How to integrate Lower Sodium Salt Substitutes (LSSS) in the overall sodium reduction strategy.

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No conflicts of interest to declare

Scope of the recommendation

- ✓ The recommendation applies to discretionary use of LSSS in the form of table salt.
- ✓ It does not apply to discretionary use of sodium-containing condiments (e.g. soy sauce, fish sauce), or non-discretionary salt already present in manufactured foods and foods served at restaurants and other out-of-home settings.
- ✓ The recommendation applies to use of LSSS in which NaCl is partially replaced with KCl.
- ✓ The recommendation is intended for adults in the general population.
- ✓ It excludes individuals with kidney impairments or with other circumstances or conditions that might compromise potassium excretion.
- ✓ The recommendation does not apply to children or pregnant women.

Unanswered questions for population-wide policy making of LSSS

Generalisability
- **BP** benefits in general population
- **CVD** benefits only in high-risk

Risk - Safety
- Modest increase in SK in general population
- No evidence in children, pregnancy
- Safety in 'at risk' groups not tested in trials

Feasibility
- **Discretionary:** Away from familiar table salt; adherence; palatability (bitter)
- **Fortification** lacks efficacy and safety data
- **Industry:** Obstacles from tight regulation, access, costs.

Specificity
- No significant reduction in Na intake
- Effects due to potassium only
- Flat dose-response to K (<30% = >30%)
- Modest BP effect in low K/high Na

Policy
- **For individuals**, K supplementation, LSSS, or diet.
- **For populations**, LSSS, industry-level use or fortification.

Implementation
- settings where most salt derives from home-cooking vs outside the home and from industry
- Iodine fortification?

Modified from Earle WB, et al. Hypertension 2024; 81: 510-5

LSSS intervention compared to regular salt in adults[1] (≥18 yrs): estimate effects on intermediate end-points

Outcome	Anticipated absolute effects (95% CI)			Relative effect (95% CI)	Studies (n)	Participants (n)	GRADE
	Risk with regular salt	Risk with LSSS	Risk difference (95% CI)				
DBP change (mmHg)	-0.74	-3.87	-2.43 (-3.50 to -1.36)	NA	19	20 830	Moderate
SBP change (mmHg)	-1.32	-7.48	-4.76 (-6.01 to -3.50)	NA	20	21 414	Moderate
Hypertension (n per 100 000)	58 019	56 278	-1741 (-5802 to 1741)	RR 0.97 (0.90 to 1.03)	1	2 566	Low
BP control (n per 100 000)	12 782	27 098	14316 (4090 to 30805)	RR 2.12 (1.32 to 3.41)	2	253	Very low

[1]not including pregnant women, individuals with kidney impairments or with other circumstances or conditions that might compromise potassium excretions. Often type 1 and 2 diabetes also excluded.

LSSS intervention compared to regular salt in adults[1] (≥18 yrs): estimate effects on CV morbidity and mortality

Outcome	Anticipated absolute effects (95% CI)			RR (95% CI)	Studies (n)	Participants (n)	GRADE
	Risk with regular salt	Risk with LSSS	Risk difference (95% CI)				
Total CVD events (n per 100 000)	1 623	1 980	357 (828 to 3310)	1.22 (0.49 to 3.04)	5	982	Very low
Non-fatal strokes (n per 100 000)	198	178	-20 (-40 to 2)	0.90 (0.80 to 1.01)	3	21 250	Moderate
Non-fatal ACS (n per 100 000)	512	358	-150 (-250 to -30)	0.70 (0.52 to 0.94)	1	20 995	Moderate
CVD deaths (n per 100 000)	786	605	-180 (-310 to 0)	0.77 (0.60 to 1.00)	3	23 200	Moderate
Stroke deaths (n per 100 000)	405	259	-145 (-270 to 100)	0.64 (0.33.to 1.25)	2	21 423	Very low

[1]not including pregnant women, individuals with kidney impairments or with other circumstances or conditions that might compromise potassium excretions. Often type 1 and 2 diabetes also excluded.

