

Effect of sodium restriction on blood pressure of unstable or uncontrolled hypertensive patients in primary care

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BACKGROUND/OBJECTIVES: The aims of the present study are: 1) to quantify sodium consumption of patients with unstable or uncontrolled hypertension, 2) to investigate if reduced sodium intake can lower BP in these patients, and 3), to assess the acceptability and feasibility of this approach.

SUBJECTS/METHODS: This study included 25 adults (age: 50+ years) with frequently elevated BP or patients with uncontrolled, uncomplicated hypertension despite drug treatment in a general practice setting. BP and salt intake (24h urinary excretion and food records) were measured at baseline and after a sodium reduced diet.

RESULTS: Mean (\pm SD) systolic (SBP) over diastolic (DBP) blood pressure (mmHg) at baseline was 150.7 (\pm 9.5)/84.149 (\pm 5.6). Mean urinary sodium excretion was 146 mmol/24h. A reduction of 28 mmol sodium excretion decreased SBP/DBP to 135.5 (\pm 13.0)/82.5 (\pm 12.8) ($P < 0.001$). After one month of no dietary advice, only in 48%, SBP was still \leq 140 mmHg.

CONCLUSION: Assessment of sodium intake using food records, 24h urine collections and probing questions to identify use of sodium containing supplements or drugs are essential for tailored advice targeted at sodium intake reduction. The results of the present study indicate that reduced sodium intake can lower BP after 4 weeks in unstable or uncontrolled hypertensive patients.

Nutrition Research and Practice 2015;9(2):180-185; doi:10.4162/nrp.2015.9.2.180; pISSN 1976-1457 eISSN 2005-6168

Keywords: Blood pressure, sodium, dietary, hypertension, salt reduction, primary care

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death worldwide [1]. About 54% of strokes and 47% of ischemic heart diseases worldwide are attributable to hypertension [2]. Furthermore, it has been estimated that 90% of the population aged between 55-65 years with normal blood pressure (BP) in developed countries will develop hypertension during their lifetime [3].

It was estimated that almost one third of BP-related deaths from coronary heart disease occur in pre-hypertensive individuals with a systolic BP (SBP) of 120 to 139 mmHg or a diastolic BP (DBP) of 80 to 89 mmHg [4]. Therefore, prevention, control and treatment of (pre) hypertension remain major public health priorities, which can be addressed in general practice as part of a broader overall population strategy. Many population-based intervention studies showed that even modest decreases in BP, could yield substantial reductions in CVD morbidity and mortality [1,3,5,6].

The American Heart Association (AHA) recommendations for

the prevention and treatment of hypertension emphasize non-pharmacological therapy, also termed "life-style modification" [7]. Large attention is given to a diet rich in vegetables, fish and fruits and low in fatty dairy products, as well as limiting salt intake and alcohol and maintaining a healthy body weight [7]. A large number of studies provide strong evidence of a causal link between high salt (sodium chloride) intake, hypertension and CVD [1,3,8,9]. The current sodium intake in most countries is 150 to 200 mmol per day (9 to 12 g of salt per day), while the World Health Organization's (WHO) recommendation is 100 mmol (5 g of salt per day) or less [1].

In the present study we assessed the sodium consumption (hidden in food, table salt, effervescent medication and dietary supplements) in patients with unstable or uncontrolled BP. The main objectives were 1) to quantify sodium consumption (hidden in processed foods, table salt, effervescent medication and dietary supplements) of patients with unstable or uncontrolled hypertension, 2) to assess the effect of a tailored dietary advice targeting sodium intake reduction on BP level in unstable or uncontrolled hypertensive patients, and 3) to

This research was supported by FWO Flanders (Fonds Wetenschappelijk Onderzoek Vlaanderen, Krediet aan navorsers-1519110N).

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Received: March 13, 2014, Revised: November 8, 2014, Accepted: November 12, 2014

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assess the acceptability of the patients and feasibility of this approach in a general practice setting.

