RESOLVE TO SAVE LIVES

The George Institute for Global Health

Johns Hopkins Bloomberg School of Public Health

Research prioritization to accelerate the global scale-up of low-sodium salt substitutes

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Abbreviations:

BP: blood pressure; CVD: cardiovascular disease; EC: executive committee; K: potassium; KCl: potassium chloride; LMIC: low- and middle-income countries; LSSS: low-sodium salt substitutes; NaCl: sodium chloride; RAASi: renin-angiotensin-aldosterone system inhibitor; RCT: randomized clinical trial; SC: steering committee; SSaSS: Salt Substitute and Stroke Study; WHO: World Health Organization.

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Executive Summary

Rationale

Excess dietary sodium is a major global driver of elevated blood pressure (BP) and cardiovascular disease (CVD). The WHO recommends <2000 mg/day sodium, yet average intake is more than double this. Replacing part of sodium chloride (NaCl) with potassium chloride (KCl) in **low-sodium salt substitutes (LSSS)** reduces BP and lowers CVD risk, with meta-analyses showing ~5 mm Hg systolic BP reduction, 14% fewer strokes, and 12% lower all-cause mortality. Large-scale modeling in China and India suggests hundreds of thousands of CVD deaths could be prevented annually, with net benefits outweighing the potential risk of hyperkalemia. However, critical evidence gaps hinder global scale-up, particularly evidence related to safety in high-risk populations, consumer acceptance, cost, and implementation.

Methods

To identify and prioritize research needs that would facilitate global uptake of LSSS, Johns Hopkins University, The George Institute, and Resolve to Save Lives conducted four thematic webinars attended by an interdisciplinary, international group of experts. The themes of the four webinars were: (1) **Safety & Efficacy** of LSSS, (2) the role of **Industry & Food Technology, (3)** strategies for **Implementation**, and **(4) Public Policy** approaches. Each webinar featured presentations on current evidence, followed by structured discussions and participant surveys where experts ranked potential research questions by importance (1–5 scale; important to critically important). Results of the research surveys were synthesized with participant comments to inform a consolidated research agenda.

Results

Safety and Efficacy research in individuals with chronic kidney disease (CKD) and diabetes as well as those taking blood pressure–lowering medications such as renin-angiotensin-aldosterone system (RAAS) inhibitors, was deemed high priority. Key questions identified in the webinars included determining the clinical relevance of modest potassium elevations in CKD, evaluating effectiveness in processed-food–dominant diets and across varying potassium chloride (KCl) proportions, and examining long-term outcomes beyond blood pressure, such as cardiovascular disease, kidney function, and the age-related rise in blood pressure. Appropriate study designs to address these research questions include pragmatic and quasi-experimental trials with integrated safety monitoring.

Industry and Food Technology research should address consumer acceptability of taste and aftertaste and should assess taste adaptation and bitterness thresholds, for discretionary and processed food uses. The functional performance of LSSS across key food types, such as bread, cheese, and meats, as well as determining how additives like iodine, calcium, magnesium, and citrate affect taste and stability were highlighted as important for global scale-up. Modeling the cost-effectiveness of subsidies, assessing supply chain capacity for food-grade KCl, and exploring alternative production methods were also thought to be high priorities.

Implementation research should focus on strategies to enhance stakeholder engagement, fostering buy-in from healthcare providers, manufacturers, the food service industry, and consumers. Labelling and messaging studies should test standardized, culturally appropriate designs that promote benefits while appropriately warning individuals at risk for CKD-related complications. Behavioral economics approaches are needed to understand how incentives, price changes, and tailored messaging

influence uptake, while ensuring such efforts do not inadvertently increase overall sodium consumption.

Finally, in the **Public Policy** arena, research should evaluate the impact of policy levers such as subsidies, reduced tariffs, and procurement mandates in public institutions. Efforts should also identify effective strategies for educating policymakers and the public on the benefits of LSSS and potassium. Integration of LSSS-related policy with existing iodization programs and sodium reduction benchmarks is important, as is determining when mandatory versus voluntary approaches are most effective.

Conclusion

Use of LSSS is a scalable, evidence-based intervention to lower BP and reduce the global burden of BP-related CVD. Addressing targeted safety questions, ensuring consumer acceptance, reducing cost, and implementing supportive policy frameworks are important next steps for accelerating adoption of LSSS worldwide.

Scope of the Problem

The World Health Organization (WHO) recommends daily intake of <2000 mg/day sodium (~< 5 g/day salt); the global mean intake is well above this, reported as 4310 mg/day sodium (~10.78 g/day salt). In 2013, WHO Member States agreed on a global target to reduce mean population sodium intake by 30% by 2030. One way in which this can be accomplished is by changing the composition of dietary salt to one in which a certain proportion of sodium chloride (NaCl) is replaced with other elements, typically potassium chloride (KCl) due to the potential added benefits of blood pressure (BP) reduction seen with greater potassium intake. Recent studies, including a large cluster randomized clinical trial (RCT), several meta-analyses, and the WHO guideline have documented the benefits of low-sodium salt substitutes (LSSS) on clinically relevant outcomes, specifically, lower BP and reduced risk of cardiovascular diseases (CVD) including stroke, and mortality.[1] Scaling up the availability and use of LSSS could therefore have significant public health benefits; however, there are key gaps in the current evidence base that make it challenging to scale up their use on a broad scale.

In this context, key thought leaders, nutrition experts, CVD researchers, and public health leaders convened for several scientific webinars to make recommendations for future research that addresses key gaps. The ultimate goal of this effort was to identify and prioritize research topics that could help accelerate global scale-up of potassium-enriched salt as a major public health intervention of the 21st century.

Methods

Approach to Webinars and Identification of Research Priorities

To identify and prioritize research topics, an Executive Committee (EC) consisting of physician scientists, global health experts, and nutrition scientists from Johns Hopkins University, The George Institute, and Resolve to Save Lives convened to decide upon the broad content areas to explore in the webinar series and identify leaders in this space to serve on the Steering Committee (SC). Over several virtual meetings, the EC and the SC reviewed and approved the following topic areas for Webinar focus: Safety and Efficacy of LSSS, Industry/Development and Food Technology, Implementation, and Public Health Policy (Figure). The EC and SC nominated external experts to invite to the Webinars, with several experts invited to present the current state of evidence and existing gaps during each webinar as a featured presentation (Appendix).

To optimize the content delivered during each of the featured presentations and to guide the development of these webinars, an initial introductory webinar was held with a high-level overview of the current landscape of LSSS and a description of the overall goals of the webinar series. During this initial Introductory webinar, the experts were asked to weigh in on important questions and subtopics for each of the four themes. This input informed subsequent webinar development and survey questions, which are detailed in each of the thematic areas to follow (Tables 1-4).

Prior to each webinar, members of the EC and the SC were asked to provide a list of 3-5 research questions that they considered to be high priority in regard to the key area to be discussed. This expert input was collated and assimilated into a survey to be administered during each webinar. The structure of each webinar was consistent: 2-3 featured presentations followed by a moderated discussion and then survey administration. The surveys requested participants in real-time to rank the research questions in order of priority (using a scale from 1 to 5; important (1), quite important (3), critically important (5)). After each webinar, a link to a recording of the webinar along with a separate survey link was provided to all invitees, to maximize participation.

The ultimate goal for ranking these research questions was to identify priorities of focus for the research community as we aim to narrow identified gaps in evidence. These efforts would then facilitate global implementation of LSSS in various contexts.

This approach was modeled after prior work by Khan, Matsushita and Salomon as they identified “Priorities for research on hypertension care delivery”.[2] Their methodology was adapted from that utilized by the WHO[3] and Nasser and colleagues.[4]

Efficacy & Safety of Low-sodium Salt Substitutes

Table 1: Expert-identified Safety/Efficacy subthemes and questions for focus during LSSS webinar series

1. **Special Populations:** Need to explore safety and efficacy in special populations (children, elderly, pregnant, normotensive, kidney disease, diabetes).
    a. **Children/Elderly:**
        i. Since the dietary salt used is the same across all members of a household, the effects, positive and negative, need to be considered not only for those with hypertension but also for the other members of the household
    b. **Chronic kidney disease (CKD):**
        i. Need to consider: (1) role of LSSS on acidosis and bone health; (2) effect of LSSS on BP in this population; (3) risk of hyperkalemia with potassium enriched salt use
        ii. Related: What is the clinical relevance of different degrees of serum potassium elevation in high-risk persons (i.e., is a potassium level of 5.5 mg/dL harmful in persons with CKD)?
        iii. Related: In settings with limited healthcare utilization and generally late diagnosis of kidney disease, how do we balance widespread LSSS use and the risk of hyperkalemia, no matter how small?
        iv. Related: Evidence suggests that increased potassium intake is beneficial for reducing progression of kidney disease; can LSSS help delay kidney disease progression?
    c. **Medication use:**
        i. Need to consider the safety/efficacy among those taking any class of medications that may increase serum potassium.

2. **Mechanism**
    a. Basic science research offers an opportunity to understand the mechanism of potassium's CV benefits and explore the potential adverse effects of potassium supplementation
        i. Potential research questions for basic scientists: (1) what are the underlying mechanisms that drive the benefits of potassium-enriched salts, (2) how are CV benefits of potassium influenced by the diet Na/K ratio, (3) beyond CKD, heart failure, RAAS inhibition/ mineralocorticoid receptor antagonists use, what puts individuals at risk for hyperkalemia, (4) are there markers/predictors for individuals who are more sensitive to hyperkalemia, (5) do medications impact the dose-response relationship between dietary potassium intake and serum potassium levels?

