

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

## An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China - Protocol of a cluster randomised controlled trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-027793
Article Type:	Protocol
Date Submitted by the Author:	07-Nov-2018
Complete List of Authors:	<p>He, Feng; Queen Mary University of London, Wolfson Institute of Preventive Medicine            Zhang, Puhong ; The George Institute at Peking University Health Science Center; University of New South Wales, Faculty of Medicine            Luo, Rong; The George Institute for Global Health at Peking University Health Science Center            Li, Yuan; The George Institute for Global Health, Peking University Health Science Centre; University of New South Wales, Faculty of Medicine            Chen, Fengge; Shijiazhuang Center for Disease Control and Prevention            Zhao, Yuhong; Changan Center for Disease Control and Prevention            Zhao, Wei; Shijiazhuang Center for Disease Control and Prevention            Li, Daoxi; Luzhou Center for Disease Control and Prevention            Chen, Hang; Luzhou Center for Disease Control and Prevention            Wu, Tianyong; Luzhou Center for Disease Control and Prevention            Yao, Jianyun; Yueyang Center for Disease Control and Prevention            Li, Jinbao; Yueyang Center for Disease Control and Prevention            Zhou, Siyuan; Yueyang Center for Disease Control and Prevention            Li , Xian; The George Institute for Global Health at Peking University Health Science Center            Wang, Changqiong; Queen Mary University of London, Wolfson Institute of Preventive Medicine            MacGregor, Graham; Queen Mary University of London, Wolfson Institute of Preventive Medicine</p>
Keywords:	Salt Reduction, Schoolchildren and Families, m-Health, Randomised Controlled Trial

SCHOLARONE™  
Manuscripts

**An app-based programme to reinforce and maintain lower salt intake (AppSalt) in  
schoolchildren and their families in China  
Protocol of a cluster randomised controlled trial**

**Feng J He,<sup>1\*</sup> Puhong Zhang,<sup>2,3\*</sup> Rong Luo,<sup>2</sup> Yuan Li,<sup>2,3</sup> Fengge Chen,<sup>4</sup> Yuhong Zhao,<sup>5</sup>  
Wei Zhao,<sup>4</sup> Daoxi Li,<sup>6</sup> Hang Chen,<sup>6</sup> Tianyong Wu,<sup>6</sup> Jianyun Yao,<sup>7</sup> Jinbao Li,<sup>7</sup> Siyuan  
Zhou,<sup>7</sup> Xian Li,<sup>2,3</sup> Changqiong Wang,<sup>1</sup> Graham A MacGregor<sup>1</sup>**

<sup>1</sup> Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine & Dentistry, Queen Mary University of London, UK

<sup>2</sup> The George Institute for Global Health at Peking University Health Science Center, China.

<sup>3</sup> Faculty of Medicine, University of New South Wales, Australia

<sup>4</sup> Shijiazhuang Center for Disease Control and Prevention, Hebei Province, China

<sup>5</sup> Changan Center for Disease Control and Prevention, Shijiazhuang, Hebei Province, China

<sup>6</sup> Luzhou Center for Disease Control and Prevention, Sichuan Province, China

<sup>7</sup> Yueyang Center for Disease Control and Prevention, Hunan Province, China

**\*Joint first author**

Correspondence to:

Professor Feng J He

Wolfson Institute of Preventive Medicine,

Barts and The London School of Medicine & Dentistry,

Queen Mary University of London,

Charterhouse Square,

London EC1M 6BQ.

Tel: 44 (0)20 7882 6266

Fax: 44 (0)20 7882 6270

E-mail: [f.he@qmul.ac.uk](mailto:f.he@qmul.ac.uk)

Professor Puhong Zhang

The George Institute for Global Health at Peking University Health Science Center,

Level 18, Tower B, Horizon Tower, No. 6 Zhichun Rd,

Haidian District | Beijing, 100088 P.R. China

Tel: +86 10 8280 0577 ext 512

Fax: +8610 8280 0177

E-mail: [zpuhong@georgeinstitute.org.cn](mailto:zpuhong@georgeinstitute.org.cn)

## ABSTRACT

**Introduction:** Salt intake is very high in China, with  $\approx 80\%$  being added by the consumers. It is difficult to reduce salt in such settings. Our previous study (School-EduSalt, School based Education programme to reduce Salt) demonstrated that educating schoolchildren who then instructed their families to reduce the amount of salt used at home, is effective in lowering salt intake in both children and adults. Our team also developed an app called “KnowSalt” which could help individuals to estimate their salt intake and the major sources of salt in the diet. Building upon School-EduSalt and KnowSalt, we propose to develop a new app (AppSalt) focusing on salt reduction through education, target setting, monitoring, evaluation, decision support and management, to achieve a progressive lower salt intake for long term. To evaluate the effectiveness of the AppSalt programme, we will carry out a cluster randomised controlled trial.

**Methods and analysis:** We will recruit 54 primary schools from urban and rural areas of 3 provinces in China. 540 children aged  $\approx 8$  years and 1080 adult family members will be randomly selected for evaluation. After baseline assessment, schools will be randomly allocated to either the intervention or control group. Children in the intervention group will be taught, with support of AppSalt, about salt reduction and assigned homework to get the whole family involved in the activities to reduce salt consumption. The duration of the intervention is two school terms (i.e. 1 year). The primary outcome is the difference between the intervention and control group in the change of salt intake as measured by 24-h urinary sodium.

**Ethics and dissemination:** The study has been approved by Queen Mary Research Ethics Committee and Peking University Health Science Centre IRB. Results will be disseminated through presentations, publications and social media.

**Trial Registration:** Registered on Chinese Clinical Trial Registry, ChiCTR1800017553.

### Strengths and limitations of this study

- Our study will develop a new approach to reducing salt intake, i.e. by the use of an innovative smartphone application through estimation of salt intake, education, target setting and monitoring, decision support and management, to achieve a sustainable progressive lower salt intake for long term.
- The study covers a wide range of the population including children and adults in diverse settings, e.g. rural and urban, north, central and south China, the results should be generally applicable to the whole Chinese population.
- The study will be carried out in China only. However, the method could be adapted by many other developing countries where most of the salt in the diet is added by the consumers.

## INTRODUCTION

Cardiovascular disease (CVD, i.e. strokes, heart attacks and heart failure) is the leading cause of death and disability worldwide. Approximately 80% of CVD deaths occur in developing countries.<sup>1</sup> Blood pressure (BP) throughout its range starting at 115/75 mmHg, is an important risk factor for CVD, accounting for 62% of strokes and 49% of coronary heart disease.<sup>2</sup> High salt intake is the major cause of raised BP,<sup>3</sup> responsible for about half of the disease burden attributable to BP. Randomised trials have demonstrated that a reduction in salt intake lowers BP in both hypertensive and normotensive individuals, in both adults and children.<sup>4,5,6</sup> There is also compelling evidence that a lower salt intake is associated with a reduced risk of CVD and total mortality.<sup>7,8</sup> Indeed, salt reduction is one of the most cost-effective measures to prevent hypertension and CVD.<sup>3,9</sup> The World Health Organisation (WHO) has recommended a 30% reduction in population salt intake by 2025, and also set a target of <5 g/d for all adults and lower levels for children.<sup>10</sup> Many developed countries have started salt reduction initiatives.<sup>11</sup> Salt intake has been successfully reduced in Finland and the UK, accompanied by falls in population BP and CVD mortality.<sup>12</sup> Developing countries, however, are lagging behind.

China is the largest developing country with one fifth of the world population. Salt intake in China is very high with an average of 12-14 g/d in adults<sup>13-15</sup> and 7 g/d in 10 years-old children,<sup>13</sup> and in some rural areas of northern China, salt intake could be as high as 18-20 g/d in adults. Approximately 80% of the salt in the Chinese diet is added by the consumers during cooking or in sauces.<sup>16</sup> It is extremely challenging to reduce salt intake in such settings due to the difficulty in changing individuals' dietary behaviours. Our previous study (School-EduSalt) has developed a novel and effective approach to reducing salt intake in northern China.<sup>13</sup> In School-EduSalt, primary schoolchildren aged ≈10 years were educated about the harmful effects of salt on health and how to reduce intake during the school's usual

1  
2  
3 health education lessons. Children then instructed their whole family to reduce salt. The  
4  
5 results showed that, over one school term ( $\approx 3.5$  months), salt intake was reduced by  $\approx 25\%$  in  
6  
7 both children and adults as measured by 24h urinary sodium excretion. The reduction in salt  
8  
9 intake led to a significant fall in systolic BP of 2.3 mmHg in adults.<sup>13</sup> It was estimated that, if  
10  
11 School-EduSalt was implemented and sustained, it would prevent  $\approx 400,000$  stroke and heart  
12  
13 attack events per year in China.  
14

15  
16  
17 Previous studies have shown that salt reduction achieved by dietary advice attenuates over  
18  
19 time and maintaining a lower salt intake long-term remains a challenge.<sup>4</sup> The School-EduSalt  
20  
21 was successful over one school term of  $\approx 3.5$  months. The question is how to continue and  
22  
23 reinforce the salt reduction education to achieve a sustainable, progressive lower intake to  
24  
25 achieve the WHO's target.  
26  
27

28  
29 Mobile technology is increasingly used in health education.<sup>17</sup> Recent studies have suggested  
30  
31 that game-based intervention has great potential in changing behaviours due to the popularity  
32  
33 of gaming.<sup>18</sup> China has the largest and fastest growing mobile internet population with 802  
34  
35 million people using internet and mobile phone penetration reached 98.3% of the population  
36  
37 by June 2018.<sup>19</sup> Mobile-based decision support system has been shown to be effective in  
38  
39 increasing medication use in individuals with high CVD risk in rural China.<sup>20</sup> Our team have  
40  
41 recently developed a smartphone app (KnowSalt) which can be used by individuals to  
42  
43 estimate their salt intake and the major sources of salt in the diet. The methodology  
44  
45 underpinning KnowSalt app had been validated in a pilot study in primary schoolchildren and  
46  
47 their families.<sup>21</sup>  
48  
49

50  
51 Our proposed study building upon School-EduSalt and KnowSalt app will develop an  
52  
53 innovative smartphone application focusing on salt reduction (AppSalt) through functional  
54  
55 modules of education, evaluation, target setting and monitoring, decision support and  
56  
57 management, with the aim of reinforcing School-EduSalt to achieve a progressive lower salt  
58  
59  
60

intake for long term. To evaluate the effectiveness and cost-effectiveness of the AppSalt programme, we will carry out a cluster randomised trial.

## METHODS AND ANALYSIS

The project consists of 2 phases: (1) Developing AppSalt platform; (2) Carrying out a cluster randomised controlled trial.

### Phase 1 – Development of AppSalt platform

AppSalt platform comprises a smartphone app named AppSalt (family end) and a WeChat mini app (teacher end). The AppSalt consists of 4 core procedures (i.e. Education, Evaluation, Decision support and Reminding) and 3 supportive modules (i.e. Competition & Award, Supervision & Communication and SaltSwitch) (Figure 1).

#### Core procedures

1. “Education” is to educate the families about the harmful effects of salt on health and how to reduce salt intake. Nine lessons are developed, each starting with a 10-min lecture on salt reduction, followed by a few questions to test whether the families have understood the content. At the same time, the questions and answers will re-enforce the key messages. Following each lesson, the families are required to complete a practical session which is designed to help the families to prepare foods with reduced salt at home and to choose lower-salt foods when shopping.
2. “Evaluation” is to estimate salt intake and the main sources of salt for every member of the family. After completing a simple questionnaire, the family will be provided with the information on the top 3 contributors of salt in their diet. This will help the family make a decision on how to effectively reduce salt intake.
3. “Decision Support” will set target for total salt intake and specific targets for top 3 contributors. Lower-salt sample recipes and specific measures, e.g. reducing the amount of

1  
2  
3 salt used during cooking by 50%, will be recommended. The recommended measures will be  
4  
5 customised as an action plan.  
6

7  
8 4. “Reminding” will remind the family how far their salt intakes are away from the targets set  
9  
10 and highlight further action plans.  
11

### 12 *Supportive modules*

13  
14  
15 1. The “Competition & Award” module will help the participants to find out their own  
16  
17 ranking position assessed by salt intake level and extent of salt reduction among all  
18  
19 participants (NB: only their own ranking will be displayed and other participants’ ranking  
20  
21 will not be revealed to them). The family with lowest salt intake and the family who achieve  
22  
23 the greatest reduction in salt intake, will be the winners of competition. They will be awarded  
24  
25 an honorary title like “Salt Reduction Pacesetter” and get a small gift.  
26  
27

28  
29 2. The “Supervision & Communication” module will be the place to exchange experience and  
30  
31 knowledge among the participants. The teachers will use this function to announce  
32  
33 instructions, newsletters, and school canteen menus, as well as providing answers to any  
34  
35 queries.  
36

37  
38 3. The “SaltSwitch” module will help the participants to choose pre-packaged foods with  
39  
40 lower salt. “SaltSwitch”, as a sub-function of “FoodSwitch”<sup>22</sup> integrated into the AppSalt, has  
41  
42 a database of over 50,000 pre-packaged food collected by the George Institute China. By  
43  
44 scanning the barcode of the pre-packaged foods, the “SaltSwitch” will provide information  
45  
46 on salt/sodium content and compare it with other similar products based on products’  
47  
48 labelling. This will help the participants to choose food with lower salt.  
49

50  
51 AppSalt will be installed in the smartphone of adult family members. Children are only  
52  
53 allowed to use AppSalt accompanied by their adult family members to complete AppSalt  
54  
55 core procedures as required. New features with a variety of presentation styles on salt  
56  
57 reduction education will be added to keep the programme attractive to the participants.  
58  
59  
60

