BMC Medicine

RESEARCH

Open Access

Effect of sodium-reduced potassium-enriched salt substitutes on stomach cancer: the Salt Substitute and Stroke Study (SSaSS)

Xinyi Zhang[1†], Xuejun Yin[2,3*†], Mei Ling Yap[4,5,6,7], Qiang Li[4], Liping Huang[4], Yishu Liu[8], Bo Zhou[9], Zhifang Li[10], Yi Zhao[11], Jixin Sun[12], Yan Yu[13], Lijing L. Yan[14,15,16,17], Yangfeng Wu[18], Bruce Neal[4,19,20] and Maoyi Tian[1,4,21*]

Abstract

Background There is an association between increased dietary sodium intake and the risk of stomach cancer. Lowering dietary sodium intake with sodium-reduced potassium-enriched salt substitutes may reduce this risk. To evaluate the effects of sodium-reduced potassium-enriched salt substitutes on the risk of stomach cancer and other types of cancer.

Methods The primary analyses of the Salt Substitute and Stroke Study (SSaSS) defined the effects of sodium-reduced potassium-enriched salt substitutes compared to regular salt on the risk of stroke. This post-hoc investigation explored effects on stomach and other cancers. SSaSS was an open-label, cluster randomised controlled trial done in 600 Chinese villages among 20,996 participants. Villages were assigned at random in a 1:1 ratio to receive sodium-reduced potassium-enriched salt substitutes or continue regular salt use. Fatal and hospitalised cancer events were identified through direct face-to-face follow-up and record linkage, with adjudication of fatal, but not non-fatal events.

Results During a mean follow-up of 4.7 years, there were 1040 cancer events (507 fatal, 533 non-fatal) recorded. There were 212 stomach cancers, 725 other cancers, and 103 cancers with an unknown primary site. There was a trend toward but not a significant effect of randomised treatment on total stomach cancer (rate ratio (RR) 0.77, 95% confidence interval (CI) 0.54 to 1.08). The RR for adjudicated fatal stomach cancer was 0.66 (95% CI 0.44 to 1.00) compared to 0.88 (95% CI 0.56 to 1.37) for unadjudicated non-fatal stomach cancer. There was no detectable effect on total cancer at any site (RR 0.94, 95% CI 0.81 to 1.08), adjudicated fatal cancer at any site (RR 0.85, 95% CI 0.69 to 1.05), or unadjudicated non-fatal cancer at any site (RR 1.04, 95% CI 0.88 to 1.23).

Conclusions There was no effect of sodium-reduced potassium-enriched salt substitutes on stomach cancer or other cancer types detected. Trends toward protection against fatal and non-fatal stomach cancer align with the observational epidemiology and warrant further investigation.

[†]Xinyi Zhang and Xuejun Yin contributed equally to this work.

*Correspondence:
Xuejun Yin
xyin@georgeinstitute.org.au
Maoyi Tian
maoyi.tian@hrbmu.edu.cn
Full list of author information is available at the end of the article

Trial registration This trial was registered in ClinicalTrials.gov as NCT02092090.

Keywords Salt substitutes, Stomach cancer, Cluster randomised controlled trial, Potassium supplementation, Sodium reduction

Background

Stomach cancer is the fifth most common type of cancer and is the fourth leading cause of cancer-related deaths worldwide [1]. Excess sodium intake has been identified as a dietary risk factor for the development of stomach cancer [2] in cross-sectional surveys [3, 4], case–control studies [5, 6], and prospective cohort studies [7, 8]. Excess sodium intake has also been linked, though less conclusively, to increased risks of other cancers, such as liver [9], lung [10], and colorectal [11] and esophageal cancers [12].

Dietary sodium consumption is far above physiological norms. During hominid evolution dietary sodium intake was likely about 0.5 g per day but average global intake is now much higher at about 4 g per day [13]. Intake is particularly high in many Asian countries, including China. The primary source of dietary sodium varies between populations but typically derives from three main sources—salt added when cooking or seasoning in the home, salt added during the manufacture of processed foods, and salt added to restaurant foods eaten outside the home [14]. In general the proportion of dietary sodium that comes from salt added in the home is greater in countries that are less economically developed.

Efforts to reduce dietary sodium have been recommended by the World Health Organisation and many other national and international agencies for many years. However, implementing successful and sustained sodium reduction has proven challenging. Sodium-reduced potassium-enriched salt substitutes, which typically replace a portion of sodium chloride with potassium chloride, have been developed as a practical solution as they can easily replace regular salt without significantly changing dietary habits [15, 16].

The Salt Substitute and Stroke Study (SSaSS) was a 5-year cluster randomised trial conducted in 600 villages in China. The trial demonstrated that switching to sodium-reduced potassium-enriched salt substitutes compared to regular salt lowered blood pressure and protected against stroke, cardiovascular events and premature death [16]. In conjunction with data from about 20 smaller studies it appears likely that these blood pressure mediated benefits will be highly generalisable across diverse population groups. While cancer outcomes were not specified a priori in the SSaSS, the large sample size and randomised design of the trial provide a unique opportunity to investigate the potential effects of sodium-reduced salt substitutes on stomach and other cancer risks. Therefore, we conducted this secondary analysis of SSaSS data to examine the effects of replacing regular salt with sodium-reduced potassium-enriched salt substitutes on the risk of stomach and other types of cancer.

