A randomized controlled trial evaluating a novel just-in-time contextual mobile application intervention to reduce sodium intake in hypertension: Design and rationale for the LowSalt4Life trial

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Abstract

Background: High sodium intake is a significant public health problem in the U.S. Interventions that lower sodium intake can decrease blood pressure and improve cardiovascular outcomes. Restaurants and grocery stores are prime targets for intervention with about 77% of all sodium intake in the average U.S. diet coming from processed and restaurant foods.

Objective: We propose that a mobile application intervention that promotes low sodium alternatives at grocery stores and restaurants will reduce dietary intake of sodium and improve confidence following a low sodium diet in hypertension (HTN).

Methods: This is a single center prospective open-label design, patients will be randomized to the mobile application or usual care for 8-week duration. Fifty patients greater than 18 years of age diagnosed with hypertension and on antihypertensive therapy for at least 3 months will be randomized in a 1:1 fashion stratified by gender. Study subjects will receive the mobile application, LowSalt4Life, or usual dietary advice for 8 weeks. LowSalt4Life provides a multifaceted intervention based on just-in-time contextual tailored messages at grocery stores and restaurants. The primary endpoint of is the change in estimated 24-hour urinary excretion of sodium from spot urine. Secondary outcomes include the change in sodium content of the food frequency questionnaire, confidence in following a low sodium diet, urine chloride and creatinine dipsticks and blood pressure.

Conclusion: This randomized controlled trial will test the efficacy of just-in-time contextual tailored messages via a novel mobile application 8-week intervention on urinary sodium excretion in patients with HTN. By testing a novel mobile application intervention, LowSalt4Life, we will address a critical evidence gap in the care of HTN patients. If effective, this intervention could be scaled to assess effects on blood pressure and cardiovascular events in HTN.

Clinical Trial Registration: ClinicalTrials.gov NCT03099343 (https://clinicaltrials.gov/ct2/show/NCT03099343)
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Introduction

High sodium intake is a significant public health problem in the U.S. In a meta-analysis of 177,025 patients, higher sodium consumption was associated with greater risk of stroke (RR 1.23, 95% CI 1.06-1.43) and a trend toward greater cardiovascular risk (RR 1.14, 95% CI 0.99-1.32).[1] Based on 2005 estimates, high dietary sodium is responsible for 102,000 deaths annually. Current federal guidelines advocate a daily sodium intake of less than 2,300 milligrams (mg) with further reduction to 1,500 mg in persons who are 51 and older and those of any age who are African American or have hypertension, diabetes, or chronic kidney disease, while the average sodium intake for all Americans ages 2 years and older is approximately 3,400 mg per day.[2]

Interventions that lower sodium intake can decrease blood pressure and improve cardiovascular outcomes. The sodium-restricted Dietary Approach to Stop Hypertension (DASH) eating plan reduced systolic blood pressure (SBP) by 7.1 mmHg in adults without HTN and 11.5 mmHg in adults with HTN.[3] In an analysis of the Trials of Hypertension Prevention, participants randomized to the low sodium interventions had a 25% lower long-term risk of cardiovascular disease (RR 0.75, 95% CI 0.57-0.99).[4] Following the 2003 introduction of a national salt reduction program in England, the 2011 national Health Survey estimated that population sodium intake decreased by ~550 mg per day.[5] During that same timeframe, population systolic blood pressure declined by 3±0.3/1.4±0.2 mmHg, which was accompanied by a 42% decrease in stroke mortality (p<0.001) and a 40% reduction in mortality due to ischemic heart disease by 40% (p<0.001). After extensive adjustment for other potential factors, dietary sodium reduction was identified as the most likely contributor.