3. **Relative risks – topics to consider:**
    a. How do the adverse effects of hyperkalemia compare to the adverse effects of current sodium intake?
    b. How does the potential risk for hyperkalemia with intake of LSSS compare to the risk with (prescribed) increased consumption of fresh fruits and vegetables?
    c. What are the risks associated with various compositions of K-salt?
        i. How does this change with the use of citrate in supplements?

Legend: BP: blood pressure; CKD: chronic kidney disease; CV: cardiovascular; CVD: cardiovascular disease; K: potassium; KCl: potassium chloride; LSSS: low-sodium salt substitutes; Na: sodium

Background

LSSS are known as low/reduced sodium salts or potassium salts. The composition varies but generally they are made up of ~75% NaCl and ~25% KCL, albeit the proportion of both has varied.

Several RCTs, cluster RCT, a recent meta-analysis, and the WHO guideline[1] have evaluated efficacy and effectiveness of LSSS on BP, CVD, and mortality. Meta-analyses by Yin et al. of 21 RCTs,[5] Brand et al. of 26 RCTs,[6] and Greenwood et al. of 16 RCTs[7] included over 30,000 participants, each, over various durations. These studies consistently showed that potassium-enriched LSSS can significantly improve BP and CV outcomes, with effect sizes as follows:

- Reduction in systolic BP by -5.12 (-6.72 to -3.52) mm Hg
- Reduction in diastolic BP -1.56 (-2.25 to -0.88) mm Hg

Importantly, this BP lowering also translated into:

- 14% reduction in stroke
- 15% reduction in major adverse CV events
- 17% reduction in CV mortality
- 12% reduction in all-cause mortality

Of the available studies, the most influential trial was the Salt Substitute and Stroke Study (SSaSS) which enrolled over 20,000 participants from rural China, all with a history of stroke or high BP, and lasted nearly five years.[8] Importantly, most trials were done in East Asia or South Asia, where discretionary salt intake was the major source of dietary sodium intake.

The impact of LSSS on lowering BP was notably greater in specific scenarios. Individuals with hypertension and older adults experienced more significant reductions. Those with higher baseline sodium intake and lower baseline potassium intake also saw more pronounced benefits. Additionally, a higher proportion of KCl in LSSS, particularly 30% or more, led to larger BP reductions. These factors collectively enhanced the effectiveness of LSSS in managing BP.

Modeling studies in India and China further show the promise of broad scale implementation of LSSS. Applying data from pragmatic trials in China on local demographic data showed that a nationwide intervention to replace all discretionary salt with potassium-enriched LSSS could prevent around 500,000 cardiovascular deaths per year, far greater than the estimated 9000 hyperkalemia-related deaths in the CKD population.[9] In addition, the LSSS interventions in SSaSS and the DECIDE-Salt study were cost-saving in China.[10,11]

Morbidity and mortality related to hyperkalemia remains one of the main concerns regarding the use of LSSS overall and in select populations. The incidence of hyperkalemia in LSSS studies have shown varying results, related to the population studied and the scientific rigor. Fortunately, serious adverse events appear to be rare. The SSaSS Stroke Study found no significant harm related to hyperkalemia, though blood potassium levels were not measured in the trial.[8] The DECIDE-Salt Study in China showed that serum potassium increased by 0.27 mmol/L over two years, with hyperkalemia prevalence rising from 2.4% to 7.4%.[12] However, it should be noted that there was also a reduction in the number of episodes of hypokalemia. Modeling studies projecting population-wide scaling up of LSSS in India and China demonstrated a net benefit from the substantial reduction in BP-related CV mortality with LSSS use, even after considering the slight increase in hyperkalemia-related mortality.[9,13]

Studies of potassium supplementation in patients with CKD have shown a slight increase in potassium levels with some patients exhibiting overt hyperkalemia. The evidence suggests that older individuals with higher baseline serum potassium levels were at greatest risk for the developmentof hyperkalemia.[14]

Emerging evidence suggests that adjusting the anion delivered with LSSS, i.e., replacing chloride with citrate, may help avoid hyperkalemia. Avoidance of certain medication, particularly those impacting the renin-angiotensin-aldosterone system (RAAS), could also help minimize the risk of hyperkalemia with potassium substitution.[15]

Participant discussion

A robust discussion followed the featured presentation, where gaps were highlighted and questions were raised. A summary of this discussion, organized by topic areas, is presented in Supplemental Table 1.

Post-webinar survey results:

Q1a: How important is it to study LSSS effectiveness in each of these patient groups?	
	% of participants who ranked as high importance*
Persons with chronic kidney disease	83%
Persons taking blood pressure lowering medications	71%
Persons with Diabetes	69%
Persons with high blood pressure levels	52%
Older aged persons	48%
Persons with Heart Failure	48%
Pregnant Women	38%
People taking SGLT2i	32%
Children/Young adults	31%
Definitions: LSSS: *low-sodium salt substitutes; RAASi: renin-angiotensin-aldosterone inhibitor; SGLT2i: sodium-glucose co-transporter 2 inhibitor* **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1a): The top three priority groups for effectiveness studies are those with common conditions where evidence on both safety and effectiveness remains limited: individuals with chronic kidney disease (CKD), those taking blood pressure–lowering medications (particularly RAAS inhibitors), and those with diabetes. Other groups were identified as lower priority because they are less likely to derive substantial benefit (e.g., children and youth, except in cases where use of LSSS might help slow the age-related rise in blood pressure), represent relatively small subpopulations (e.g., SGLT2 inhibitor users), or involve complex medical management (e.g., individuals with heart failure). It is worth noting that persons with hypertension have frequently been included in LSSS trials, where blood pressure has typically served as the primary outcome.

Q1b: How important is it to study LSSSS effectiveness in each of these scenarios?	
	% of participants who ranked as high importance*
Determining the dose response relationship between % potassium content and blood pressure reduction	75%
In populations where most sodium intake comes from processed food	66%
In populations where potassium intake is high at baseline	44%
LSSS with potassium citrate instead of potassium chloride	39%
In regions with hot climates (and potential sodium loss via sweat)	34%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1b): The highest-priority scenarios focus on unresolved research questions regarding the optimal dose of LSSS and its effectiveness in populations where the majority of sodium intake comes from processed and restaurant foods rather than from discretionary salt added during cooking or at the table. A key potential confounder is that most existing LSSS trials have been conducted in South and Southeast Asia, where sodium intake is primarily discretionary, dietary potassium intake is low, and serum potassium levels may also be low (i.e., hypokalemia).

Q1c: Please indicate the importance of each as a research topic.	
	% of participants who ranked as high importance*
Long term outcomes (CVD risk, stroke, and mortality)	90%
Renoprotective effects	79%
Age-related rise in blood pressure	62%
Change in population intake of salt	59%
Benefits over other health activities like exercise and diet	33%
Impact on glycemia	25%
Definitions: CVD: cardiovascular disease **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1c): These topics address outcome variables beyond BP. Long-term clinical outcomes was rated as most important to study. The next highest priority was preservation of kidney function, an area where evidence remains limited. Interest in the age-related rise in BP reflects a focus on the potential long-term effects of LSSS in lowering BP and preventing hypertension. Finally, changes in population sodium intake could provide surrogate evidence of benefit in the absence of direct clinical outcomes such as BP or disease events.

Q1d: How important is it to study LSSS safety in each of these patient groups?	
	% of participants who ranked as high importance*
Persons with chronic kidney disease	93%
Persons with Heart Failure	74%
Persons taking blood pressure lowering medications	74%
Persons with Diabetes	63%
Older aged persons	62%
Persons with high blood pressure levels	54%
Pregnant Women	33%
Children/Young adults	19%
Definitions: CKD: chronic kidney disease; LSSS: low-sodium salt substitutes; RAASi: renin-angiotensin-aldosterone system inhibitor	
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1d): Respondents identified several patient subgroups as important to study when evaluating the safety of LSSS, largely because these groups face a higher-than-average risk of hyperkalemia. However, some subgroups may introduce confounding; for example, rather than focusing broadly on older adults, it may be more appropriate to study individuals with chronic kidney disease (CKD) or those using RAAS inhibitors. In contrast, patients with uncomplicated hypertension who do not have CKD, diabetes, or RAASi use are not considered at high risk for hyperkalemia. Similarly, the likelihood of LSSS-related adverse events is low in uncomplicated pregnancies and in healthy children and young adults, and thus these groups were not deemed priority populations for safety studies.

Q1e: How important are the following research topics related to hyperkalemia?	
	% of participants who ranked as high importance*
What is the clinical relevance of high potassium levels (e.g. 5-5.9 mmol/L) in persons with CKD?	81%
How does using LSSS affect long term renal function in hypertensive individuals?	65%
What is the risk of hyperkalemia from LSSS by level of dietary potassium intake?	65%
Would substituting chloride by citrate reduce the risk of hyperkalemia with LSSS?	56%
Determining clinical risk factors that predict hyperkalemia (eGFR stage, proteinuria stage, biomarkers) among those using LSSS.	54%
Is the increased use of potassium in LSSS linked to a risk of heart attacks and strokes?	48%
What frequency of monitoring of potassium levels is needed to ensure LSSS safety?	46%
Does LSSS increase the risk of postprandial hyperkalemia?	36%
Definitions: CKD: chronic kidney disease; K: potassium; LSSS: low-sodium salt substitutes	
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1e): Most of these questions are clinically relevant and could help guide the use of LSSS in patient care. Some, however, address broader issues not specific to LSSS—for example, the clinical significance of modestly elevated serum potassium in individuals with CKD, where such elevations may carry greater risk than in those without CKD. Exploring the combined impact of high dietary potassium intake and LSSS, as well as identifying predictors of hyperkalemia in LSSS users, could inform clinical management but may have limited value for public health guidance. Substituting potassium citrate or gluconate for potassium chloride may also offer advantages, including reduced risks of hyperkalemia and metabolic acidosis, particularly in patients with CKD.