Effect of potassium supplementation on potassium and renal function: meta-analysis of RCTs

	Mean	95% C.I.	P value
Trials - Samples (n)	20 - 21	-	-
Participants (n)	1127/89	-	-
Type of supplement	KCl	-	-
Duration of supplement (weeks)	2 - 24	-	-
Dose of supplement (mmol/day)	22 -140	-	-
Urinary potassium (mmol/24h – mg)	45.7 (1784)	37.8 to 53.7	<0.001
Urinary sodium (mmol/24h – mg)	4.42 (75)	-4.84 to 13.69	0.30
Serum potassium (mmol/L)	0.14	0.09 to 0.19	<0.001
Serum creatinine (umol/L)	0.30	-1.19 to 1.78	0.70

Cappuccio FP, et al. BMJ Open 2016; 6: e011716

Conversions: 90 mmol=3,510 mg=3.51g of K

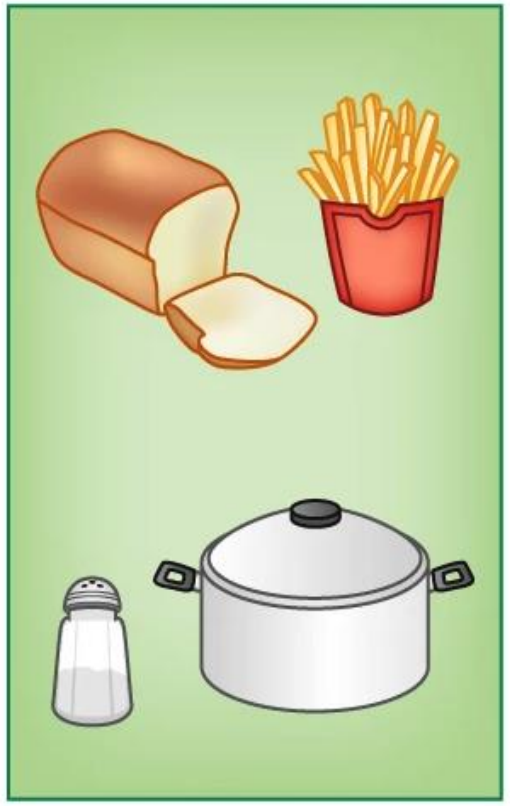
LSSS intervention compared to regular salt in adults[1] (≥18 yrs): estimate effects on potassium

Outcome	Anticipated absolute effects (95% CI)			RR (95% CI)	Studies (n)	Participants (n)	GRADE
	Risk with regular salt	Risk with LSSS	Difference (95% CI)				
Change in blood K^+ (mM)	0.01	0.09	0.12 (0.07 to 0.18)	-	6	784	Moderate
Hyperkalaemia (n per 100 000)	88	91	4 (-47 to 121)	1.04 (0.46 to 2.38)	5	22 849	Moderate

[1]not including pregnant women, individuals with kidney impairments or with other circumstances or conditions that might compromise potassium excretions. Often type 1 and 2 diabetes also excluded.

Potassium-enriched salt substitution trials

Community-wide salt substitution in Peruvian villages



Design: Stepped-wedge cluster RCT
Setting: 6 villages in Tumbes, Perù
Population: All aged ≥ 18+ yrs
Exclusions: self-reported history of CKD or heart disease on digoxin
Sample size: n = 2,376
Intervention: Regular salt in household replaced free-of-charge with a LSSS (75% NaCl + 25% KCl)
Primary outcomes: SBP and DBP
Follow-up: 4 to 24 mo. after 4 mo. intervention

