

低ナトリウム塩の使用で 心血管イベントと死亡は減るか

Effect of Salt Substitution on Cardiovascular Events and Death

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症例提示

- 74歳男性、認知症なし、ADL自立
- 既往歴：高血圧、脂質異常症、脳梗塞
- 内服薬：バイアスピリン、CCB、スタチン
- past smoker
- 直近の腎機能: Cr 0.7mg/dL
- 定期外来の受診時、
「“やさしお®”が体に良いと聞いて、妻が料理に使い始めました。長生きしてほしいから、って言うんです。先生、私の体にも良いのでしょうか。」



症例の疑問点まとめ

- 低ナトリウム塩の使用は、生命予後を改善するのか？



低ナトリウム塩とは

- salt substitutes (低ナトリウム塩、代替塩)
 - ナトリウム塩の割合を減らし、代わりにカリウム塩を使用した調味料
 - 塩味を薄めずに、ナトリウム摂取量を減らすことが可能
 - 同時にカリウム補充もできる



EBMの実践 5steps

- Step1 疑問の定式化
- Step2 論文の検索
- Step3 論文の批判的吟味
- Step4 症例への適応
- Step5 Step1-4の見直し

Step1 疑問の定式化

P	高血圧、脳梗塞の既往がある 74歳男性
I	低ナトリウム塩の使用
C	普通塩の使用と比較
O	死亡が減る

✓「治療」で検索

EBMの実践 5steps

Step1 疑問の定式化

Step2 論文の検索

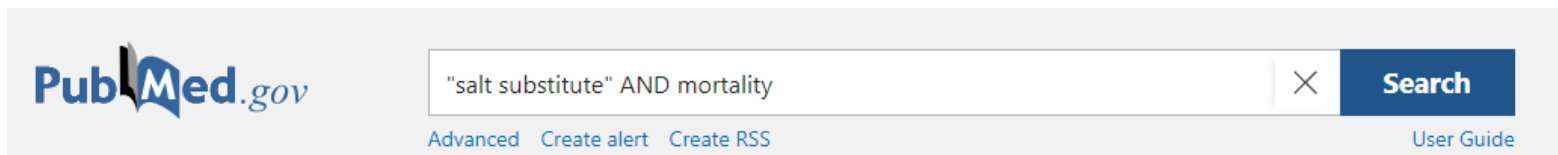
Step3 論文の批判的吟味

Step4 症例への適応

Step5 Step1-4の見直し

Step2 論文の検索

- 低ナトリウム塩による予後改善効果を調べたい
 - ✓ “salt substitute” AND mortalityでPubmed検索
 - ✓ Systematic Reviewで絞り込み →1件ヒット



Filters applied: Systematic Review. [Clear all](#)

[Meta-Analysis](#) > [Heart](#). 2019 Jun;105(12):953-960. doi: 10.1136/heartjnl-2018-314036.

Epub 2019 Jan 19.

Effect of low-sodium salt substitutes on blood pressure, detected hypertension, stroke and mortality

Adrian V Hernandez ^{1 2}, Erin E Emonds ¹, Brett A Chen ¹, Alfredo J Zavala-Loayza ³, Priyaleela Thota ⁴, Vinay Pasupuleti ⁵, Yuani M Roman ¹, Antonio Bernabe-Ortiz ^{3 6}, J Jaime Miranda ³

Affiliations + expand

PMID: 30661034 DOI: [10.1136/heartjnl-2018-314036](https://doi.org/10.1136/heartjnl-2018-314036)

ORIGINAL RESEARCH ARTICLE

Effect of low-sodium salt substitutes on blood pressure, detected hypertension, stroke and mortality

Adrian V Hernandez,^{1,2} Erin E Emonds,¹ Brett A Chen,¹ Alfredo J Zavala-Loayza,³ Priyaleela Thota,⁴ Vinay Pasupuleti,⁵ Yuani M Roman,¹ Antonio Bernabe-Ortiz,^{3,6} J Jaime Miranda³

Study selection

We included (1) RCTs evaluating salt substitutes versus control (regular salt), (2) studies evaluating clinical and/or intermediate outcomes (ie, CV risk factors) and (3) studies evaluating hypertensive, normotensive and mixed populations.

RESULTS

Eligible studies

We identified 3081 publications. After removing duplicates and screening titles and abstracts, 29 articles were selected. After full-text screening, 19 articles [w1–w19] were included. Two articles [w12, w18] encompassed two separate RCTs; therefore, 21 RCTs (n=7403) were included (online supplementary figure S1).

血管リスク因子をアウトカムとした
低ナトリウム塩 vs 通常塩のRCTを検索
→21のRCTをsystematic review

Overall mortality was non-significantly reduced in two trials (n=2159) (RR 0.89, 95% CI 0.77 to 1.03, p=0.12, I²=0%) (online supplementary figure S3). Only one (n=608) [w9] trial reported stroke incidence (RR 1.58, 95% CI 0.52 to 4.77, p=0.42).

There were data from only one trial for waist circumference, C-peptide and CV mortality, and therefore we could not meta-analyse these outcomes.

Mortality (n=2159), stroke (n=608), CV mortalityを直接アウトカムとした RCTは少ない

ORIGINAL RESEARCH ARTICLE

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Limitations

Our study had several limitations. First, we evaluated heterogeneous salt substitutes, with NaCl contents ranging between 0% to 97% and potassium chloride as the main replacer. Second, although we reported effects for all trials, our primary analyses showed no significant differences in effects across study populations for all outcomes with sufficient data. Third, five trials had high risk of bias; sensitivity analyses without these five trials showed similar results for all outcomes. However, the quality of evidence was at most moderate for overall mortality, and all other outcomes had worse quality of evidence. Fourth, there was scarce data on important outcomes such as stroke or CV mortality. The ongoing salt substitute SSaSS trial features stroke as primary outcome.²⁸ Fifth, we included RCTs with all ranges of follow-up times. However, trials of >3 months of follow-up had similar effects than shorter studies for most of outcomes.

CONCLUSIONS

In a broad range of individuals and acknowledging their heterogeneous composition, low-sodium salt substitutes are associated with significant reductions in SBP and DBP, reduction of urinary sodium excretion, and increase in urinary potassium and calcium excretions. There was no effect on detected hypertension, overall mortality or other intermediate outcomes. We could not conclude on the effects of salt substitutes' stroke or CV mortality due to the scarcity of data.