Q1f: Please indicate the importance of each of these topics regarding risk of hyperkalemia.	
	% of participants who ranked as high importance*
What is the safety profile in populations where many people are unaware of kidney disease?	80%
What is an appropriate warning label for LSSS?	72%
Which population categories need to have kidney function tested before switching to LSSS?	60%
What amounts of LSSS can safely be used per day?	58%
What is the risk in countries where less than 25% of salt is discretionary?	50%
Are there populations or countries for which there is unequivocal safety?	42%
Deinitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1f): These questions pertain to the safety of public health initiatives that promote use of LSSS. Most focus on identification and mitigation of risks related to hyperkalemia, with particular attention to those who may not be aware of their increased risk. Research priorities should also focus on determining what degree of potassium elevation is harmful; this will then allow for determinations regarding the amount of potassium that can be safely ingested.

Q1g: Please indicate how important it is to study each of these medications.	
	% of participants who ranked as high importance*
Potassium-sparing Diuretics	72%
Renin-angiotensin-aldosterone system inhibitors, including ACEi, ARB, RI	67%
SGLT2i (sodium-glucose co-transporter-2 inhibitors)	50%
Bactrim and other sulfa antibiotics	33%
NSAIDs (non-steroidal anti-inflammatory drugs)	33%
Non-Potassium-sparing diuretics	17%
Definitions: ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker; CKD: chronic kidney disease; LSSS: low-sodium salt substitutes; RI: renin inhibitor **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q1g): These questions focus on the safety of medications known to raise serum potassium levels. Some, such as RAAS inhibitors, are widely prescribed in patients with hypertension and CKD. Others, including SGLT2 inhibitors and potassium-sparing diuretics, are newer or less commonly used but are increasing in prevalence. Feasibility considerations include how frequently and how long these medications are taken—for example, sulfa antibiotics are prescribed for short episodes of infection, whereas NSAIDs may be used chronically for pain. To determine whether research on these drug classes is warranted, it is important to assess current patterns and trends in use. For instance, it remains unclear whether potassium-sparing diuretics are used often enough to justify dedicated studies of their interaction with LSSS. Notably, a recent *JAMA Internal Medicine* publication reported that SGLT2 inhibitors do not increase the risk of hyperkalemia.[13]

Interpretation and recommendations

- Effectiveness of LSSS to lower BP and prevent CVD events is well-documented, largely from studies conducted in regions of the world with high sodium and low potassium intake (South and Southeast Asia) where the source of sodium is discretionary, highlighting the need to study LSSS in other regions where discretionary intake of sodium is not a common source.

- Effectiveness outcomes of interest were mostly clinical events (CVD events, kidney disease progression) and long-term effects, particularly the age-related rise in BP. Amelioration of hypokalemia is a potential benefit that might outweigh the frequency of hyperkalemia.

- Priority populations identified for both effectiveness and safety questions (q3a and q3d) were largely the same: individuals with CKD, those taking blood pressure medications (especially RAAS inhibitors), and those with diabetes—clinical contexts where impaired potassium excretion increases the risk of hyperkalemia. The consistency in responses underscores an interest in understanding the net health impact of LSSS, specifically whether its benefits outweigh its potential risks.

- Low-priority populations included pregnant women and children/young adults, likely because the risks of LSSS are considered minimal in the absence of underlying disease.

- Apart from hyperkalemia, no major safety concerns were identified.

- A recurring concern was how the effectiveness and safety of LSSS may vary depending on concomitant diet, particularly in the context of high dietary potassium intake.

- Several public health issues were rated as high priority, such as strategies for populations with low CKD awareness and the potential use of warning labels.

Industry/ Development & Food Technology

Table 2: Expert-identified Industry/Development and Food Technology subthemes for focus during LSSS webinar series

1. **Taste/Texture/Appearance**
    a. Taste needs to be prioritized because taste is key to consumer uptake, acceptance, and adherence
        i. Need to consider that the impact of LSSS on taste may be different depending on when its added (before/during or after cooking)
        ii. Need to be mindful about not flooding the marketplace with poor tasting LSSS as this will impact future spending/product choice
        iii. Need to consider the role of KCl content on taste (i.e. higher proportions of KCl can lead to a bitter, metallic taste; potassium is less salty than sodium)
        iv. Need to consider the role of taste adaptation; if people maintain the same preference for salty taste, when using a KCl-enriched salt do we send mixed messages; use of LSSS do not decrease one's affinity for salty foods
    b. LSSS may change texture in some products (i.e. cheese)
    c. Need more data on consumer science – what will lead to consistent use, adherence? How can we make people stick with the product?
2. **Cost**
    a. Can be barrier: manufacturers will be unwilling to make voluntary change if its more expensive
    b. The main raw material for K+ salt is potash which is a traded commodity, thus is subject to market conditions
    c. Need innovation in technology that might make K salts more affordable
    d. May be less of a barrier to buyers in high-middle income countries: data suggests the sale price of LSSS products is not an issue to consumer; no data for low- and middle-income countries (LMIC)
3. **Composition of substitutes – considerations for LSSS:**
    a. Incorporating less than 25% of salt as KCl
    b. Adding Calcium and Magnesium with Potassium
    c. Replacing chloride with citrate
        i. Potential benefit: addition of citrate might reduce the risk of hyperkalemia and antagonize the negative effects of chloride on BP
    d. Iodine
    e. Iron
        i. Note: Iron fortified salts are currently being promoted in some LMIC
    f. Pre-blended salt substitute
4. **Consumer needs/wants**
    a. Food industry is currently focusing on what they *think* the consumer wants
    b. Current gap: taste tests considered along with consumer sales
5. **Food safety when replacing NaCl**
    a. Shelf life

Background

Practically, replacing some NaCl from usual salt with KCl and other substitutes is easily done. A LSSS that is 75% NaCl: 25% KCl is simple to make and is already widely commercially available in several countries.

Technical functionality of low-sodium salt substitutes

The role of salt in food preparation is complex and varies by type of food. However, three general functionalities of salt can be identified:

- Taste: enhances the overall food flavour and masks undesired off-tastes like bitterness.
- Preservative effectiveness: reduces the water activity (aw) and drives osmosis, important for drying/curing, controlling fermentation processes, and limiting the opportunities for microbial growth.
- Technical functionality: modulates the functionality of proteins, which are very important for food processing and food texture formation (e.g. the water binding properties of meat protein).

For any NaCl substitute, the ability to function similar to NaCl is key. Potassium has been considered by most as an ideal substitute due to its chemical similarity to sodium and because it also has BP lowering properties. Although potassium's higher molecular weight makes its techno-functionality somewhat less effective than sodium, it provides a more favorable taste profile compared with other alternatives such as magnesium. While NaCl is characterized by its clean, pure salty taste, KCl is known to impart a bitter and metallic note, particularly at higher K:Na ratios. To address some of the health aspects related to potassium supplementation, cations to replace chloride have been considered (citrate, lactate, succinate, sulphate), however, these supplements technologically behave differently in foods (e.g. as acidulant) and induce a different taste than NaCl.

Potassium Chloride (KCl) is therefore the most common component of LSSS. Studies indicate that partially replacing NaCl with KCl (30–50%) yields comparable results in processing properties, texture, preservation, and taste.[17-19] However, because KCl is less effective than NaCl in its interactions with proteins (affecting texture) and with water (affecting drying, curing, and microbial stability), a partial sodium replacement of about 25% has been proposed as the optimal ratio. This proportion will lead to only a slight reduced technical effectiveness of ~5% which is feasible for most all food categories. Only in exceptional cases do challenges occur, and these can be solved through taste-maskers and preservation techniques. Concerns remain regarding how specific consumer groups like 'super-tasters' respond to products with LSSS, and whether taste adaptation to KCl in foods occur over time.

Consumer acceptability of LSSS as discretionary salt seems to be very high in human intervention studies,[20] which is confirmed by the commercial experiences of LSSS with high K-content on the market. However, it should be noted that these results are biased to specific target groups: health-conscious consumers or patients who are relatively older and likely more motivated to stick to the intervention.

Feasibility of producing and scaling low-sodium salt substitutes

Potassium chloride is not mined directly but is produced from potash, a natural mixture of potassium-rich minerals. In addition to the higher processing costs, potash is not as widely found on earth compared to sodium, making the production and distribution more costly. Potash is mainly (>95%) used for non-food applications such as fertilizers and is traded in a market similar to the oil and gas trade. On this global market, the price of potash is influenced by various factors such as:

- supply and demand (population growth, increasing food demand, and changing agricultural practices)
- production costs (mining, processing, transportation, energy, labour, and regulatory requirements)
- market conditions (global economic conditions, currency exchange rates, and trade policies)

In general, LSSS will always be more costly than NaCl salt, with the potassium enrichment level being the main driver of cost. Currently, food grade KCl costs six times more than food grade NaCl. Because costs are tied to the global potassium market, widespread adoption and scaling of LSSS are not expected to lower the price of potash. Importantly, potash supply is not a limiting factor—current mining capacity can readily meet potential demand. Instead, the main constraint lies in the relatively small number of manufacturers capable of producing high-quality, food-grade KCl with the required particle size, which may restrict global implementation.

Participant discussion

A robust discussion followed the featured presentation, where gaps were highlighted and questions were raised. A summary of this discussion, organized by topic areas, is presented in Supplemental Table 2.