From a policy perspective in the United States, reducing sodium intake by 1200 mg per day is projected to prevent 60,000 to 120,000 coronary heart disease events, 32,000 to 66,000
strokes, 54,000 to 99,000 myocardial infarctions and 44,000 to 99,000 deaths from any cause on an annual basis.[6] This reduction in sodium intake would also lead to $10 billion to $24 billion savings in the healthcare system. Restaurants and grocery stores are prime targets for intervention with about 77% of all sodium intake in the average U.S. diet coming from processed and restaurant foods.[7,8] Over half of Americans consume 1-3 restaurant meals per week and 23% consume ≥ 4 restaurant meals per week. The use of pre-packaged foods in home meal preparation has also increased substantially in recent years. The AHA guideline for the dietary approach to prevent and treat hypertension states, “any meaningful strategy to reduce salt intake must involve efforts of food manufacturers and restaurants.”[9]

Patients need assistance at grocery stores and restaurants to follow a low sodium diet. Over half of Americans consume 1-3 restaurant meals per week and 23% consume ≥ 4 restaurant meals per week. The use of pre-packaged foods in home meal preparation has also increased substantially in recent years. Restaurants and grocery stores are prime targets for intervention with about 77% of all sodium intake in the average U.S. diet coming from processed and restaurant foods.[7,8] In a recent study on consumer knowledge of sodium intake and food labeling, only half of the over 400 grocery store shoppers were able to accurately use sodium label information to choose low sodium food options.[10] The AHA guideline for the dietary approach to prevent and treat hypertension states, “any meaningful strategy to reduce salt intake must involve efforts of food manufacturers and restaurants.”[9]

Patients need assistance at grocery stores and restaurants to follow a low sodium diet. In a recent study on consumer knowledge of sodium intake and food labeling, only half of over 400 grocery store shoppers were able to accurately use sodium label information to choose low sodium food options.[10] We are currently witnessing broad social changes in the ways in which individuals expect to find and use information about their health. According to the Pew Research
Center’s Internet and American Life Project, nearly 90% of households now have at least basic Internet access and 70% of households actually have broad band service.[11] Use of mobile phones has nearly become ubiquitous (with 90% of individuals owning a mobile phone) with a growing majority of individuals (65%) using smartphones.[12] We believe that a mobile application that provides location-based, tailored messages can reduce dietary sodium intake and increase participant confidence in following a low sodium diet.

**Aim and hypothesis**

The LowSalt4Life Trial will study the effectiveness of a newly developed mobile application that provides mobile phone sensor based contextual push messages related to following a low sodium diet. We will randomize hypertensive patients to the mobile application or standard of care for 8 weeks. From baseline to 8 week follow up, we will assess the impact of the mobile application on dietary intake of sodium (measured by 24-hour dietary recall and 24-hour urinary sodium excretion) and confidence following a low sodium diet (measured by the Self-care Confidence in Following a Low-sodium Diet Scale). Our hypothesis is that the group randomized to the mobile application will demonstrate improvement in these measurements compared to the control group.

**Methods**

**Trial registration and funding**

This trial is registered at ClinicalTrials.gov (NCT03099343, received March 28, 2017) and is funded by the Agency for Healthcare Research and Quality (R21 HS024567). The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

**General design**

This is a single center prospective open-label designed clinical trial. Patients will be randomized to the mobile application or usual care in a 1:1 fashion. Patients randomized to the mobile application receive a 30-minute training session about the mobile application and be instructed to use the mobile application for 8 weeks.
**Study subjects**

Fifty patients greater than 18 years of age diagnosed with hypertension and on antihypertensive therapy for at least 3 months will be included. Patients will be excluded if they have chronic kidney disease (CKD), heart failure, systolic blood pressure > 180 mmHg, diastolic blood pressure > 110 mmHg, insulin-requiring diabetes mellitus, or are taking a loop diuretic, corticosteroid, or non-steroidal anti-inflammatory medication. CKD is defined as known kidney damage (structural or functional abnormalities) or estimated Glomerular Filtration Rate (eGFR) less than 60 mls/min/1.73m² (CKD Stage 3, 4, or 5). Initially consented participants will complete the Block Food Frequency Questionnaire (NutritionQuest),[13] and those with estimated baseline sodium intake less than 2300mg per day will be excluded before randomization.

**Intervention**

The intervention with the mobile application includes two parts: 1) just-in-time contextual tailored messages that promote behavior change when a patient enters a grocery store and restaurant; 2) the ability to easily scan and search for the foods at grocery stores and restaurants to find options containing lower sodium content.