Methods

This study is a post-hoc analysis of data from SSaSS (ClinicalTrials.gov identifier: NCT02092090). Full details of the SSaSS design and the main results have been reported previously [16, 17]. Approval to conduct the study was received from the ethics committees at the Peking University Health Science Centre in China and the University of Sydney in Australia. Written informed consent was obtained from all participants.

Study recruitment and participants

The study was done in 600 rural villages from ten counties in five provinces in northern China (Additional file 1: Fig. S1). Approximately 35 participants who had a history of stroke or were older than 60 years with uncontrolled blood pressure (systolic blood pressure $\geq$ 140 mm Hg if on blood pressure lowering medication or $\geq$ 160 mm Hg if not on blood pressure lowering medication) were recruited from each village. Participant inclusion criteria were designed to maximise the capacity to address the primary hypothesis of protections against stroke.

Randomisation, intervention, and control

Villages were randomly assigned in a 1:1 ratio to the intervention or the control group. Randomisation was done by an independent biostatistician through a central computerised process. Participants in the intervention villages were provided with sodium-reduced potassium-enriched salt substitutes free-of-charge in a sufficient quantity to replace all use of regular salt for cooking, seasoning, and preserving foods at home. The sodium-reduced potassium-enriched salt substitutes had a composition of 75% sodium chloride and 25% potassium chloride by mass. Participants in the control villages continued to use regular salt (100% sodium chloride) as previously.

Follow-up and data collection

Follow-up was conducted at 6-month intervals and focused on the identification of the primary and secondary outcomes of stroke, other major adverse cardiovascular events and death. The occurrence of all hospitalisations and other serious illnesses was also recorded. Information was collected face-to-face from participants or family members as well as through searches of routinely collected data. These routinely collected data sources included the health insurance records held within the New Rural Cooperative Medical Scheme and the National Mortality Surveillance System. Fatal and non-fatal cancer events were identified through these processes.

Outcomes

The primary outcome of interest for these analyses was stomach cancer comprising both fatal and non-fatal events. Fatal stomach cancer was defined as death adjudicated to be directly caused by stomach cancer, determined by an independent endpoint adjudication committee blinded to treatment allocation. Non-fatal stomach cancer events were identified through hospitalisation records with cancer-related discharge diagnoses. The secondary outcomes of interest were cancers occurring at other specific sites, all cancers occurring at any site and a composite outcome, consisting of stomach, liver, colorectal and lung cancers. Separate analyses were also done in each case for fatal cancers and for non-fatal cancer hospitalisations because the former were adjudicated while the latter were not.

For all deaths, the immediate and underlying causes of death were determined by an endpoint adjudication committee composed of physicians blinded to group assignment. We included all deaths which had a cancer outcome of interest listed as either the immediate or an underlying cause of death in these analyses.

The Adjudication Committee used a pre-defined adjudication procedure for assigning causes of death. Information provided to the adjudicators to support their decision making included data extracted from the National Mortality Surveillance System [18], the New Rural Cooperative Medical Scheme [19], medical documentation held by the participant or family members, responses to structured SSaSS questionnaires administered face-to-face with the participant or family members, and the output of a verbal autopsy process.

Non-fatal cancer hospitalisations were identified by searching the data from New Rural Cooperative Medical Scheme for hospitalisations assigned to cancer codes. Briefly, every discharge diagnosis for a study participant within the New Rural Cooperative Medical Scheme dataset was reviewed by clinically trained coders masked to participant treatment allocation. The most relevant Medical Dictionary for Regulatory Activities (MedDRA) code was assigned for each discharge diagnosis with these analyses based on events falling under the MedDRA preferred term "cancer."

For every participant with more than one cancer event, two clinicians reviewed the data to determine whether there were two separate cancer types, or a primary cancer and a metastasis.

Statistical analysis

We conducted intention-to-treat comparisons using time-to-event analyses of the first occurrence of each event of interest among participants in the sodium-reduced potassium-enriched salt substitutes group compared to those in the regular salt group. Adjustment for clustering was made with the use of a hierarchical Poisson regression model, with follow-up time as an offset. Cumulative event curves were generated using the Kaplan–Meier method. If there were multiple non-fatal events for the same cancer type for a single participant only, the first non-fatal event was included in the analysis. If a participant had multiple non-fatal cancer events of different types, after review by two clinicians, all distinct cancer types were retained and counted as a cancer event in the analysis of effects on "all" cancers. If a participant had non-fatal and fatal events regardless of the cancer type, and these events occurred within one month, only the fatal event was included in the analysis. If the fatal and non-fatal events, regardless of the cancer type, occurred more than one month apart, all events were counted.

Cause-specific rate ratios (RR) and 95% confidence intervals were determined for fatal and non-fatal cancer combined for stomach cancer, all cancer, cancer occurring at specific sites (breast, colorectal, liver, lung, esophagus, pancreas, and others) and cancers of unknown primary site.

Subsidiary analyses examined the separate effects on fatal and non-fatal events as well as the effects on stomach cancer and cancers at any site in the participant subgroups pre-defined for the primary SSaSS analyses (including age, sex, body mass index, history of diseases, smoking status and the use of medication). We did not do hypothesis testing given the post hoc nature of the analyses and the limited statistical power for most outcomes. Statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute).