Bernabe-Ortix A, et al. Nature Med 2020; 26: 374-8

Potassium-enriched salt substitution trials

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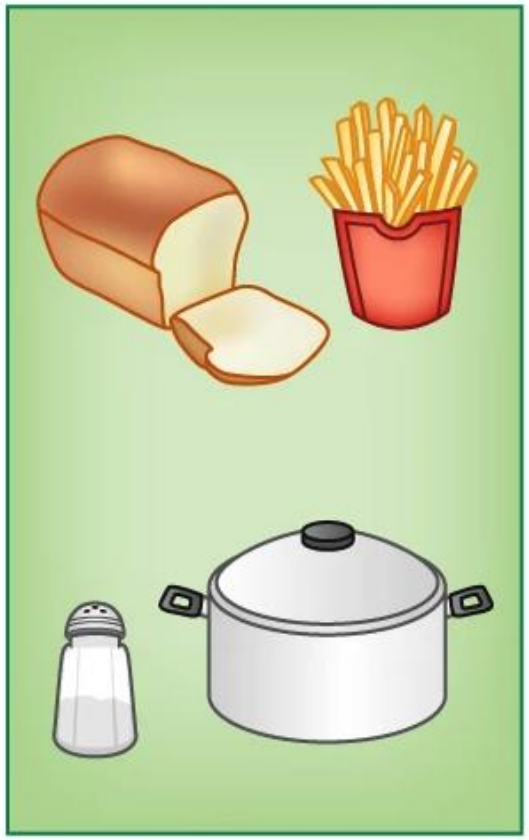


I.T.T.

3.94 to 3.95 g
171 to 172 mM

1.97 to 2.60 g
50.3 to 66.5 mM

Variable	difference	95% CI
SBP (mmHg)	**-1.29**	**-2.17, -0.41**
DBP (mmHg)	**-0.76**	**-1.39, -0.13**
Hypertension* (HR)	**0.49**	**0.34, 0.71**
Sodium (g/d)**	0.01	-0.23, 0.25
Potassium (g/d)**	**0.63**	**0.47, 0.78**
Serum K	NOT REPORTED - No adverse effects	

Bernabe-Ortix A, et al. Nature Med 2020; 26: 374-8

*among 1,891 participants without hypertension at baseline
**estimated from 24h urine collections in a random sample of 600 participants
Conversions: 90 mmol=3,510 mg=3.51g of K

Potassium-enriched salt substitution trials

Design: unblinded cluster RCT
Setting: 600 villages in rural China
Population: history of stroke or age ≥60 yrs with uncontrolled high BP
Sample size: n = 20,995
Intervention: assigned LSSS (75% NaCl, 25% KCl) for all household cooking and food preservation or to continue using regular salt.
Primary outcome: fatal and non-fatal stroke
Mean follow-up: 4.74 yrs

Neal B, et al. N Engl J Med 2021; 385: 1067-77

Potassium-enriched salt substitution trials

Outcomes	Salt Substitute	Regular Salt	Rate Ratio (95% CI)	P Value
	no. of events per 1000 person-yr			
Stroke	29.14	33.65	0.86 (0.77–0.96)	P=0.006
Major Adverse CV Events	49.09	56.29	0.87 (0.80–0.94)	P<0.001
Death from Any Cause	39.28	44.61	0.88 (0.82–0.95)	P<0.001
Hyperkalemia	3.35	3.30	1.04 (0.80–1.37)	P=0.76

4.30 to 3.95 g
187 to 172 mM

1.4 to 2.2 g
35.8 to 56.2 mM

SBP (mmHg)	**-3.34**	**-4.51, -2.18**
DBP (mmHg)	-0.67	-1.39, 0.05
Sodium (g/d)	**-0.35**	**-0.54, -0.15**
Potassium (g/d)	**0.80**	**0.71, 0.90**
Serum K (mM)	NOT REPORTED - No adverse risk of events	