Just-in-time contextual tailored messages are generated based on a multifaceted system. Initially, participants complete the Block Sodium Screener (NutritionQuest) and survey to assess their confidence in following a low sodium diet. The users then creates alternatives to the high 5 sodium containing foods and map these items to locations. In order to properly target messages, we use artificial intelligence algorithms that analyze the changes in mobile phones sensors (including Wi-Fi, Bluetooth, accelerometer, gyroscope, magnetometer, GPS). This takes each individual user’s past, recognizes his or her present context and predicts future activity. These predictions then alert the mobile application that the user is entering a grocery store or restaurant. Once the mobile application knows the user’s context, the user receives a tailored message based
on the context (grocery store or restaurant), their individual high 5 sodium containing foods (from the Block Sodium Screener) and their confidence following a low sodium diet. These messages are delivered by push notifications.

When a user taps on a just-in-time contextual tailored message, the application is opened to the appropriate section for their context, grocery store or restaurant. The grocery store section provides the user with the ability to scan Universal Product Codes (UPC) on food packaging or text search at the grocery store. The mobile application provides feedback on the sodium content of the food using a traffic light signal red (≥ 480mg per serving), yellow (≥ 120mg to < 480mg per serving) and green (< 120mg sodium per serving) to show consumers, at a glance, whether a product is high, medium or low in sodium.[14-16] In addition, the application will list lower sodium options in the same food category (See figure 2). In restaurants, users are presented 3 low sodium meals for that specific restaurant that were curated by the investigators and be able to search the restaurant’s menu with items order by sodium content, lowest to highest.

Outcomes

The Automated Self-administered 24-Hour Dietary Recall (ASA24), developed by the National Cancer Institute for dietary research, will be used to estimate dietary sodium intake during the trial. The ASA24 is an electronic 24-hour recall website that allows patients to self-administer the survey in a user-friendly manner. The ASA24 allows researchers to send the survey at defined intervals and automatically performs a dietary analysis by converting the dietary recall data into nutrient information based on the Food and Nutrient Database for Dietary Studies (FNDDS). In order to provide a detailed interview, the website includes a meal-based quick list, meal gap review, review of forgotten foods, a final review and a question about whether the day’s intake was usual or not. We will obtain the sodium content per day from the FNDDS-based sodium content analysis completed by the ASA24 website. The ASA24 will be administered at week 0 and 8 of the study. See figure 1 for details of outcomes.
The most widely used method for monitoring sodium intake is urinary sodium excretion measured by a 24-hour urine collection. Patients will be instructed to collect all urine voids for 24 hours and return them for analysis for sodium excretion. Twenty-four hour urine excretion will be collected at baseline and after 8 weeks. This method is not convenient (e.g. difficult to perform collections at work), and some participants may have incomplete urine collections. Because of these challenges, we will also explore other methods to estimate sodium excretion that would be more practical for use in larger trials.

The first method to estimate 24-hour urinary sodium excretion is spot morning urine excretion of sodium. The Kawasaki formula will be used to estimate 24-hour sodium urinary excretion from a fasting morning urine sample.[17] This approach has been proven to provide a valid estimate of sodium intake in several patient populations and in large-scale epidemiological studies.[18] Participants will be instructed to fast overnight, void in the morning and provide us a second morning urine sample on the day of the assessment. This measurement will be assessed at baseline and after 8 weeks of the study.

The second method for estimating 24-hour urinary sodium excretion is with a spot urine sample using chloride and creatinine dipsticks. The dipstick method has been validated in hypertensive patients and correlates well with 24-hour urinary sodium excretion (r=0.86).[19] The chloride dipstick is used as a surrogate for sodium excretion. The Quantab chloride dipstick (Hach, Loveland, CO) is placed in a container filled less than half way with urine. The chloride concentration is determined by observation of the change in color from brown to pale on the dipstick, which is the formation of silver chloride. The creatinine dipstick is similar to the chloride dipstick. The MultistixPro-10LS (Bayer, Elkhart, IN) is a dipstick that includes a color pad for creatinine after it is placed in a container filled with urine. The color pad turns from yellow to green to indicate the creatinine concentration. The predicted 24-hour urinary sodium
excretion is calculated based on the 24-hour creatinine concentration calculated using sex,
weight, race and age. This model has been validated and correlates highly (r=0.93) with 24-hour
measurements of creatinine.[20] This measurement will be performed at baseline and after week
2, 4, 6 and 8.