1  
2  
3 The school teachers will use the WeChat mini app (teacher end) to send messages to the  
4 families, provide timely feedback to any queries, and check families' progress and ensure all  
5 families complete the procedures in time. The teachers will also report any issues to the site  
6 managers and the research team where appropriate.  
7  
8  
9  
10  
11  
12

## 13 **Phase 2 — Cluster randomised controlled trial (RCT)**

14  
15 To test the effectiveness and cost-effectiveness of the AppSalt programme, we will carry out  
16 a cluster randomised controlled trial (Figure 2).  
17  
18  
19

### 20 ***Study Setting and participants***

21  
22 Considering the geographical location, economic level and dietary habit, our study will be  
23 undertaken in selected primary schools from urban and rural areas of 3 provinces in northern  
24 (Hebei), central (Sichuan) and southern (Hunan) China.  
25  
26  
27  
28

29 To recruit schools, we will firstly contact the local education authority through local health  
30 Bureau or Centre for Disease Control (CDC) to gain their opinion, support and approval. We  
31 will then contact schools' head teachers to request their participation in the study. In each  
32 school, there are 6 grades with age ranging from 7 to 12 years and our study will be carried  
33 out in grade 3 (age ≈8 years). Head-teacher will choose one class whose teacher in charge is  
34 willing to collaborate with the researchers. From each class, we will randomly select 10  
35 children and 20 adult family members (i.e. 1 child and 2 adults per family) for evaluation.  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45

46 The inclusion criteria are (1) Children and their adult family members have to eat homemade  
47 meals at least four times per week; (2) One of the adults in the family has a mobile device  
48 with access to Internet; (3) If more than 2 adults in one family agree to take part in the  
49 evaluation, we will select two in the order of grandparents, parents, uncles and aunts; (4)  
50 Participants have been local residents for over 6 months, without moving plan within 24  
51 months. We will exclude the individuals who cannot or refuse to collect 24-hour urine.  
52  
53  
54  
55  
56  
57  
58

### 59 ***Randomisation***

1  
2  
3 Schools (clusters) will be randomly assigned (1:1) to either the intervention or the control  
4  
5 group. Randomisation will be stratified by the location of schools (i.e. south or north, urban  
6  
7 or rural) and the size of the class. The randomisation will be carried out using computer  
8  
9 generated random number by an independent statistician who is blind to the identity of the  
10  
11 schools. The randomisation will take place after the completion of baseline assessments.  
12  
13  
14 Therefore, the participants, school-teachers and local investigators who undertake recruitment  
15  
16 and data collection, will be unaware of the allocation until the point prior to the  
17  
18 commencement of the intervention.  
19  
20

### 21 ***Intervention***

22  
23 Our goal is to lower salt intake (measured by 24h urinary sodium) by a minimum of 15%  
24  
25 ( $\approx 1.5$ g salt) for both children and their families. To achieve this goal, a strategy towards a  
26  
27 50% reduction should be implemented. To make the decision-support algorithm simple in the  
28  
29 AppSalt, we will set targets for the top 3 contributors to salt intake, such as cooking salt, soy  
30  
31 sauce, pickles. Targets and priority actions will be individualised depending on the sources of  
32  
33 salt in the individual's diet which will be provided by AppSalt.  
34  
35  
36

37  
38 In the intervention group, the AppSalt intervention package will be delivered to all children  
39  
40 and their families in the whole class, despite only 10 children and their families being  
41  
42 randomly selected for evaluation. Children's adult family members will be authorized to  
43  
44 install and operate the AppSalt programme, while children will be assigned homework to get  
45  
46 the whole family to reduce salt with the support of AppSalt. Children's homework will  
47  
48 include: (a) helping the family to set salt reduction target and reminding the whole family of  
49  
50 this target on a regular basis; (b) getting the whole family involved in salt reduction activities  
51  
52 and persuading the person who does the cooking to reduce the amount of salt used during  
53  
54 food preparations at home; (c) working with their family members to complete the AppSalt  
55  
56 core procedures, including education, evaluation, target setting and monitoring. In addition to  
57  
58  
59  
60

1  
2  
3 the online lessons, school teachers will organise three face-to-face seminars for both children  
4 and adults during the one-year intervention period. This will provide an opportunity for the  
5 participants to share experiences and discuss challenges and solutions. These seminars will be  
6  
7 integrated into the schools' routine parent meetings.  
8  
9

10  
11 Trained teachers will provide guidance on AppSalt utilisation, assign and check children's  
12 homework including monitoring the progress of salt reduction. They will also create salt-  
13 reduction environment, e.g. putting up posters in classroom, campus and canteens. The  
14 AppSalt will be activated at the beginning of the intervention for all families in the  
15 intervention group. Throughout the study, participants will receive salt reduction messages  
16 and newsletters via AppSalt on a monthly basis. Participants will be encouraged to use  
17 AppSalt and communicate with the teachers and other families to share experiences. The  
18 mandatory tasks for the participants include completing the online lessons and the related  
19 Q&As (Questions and Answers) at baseline and every month thereafter, and completing the  
20 core procedures, i.e. salt intake estimation, target setting at baseline and every 3 months  
21 thereafter. In addition to the mandatory tasks, the participants are encouraged to repeat the  
22 core procedures as often as they wish, in order to monitor their progress and achieve  
23 progressive reductions in salt intake. Based on the progress monitored from the WeChat mini  
24 app, the teachers will remind children that they should complete their homework which is to  
25 help the family complete the AppSalt procedures in time and to instruct the family members  
26 to reduce salt to the target.  
27  
28

29  
30 The records from AppSalt, e.g. salt intake and how far the intake is different from the target  
31 set, will be used to monitor compliance. During follow-up, the participant who fails to  
32 achieve the salt reduction target, will be sent a specially designed message via AppSalt and a  
33 letter to the child through his/her teacher to remind the family of the salt reduction target.  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 The intervention duration is 2 school terms, i.e. 1 year. After the trial is completed, we will  
4 introduce the AppSalt to all schoolchildren including those in the control group.  
5  
6

### 7 ***Sample size calculation***

8  
9  
10 Based on the School-EduSalt trial,<sup>13</sup> assuming a standard deviation of 24-hour sodium  
11 excretion is 85mmol/day, and intraclass correlation coefficient (ICC) is 0.05, we estimate that  
12 a sample size of 540 children from 54 schools (18 primary schools from each province in  
13 both urban and rural area, and 10 children per school) would provide a power of 80% (with a  
14 two-sided alpha=0.05) to detect a difference in mean 24-hour urinary sodium  $\geq 28$ mmol/day  
15 (1.5 g/d salt) between intervention and control group, allowing for a 20% drop-out rate of  
16 participants. We aim to recruit 2 adults per family, therefore 1080 adults will be recruited into  
17 the study for evaluation.  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27

### 28 ***Outcome measures***

29  
30  
31 The primary outcome is the difference between the intervention and control group in the  
32 change of salt intake as measured by 24-hour urinary sodium from baseline to the end of the  
33 trial. The secondary outcome is the difference between the two groups in the change of  
34 systolic BP for adults.  
35  
36  
37  
38  
39

### 40 ***Outcome assessments***

41  
42 All outcome measurements and assessments will be carried out at baseline and at the end of  
43 the trial in exactly the same way in all schools for all participants, irrespective of their  
44 assignment to intervention or control group.  
45  
46  
47  
48

49 We will carry out two consecutive 24-hour urine collections using the stringent protocol  
50 which we developed in the School-EduSalt study.<sup>13</sup> The participants will be carefully  
51 instructed on how to accurately collect 24h urine by trained research staff. On the first day,  
52 the participants will be asked to come to the schools. The researchers will ask the participants  
53 to empty bladder and discard the urine. The researchers will record the start time and date of  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 the 24h urine collection. They will then give the participants the collection equipment  
4 including containers and collection aids such as carrier bags. The participants will be  
5 instructed to collect all subsequent urine voids over the next 24h period. On the second day at  
6 the same time, the participants will be asked to bring the urine collection bottles back to the  
7 schools and they will be asked to pass the last urine into the container. The researchers will  
8 record the finish time of the first 24h urine collection. The researchers will then give the  
9 participants the collection equipment for the second 24h urine collection and repeat the  
10 process. During the 24h urine collection period, the participants will be asked to take spare  
11 urine containers with them when they go to school or work. Spare collection equipment will  
12 also be available in the schools, in case children forget to bring them. In the case that the  
13 participant misses one or more urine voids or spillage occurs, the participant will be asked to  
14 do a further 24-hour urine collection. The 24-hour urine collections will be made either at  
15 weekdays or at weekends. For each participant, the 24-hour urines will be collected on the  
16 same days of the week for baseline and for follow-up at the end of the trial.

17 We will measure urine volume, sodium, potassium and creatinine. Ion-selective electrode  
18 method will be used for sodium and potassium analysis and enzymatic method for creatinine  
19 assay. 24-hour urinary creatinine together with urine volume will be used to determine if the  
20 collection is likely to be complete. The biochemist who performs the measurements of  
21 urinary electrolytes will not be told which group the participant is allocated.

22 In addition to 24-hour urine collection, we will measure BP and heart rate using a validated  
23 automatic machine with the appropriate size of cuff. Three readings will be taken in the right  
24 arm at 1-2-minute intervals at sitting position after the participant has had 10 minutes' rest in  
25 a quiet room. Body weight, height and waist circumference will also be measured. Survey on  
26 Knowledge, Attitude and Practice (KAP) related to salt will be completed via questionnaire.

## Data collection, management and analysis

### *Data collection*

Our study will have two major data outputs. One is the “App Data” generated automatically when the AppSalt platform is used by the families in intervention group to support salt reduction. The App Data include information on demographic characteristics, eating habits, amount and sources of salt in the diet, as well as information (or App logs) on the use of AppSalt. The other data output is the “RCT Data” which is generated by both intervention and control groups during the RCT. The RCT Data will be collected through a specially designed mobile device based electronic data capture system (mEDC) by well-trained field investigators. The mEDC has been validated and widely used in other clinical trials<sup>23</sup> with more advantages on process and quality control compared with traditional EDC. The RCT data include information on demographics, social-economic information, KAP, measurement of height, weight, waist circumference, BP, heart rate, 24-h urine volume and electrolytes, as well as information on costs for all the components of intervention conducted through the AppSalt programme.

### *Data management*

All cleaned and locked datasets together with the study design, questionnaire, code list and definition of database and variables will be stored with a unique ID number attached but no personal identifiers in The George Institute China (TGI), following an established standard operating procedure for data security. To guarantee the data security, the mobile app developer (i.e. the IT team at Beihang University) must follow the “Mobile Application Information Service Regulation” issued by the Cyberspace Administration of China in 2016. Although personal data are accessible to app developer, disclosure of such information is prohibited. In addition to the development and maintenance of the AppSalt and mEDC, IT

1  
2  
3 team will also provide data management service during the study to guarantee the safety,  
4 integrity and proper use of the data collected through AppSalt and mEDC.  
5  
6

### 7 8 ***Statistical Analysis*** 9

10 The effect of the intervention on the outcomes will be tested using linear mixed models with  
11 participants nested within family units and families nested within schools. We will include  
12 group (intervention, control), time (baseline, end of trial), and time×group interaction, with  
13 the time×group interaction term indicating differential change by group from baseline to the  
14 end of the trial. We will adjust for the stratification variables at randomization and potential  
15 confounding variables. Various sensitivity analyses will be carried out to examine the  
16 robustness of the conclusions of the primary analysis. Results will be reported as mean, SD,  
17 SE, and 95% confidence interval when appropriate. All analyses will be two sided and  
18 P<0.05 is considered significant. SAS will be used for the analyses.  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31

### 32 ***Economic evaluation and process evaluation*** 33

34 Economic evaluations will be carried out from health sector perspective to compare the m-  
35 Health strategy with usual care and it will entail two components: a trial-based economic  
36 evaluation and a modelled economic evaluation of long-term costs and outcomes.  
37  
38

39 Intervention costs will include those in running the programme but exclude any research and  
40 development costs. The trial-based economic evaluation will be assessed initially in terms of  
41 incremental cost per unit reduction in salt intake and systolic BP. The modelled economic  
42 evaluation with discounting will examine the cost, survival, quality of life over lifetime, via  
43 capturing various health states (including death and CVD events) to estimate incremental cost  
44 per life year saved and cost per Quality-Adjusted Life Year (QALY) gained. The transition  
45 probabilities across health states and costs attached to various health states will be based on  
46 literatures and the long-term effects of salt reduction or systolic BP will be derived from the  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 trial findings and/or literatures of disease progression. Sensitivity analyses will be carried out  
4  
5 to estimate uncertainty about the primary findings associated with varying key parameters.  
6  
7

8 Mixed-method process evaluations will be conducted during and at the end of the study using  
9  
10 data from AppSalt, key informant interviews with researchers and teachers, and focus groups  
11  
12 interviews with participants. This will help understand the barriers and facilitators of the  
13  
14 intervention as well as the acceptance and effect of the AppSalt programme.  
15  
16

### 17 **Project status and timelines**

18  
19 Recruitment of schools and participants started in September 2018. Baseline assessments are  
20  
21 underway with one province (Hebei) completed and the other two provinces are to complete  
22  
23 baseline surveys by November 2018. As the intervention duration is one year, the final  
24  
25 follow-up assessments will be carried out between September and November 2019.  
26  
27

### 28 **Expected outcome and potential impact**

29  
30 The study will provide a novel, feasible and effective approach to achieving sustainable  
31  
32 reduction in salt intake in both children and adults. The use of AppSalt platform in delivering  
33  
34 health education is particularly advantageous over the traditional school education method in  
35  
36 terms of reducing the burden on teaching staff. Furthermore, our study covers a wide range of  
37  
38 the populations (children and adults, rural and urban, north and south), the results should  
39  
40 therefore be generally applicable to the whole country. If the programme is implemented and  
41  
42 sustained across China, it will reduce population salt intake and thereby prevent hundreds of  
43  
44 thousands of strokes, heart attacks and heart failure each year, and lead to major cost-savings  
45  
46 to individuals, their families and the health service.  
47  
48

49  
50 Although our study will be carried out in China, the AppSalt programme could potentially be  
51  
52 adapted by many other countries. Additionally, our model on salt reduction could possibly be  
53  
54 adapted for other dietary and lifestyle changes to prevent CVD and other non-communicable  
55  
56 diseases, which will have major public health implications.  
57  
58  
59  
60

## ETHICS AND DISSEMINATION

The study has been approved by Queen Mary Research Ethics Committee in the UK (QMERC2018/13) and Peking University IRB in China (IRB00001052-18051). Written consent will be obtained from all participants according to well-established practices. For children, participant assent and parental written consent will be obtained. All participants will be free to discontinue their participation at any time with no explanation required.