Results

Participants

A total of 20,995 persons were recruited and assigned to either the sodium-reduced potassium-enriched salt

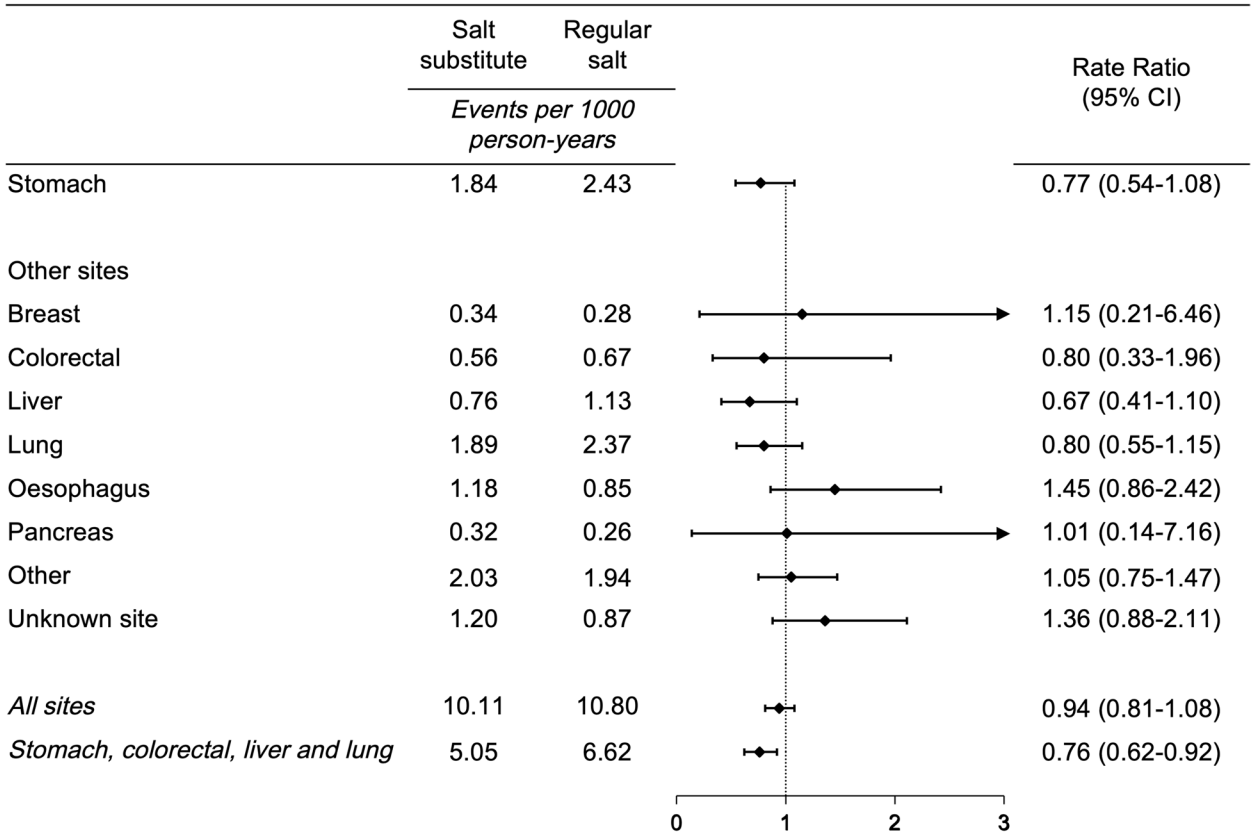

Fig. 1 Effects of sodium-reduced potassium-enriched salt substitutes versus regular salt on fatal or non-fatal stomach cancer, fatal or non-fatal cancers at other sites, fatal or non-fatal cancers of unknown primary site, fatal or non-fatal cancers at all sites and a composite outcome consisting of stomach, colorectal, liver and lung cancers

substitutes or continued regular salt group (Additional file 1: Table S1). The mean follow-up was for 4.7 years with 4172 participants dying during the trial period. There was complete follow-up of all participants for fatal cancer events and 80% complete follow-up of participants for non-fatal cancer events. The incomplete follow-up for non-fatal cancer events, accounting for 20% of participants, was due to restricted access to one county's medical insurance database.

At baseline, the mean age of all SSaSS participants was 65.4 years and 49.5% were female. The mean body mass index was 24.8 kg/m^2, 18.8% were current smokers and 33.5% had smoked at any time. There were 72.7% of participants with a history of stroke, 59.3% with uncontrolled blood pressure, 16.1% with ischemic heart disease and 10.6% with diabetes. Forty percent of participants were taking aspirin or other antiplatelet agents, and 12.3% were taking a statin or other lipid-lowering agent. The mean 24-h urinary sodium excretion in the subset of 614 participants in which it was measured was 4.3 g/day which equated to daily salt consumption of about 11.9 g/day (Additional file 1: Table S1). All baseline characteristics were well balanced across randomised groups.

Effects on fatal and non-fatal stomach cancer

In the sodium-reduced potassium-enriched salt substitutes group, 92 fatal or non-fatal stomach cancer events, from 82 participants (1.84/1000 patient years, pt years), were recorded. Whereas in the regular salt group, 120 fatal or non-fatal stomach cancer events, from 97 participants (2.43/1000 pt years), were recorded. The RR between the groups was 0.77 (95% CI 0.54 to 1.08) (Figs. 1 and 2). There were 110 adjudicated fatal stomach cancer events and the RR was 0.66 (95% CI 0.44 to 1.00). For the 102 unadjudicated non-fatal stomach cancer events the RR was 0.88 (95% CI 0.56 to 1.37). There was no strong evidence of any differences in effects on stomach cancer across participant subgroups (Additional file 1: Fig. S2).

