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Filippou CD, Tsioufis CP, Thomopoulos CG, Mihas CC, Dimitriadis KS, Sotiropoulou LI, et al. Dietary Approaches to Stop Hypertension (DASH) Diet and Blood Pressure Reduction in Adults with and without Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2020;1–11.

What We Know, Think We Know, or Are Starting to Know

It' s over 20yrs since the initial publication of the Dietary Approaches to Stop Hypertension [DASH] trial [(1)]. What in the initial intervention was known as the "combination diet", a diet rich in fruit, vegetables, low-fat dairy, whole-grains, white meats, and nuts, was designed to be low in sodium and saturated fat, and rich in potassium: this became known as "the DASH diet" following the intervention.

The DASH trial was not, however, the first time the relationship between sodium and cardiovascular risk was considered. The relationship between sodium and cardiovascular risk was well-established by the early 1990' s, evident in a 1991 analysis of 78 trials on salt reduction and blood pressure [(2)]. This analysis modelled the predicted reduction in mortality from salt reduction, based on mortality risk evident at different levels of blood pressure in population studies: reducing salt by 1,500mg/d [bear in mind intakes were on average over 10g salt - 4,000mg sodium - per day] across the whole population was predicted to reduce stroke deaths by 22% and ischaemic heart disease deaths by 16% [(2)].

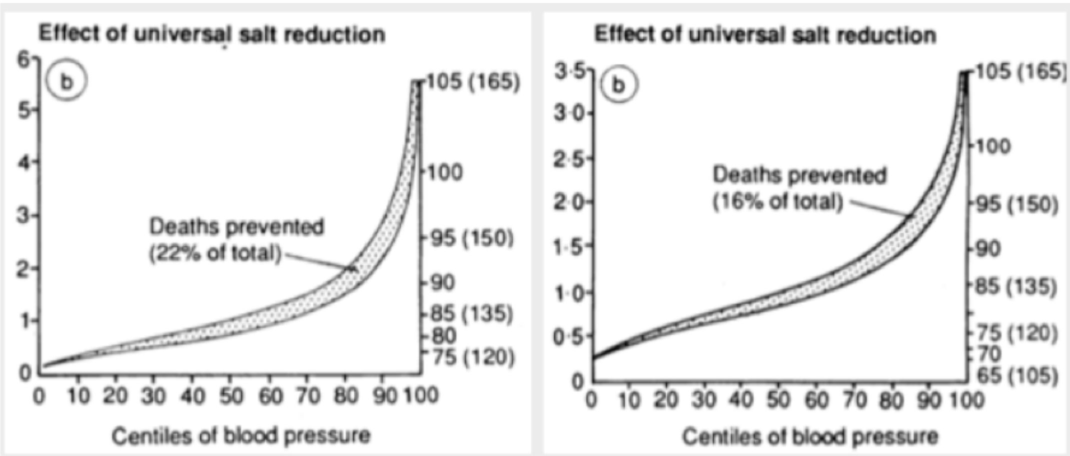


***Figure** from [(2)] illustrating the modelled effects on stroke and ischaemic heart disease mortality from a population-wide reduction of 1,500mg sodium.*

The initial DASH intervention examined whether reducing sodium from average levels in the US diet [3.5g of sodium [Na] / 8.7g of salt [sodium chloride, NaCl] to below recommended levels would lower blood pressure to a greater degree than the target levels alone. The controlled feeding intervention compared the DASH diet to a control standard American diet at three different levels of sodium intake: 3,300mg/d, 2,500mg/d, and 1,500mg/d. At every level of sodium intake, the DASH diet lowered blood pressure [(1)].

The initial publications from DASH included specific subgroup analyses to analyse the effects of the intervention mediated by factors like by age, hypertension status, ethnicity, medication use, alcohol intake, physical activity, and body weight: across all subgroups, the lower sodium diets resulted in more substantial reductions in blood pressure, an effect which was particularly pronounced in Black participants [3,4].

This is quite relevant: many who question the relationship between sodium and cardiovascular disease emphasise that in people with normal blood pressure [normotensive], lower body weight, and other health-associated behaviours, there is little effect of adjusting salt intake.

In the 20yrs since the initial DASH diet intervention was published, it has become one of the most well-established dietary patterns in nutrition, with a substantial body of intervention studies. The present study was a meta-analysis of the effects of DASH diet interventions on blood pressure in both hypertensive and normotensive subjects.