The findings of this study will be disseminated widely through conference presentations, peer-reviewed publications, press release and social media. Furthermore, the results will be disseminated worldwide through World Action on Salt and Health<sup>24</sup> which is a global non-profit organisation of 600 members from 100 countries with the mission to improve the health of populations by reducing salt intake.

**Authors' contributions:** FJH and PZ conceived the project and contribute equally to the work. FJH, PZ, YL and RL designed the study. All authors contributed to the development of the AppSalt intervention and evaluation. FH wrote the first draft of the manuscript. All authors contributed to the refinement of the study protocol and approved the final manuscript.

**Funding statement:** This work is supported by the National Institute of Health Research using Official Development Assistance (ODA) funding (16/136/77). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

**Competing interests:** FJH is a member of Consensus Action on Salt & Health (CASH) and World Action on Salt & Health (WASH). Both CASH and WASH are non-profit charitable organisations and FJH does not receive any financial support from CASH or WASH. GAM is Chairman of Blood Pressure UK (BPUK), Chairman of CASH and Chairman of WASH. BPUK, CASH and WASH are non-profit charitable organisations. GAM does not receive any financial support from any of these organisations. Other authors declare no competing interests.

**Word Count:** 3894 words.

## References

1. Lawes CM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. *Lancet* 2008;371:1513-8.
2. World Health Report 2002: Reducing risks, promoting healthy life. Geneva, Switzerland: World Health Organisation, 2002. [www.who.int/whr/2002](http://www.who.int/whr/2002).
3. He FJ, MacGregor GA. Reducing population salt intake worldwide: from evidence to implementation. *Prog Cardiovasc Dis* 2010;52:363-82.
4. He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *BMJ* 2013;346:f1325.
5. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. *Hypertension* 2006;48:861-9.
6. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ* 2013;346:f1326.
7. He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. *Lancet* 2011;378:380-2.
8. He FJ, Campbell NRC, Ma Y, et al. Errors in estimating usual sodium intake by the Kawasaki formula alter its relationship with mortality — Implications for public health. *Int J Epidemiol* 2018.
9. Asaria P, Chisholm D, Mathers C, et al. Chronic disease prevention: health effects and financial costs of strategies to reduce salt intake and control tobacco use. *Lancet* 2007;370:2044-53.
10. WHO issues new guidance on dietary salt and potassium, 31 January 2013. [http://www.who.int/mediacentre/news/notes/2013/salt\\_potassium\\_20130131/en/](http://www.who.int/mediacentre/news/notes/2013/salt_potassium_20130131/en/) (Accessed 30 January 2017).
11. Trieu K, Neal B, Hawkes C, et al. Salt Reduction Initiatives around the World - A Systematic Review of Progress towards the Global Target. *PLoS One* 2015;10:e0130247.
12. He FJ, Pombo-Rodrigues S, MacGregor GA. Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease mortality. *BMJ Open* 2014;4:e004549.
13. He FJ, Wu Y, Feng XX, et al. School based education programme to reduce salt intake in children and their families (School-EduSalt): cluster randomised controlled trial. *BMJ* 2015;350:h770.
14. Zhou BF, Stamler J, Dennis B, et al. Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: the INTERMAP study. *J Hum Hypertens* 2003;17:623-30.
15. Zhang JY, Yan LX, Tang JL, et al. Estimating daily salt intake based on 24 h urinary sodium excretion in adults aged 18-69 years in Shandong, China. *BMJ Open* 2014;4:e005089.
16. Anderson CA, Appel LJ, Okuda N, 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;110:736-45.
17. Burke LE, Ma J, Azar KM, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: a scientific statement from the American Heart Association. *Circulation* 2015;132:1157-213.

18. Payne HE, Moxley VB, MacDonald E. Health Behavior Theory in Physical Activity Game Apps: A Content Analysis. *JMIR Serious Games* 2015;3:e4.
19. CNNIC. The 42nd Statistical Report on the Development of China's Internet Network, 10 August 2018. [https://cnnic.net.cn/gywm/xwzx/rdxw/20172017\\_7047/201808/t20180820\\_70486.htm](https://cnnic.net.cn/gywm/xwzx/rdxw/20172017_7047/201808/t20180820_70486.htm) (Accessed 1 Nov 2018).
20. Tian M, Ajay V, Dunzhu D, et al. A Cluster-Randomized Controlled Trial of a Simplified Multifaceted Management Program for Individuals at High Cardiovascular Risk (SimCard Trial) in Rural Tibet, China, and Haryana, India. *Circulation* 2015;132:815-24.
21. Zhang L, Zhao F, Zhang P, et al. A pilot study to validate a standardized one-week salt estimation method evaluating salt intake and its sources for family members in China. *Nutrients* 2015;7:751-63.
22. Dunford E, Trevena H, Goodsell C, et al. FoodSwitch: a mobile phone app to enable consumers to make healthier food choices and crowdsourcing of national food composition data. *JMIR mHealth and uHealth* 2014;2:e37.
23. Zhang J, Sun L, Liu Y, et al. Mobile Device–Based Electronic Data Capture System Used in a Clinical Randomized Controlled Trial: Advantages and Challenges. *J Med Internet Res* 2017;19:e66.
24. World Action on Salt and Health. <http://www.worldactiononsalt.com>

1  
2  
3 **Figure Legends**  
4  
5

6  
7 **Figure 1.** AppSalt core procedures and modules.  
8

9  
10 **Figure 2.** Appsalt trial design. BP: Blood Pressure.  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

Enseignement Supérieur (ABES) .  
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

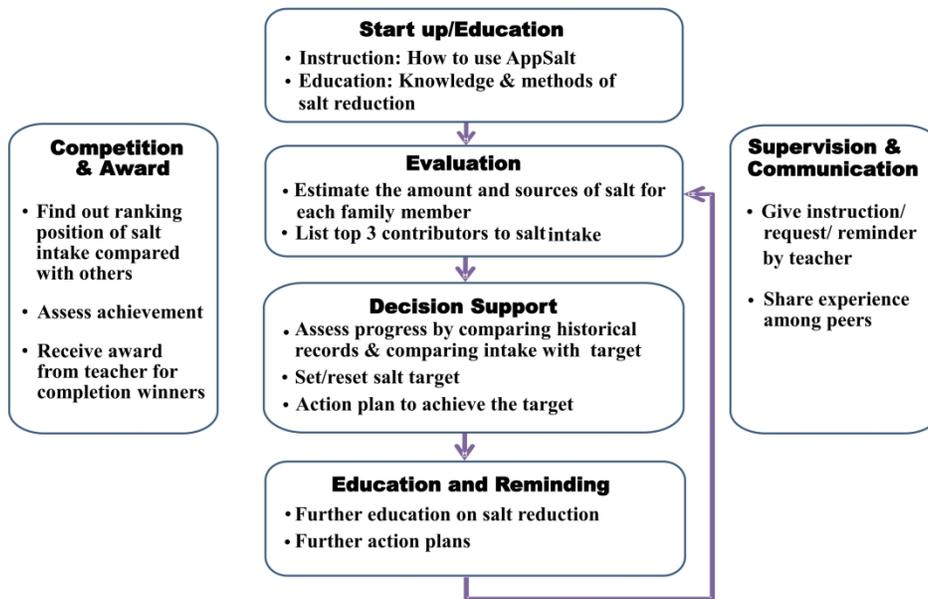


Figure 1 AppSalt core procedures and modules.

279x183mm (300 x 300 DPI)

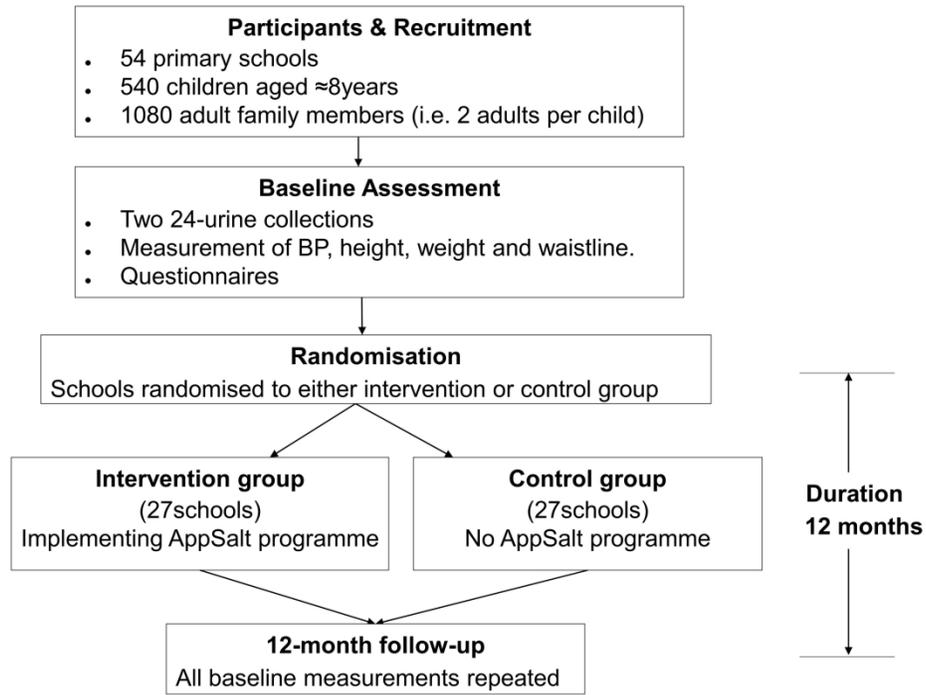


Figure 2 Appsalt trial design. BP: Blood Pressure.

266x190mm (300 x 300 DPI)



# CONSORT 2010 checklist of information to include when reporting a randomised trial\*

Section/Topic	Item No	Checklist item	Reported on page No
<b>Title and abstract</b>			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance, see CONSORT for abstracts)	2-3
<b>Introduction</b>			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	5
<b>Methods</b>			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-10
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Not applicable
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	11-12
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Not applicable
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not applicable
<b>Randomisation:</b>			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	12

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	Not applicable
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	14
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	14
<b>Results</b>			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Not applicable
	13b	For each group, losses and exclusions after randomisation, together with reasons	Not applicable
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Not applicable
	14b	Why the trial ended or was stopped	Not applicable
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Not applicable
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Not applicable
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimate of effect size and its precision (such as 95% confidence interval)	Not applicable
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Not applicable
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Not applicable
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for Harms)	Not applicable
<b>Discussion</b>			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	3
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15
<b>Other information</b>			
Registration	23	Registration number and name of trial registry	2
Protocol	24	Where the full trial protocol can be accessed, if available	Reference 24
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	16

\*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see [www.consort-statement.org](http://www.consort-statement.org).

# BMJ Open

## An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China - Protocol of a cluster randomised controlled trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-027793.R1
Article Type:	Protocol
Date Submitted by the Author:	18-Feb-2019
Complete List of Authors:	<p>He, Feng; Queen Mary University of London, Wolfson Institute of Preventive Medicine            Zhang, Puhong ; The George Institute at Peking University Health Science Center; University of New South Wales, Faculty of Medicine            Luo, Rong; The George Institute for Global Health at Peking University Health Science Center            Li, Yuan; The George Institute for Global Health, Peking University Health Science Centre; University of New South Wales, Faculty of Medicine            Chen, Fengge; Shijiazhuang Center for Disease Control and Prevention            Zhao, Yuhong; Changan Center for Disease Control and Prevention            Zhao, Wei; Shijiazhuang Center for Disease Control and Prevention            Li, Daoxi; Luzhou Center for Disease Control and Prevention            Chen, Hang; Luzhou Center for Disease Control and Prevention            Wu, Tianyong; Luzhou Center for Disease Control and Prevention            Yao, Jianyun; Yueyang Center for Disease Control and Prevention            Li, Jinbao; Yueyang Center for Disease Control and Prevention            Zhou, Siyuan; Yueyang Center for Disease Control and Prevention            Liu, Yu; Beihang University, School of Computing            Li , Xian; The George Institute for Global Health at Peking University Health Science Center            Wang, Changqiong; Queen Mary University of London, Wolfson Institute of Preventive Medicine            MacGregor, Graham; Queen Mary University of London, Wolfson Institute of Preventive Medicine</p>
<b>Primary Subject Heading</b>:	Public health
Secondary Subject Heading:	Global health, Public health
Keywords:	Salt Reduction, Schoolchildren and Families, m-Health, Randomised Controlled Trial

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



**An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China**

**Protocol of a cluster randomised controlled trial**

**Feng J He,<sup>1\*</sup> Puhong Zhang,<sup>2,3\*</sup> Rong Luo,<sup>2</sup> Yuan Li,<sup>2,3</sup> Fengge Chen,<sup>4</sup> Yuhong Zhao,<sup>5</sup>**

**Wei Zhao,<sup>4</sup> Daoxi Li,<sup>6</sup> Hang Chen,<sup>6</sup> Tianyong Wu,<sup>6</sup> Jianyun Yao,<sup>7</sup> Jinbao Li,<sup>7</sup> Siyuan**

**Zhou,<sup>7</sup> Yu Liu,<sup>8</sup> Xian Li,<sup>2,3</sup> Changqiong Wang,<sup>1</sup> Graham A MacGregor<sup>1</sup>**

<sup>1</sup> Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine & Dentistry, Queen Mary University of London, UK

<sup>2</sup> The George Institute for Global Health at Peking University Health Science Center, China.