Mortality、stroke、CV mortalityなど重要なアウトカムはデータが不足

strokeやmortalityを主要アウトカムとした大規模RCT (SSaSS trial)が進行中
→ 検索してみる

Save

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Display options

- ☐ 1 Interim effects of **salt substitution** on urinary electrolytes and blood pressure in the China **Salt Substitute and Stroke Study (SSaSS)**.
Cite Huang L, Tian M, Yu J, Li Q, Liu Y, Yin X, Wu JH, Marklund M, Wu Y, Li N, Elliott P, Yan LL, Labarthe DR, Hao Z, Shi J, Feng X, Zhang J, Zhang Y, Zhang R, Zhou B, Li Z, Sun J, Zhao Y, Yu Y, Neal B.
Share Am Heart J. 2020 Mar;221:136-145. doi: 10.1016/j.ahj.2019.12.020. Epub 2020 Jan 7. PMID: 31986290 Clinical Trial.
The **Salt Substitute and Stroke Study** is an ongoing 5-year large-scale cluster randomized trial investigating the effects of potassium-enriched **salt substitute** compared to usual **salt** on the risk of **stroke**. ... Use of **salt** ...
- ☐ 2 Feasibility and validity of using death surveillance data and SmartVA for fact and cause of death in clinical trials in rural China: a substudy of the China **salt substitute and stroke study (SSaSS)**.
Cite Huang L, Yu J, Neal B, Liu Y, Yin X, Hao Z, Wu Y, Yan LL, Wu JH, Joshi R, Shi J, Feng X, Zhang J, Zhang Y, Zhang R, Zhou B, Li Z, Sun J, Zhao Y, Yu Y, Pearson SA, Chen Z, Tian M.
Share J Epidemiol Community Health. 2020 Dec 7;jech-2020-214063. doi: 10.1136/jech-2020-214063. Online ahead of print. PMID: 33286656
METHODS: We used mortality data from the first 24 months of the China **Salt Substitute and Stroke Study (SSaSS)** trial and assessed the agreement between (1) mortality surveillance data and face-to-face visits for fact of death; (2) mortality surv ...
- ☐ 3 Rationale, design, and baseline characteristics of the **Salt Substitute and Stroke Study (SSaSS)**-A large-scale cluster randomized controlled trial.
Cite Neal B, Tian M, Li N, Elliott P, Yan LL, Labarthe DR, Huang L, Yin X, Hao Z, Stepien S, Shi J, Feng X, Zhang J, Zhang Y, Zhang R, Wu Y.
Share Am Heart J. 2017 Jun;188:109-117. doi: 10.1016/j.ahj.2017.02.033. Epub 2017 Mar 14. PMID: 28577665 Free article. Clinical Trial.
Lowering **sodium** intake with a reduced-**sodium**, added potassium **salt substitute** has been proved to lower blood pressure levels. Whether the same strategy will also reduce the risks of vascular outcomes is uncertain and controversial. The **SSaSS** has ...
- ☐ 4 Protocol for the economic evaluation of the China **Salt Substitute and Stroke Study (SSaSS)**.
Cite Li KC, Tian M, Neal B, Huang L, Yu J, Liu Y, Yin X, Zhang X, Wu Y, Li N, Elliott P, Yan L, Labarthe D, Hao Z, Shi J, Feng X, Zhang J, Zhang Y, Zhang R, Zhou B, Li Z, Sun J, Zhao Y, Yu Y, Si L, Lung T.
Share BMJ Open. 2021 Jul 20;11(7):e045929. doi: 10.1136/bmjopen-2020-045929. PMID: 34285006 Free PMC article.
This **study** protocol describes the planned within-trial economic evaluation of a low-**sodium salt substitute** intervention designed to reduce the risk of **stroke** in China. METHODS AND ANALYSES: The economic evaluation will be conducted alongside the ...
- ☐ 5 Effect of **Salt Substitution** on Cardiovascular Events and Death.
Cite Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, Zhang J, Tian M, Huang L, Li Z, Yu Y, Zhao Y, Zhou B, Shi J, Liu Y, Yin X, Hao Z, Yu J, Li KC, Zhang X, Duan P, Wang F, Ma B, Shi W, Di Tanna GL, Stepien S, Shan S, Pearson SA, Li N, Yan LL, Labarthe D, Elliott P.
Share N Engl J Med. 2021 Sep 16;385(12):1067-1077. doi: 10.1056/NEJMoa2105675. Epub 2021 Aug 29. PMID: 34459569 Clinical Trial.
The villages were randomly assigned in a 1:1 ratio to the intervention group, in which the participants used a **salt substitute** (75% **sodium chloride** and 25% potassium **chloride** by mass), or to the control group, in which the participants continued ...

SSaSS trialを検索
→ 完了して結果が出ている

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B. Neal, Y. Wu, X. Feng, R. Zhang, Y. Zhang, J. Shi,* J. Zhang, M. Tian, L. Huang, Z. Li, Y. Yu, Y. Zhao, B. Zhou, J. Sun, Y. Liu, X. Yin, Z. Hao, J. Yu, K.-C. Li, X. Zhang, P. Duan, F. Wang, B. Ma, W. Shi, G.L. Di Tanna, S. Stepien, S. Shan, S.-A. Pearson, N. Li, L.L. Yan, D. Labarthe, and P. Elliott

低ナトリウム塩と通常塩の使用による心血管イベント・死亡を比較したRCT

The Salt Substitute and Stroke Study (SSaSS)

N Engl J Med 2021;385:1067-77.

EBMの実践 5steps

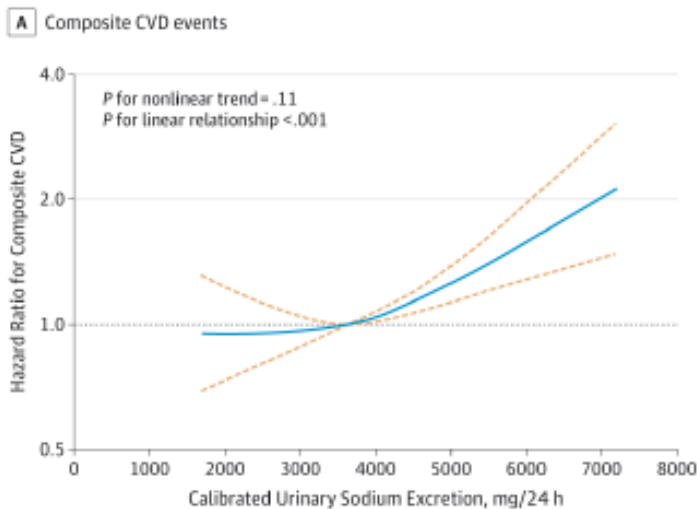
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Step3 批判的吟味

- ① 論文の背景
- ② 論文のPICO
- ③ 結果は妥当か
 - ランダム割付、隠蔽化、群間差
 - 盲検化
 - 解析(追跡率・脱落、割付)
- ④ 結果は何か

①論文の背景

- ナトリウム摂取過剰、カリウム摂取不足は、高血圧と心血管疾患との関連が示唆されている



Multiple-Adjusted Hazard Ratios and 95% Confidence Intervals of Cardiovascular Diseases Associated With Calibrated 24-Hour Urinary Sodium Excretion

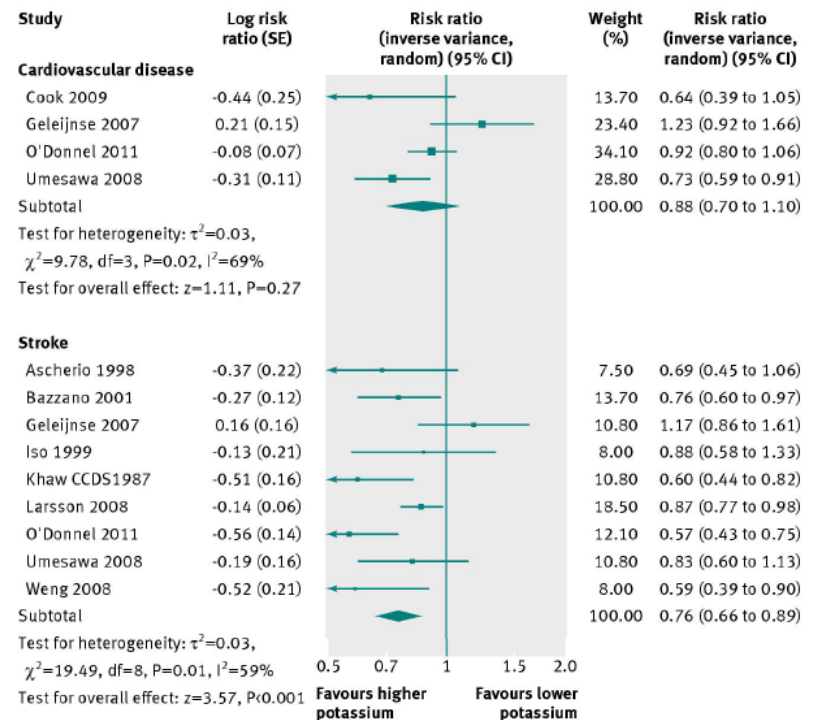
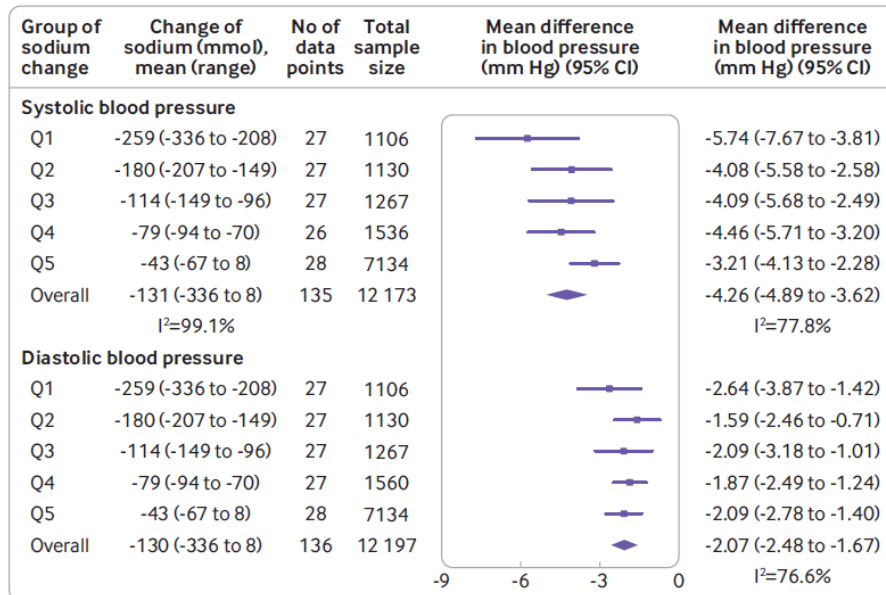


