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EDITORIAL



The best of 'best buys': public health values of potassium-enriched salt substitute

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1. Introduction

Salt substitute is a type of salt in which a portion of regular salt (nearly 100% NaCl) is replaced by alternative materials that are devoid of sodium but still impart a salty flavor, ensuring minimal alteration to the taste of prepared dishes. The most commonly used alternative material is potassium chloride. This potassium-enriched salt substitute, hereafter referred to as simply 'salt substitute,' effectively reduces blood pressure by concurrently diminishing sodium intake and augmenting potassium intake.

However, its potential values in the prevention and control of hypertension and cardiovascular diseases largely remained overlooked until the recent release of two groundbreaking studies conducted in China: the Salt Substitute and Stroke Study (SSaSS) [1] and the Diet, Exercise, and Cardiovascular Health (DECIDE – Salt Reduction Strategies for Seniors in Residential Facilities (DECIDE-Salt) study [2]. This oversight is largely due to the lack of evidence on hard clinical outcomes and concerns about the potential risk of hyperkalemia resulting from the increase in potassium intake.

With new evidence from these two studies, we now possess confidence to advocate a population-wide shift toward replacing regular salt with salt substitutes as a fundamental strategy for prevention and control of hypertension and cardiovascular disease. For clarity, we propose a set of ten criteria for evaluation of the best public health interventions. We adopt the five criteria outlined in the OECD (2022) Guidebook on Best Practices in Public Health [3]: effectiveness, efficiency, equity, evidence-based, and extent of coverage. Additionally, we incorporate five additional criteria: relevance, easy-to-do, acceptability, availability, and suitability. (Table 1) Following this, we scrutinize the strategy of substituting regular salt with a salt substitute, along with other approaches endorsed in the WHO's 'best buys,' through the lens of these ten criteria.

2. Ten Criteria for the best public health interventions and supporting evidence for salt substitutes against each

2.1. Relevance

The number one criterion for the best public health interventions should be that the intervention is addressing a major public

health challenge. Hypertension is the leading cause of death and disability globally [4]. Compelling evidence supports that lowering sodium intake and increasing potassium intake reduce blood pressure [5,6].

The WHO's global NCD action plan for 2013–2020 [7] and its newly updated version [8] included salt reduction as one of its designated 'best buys' and established a worldwide target to reduce the average population intake of salt/sodium by 30% [9]. In terms of potassium intake, the current WHO guideline recommends >3.5 g/day [10].

However, meeting the WHO's global targets for salt reduction and potassium increase remains a significant challenge worldwide [9,10]. Among the various strategies proposed, salt substitution stands out as the only one that 'kill two birds with one stone' – reduce sodium intake and increase potassium intake at the same time.

2.2. Effectiveness

A comprehensive meta-analysis [11] involving 21 randomized controlled trials and 31,949 participants reported an overall reduction in systolic blood pressure (SBP) of -4.61 mm Hg (95% CI -6.07 to -3.14) and in diastolic blood pressure (DBP) of -1.61 mm Hg (95% CI -2.42 to -0.79). However, the meta-analysis, without differentiation on the method of application, may lead to an underestimation of the intervention effect. In the DECIDE-Salt trial [2], participants collectively consume meals prepared by the kitchens. The salt substitution demonstrated a mean treatment effect of 7.1 mmHg in SBP and 3.8 mmHg in DBP, an effect equivalent to that of anti-hypertensive medications.

Furthermore, the SSaSS trial [1], involving nearly 21,000 individuals with high cardiovascular risk, demonstrated that substituting regular salt with a salt substitute over a 5-year period led to a 13% reduction in newly developed major cardiovascular events and a 12% reduction in all-cause deaths.

2.3. Efficiency

The cost-effectiveness analysis based on the SSaSS and DECIDE-Salt trials demonstrates that salt substitution is not only effective but also cost-saving, despite its higher price

Table 1. Ten Criteria in order of relevance proposed for assessing the best public health interventions and the evaluations on salt substitution against to these criteria.