<sup>3</sup> Faculty of Medicine, University of New South Wales, Australia

<sup>4</sup> Shijiazhuang Center for Disease Control and Prevention, Hebei Province, China

<sup>5</sup> Changan Center for Disease Control and Prevention, Shijiazhuang, Hebei Province, China

<sup>6</sup> Luzhou Center for Disease Control and Prevention, Sichuan Province, China

<sup>7</sup> Yueyang Center for Disease Control and Prevention, Hunan Province, China

<sup>8</sup> School of Computing, Beihang University, Beijing, China

**\*Joint first author**

Correspondence to:

Professor Feng J He

Wolfson Institute of Preventive Medicine,  
Barts and The London School of Medicine & Dentistry,

Queen Mary University of London,

Charterhouse Square,

London EC1M 6BQ.

Tel: 44 (0)20 7882 6266

Fax: 44 (0)20 7882 6270

E-mail: [f.he@qmul.ac.uk](mailto:f.he@qmul.ac.uk)

Professor Puhong Zhang

The George Institute for Global Health at Peking University Health Science Center,

Level 18, Tower B, Horizon Tower, No. 6 Zhichun Rd,

Haidian District | Beijing, 100088 P.R. China

Tel: +86 10 8280 0577 ext 512

Fax: +8610 8280 0177

E-mail: [zpuhong@georgeinstitute.org.cn](mailto:zpuhong@georgeinstitute.org.cn)

## ABSTRACT

**Introduction:** Salt intake is very high in China, with  $\approx 80\%$  being added by the consumers. It is difficult to reduce salt in such settings. Our previous study (School-EduSalt, School based Education programme to reduce Salt) demonstrated that educating schoolchildren who then instructed their families to reduce the amount of salt used at home, is effective in lowering salt intake in both children and adults. Our team also developed an app called “KnowSalt” which could help individuals to estimate their salt intake and the major sources of salt in the diet. Building upon School-EduSalt and KnowSalt, we propose to develop a new app (AppSalt) focusing on salt reduction through education, target setting, monitoring, evaluation, decision support and management, to achieve a progressive lower salt intake for long term. To evaluate the effectiveness of the AppSalt programme, we will carry out a cluster randomised controlled trial.

**Methods and analysis:** We will recruit 54 primary schools from urban and rural areas of 3 provinces in China. 594 children aged  $\approx 8$  years and 1188 adult family members will be randomly selected for evaluation. After baseline assessment, schools will be randomly allocated to either the intervention or control group. Children in the intervention group will be taught, with support of AppSalt, about salt reduction and assigned homework to get the whole family involved in the activities to reduce salt consumption. The duration of the intervention is two school terms (i.e. 1 year). The primary outcome is the difference between the intervention and control group in the change of salt intake as measured by 24-hour urinary sodium.

**Ethics and dissemination:** The study has been approved by Queen Mary Research Ethics Committee and Peking University Health Science Centre IRB. Results will be disseminated through presentations, publications and social media.

**Trial Registration:** Registered on Chinese Clinical Trial Registry, ChiCTR1800017553.

### Strengths and limitations of this study

- Our study will develop a new approach to achieving a sustainable progressive lower salt intake for long term.
- The study will use an innovative smartphone application through estimation of salt intake, education, target setting and monitoring, decision support and management to implement a salt reduction programme.
- The study covers a wide range of the population including children and adults in diverse settings, e.g. rural and urban, north, central and south China.
- The results should be generally applicable to the whole Chinese population.
- The study will be carried out in China only, however, the method could potentially be adapted by many other developing countries where most of the salt in the diet is added by the consumers.

## INTRODUCTION

Cardiovascular disease (CVD, i.e. strokes, heart attacks and heart failure) is the leading cause of death and disability worldwide. Approximately 80% of CVD deaths occur in developing countries.<sup>1</sup> Raised blood pressure (BP) is an important risk factor for CVD, accounting for 62% of strokes and 49% of coronary heart disease.<sup>2</sup> High salt intake is the major cause of raised BP.<sup>3</sup> Randomised trials have demonstrated that a reduction in salt intake lowers BP in both hypertensive and normotensive individuals, in both adults and children.<sup>4,5,6</sup> There is also compelling evidence that a lower salt intake is associated with a reduced risk of CVD and total mortality.<sup>7,8</sup> Indeed, salt reduction is one of the most cost-effective measures to prevent hypertension and CVD.<sup>3,9</sup> The World Health Organisation (WHO) has recommended a 30% reduction in population salt intake by 2025, and also set a target of <5 g/d for all adults and lower levels for children.<sup>10</sup> Many developed countries have started salt reduction initiatives.<sup>11</sup> Salt intake has been successfully reduced in Finland and the UK, accompanied by falls in population BP and CVD mortality.<sup>12</sup> Developing countries, however, are lagging behind. China is the largest developing country with one fifth of the world population. Salt intake in China is very high with an average of 12-14 g/d in adults<sup>13-15</sup>, and in some rural areas of northern China, salt intake could be as high as 18-20 g/d.<sup>16</sup> Approximately 80% of the salt in the Chinese diet is added by the consumers during cooking or in sauces.<sup>17</sup> It is extremely challenging to reduce salt intake in such settings due to the difficulty in changing individuals' dietary behaviours. Our previous study (School-EduSalt) has developed a novel and effective approach to reducing salt intake in northern China.<sup>13</sup> In School-EduSalt, primary schoolchildren aged  $\approx 10$  years were educated about the harmful effects of salt on health and how to reduce intake during the school's usual health education lessons. Children then instructed their families to reduce salt. The results showed that, over one school term ( $\approx 3.5$  months), salt intake was reduced by  $\approx 25\%$  in both children and adults as measured by 24-

1  
2  
3 hour urinary sodium excretion. The reduction in salt intake led to a significant fall in systolic  
4  
5 BP of 2.3 mmHg in adults.<sup>13</sup> It was estimated that, if School-EduSalt was implemented and  
6  
7 sustained, it would prevent ≈400,000 stroke and heart attack events per year in China.

8  
9  
10 Previous studies have shown that salt reduction achieved by dietary advice attenuates over  
11  
12 time and maintaining a lower salt intake long-term remains a challenge.<sup>4</sup> The School-EduSalt  
13  
14 was successful over one school term of ≈3.5 months. The question is how to continue and  
15  
16 reinforce the salt reduction education to achieve a sustainable, progressive lower intake to  
17  
18 achieve the WHO's target.

19  
20  
21 Mobile technology is increasingly used in health education.<sup>18</sup> Recent studies have suggested  
22  
23 that game-based intervention has great potential in changing behaviours due to the popularity  
24  
25 of gaming.<sup>19</sup> China has the largest and fastest growing mobile internet population with 802  
26  
27 million people using internet and mobile phone penetration reached 98.3% of the population  
28  
29 by June 2018.<sup>20</sup> Mobile-based decision support system has been shown to be effective in  
30  
31 increasing medication use in individuals with high CVD risk in rural China.<sup>21</sup> Our team have  
32  
33 recently developed a smartphone app (KnowSalt) which can be used by individuals to  
34  
35 estimate their salt intake and the major sources of salt in the diet. The methodology  
36  
37 underpinning KnowSalt app had been validated in a pilot study in primary schoolchildren and  
38  
39 their families.<sup>22</sup>

40  
41  
42 Our proposed study building upon School-EduSalt and KnowSalt app will develop an  
43  
44 innovative smartphone application focusing on salt reduction (AppSalt) through functional  
45  
46 modules of education, evaluation, target setting and monitoring, decision support and  
47  
48 management, with the aim of reinforcing School-EduSalt to achieve a progressive lower salt  
49  
50 intake for long term. To evaluate the effectiveness and cost-effectiveness of the AppSalt  
51  
52 programme, we will carry out a cluster randomised trial.  
53  
54  
55  
56  
57  
58  
59  
60

## METHODS AND ANALYSIS

The project consists of 2 phases: (1) Developing AppSalt platform; (2) Carrying out a cluster randomised controlled trial.

### Phase 1 – Development of AppSalt platform

AppSalt platform comprises a smartphone app named AppSalt (family end) and a WeChat mini app (teacher end). The AppSalt consists of 4 core procedures (i.e. Education, Evaluation, Decision support and Reminding) and 3 supportive modules (i.e. Competition & Award, Supervision & Communication and SaltSwitch) (Figure 1).

#### Core procedures

1. “Education” is to educate the families about the harmful effects of salt on health and how to reduce salt intake. Nine lessons are developed, each starting with a 10-min lecture on salt reduction, followed by a few questions to test whether the families have understood the content. At the same time, the questions and answers will re-enforce the key messages. Following each lesson, the families are required to complete a practical session which is designed to help the families to prepare foods with reduced salt at home and to choose lower-salt foods when shopping.
2. “Evaluation” is to estimate salt intake and the main sources of salt for every member of the family. After completing a simple questionnaire, the family will be provided with the information on the top 3 contributors of salt in their diet. This will help the family make a decision on how to effectively reduce salt intake.
3. “Decision Support” will set target for total salt intake and specific targets for top 3 contributors. Lower-salt sample recipes and specific measures, e.g. reducing the amount of salt used during cooking by 50%, will be recommended. The recommended measures will be customised as an action plan.

1  
2  
3 4. “Reminding” will remind the family how far their salt intakes are away from the targets set  
4  
5 and highlight further action plans.  
6

### 7 Supportive modules

8  
9  
10 1. The “Competition & Award” module will help the participants to find out their own  
11 ranking position assessed by salt intake level and the extent of salt reduction among all  
12 participants (NB: only their own ranking will be displayed and other participants’ ranking  
13 will not be revealed to them). The family with lowest salt intake and the family who achieve  
14 the greatest reduction in salt intake, will be the winners of competition. They will be awarded  
15 an honorary title like “Salt Reduction Pacesetter” and get a small gift.  
16  
17

18  
19 2. “Supervision & Communication” module: The teachers and researchers will use the  
20 function “Supervision” to announce instructions, newsletters, and school canteen menus, as  
21 well as to provide answers to any queries. The participants will use the function  
22 “Communication” to ask any questions and also to exchange experience and knowledge with  
23 other participants.  
24

25  
26 3. The “SaltSwitch” module will help the participants to choose pre-packaged foods with  
27 lower salt. “SaltSwitch”, as a sub-function of “FoodSwitch”<sup>23</sup> integrated into the AppSalt, has  
28 a database of over 50,000 pre-packaged food collected by the George Institute China. By  
29 scanning the barcode of the pre-packaged foods, the “SaltSwitch” will provide information  
30 on salt/sodium content and compare it with other similar products based on products’  
31 labelling. This will help the participants to choose food with lower salt.  
32  
33

34  
35 AppSalt will be installed in the smartphone of adult family members. Children are only  
36 allowed to use AppSalt accompanied by their adult family members to complete AppSalt  
37 core procedures as required. New features with a variety of presentation styles on salt  
38 reduction education will be added to keep the programme attractive to the participants.  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 The school teachers will use the WeChat mini app (teacher end) to send messages to the  
4 families, provide timely feedback to any queries, and check families' progress and ensure all  
5 families complete the procedures in time. The teachers will also report any issues to the site  
6 managers and the research team where appropriate.  
7  
8  
9  
10  
11  
12

## 13 **Phase 2 — Cluster randomised controlled trial (RCT)**

14  
15 To test the effectiveness and cost-effectiveness of the AppSalt programme, we will carry out  
16 a cluster randomised controlled trial (Figure 2).  
17  
18

### 19 ***Study Setting and participants***

20  
21 Considering the geographical location, economic level and dietary habit, our study will be  
22 undertaken in selected primary schools from urban and rural areas of 3 provinces in northern  
23 (Hebei), central (Sichuan) and southern (Hunan) China.  
24  
25  
26  
27  
28

29 To recruit schools, we will firstly contact the local education authority through local  
30 Health/Education Bureau or Centre for Disease Control (CDC) to gain their opinion, support  
31 and approval. We will then contact schools' head-teachers to request their participation in the  
32 study. In each school, there are 6 grades with age ranging from 7 to 12 years and our study  
33 will be carried out in grade 3 (age ≈8 years). Head-teacher will choose one class whose  
34 teacher in charge is willing to collaborate with the researchers. From each class, we will  
35 randomly select 11 children and 22 adult family members (i.e. 1 child and 2 adults per  
36 family) for evaluation.  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46

47 The inclusion criteria are (1) Children and their adult family members have to eat homemade  
48 meals at least four times per week; (2) One of the adults in the family has a mobile device  
49 with access to Internet; (3) If more than 2 adults in one family agree to take part in the  
50 evaluation, we will select two in the order of grandparents, parents, uncles and aunties; (4)  
51 Participants have been local residents for over 6 months, without moving plan within 24  
52 months. We will exclude the individuals who cannot or refuse to collect 24-hour urine.  
53  
54  
55  
56  
57  
58  
59  
60

### ***Randomisation***

Schools (clusters) will be randomly assigned (1:1) to either the intervention or the control group. Randomisation will be stratified by the location of schools (i.e. south or north, urban or rural) and the size of the class. The randomisation will be carried out using computer generated random number by an independent statistician who is blind to the identity of the schools. The randomisation will take place after baseline data collection has completed. Therefore, the participants, school-teachers and local investigators who undertake recruitment and data collection, will be unaware of the allocation until the point prior to the commencement of the intervention.