Fig 4 Association between higher potassium intake and risk of incident cardiovascular disease, stroke,

①論文の背景

- ナトリウム摂取減少およびカリウム摂取補充による降圧効果は、メタアナリシスで示されている



Association of magnitude of sodium reduction (mmol) with size of blood pressure reduction (mm Hg)

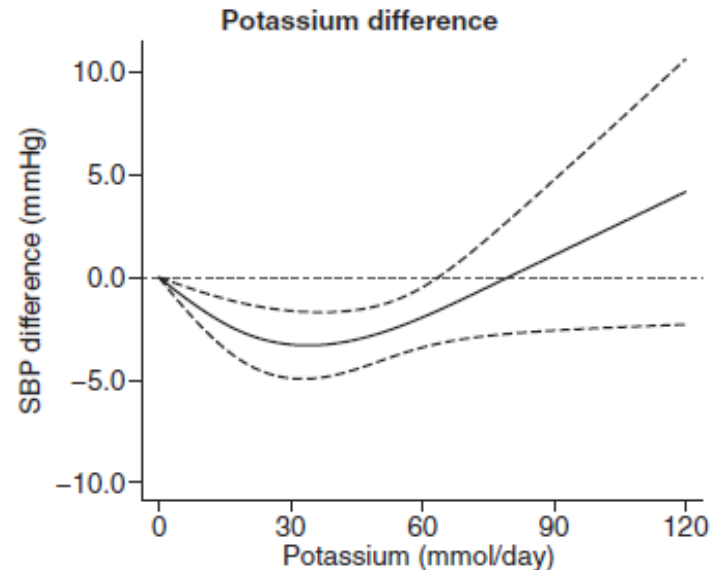
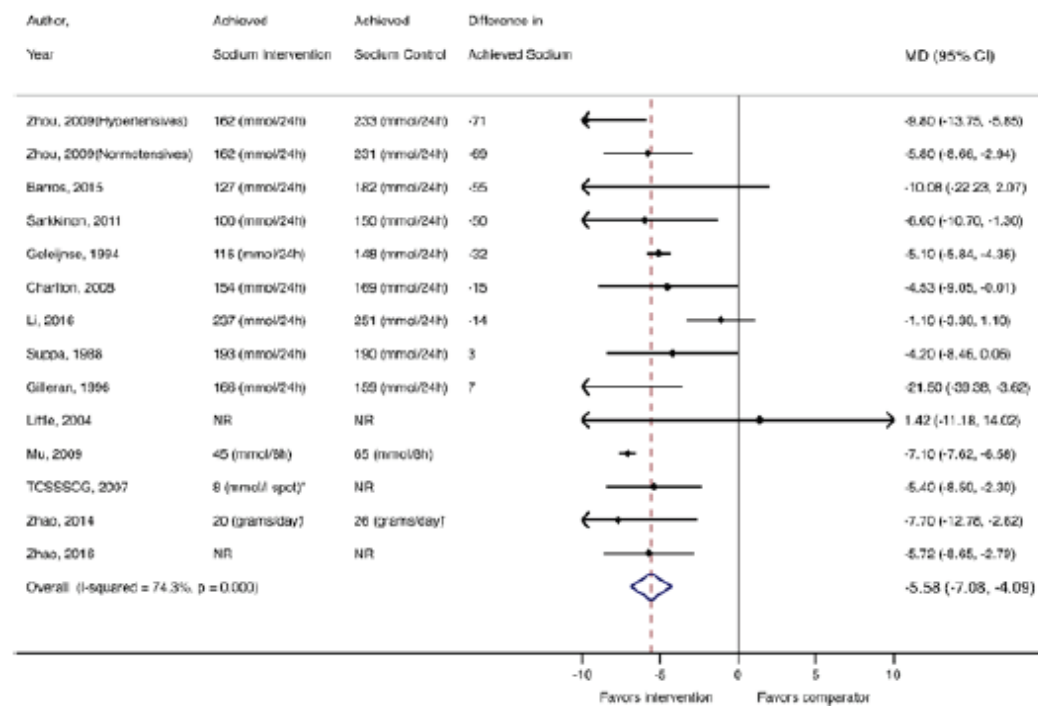


Figure 2. Dose-response meta-analysis of changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels (as mm Hg), according to differences in potassium excretion between the treatment arms (potassium supplemented and control group) at the end of the trials.

①論文の背景

- 低ナトリウム塩による降圧効果は示されているが、重要なアウトカム（脳卒中、冠動脈疾患、死亡）に関する効果を示した大規模研究はまだ存在しない



①論文の背景

- 理論上、低ナトリウム塩使用による高カリウム血症が懸念される
- 低ナトリウム塩の使用による、重要アウトカム(脳卒中・心血管イベント・死亡)とリスク(高カリウム血症)を調べるため、大規模RCTが行われた

②Patients

Inclusion criteria

- 脳卒中の既往
and/or
- 60歳以上でコントロール不良の高血圧
 - 降圧薬内服中で SBP $\geq$ 140
 - 降圧薬なしで SBP $\geq$ 160
- 電話を所有 (同居家族でも可)

➤ 倫理的配慮あり

北京大学医学部、シドニー大学の倫理委員会の承認
全参加者がインフォームド・コンセントを記載

Exclusion criteria

- 参加者または同居家族が
 - カリウム保持性利尿薬を使用
 - カリウム補充を使用
 - 重度の腎障害あり
 - 低ナトリウム塩使用にあたって他に懸念事項あり
- 参加者が
 - 推定予後6ヶ月未満
 - ほとんどの食事が外食
 - 同居家族がすでに研究に参加

