



Sodium Reduction Strategies at Population and Patient Level: Reformulation, Substitutes and Measurable Effect

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Abstract

The effect attributable to sodium reduction shrinks as the population widens, and reading across those levels is where this literature is most often misused. A cluster-randomised trial in 600 villages and 20,995 participants using a substitute of 75 per cent sodium chloride and 25 per cent potassium chloride reported reductions of 14 per cent in stroke, 13 per cent in major cardiovascular events and 12 per cent in premature death over five years. Meta-analysis of substitute trials gives a systolic reduction of 5.58 mmHg (95% CI 4.09 to 7.08). A provincial programme across four intervention counties produced an adjusted net systolic difference of 1.3 mmHg (95% CI 0.5 to 2.1). All three are real. Whether the benefit comes from less sodium or more potassium has been modelled rather than measured, and substitutes carry hyperkalaemia risk where excretion is impaired.

Keywords: Sodium reduction; Salt substitutes; Reformulation; Blood pressure; Population health

Introduction

Excess dietary salt is responsible for around three million deaths annually worldwide, and reducing sodium intake produces dose-dependent declines in systolic and diastolic blood pressure [1,2]. The World Health Organization recommends that salt intake should not exceed 5 grams daily and describes salt reduction as among the most cost-effective measures available to a country [1,12]. Global sodium consumption has been related to death from cardiovascular causes across populations [13].

Two broad approaches exist. Reformulation and voluntary industry targets act on the food supply, while substitution replaces a proportion of sodium chloride with potassium chloride in cooking or at the table [1,3]. Both are described as population strategies although they operate differently [3].

This review examines what each achieves, why effect sizes differ so markedly between study designs, and what is not established about the mechanism or the safety of the substitution approach.

Objective

This review sets out to establish four things from the published literature. First, what substitution achieves on hard outcomes where it has been tested in a randomised trial. Second, how the blood pressure effect compares across individual, trial and programme levels. Third, whether the benefit is attributable to sodium reduction or to potassium increase. And fourth, in whom substitution is unsuitable and what the population approach has achieved by comparison.

Literature Review

What substitution achieved on outcomes: An open-label cluster-randomised trial enrolled 20,995 people from 600 villages in rural China who had a history of stroke or were aged 60 or over with high blood pressure. Villages were randomised to a substitute of 75 per cent sodium chloride and 25 per cent potassium chloride by mass, or to continued regular salt (Figure 6) [4]. Over five years the trial reported significant reductions in stroke of 14 per cent ($p = 0.006$), in major cardiovascular events of 13 per cent ($p < 0.001$) and in premature death of 12 per cent ($p < 0.001$) (Figure 1) [5].

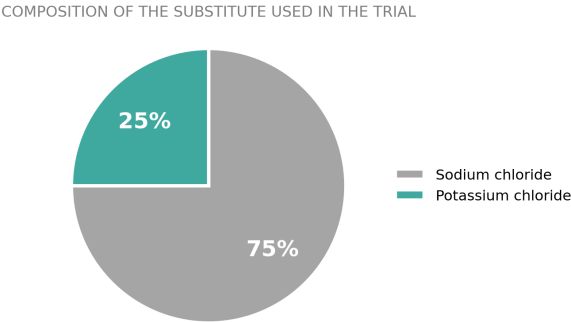


Figure 6: Composition of the substitute used in the trial [4]

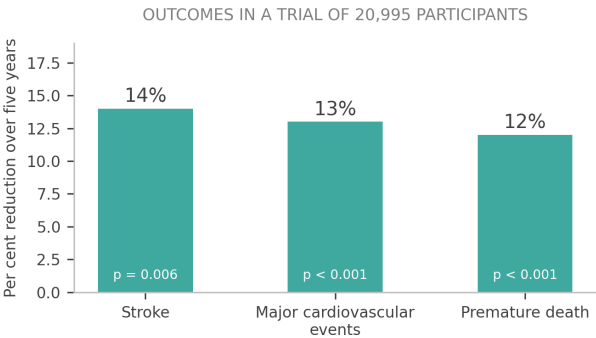


Figure 1: Outcomes in a trial of 20,995 participants [5]

How the blood pressure effect scales: Empirical evidence indicates that replacing sodium chloride with potassium-enriched substitutes lowers systolic blood pressure by a net 5.58 mmHg (95% CI 4.09 to 7.08) and diastolic by 2.88 mmHg (1.83 to 3.93), with a weighted mean difference in sodium excretion of 18 mmol; over half the included trials used substitutes containing 30 per cent potassium chloride or less [3]. A phase I study in 43 hypertensive patients, of whom 39 completed, using an 18 per cent substitute reported morning systolic reduction of 10.0 mmHg (95% CI 3.5 to 16.5, $p = 0.003$) and night-time systolic reduction of 10.2 mmHg (4.3 to 16.1, $p = 0.001$) (Figure 2) [6].