### ***Intervention***

Our goal is to lower salt intake (measured by 24-hour urinary sodium) by a minimum of 15% ( $\approx 1.5$ g salt) for both children and their families. To achieve this goal, a strategy towards a 50% reduction should be implemented. To make the decision-support algorithm simple in the AppSalt, we will set targets for the top 3 contributors to salt intake, such as cooking salt, soy sauce. Targets and priority actions will be individualised depending on the sources of salt in the individual's diet which will be provided by AppSalt.

In the intervention group, the AppSalt intervention package will be delivered to all children and their families in the whole class, despite only 11 children and their families being randomly selected for evaluation. The adult family members will be authorized to install and operate the AppSalt programme, while children will be assigned homework to get the whole family to reduce salt with the support of AppSalt. Children's homework will include: (a) helping the family to set salt reduction target and reminding the whole family of this target on a regular basis; (b) getting the whole family involved in salt reduction activities and persuading the person who does the cooking to reduce the amount of salt used during food preparations at home; (c) working with their family members to complete the AppSalt core

1  
2  
3 procedures, including education, evaluation, target setting and monitoring. In addition to the  
4  
5 online lessons, school teachers will organise three face-to-face seminars for both children and  
6  
7 adults during the one-year intervention period. This will provide an opportunity for the  
8  
9 participants to share experiences and discuss challenges and solutions. These seminars will be  
10  
11 integrated into the schools' routine parent meetings.  
12  
13

14 Trained teachers will provide guidance on AppSalt utilisation, assign and check children's  
15  
16 homework including monitoring the progress of salt reduction. They will also create salt-  
17  
18 reduction environment, e.g. putting up posters in classroom, campus and canteens. The  
19  
20 AppSalt will be activated at the beginning of the intervention for all families in the  
21  
22 intervention group. Throughout the study, participants will receive salt reduction messages  
23  
24 and newsletters via AppSalt on a monthly basis. Participants will be encouraged to use  
25  
26 AppSalt and communicate with the teachers and other families to share experiences. The  
27  
28 mandatory tasks for the participants include completing the online lessons and the related  
29  
30 Q&As (Questions and Answers) at baseline and every month thereafter, and completing the  
31  
32 core procedures, i.e. salt intake estimation, target setting at baseline and every 3 months  
33  
34 thereafter. In addition to the mandatory tasks, the participants are encouraged to repeat the  
35  
36 core procedures as often as they wish, in order to monitor their progress and achieve  
37  
38 progressive reductions in salt intake. Based on the progress monitored from the WeChat mini  
39  
40 app, the teachers will remind children that they should complete their homework which is to  
41  
42 help the family complete the AppSalt procedures in time and to instruct the family members  
43  
44 to reduce salt to the target.  
45  
46  
47  
48  
49  
50

51 The records from AppSalt, e.g. salt intake and how far the intake is different from the target  
52  
53 set, will be used to monitor compliance. During follow-up, the participant who fails to  
54  
55 achieve the salt reduction target, will be sent a specially designed message via AppSalt and a  
56  
57 letter to the child through his/her teacher to remind the family of the salt reduction target.  
58  
59  
60

1  
2  
3 The intervention duration is 2 school terms, i.e. 1 year. After the trial is completed, we will  
4 introduce the AppSalt to all schoolchildren and their families including those in the control  
5  
6 group.  
7  
8

### 9 10 ***Sample size calculation***

11  
12 Based on the School-EduSalt trial,<sup>13</sup> assuming a standard deviation of 24-hour sodium  
13 excretion is 85mmol/day, and intraclass correlation coefficient (ICC) is 0.05, we estimate that  
14 a sample size of 594 children from 54 schools (18 primary schools from each province in  
15 both urban and rural area, and 11 children per school) would provide a power of 80% (with a  
16 two-sided alpha=0.05) to detect a difference in mean 24-hour urinary sodium  $\geq 26$ mmol/day  
17 (1.5 g/d salt) between intervention and control group, allowing for a 15% drop-out rate of  
18 participants. We aim to recruit 2 adults per family, therefore 1188 adults will be recruited into  
19 the study for evaluation.  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29

### 30 31 ***Outcome measures***

32  
33 The primary outcome is the difference between the intervention and control group in the  
34 change of salt intake as measured by 24-hour urinary sodium from baseline to the end of the  
35 trial. The secondary outcome is the difference between the two groups in the change of  
36 systolic BP for adults.  
37  
38  
39

### 40 41 42 ***Outcome assessments***

43  
44 All outcome measurements and assessments will be carried out at baseline and at the end of  
45 the trial in exactly the same way in all schools for all participants, irrespective of their  
46 assignment to intervention or control group.  
47  
48  
49

50  
51 We will carry out two consecutive 24-hour urine collections using the stringent protocol  
52 which we developed in the School-EduSalt study.<sup>13</sup> The participants will be carefully  
53 instructed on how to accurately collect 24-hour urine by trained research staff. On the first  
54 day, the participants will be asked to come to the schools. The researchers will ask the  
55  
56  
57  
58  
59  
60

1  
2  
3 participants to empty bladder and discard the urine. The researchers will record the start time  
4  
5 and date of the 24-hour urine collection. They will then give the participants the collection  
6  
7 equipment including containers and collection aids such as carrier bags. The participants will  
8  
9 be instructed to collect all subsequent urine voids over the next 24-hour period. On the  
10  
11 second day at the same time, the participants will be asked to bring the urine collection  
12  
13 bottles back to the schools and they will be asked to pass the last urine into the container. The  
14  
15 researchers will record the finish time of the first 24-hour urine collection. The researchers  
16  
17 will then give the participants the collection equipment for the second 24-hour urine  
18  
19 collection and repeat the process. During the 24-hour urine collection period, the participants  
20  
21 will be asked to take spare urine containers with them when they go to school or work. Spare  
22  
23 collection equipment will also be available in the schools, in case children forget to bring  
24  
25 them. In the case that the participant misses one or more urine voids or spillage occurs, the  
26  
27 participant will be asked to do a further 24-hour urine collection. The 24-hour urine  
28  
29 collections will be made either at weekdays or at weekends. For each participant, the 24-hour  
30  
31 urines will be collected on the same days of the week for baseline and for follow-up at the  
32  
33 end of the trial.

34  
35 We will measure urine volume, sodium, potassium and creatinine. Ion-selective electrode  
36  
37 method will be used for sodium and potassium analysis and enzymatic method for creatinine  
38  
39 assay. 24-hour urinary creatinine together with urine volume will be used to determine if the  
40  
41 collection is likely to be complete. The biochemist who performs the measurements of  
42  
43 urinary electrolytes will not be told which group the participant is allocated.

44  
45 In addition to 24-hour urine collection, we will measure BP and heart rate using a validated  
46  
47 automatic machine with the appropriate size of cuff. Three readings will be taken in the right  
48  
49 arm at 1-2-minute intervals at sitting position after the participant has had 10 minutes' rest in  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 a quiet room. Body weight, height and waist circumference will also be measured. Survey on  
4 Knowledge, Attitude and Practice (KAP) related to salt will be completed via questionnaire.  
5  
6  
7

## 8 **Data collection, management and analysis**

### 9 *Data collection*

10  
11 Our study will have two major data outputs. One is the “App Data” generated automatically  
12 when the AppSalt platform is used by the families in intervention group to support salt  
13 reduction. The App Data include information on demographic characteristics, eating habits,  
14 amount and sources of salt in the diet, as well as information (or App logs) on the use of  
15 AppSalt. The other data output is the “RCT Data” which is generated by both intervention  
16 and control groups during the RCT. The RCT Data will be collected through a specially  
17 designed mobile device based electronic data capture system (mEDC) by well-trained field  
18 investigators. The mEDC has been validated and widely used in other clinical trials<sup>24</sup> with  
19 more advantages on process and quality control compared with traditional EDC. The RCT  
20 data include information on demographics, social-economic information, KAP, measurement  
21 of height, weight, waist circumference, BP, heart rate, 24-hour urine volume and electrolytes,  
22 as well as information on costs for all the components of intervention conducted through the  
23 AppSalt programme.  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42

### 43 *Data management*

44 All cleaned and locked datasets together with the study design, questionnaire, code list and  
45 definition of database and variables will be stored with a unique ID number attached but no  
46 personal identifiers in The George Institute China (TGI), following an established standard  
47 operating procedure for data security. To guarantee the data security, the mobile app  
48 developer (i.e. the IT team at Beihang University) must follow the “Mobile Application  
49 Information Service Regulation” issued by the Cyberspace Administration of China in 2016.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Although personal data are accessible to app developer, disclosure of such information is  
4 prohibited. In addition to the development and maintenance of the AppSalt and mEDC, IT  
5 team will also provide data management service during the study to guarantee the safety,  
6 integrity and proper use of the data collected through AppSalt and mEDC.  
7  
8  
9

### 10 11 12 ***Statistical Analysis***

13  
14  
15 Data analyses will be performed according to the intention-to-treat approach. The effect of  
16 the intervention on the outcomes will be tested using linear mixed models with participants  
17 nested within family units and families nested within schools. We will include group  
18 (intervention, control), time (baseline, end of trial), and time×group interaction, with the  
19 time×group interaction term indicating differential change by group from baseline to the end  
20 of the trial. We will adjust for the stratification variables at randomization and potential  
21 confounding variables. Various sensitivity analyses will be carried out to examine the  
22 robustness of the conclusions of the primary analysis. Results will be reported as mean, SD,  
23 SE, and 95% confidence interval where appropriate. All analyses will be two sided and  
24 P<0.05 is considered significant. SAS will be used for the analyses.  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38

### 39 40 ***Economic evaluation and process evaluation***

41  
42 Economic evaluations will be carried out from health sector perspective to compare the m-  
43 Health strategy with usual care and it will entail two components: a trial-based economic  
44 evaluation and a modelled economic evaluation of long-term costs and outcomes.  
45  
46 Intervention costs will include those in running the programme but exclude any research and  
47 development costs. The trial-based economic evaluation will be assessed initially in terms of  
48 incremental cost per unit reduction in salt intake and systolic BP. The modelled economic  
49 evaluation with discounting will examine the cost, survival, quality of life over lifetime, via  
50 capturing various health states (including death and CVD events) to estimate incremental cost  
51 per life year saved and cost per Quality-Adjusted Life Year (QALY) gained. The transition  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 probabilities across health states and costs attached to various health states will be based on  
4 literatures and the long-term effects of the reduction in salt intake or systolic BP will be  
5 derived from the trial findings and/or literatures of disease progression. Sensitivity analyses  
6 will be carried out to estimate uncertainty about the primary findings associated with varying  
7 key parameters.  
8  
9

10  
11 Mixed-method process evaluations will be conducted during and at the end of the study using  
12 data from AppSalt, key informant interviews with researchers and teachers, and focus groups  
13 interviews with participants. This will help understand the barriers and facilitators of the  
14 intervention as well as the acceptance and effect of the AppSalt programme.  
15  
16

### 17 **Project status and timelines**

18  
19 Recruitment of schools and participants started in September 2018. Baseline assessments  
20 were carried out between September and December 2018. As the intervention duration is one  
21 year, the final follow-up assessments will be carried out between September and December  
22 2019.  
23  
24

### 25 **Expected outcome and potential impact**

26  
27 The study will provide a novel, feasible and effective approach to achieving a sustainable  
28 reduction in salt intake in both children and adults. The use of AppSalt platform in delivering  
29 health education lessons is particularly advantageous over the traditional school education  
30 method in terms of reducing the burden on teaching staff. Furthermore, our study covers a  
31 wide range of the population (children and adults, rural and urban, north and south), the  
32 results should therefore be generally applicable to the whole Chinese population. If the  
33 programme is implemented and sustained across China, it will reduce population salt intake  
34 and thereby prevent hundreds of thousands of strokes, heart attacks and heart failure each  
35 year, and lead to major cost-savings to individuals, their families and the health service.  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 Although our study will be carried out in China, the AppSalt programme could potentially be  
4 adapted by many other countries. Additionally, our model on salt reduction could possibly be  
5 adapted for other dietary and lifestyle changes to prevent CVD and other non-communicable  
6 diseases, which will have major public health implications.  
7  
8  
9  
10  
11  
12

### 13 **Patient and Public Involvement**

14  
15 During the development of the study protocol, we had 2 round-table meetings with 6 head-  
16 teachers from 3 different cities and numerous telephone meetings with teachers and  
17 children's parents to gain their opinion, particularly on the feasibility of carrying out the  
18 study in school settings and how to incorporate the intervention programme into the school  
19 curriculum. During the study, school teachers will assign and check children's homework.  
20 Both teachers and head-teachers will be informed of the study progress by monthly  
21 communication via newsletters, WeChat and website. Upon completion of the study, we will  
22 disseminate the results to head-teachers, teachers, children and their parents. We will also  
23 discuss with them and other stakeholders on how to transfer research findings into practice.  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35

### 36 **ETHICS AND DISSEMINATION**

37  
38 The study has been approved by Queen Mary Research Ethics Committee in the UK  
39 (QMERC2018/13) and Peking University IRB in China (IRB00001052-18051). Written  
40 consent will be obtained from all participants according to well-established practices. For  
41 children, participant assent and parental written consent will be obtained. All participants will  
42 be free to discontinue their participation at any time with no explanation required.  
43  
44  
45  
46  
47  
48  
49

50 The findings of this study will be disseminated widely through conference presentations,  
51 peer-reviewed publications, press release and social media. Furthermore, the results will be  
52 disseminated worldwide through World Action on Salt and Health<sup>25</sup> which is a global non-  
53 profit organisation of 600 members from 100 countries with the mission to improve the  
54 health of populations by reducing salt intake.  
55  
56  
57  
58  
59  
60

**Authors' contributions:** FJH and PZ conceived the project and contribute equally to the work. FJH, PZ, YLi and RL designed the study and oversaw the conceptualisation and development of the app. PZ, YLi, RL, FC, YZ, WZ, DL, HC, TW, JY, JL and SZ facilitates Patient and Public Involvement and were responsible for setting up the study in each site. YLiu and RL are leading the development and maintenance of the app. XL and CW contributed to sample size calculation and analysis plan. All authors contributed to the development of the intervention and evaluation. FJH wrote the first draft of the manuscript, and PZ, YLi, RL, CW and GAM revised the draft. All authors contributed to the refinement of the study protocol and approved the final manuscript.