Post-webinar survey questions:

Q2a: How important is it to assess sensory and quality attributes when developing a new processed food product with LSSS?	
	% of participants who ranked as high importance*
Overall consumer acceptability	84%
Taste and aftertaste	75%
Shelf life/stability	57%
Degree of saltiness	50%
Appearance (including color)	46%
Smell	41%
Texture	38%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2a): Assessing consumer acceptability of salt substitutes in food products was identified as the top research priority. For a public health initiative to succeed, consumer buy-in is essential, and taste—including both flavor and aftertaste—is central to acceptance. Determining how to test and optimize the shelf life and stability of the product was also ranked highly; consumers want food products that don't expire quicky and industry benefits from substitutes that keep their products safely on the shelf for longer periods of time.

Q2b: How important is it to assess attributes when developing a new LSSS product for discretionary use?	
	% of participants who ranked as high importance*
Overall consumer acceptability	87%
Taste and aftertaste	79%
Degree of saltiness	65%
Shelf life/stability	35%
Smell	35%
Appearance (including color)	34%
Texture	30%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2b): For LSSS intended for discretionary use, consumer acceptability and taste/aftertaste were ranked as top priorities, consistent with findings for LSSS in processed foods. A key distinction, however, was that establishing the perceived degree of saltiness was considered a higher priority for discretionary salt use.

Q2c: How important is it to study the functionality of the following types of food/uses?	
	% of participants who ranked as high importance*
Use for home cooking	80%
Meat Products	80%
Bread products	80%
Use for post-cooking flavor	70%
Cheese products	50%
Pickled foods	40%
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2c): The majority of these options were felt to be sufficiently important to study in terms of retaining functionality when LSSS are incorporated. With much of the salt use in LMIC being discretionary, ensuring the salt used for home cooking retained its function was ranked most highly. Meat and bread products make up most of the food products consumed in higher resourced countries, elevating their importance above the other listed products.

Q2d: How important is it to study how LSSS additives and personal factors affect taste?	
	% of participants who ranked as high importance*
Ability to adapt one's taste preference over time	85%
Impact of individual characteristics (age, sex, usual salt intake) on taste perception	85%
Potassium thresholds where saltiness and taste become negatively impacted	70%
How molarity, size, and structure of LSSS impacts saltiness	60%
Impact of individual biology on LSSS taste perception ("super-tasters"? "salt-sensitivity"?)	60%
Impact of other LSSS components (citrate, magnesium, calcium) on taste	40%
Impact of food grade vs. refined chemical grade KCl on taste	30%
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2d): Consumer acceptability and taste are the underpinnings of these results. Determining the personal characteristics that impact taste perception of LSSS and the ability to alter one's taste over time have potential implications not just for product development but for roll out of public health initiatives. While not linked to these two concepts, per se, determining the potassium thresholds where taste and saltiness become negatively impacted – when, and by whom – could also aid product development and ultimately implementation efforts.

Q2e: How important is it to study the following product characteristics on consumer acceptability?	
	% of participants who ranked as high importance*
Incorporation of taste enhancers	65%
Iodine enrichment of LSSS	59%
Sodium coating of LSSS	53%
Iron enrichment of LSSS	42%
Use of spray drying and atomization techniques	41%
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2e): The most important research priorities were understanding how consumer acceptability depends on palatability—shaped by factors such as taste enhancers, sodium coating, and their effects on texture—and on whether these products include other key health-related ingredients, such as iodine.

Q2f: How important is it to study LSSS regarding cost?	
	% of participants who ranked as high importance*
Cost-effectiveness of subsidizing LSSS	94%
Projected costs when LSSS are used/sold on a global scale	76%
Projected regional costs when KCl supplies are abundant (no need for import) vs. limited (need for impots or alternative production)	69%
Impact of salt reformulation strategies on production and retail costs	69%
Cost effectiveness of producing KCl from other local methods (ie Bittern) vs. importing potash	50%
Cost when additional additives are included in LSSS (calcium, magnesium, citrate)	44%
Definitions: KCl: potassium chloride; LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2f): Cost emerged as a high-priority area for research to support large-scale implementation of LSSS. Determining the cost-effectiveness of government subsidies was viewed as especially critical. Respondents also emphasized the importance of assessing how supply–demand dynamics influence cost, including the financial impact of global versus regional sales and the effect of abundant versus limited regional supply. In addition, evaluating how innovative salt reformulation strategies affect cost was identified as a key priority.

Q2g: How important is it to estimate factors related to demand, supply, and cost of LSSS?	
	% of participants who ranked as high importance*
A business model for food manufacturers that justifies a slightly higher cost for LSSS in their products	82%
The amount of food grade KCl needed to produce enough LSSS to have a meaningful impact on population-wide BP levels	81%
Potential savings with alternative strategies for LSSS production	69%
The amount of food grade KCl needed to meet demand for global LSSS implementation	69%
The amount of potash (raw KCl) needed to meet demand for global LSSS implementation	63%
The amount of potash (raw KCl) needed to produce enough LSSS to have a meaningful impact on population-wide BP levels	50%
Definitions: BP: blood pressure; KCl: potassium chloride; LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q2g): The top two items identified relate to how to best aid efforts for widespread use of LSSS. Working with industry to determine how to incorporate LSSS in their products from a business perspective, recognizing that the product cost may increase slightly, is key to scale up. While determining how much food grade KCl is needed to have the intended and expected public health impact is a goal with merit on its own, it also links back to aiding industry (and others) in accepting a slightly higher cost for potential long-term gain. The third and fourth most highly ranked questions are similar in scope, aiming to study ways to decrease cost with innovative production methods and determine global supply needed for optimal impact.

Responses to Open Text Question

1) *Key factors contributing to higher cost of LSSS*
   Several factors were identified: challenges with procurement of KCl, higher price of potash, regulatory constraints, and cost of food grade production. The low demand for KCl was noted as another cause for higher prices. Government subsidies was one proposed solution to overcome this barrier by increasing demand and guiding industry behavior.

Interpretation and recommendations

- While there is general consensus regarding the promise of LSSS on CV health, how to ensure consumer acceptability from a taste and cost perspective remain challenges.

- Many experts recommend an LSSS formulation of 75% NaCl and 25% KCl, as this ratio has demonstrated efficacy, is relatively easy to produce, and is widely accessible. However, it remains uncertain whether this proportion will be acceptable across all food categories and among diverse consumers. Assessing consumer acceptability—both at first taste and with continued use—may be critical to ensuring early adoption and sustained uptake.

- Minimizing cost is essential to ensuring widespread uptake of LSSS is feasible. Some drivers of cost will be lessened once there is market demand and greater numbers of manufacturers mine and refine potash into food grade KCl.

- Lobbying for government mandating the use of LSSS in processed foods—and ensuring their enforcement—could stimulate demand and help lower costs.

- In LMIC, advocacy for measures such as subsidies, import tariffs, and taxes may be especially important to offset costs and support broad dissemination.

Implementation of LSSS

Table 3: Expert-identified Implementation subthemes for focus during LSSS webinar series

1. **Health care/medical professional buy-in**
    a. Medical professionals recommending LSSS as treatment/prevention will increase consumer use
    b. Discussing LSSS in the context of overall health will increase buy-in from those who are intrinsically health conscious
    c. Current need: behavioral change communication approaches for health care professionals recommending LSSS
2. **Manufacturer buy-in**
    a. Important for widespread replacement in prepackaged foods
3. **Food service industry buy-in**
    a. Many don't see the value of sodium reduction/supplementation
        i. Need to focus efforts/target marketing to CEOs of restaurant chains and sports stadiums, retail executives
4. **Consumer buy-in**
    a. Need to determine: (1) consumer willingness to purchase LSSS products, (2) comparative effectiveness of LSSS when use is voluntary vs. implemented as public policy, (3) consumer acceptability
5. **Government buy-in**
    a. Most national salt targets for packaged foods are not currently mandatory
        i. Need to determine if sodium target mandates would impact the sodium content of packaged foods
6. **Availability**
    a. Increased perception of availability will lead to greater consumer purchase/use
        i. Area of focus: (1) encourage retail outlets to offer healthier salt alternatives everywhere (much like with sugar substitutes), (2) increase product availability on grocery store shelves
7. **Labelling**
    a. Needs to be standardized
    b. Should promote LSSS as healthier alternative
    c. Consider analogous labelling to that done for food allergens
    d. Identified gap: impact of labelling on consumer uptake
8. **Advocacy**
    a. Needed among the key stakeholders - specifically clinicians and academicians – but need to increase education/knowledge first
    b. Awareness, availability, and affordability are challenges in implementation. Even if the health care provider recommends the use of LSSS, LSSS may not be available.
    c. Improving awareness and correct messaging is critical to increasing product demand

9. **Future research focus**
    a. Implementation research regarding NaCl replacement with K-salt in public food procurement.
    b. Feasibility, demonstration projects, cost effective analyses, and studies regarding acceptability by settings and contexts – this data is key for large scale implementation and sustainability.
    c. Set “progression criteria” like is done in pilot trials
    d. Targeted or population-wide approach will determine the potential to include LSSS in food distribution systems.
    e. Impact of LSSS on measured sodium and potassium level changes
    f. Implications of LSSS on total potassium intake
    g. Impact of LSSS on discretionary salt intake
        i. Ie: is there an inadvertent increase of discretionary salt use when LSSS are used due to perceived health benefit/less salty taste of LSSS?

Background

For LSSS to be successful, they need to be well-tolerated by consumers, in terms of taste and ease of use, and they need to be relatively low-cost to manufacture. To be maximally effective as a public health strategy to improve CV health, they also need to function as a universal salt replacer in food production (e.g., packaged foods) and for discretionary use (e.g., table salt). This is an important aspect for any global LSSS intervention, because dietary salt intake varies substantially between countries. In high-income markets with Western diets, most salt intake comes from packaged foods, such as base foods like bread, processed meats, and cheese. The situation in low-income countries differs and is rapidly evolving. Previously, most salt intake in low-income countries was discretionary, i.e. salt added at home during cooking or at the table when consuming the food. However, given rapid food transitions occurring in these countries, sodium in processed foods appears to be a major source as well.