Effects on all cancer and cancers at specific sites

A total of 1040 cancer events were recorded (507 fatal events and 533 non-fatal cancer events). There were 507 fatal or non-fatal events, from 395 participants

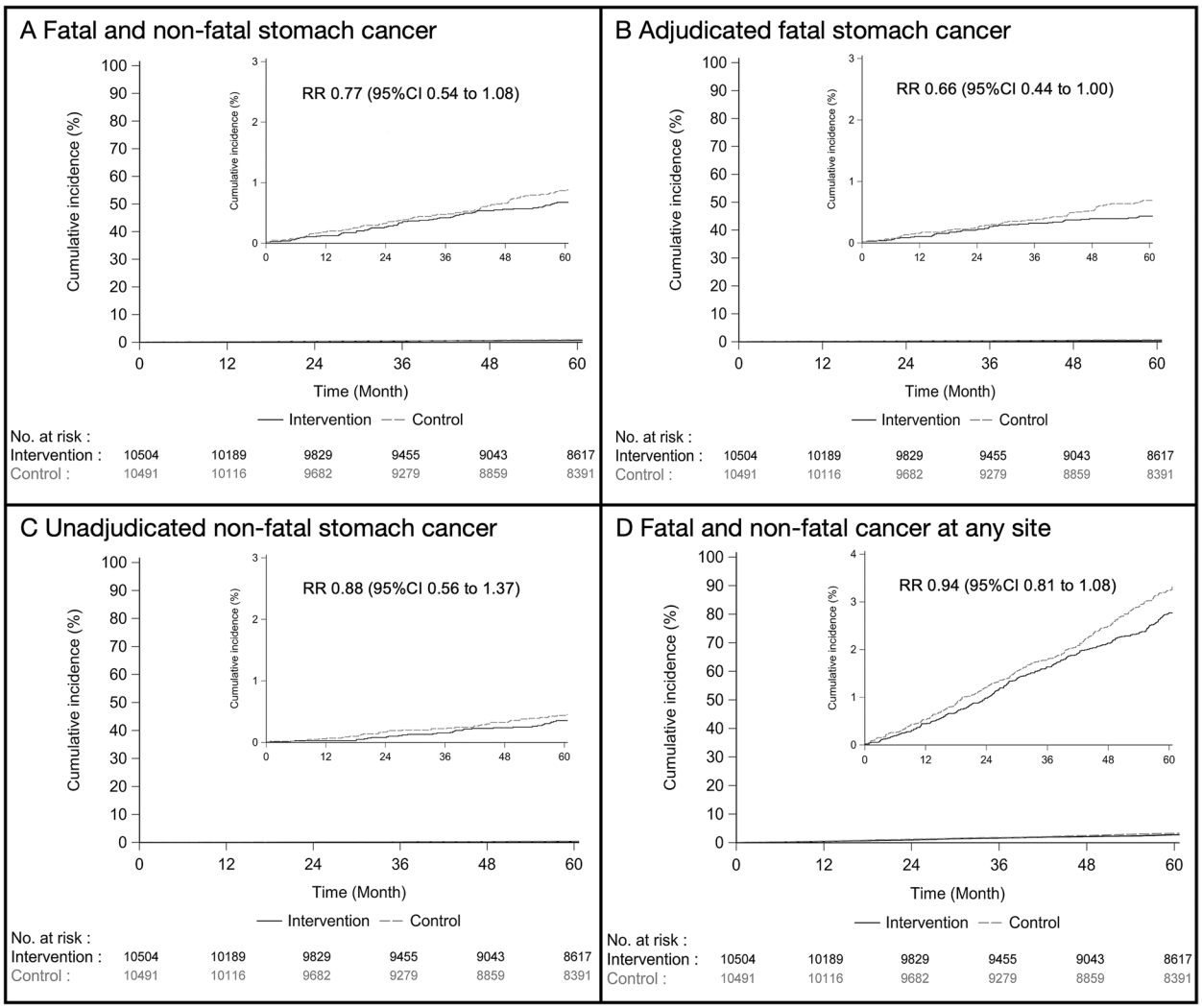

Fig. 2 Effects of sodium-reduced potassium-enriched salt substitutes compared to regular salt on **A** total stomach cancer, **B** fatal stomach cancer, **C** non-fatal stomach cancer, and **D** fatal and non-fatal cancer at any site

(10.1/1000 pt years), in the sodium-reduced potassium-enriched salt substitutes group. Whereas in the regular salt group, 533 fatal and non-fatal cancer events were recorded, from 421 participants (10.8/1000 pt years). The RR for fatal or non-fatal cancer at any site between the groups was 0.94 (95% CI 0.81 to 1.08). Effects on cancer at any site were consistent across subgroups with a trend toward larger effects among younger people (< 60 years old) and participants without hypertension (Fig. 3). The separate estimate for total adjudicated fatal cancer was a RR of 0.85 (95% CI 0.69 to 1.05) and for total unadjudicated non-fatal cancer was a RR of 1.04 (95% CI 0.88 to 1.23) (Additional file 1: Table S2). There was no clear effect of potassium-enriched salt compared to regular salt on the risk of cancer at any specific site (Fig. 1). The composite outcome, consisting of stomach, colorectal, liver and lung cancers showed a RR between the groups of 0.76 (95% CI 0.62 to 0.92) (Fig. 1).