Criteria	Evaluation of salt substitution	Reference
Relevance: Extent to which the intervention is relevant to the global major health challenges	Effectively lowers blood pressure and risk of CVD and total deaths, has impact on leading causes of global mortality	[4–10]
Effectiveness*: Extent to which the objectives of the intervention were achieved	Consistent large effect size in lowering blood pressure that is equivalent to that from anti-hypertension medications; Significantly lower major cardiovascular adverse events and all-causes mortality.	[1,2,11]
Efficiency*: Extent to which inputs were used to achieve desired outcomes	Proved not only effective but cost-saving, outperforming other proposed 'best buys.'	[12–14]
Evidence-based*: The strength and validity of evidence supporting the intervention	Rigorous trials support salt substitution's effectiveness, attaining the highest credibility.	[1,2,11]
Acceptability: Extent to which the intervention is embraced and accepted by the entire target population.	Salt substitute's taste preservation and high user retention underscore its acceptability	[1,2,15]
Equity*: Extent to which the intervention reduces inequalities in society;	With little dependency on socio-economic status, great potential to enhance health equity.	[1,2,16–18]
Easy-to-do: Extent of difficulty in producing and implementing the intervention	Implementing salt substitution is straightforward, making it one of the most accessible strategies.	[19,20]
Extent of coverage*: Extent to which the intervention reached the target population.	Unlike medications, salt substitutes applicable to whole population, offering broad public health benefits.	[2,19]
Availability: Extent to which the intervention is available to the target population.	Available in major markets but may compete with increasing fertilizer manufacturing for resources.	[21–26]
Suitability: Extent to which a product fits into the global or local situation	Aligns perfectly with the urgent need to reduce sodium intake and increase potassium intake globally.	[9,10,27–30]

*Criteria adopted from OECD five best practice criteria.

compared to regular salt [12,13]. For example, over two years in the DECIDE-Salt trial, the cost of salt substitute per person was \$18.7 compared to \$6.1 for regular salt. However, the corresponding treatment costs for major adverse cardiovascular events were \$72.9 and \$111.2, respectively, resulting a total incremental cost saving of \$25.9 per person [13]. A similar conclusion was drawn from the modeling studies as well [14]. This level of cost-effectiveness was not observed with other proposed 'best buy' strategies for reducing sodium intake, despite they were assessed as highly cost-effective.

2.4. Evidence-based

The effectiveness and safety of the strategy replacing regular salt with a salt substitute have garnered robust support from randomized controlled trials, including double-blind studies, which are widely recognized as the gold standard in methodology for evaluating the effectiveness and safety of interventions [11]. The strength and validity of the evidence supporting the replacement of regular salt with a salt substitute have attained the highest level of credibility [1,2,11].

2.5. Acceptability

Potassium chloride itself has a bitter taste, which is not as palatable as sodium chloride. However, when the potassium chloride content in a salt substitute is 30% or lower, over 80% of participants are unable to distinguish between regular salt and salt substitute or tend to use salt substitute [15]. The failure of the progressive restriction of salt supply, in contrast to the success of the salt substitution for blood pressure reduction in the DECIDE-Salt study [2], strongly underscores the importance of acceptability as a criterion for determining the most effective public health interventions.

The amount of salt in foods is closely linked to their taste. Salt substitute, both in theory and in practice, allows for a reduction in sodium intake without sacrificing the taste of

foods; hence it is highly acceptable. This is because the addition of potassium chloride in the salt substitute imparts a salty taste. Compared to other strategies for reducing sodium intake, salt substitution enjoys higher levels of acceptability. In the SSaSS trial [1], after 5 years of intervention, an impressive 92% of participants in the intervention group continued to use salt substitute.

2.6. Equity

The use of salt and intake of sodium apply to nearly everyone. It may seem that any strategy aimed at reducing sodium intake would lead to improved health equity, or at the very least, not worsen it. However, this may not be the case in practice. For instance, collaborative efforts with the food industry to lower sodium levels in processed foods have demonstrated success only in high-income countries [16]. For populations with low levels of education and higher rates of illiteracy, the impact of health education and mass media campaigns is also limited [17]. In contrast, the implementation of salt substitutes is not contingent on the level of education of an individual or a population [1,2], nor is it tied to the level of food industry development. In fact, salt substitution is the only sodium reduction strategy that has been demonstrated cost-saving through randomized clinical trials [12,13], although It has a higher price [18]. Promoting the use of salt substitutes could significantly enhance health equity among the world's poorest populations while benefit its economy, due to the cost-saving nature.