The Study

A systematic review and meta-analysis of DASH intervention trials was conducted. The eligibility criteria for studies to be included was as follows:

- Randomised controlled trials
- Compared effects of the DASH diet vs. a control diet
- Attained blood pressure [systolic and diastolic] as the primary or secondary outcome
- Both normotensive and hypertensive participants
- With or without comorbodities, i.e., type-2 diabetes, metabolic syndrome
- With or without lifestyle changes, i.e., weight loss, physical activity

The authors also considered data, if available in the primary included studies, on potentially important mediating factors, for example change in 24hr urinary sodium excretion during follow-up period of trials, whether trials involved energy restriction, controlled vs. uncontrolled feeding, specific sodium restriction in addition to the diets, physical activity, and age. Subgroup analysis was undertaken to examine the effects of the DASH diet vs. control diet relative to these factors.

*Geek Box: Average Treatment Effect

One of the main reasons why RCTs are considered more reliable than other research designs is that the size of the effect (if any) is presumed to be more accurate. When it comes to effect sizes, what intervention trials look at is the average treatment effect (ATE). This is the difference between the average (mean) effect in the intervention group vs. the average effect in the control group. This can be an issue in trials looking at the effects of a supplemental nutrient, as often the control group has adequate intake of that nutrient anyway from diet, and the difference in the ATE between the intervention and control group is not large and is statistically insignificant. To calculate the ATE in both arms of a trial, the general standard approach is to compare the difference between the baseline value (for whatever is being measured) and the end value. Let's say, for example, that a group start a trial in the intervention group with a blood glucose reading of 6.5mmol/L and finish with a mean level of 4.5mmol/L: a mean difference of 2.0mmol/L. Now, one limitation of the ATE is that we look at the mean, and cannot see individual effects. Some people may have larger or smaller responses. The other factor to bear in mind is that the ATE for the same exposure or intervention may differ from trial to trial, for example if the baselinevalues are higher or lower, if the achieved level is higher or lower, if the duration of the trial differs, etc. This means, from a meta-analysis perspective, to compare these trials could bias the outcome and over or underestimate the effects of an intervention. In the present meta-analysis, rather than take the ATE of each included study, the used the actual level of blood pressureafter the intervention, and the difference between attained levels. Let's come back to our example above, and let's say in that study the control group increased from 6.5 to 7.0mmol/L. In this example, the mean post-intervention difference between intervention and control would be 2.5mmol/L. This means the effect size isn't the difference between baseline and end of study, which is influenced by the factors mentioned above, but the actual difference between intervention and control values after the intervention.

Results: 30 studies were included in the analysis, including 5,545 participants, 45% men and 55% women, mean age 51yrs, mean BMI 29.2kg/m2, mean baseline SBP was 134.3mmHg and DBP 84.9mmHg, mean follow-up period of 15.3 weeks.

In the main analysis including all 30 trials together, the following mean differences between intervention and control groups in attained blood pressure were highly significant:

- ***SBP:***
  −3.2mmHg [95% CI −4.2 to −2.3]
- ***DBP:***
  −2.5mmHg [95% CI −3.5 to −1.5]

Confining the analysis to studies graded as 'high quality' did not change the results.

In the analysis comparing the effects of the DASH diet in normotensive vs. hypertensive participants, the following mean differences in attained blood pressure were found:

- ***Normotension:***
  SBP −3.9mmHg [95% CI −5.5 to −2.4], DBP −2.5mmHg[95% CI −3.9 to −1.1]
- ***Hypertension:***
  SBP −3.9mmHg [95% CI −6.0 to −1.8], DBP −2.1mmHg [95% CI −4.0 to −0.2]
- ***Untreated hypertension:***
  SBP −5.9mmHg [95% CI −9.9 to −1.8], DBP −3.3mmHg [95% CI −5.5 to −1.2]
- ***SBP >140mmHg:***
  SBP −2.9mmHg [95% CI −5.1 to −0.7], DBP −3.0mmHg [95% CI −5.0 to −1.0]
- ***SBP <140mmHg:***
  SBP −3.4mmHg [95% CI −4.5 to −2.3], DBP −2.3mmHg [95% CI −3.5 to −1.2]

In the subgroup analysis of potential modifying factors, the following factors were statistically significant [for ease only mean differences are shown, not confidence intervals]:

- ***Age >50yrs:***
  SBP −2.0mmHg [95% CI−2.4 to −1.8], DBP −1.3mmHg [95% CI −2.2 to −0.4]
- ***Age <50yrs:***
  SBP −4.9mmHg [95% CI−6.2 to −3.5], DBP −3.5mmHg [95% CI −4.8 to −2.1]
- ***Daily Sodium intake >2,400mg***
  SBP −4.5mmHg [95% CI−6.1 to −3.0], DBP −2.7mmHg [95% CI −3.8 to −1.6
- ***Daily Sodium intake <2,400mg:***
  SBP −2.1mmHg [95% CI −2.5 to −1.8], DBP −1.9mmHg [95% CI −3.3 to −0.6]

Neither BMI, whether the study controlled feeding, whether the study involved energy restriction, whether the follow-up period was over or under 3-months, or the method of blood pressure measurement, had any effect on either SBP or DBP.