② Intervention/Comparison

Intervention group

- 通常塩と同じ量の低ナトリウム塩(下記)を使用
- 低ナトリウム塩は無料で配布

comparison group

- 普段と同様に通常塩を使用

- ✓ 一般的な脳梗塞予防として、ガイドラインに沿った薬物療法は許可
- ✓ 研究開始時に減塩を勧めてもよいが、介入期間中には再指導はしない

通常塩

NaCl 100%

低ナトリウム塩

KCl 25%

NaCl 75%

② Outcome

Primary outcome

- 脳卒中（死亡または24時間以上持続する巣症状）

Secondary outcome

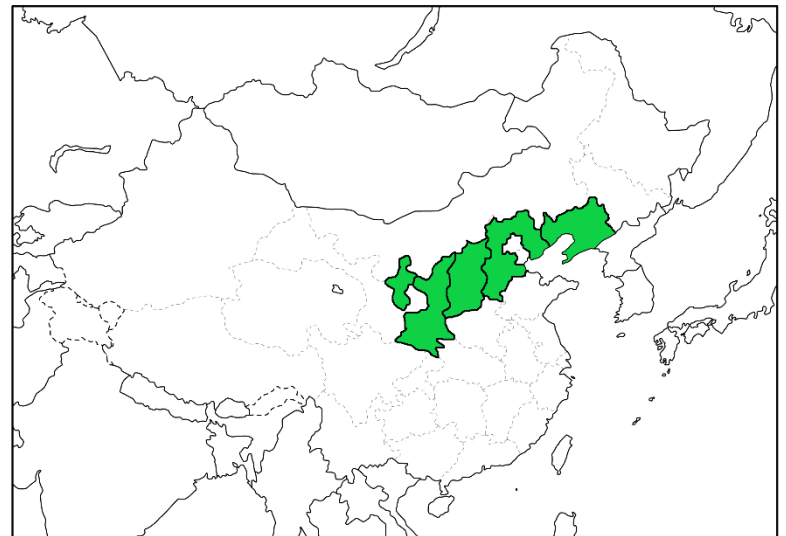
- 主要な心血管イベント（以下の複合アウトカム）
非致死的脳卒中、非致死的急性冠症候群、血管疾患による死亡
- 全死亡

Safety outcome

- 高カリウム血症（ $K > 6.0 \text{ mmol/L}$ or $K > 5.5$ かつ心電図変化あり）
- 突然死

③研究デザイン

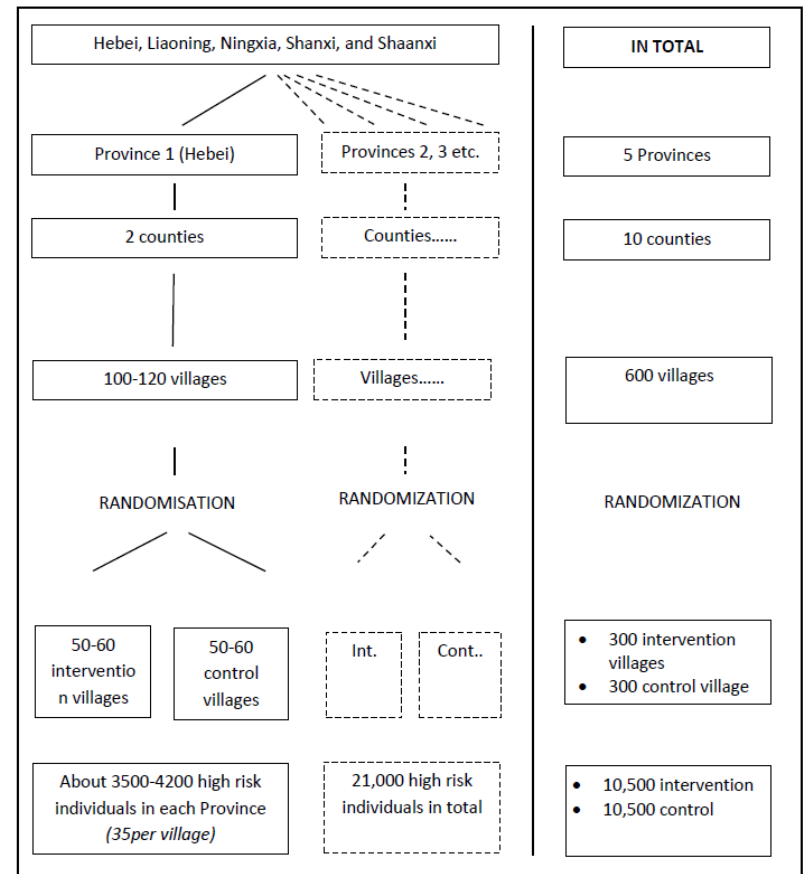
- 多施設、Open-label、クラスターRCT
- 中国の5つの省（河北省、遼寧省、寧夏回族自治区、山西省、陝西省）の農村部にある600の村
- 2014年4月-2015年1月に登録
- 5年間の追跡期間を予定



③ランダム化・隠蔽化

- 村をひとつの単位(クラスター)としてランダム化
- 郡ごとに層別化
- central computerized processを使用し隠蔽化

Figure 1 – Study flow chart – site selection and randomization



③背景因子の群間差

	Intervention (10,505)	Control (10,491)	Total (20,996)
Age (y), mean (SD)	65.2 (8.5)	65.5 (8.5)	65.4 (8.5)
Body mass index (kg/m ²), mean (SD)	24.8 (3.6)	24.9 (3.7)	24.8 (3.6)
Female (%)	49.7	49.2	49.5
Past smokers (%)	32.8	34.2	33.5
Current smokers (%)	18.7	18.9	18.8
Systolic blood pressure (mm Hg), mean (SD)	153.8 (23.4)	154.2 (23.6)	154.0 (23.5)
<140 mm Hg (%)	26.8	26.2	26.5
≥140 and <160 mm Hg (%)	34.6	35.7	35.1
≥160 mm Hg (%)	38.7	38.2	38.4
Diastolic blood pressure (mm Hg), mean (SD)	89.1 (14.0)	89.4 (14.0)	89.2 (14.0)
<90 mm Hg (%)	52.0	51.7	51.8
≥90 and <100 mm Hg (%)	25.7	25.3	25.6
≥100 mm Hg (%)	22.3	23.0	22.7
Urinary sodium* (g/d), mean (SD)	4.4 (1.8)	4.2 (1.8)	4.3 (1.8)
Urinary potassium* (g/d), mean (SD)	1.4 (0.6)	1.4 (0.6)	1.4 (0.6)
Education			
Primary school or lower (%)	72.3	72.6	
Junior high school (%)	23.2	22.4	
Senior high school or above (%)	4.5	5.0	
Medication use			
Diuretic (%)	11.5	11.2	
ACE inhibitor or ARB (%)	23.1	23.0	
α-Blocker (%)	0.7	1.1	
β-Blocker (%)	5.0	6.3	
Calcium antagonist (%)	43.3	40.6	
Any of the above medications (%)	79.9	78.7	
Other antihypertensive agent† (%)	38.2	37.5	
Any antihypertensive medication‡ (%)	79.9	78.7	
Statin or other lipid-lowering agent (%)	12.6	12.0	
Aspirin or other antiplatelet agent (%)	40.0	39.4	
Disease history			
Stroke (%)	73.3	72.0	72.7
Uncontrolled high blood pressure§ (%)	59.4	59.2	59.3
Transient ischemic attack (%)	13.2	14.9	14.1
Ischemic heart disease (%)	16.4	15.7	16.1
Diabetes mellitus (%)	10.6	10.5	10.6
Knowledge and behaviors related to salt			
Trying to reduce salt intake (%)	64.8	64.4	64.6
Eating pickled vegetables most days (%)	27.0	26.0	26.5
Adding salt to most meals (%)	8.1	8.9	8.5
Adding MSG to most meals (%)	42.8	41.4	42.1
Trying to eat less if the food is very salty (%)	74.7	75.0	74.8
Have heard about salt substitute (%)	5.9	6.0	5.9
Household uses salt substitute (%)	1.3	1.5	1.4
Know too much salt affects health (%)	90.0	90.9	90.4
Know too much salt affects risk of stroke (%)	32.1	33.4	32.8
Know too much salt affects blood pressure (%)	47.1	47.4	47.3

Baseline characteristicsに
両群間で大きな差はない

Abbreviations: ACE, Angiotensin-converting enzyme; ARB, angiotensin receptor blocker; MSG, monosodium glutamate.

*Urinary sodium and potassium were calculated from 539 complete 24-hour urine collections.

†Comprises mostly Chinese traditional medicine.

‡Any hypertensive medication is defined if the participant self-reported any of the following medications: diuretic, ACE inhibitor or ARB, α-blocker, β-blocker, calcium antagonist, or other antihypertensive agent.