**Funding statement:** This work is supported by the National Institute of Health Research using Official Development Assistance (ODA) funding (16/136/77). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

**Competing interests:** FJH is a member of Consensus Action on Salt & Health (CASH) and World Action on Salt & Health (WASH). Both CASH and WASH are non-profit charitable organisations and FJH does not receive any financial support from CASH or WASH. GAM is Chairman of Blood Pressure UK (BPUK), Chairman of CASH and Chairman of WASH. BPUK, CASH and WASH are non-profit charitable organisations. GAM does not receive any financial support from any of these organisations. Other authors declare no competing interests.

**Acknowledgement:** We would like to thank the head-teachers, teachers and parents who generously shared their opinion on the development of the intervention programme.

**Word Count:** 4008 words.

## References

1. Lawes CM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. *Lancet* 2008;371:1513-8.
2. World Health Report 2002: Reducing risks, promoting healthy life. Geneva, Switzerland: World Health Organisation, 2002. [www.who.int/whr/2002](http://www.who.int/whr/2002).
3. He FJ, MacGregor GA. Reducing population salt intake worldwide: from evidence to implementation. *Prog Cardiovasc Dis* 2010;52:363-82.
4. He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *BMJ* 2013;346:f1325.
5. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. *Hypertension* 2006;48:861-9.

- 1
  - 2
  - 3
  - 4
  - 5
  - 6
  - 7
  - 8
  - 9
  - 10
  - 11
  - 12
  - 13
  - 14
  - 15
  - 16
  - 17
  - 18
  - 19
  - 20
  - 21
  - 22
  - 23
  - 24
  - 25
  - 26
  - 27
  - 28
  - 29
  - 30
  - 31
  - 32
  - 33
  - 34
  - 35
  - 36
  - 37
  - 38
  - 39
  - 40
  - 41
  - 42
  - 43
  - 44
  - 45
  - 46
  - 47
  - 48
  - 49
  - 50
  - 51
  - 52
  - 53
  - 54
  - 55
  - 56
  - 57
  - 58
  - 59
  - 60
6. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ* 2013;346:f1326.
  7. He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. *Lancet* 2011;378:380-2.
  8. He FJ, Campbell NR, Ma Y, et al. Errors in estimating usual sodium intake by the Kawasaki formula alter its relationship with mortality: implications for public health. *International Journal of Epidemiology* 2018;47:1784-95.
  9. Asaria P, Chisholm D, Mathers C, et al. Chronic disease prevention: health effects and financial costs of strategies to reduce salt intake and control tobacco use. *Lancet* 2007;370:2044-53.
  10. WHO issues new guidance on dietary salt and potassium, 31 January 2013. [http://www.who.int/mediacentre/news/notes/2013/salt\\_potassium\\_20130131/en/](http://www.who.int/mediacentre/news/notes/2013/salt_potassium_20130131/en/) (Accessed 30 January 2017).
  11. Trieu K, Neal B, Hawkes C, et al. Salt Reduction Initiatives around the World - A Systematic Review of Progress towards the Global Target. *PLoS One* 2015;10:e0130247.
  12. He FJ, Pombo-Rodrigues S, MacGregor GA. Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease mortality. *BMJ Open* 2014;4:e004549.
  13. He FJ, Wu Y, Feng XX, et al. School based education programme to reduce salt intake in children and their families (School-EduSalt): cluster randomised controlled trial. *BMJ* 2015;350:h770.
  14. Zhou BF, Stamler J, Dennis B, et al. Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: the INTERMAP study. *J Hum Hypertens* 2003;17:623-30.
  15. Zhang JY, Yan LX, Tang JL, et al. Estimating daily salt intake based on 24 h urinary sodium excretion in adults aged 18-69 years in Shandong, China. *BMJ Open* 2014;4:e005089.
  16. Zhang L, Zhao F, Zhang P, et al. A pilot study to validate a standardized one-week salt estimation method evaluating salt intake and its sources for family members in China. *Nutrients* 2015;7:751-63.
  17. Anderson CA, Appel LJ, Okuda N, 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;110:736-45.
  18. Burke LE, Ma J, Azar KM, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: a scientific statement from the American Heart Association. *Circulation* 2015;132:1157-213.
  19. Payne HE, Moxley VB, MacDonald E. Health Behavior Theory in Physical Activity Game Apps: A Content Analysis. *JMIR Serious Games* 2015;3:e4.
  20. CNNIC. The 42nd Statistical Report on the Development of China's Internet Network, 10 August 2018. [https://cnnic.net.cn/gywm/xwzx/rdxw/20172017\\_7047/201808/t20180820\\_70486.htm](https://cnnic.net.cn/gywm/xwzx/rdxw/20172017_7047/201808/t20180820_70486.htm) (Accessed 1 Nov 2018).

- 1
- 2
- 3
- 4 21. Tian M, Ajay V, Dunzhu D, et al. A Cluster-Randomized Controlled Trial of a Simplified
- 5 Multifaceted Management Program for Individuals at High Cardiovascular Risk
- 6 (SimCard Trial) in Rural Tibet, China, and Haryana, India. *Circulation* 2015;132:815-24.
- 7
- 8 22. Zhang L, Zhao F, Zhang P, et al. A pilot study to validate a standardized one-week salt
- 9 estimation method evaluating salt intake and its sources for family members in China.
- 10 *Nutrients* 2015;7:751-63.
- 11
- 12 23. Dunford E, Trevena H, Goodsell C, et al. FoodSwitch: a mobile phone app to enable
- 13 consumers to make healthier food choices and crowdsourcing of national food
- 14 composition data. *JMIR mHealth and uHealth* 2014;2:e37.
- 15
- 16 24. Zhang J, Sun L, Liu Y, et al. Mobile Device–Based Electronic Data Capture System Used
- 17 in a Clinical Randomized Controlled Trial: Advantages and Challenges. *J Med Internet*
- 18 *Res* 2017;19:e66.
- 19
- 20 25. World Action on Salt and Health. <http://www.worldactiononsalt.com>
- 21
- 22
- 23
- 24
- 25
- 26
- 27
- 28
- 29
- 30
- 31
- 32
- 33
- 34
- 35
- 36
- 37
- 38
- 39
- 40
- 41
- 42
- 43
- 44
- 45
- 46
- 47
- 48
- 49
- 50
- 51
- 52
- 53
- 54
- 55
- 56
- 57
- 58
- 59
- 60

1  
2  
3 **Figure Legends**  
4  
5  
6

7 **Figure 1.** AppSalt core procedures and modules.  
8  
9

10 **Figure 2.** Appsalt trial design. BP: Blood Pressure.  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

Enseignement Supérieur (ABES) .  
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

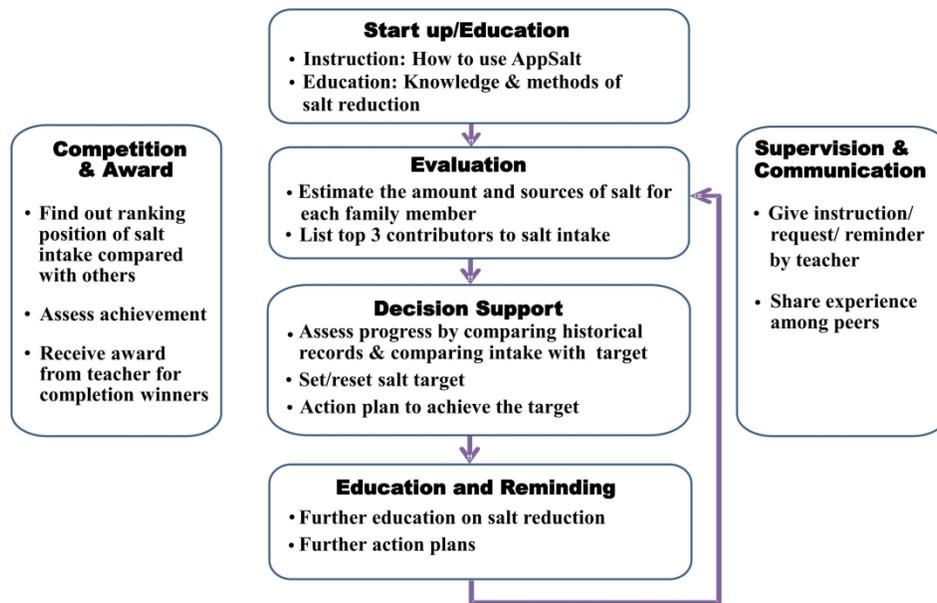


Figure 1 AppSalt core procedures and modules.

278x181mm (300 x 300 DPI)

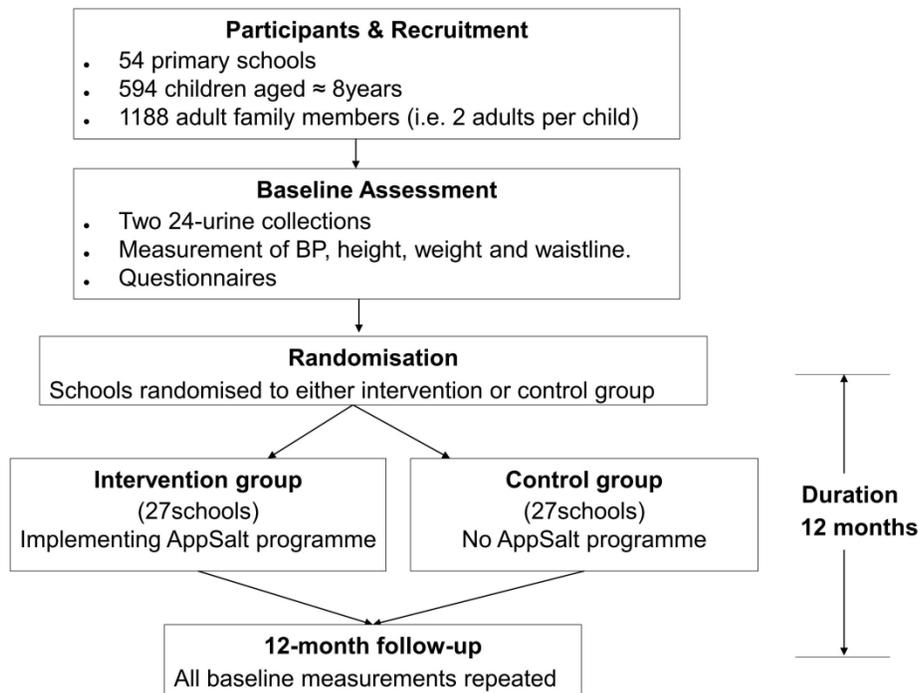


Figure 2 Appsalt trial design. BP: Blood Pressure.