The Critical Breakdown

Pros: The large amount of trials and included participants yielded a comprehensive analysis, and allowed for multiple potential moderating factors to be examined in subgroup analysis. Rather than compare the mean difference between baseline and end of intervention, which is prone to bias influenced by varying baseline levels in both intervention and control groups, the analysis compared the attained levels of blood pressure in both groups after the intervention; this would allow for a more ' true' comparison of the difference between the diet vs. control groups.

Cons: Given the substantial racial differences in hypertension, and effects of sodium restriction, between Black and Caucasian populations, there was no analysis based on this factor [assuming not all 30 studies included were exclusively Caucasian, but this potential limitation is not mentioned]. There was also no subgroup analysis based on sex due to limited data in the included studies. The exact dietary prescriptions in included studies varied in macronutrient and micronutrient content, which may have influenced the outcomes.

Key Characteristic

The subgroup analyses teased out a number of important factors that typically arise in discussion around sodium, diet, and health. This generated a number of important findings.

First, the magnitude of effect was similar in both normotensive and hypertensive participants [more under ***Interesting Finding***, below].

Second, the magnitude of effect of the DASH diet was mediate strongly by age, with significantly greater reductions in BP in participants <50yrs compared to >50yrs.

Third, treatment for hypertension mediated the effect [which could be expected]; hypertensive patients without any anti-hypertensive medications benefitted more than all hypertensive patients considered together, however, there was even a benefit of the DASH diet evident in subgroups treated with antihypertensive medications.

Fourth, the treatment effect of the DASH diet was more pronounced on SBP reduction participants with sodium intake >2400mg/d.

Fifth, the effect was independent of baseline BP levels - either SBP >140mmHG vs. <140mmHG or DPB >80mmHG vs. <80mmHG.

Finally, the effects of the DASH diet were independent of energy restriction.

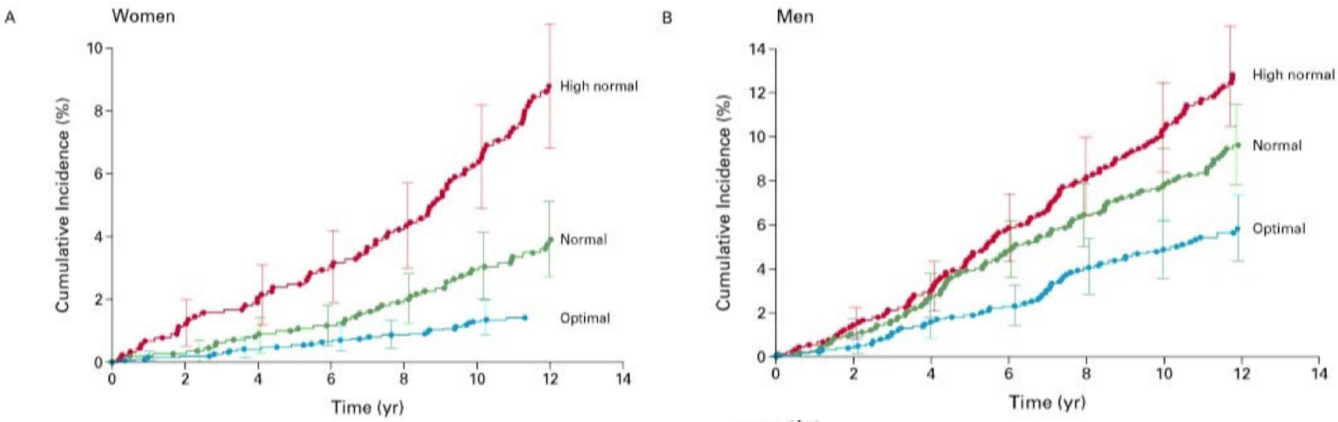
Interesting Finding

The finding that the DASH diet was as effective in normotensive as hypertensive participants. In normotensive participants, SBP decreased −3.9mmHg and DBP decreased −2.5mmHg; in hypertensive participants SBP decreased −3.9mmHg and DBP decreased −2.1mmHg.

This is relevant as there are questions over whether normotensive individuals benefit from sodium reduction [(5)]. Such studies are often cited to suggest that otherwise healthy individuals with normal BP need not consider sodium/salt intake, that the consideration is largely for individuals with hypertension [(6)].