Neal B, et al. N Engl J Med 2021; 385: 1067-77

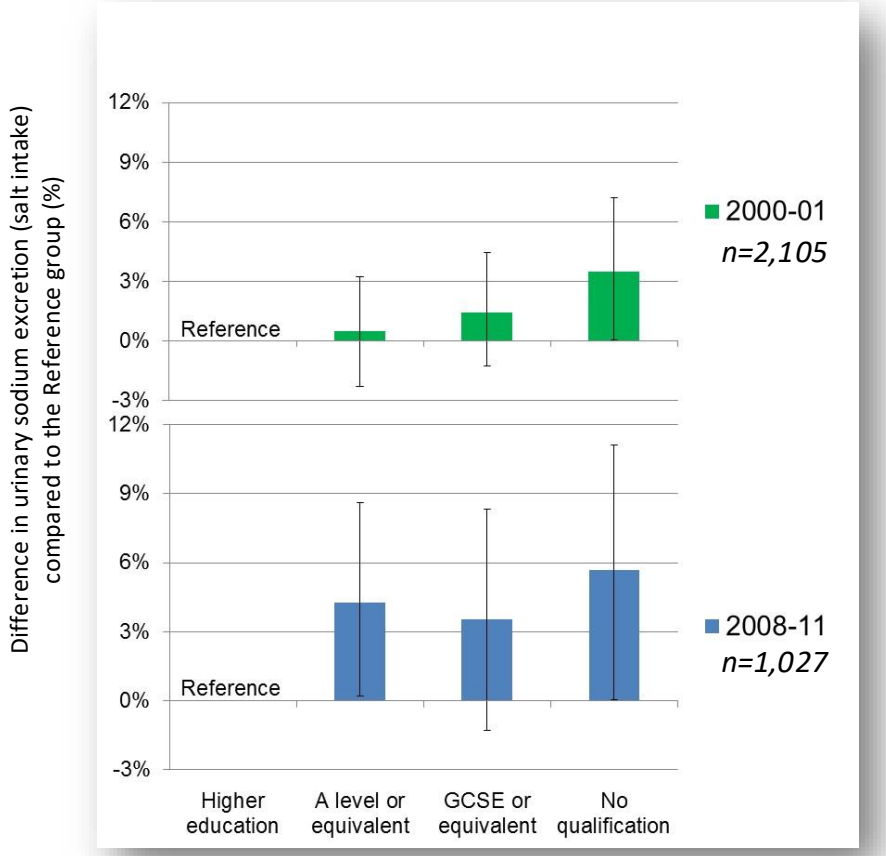
Conversions: 90 mmol=3,510 mg=3.51g of K

Unwanted effects

1. Widening health inequalities
2. Disincentives for industry to reduce Na
3. Excess Na causes increased thirst -> consumption of unhealthy beverages -> adverse health outcomes

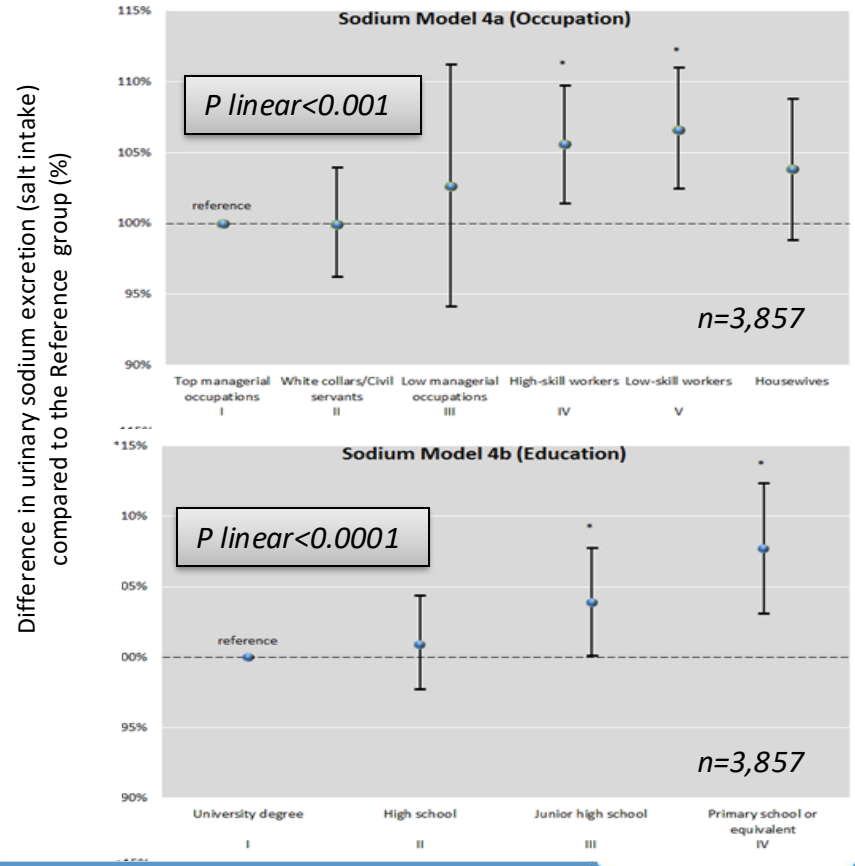
1. Widening health inequalities: **Social inequalities in salt intake**