267x190mm (300 x 300 DPI)



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description
<b>Administrative information</b>		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym <b>An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China Protocol of a cluster randomised controlled trial</b>
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry <b>ChiCTR1800017553</b>
	2b	All items from the World Health Organization Trial Registration Data Set <b>Yes</b>
Protocol version	3	Date and version identifier <b>N/A</b>
Funding	4	Sources and types of financial, material, and other support <b>Page 17</b>
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors <b>Page 17</b>
	5b	Name and contact information for the trial sponsor <b>Queen Mary University of London</b>
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities <b>None</b>
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) <b>N/A</b>

## Introduction

- Background and rationale
- 6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention  
**Page 4-5**
- 6b Explanation for choice of comparators  
**Page 11-12**
- Objectives
- 7 Specific objectives or hypotheses  
**Page 9**
- Trial design
- 8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)  
**Page 8-10**

## Methods: Participants, interventions, and outcomes

- Study setting
- 9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained  
**Page 8**
- Eligibility criteria
- 10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)  
**Page 8**
- Interventions
- 11a Interventions for each group with sufficient detail to allow replication, including how and when they will be administered  
**Page 9-10**
- 11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)  
**N/A**
- 11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)  
**Page 10**
- 11d Relevant concomitant care and interventions that are permitted or prohibited during the trial  
**N/A**

1			
2	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended
3			<b>Page 11-12</b>
4			
5			
6			
7			
8			
9			
10			
11	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)
12			<b>Page 15</b>
13			
14			
15			
16			
17	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations
18			<b>Page 11</b>
19			
20			
21			
22			
23	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size
24			<b>Page 8</b>
25			
26			

### Methods: Assignment of interventions (for controlled trials)

#### Allocation:

27			
28			
29			
30			
31	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions
32			<b>Page 8-9</b>
33			
34			
35			
36			
37			
38			
39			
40			
41	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned
42			<b>Page 8-9</b>
43			
44			
45			
46			
47			
48	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions
49			<b>Page 9</b>
50			
51			
52	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how
53			<b>Page 12</b>
54			
55			
56			
57			
58			
59			
60			

- 1  
2  
3  
4  
5  
6  
7
- 17b If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial  
N/A

8  
9

**Methods: Data collection, management, and analysis**

10  
11  
12  
13  
14  
15  
16  
17

Data collection methods 18a Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol

18  
19

**Page 13**

- 20  
21  
22  
23
- 18b Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols

24  
25

**Page 7-8**

26  
27  
28  
29  
30

Data management 19 Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol

31  
32

**Page 13-14**

33  
34  
35  
36

Statistical methods 20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol

37  
38

**Page 14**

- 39  
40  
41
- 20b Methods for any additional analyses (eg, subgroup and adjusted analyses)

42  
43

**Page 14**

- 44  
45  
46
- 20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)

47  
48

**Page 14**

49

**Methods: Monitoring**

50  
51  
52  
53  
54  
55

Data monitoring 21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed

56  
57  
58  
59  
60

**N/A**

1		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial
2			<b>N/A</b>
3			
4			
5			
6			
7	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct
8			<b>N/A</b>
9			
10			
11			
12			
13	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor
14			<b>N/A</b>
15			
16			
17			
18			
19	<b>Ethics and dissemination</b>		
20			
21	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval
22			<b>Page 16</b>
23			
24			
25	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)
26			<b>Page 16</b>
27			
28			
29			
30			
31			
32	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)
33			<b>Page 16</b>
34			
35			
36			
37		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable
38			<b>N/A</b>
39			
40			
41	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial
42			<b>Page 13-14</b>
43			
44			
45			
46			
47	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site
48			<b>Page 17</b>
49			
50			
51	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators
52			<b>Page 13-14</b>
53			
54			
55			
56			
57			
58			
59			
60			

1			
2	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for
3	post-trial care		compensation to those who suffer harm from trial participation
4			<b>N/A</b>
5			
6	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to
7	policy		participants, healthcare professionals, the public, and other relevant
8			groups (eg, via publication, reporting in results databases, or other
9			data sharing arrangements), including any publication restrictions
10			<b>Page 16</b>
11			
12		31b	Authorship eligibility guidelines and any intended use of professional
13			writers
14			<b>N/A</b>
15			
16		31c	Plans, if any, for granting public access to the full protocol, participant-
17			level dataset, and statistical code
18			<b>N/A</b>
19			
20			
21			
22			
23	<b>Appendices</b>		
24	Informed consent	32	Model consent form and other related documentation given to
25	materials		participants and authorised surrogates
26			<b>Available Upon Request</b>
27			
28			
29	Biological	33	Plans for collection, laboratory evaluation, and storage of biological
30	specimens		specimens for genetic or molecular analysis in the current trial and for
31			future use in ancillary studies, if applicable
32			<b>N/A</b>
33			

---

\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.



## CONSORT 2010 checklist of information to include when reporting a randomised trial\*

Section/Topic	Item No	Checklist item	Reported on page No
<b>Title and abstract</b>			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2-3
<b>Introduction</b>			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	5
<b>Methods</b>			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-10
	3b	Important changes to methods after trial commencement (such as eligibility criteria) with reasons	Not applicable
Participants	4a	Eligibility criteria for participants	8
	4b	Settings and locations where the data were collected	8
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9-10
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	11-12
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Not applicable
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not applicable
<b>Randomisation:</b>			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9

1	Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
2				
3	Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	12
4				
5		11b	If relevant, description of the similarity of interventions	Not applicable
6				
7	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	14
8		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	14
9				
10	<b>Results</b>			
11	Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Not applicable
12				
13		13b	For each group, losses and exclusions after randomisation, together with reasons	Not applicable
14	Recruitment	14a	Dates defining the periods of recruitment and follow-up	Not applicable
15				
16		14b	Why the trial ended or was stopped	Not applicable
17	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Not applicable
18	Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Not applicable
19				
20				
21	Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Not applicable
22				
23		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Not applicable
24	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Not applicable
25				
26				
27	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Not applicable
28				
29	<b>Discussion</b>			
30	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	3
31	Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15
32	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15
33				
34	<b>Other information</b>			
35	Registration	23	Registration number and name of trial registry	2
36	Protocol	24	Where the full trial protocol can be accessed, if available	Not applicable
37	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	17
38				
39				
40				
41				
42				

1 \*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also  
2 recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials.  
3 Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see [www.consort-statement.org](http://www.consort-statement.org).  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-027793 on 3 July 2019. Downloaded from <http://bmjopen.bmj.com/> on June 12, 2025 at Agence Bibliographique de l'Enseignement Supérieur (ABES).  
Including for uses related to text and data mining, AI training, and similar technologies.

# BMJ Open

## An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China Protocol of a cluster randomised controlled trial

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-027793.R2
Article Type:	Protocol
Date Submitted by the Author:	28-Mar-2019
Complete List of Authors:	<p>He, Feng; Queen Mary University of London, Wolfson Institute of Preventive Medicine  Zhang, Puhong ; The George Institute at Peking University Health Science Center; University of New South Wales, Faculty of Medicine  Luo, Rong; The George Institute for Global Health at Peking University Health Science Center  Li, Yuan; The George Institute for Global Health, Peking University Health Science Centre; University of New South Wales, Faculty of Medicine  Chen, Fengge; Shijiazhuang Center for Disease Control and Prevention  Zhao, Yuhong; Changan Center for Disease Control and Prevention  Zhao, Wei; Shijiazhuang Center for Disease Control and Prevention  Li, Daoxi; Luzhou Center for Disease Control and Prevention  Chen, Hang; Luzhou Center for Disease Control and Prevention  Wu, Tianyong; Luzhou Center for Disease Control and Prevention  Yao, Jianyun; Yueyang Center for Disease Control and Prevention  Li, Jinbao; Yueyang Center for Disease Control and Prevention  Zhou, Siyuan; Yueyang Center for Disease Control and Prevention  Liu, Yu; Beihang University, School of Computing  Li , Xian; The George Institute for Global Health at Peking University Health Science Center  Wang, Changqiong; Queen Mary University of London, Wolfson Institute of Preventive Medicine  MacGregor, Graham; Queen Mary University of London, Wolfson Institute of Preventive Medicine</p>
<b>Primary Subject Heading</b>:	Public health
Secondary Subject Heading:	Global health, Public health
Keywords:	Salt Reduction, Schoolchildren and Families, m-Health, Randomised Controlled Trial

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



**An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China**

**Protocol of a cluster randomised controlled trial**

**Feng J He,<sup>1\*</sup> Puhong Zhang,<sup>2,3\*</sup> Rong Luo,<sup>2</sup> Yuan Li,<sup>2,3</sup> Fengge Chen,<sup>4</sup> Yuhong Zhao,<sup>5</sup>**

**Wei Zhao,<sup>4</sup> Daoxi Li,<sup>6</sup> Hang Chen,<sup>6</sup> Tianyong Wu,<sup>6</sup> Jianyun Yao,<sup>7</sup> Jinbao Li,<sup>7</sup> Siyuan**

**Zhou,<sup>7</sup> Yu Liu,<sup>8</sup> Xian Li,<sup>2,3</sup> Changqiong Wang,<sup>1</sup> Graham A MacGregor<sup>1</sup>**

<sup>1</sup> Wolfson Institute of Preventive Medicine, Barts and The London School of Medicine & Dentistry, Queen Mary University of London, UK

<sup>2</sup> The George Institute for Global Health at Peking University Health Science Center, China.

<sup>3</sup> Faculty of Medicine, University of New South Wales, Australia

<sup>4</sup> Shijiazhuang Center for Disease Control and Prevention, Hebei Province, China

<sup>5</sup> Changan Center for Disease Control and Prevention, Shijiazhuang, Hebei Province, China

<sup>6</sup> Luzhou Center for Disease Control and Prevention, Sichuan Province, China

<sup>7</sup> Yueyang Center for Disease Control and Prevention, Hunan Province, China

<sup>8</sup> School of Computing, Beihang University, Beijing, China

**\*Joint first author**

Correspondence to:

Professor Feng J He

Wolfson Institute of Preventive Medicine,  
Barts and The London School of Medicine & Dentistry,

Queen Mary University of London,

Charterhouse Square,

London EC1M 6BQ.

Tel: 44 (0)20 7882 6266

Fax: 44 (0)20 7882 6270

E-mail: [f.he@qmul.ac.uk](mailto:f.he@qmul.ac.uk)

Professor Puhong Zhang

The George Institute for Global Health at Peking University Health Science Center,

Level 18, Tower B, Horizon Tower, No. 6 Zhichun Rd,

Haidian District | Beijing, 100088 P.R. China

Tel: +86 10 8280 0577 ext 512

Fax: +8610 8280 0177

E-mail: [zpuhong@georgeinstitute.org.cn](mailto:zpuhong@georgeinstitute.org.cn)

## ABSTRACT

**Introduction:** Salt intake is very high in China, with  $\approx 80\%$  being added by the consumers. It is difficult to reduce salt in such settings. Our previous study (School-EduSalt, **School-based Education** programme to reduce **Salt**) demonstrated that educating schoolchildren who then instructed their families to reduce the amount of salt used at home, is effective in lowering salt intake in both children and adults. Our team also developed an app called “KnowSalt” which could help individuals to estimate their salt intake and the major sources of salt in the diet. Building upon School-EduSalt and KnowSalt, we propose to develop a new app (AppSalt) focusing on salt reduction through education, target setting, monitoring, evaluation, decision support and management, to achieve a progressive lower salt intake for long term. To evaluate the effectiveness of the AppSalt programme, we will carry out a cluster randomised controlled trial.

**Methods and analysis:** We will recruit 54 primary schools from urban and rural areas of 3 provinces in China. 594 children aged 8-9 years and 1188 adult family members will be randomly selected for evaluation. After baseline assessment, schools will be randomly allocated to either the intervention or control group. Children in the intervention group will be taught, with support of AppSalt, about salt reduction and assigned homework to get the whole family involved in the activities to reduce salt consumption. The duration of the intervention is two school terms (i.e. 1 year). The primary outcome is the difference between the intervention and control group in the change of salt intake as measured by 24-hour urinary sodium.

**Ethics and dissemination:** The study has been approved by Queen Mary Research Ethics Committee and Peking University Health Science Centre IRB. Results will be disseminated through presentations, publications and social media.

**Trial Registration:** Registered on Chinese Clinical Trial Registry, ChiCTR1800017553.

### Strengths and limitations of this study

- Our study will develop a new approach to achieving a sustainable progressive lower salt intake for long term.
- The study will use an innovative smartphone application through estimation of salt intake, education, target setting and monitoring, decision support and management to implement a salt reduction programme.
- The study covers a wide range of the population including children and adults in diverse settings, e.g. rural and urban, northern, central and southern China.
- The results should be generally applicable to the whole Chinese population.
- The study will be carried out in China only, however, the method could potentially be adapted by many other developing countries where most of the salt in the diet is added by the consumers.

## INTRODUCTION

Cardiovascular disease (CVD, i.e. strokes, heart attacks and heart failure) is the leading cause of death and disability worldwide. Approximately 80% of CVD deaths occur in developing countries.<sup>1</sup> Raised blood pressure (BP) is an important risk factor for CVD, accounting for 62% of strokes and 49% of coronary heart disease.<sup>2</sup> High salt intake is the major cause of raised BP.<sup>3</sup> Randomised trials have demonstrated that a reduction in salt intake lowers BP in both hypertensive and normotensive individuals, in both adults and children.<sup>4,5,6</sup> There is also compelling evidence that a lower salt intake is associated with a reduced risk of CVD and total mortality.<sup>7,8</sup> Indeed, salt reduction is one of the most cost-effective measures to prevent hypertension and CVD.<sup>3,9</sup> The World Health Organisation (WHO) has recommended a 30% reduction in population salt intake by 2025, and also set a target of <5 g/d for all adults and lower levels for children.<sup>10</sup> Many developed countries have started salt reduction initiatives.<sup>11</sup> Salt intake has been successfully reduced in Finland and the UK, accompanied by falls in population BP and CVD mortality.<sup>12</sup> Developing countries, however, are lagging behind. China is the largest developing country with one fifth of the world population. Salt intake in China is very high with an average of 12-14 g/d in adults<sup>13-15</sup>, and in some rural areas of northern China, salt intake could be as high as 18-20 g/d.<sup>16</sup> Approximately 80% of the salt in the Chinese diet is added by the consumers during cooking or in sauces.<sup>17</sup> It is extremely challenging to reduce salt intake in such settings due to the difficulty in changing individuals' dietary behaviours. Our previous study (School-EduSalt, **School-based Education programme to reduce Salt**) has developed a novel and effective approach to reducing salt intake in northern China.<sup>13</sup> In School-EduSalt, primary schoolchildren aged ≈10 years were educated about the harmful effects of salt on health and how to reduce intake during the school's usual health education lessons. Children then instructed their families to reduce salt. The results showed that, over one school term (≈3.5 months), salt intake was reduced by

1  
2  
3 ≈25% in both children and adults as measured by 24-hour urinary sodium excretion. The  
4  
5 reduction in salt intake led to a significant fall in systolic BP of 2.3 mmHg in adults.<sup>13</sup> It was  
6  
7 estimated that, if School-EduSalt was implemented and sustained, it would prevent ≈400,000  
8  
9 stroke and heart attack events per year in China.  
10  
11

12  
13 Previous studies have shown that salt reduction achieved by dietary advice attenuates over  
14  
15 time and maintaining a lower salt intake long-term remains a challenge.<sup>4</sup> The School-EduSalt  
16  
17 was successful over one school term of ≈3.5 months. The question is how to continue and  
18  
19 reinforce the salt reduction education to achieve a sustainable, progressive lower intake to  
20  
21 achieve the WHO's target.  
22  
23

24  
25 Mobile technology is increasingly used in health education.<sup>18</sup> Recent studies have suggested  
26  
27 that game-based intervention has great potential in changing behaviours due to the popularity  
28  
29 of gaming.<sup>19</sup> China has the largest and fastest growing mobile internet population with 802  
30  
31 million people using internet and mobile phone penetration reached 98.3% of the population  
32  
33 by June 2018.<sup>20</sup> Mobile-based decision support system has been shown to be effective in  
34  
35 increasing medication use in individuals with high CVD risk in rural China.<sup>21</sup> Our team have  
36  
37 recently developed a smartphone app (KnowSalt) which can be used by individuals to  
38  
39 estimate their salt intake and the major sources of salt in the diet. The methodology  
40  
41 underpinning KnowSalt app had been validated in a pilot study in primary schoolchildren and  
42  
43 their families.<sup>22</sup>  
44  
45  
46  
47

48  
49 Our proposed study building upon School-EduSalt and KnowSalt app will develop an  
50  
51 innovative smartphone application focusing on salt reduction (AppSalt) through functional  
52  
53 modules of education, evaluation, target setting and monitoring, decision support and  
54  
55 management, with the aim of reinforcing School-EduSalt to achieve a progressive lower salt  
56  
57 intake for long term. To evaluate the effectiveness and cost-effectiveness of the AppSalt  
58  
59 programme, we will carry out a cluster randomised trial.  
60

## METHODS AND ANALYSIS

The project consists of 2 phases: (1) Developing AppSalt platform; (2) Carrying out a cluster randomised controlled trial.