The Self-care Confidence in Following a Low-sodium Diet Scale will be used to measure
the patient’s confidence in following a low sodium diet. It assesses the patient’s confidence in the
ability to select and prepare low-sodium foods.[21] The tool consists of 7 items with 4 response
options per item. The items ask the patient to rate their level of confidence reading food labels,
choosing low sodium food during shopping, choosing low sodium foods at restaurants, cooking
low sodium foods, choosing low sodium foods at relatives or friends homes, estimating how
much sodium the patient eats each day and substituting low sodium foods for high sodium foods.
The 4 response options are assigned a score of 1-4 (1=Not confident, 2=Somewhat confident,
3=Very confident, 4=Extremely confident) then added for each question. Possible scores range
from 7 to 28 and the higher the score indicates greater confidence. The Self-care Confidence in
Following a Low-sodium Diet Scale will be administered at baseline and after week 8 of the
study.

Mobile device analytics will be collected to determine the extent to which the mobile
application was used. After a participant receives a push notification on entry to a grocery store
and restaurant, we will provide them with a push notification on exit asking them if they chose
any of our alternative options. We will also collect any scanned items to better understand the
specific foods that participants are seeking more information about. Blood pressure will be
monitored on a weekly basis by the patient and the results will be entered into the mobile
application and graphically represented.

Statistical approach
The primary endpoint this study is powered for is the estimated 24-hour urinary excretion of sodium from spot urine. Based on data in hypertension patients, we conservatively expect the 24-hour urinary excretion of sodium to decrease from 3400±1200 mg/24 hr to 2400±1200 mg/24 hr (35% reduction in sodium intake) in the mobile application group and a decrease from 3400±1200 mg/24 hr to 3300±1200 mg/24 hr in the usual care group.[22] A total sample size of 24 patients (12 in each group) and 32 patients (16 in each group) will provide 80% and 90% power, respectively, for a 35% reduction in sodium intake. In order to account for patients dropping out or incomplete follow up, we are enrolling a total sample of 50 patients (25 in each group). We will use a two-sided t-test to compare the change in each outcome over time in the mobile application group versus the usual care group. Other quantitative measures of sodium intake will be 24-hour urine collected urinary sodium excretion and estimated 24-hour urine sodium excretion estimated from the chloride and creatinine dipsticks will be analyzed using a two-sided t-test and repeated measures ANOVA, respectively.

Although not powered to determine the impact, other measures of the effectiveness of this intervention will be summarized and evaluated. The percent change in confidence following a low sodium diet will be analyzed using two-sided t-test. The change in blood pressure over time will be analyzed using repeated measures ANOVA.

Data safety and monitoring

A Data Safety and Monitoring Plan has been developed for this small intervention trial. Adverse events will be recorded from the day of first study related contact and reported to the institutional review board. All participants that experience an adverse event will be referred for treatment. No formal stopping rule for harm has been established for this pilot study, as it evaluates standard-of-care treatment in a low-risk population.

Discussion
The purpose of this randomized controlled trial is to test the efficacy of just-in-time contextual tailored messages via a mobile application for 8 weeks in patients with hypertension. This is a novel, first of a kind patient-centered decision support tool using geofencing technologies. We hypothesize that this intervention will improve sodium intake compared to the control group. By testing this novel approach, we could be developing a highly scalable mHealth model to help patients optimize their dietary habits in grocery stores and restaurants. If effective, the broader implications to other cardiovascular diseases and clinical outcomes should be explored.
Acknowledgments:

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Sources of Funding:

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Conflicts of Interest:

The authors have no conflict of interest related to this study.
References


Figure 1. Summary of outcomes in the trial.

- **Dietary assessment** - ASA24, FFQ with sodium screen
- **Self-care** - SCFLDS
- **Clinical measures** - 24-hr urinary sodium excretion, spot urinary excretion of sodium, dipstick chloride, dipstick creatinine, blood pressure

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Abbreviations – ASA24 = Automated Self-administered 24-Hour Dietary Recall, FFQ = Food Frequency Questionnaire, SCFLDS = Self-care Confidence in Following a Low-sodium Diet Scale
Figure 2. Example of the grocery store result screen for tomato soup using a traffic light signal.