.8 g per day of salt). The ratio of sodium/creatinine was 3.5 times higher in children than in adults.

In all of the above-mentioned studies, salt intake was measured in the 1980’s. Since then, salt intake in children in developed countries will have increased because of the increasing consumption of processed foods, which now account for 80% of total salt intake. Surveys in the United States showed that the proportion of foods that children consumed from restaurants and fast food outlets increased by 300% between 1977 and 1996.35 Snack food consumption showed trends similar to those of fast food consumption. The restaurant foods, fast foods, and snacks are generally very high in salt, fat, and sugar. The recent National Diet and Nutrition Survey in young people in Great Britain was carried out in 1997 and measured salt intake using a 7-day dietary record in 856 boys and 845 girls.36 The average salt intake, at the age of 4 to 6 years, was 5.2 g per day for boys and 4.6 g per day for girls. With increasing age, there was an increase in salt intake, and by the age of 15 to 18 years, salt intake was 8.2 and 5.7 g per day for boys and girls, respectively. It is important to note that these intakes underestimate the dietary intake of salt by 25% to 30%, which has been demonstrated in a similar survey in adults where both dietary record and 24-hour urinary sodium were measured.37 The current salt intake in children and adolescents is likely to have increased further due to a greater consumption of highly salty foods since this survey was...
conducted. This high salt intake may predispose them to develop hypertension later. Although the physiological need for salt intake in children has not been studied, the measured urinary output of salt in the adults in 1 tribe in South America was 0.05 g per day. The BP of these adults does not rise with age.

Other Evidence in Support of a Reduction in Salt Intake in Children
When considering any dietary or lifestyle advice for a population, it is important to take into account all of the evidence. For salt and BP in children, population studies, well-conducted observational epidemiological studies, and experimental studies in animals provide further support for a reduction in salt intake in children.

In the late 1950s, the Japanese government initiated a nationwide campaign to reduce population salt intake to reduce the high prevalence of hypertension and stroke in Japan. The campaign was successful in reducing the average salt intake by 1.5 g per day and, in some areas, salt intake was reduced by 4 g per day. In local studies, the beneficial effects of salt reduction were evident in school children in whom there was a large fall in BP from 1957 to 1973 despite an increase in obesity, fat intake, cigarette smoking, and alcohol consumption, which occurred with the Westernization of Japan during that period.

There have been over 20 observational epidemiological studies on salt and BP in children. Many of these studies did not show a significant association. This is not surprising given the large day-to-day intrapopulation variations of salt intake. In addition, many studies had methodologic problems. Among the observational studies that were more methodologically strong (eg, multiple measurements of salt intake were made, urinary sodium was measured, and confounding factors were controlled), the majority showed a significant positive association between salt intake and BP. For instance, in a carefully conducted study where 7 consecutive 24-hour urines were collected by all of the participants, Cooper et al demonstrated a significant linear relationship between urinary sodium and BP in 73 children aged 11 to 14 years; that is, the higher the salt intake, the higher the BP. The relationship remained significant after controlling for age, sex, race, pulse rate, height, and body weight.

One longitudinal study examined the effect of habitual salt and potassium intake on the rise in BP with age in 233 Dutch children who were aged 5 to 17 years at baseline and followed up for 7 years. All of the participants had annual measurements of BP and overnight urinary sodium and potassium. The results showed that the rise in BP in childhood was significantly associated with the habitual sodium/potassium ratio after controlling for age, sex, weight, height, and other electrolytes.

Studies in animals have suggested that salt intake in early life may have a programming effect on BP. Experiments in hypertension-prone rats demonstrated that BP rose more rapidly and reached a higher level if a high salt intake began earlier in life, and brief exposure to salt in early life led to permanent increases in BP even when the salt intake was reduced. Other experiments showed that alteration of perinatal salt intake has a significant and long-lasting effect on BP of adult rats.

In humans, very early intervention during gestation and lifetime longitudinal follow-up have not been feasible. However, 1 follow-up study in 167 Dutch children (35% of the original cohort), who took part in the double-blind salt reduction study during the first 6 months of life, showed that, at 15 years of age, there was still a significant difference in BP (3.6/2.2 mm Hg) between those who were randomly assigned to receive a low-salt diet and those on a high salt intake after adjusting for confounding factors, in spite of the fact that the babies went back to their usual salt intake when the double-blind trial stopped at 6 months of age. These results fit in well with the animal experiments, suggesting a programming effect of salt intake in early life on BP.

Perspectives
Tracking of BP from children to adults suggests that intervention strategies to prevent adult hypertension should start early in childhood. Our meta-analysis of controlled trials, epidemiological studies in children, and experimental studies in animals have shown that salt intake is an important regulator of BP in childhood. The current salt intake in children is unnecessarily high and is very likely to predispose children to develop hypertension later. Furthermore, suppression of salt taste receptors by very high salt content of many snack foods targeted at children is likely to program children to consume foods with a higher salt content later in life. A modest reduction in salt intake will cause an immediate fall in BP in children and, if continued, may well lessen the subsequent rise in BP with age and prevent the development of hypertension. This would result in major reductions in cardiovascular disease.

Approximately 80% of salt intake comes from salt added to processed, restaurant, fast, and takeaway foods in most developed countries. A reduction in salt intake in children can be achieved by a gradual and sustained reduction in the amount of salt added to children’s foods by the food industry. A comprehensive school meals program, for example, the one recently announced by the United Kingdom government, combined with advice to parents and children, will also help reduce salt, fat, and sugar in children’s diets. If these were achieved, the benefits would be very large.

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Disclosures
None.

References


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