Table 1: Reported systolic effect by level of intervention

Where substitution is unsafe: The risks of potassium-enriched substitutes include possible increased risk of hyperkalaemia and its principal adverse consequences, arrhythmia and sudden cardiac death, especially in people with conditions impairing potassium excretion such as chronic kidney disease (Figure 4) [3]. The trial specified clinical hyperkalaemia as its safety outcome [4].

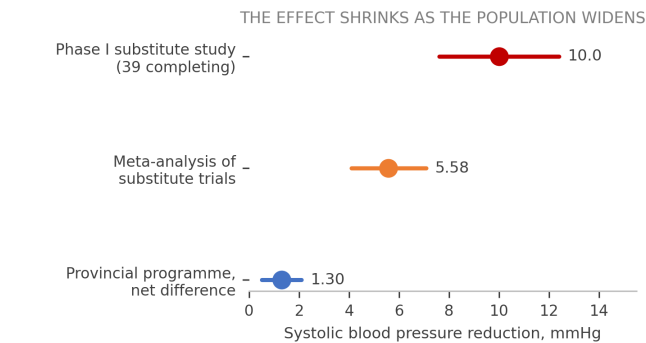


Figure 2: The effect shrinks as the population widens [3,6,7]

What a programme achieved across a province: A salt reduction and hypertension prevention project surveyed 7,512 participants across five counties at baseline, randomly selecting four for a multifaceted intervention with one as reference. Urinary potassium excretion rose from 1,441.3 to 1,676.9 mg daily ($p < 0.001$), and the adjusted net difference in urinary sodium change was 394.1 mg daily (95% CI 133.2 to 655.0, $p = 0.003$). Systolic pressure fell from 131.2 to 129.8 mmHg and diastolic from 80.8 to 78.9, with adjusted net differences against the reference county of 1.3 mmHg (0.5 to 2.1) and 1.4 mmHg (0.9 to 2.0) [7] (Table 1).

Level of intervention	Systolic effect	Interval
Phase I substitute study	10.0 mmHg	3.5 to 16.5 [6]
Meta-analysis of substitute trials	5.58 mmHg	4.09 to 7.08 [3]
Provincial programme, net difference	1.3 mmHg	0.5 to 2.1 [7]

Which component is responsible: The trial was premised on the joint blood pressure-lowering effects of sodium reduction and potassium supplementation, and a minimum 3.0 mmHg systolic lowering was assumed for its power calculation [8]. A subsequent analysis states that the contribution of sodium reduction against potassium increase to these effects is unknown, and identified four separate data sources from which to model the proportions attributable to each (Figure 3) [8]. Randomised trials reducing sodium and trials supplementing potassium have each demonstrated blood pressure lowering independently [8].

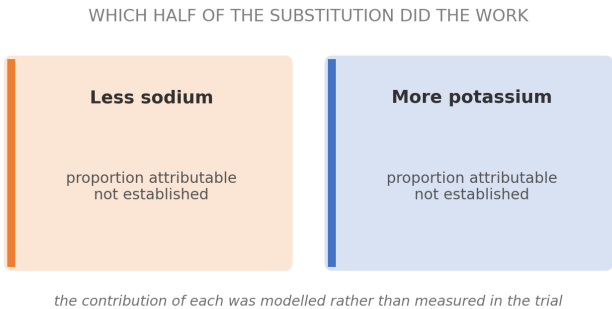


Figure 3: Which half of the substitution did the work [8]

Table 2: Summary of reported findings across levels

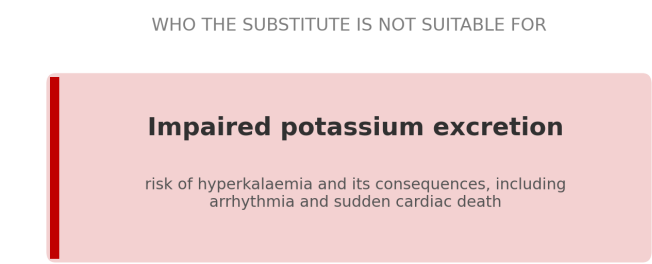


Figure 4: Who the substitute is not suitable for [3,4]

What the population approach has looked like: One national salt reduction programme began in 2003 with voluntary targets, product labelling, a public and political awareness campaign and monitoring. Updated targets for industry were published in 2009, 2011, 2014, 2017 and 2020, the last to be met by 2024, while the campaigning element of the programme has diminished over that period (Figure 5) [9].