Discussion

In this post hoc analysis of the SSaSS trial, we identified no clear effect of the sodium-reduced potassium-enriched salt substitutes compared to the regular salt on stomach, total cancer, fatal cancer, non-fatal cancer or cancer at any specific site. The study was, however, limited by the relatively small number of stomach cancer events recorded and the fairly short duration of follow-up. Both the observation that the survival curves appeared to be separating later in follow-up and the strong trend towards protection observed for adjudicated fatal stomach cancer suggest that further

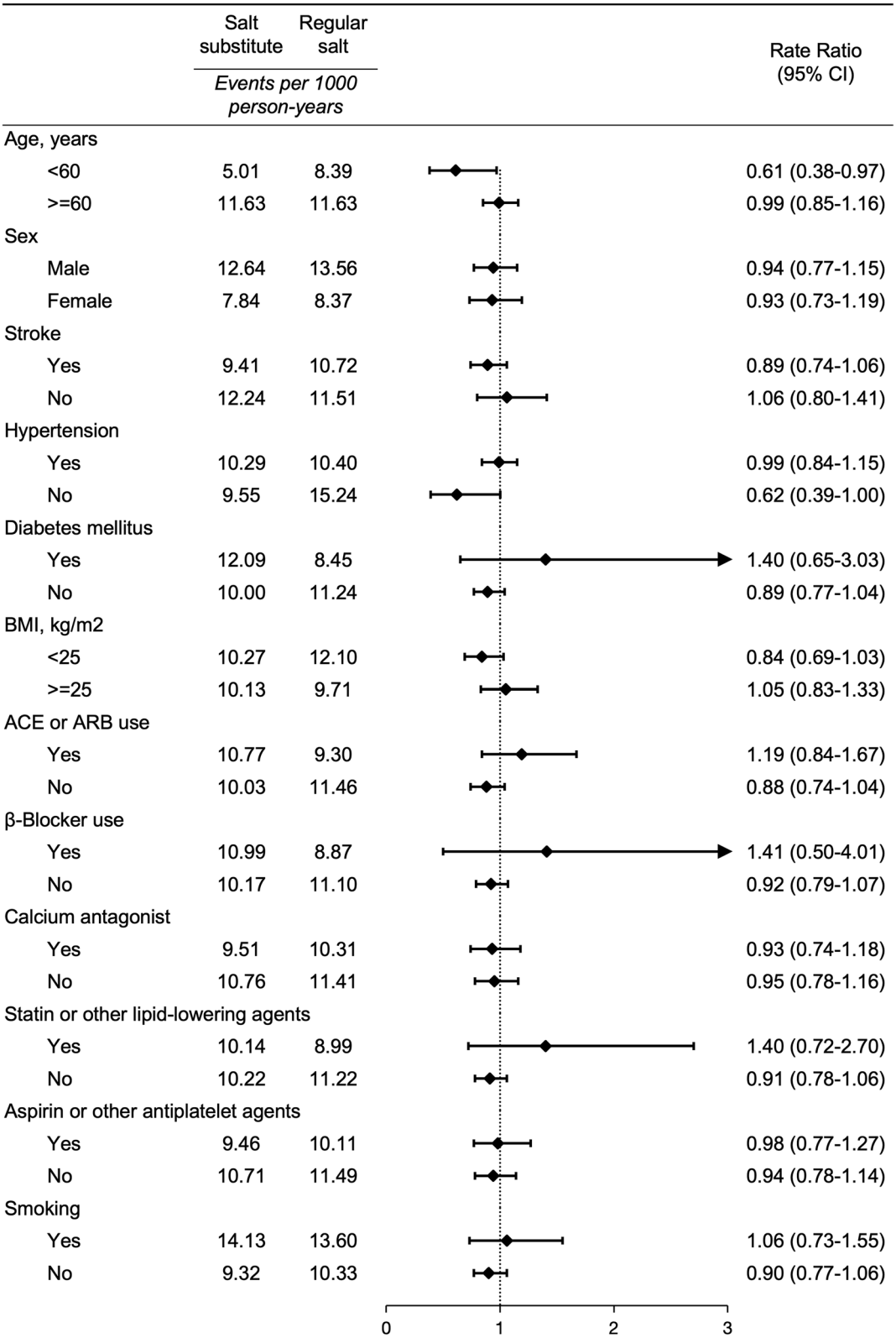

Fig. 3 Effects of sodium-reduced potassium-enriched salt substitutes versus regular salt on fatal and non-fatal cancer occurring at any site in participant subgroups. Abbreviations: BMI, body mass index; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers

investigation of this question is warranted. In particular, longer follow-up of SSaSS participants to accommodate lag in the effects of sodium-reduced potassium-enriched salt substitutes on stomach cancer risk, the accrual of larger numbers of events over time, and adjudication of all events to minimise errors in the classification of cancer types would enhance the power of the analyses.