§Uncontrolled high blood pressure is defined as 2 measures of systolic blood pressure ≥ 140 mm Hg and using blood pressure-lowering treatment, or 2 measures of systolic blood pressure ≥ 160 mm Hg and not using blood pressure-lowering treatment.

③背景因子の群間差

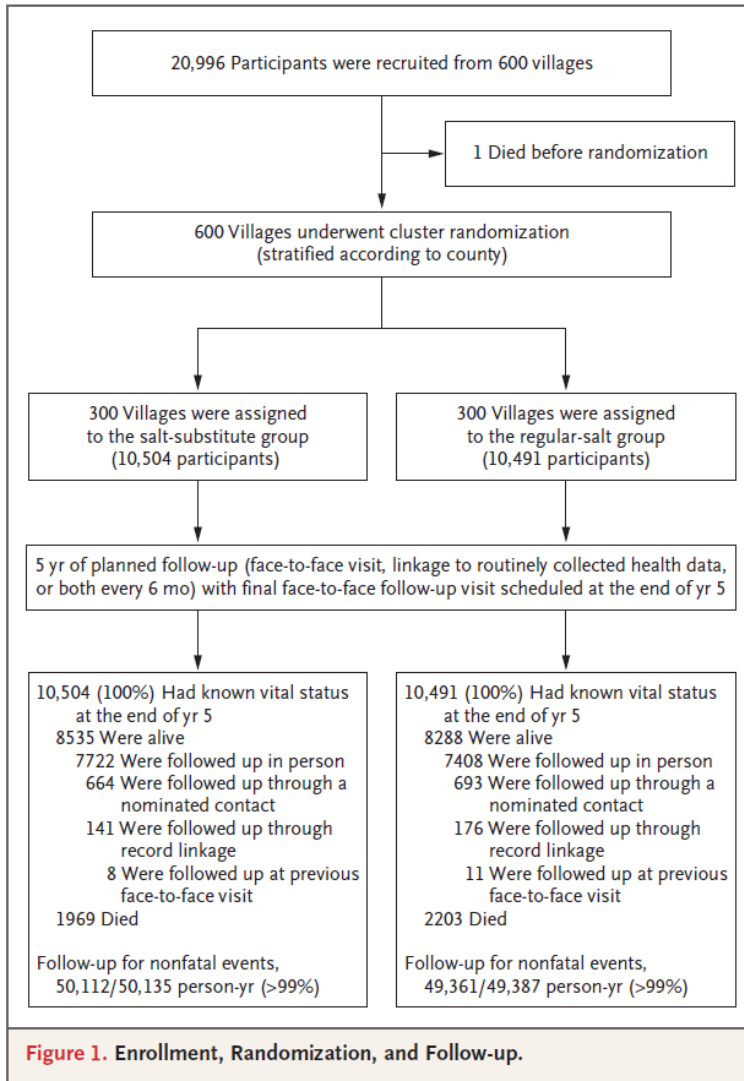
	Intervention (10,505)	Control (10,491)	Total (20,996)
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Age (y), mean (SD)
 Body mass index (kg/m²), mean (SD)
 Female (%)
 Past smokers (%)
 Current smokers (%)
 Systolic blood pressure (mm Hg), n
 <140 mm Hg (%)
 ≥140 and <160 mm Hg (%)
 ≥160 mm Hg (%)
 Diastolic blood pressure (mm Hg), n
 <90 mm Hg (%)
 ≥90 and <100 mm Hg (%)
 ≥100 mm Hg (%)
 Urinary sodium (g/d), mean (SD)
 Urinary potassium (g/d), mean (SD)
 Education
 Primary school or lower (%)
 Junior high school (%)
 Senior high school or above (%)
 Medication use
 Diuretic (%)
 ACE inhibitor or ARB (%)
 α-Blocker (%)
 β-Blocker (%)
 Calcium antagonist (%)
 Any of the above medications (%)
 Other antihypertensive agent† (%)
 Any antihypertensive medication (%)
 Statin or other lipid-lowering agent (%)
 Aspirin or other antiplatelet agent (%)
 Disease history
 Stroke (%)
 Uncontrolled high blood pressure (%)
 Transient ischemic attack (%)
 Ischemic heart disease (%)
 Diabetes mellitus (%)
 Knowledge and behaviors related to salt intake
 Trying to reduce salt intake (%)
 Eating pickled vegetables most days (%)
 Adding salt to most meals (%)
 Adding MSG to most meals (%)
 Trying to eat less if the food is very salty (%)
 Have heard about salt substitute (%)
 Household uses salt substitute (%)
 Know too much salt affects health (%)
 Know too much salt affects risk of stroke (%)
 Know too much salt affects blood pressure (%)

- 年齢 平均65.4歳
- 性別 ほぼ1:1
- 介入前の血圧 154/89 mmHg
- 降圧薬内服 79%が1剤以上
- 降圧薬の種類 CCB 42%, ACE-I/ARB 23%, 利尿剤 11%
- 脳卒中の既往 72.6%
- 虚血性心疾患の既往 16%
- 抗血小板内服 40%
- 糖尿病 11%
- BMI 25%
- 喫煙歴 current 19%, past 33%

Abbreviations: ACE, Angiotensin-converting enzyme; ARB, angiotensin receptor blocker.
 *Urinary sodium and potassium were calculated from a 24-hour urine collection.
 †Comprises mostly Chinese traditional medicine.
 ‡Any hypertensive medication is defined as any antihypertensive agent.
 §Uncontrolled high blood pressure is defined as 2 measures of systolic blood pressure ≥ 140 mm Hg and using blood pressure-lowering treatment, or 2 measures of systolic blood pressure ≥ 160 mm Hg and not using blood pressure-lowering treatment.

③解析(追跡・脱落)



- Intention-to-treat解析
- 両群とも脱落なし

③解析(割付遵守率)

- 介入期間は平均4.74年、中央値5.12年
- 5年後のフォローアップ時、
 - 介入群の91.7%が低ナトリウム塩を使用
 - 対照群の6.4%が低ナトリウム塩を使用

→ 9割以上が割付通りの治療を行っている
(ただし、外食などの割合については評価していない)