Broad scale implementation of LSSS as a public health initiative to decrease CVD will rely on three implementation pathways:

(1) substitution of table salt with LSSS, intended for discretionary use by food consumers at the household level

(2) replacement of salt with LSSS in processed/packaged foods by food manufacturers

(3) replacement of table salt with LSSS in foods prepared in restaurants and other settings where food is sold

Understanding how evidence-based interventions can be implemented successfully in real-world contexts will drive meaningful change. As an early proof-of-concept, China has implemented several initiatives to increase potassium-rich salt production. These have included the following: salt-manufacturer distribution of a 2-gram salt-limited spoon along with videos and other health promotion materials to promote the healthy use of salt in communities and supermarkets; launch of a series of LSSS products designed to meet the needs of various customer groups; and a switch to LSSS in the cafeterias of schools, public institutions, and other enterprises.[21]

Despite these efforts, consumer buy-in remains suboptimal. Warning labels targeting specific groups that do not also include information regarding potential health benefits, high production cost and thus high market prices, and low overall awareness of the health benefits of LSSS have limited their use. The emerging dominance of prepackaged or ready-made foods, particularly in urban areas, requires a similar shift in terms of effort allocation for implementation.

Enhancing the engagement and buy-in of each stakeholder – general population, health care professionals, food manufacturers, and food-service industry - is key to implementation. One underutilized strategy includes educating and encouraging health care professionals to prescribe potassium-rich salt to those at increased CVD risk. In some countries, such as China, this strategy will require a nuanced approach as there can be a perception that doctors sell products for financial gain.

Consumer perceptions of LSSS taste have been mixed; however, studies show that acceptability and willingness to use substitutes increase significantly after consumers try the products. Standardizing product labels and associated health claims could further support implementation. Currently, the absence of such standardization is viewed as a key barrier to large-scale adoption.[22] To illustrate this point, common salt (NaCl) can be labeled simply as a natural ingredient (“salt” or “sea salt”), while

products containing sodium replacers like potassium must be labeled as additives, which can create barriers for both industry and consumer acceptance. Adding positive health claims to labels could encourage use, but such claims depend on the specific LSSS formulation and may conflict with or confuse existing warning labels. To address these challenges, some have proposed an industry-wide shift to treating LSSS as the default form of salt, eliminating the need for special warnings or ingredient-specific claims regarding KCl.

Participant discussion

Post-webinar survey questions:

Q3a: How important is it to study the impact of the following governmental roles in widespread uptake of LSSS?	
	% of participants who ranked as high importance*
Public health policy development (e.g., WHO guidelines or recommendations, national or regional public health guidelines)	72%
Education of medical professionals	71%
Regulation (e.g., LSSS subsidies, regulations allowing health claims on product packaging)	68%
Education of citizens	67%
Promotion (e.g., media campaigns, advocacy with salt manufacturers and the food service sector)	60%
Collaboration with LSSS manufacturers and food services	52%
Evidence generation (research, public health surveys)	48%
Financial support and incentives (e.g., grants to LSSS manufacturers and/or retailers)	48%
Definitions: LSS: low-sodium salt substitutes; WHO: World Health Organization **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q3a): There was broad interest in defining government roles to promote LSSS. The most highly rated roles were not traditional research activities but rather actions governments can take, such as developing policy documents and recommendations, educating health professionals and the public, and promoting LSSS through regulations, including health claims and subsidies. Some of these functions—such as education of health professionals and the public—could also be carried out by non-governmental organizations, such as professional societies.

Q3b: How important is it to study the following potential concerns and considerations of the food service industry?	
	% of participants who ranked as high importance*
Concerns regarding impact of LSSS use and customer satisfaction	63%
Availability and cost of LSSS	56%
Willingness to incorporate LSSS into menus	54%
Type of incentives required by each industry/service	50%
Need for financial support/incentives to use LSSS	46%
Perceived health benefits and risks	42%
Suitability of adding LSSS to local foods	38%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q3b): The food service industry's main concerns center on consumers—specifically customer satisfaction and the cost of incorporating LSSS into food products. Their willingness to adopt LSSS is less of a barrier; instead, the focus lies in developing and testing products and assessing consumer acceptance, which are already standard practices in the industry. Interestingly, there was less emphasis on health benefits or financial incentives. Addressing these issues may be best achieved through surveys, focus groups, and key informant interviews rather than traditional biomedical research.

Q3c: How important is it to study the following manufacturer concerns in promoting the use of LSSS?	
	% of participants who ranked as high importance*
Market demand	76%
LSSS Cost and ultimate product price	68%
Ability to ensure quality and safety	52%
Technical challenges	52%
Need for financial support/incentives to use LSSS	50%
Development of food for mass/institutional consumption	36%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q3c): For manufacturers, the primary concerns were market demand and the cost of LSSS. Demand is likely shaped by consumer perceptions of taste, price, and, for some groups, health benefits. Unlike responses to other questions, product cost and pricing ranked especially high in importance. The issues raised may be best addressed through surveys, focus groups, and key informant interviews rather than traditional biomedical research.

Q3d: How important is it to study the following aspects of product label design?	
	% of participants who ranked as high importance*
How specific features of the label impact consumer purchase intent	64%
What information consumers want on the labels	59%
How details regarding potassium content impact consumer purchase intent	45%
How specific features of the label influence consumer perception of health benefits	41%
Saturation point (e.g., how long do the labels have an influence? Are the effects sustained over time?)	23%
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q3d): Product labels serve as key tools for conveying information at the point of purchase, using both messaging and visual elements such as size, shape, color, and icons. In this survey, both the content of messages and the design features of labels were rated highly. Consumer research will be essential to address these issues, though findings may vary depending on label type: labels emphasizing benefits differ from those designed as warnings. For example, colorful designs may enhance appeal and effectiveness for benefit-oriented labels but may not be appropriate for warning labels.

Q3e: How important is it to study the following and how it may relate to implementation?	
	% of participants who ranked as high importance*
The architecture of incentives and delivery channels to facilitate the purchasing and use of LSSS	75%
Motivation for consumer purchase and consistent use of LSSS	70%
Content of advertisements and public health messaging that could increase consumer acceptability of LSSS	70%
The impact of warning labels designed to inform people with CKD about the high potassium content of LSSS	65%
Taste/Texture perception of LSSS compared to regular salt	60%
Current level of consumer knowledge regarding benefits of potassium	45%
Consumer concerns regarding side-effects of potassium consumption	45%
Methods to prevent increased sodium consumption overall from positive messages regarding LSSS	30%
Consumer experiences with other enriched products	25%
Definitions: CKD: chronic kidney disease; LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q3e): The highest rated topic was the 'architecture' of incentives, which might be relevant for consumers as well as food manufacturers and food service providers. Understanding the motivation for purchase of LSSS was also rated highly, presumably to understand the contributions of price, taste and potential health benefits. Advertisements and public health messaging were highly rated, but might have limited impact because of cost, limited reach and the challenges of mass campaigns to change individual-level of behavior. Interest in warning labels presents a quandary, i.e. conveying a message of harm that is difficult to reconcile with concurrent messaging that emphasize benefit. Again, consumer research will be needed to address these topics.

Q3f: How important is it to study each of the following features that might impact consumer demand for LSSS?	
	% of participants who ranked as high importance*
Perception of LSSS health benefits	74%
Impact of price and availability in stores	68%
Public health campaign strategies	64%
Government strategies	63%
Targeted strategies to reach those most likely to benefit from LSSS	58%
Role of social media	47%
Socio-demographic groups (e.g., does demand for LSSS vary by age, sex, race, family income level, education level etc.)	32%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q3f): The highest rated topic was perception of LSSS health benefits, followed closely by impact of price. Given that the respondents to the webinars were namely persons in medical fields, it is not surprising that perception of health benefits was rated so highly. Yet, research on food purchasing behavior tends to emphasize the key roles of taste and price. Those most likely to benefit, presumably persons with hypertension, was of high interest, and could be a target population given the high prevalence of hypertension. Interest in government strategies likely reflects the need for leadership given the complexity of a campaign to promote broad and sustained uptake of LSSS, which is beyond the scope of industry and academia.

Interpretation and recommendations

- Successful implementation will require joint and coordinated efforts by government, medical professionals, food manufacturers, food service producers, and consumers to address a diverse array of issues related to promotion of LSSS. Government will likely need to assume a leadership role.

- The topic of cost/price was often highly rated as a research topic, presumably because LSSS, while not expensive per se, is nonetheless more expensive than routine table salt. Implementation studies testing (1) the impact of financial incentives and subsidies, and (2) the additional cost of using LSSS incurred by the food industry are needed to ultimately lower the cost of LSSS.

- There was considerable interest in emphasizing health benefits to consumers to promote LSSS uptake. Such efforts might focus on health care providers who could recommend LSSS to lower BP in persons with hypertension. To this end, guidelines that explicitly mention LSSS would be particularly useful.

- Product labeling can highlight both health benefits and potential health risks. A key challenge for LSSS is that labels may need to communicate both: benefits for the general population—particularly individuals with hypertension—alongside potential risks for people with chronic kidney disease.

- There was considerable interest in understanding consumer motivations, acceptance of LSSS, and perceptions of labeling features and health benefits. To explore these issues, respondents suggested market research methods—such as surveys, focus groups, and key informant interviews—rather than traditional biomedical research. Product development and evaluation were also considered important, though this area received less emphasis during the webinar, in part because such studies are often conducted as proprietary industry research.