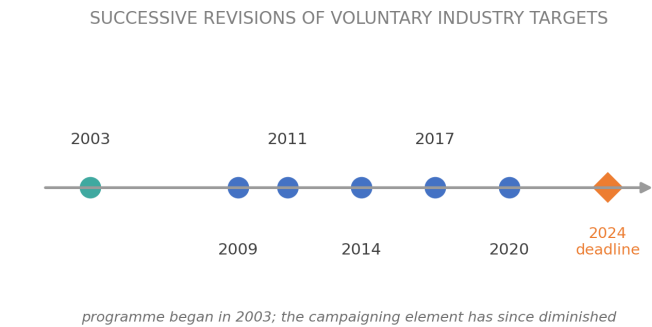


Figure 5: Successive revisions of voluntary industry targets [9]

Effects beyond blood pressure: A pre-specified analysis of the same trial evaluated the effect of long-term reduced-sodium, added-potassium salt on headache frequency and severity, noting prior evidence that short to medium term sodium reduction reduces headache symptoms [10]. Feasibility work in general practice has tested a behavioural intervention to reduce salt in purchased foods, with outcomes including salt content of purchases, 24-hour urinary sodium and blood pressure [11] (Table 2).

Finding	Source
Stroke reduced 14 per cent	Cluster-randomised trial [5]
Systolic reduced 5.58 mmHg	Meta-analysis of substitutes [3]
Net systolic difference 1.3 mmHg	Provincial programme [7]
Attribution between components	Modelled, not measured [8]
Hyperkalaemia risk	In impaired excretion [3]

The underlying dose-response: Cochrane review has assessed longer-term modest sodium reduction on blood pressure [2], and systematic reviews with meta-analysis have examined lower sodium intake on health outcomes [14] and increased potassium intake on cardiovascular risk factors and disease [15]. A separate Cochrane review compared low against high sodium diets across

a wider range of biochemical outcomes [16]. Guidance sets recommended intake for adults and children [12], and a scientific statement addresses population reduction and cardiovascular risk directly [17].

What programmes have achieved elsewhere: Salt reduction in one country between 2003 and 2011 has been related to blood pressure, stroke and ischaemic heart disease mortality [18]. Systematic reviews have catalogued initiatives worldwide and progress against global targets [19,21], and have asked whether an effectiveness hierarchy exists among policy types [20]. Where dietary salt comes from differs markedly between countries [22,23], which determines whether reformulation or substitution is the applicable lever [3,22].

Substitution beyond the single trial: Modelling has estimated population-wide benefits and risks of potassium-enriched substitution [24], and a community-wide trial has examined effects on blood pressure and hypertension incidence [25]. Systematic review and meta-analysis has pooled clinical outcomes across substitute trials [26], and a separate trial examined incidence of both hypertension and hypotension among normotensive adults [27], which is the counterpart risk to the intended effect [24,27].

Where the epidemiology is contested: Sodium excretion and blood pressure have been analysed within and across populations [28], and dietary sodium with cardiovascular risk has been argued to depend heavily on measurement method [31]. Community-level prospective data have been read as suggesting a more complex association [32], while analyses using repeated 24-hour collections report a positive relationship [33], and dose-response meta-analysis has been conducted [34]. Trial evidence combining sodium reduction with a dietary pattern remains among the strongest [29], and professional guidelines incorporate sodium targets into hypertension management [30] (Table 3).

Table 3: What is and is not established across the two approaches

Question	What the evidence supports
Does substitution reduce stroke?	Yes, by 14% in one large trial [5]
How large is the pressure effect?	Depends on the level measured [3,6,7]
Sodium or potassium?	Not established; modelled only [8]
Is substitution safe for all?	No; impaired excretion excluded [3]
Do population programmes work?	Small net differences reported [7,18]

Method

Search strategy: PubMed and the archives of the major cardiology, public health and nutrition journals were searched for studies of sodium reduction and salt substitution. Search terms combined salt substitute and sodium reduction with blood pressure, reformulation, potassium chloride, population intervention and hyperkalaemia. Reference lists of the substitute meta-analysis [3] and the cluster-randomised trial [4] were screened by hand for primary sources.