③盲検化

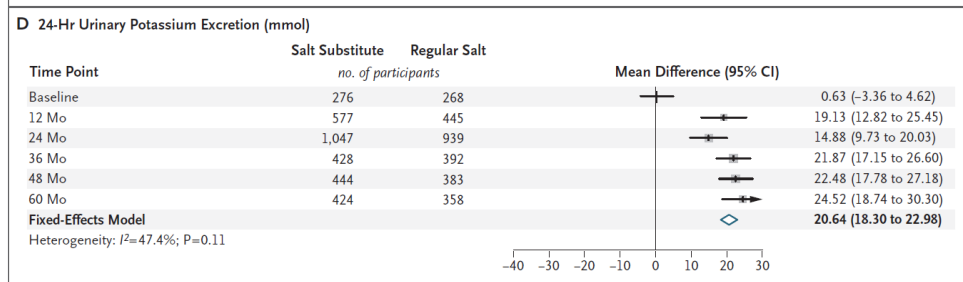
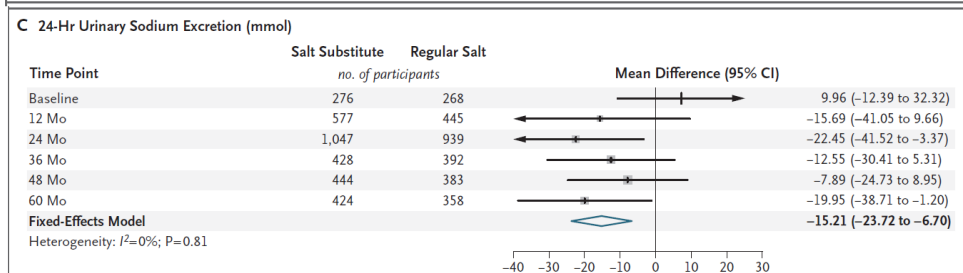
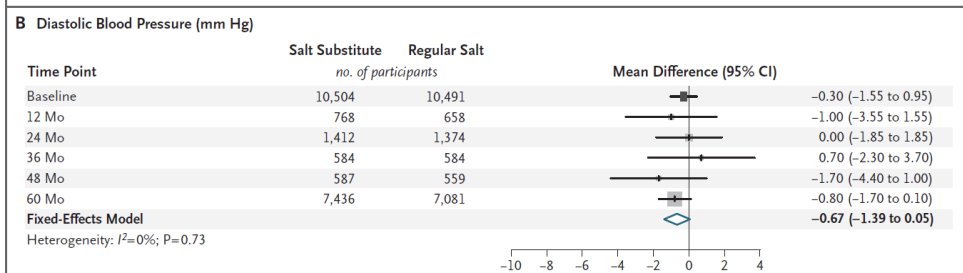
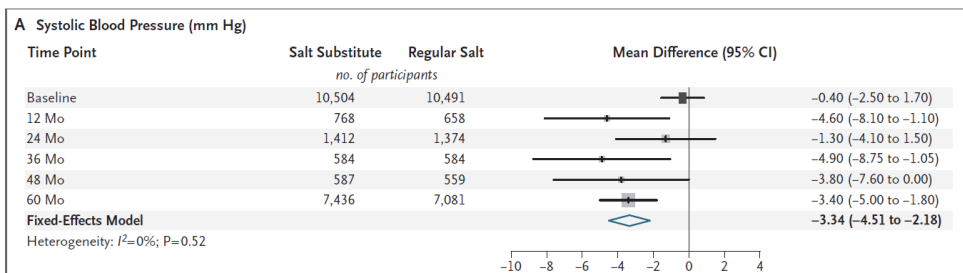
- 患者、医師は非盲検
- 研究評価者は盲検化し、可能な限り客観的なアウトカムを使用

③症例数

- 各群における脳卒中の発症率の差を13%と予想
- 検出力 90%
- 両側検定 $\alpha=0.05$

→ 全体で21000名の参加者が必要
(各クラスターに35名ずつ、両群300クラスターずつ)

④結果の評価



介入群では、

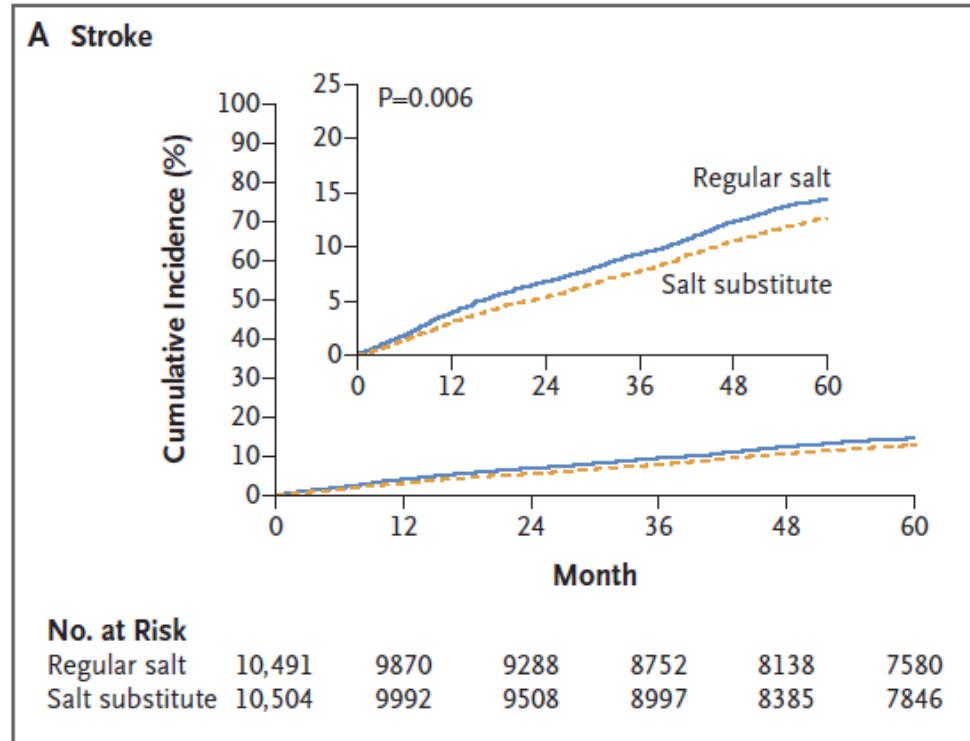
- 血圧が低下
- 尿中ナトリウム排泄が減少
- 尿中カリウム排泄が増加



過去の研究と一致

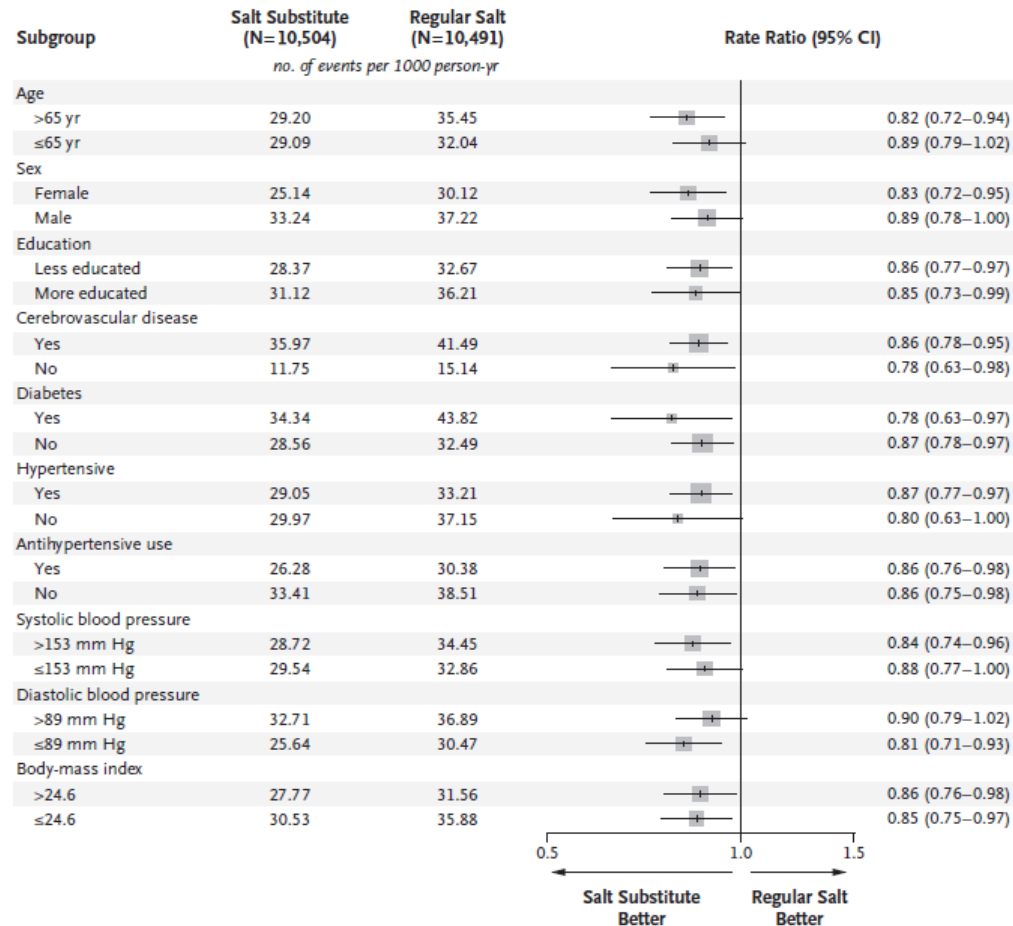
- ✓ 低ナトリウム塩を摂取していたことの裏付け
- ✓ 中間因子と思われる血圧低下を確認