Public Policy for Low-sodium Salt Substitutes

Table 4: Expert-identified Public Policy subthemes for focus during LSSS webinar series

1. **General:**
    a. Partnering with the World Health Organization would facilitate public policy support of implementation
    b. Need to consider: should LSSS be a "medicalized" prescription for people with high BP/hypertension/high CVD risk, a "public health" population-wide approach, or both?
2. **Potential barrier for government uptake:**
    a. LSSS still taste salty; proposing use of a salty product will not achieve the goal of changing people's palates (i.e. will not help with the goal of voluntary reduction of sodium intake because they want to eat less salty food)
    b. Need to consider: (1) how a public policy approach will align with other sodium reduction initiatives like SHAKE, (2) how this will be included in food distribution systems, (3) how the food industry will achieve mandatory salt limits in prepackaged food?
    c. Potential motivators for public policy uptake: (1) subsidies for K-salts, (2) financial incentives for manufacturing LSSS
3. **Iodinization**
    a. Manufacturers may need to tailor products to individual countries based on the iodinization regulation; this standard is set by the Ministry of Health.
4. **Advocacy**
    a. Efforts that highlight the benefits of increased K intake in addition to reduced Na are needed

Legend: CKD: chronic kidney disease; CV: cardiovascular; CVD: cardiovascular disease; K: potassium; KCl: potassium chloride; LMIC: low- and middle-income countries; LSSS: low-sodium salt substitutes; Na: sodium

Background

Most of the existing public policies that relate to sodium reduction are concentrated in high-income countries which limits applicability to lower income countries with fewer resources. To address this gap, in 2024 the WHO published an updated SHAKE guideline which had three overall program objectives:

(1) Reduce sodium content in manufactured foods
(2) Reduce consumer demand for high sodium foods
(3) Change consumer practices

The preferred public policy approach to achieve these objectives is food reformulation rather than direct salt replacement. To be most effective, such policies must be comprehensive, grounded in evidence, and supported by clear objectives, administrative visibility, adequate financial resources, and practical logistics. The WHO has developed global sodium benchmarks across food categories to guide this process.

A scoping review by Kong et al, published in 2023, reviewed national and international initiatives related to LSSS across 11 countries and 3 international organizations. The authors identified 35 initiatives, which can be grouped into four broad categories:

- **Benefit and risk assessments** – e.g., determining the appropriate proportion of sodium to replace with potassium chloride.
- **Plans and actions** – e.g., incorporating salt substitutes into national salt reduction strategies and policy guidelines.
- **Regulations, standards, and labelling** – e.g., health claims, nutrient composition requirements, and product classification.
- **Food reformulation and industry/media collaboration** – e.g., introducing LSSS into processed foods and engaging the media to raise awareness.

Although this review was limited by its focus on national initiatives (excluding sub-national efforts) and its reliance solely on web-based data sources rather than expert or key informant interviews, it nonetheless offers a useful foundation for evaluating public policy initiatives across different contexts. High income countries such as the UK, USA, Germany, Norway, Canada, Australia, Ireland, Finland and Singapore focused on processed food reformulation, whereas China focused on a population wide approach to lowering discretionary salt intake and India focused on Food Safety and Standards Authority of India (FSSAI) recommendations for usage under medical supervision. Notably, the review found no reports on monitoring LSSS usage and identified no national LSSS initiatives in certain regions, including Latin America and Africa.

WHO global sodium benchmarks and policies

Most countries utilize a mix of mandatory and voluntary benchmarks for sodium reduction. The WHO sets global sodium benchmarks for various food categories, with bread products, snacks, and ready meals being the most commonly benchmarked categories. Optimizing food labelling to be clear and easily understandable is essential for countries aiming to meet these targets, as is targeted food marketing, public procurement to promote healthier food options, taxation for foods that do not contribute to a healthy diet, and overall policy coherence. The WHO sodium scorecard is a tool to assess policy coherence for sodium reduction; increasing scores by 2 levels could help achieve sodium reduction targets by 2030.

The role of government

Governments play a critical role in promoting the production and consumption of LSSS and in creating incentives for businesses to support public policies aimed at reducing salt intake. Key actions include:

- Developing national guidelines for LSSS production and use
- Setting standards for LSSS and permissible health claims
- Issuing health advisories regarding the use of LSSS
- Determining what salt reduction policies should be mandatory vs. voluntary
- Regulating the price of LSSS to encourage uptake e.g., subsidies/ incentives for industry, tax incentives (removing tariffs on potassium enriched salt or KCl, removal of sales taxes)
- Assessing and providing budgetary needs for program implementation.
- Promoting LSSS use and distribution through public food programs and government health centers

Participant discussion

Participants highlighted several strategies for sensitizing policymakers to LSSS as a realistic and cost-effective intervention for improving health outcomes. These included:

- Raising awareness through diverse channels such as events, success stories, roundtable discussions, policy toolkits, policy briefs, and storytelling
- Knowledge mobilization of the science, technology, and economics of LSSS as well as cost effectiveness.
- Dissemination of WHO guidelines when available
- Engaging broadly on cross-cutting issues beyond health and nutrition, including supply chain, procurement, and distribution

Post-Webinar Survey questions:

Q4a: How important is it to conduct research on the following policy approaches on strategies to implement LSSS?	
	% of participants who ranked as high importance*
Strategies to enhance public and policy makers' understanding of LSSS and their health benefits	72%
Policies to enhance the understanding of the health benefits of potassium	65%
Procurement policies for use of LSSS in public institutions (hospitals, domicile facilities, schools, jails etc)	61%
Policies that target high risk populations who would benefit from LSSS	61%
LSSS policies that span multiple sectors such as cross-sector initiatives that encourage collaboration across different industries (beyond the healthcare and nutrition sectors)	57%
Health messaging with the term sodium vs. the term salt	55%
Integration of messaging to consume LSSS with messaging to reduce overall sodium intake	53%
Integration of policies for potassium-enriched salt with policies for iodization of salt	52%
Changing the definition of "salt" to one that includes all minerals, with labeling required to detail the mineral composition	43%
Policies and messaging to ensure patients at high risk for hyperkalemia avoid LSSS (for example, advanced CKD)	39%
How LSSS can achieve mandatory vs. voluntary sodium reformulation targets	24%
Definitions: LSSS: low-sodium salt substitutes **High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q4a): The top-rated research priorities for policy approaches to LSSS centered on education—specifically, identifying effective strategies to improve public and policymaker understanding of the health benefits of LSSS and potassium more broadly. Building awareness and securing buy-in from these stakeholders is expected to facilitate more successful policy adoption and

scale-up. Additional priorities included examining procurement policies for incorporating LSSS into public institutions and conducting trials to evaluate effectiveness in settings where barriers to implementation may exist but impact could be substantial. Finally, identifying and assessing policies that target high-risk individuals was also considered a high priority.

Q4b: How important is it to conduct research on the following approaches to increase use of LSSS?	
	% of participants who ranked as high importance*
Subsidies for manufacturers	88%
Subsidies for consumers	76%
Reduced tariffs for Potash	63%
Strategies to provide governments a financial benefit for promoting use of LSSS (as they do with taxation on sugar or alcohol)	63%
Joint impact of subsidizing LSSS while taxing use of sodium chloride	50%
Food as medicine initiatives- recommendation of LSSS at reduced or no cost by healthcare professionals as part of treatment	50%
Coverage by health insurance companies	38%
**High importance—rated 4 or 5 on Likert scale of importance*	

Comment (Question Q4b): Public policies that are financially beneficial are more likely to succeed, which likely explains the strong emphasis on research into subsidies, tariff reductions, and other financial incentives.

Responses to Open Text Questions

1) *How can we help policymakers be aware of the existence of LSSS and see them as a realistic and cost-effective public intervention to improve health outcomes?*

   Several suggestions were provided:

   - Create a campaign based on personal stories; identify “champions” or “ambassadors” who have experienced the health consequences related to CVD outcomes such as stroke and myocardial infarction. These personal stories may be more impactful in changing public policy than the evidence provided by researchers.
   - Consolidate messaging on how LSSS could decrease hypertension burden and improve cardiovascular health by incorporating information regarding the science, technology, and economics of LSSS production and access. Include success stories.
   - Adjust the context in which LSSS are promoted; instead of focusing solely on LSSS as a nutritional supplement, discuss LSSS as you might discuss vaccines – something that can prevent disease, is safe, but requires ongoing monitoring.
   - Increase news media coverage, host round-table discussions at forums that they attend, lobby medical groups, publish policy briefs
   - Develop a policy makers engagement toolkit which details current evidence and best practices from various countries for use in policy engagement
   - Request that the WHO write a guideline that not only reflects the evidence on LSSS but also highlights how/why current salt reduction strategies are ineffective. Ensure this document is broadly disseminated

Interpretation and recommendations

- Food reformulation is the preferred public policy approach to achieve widespread sodium reduction.

- Successful public policy approaches are comprehensive and clear, are evidence based, and have financial benefits and incentives. With that in mind, research to (1) identify effective strategies to increase stakeholder awareness regarding health benefits of potassium and LSSS and (2) demonstrate the effectiveness of subsidies, reduces tariffs, and financial benefits on LSSS implementation have the potential to be high yield.