Eligibility: Studies were included if they reported blood pressure, sodium or potassium excretion, or clinical outcomes following substitution or a population reduction programme. Modelling analyses are cited for what they estimate and are identified as such.

Data extraction and handling: Population, intervention, comparator, the level at which the intervention operated and the reported effect were extracted as published. The level is stated alongside every effect size, because individual substitute studies, pooled substitute trials and whole-population programmes report systolic reductions differing by nearly an order of magnitude and are frequently quoted interchangeably in support of the same policy. This review reports published findings and does not constitute dietary, salt intake or antihypertensive guidance for any individual, and notably no recommendation regarding salt substitutes, which are unsuitable for some patients. No pooling or re-analysis was performed. Figures 1 to 6 and Tables 1 to 3 reproduce published values only. This is a narrative synthesis of published literature and was not registered as a systematic review.

Concluding Remarks

Three systolic effects appear in this literature and they differ by nearly tenfold: 10.0 mmHg in a small phase I substitute study, 5.58 mmHg pooled across substitute trials, and a net difference of 1.3 mmHg from a provincial programme [3,6,7]. None is wrong. They measure different things, and quoting the largest in support of the smallest intervention is the characteristic error in this field.

The hard outcome evidence is genuinely strong and deserves to be stated without hedging. Twenty thousand nine hundred and ninety-five participants, cluster-randomised, five years, with stroke reduced 14 per cent and premature death 12 per cent [4,5]. Few dietary interventions have evidence of that quality on outcomes that matter this much.

Its generalisability is the qualification. The trial recruited people with prior stroke or aged over 60 with high blood pressure, in rural villages where salt is added during home cooking [4]. In countries where most sodium arrives already incorporated into manufactured food, a substitute in the kitchen reaches a smaller share of intake, and the reformulation route becomes the relevant one [3,9].

The attribution question is more than academic and remains open. The intervention changed two things at once, and the analysis addressing it states that the contribution of each is unknown and proceeds by modelling from separate data sources [8]. If much of the benefit is potassium rather than sodium, then a reformulation programme that removes sodium without adding potassium is a different intervention from the one that was tested.

The safety limit is what most sharply separates the two approaches. Potassium-enriched substitutes carry hyperkalaemia risk in people with impaired potassium excretion, including chronic kidney disease, with arrhythmia and sudden cardiac death as the consequences [3]. Reformulation of the food supply carries no equivalent hazard, which is a substantial argument for it in unselected populations even where its measured effect is smaller.

On the population programme, the timeline is the finding. Targets revised in 2009, 2011, 2014, 2017 and 2020, with the campaigning element diminishing across the same period [9]. Repeated revision of voluntary targets is not evidence of failure in itself, but a programme whose enforcement mechanism is publicity and whose publicity has faded is relying on something it no longer does.

Three limitations belong with these conclusions. The outcome trial is open-label, so participants and local investigators knew the allocation, and it was conducted in a single country in a high-risk population [4]. The provincial programme compares four intervention counties against one reference county, which is a weak unit of comparison for a population intervention [7]. And the modelling of component attribution draws on four external data sources rather than on within-trial randomisation, so its estimates are inferences about the trial rather than results from it [8].

A distinction worth holding is between the two interventions the word substitution covers. Replacing salt in the kitchen is a household behaviour; replacing sodium chloride during manufacture is reformulation with a potassium-enriched ingredient [3]. The trial evidence on outcomes concerns the first [4,5], while the population modelling and the target-based programmes concern the second [9,24]. They share a mechanism and differ in who has to act.

The measurement disputes running through this literature deserve acknowledgement rather than resolution here. Analyses using single spot estimates and those using repeated 24-hour collections have reached different conclusions about the shape of the association at lower intakes [31,32,33]. That disagreement concerns observational epidemiology and does not bear on the randomised outcome evidence, which is where the strongest claims in this review rest [4,5,26].

What follows for practice is modest and specific. The intervention with outcome evidence was tested in people at high

cardiovascular risk who cook with added salt and have normal potassium handling [4]. That is a describable group rather than a population, and it is the group in whom the reviewed evidence most directly applies [3,4,27].

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Conflict of Interest

The authors declare no competing interests.

Ethics Statement

This article reviews previously published studies only. No new patient data were collected and no participants were recruited, so ethical approval was not required.

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