Stomach cancer risk is associated with a series of modifiable risks including alcohol consumption, smoking, and an unhealthy diet [20]. Higher levels of dietary sodium intake have been identified as a particularly strong dietary risk in multiple human studies. In a meta-analysis of 38 case–control studies, higher sodium intake compared to lower sodium intake was associated with an approximate 50% increased risk of stomach cancer [21]. A parallel meta-analysis of 10 prospective cohort studies identified a directly comparable strength of association for higher sodium intake compared to lower sodium intake, but also demonstrated a dose–response relationship, with moderate sodium intake showing adverse effects compared to lower intake [2]. Notably, follow-up durations in these observational studies were typically longer than in SSaSS, and the differences in sodium exposure between study groups were likely greater. In combination, these considerations mean that the SSaSS data would be expected to show smaller risk differences between groups and that the present analyses would have limited power to demonstrate the most likely effects of sodium reduction on stomach cancer.

Although prior observational studies have suggested an association between high dietary sodium intake and increased esophageal cancer risk [12], our exploratory analysis did not identify a significant protective effect from sodium-reduced potassium-enriched salt substitution on esophagus cancer (RR 1.45, 95% CI: 0.85 to 1.42). The limited number of esophageal cancer events resulted in wide confidence intervals, indicating insufficient statistical power to draw definitive conclusions. Moreover, unlike stomach cancer, there is less clearly defined biological plausibility linking sodium intake directly to esophageal cancer risk. Given these uncertainties, future well-powered studies to detect effects on esophageal cancer—with more events and longer-term follow-up—are required to clarify this relationship further.

Our exploratory analysis found a protective effect in stomach cancer, colorectal cancer, liver cancer and lung cancer, though the results were not statistically significant. The associations of higher sodium intake with increased risks of primary cancers at other sites such as the lung, colon and liver [9, 10] have been observed less frequently and mechanisms of causation are less well defined. The findings of observational studies describing associations of sodium intake with stomach cancer could be attributable to confounding factors [21] and the present analyses of SSaSS do not resolve this uncertainty. Limited numbers of events and the potential for errors in classification of cancer types due to the limited capacity to adjudicate events has likely also reduced the capacity of the study to detect the real effects of sodium. The analysis of the composite outcome (combining fatal and non-fatal events of stomach, colorectal, liver and lung cancers) observed a statistically significant protective effect of sodium-reduced potassium-enriched salt substitutes. This exploratory analysis further suggests that extending the study follow-up duration and increasing the number of outcome events might maximise the statistical power to detect differences between the groups.

The intervention used in this study involved replacing regular salt with sodium-reduced potassium-enriched salt substitutes, simultaneously reducing sodium intake and increasing potassium intake. Both sodium reduction and potassium supplementation have established independent and synergistic benefits on lowering blood pressure and reducing the risk of cardiovascular events, as clearly demonstrated in the SSaSS trial [16]. However, this joint effect on cancer outcomes remains unclear. While sodium reduction alone was associated with reduced stomach cancer risk in observational studies [21], the role of potassium supplementation in cancer prevention is less clearly defined. Thus, although the sodium-reduced potassium-enriched salt substitute showed clear benefits on cardiovascular events, its effects on cancer require cautious interpretation. Further research is required to elucidate the specific roles and potential interactions of sodium reduction and potassium supplementation on cancer risk. Moreover, antihypertensive drugs and aspirin were also widely used by the SSaSS population, and both have been associated with effects on cancer risks [22, 23]. However, randomisation resulted in good balance between randomised groups so effects of these agents should not have biased the findings of the present analyses.

The SSaSS data provide a unique opportunity to explore questions about the effects of sodium on cancer causation with a robust randomised research design. Randomisation has controlled for confounding factors in a way that cannot be achieved in observational studies and event adjudication by experienced clinicians blinded to group allocation has ensured independent and unbiased determination of fatal cancer outcomes. Despite the strength of the study, there are also limitations to the present analyses. Firstly, history of cancer was not collected at the baseline, which may potentially introduce bias. However, the current baseline characteristics were well balanced between the groups, there is the reason to

believe there was no significant difference in cancer history between the two groups at the baseline. Secondly, the limited number of the cancer events may hinder the interpretation of the study results. There is clear potential for enhancing future analyses by performing longer-term follow-up of the SSaSS participants to capture more events and allow an opportunity for the effects of differential exposure to sodium on cancer across randomised groups to fully evolve. Consent for linkage to fatal and non-fatal events, as well as the collection of data for adjudication of cancer events, has been secured for this purpose and resourcing to enable data collection is now undergoing.

Conclusions

Sodium-reduced potassium-enriched salt substitutes are emerging as a novel, scalable [24], practical [25] and affordable mechanism [26, 27] for addressing sodium and potassium intake amongst populations, with very large projected net health benefits for cardiovascular outcomes [28, 29]. This study provides further analyses for effects of sodium consumption on the risk of stomach cancer and potentially also other cancer types. However, no clear effect of sodium-reduced potassium-enriched salt substitutes on stomach cancer or other cancer types was found. The limited number of cancer events and relatively short follow-up duration constrained the statistical power of this post-hoc analysis. There is clear potential for enhancing future analyses with additional follow-up of participants for cancer outcomes and providing clarity about effects of sodium-reduced potassium-enriched salt substitutes on cancer outcomes would be highly worthwhile. Future evidence of protection against cancer outcomes would further support the transition from regular salt to sodium-reduced potassium-enriched salt substitutes.

Abbreviations

ACE	Angiotensin-converting enzyme
ARB	Angiotensin receptor blockers
BMI	Body mass index
CI	Confidence interval
MedDRA	Medical Dictionary for Regulatory Activities
RR	Rate ratio
SD	Standard deviation
SSaSS	Salt Substitute and Stroke Study

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-04068-0.