Results

Table 5: Priority areas for research with suggested study designs

Research priority	Study designs	Justification	Notes/Comments
Assess the efficacy and safety of LSSS among different population	Intervention studies such as randomized controlled trials (including cluster randomized and practice-based designs) and non-randomized studies; quasi experimental studies; modelling studies to estimate population-wide health effects	Different populations, such as persons with chronic kidney disease, those taking blood pressure-lowering medications, and those with diabetes, were rated as high priorities in the survey for studying both efficacy and safety. These trials will provide robust evidence to tailor LSSS use to specific patient needs while minimizing risks, particularly hyperkalemia.	Some experts suggest that efficacy trials are no longer needed. However, there are many high priority populations (e.g. persons with CKD) where effectiveness has not been demonstrated and where safety is a commonly expressed concern. Trials that test effectiveness and report safety may be most appropriate, especially given the ethical challenges of studies primarily focused on determining safety. In addition to reporting on safety, reporting on unexpected consequences should be prioritized. RCTs are typically expensive and logistically challenging and not appropriate for certain research questions, e.g. optimal label design. Quasi-experimental studies with population surveillance might be appropriate to detect uncommon outcomes, e.g. episodes of clinical hyperkalemia.

Assess the functionality and feasibility of LSSS	Experimental trials and real-world feasibility studies	Functionality factors such as taste, texture, appearance, and shelf life were identified as key determinants of consumer acceptability. Controlled food trials can optimize LSSS formulations, while real-world feasibility studies assess how well LSSS can be integrated into dietary habits across different cultural and economic contexts.	
Assess stakeholder and consumer buy-in for LSSS implementation	Market research, feasibility studies, cost-benefit analyses, consumer perception studies.	Adoption depends on industry feasibility and consumer acceptance. Key concerns include cost, market demand, technical challenges, taste, and labeling. Research should focus on implementation strategies to promote LSSS use.	
Evaluate public policy for LSSS implementation	Modelling studies, policy analysis	Detailed policies to evaluate benefit and potential risk of LSSS.	

Conclusions

Based on the evidence provided during the webinars, including the key gaps identified in the featured presentations, during the online discussion, and in the survey responses, experts identified key research priorities to support the global scale-up of LSSS. Priority areas for investigation include:

Efficacy and safety

- Evaluating the efficacy and safety of LSSS in high-risk subpopulations for hyperkalemia, particularly individuals with CKD, diabetes, or those taking renin–angiotensin–aldosterone system inhibitors.
- Assessing potential health benefits of LSSS beyond blood pressure and cardiovascular outcomes, such as reducing the age-related rise in systolic BP, alleviating hypokalemia in populations with low potassium intake, improving bone health, and slowing CKD progression and its sequelae (e.g., metabolic acidosis).
- Examining the benefits of LSSS in populations where sodium intake primarily comes from non-discretionary sources—such as processed foods and meals prepared outside the home—especially in countries beyond South and Southeast Asia.
- Investigating the health effects of dietary potassium intake both in the general population and in specific subgroups with impaired potassium excretion or high potassium intake.
- Clarifying the clinical significance of moderately elevated potassium levels (5.0–5.9 mmol/L) in individuals with risk factors such as CKD, advanced age, heart failure, diabetes, or hypertension, and whether these risks differ depending on the potassium source (processed foods, fresh fruits/vegetables, or LSSS).

Food Technology and Implementation

- Dose-response studies to establish harmonized LSSS formulations that are acceptable across different food groups.
- While LSSS appears cost-effective when health care savings are considered, tailored funding strategies are needed for diverse geographic and economic contexts. Research should therefore estimate the impact of government subsidies, import tariffs, and global versus regional sales, accounting for variations in KCl supply (abundant vs. limited) and use (discretionary vs. non-discretionary).

Public Policy for Low-sodium Salt Substitutes

- Identify barriers and facilitators to LSSS implementation across stakeholders—including governments, the food industry, health professionals, and consumers—and determine effective incentive mechanisms to expand availability.
- Explore optimal labelling strategies for LSSS, such as warnings for individuals at high risk of hyperkalemia, health-promoting labels for the general population, and approaches to address consumer perceptions when labels present conflicting messages (e.g., LSSS as beneficial for most people but potentially harmful for some).

Beyond research, there is a great need for scale up of other activities (e.g. advocacy, policy analysis, consumer education and promotion) and coordinated, strategic planning with government officials, ministries of health, and professional organizations to advance global uptake of LSSS.

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Appendix A. Executive and Steering Committee members

Name	Affiliation
Tammy Brady* **(Lead)**	Johns Hopkins University, USA
Lawrence J. Appel* **(Co-Lead)**	Johns Hopkins University, USA
Annet Hoek*	The George Institute, Australia
Tazeen Jafar	Duke Univ Global Health Institute, USA
Jaime Miranda	Sydney School of Public Health, Australia
Penjani Mkambula	Global Alliance for Improved Nutrition, Nigeria
Martijn Noort	Wageningen University, The Netherlands
Kathy Trieu*	The George Institute, Australia
Lindsay Steele*	Resolve to Save Lives, USA
Laura Cobb*	Resolve to Save Lives, USA

*Executive Committee members

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Appendix B. Webinar topics and invited experts

Webinar	Date	Topic	Lead	Presenters	Number of Attendees
1	2024-05-21	Research prioritization for scaling the use of low-sodium salt substitutes	Tammy Brady, Johns Hopkins University	"**Overview of the current landscape of Low-sodium Salt Substitutes (LSSS)**" Bruce Neal The George Institute	33
2	2024-06-26	Safety and Efficacy	Tazeen Jafar, Duke Univ Global Health Institute	"**Efficacy of Low-sodium Salt Substitutes**" Matti Marklund Johns Hopkins University, SPH **"Safety of Low-sodium Salt Substitutes"** Ewout Hoorn Erasmus University	29
3	2024-08-19	Industry Development and Food Technology	Martijn Noort, Wageningen University	"**Functionality of Low-sodium Salt Substitutes**" Martijn Noort Wageningen University and Research "**Feasibility of upscaling Low-sodium Salt Substitutes: Considerations for producing a LSSS**" Carolyne Klinge	23

				Klinge Chemicals Ltd	
4	2024-09-16	Implementation of Low-sodium Salt Substitutes	Jaime Miranda, Sydney School of Public Health	"**Implementation considerations – stakeholder buy-in**" Maoyi Tian University of New South Wales "**Implementation considerations – consumer buy-in**" Jaime Miranda Sydney School of Public Health; Kathy Trieu The George Institute	17
5	2024-10-22	Public Policy and Low-sodium Salt Substitutes	Penjani Mkambula, Global Alliance for Improved Nutrition	"**WHO recommendations and Policy Integration**" Luz de Regil World Health Organization "**Role of Government**" Marthi Venkatesh Mannar University of Toronto	20

Appendix C. List of webinar attendees

Name	Affiliation	Country	Number of Webinars Attended	Webinars
Caroline Klinge	Klinge Chemicals	United Kingdom	5	1, 2, 3, 4, 5
Matti Marklund	Johns Hopkins University, SPH	USA	5	1, 2, 3, 4, 5
Nikhil Srinivasaura Venkteshesmurthy	Public Health Foundation of India	India	5	1, 2, 3, 4, 5
Venkatesh Mannar	University of Toronto	Canada	5	1, 2, 3, 4, 5
Andrew Moran	Resolve to Save Lives	USA	4	1, 2, 3, 4
Bruce Neal	The George Institute	Australia	4	1, 2, 4, 5
Janice Johnson	Cargill	USA	4	1, 2, 3, 5
Lijing Yan	Duke University	USA	4	2, 3, 4, 5
Manika Sharma	Resolve to Save Lives	India	4	1, 2, 4, 5
Michael Durst	Unilever/ Culinaria Europe	The Netherlands	4	2, 3, 4, 5
Ranjan Jha	Nutrition International	India	4	1, 2, 3, 5
Robert Kalyesubula	Makerere University	Uganda	4	1, 2, 3, 5
Yazied Chothia	Stellenbosch Univ & Tygerberg Hosp	South Africa	4	2, 3, 4, 5
Abdullah Al-Mamun	ACI Salt Limited	Bangladesh	3	2, 3, 5
Albertino Damasceno	Eduardo Mondlane University	Mozambique	3	1, 3, 5

Name	Affiliation	Country	Number of Webinars Attended	Webinars
Arpana Iyengar	St.John's Nat'l Academy of Health Sci	India	3	2, 3, 4
Marianne Geleijnse	Wageningen University	The Netherlands	3	1, 3, 4
Markisa Dotch	Unilever/ Culinaria Europe	The Netherlands	3	2, 3, 4
Rain Yamamoto	World Health Organization	Switzerland	3	1, 3, 5
Surya Goud	ICMR-National Institute of Nutrition	India	3	1, 2, 3
Ge Zeng	Vital Strategies	China	3	1, 2,5
Bolanle Banigbe	Resolve to Save Lives	USA	2	1, 3
Dr. Roopa	ICMR	India	2	4, 5
Ewout Hoorn	Erasmus University	The Netherlands	2	1, 2
Ganesh Iyer	RTSL Consultant (ex Tata Salt)	India	2	1, 2
P Raghavendra	ICMR-National Institute of Nutrition	India	2	1, 2
Paul Welling	Johns Hopkins School of Medicine	USA	2	1, 2
Robin McKinnon	Food and Drug Administration	USA	2	1, 2
Satyanarayana Reddy	Tata Asset Management Limited	India	2	2, 5
Valerie Luyckx	University of Zurich	Switzerland	2	2, 3

Name	Affiliation	Country	Number of Webinars Attended	Webinars
Yangfeng Wu	Peking University	China	2	1, 2
Ifeoma Ulasi	University of Nigeria	Nigeria	2	4,5
Maoyi Tian	University of New South Wales	Australia	2	1,4
Luz de Regil	World Health Organization	Geneva	1	5
Yuxuan Zhou	NA	China	1	4
John Drinkwater	Cerebos	South Africa	1	3
Luna Xu	University of New South Wales	Australia	1	3
Zulfiqar Bhutta	Aga Khan University	Pakistan	1	3
Laoi Albarqouni	Bond University	Australia	1	2
Rajan Sudhir	The George Institute	India	1	2
Vilarmina Ponce	Consultant	Peru	1	2
Mary Chong	National University	Singapore	1	1
Moes Sanaa	World Health Organization	Geneva	1	1
Priya Nandimath	Padmashree School of Public Health	India	1	1
Sakshi Jain	Nutrition International	India	1	1
Shivashankar Roopa	ICMR-National Institute of Nutrition	India	1	1