2.7. Easy-to-do

Among all the strategies listed in the 'best buys' for reducing sodium intake, the knowledge and skills needed to implement a salt substitute strategy are likely the least demanding [19]. The techniques used to manufacture salt substitute are straightforward; any facility producing regular salt should be

capable of producing salt substitute if food-grade potassium chloride is available [20]. The existing marketing and sales infrastructure would readily distribute the product to end-users if reasonable prices are guaranteed. What the end-users need to do is just to 'buy and use it' - nothing more.

2.8. Extent of coverage

Unlike hypertension medications that are suitable only for hypertensive patients, salt substitute has great potential to be used as a population-wide public health strategy. The reason salt substitute has not yet been included in the WHO 'best buys' and not widely promoted across the world is probably mainly due to concerns about its safety, particularly the risk of hyperkalemia from the increase in potassium intake [19]. The recent DECIDE-Salt trial demonstrated that replacing regular salt with a salt substitute increased the risk of hyperkalemia, but this risk was not stable over time and was not associated with clinical outcomes [2]. Current cumulative evidence indicates that further research is warranted on the definition of hyperkalemia and its clinical significance. Nevertheless, except for those with hyperkalemia, end-stage kidney disease, or those on long-term use of potassium-preserving medications, salt substitute should benefit all individuals.

2.9. Availability

Salt substitutes are available in all global major markets and regions, though not in every country [21]. Regular salt includes well salt and sea salt, its sources are basically unlimited. However, manufacturing salt substitutes requires sufficient potassium chloride supply and may compete with potassium fertilizer production. The current world production of potash is around 70 million tons a year [22], and about 90% is used for fertilizers and the supply has caused concerns due to the increasing demands in agriculture development [23]. Switching from using regular salt to salt substitutes should increase competition. The solutions to alleviate the insufficiency of potassium fertilizer largely rely on technical development using alternative fertilizers, which fortunately has been underway [24–26]. As more research evidences are accumulated and consumers' awareness of its health values, the size of the salt substitute market will definitely increase, and companies in the business will certainly increase production, improving availability as a consequence. This was exactly the case in China.

2.10. Suitability

This term emphasizes how well a product or service aligns with the specific needs, conditions, and context of a particular locality or environment. The WHO recommends that adults consume less than 2000 mg of sodium per day (equivalent to 5 grams of salt) [27] and at least 3510 mg of potassium per day [28] to reduce the risk of hypertension and related diseases. However, the global average sodium intake is estimated to be 4310 mg/day (equivalent to 10.8 g of salt per day), more than double the recommended intake advised by the WHO [9], whereas the global average potassium intake is estimated to

be 2.25 g/day, only two-thirds of the recommended level [10]. In this context, salt substitute proves to be highly pertinent and applicable on a global scale.

Although that being said, suitability may still vary between countries with different cultures and dietary behaviors. In countries where sodium intake is mainly from salt added during home cooking, like China, consumers can easily replace regular salt with salt substitute. In countries where sodium intake is mainly from processed foods, the discretionary use of salt substitutes may have little effect [29]. However, the food industries could take action to replace regular salt with salt substitute or develop new formula that increases potassium and reduce sodium in the products. Fortunately, these actions have been taking place [30]. Researchers have found that the use of salt substitutes can significantly reduce the sodium content in foods such as meat products, bread, pizza, and cheese without compromising the quality and taste of the food. Consumers have a higher acceptance of processed foods prepared with salt substitutes, as they are able to adapt to new flavors and continue to purchase these products. This further supports the acceptability of using salt substitutes as a strategy for reducing sodium in processed foods.

3. Conclusion

In conclusion, there is ample evidence supporting the inclusion of salt substitutes in the WHO's 'best buys' as a population-wide strategy for prevention and control of hypertension and cardiovascular disease. Compared to other proposed strategies for sodium intake reduction and potassium increase, salt substitutes have stronger scientific evidence and demonstrate greater effectiveness. They also have a higher potential for improving health equity, ensuring widespread coverage across the entire population, and garnering higher acceptability among end-consumers. Additionally, their implementation is straightforward, aligning well with the global prevalence of high sodium and low potassium intake. Furthermore, this intervention promises cost savings in healthcare and is readily available in major global markets, with the capacity for increased availability in response to demand. Without a doubt, salt substitutes stand out as the best public health intervention among the 'best buys.'

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Declaration of interest

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