SUBJECTS AND METHODS

Subjects

Patients were recruited during their visit at a general practice after screening by a general practitioner who reviewed inclusion and exclusion criteria using a standardized screening checklist (Table 1). Both male and female patients aged 50 years or older with frequent elevated BP with or without antihypertensive medication (unstable BP) and patients with uncontrolled, uncomplicated hypertension despite medication at pharmacologically effective doses (β -blocker, calcium channel blockers, diuretics, angiotensin receptor blockers and angiotensin-converting inhibitors) were eligible for inclusion. Patients should have an average SBP on two of the three previous visits of 140 mmHg (130 mmHg in diabetics) or more and an average DBP of 80-100 mmHg. All subjects had been on a stable antihypertensive regimen, including diuretics, for at least four weeks before enrollment and no medications were discontinued before evaluation. Exclusion criteria were heart failure, renal insufficiency, secondary hypertension or isolated diastolic hypertension, lactation/pregnancy, active malignancy, an active low sodium diet or changing the use of antihypertensive drugs or other medications that would affect BP (e.g. NSAID, oral contraceptive hormones, cortisone) four weeks prior to inclusion.

Study design and protocol

During the first visit, BP was measured (BP₁), oral and written study information was provided and patients completed a general questionnaire. In addition, height and weight were measured at inclusion and patients were discouraged to lose weight or change exercise habits during the study. BP was measured with a hand aneroid sphygmomanometer (Durashock DS55) with an appropriate size cuff after 5 minutes of rest with the standardized technique according to the AHA guidelines [5].

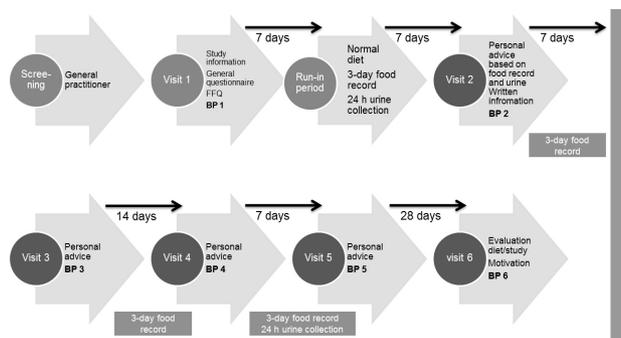


Fig. 1. Schematic overview of the study design. BP; Blood pressure

Two readings were made at each visit and the average was considered for analysis. Body weight and height were measured using a flat scale and a wall stadiometer respectively. Body mass index was calculated as weight (kg) / height (m)². Within seven days after the first visit, a run-in-period of one week was used to collect baseline data. Participants were instructed to follow their normal diet and completed a 3-day food record and supplied a 24-hour urine collection. In the following weeks, five additional visits to the general practice were scheduled (Fig. 1). During these visits, BP was measured (BP₂-BP₆). Each study visit lasted 15 to 30 minutes. The study visits were free of charge and patients were not paid for participation in the study. Based on the results of the food records and urinary sodium concentration collected during the run-in-period, patients were made aware of their dietary sources of sodium and received personalized advice to decrease sodium consumption during the second visit. This advice consisted of printed education materials such as written information about the relation between sodium and hypertension, nutritional charts and advice to reduce their sodium intake. Each patient intended to change his/her diet for at least 28 days taking into consideration the provided dietary advice. During the third and fourth visit, personal dietary advice was provided based on completed

Table 1. In- and exclusion criteria for enrollment in the clinical trial

Inclusion criteria	Exclusion criteria
An average SBP on 2 of the 3 previous visits of 140 mmHg or more (130 mmHg for diabetics) and an average DBP 80 to 100 mmHg	- An active sodium low diet - Changing the use of antihypertensive drugs or other medications that would affect BP for the past four weeks
At least 3 of the following criteria: 1. Using table salt 2. 2-3 times per week consumption of - prepared meals (butchery, warehouse, etc) - effervescent tablets - smoked fish/meat - stock block - broth - soup (self-made or condensed) - cookies - canned vegetables - vegetable juice - snacks (chips, cheese, nuts, etc) 3. Daily consumption of - cheese/cold cuts - (salted) butter/margarine	- heart failure (ejection fraction < 35) - renal insufficiency (creatinine clearance < 60 ml/min) - secondary hypertension - isolated systolic/diastolic hypertension - BP difference \geq 10 mmHg between left and right arm
Blood analysis (fasting glycaemia, creatinine, total cholesterol, high-density lipoprotein cholesterol) in the last 6 month	- lactation or pregnancy - active malignancy - impaired cognitive functioning - planning a smoke cessation