Name	Affiliation	Country	Number of Webinars Attended	Webinars
Suparna Ghosh	The George Institute	India	1	1
Vijaya Rajendram	Neptune Bio-Innovations	Australia	1	1
Vivek Jha	The George Institute	India	1	1
Yuxin Lin	China Development Research Fdn.	China	1	1
Alta Schutte	University of New South Wales	Australia	1	1

Appendix D. Supplementary Tables 1-2

Supplemental Table 1: Participant Discussion after Webinar 2, Safety and Efficacy of LSSS

Efficacy:

1. Intake of > 90 mmol/d of potassium is extremely high, so meta-analyses that report such high intakes need to be interpreted with caution
2. The effect of low-sodium on BP reduction is not homogeneous for hypertensive patients. The effect will be greatest in salt-sensitive (SS) hypertensive individuals.
3. There are methodological issues with some published SS literature related to BP measurement error at the individual level. Much of the BP variability described is due to noise. By eliminating BP measurement error, it is likely that most people are salt sensitive
4. Salt sensitivity is exacerbated by reduced kidney function. One in five individuals with hypertension has a reduced GFR. Query: Are there studies that have evaluated this association at a population level?
    a. 6 -10% of people with CKD are aware of their diagnosis in LMICs, and even mild reduction in kidney function (as can occur with living kidney donation) can increase BP
5. Populations/conditions/patient characteristics in which efficacy of LSSS should be assessed:
    a. Rather than age per se, focus on conditions associated with older age, e.g. CKD
6. Efficacy trial considerations with some examples
    a. Design
        i. Pragmatic trials in school feeding programs
            1. Randomize districts to different levels of K vs Na intake
        ii. Randomized trials to study the impact of LSSS use by cooks & street food vendors on sales
        iii. Quasi-experimental studies: e.g. using an interrupted time series analysis, assess the occurrence of hyperkalemia and CV benefits in countries already actively promoting LSSS, such as Singapore.
    b. Intervention:
        i. In order to observe a dose response of potassium on BP, will need a large difference in potassium content in trial arms which is challenging/impractical because of taste considerations
        ii. LSSS with citrate instead of chloride
            1. Some experts are of the opinion that chloride is more important, rather than sodium
                a. Chloride may be exchanged for bicarbonate in the kidney in the distal nephron (the pendrin channel).
    c. Outcomes:
        i. Sales
        ii. Cognitive outcomes including dementia
        iii. Sodium sufficiency/deficiency
            1. Comment: LSSS leading to sodium deficiency seems very unlikely: for most of hominid evolution sodium consumption was likely about 0.5g/day. That is really 'normal' intake from a human physiology perspective. Global average consumption is now 8 to 10 times that. The interventions we are talking about here will not get anywhere near that level of restriction.

Safety:

1. LSSS components that might increase safety:
    a. Citrate, particularly in advanced CKD, as it would treat metabolic acidosis and help prevent rises in serum potassium.
        i. Potassium citrate is regularly used for renal tubular acidosis in children; no anecdotal clinical evidence this has a major effect on BP
2. Populations in whom safety of potassium enriched LSSS needs to be determined:
    a. Chronic kidney disease
        i. Comments: there is data that describes an "unexpected" finding of safety with LSSS in this group that suggests there is no justification for exclusion of people with CKD from LSSS trials – however, creatinine should be checked at least initially to confirm the findings on a broader scale, particularly as CKD prevalence is high
    b. Heart failure
    c. Patients taking ACEi/ARB
        i. Comment: There is unpublished data to show that there was no difference in hyperkalemia in subgroups taking an ACEi or ARB
        ii. Comment: Guidelines recommend screening for hyperkalemia with ACEi/ARB use and dose reduction when hyperkalemia occurs
        iii. Query: Do potassium-increasing drugs impact the dose-response relationship of diet-to-serum potassium?
    d. Pregnant women and the growing fetus (assess for impact on developmental programming)
    e. Children
        i. Specific considerations: importance of maintaining sodium intake based on age and body weight for normal growth and development
    f. Family studies (e.g. households with multiple generations living under the same roof)
3. Considerations for using LSSS with citrate or other non-KCl substitutes:
    a. Feasibility (from food technological perspective)
    b. Acceptability (e.g. taste)
    c. Cost
    d. Availability
4. Additional considerations regarding potassium delivery on safety:
    a. Salt substitutes have a very high bioavailability of 80-90%
    b. Potassium in fruits and vegetables have a bioavailability of ~60%.
    c. Co-ingestion of foods that stimulate insulin secretion will lower the rise in serum potassium with intake
        i. Query: Is it potassium intake or potassium level in the blood/tissues? Is there a serum K above which K supplementation is not helpful?
5. Trial considerations testing safety:
    a. It will be hard to do trials that focus primarily on safety. Best to have trials focused on benefits that simultaneously collect information regarding risks.
    b. Trials should be long and large enough to permit robust conclusions.
6. Steps to increase buy-in, allay safety concerns, trial participation:
    a. Implement product information labels instead of product warning labels
        i. Excessive consumer information labeling may lead people to confuse LSSS with a medication
        ii. Use labels to convey health benefits
    b. Minimize cost to avoid financial deterrents to use
    c. Reach out to those who worked on buy-in of COVID-19 mRNA vaccines to learn strategies regarding communication around safety and risks for population-wide interventions
    d. Determine the upper limit of potassium intake for safety
        i. EFSA gives some guidance

Definitions: *ACEi: angiotensin converting enzyme inhibitor; ARB: angiotensin II receptor blocker; BP: blood pressure; CKD: chronic kidney disease; CV: cardiovascular; EFSA: European Food Safety Authority; GFR: glomerular filtration rate; K: potassium; LMIC: low- and middle-income countries; LSSS: low-sodium salt substitutes; Na: sodium; SS: salt sensitive*

Supplemental Table 2: Participant Discussion after Webinar 3, Functionality & Feasibility of LSSS

Functionality:

1. Composition of LSSS in specific products
    a. Typically, LSSS are composed of 75% NaCl and 25% KCl
    b. Some food products use or require different compositions:
        i. 50% NaCl : 50% K Lactate composition in bread products helps prevent listeria growth
    c. Yeast extract is a natural ingredient sometimes used as a flavor enhancer when KCl is used as a substitute for NaCl. The concern is that the cost is high.
    d. MSG is also used as a flavor enhancer which is more of a concern when it comes to labelling LSSS products.
2. Acceptability (taste)
    a. 50% NaCl : 50% KCl is acceptable for bread and meat
    b. 66% NaCl : 33% KCl is acceptable for bread
    c. 85% NaCl : 15% KCl would be acceptable; there would be minor differences in preservation and processing compared to normal salt
    d. There are products like light chicken broth and potato crisps with natural flavor where the bitterness of KCl, even at 25%, is less accepted
    e. Replacement of NaCl with LSSS using 25% KCl for 'baked goods' (e.g. cakes, pastry) is acceptable; the chemical leavening (baking powder) in these products contributes to sodium content which may explain this. When low-sodium baking powders are used, the products are not always accepted and can be more expensive
    f. Bouillon cubes are an important source of sodium in some parts of the world. Replacing 25% of NaCl with KCl is feasible – regarding acceptability, when used in a stew, high acceptability is expected, when ingested directly, limited acceptability is expected due to bitterness/metallic taste.
    g. One approach to help with taste: distribute the sodium within or on the surface of a product – this allows one to lower the salt content without changing salt perception.
        i. Caveat: Salt diffuses in many products, so it is mainly effective in fresh products and thus the strategy is not universally applicable.
    h. Query: Approximately 25% of the general population are so-called supertasters. How does this affect palatability?

Feasibility:

1. For low-income countries, price will be a major barrier unless LSSS are supported by the government
    a. In LMIC, the high discretionary NaCl intake is mainly driven by affordability and accessibility. Na-containing foods are cheap, while fresh food products are expensive and unaffordable.
    b. Non-subsidy option for governments: reducing import tariffs / taxes
    c. Another option to reduce costs: implement larger scale manufacturing locally
2. Impact of potash being a global commodity on cost
    a. A key issue to cost seems to be the world reserves of potash. For many commodities, new reserves are often found, even for commodities where supply appears to be very limited.
        i. <2% of the world's Potash resource is being used for food applications
    b. Price is driven by the potash mine owners, analogous to oil/gas pricing
    c. While the last time a new mine came online was 1980 when Canadian reserves were extended, potash is not in limited supply.
3. Impact of labelling on uptake
    a. Consumer advocates in Germany raise (incorrect) concerns regarding yeast being 'MSG in disguise', which has led to poor consumer opinion and use of these products
    b. In general, consumers do not like chemical-sounding terms on ingredient lists (e.g. 'Chloride' sounds like a pool disinfectant)
        i. Some countries allow NaCl to be listed as salt in the ingredients list instead of sodium chloride whereas KCl is required to be listed as potassium chloride
        ii. The Netherlands uses 'bread salt' for labelling 'iodine enriched salt'
            1. Need to weigh this approach with the concern that it lacks transparency (labelling is not clearly informing consumer that iodine has been added).
    c. Labelling considerations need to include geography and cultural context to maximize uptake

Definitions: KCl: potassium chloride; LMIC: low- and middle-income countries; LSSS: low-sodium salt substitutes; NaCl: sodium chloride