However, further scrutiny reveals these studies may be the exception, rather than the norm, and a number of acute studies have demonstrated that salt raises blood pressure in otherwise normotensive participants [(7,8)]. A 1997 analysis of RCTs also demonstrated reductions in blood pressure in normotensive participants, albeit the magnitude of this effect was less than in hypertensive participants [(9)]. But more importantly - and many people seem totally unaware of this fact - most deaths related to high BP occur in people with moderately elevated BP in the normotensive range between 120/80mmHg to 140/90mmHg [(10)].

The finding in the present meta-analysis may reflect the difference in method of analysis; looking at attained BP level post-intervention, rather than the difference between baseline and post-intervention, as many studies in normotensive participants are very short-term - <4weeks or often 1-day experimental studies - which exaggerates the purported difference between normotensive and hypertensive participants [(2)].



No. at Risk							
Optimal	1875	1867	1851	1839	1821	1734	887
Normal	1126	1115	1097	1084	1061	974	649
High normal	891	874	859	840	812	722	520

Figure *from* [(10)] *illustrating the incidence of cardiovascular events in women (top) and men (bottom) relative to baseline blood pressure levels: the 'high-normal' range in this study was defined as SBP of 130-139mmHg or a DBP of 85-89mmHg.*

Relevance

This meta-analysis differed by looking at the effect of DASH vs. control diet on attained BP reduction [i.e., what was the actual level of blood pressure achieved in the study vs. the mean difference between baseline to post intervention]. The various subgroup analyses yielded important findings in the context of wider question marks over what populations may benefit from lowering sodium intake. What this analysis suggests is that lowering sodium earlier in the lifespan may yield greater reductions in BP, and that DASH dietary interventions may benefit BP independent of energy restriction. Of note, individuals with higher sodium intake may have a greater benefit in reducing BP. This is particularly relevant when we consider the benefit to salt reformulation policies in public health nutrition over the past decade or so:

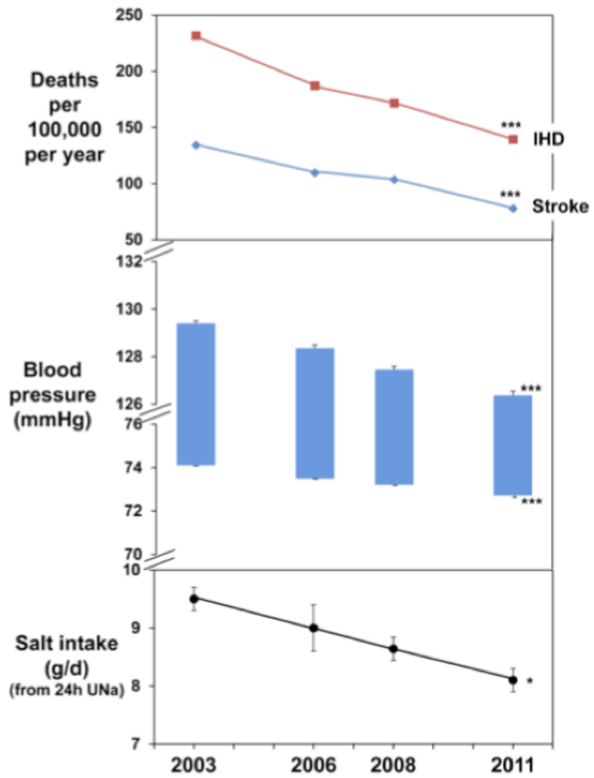


***Figure** from [(10)] illustrating the decline in stroke and ischaemic heart disease mortality in the UK population between 2003-2011 following introduction of salt reformulation, and the correlation with reductions in population-wide blood pressure levels accompanying significant declines in salt intake.*

These data from the UK mirror the data from public health interventions in both Japan and Finland targeting reductions in salt intake, all countries of which have observed significant reductions in stroke and ischaemic heart disease mortality [(11)].

Diet-disease relationships are moderated or mediated relationships: not 'A=B', but 'A=C via B'. This meta-analysis was of studies with the intermediate risk factor - BP - as the outcome. Nonetheless, BP lies on the causal chain between diet, hypertension, and CVD.

The present meta-analysis demonstrates that the DASH diet is effective in lowering BP across a range of participant characteristics.

Application to Practice

The DASH diet is one of the most well-established dietary pattern interventions, and most practitioners will be familiar with its main dietary constituents. The present study synthesises good quality available intervention studies, confirming the effectiveness of the diet in reducing blood pressure. Of note for practitioners, this reduction in BP is evident in individuals with normal blood pressure, may occur independent of energy restriction, and is more pronounced in people <50yrs.

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