④ Primary Outcome



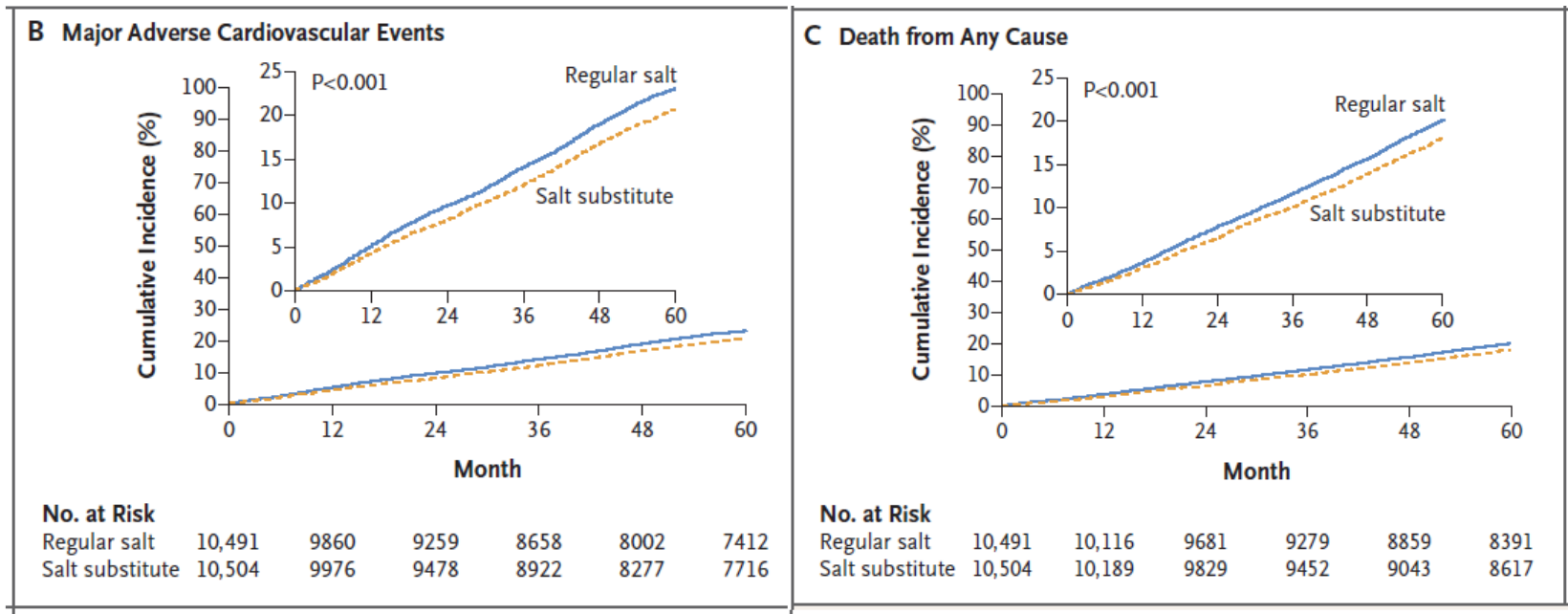
- 脳卒中は介入群で減少 [RR 0.86; 95%CI, 0.77 -0.96; P=0.006]

④ Primary Outcome



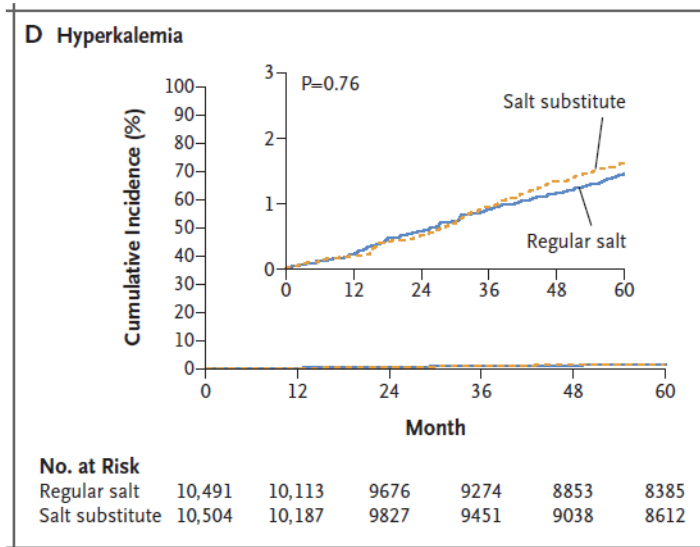
- すべてのサブグループ解析で、介入群が優れる

④ Secondary Outcome



- 主要な心血管イベントは介入群で減少 [RR 0.87; 95%CI, 0.80-0.95; $P < 0.001$]
- 全死亡も介入群で減少 [RR 0.88; 95%CI, 0.82-0.95; $P < 0.001$]

④ Safety Outcome

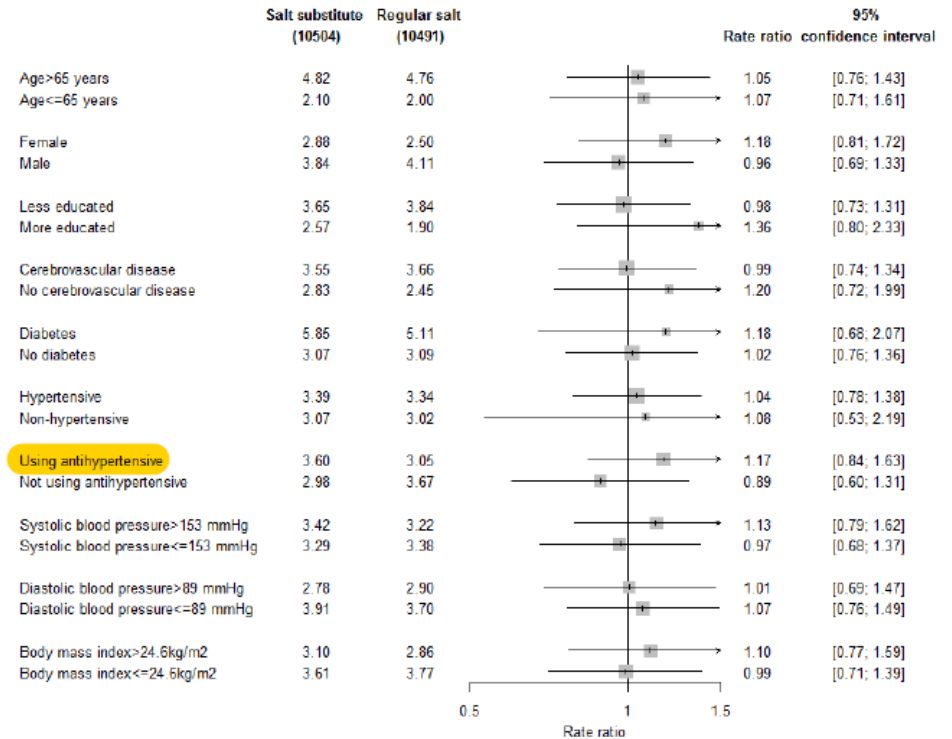


- 高カリウム血症の発症率は両群で有意差なし

[RR 1.04; 95%CI, 0.80-1.37; P=0.76]

- ACE-I/ARB内服は各群23%

Number of events per 1000 person-years



Effects of salt substitute on hyperkalemia in participant subgroups

- サブグループ解析は「降圧薬使用」のみで、降圧薬の種類別の記載はなし
- 「降圧薬使用あり」でRR上昇傾向がみられるが、ACE-I/ARBの影響かどうかは不明

EBMの実践 5steps

- Step1 疑問の定式化
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- Step5 Step1-4の見直し