BP, Blood pressure; SBP, Systolic blood pressure; DBP, Diastolic blood pressure

3-day food records. After 28 days of dietary intervention, patients provided a second 24-hour urine collection and filled in an evaluation questionnaire to assess their viewpoint about the different procedures and methods used during the trial. One month later, during a sixth and final visit, BP was measured and after a closing session patients left the study. The field work took place between April 2010 and March 2011 in a general practice in Bruges, Belgium. The study protocol was approved as clinical trial by the ethical committee of the Ghent University Hospital (Belgian registration number: B67020108595, study number EC/2010/233) and all patients gave written informed consent.

General questionnaire

Patients were asked about their life-style (e.g. smoking status, physical activity), nutritional habits (e.g. supplement use, with special attention to effervescent tablets) and personal salt consumption (e.g. frequency of consumption of table salt, salt use during cooking). This questionnaire could be completed at home. Patients who returned incomplete questionnaires were contacted by phone to obtain any missing information.

3-day food record

A self-reported 3-day structured record was used to assess dietary sodium intake information. Patients were instructed on how to complete the food record, also a written example of a completed record day was included for future reference. Nutrition calculations were performed using the BECEL data entry software (version 5.0). The following food composition tables were used to perform nutrient calculations: the Belgian food composition tables NUBEL (NUBEL, 2004) and the Dutch food composition database NEVO (NEVO, 2001).

24-h urine collections

Patients were provided with two 2L containers and a 1L specimen to collect all produced urine during 24 hours. The collection started after voiding the first morning urine at awakening and continued for 24 hours including one last voiding of the bladder the next day. Sodium, chloride and potassium in urine were analyzed by ion-selective electrodes in the Modular ISE 900-module (Hitachi High-Technologies Corporation, Tokyo, Japan). Completeness of the 24-hour urine collections was assessed through the ratio creatinine (mg/day)/body mass (kg). Cut off values for a complete collection were < 25.2 and > 10.8 [10]. Creatinine concentration was analyzed by the Jaffé method in the Modular P-800 module (Hitachi High-Technologies Corporation, Tokyo, Japan). All samples were analyzed in by the same accredited laboratory.

Participant's evaluation

Using a set of multiple choice questions, the work-load and acceptance of the questionnaires, food records, urine collections, dietary advice and visits were scored using relative scores ranging from 'to a low degree', 'to some degree', 'to a fairly high degree' and 'to a high degree'. The awareness of the patients' own salt consumption and motivation to continue were also considered. The evaluation questionnaire was based upon questions asked in the evaluation questionnaire of the

EFCOVAL study [11]. The answers from this questionnaire, allowed us to make an inventory of the problems and barriers coinciding our sodium intervention. This information can be used to successfully implement this intervention in general practice.

Statistical analysis

Statistical tests were performed using SPSS 17.1 (Chicago, IL, USA). Baseline BP was calculated as the average of the measurement taken during the screening and run-in period (mean of BP₁ and BP₂). Difference in BP, sodium intake and urinary sodium excretion pre and post intervention was computed for every patient. Results are reported as means (\pm SD) and medians. A Paired-samples Wilcoxon Signed Rank Tests was used to compare sodium intake and urinary sodium excretions. Finally, a Friedman test was used to assess differences in SBP and DBP and post-hoc tests using Wilcoxon Signed Rank Test with Bonferroni correction was used to investigate pairwise differences. Unless stated different, a *P*-value of < 0.05 was used as a threshold for significance.

RESULTS

Subject characteristics

Twenty-five patients were enrolled, 16 females and 9 males. Two patients were withdrawn because they needed change in antihypertensive medication during the study period. The mean age was 64 years (ranging from 52 to 77 years). All baseline characteristics are presented in Table 2. Patients used on average one antihypertensive drug (ranging from 0 to 3).

Sodium intake and excretion

Mean sodium intake during normal diet was 161 mmol/day (9.3 g of salt) compared to 108.1 mmol/day (6.2 g of salt) during the reduced sodium diet ($Z = -3.194$, $P < 0.001$) (Table 3). Mean urinary sodium excretion during the run-in period was 146.4 mmol/day (8.4 g of salt) compared to 119 mmol/day (6.8 g of salt) after the intervention period ($Z = -2.008$, $P < 0.05$).