Additional file 1: Figure S1-S2. Figure S1. Participant flow chart. Figure S2. Effects of sodium-reduced potassium-enriched salt substitutes versus regular salt on fatal and non-fatal stomach cancer in participant subgroups. Table S1-S2. Table S1. Baseline characteristics of all trial participants (*n*=20,995). Table S2. Effects of sodium-reduced potassium-enriched salt substitutes on fatal cancer and cancer hospitalisations by site for fatal and non-fatal events.

Acknowledgements

The authors like to thank the implementation team and all trial participants. In addition, we would like to acknowledge Professor Jingpu Shi, from the Department of Evidence-Based Medicine, First Hospital of China Medical University, who died on October 27, 2020, for his leadership to implement the SSaSS trial in Liaoning Province.

Authors' contributions

MT and BN led the conception of this study. XY and XZ led the analysis and drafted the manuscript. MT, BN, MY, LY made substantial edits to the draft. YL, BZ, ZL, YZ, JS, YY, LY, YW, BN and MT contributed to the acquisition, analysis, and interpretation of data. QL and LH assisted in the data analysis and validated the analytical process. All authors provided critical comments and revised the manuscript. All authors read and approved the final manuscript.

Funding

Salt Substitute and Stroke Study was funded by research grants (APP1164206 and APP1049417) from the National Health and Medical Research Council of Australia. The sodium-reduced potassium-enriched salt substitutes used in the trial was donated by Jiangsu Sinokone Technology Co Ltd for years three and four of the trial. The funders of the study had no role in the study design, in the collection, analysis, and interpretation of data, or in the writing of the report. The funding sources had no restrictions regarding the submission of publication.

Data availability

Data and related documents for the SSaSS study and for this post-hoc analysis, including the study protocol, informed consent forms, complete de-identified patient data set, a data dictionary defining each field and analytic/statistical code can be requested from the co-author, Professor Bruce Neal, via the email: bneal@georgeinstitute.org.au. Once the data access is granted, data can be accessed via a secured environment hosted by The George Institute for Global Health, China, in-line with China's Cyber Security Law.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committees at the Peking University Health Science Centre in China (IRB00001052-13069) and the University of Sydney in Australia (2013/888). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]School of Public Health, Harbin Medical University, Harbin, China. [2]School of Public Health, Jiangxi Medical College, Nanchang University, Nanchang, China. [3]Jiangxi Provincial Key Laboratory of Disease Prevention and Public Health, Nanchang University, Nanchang, China. [4]Faculty of Medicine and Health, The George Institute for Global Health, University of New South Wales, Sydney, Australia. [5]Liverpool and Macarthur Cancer Therapy Centres, South-West Sydney Local Health District, Sydney, NSW, Australia. [6]Collaboration for Cancer Outcomes, Research and Evaluation (CCORE), Sydney Clinical School, Ingham Institute, University of New South Wales, South-Western, Sydney, Australia. [7]School of Medicine, Western Sydney University, Campbelltown, Australia. [8]School of Public Health, Nanjing Medical University, Nanjing, China. [9]Department of Evidence-Based Medicine, First Affiliated Hospital of China Medical University, Shenyang, China. [10]School of Public Health, Changzhi Medical College, Changzhi, China. [11]School of Public Health, Ningxia Medical University, Yinchuan, China. [12]Department of Chronic and Noncommunicable Disease Prevention and Control, Hebei Provincial Center for Disease Prevention and Control, Shijiazhuang, China. [13]School of Public Health, Jiaotong University Health Science Centre, Xi'an, China. [14]Global Health Research Centre, Duke Kunshan University, Kunshan, China. [15]Duke Global Health Institute, Duke University, Durham, NC, USA. [16]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA. [17]School

of Public Health, Wuhan University, Wuhan, China. [18]School of Public Health, Peking University Clinical Research Instituteand, Peking University, Beijing, China. [19]The Charles Perkins Centre, University of Sydney, Sydney, Australia. [20]Department of Epidemiology and Biostatistics, Imperial College London, London, UK. [21]Department of General Practice, The Second Affiliated Hospital of Harbin Medical University Harbin, Harbin, China.