Great Britain



Ji C et al BMJ Open 2012; 2: e002246
Ji C & Cappuccio FP. BMJ Open 2014; 4: e005683

Italy



Cappuccio FP et al. BMJ Open 2015;5:e007467

2. Disincentives for industry to reduce Na: **Industry vs Public Health priorities**

Industry

- Sodium-based salts contribute to food safety
- Sodium-based salts increase shelf-life
- Sodium-based salts make unpalatable food edible at virtually no cost
- Habituation to high sodium-based foods increases demand – profit on these foods tends to be greater
- Increasing sodium concentration in meat products increases water binding capacity by up to 20%
- Salt intake is the main drive to thirst and thereby increases soft drinks, beer, wine and mineral water consumption

Public health

- Lower sodium intake reduces ill-health and prevents diseases (CV and non-CV) and the risk of other condition (CKD progression, bone demineralisation and osteoporosis, gastric cancer)
- Lower sodium intake reduces the consumption of sugar-containing drinks, alcohol, hence calories
- Lower sodium intake is highly cost-effective for society (reduced healthcare costs)
- Lower sodium intake reduces addiction
- Moderate population reduction in sodium intake is feasible, efficacious, cost-effective

Cappuccio FP, Capewell S. Functional Food Reviews 2015; 7(1): 41-61.

3. Excess Na causes increased thirst -> consumption of unhealthy beverages -> adverse health outcomes: **Profit vs Public benefit**

High salt (Na-based salts) in processed and manufactured food leads to profit to industry, not to health benefits!