Blood pressure

The mean BP (mmHg) at baseline was 150.7 (± 9.5)/84.4 (± 5.6) (median 148.3/84.8). After four weeks of intervention, systolic and diastolic BP were reduced to 135.5 (± 13.0) mmHg (median 135 mmHg) and 82.5 (± 12.8) mmHg (median 80 mmHg) respectively ($\chi^2(4) = 34.505$, $P < 0.001$ for SBP and $\chi^2(4)$

Table 2. Baseline characteristics of patients who completed the study (n = 23)

	Mean/n	SD	Median
Age (yrs)	64 (52-77)	7.2	64
Male/female (n)	8/15		
Body mass index (kg/m ²)	27.4	3.3	27.2
No. of antihypertensive drugs (n)	1		1
AHT: uncontrolled [†] /unstable [‡] (n)	15/8		
Diabetes mellitus (n)	2		

BP indicates blood pressure

[†] Uncontrolled, uncomplicated hypertension despite medication at pharmacologically effective doses

[‡] Frequently elevated BP with or without antihypertensive medications

Table 3. Sodium intake, urinary sodium before and after the dietary intervention and blood pressure evolution during the trial (n = 23)

	Mean	SD	Median	P-value
Sodium intake (mmol/d)				
Before intervention (run-in period)	161.1	71.2	159.8	0.002*
After intervention (between visit 4 & 5)	108.1	33.8	113.7	
Urinary sodium excretion (mmol/d)				
Before intervention (run-in period)	146.4	57.8	129.0	0.045*
After intervention (between visit 4 & 5)	118.8	42.3	108.0	
Systolic blood pressure (mmHg)				
SBP baseline ((BP ₁ +BP ₂)/2)	150.7	9.5	148.3	< 0.001 [†]
SBP after 7 days diet (BP ₃)	143.5	11.9	142.3	
SBP after 14 days diet (BP ₄)	139.5	12.6	137.0	
SBP after 28 days diet (BP ₅)	135.5	13.0	135.0	
SBP after 30 days of no contact (BP ₆)	140.7	13.6	140.0	
Diastolic blood pressure (mmHg)				
DBP baseline ((BP ₁ +BP ₂)/2)	84.4	5.6	84.8	< 0.001 [†]
DBP after 7 days diet (BP ₃)	82.4	5.1	80.5	
DBP after 14 days diet (BP ₄)	81.0	6.0	80.0	
DBP after 28 days diet (BP ₅)	82.5	12.8	80.0	
DBP after 30 days of no contact (BP ₆)	82.8	7.0	81.5	

* Wilcoxon signed-rank test

[†] Friedman test

= 27.5, $P < 0.01$ for DBP). Post hoc analysis with Wilcoxon signed-rank tests was conducted with a Bonferroni correction applied, resulting in a significance level set at $P < 0.0125$. For SBP, there was a significant reduction at all visits compared to the baseline values ($P < 0.001$). For DBP, there were no significant differences between baseline BP and the third (BP₃) and sixth (BP₆) measurements ($Z = -2.332$, $P = 0.020$ and $Z = -2.876$, $P = 0.025$ respectively).

After one month of no advice at the practice center, 48% of the cases had a SBP < 140 mmHg compared to none before the start of the intervention (mean SBP 140.7 (\pm 13.6) mmHg).

Medication and sodium use

Before personalized advice, five patients used daily effervescent tablets (paracetamol (527 mg of sodium per tablet) and calcium supplements respectively) and three patients used food supplements or over the counter products that could affect BP (St. John's Wort, soda bicarbonate for pyrosis, multivitamin complexes) [5]. During personalized advice, a sodium poor alternative was introduced for the calcium supplements (only 10 mg of sodium per tablet) and paracetamol was substituted into tablets. St. John's Wort and the vitamins were discontinued and the use of soda bicarbonate was minimized. Seven patients were using table salt, but all succeeded discontinuing the use.