Received: 3 July 2024 Accepted: 10 April 2025
Published online: 23 April 2025

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209–49.
2. D'Elia L, Rossi G, Ippolito R, Cappuccio FP, Strazzullo P. Habitual salt intake and risk of gastric cancer: a meta-analysis of prospective studies. Clin Nutr. 2012;31(4):489–98.
3. Joossens JV, Hill M, Elliott P, Stamler R, Stamler J, Lesaffre E, et al. Dietary salt, nitrate and stomach cancer mortality in 24 countries. Int J Epidemiol. 1996;25(3):494–504.
4. Park B, Shin A, Park SK, Ko K-P, Ma SH, Lee E-H, et al. Ecological study for refrigerator use, salt, vegetable, and fruit intakes, and gastric cancer. Cancer Causes Control. 2011;22(11):1497–502.
5. Xibin S, Moller H, Evans HS, Dixing D, Wenjie D, Jianbang L. Residential environment, diet and risk of stomach cancer: a case-control study in Linzhou. China Asian Pac J Cancer Prev. 2002;3:167–72.
6. Salvador I, Mercado A, Bravo GL, Baldeón M, Fornasini M. Risk and protective factors for gastric metaplasia and cancer: a hospital-based case-control study in Ecuador. Nutr Hosp. 2015;32(3):1193–9.
7. Tsugane S, Sasazuki S, Kobayashi M, Sasaki S. Salt and salted food intake and subsequent risk of gastric cancer among middle-aged Japanese men and women. Br J Cancer. 2004;90(1):128–34.
8. Kim J, Park S, Nam B-H. Gastric cancer and salt preference: a population-based cohort study in Korea. Am J Clin Nutr. 2010;91(5):1289–93.
9. Liu T, Zhang Q, Xiao X, Wang Y, Ma X, Song M, et al. High salt intake combined with hypertension elevated the risk of primary liver cancer: a prospective cohort study. Front Oncol. 2022;12: 916583.
10. You D, Zhang M, He W, Wang D, Yu Y, Yu Z, et al. Association between dietary sodium, potassium intake and lung cancer risk: evidence from the prostate, lung, colorectal and ovarian cancer screening trial and the Women's Health Initiative. Translational Lung Cancer Research. 2021;10(1):45.
11. Kune GA, Kune S, Watson LF. Dietary sodium and potassium intake and colorectal cancer risk. Nutr Cancer. 1989;12(4):351–9.
12. Banda KJ, Chiu HY, Hu SH, Yeh HC, Lin KC. Huang HC. Associations of dietary carbohydrate and salt consumption with esophageal cancer risk: a systematic review and meta-analysis of observational studies. Nutr Rev. 2020;78(8):688–98.
13. Yin X, Tian M, Neal B. Sodium Reduction: How Big Might the Risks and Benefits Be? Heart Lung Circ. 2021;30(2):180–5.
14. Anderson CA, Appel LJ, Okuda N, Brown IJ, Chan Q, Zhao L, et al. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. J Am Diet Assoc. 2010;110(5):736–45.
15. Greer RC, Marklund M, Anderson CAM, Cobb LK, Dalcin AT, Henry M, et al. Potassium-Enriched Salt Substitutes as a Means to Lower Blood Pressure: Benefits and Risks. Hypertension. 2020;75(2):266–74.
16. Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, et al. Effect of salt substitution on cardiovascular events and death. N Engl J Med. 2021;385(12):1067–77.
17. Neal B, Tian M, Li N, Elliott P, Yan LL, Labarthe DR, et al. Rationale, design, and baseline characteristics of the Salt Substitute and Stroke Study (SSaSS)—a large-scale cluster randomized controlled trial. Am Heart J. 2017;188:109–17.
18. Yang G, Hu J, Rao KQ, Ma J, Rao C, Lopez AD. Mortality registration and surveillance in China: History, current situation and challenges. Popul Health Metr. 2005;3(1):3.
19. You X, Kobayashi Y. The new cooperative medical scheme in China. Health Policy. 2009;91(1):1–9.
20. Thrift AP, Wenker TN, El-Serag HB. Global burden of gastric cancer: epidemiological trends, risk factors, screening and prevention. Nat Rev Clin Oncol. 2023;20(5):338–49.
21. Wu X, Chen L, Cheng J, Qian J, Fang Z, Wu J. Effect of Dietary Salt Intake on Risk of Gastric Cancer: A Systematic Review and Meta-Analysis of Case-Control Studies. Nutrients. 2022;14(20):4260.
22. Tingle SJ, Severs GR, Moir JAG, White SA. Calcium channel blockers in pancreatic cancer: increased overall survival in a retrospective cohort study. Anticancer Drugs. 2020;31(7):737–41.
23. Kim ST, Park KH, Oh SC, Seo JH, Kim JS, Shin SW, et al. How does inhibition of the renin-angiotensin system affect the prognosis of advanced gastric cancer patients receiving platinum-based chemotherapy? Oncology. 2012;83(6):354–60.
24. Bernabe-Ortiz A, Trieu K, Markland M, Hy WuJ, Saavedra-Garcia L, Hart AC, et al. The potential scalability of salt substitutes as an intervention to lower population sodium levels. Salud Publica Mex. 2022;64:S6–13.
25. Liu Y, Chu H, Peng K, Yin X, Huang L, Wu Y, et al. Factors Associated With the Use of a Salt Substitute in Rural China. JAMA Netw Open. 2021;4(12): e2137745.
26. Li KC, Huang L, Tian M, Di Tanna GL, Yu J, Zhang X, et al. Cost-Effectiveness of a Household Salt Substitution Intervention: Findings From 20 995 Participants of the Salt Substitute and Stroke Study. Circulation. 2022;145(20):1534–41.
27. Yin X, Liu H, Webster J, Trieu K, Huffman MD, Miranda JJ, et al. Availability, Formulation, Labeling, and Price of Low-sodium Salt Worldwide: Environmental Scan. JMIR Public Health Surveill. 2021;7(7): e27423.
28. Marklund M, Singh G, Greer R, Cudhea F, Matsushita K, Micha R, et al. Estimated population wide benefits and risks in China of lowering sodium through potassium enriched salt substitution: modelling study. BMJ. 2020;369: m824.
29. Marklund M, Tullu F, Raj Thout S, Yu J, Brady TM, Appel LJ, et al. Estimated Benefits and Risks of Using a Reduced-Sodium, Potassium-Enriched Salt Substitute in India: A Modeling Study. Hypertension. 2022;79(10):2188–98.

Publisher's Note