Step4 症例への適応

	Intervention (10,505)	Control (10,491)	Total (20,996)
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Age (y), mean (SD)
 Body mass index (kg/m²), mean (SD)
 Female (%)
 Past smokers (%)
 Current smokers (%)
 Systolic blood pressure (mm Hg), mean (SD)
 <140 mm Hg (%)
 ≥140 and <160 mm Hg (%)
 ≥160 mm Hg (%)
 Diastolic blood pressure (mm Hg), mean (SD)
 <90 mm Hg (%)
 ≥90 and <100 mm Hg (%)
 ≥100 mm Hg (%)
 Urinary sodium (g/d), mean (SD)
 Urinary potassium (g/d), mean (SD)
 Education
 Primary school or lower (%)
 Junior high school (%)
 Senior high school or above (%)
 Medication use
 Diuretic (%)
 ACE inhibitor or ARB (%)
 α-Blocker (%)
 β-Blocker (%)
 Calcium antagonist (%)
 Any of the above medications (%)
 Other antihypertensive agent† (%)
 Any antihypertensive medication (%)
 Statin or other lipid-lowering agent (%)
 Aspirin or other antiplatelet agent (%)
 Disease history
 Stroke (%)
 Uncontrolled high blood pressure (%)
 Transient ischemic attack (%)
 Ischemic heart disease (%)
 Diabetes mellitus (%)
 Knowledge and behaviors related to salt intake
 Trying to reduce salt intake (%)
 Eating pickled vegetables most days (%)
 Adding salt to most meals (%)
 Adding MSG to most meals (%)
 Trying to eat less if the food is very salty (%)
 Have heard about salt substitute (%)
 Household uses salt substitute (%)
 Know too much salt affects health (%)
 Know too much salt affects risk of heart disease (%)
 Know too much salt affects blood pressure (%)

- 年齢 平均65.4歳
- 性別 ほぼ1:1
- 介入前の血圧 154/89 mmHg
- 降圧薬内服 79%が1剤以上
- 降圧薬の種類 CCB 42%, ACE-I/ARB 23%, 利尿剤 11%
- 脳卒中の既往 72.6%
- 虚血性心疾患の既往 16%
- 抗血小板内服 40%
- 糖尿病 11%
- BMI 25%
- 喫煙歴 current 19%, past 33%

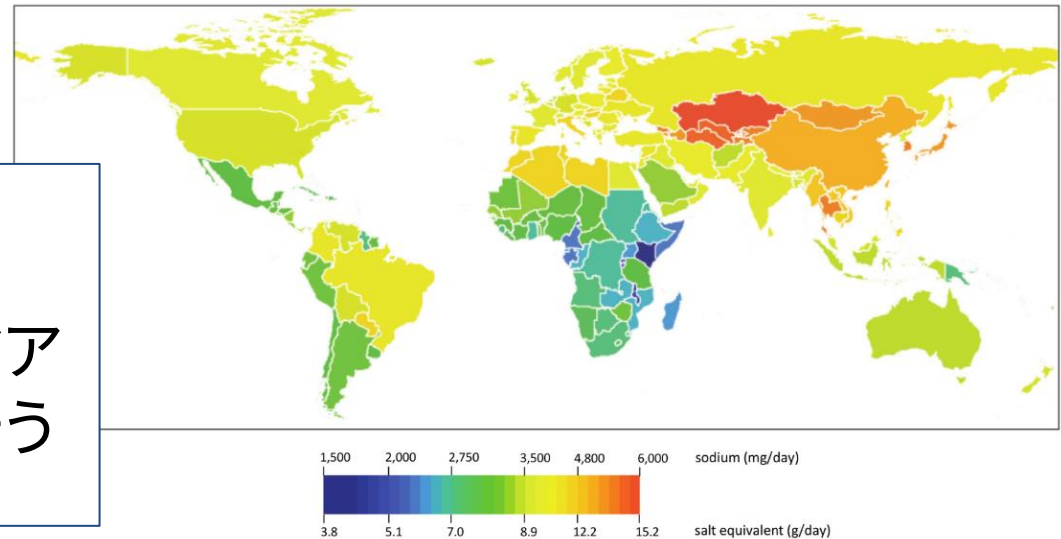
研究参加者と患者の特徴に
 大きなズレはない
 exclusionにも該当しない

Abbreviations: ACE, Angiotensin-converting enzyme; ARB, angiotensin receptor blocker.
 *Urinary sodium and potassium were calculated from a 24-hour urine collection.
 †Comprises mostly Chinese traditional medicine.
 ‡Any hypertensive medication is defined as any antihypertensive agent.
 §Uncontrolled high blood pressure is defined as 2 measures of systolic blood pressure ≥ 140 mm Hg and using blood pressure-lowering treatment, or 2 measures of systolic blood pressure ≥ 160 mm Hg and not using blood pressure-lowering treatment.

Step4 症例への適応

- この研究での塩分摂取量 10.75g/日
(24時間尿中ナトリウム排泄量からの推定量)
- 日本人の塩分摂取量 平均 10.1g/日
(2019年国民健康・栄養調査結果より)
- 塩分摂取量は、中国と日本では同程度 (下図)

塩分摂取量が同程度で、
脳卒中の疫学も似た東アジア
人の研究であり、適応できそう



Step4 症例への適応

- 通常塩と比較すると、少し価格が高い
 - 現実世界での実行率や長期使用率は下がる可能性もあるが、
最安価の商品なら、普通塩との差は年間840円、安価な薬剤とはほぼ同額

	通常塩	低ナトリウム塩 (市販品)	1:1混合塩 注1) (本研究相当塩)	アムロジン5mg (3割負担の場合)
価格 (例)	約100～200円/kg	約200円/300g ～400円/180g		1錠 10.1円
1日あたり注2)	1～2円	6.6～22円	3.3～12円	10.1円(3円)
1年あたり	365～730円	2,409～8,030円	1,204～4,380円	3,687円(1,095円)

注1) 市販品は50%減塩のため、通常塩：低ナトリウム塩(市販品)＝1：1の混合塩が今回の研究で使用された低ナトリウム塩に相当 注2) 1日あたり塩10gを使用すると仮定して計算

- 外食中心の患者では、塩分代替効果が不十分

当然、使用量の影響を受けるため、必ずしも今回の研究と同等の効果が期待できるわけではない

Step4 症例への適応

- 腎不全やカリウム保持性利尿剤の使用がなければ、高カリウム血症は増加はせず比較的安全
- ただし、ACE-I/ARB使用については、今回の研究結果からは高カリウム血症が増加する可能性が不明であり、注意が必要

市販の低ナトリウム塩は、塩分代替割合が40～50%の商品が多く、今回の研究よりもカリウム含有量が多いことにも注意

Step4 症例への適応

- 以上より、外的妥当性はあるそう
- 副作用が少なく、重要アウトカムを改善する効果を考慮すると、低ナトリウム塩の使用は費用対効果が大きいと考えられる

冒頭症例の患者には、費用が問題でなければ、そのまま低ナトリウム塩の使用継続を勧めた。

今後、ACE-I/ARBやカリウム保持性利尿薬を新規に開始する際に留意するよう、カルテ記載した。

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Step5 Step1-4の見直し

Step1 疑問の定式化

臨床的疑問をPICOを用いて形式化した

Step2 論文の検索

情報収集し、重要なアウトカムを評価した論文を選択した

Step3 論文の批判的吟味

内的妥当性を評価し、概ね問題ないと判断した

Step4 症例への適応

論文の患者群と比較的一致し、外的妥当性はあると判断した

論文のまとめ

- 従来の生活指導(減塩、禁煙、運動など)や薬物療法を継続することが大前提だが、
高血圧、脳卒中の既往がある患者に、低ナトリウム塩の使用を勧めることは妥当と思われる
- (同居家族も含め)腎不全患者やカリウム保持性利尿剤内服患者では、安全性が不明であり、低ナトリウム塩は避けるべきだろう
 - 効果の程度は不明だが、塩化カリウム不使用の低ナトリウム塩製品であれば安全と思われる