Participant's evaluation

After being informed of the results of the urine collection and food records, 15 patients said to be aware of their sodium consumption (5 to fairly high degree and 9 to some degree). All patients wanted to continue the reduced sodium diet in greater or lesser extent. Cited reasons to continue their reduced sodium diet included: taking less medication (n = 20) and a more healthy life-style (n = 10). Moreover, 19/23 would like to

have a yearly 24-hour urine collection to check their sodium intake and 22/23 would like to redo the trial in the future.

Seven persons felt constrained to some degree because of the diet and 13 persons experienced the diet as a task (3 to fairly high degree and 10 to some degree). The largest barriers were eating less cold cuts (especially smoked ham, bacon, salami), cheese, dressings, smoked fish, using less stock cubes and adding less salt to potatoes. Six patients mentioned that they experienced problems with the questionnaires and 3 with the food records. The 24-hour urine collection gave only in 3 cases a minor discomfort. All patients declared that their 24-hour urine collections were complete, which was confirmed with the ratio of urinary creatinine (mg/d) to body mass (kg) (data not shown). Nobody had problems with the frequency of visits.

DISCUSSION

To our knowledge, this is the first study to assess the effects of low dietary sodium ingestion in adults aged 50 years or older with unstable BP with or without antihypertensive medications and patients with unstable or uncontrolled BP despite medication in a general practice. This trial demonstrated that sodium reduction alone can favorably affect BP in hypertensive individuals. Sodium intake decreased from 161 mmol/24 h (9.3 g of salt) to 108 mmol/24 h (6.2 g of salt) and from a 146 mmol/24 h baseline mean sodium excretion, net decrease was 28 mmol/24 h after intervention. Corresponding net decreases in SBP/DBP were 15.2/1.9 mmHg ($P < 0.001$). After one month of no advice and no contacts, only in 48% of the cases, SBP was still \leq 140 mmHg.

A remarkable finding in the present trial is that the degree of BP reduction was much larger than reductions previously observed in unselected hypertensive subjects. For example, in a meta-analysis [6], a median reduction in urinary sodium of 78 mmol/day (4.6 g salt/day) in hypertensive individuals lowered SBP and DBP by 5.0 and 2.7 mmHg. The sodium reduction in our trial was considerably lower but even yielded a larger BP reduction. This suggests that patients with hypertension despite medications or with unstable BP are particularly sodium sensitive and it emphasizes the importance of low dietary sodium intake in the clinical management of hypertension [12].

The best way to study the dose-response relation between sodium intake and BP is to look how the BP responds to several levels of sodium intake. Only trials lasting more than four weeks can show the full effects of long-term reduction in sodium intake on BP [6]. In one meta-analysis [6], a median reduction in urinary sodium of 78 mmol/day (4.6 g salt/day) in hypertensive individuals lowered SBP and DBP by 5.0 and 2.7 mmHg (and 2.0 and 1.0 mmHg in normotensive). There are two well-controlled trials that studied three levels of salt intake, each for four weeks [13,14]. They all documented statistically significant, direct, progressive dose-response relationships. The first is a double-blind study in 19 patients with untreated essential hypertension. Effects of three different salt levels were tested. The BP decreased by 8/5 mmHg when salt intake, as judged by 24-hour urinary sodium, changed from 190 to 108 mmol/day

(11.1 to 6.3 g of salt/day), and the BP decreased by 8/4 mmHg when salt intake changed from 108 to 49 mmol/day (6.3 to 2.9 g salt/day) [13]. The largest trial is the DASH (Dietary Approaches to Stop Hypertension)-Sodium trial which tested the effects of three different sodium levels (low (a target of 2.9 g of salt/day), intermediate (a target of 5.8 g of salt/day) and high (a target of 8.9 g of salt/day)) on BP in two separate diets: the DASH (rich in fruits, vegetables, and low-fat dairy products) diet [15] and a control diet (the normal American diet). Both the type of diet and sodium reduction were effective in lowering BP. Comparing the high- with low-sodium groups, the differences in SBP were 6.7 mmHg among those on the control diet and 3.0 mmHg among those on the DASH diet. The corresponding differences in DBP were 3.5 and 1.6 mmHg respectively. These results show that BP can be lowered in either a diet that is typical in the US or the DASH diet by reducing the sodium intake [14].