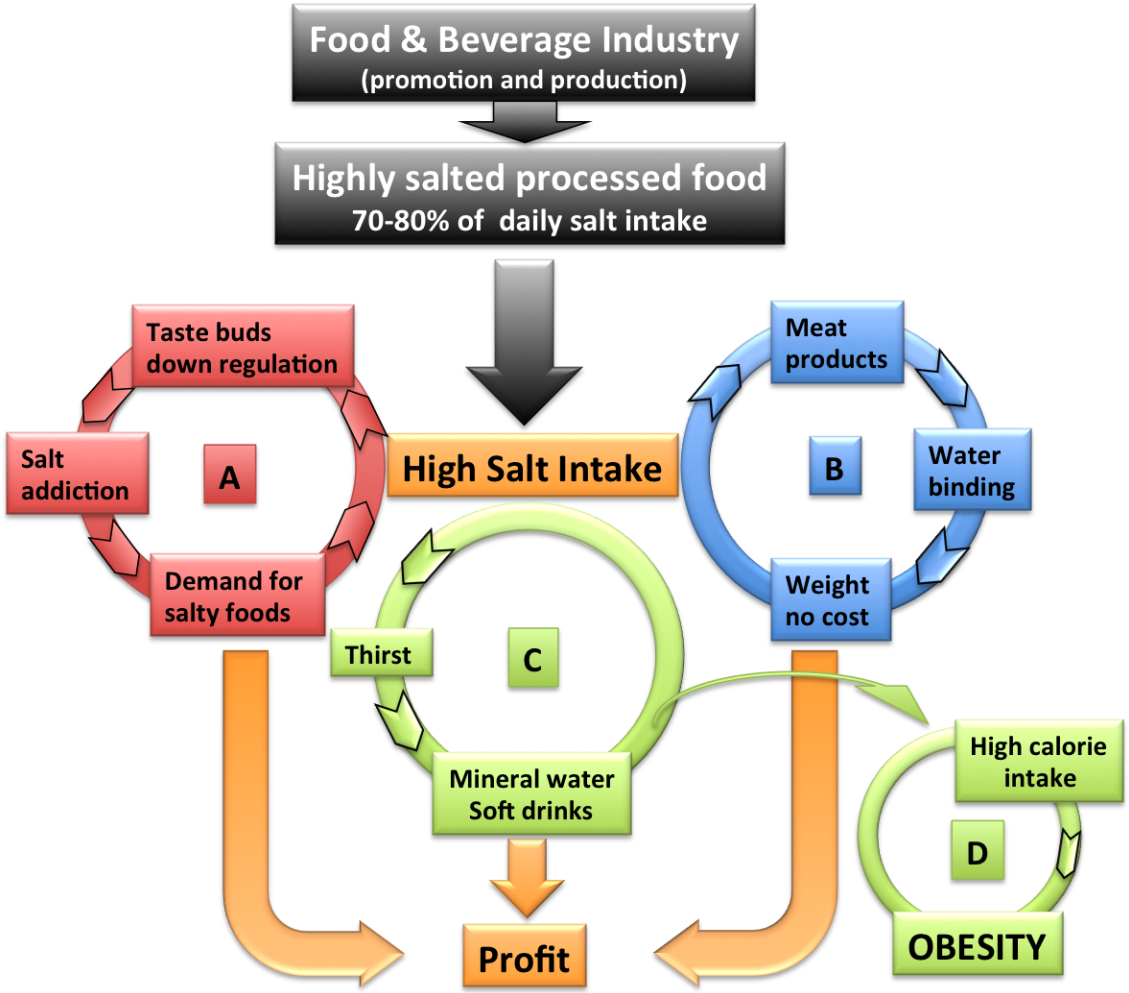
A. Palatability – bad food edible

A. Taste addiction – demand

B. Hygroscopic properties – weight at extra cost

C. Thirst - drinks (sugary, carbonated, alcoholic)

D. Obesity



Cappuccio FP, Capewell S. Functional Food Reviews 2015; 7(1): 41-61.

W.H.O. recommendation

- To reduce blood pressure and risk of cardiovascular diseases, WHO has recommended reducing sodium intake to less than 2 g/day (strong recommendation[1]).
- In this context, using less regular table salt is an important part of an overall sodium reduction strategy.
- If choosing to use table salt, WHO suggests replacing regular table salt with lower-sodium salt substitutes that contain potassium (conditional recommendation[2]).
- This recommendation is intended for adults (not pregnant women or children) in general populations,
- It excludes individuals with kidney impairments or with other circumstances or conditions that might compromise potassium excretion.

The use of LSSS should be aligned with current WHO recommendations on sodium intake[3] (Core principle). It is only one of many means in an overall strategy to reduce sodium intake[4].

[1] *Strong* recommendation: WHO confident that the desirable consequences of implementing the recommendation will outweigh the undesirable consequences in nearly all circumstances and can be adopted as practice or policy in most situations.

[2] *Conditional* recommendation: WHO is less certain that the desirable consequences of implementing the recommendation outweigh the undesirable consequences generally or in certain settings or when the anticipated net benefits are very small. Therefore, discussion may be required, including about setting-specific issues, before a conditional recommendation can be adopted as policy and implemented.

WHO Guideline, 2025

[3]Guideline: sodium intake for adults and children. Geneva: World Health Organization; 2012
[4]The SHAKE technical package for salt reduction. Geneva: World Health Organization; 2016

Thank you!