Our study showed that BP decrease was time dependent. An explanation for this time-effect in both DBP and SBP reduction could be that during intermediate visits personal advice, tailored to the patients' situation, was provided so sodium intake reduction could be further improved with consecutive visits. Consequently, with lowering sodium intake in time, BP measurement readings also decreased. If we would have been able to collect 24h urine collections on all intermediate visits, urinary sodium excretion could be analyzed to support this hypothesis.

From the evaluation questionnaire, it could be concluded that none of the study patients had problems with the (frequency of) visits. A possible explanation is that the consultations were free of charge. A screening visit and the feedback and advice visit lasted minimum 30 minutes, while a regular visit in general practice takes about 15 minutes. This time-frame can be a potential barrier in future as well as the financial implications for the general practitioner. This problem could be overcome by referring patients to a skilled dietitian. The costs will increase for the patient, unless this is (partly) refunded by the health care insurance. This can be done by creating nomenclature numbers that attribute more time for the coaching of hypertensive patients. A remaining question for further research is whether patients are willing to pay extra for BP-coaching and if it will be cost-effective for the community. Still, even without the assistance of support personnel or programs, physicians should routinely encourage life-style modification [4,16,17]. The evaluation questionnaire also showed that the reduced sodium diet was well tolerated. However some patients experienced the diet as a burden, because they had to search for sodium poor alternatives for their bread fillings/toppings and had to get used to the less salty taste.

Generally, 24-hour urine collections are considered to be the most reliable method to evaluate sodium intake because most of the sodium a subject consumes is excreted via the urine [18]. However, this method is not readily conducted in general practice. Although our patients did not mind the urine collections, other studies have proposed predictive equations for population mean sodium intake based on single spot urine samples [19]. Nevertheless, none of the equations presented provided unbiased estimates of individual 24-h sodium excretion [19].

Screening for the use of supplements (and over the counter products) and effervescent tablets is important, since these products can affect BP [20]. As patients don't report spontaneously about the use of over the counter products (e.g. soda bicarbonate, St. John's Wort, multivitamins...) or effervescent tablets (e.g. calcium supplements, paracetamol), they will only be detected by active screening by providing examples.

A weakness of our study was the low sample size (23 patients). Estimation of usual sodium intake is labor intensive. Two 3-day food records might be insufficient to represent the usual dietary intake among patients, however, the observed decrease in sodium intake was also reflected in urinary excretion indicating that the food records are capable of detecting relative differences in sodium intake. The nutrition calculations were performed with databases based on NUBEL-95 and NEVO-96. It should be noted that the food composition data used for calculating sodium intake might also introduce some bias.

A control group with the same characteristics as the experimental group and not receiving the tailored dietary intervention could have been interesting to compare the salt intakes and BP reductions. Due to restrictions of available budget this was not performed.

The strengths of the present study include the general practice setting (an outpatient setting), its eight-week evaluation and the evaluation of several measurements of BP, which is important in the management of hypertension. Also, the urine collections were an important strength of this study and through the multiple follow-up visits, the trial was highly controlled. Despite the low sample size, there was a significant SBP reduction identified due to the reduced sodium diet ($P < 0.001$). An extra advantage is the use of food records so that sources of salt intake could be determined which allowed tailored intervention.

The current challenge in primary care is to reduce sodium intake of hypertensive patients and to make sodium restriction part of the overall treatment of hypertension. Assessment of sodium intake using food records, 24-hour urine collections and probing questions to identify use of sodium containing supplements or drugs are essential for tailored advice targeted at sodium intake reduction. This trial could serve as a basis for further study and development of a guideline for non-pharmacological management of hypertension in general practice. Further exploration for a good screening form, which is validated, and up-to date nutritional charts should be developed for use in a general practice.

This intervention trial shows that in a general practice setting significant reductions in both systolic and diastolic blood pressure can be achieved in patients with uncontrolled or unstable hypertension by lowering sodium intake. Participants' evaluation indicated good acceptance of this approach.

ACKNOWLEDGMENTS

The authors indebted to the trial participants and the staff of labo Nuytinck Brugge for their substantial commitment to this study. IH, KT & SDH designed the study protocol and instruments. KT conducted all the fieldwork. WDK & JA assisted in the development of the instruments and assisted in the

interpretation of the results. WDK and KT wrote the manuscript. IH and WDK conducted the statistical analyses. All authors have read and agreed upon the final version of the manuscript.

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