### Phase 1 – Development of AppSalt platform

AppSalt platform comprises a smartphone app named AppSalt (family end) and a WeChat mini app (teacher end). The AppSalt consists of 4 core procedures (i.e. Education, Evaluation, Decision support and Reminding) and 3 supportive modules (i.e. Competition & Award, Supervision & Communication and SaltSwitch) (Figure 1).

#### *Core procedures*

1. “Education” is to educate the families about the harmful effects of salt on health and how to reduce salt intake. Nine lessons are developed, each starting with a 10-min lecture on salt reduction, followed by a few questions to test whether the families have understood the content. At the same time, the questions and answers will re-enforce the key messages. Following each lesson, the families are required to complete a practical session which is designed to help the families to prepare foods with reduced salt at home and to choose lower-salt foods when shopping.
2. “Evaluation” is to estimate salt intake and the main sources of salt for every member of the family. After completing a simple questionnaire, the family will be provided with the information on the top 3 contributors of salt in their diet. This will help the family make a decision on how to effectively reduce salt intake. Evaluation of the top 3 contributors (i.e. top 3 sources of dietary salt) will be based on a 7-day salt surveillance method. Participants will record frequency of dining out, consumption of processed foods and the amount of salt added during cooking. The added salt will be assessed by weighing salt, soy sauce and other primary salty condiments on the first and last day of the evaluation period.<sup>23</sup>

1  
2  
3 3. “Decision Support” will set target for total salt intake and specific targets for top 3  
4 contributors. Lower-salt sample recipes and specific measures, e.g. reducing the amount of  
5 salt used during cooking by 50%, will be recommended. The recommended measures will be  
6 customised as an action plan.  
7  
8  
9

10  
11  
12 4. “Reminding” will remind the family how far their salt intakes are away from the targets set  
13 and highlight further action plans.  
14  
15

### 16 *Supportive modules*

17  
18  
19 1. The “Competition & Award” module will help the participants to find out their own  
20 ranking position assessed by salt intake level and the extent of salt reduction among all  
21 participants (NB: only their own ranking will be displayed and other participants’ ranking  
22 will not be revealed to them). The family with the lowest salt intake and the family who  
23 achieve the greatest reduction in salt intake, will be the winners of competition. They will be  
24 awarded an honorary title like “Salt Reduction Pacesetter” and get a small gift.  
25  
26  
27

28  
29 2. “Supervision & Communication” module: The teachers and researchers will use the  
30 function “Supervision” to announce instructions, newsletters, and school canteen menus, as  
31 well as providing answers to any queries. The participants will use the function  
32 “Communication” to ask any questions and also to exchange experience and knowledge with  
33 other participants.  
34  
35  
36  
37  
38  
39

40  
41 3. The “SaltSwitch” module will help the participants to choose pre-packaged foods with  
42 lower salt. “SaltSwitch”, as a sub-function of “FoodSwitch”<sup>24</sup> integrated into the AppSalt, has  
43 a database of over 50,000 pre-packaged foods collected by the George Institute China. By  
44 scanning the barcode of the pre-packaged foods, the “SaltSwitch” will provide information  
45 on salt/sodium content and compare it with other similar products based on products’  
46 labelling.  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 AppSalt will be installed in the smartphone of adult family members. Children are only  
4  
5 allowed to use AppSalt accompanied by their adult family members to complete AppSalt  
6  
7 core procedures as required. New features with a variety of presentation styles on salt  
8  
9 reduction education will be added to keep the programme attractive to the participants.  
10  
11

12  
13 The school teachers will use the WeChat mini app (teacher end) to send messages to the  
14  
15 families, provide timely feedback to any queries, and check families' progress and ensure all  
16  
17 families complete the procedures in time. The teachers will also report any issues to the site  
18  
19 managers and the research team where appropriate.  
20  
21

## 22 23 **Phase 2 — Cluster randomised controlled trial (RCT)**

24  
25 To test the effectiveness and cost-effectiveness of the AppSalt programme, we will carry out  
26  
27 a cluster randomised controlled trial (Figure 2).  
28  
29

### 30 *Study Setting and participants*

31  
32 Considering the geographical location, economic level and dietary habit, our study will be  
33  
34 undertaken in selected primary schools from urban and rural areas of 3 provinces in northern  
35  
36 (Hebei), central (Sichuan) and southern (Hunan) China.  
37  
38

39 To recruit schools, we will firstly contact the local education authority through local  
40  
41 Health/Education Bureau or Centre for Disease Control (CDC) to gain their opinion, support  
42  
43 and approval. We will then contact schools' head-teachers to request their participation in the  
44  
45 study. In each school, there are 6 grades with age ranging from 7 to 12 years and our study  
46  
47 will be carried out in grade 3 (age 8-9 years). Head-teacher will choose one class whose  
48  
49 teacher in charge is willing to collaborate with the researchers. From each class, we will  
50  
51 randomly select 11 children and 22 adult family members (i.e. 1 child and 2 adults per  
52  
53 family) for evaluation. The inclusion criteria are (1) Children and their adult family members have  
54  
55 to eat homemade meals at least four times per week; (2) One of the adults in the family has a mobile  
56  
57 device with access to Internet; (3) If more than 2 adults in one family agree to take part in the  
58  
59  
60

1  
2  
3 evaluation, we will select two in the order of grandparents, parents, uncles and aunts; (4)

4  
5 Participants have been local residents for over 6 months, without moving plan within 24 months. We  
6  
7 will exclude the individuals who cannot or refuse to collect 24-hour urine.  
8

### 9 ***Randomisation***

10  
11 Schools (clusters) will be randomly assigned (1:1) to either the intervention or the control  
12  
13 group. Randomisation will be stratified by the location of schools (i.e. south or north, urban  
14  
15 or rural) and the size of the class. The randomisation will be carried out using computer  
16  
17 generated random number by an independent statistician who is blind to the identity of the  
18  
19 schools. The randomisation will take place after baseline data collection has completed.  
20  
21

22  
23 Therefore, the participants, school-teachers and local investigators who undertake recruitment  
24  
25 and data collection, will be unaware of the allocation until the point prior to the  
26  
27 commencement of the intervention.  
28

### 29 ***Intervention***

30  
31 Our goal is to lower salt intake (measured by 24-hour urinary sodium) by a minimum of 15%  
32  
33 ( $\approx 1.5$ g salt) for both children and their families. To achieve this goal, a strategy towards a  
34  
35 50% reduction should be implemented. To make the decision-support algorithm simple in the  
36  
37 AppSalt, we will set targets for the top 3 contributors to salt intake, such as cooking salt.  
38  
39

40  
41 Targets and priority actions will be individualised depending on the sources of salt in the  
42  
43 individual's diet which will be provided by AppSalt. During the education lessons delivered  
44  
45 through AppSalt, the participants will be taught the methods on how to effectively reduce salt  
46  
47 intake, e.g. reducing the amount of salt, soy sauce and bean paste used during cooking.  
48  
49

50  
51 Garlic, ginger and herbs are recommended for enhancing food flavour. We also recommend  
52  
53 replacing pickles with fresh vegetables, and replacing salted eggs and peanuts with unsalted  
54  
55 ones.  
56

57  
58 In the intervention group, the AppSalt intervention package will be delivered to all children  
59  
60 and their families in the whole class, despite only 11 children and their families being

1  
2  
3 randomly selected for evaluation. The adult family members will be authorized to install and  
4 operate the AppSalt programme, while children will be assigned homework to get the whole  
5 family to reduce salt with the support of AppSalt. Children's homework will include: (a)  
6 helping the family to set salt reduction target and reminding the whole family of this target on  
7 a regular basis; (b) getting the whole family involved in salt reduction activities and  
8 persuading the person who does the cooking to reduce the amount of salt used during food  
9 preparations at home; (c) working with their family members to complete the AppSalt core  
10 procedures, including education, evaluation, target setting and monitoring. In addition to the  
11 online lessons, school teachers will organise three face-to-face seminars for both children and  
12 adults during the one-year intervention period. This will provide an opportunity for the  
13 participants to share experiences and discuss challenges and solutions. These seminars will be  
14 integrated into the schools' routine parent meetings.

15 Trained teachers will provide guidance on AppSalt utilisation, assign and check children's  
16 homework including monitoring the progress of salt reduction. They will also create salt-  
17 reduction environment, e.g. putting up posters in classroom, campus and canteens. The  
18 AppSalt will be activated at the beginning of the intervention for all families in the  
19 intervention group. Throughout the study, participants will receive salt reduction messages  
20 and newsletters via AppSalt on a monthly basis. Participants will be encouraged to use  
21 AppSalt and communicate with the teachers and other families to share experiences. The  
22 mandatory tasks for the participants include completing the online lessons and the related  
23 Q&As (Questions and Answers) at baseline and every month thereafter, and completing the  
24 core procedures, i.e. salt intake estimation, target setting at baseline and every 3 months  
25 thereafter. In addition to the mandatory tasks, the participants are encouraged to repeat the  
26 core procedures as often as they wish, in order to monitor their progress and achieve  
27 progressive reductions in salt intake. Based on the progress monitored from the WeChat mini  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 app, the teachers will remind children that they should complete their homework which is to  
4 help the family complete the AppSalt procedures in time and to instruct the family members  
5 to reduce salt to the target.  
6  
7  
8  
9

10 The records from AppSalt, e.g. salt intake and how far the intake is different from the target  
11 set, will be used to monitor compliance. During follow-up, the participant who fails to  
12 achieve the salt reduction target, will be sent a specially designed message via AppSalt and a  
13 letter to the child through his/her teacher to remind the family of the salt reduction target.  
14  
15  
16  
17  
18

19 The intervention duration is 2 school terms, i.e. 1 year. Children in the control group will  
20 carry on with their usual health education lessons as in the curriculum. After the trial is  
21 completed, we will introduce the AppSalt to all schoolchildren and their families including  
22 those in the control group.  
23  
24  
25  
26  
27  
28

### 29 ***Sample size calculation***

30 Based on the School-EduSalt trial,<sup>13</sup> assuming a standard deviation of 24-hour sodium  
31 excretion is 85mmol/day, and intraclass correlation coefficient (ICC) is 0.05, we estimate that  
32 a sample size of 594 children from 54 schools (18 primary schools from each province in  
33 both urban and rural area, and 11 children per school) would provide a power of 80% (with a  
34 two-sided alpha=0.05) to detect a difference in mean 24-hour urinary sodium  $\geq 26$ mmol/day  
35 (1.5 g/d salt) between intervention and control group, allowing for a 15% drop-out rate of  
36 participants. We aim to recruit 2 adults per family, therefore 1188 adults will be recruited into  
37 the study for evaluation.  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48

### 49 ***Outcome measures***

50 The primary outcome is the difference between the intervention and control group in the  
51 change of salt intake as measured by 24-hour urinary sodium from baseline to the end of the  
52 trial. The secondary outcome is the difference between the two groups in the change of  
53 systolic BP for adults.  
54  
55  
56  
57  
58  
59  
60

### ***Outcome assessments***

All outcome measurements and assessments will be carried out at baseline and at the end of the trial in exactly the same way in all schools for all participants, irrespective of their assignment to intervention or control group.

Two consecutive 24-hour urine collections will be made at each time point, using the stringent protocol which we developed in the School-EduSalt study.<sup>13</sup> Although there are other more convenient methods for assessing salt intake, e.g. a food diary, they are not reliable, and the most accurate method is 24-hour urine collection.<sup>25</sup> Our previous studies have shown that it is entirely feasible to collect 24-hour urine in both children and adults.<sup>13</sup> The participants will be carefully instructed on how to accurately collect 24-hour urine by trained research staff. On the first day, the participants will be asked to come to the schools. The researchers will ask the participants to empty bladder and discard the urine. The researchers will record the start time and date of the 24-hour urine collection. They will then give the participants the collection equipment including containers and collection aids such as carrier bags. The participants will be instructed to collect all subsequent urine voids over the next 24-hour period. On the second day at the same time, the participants will be asked to bring the urine collection bottles back to the schools and they will be asked to pass the last urine into the container. The researchers will record the finish time of the first 24-hour urine collection. The researchers will then give the participants the collection equipment for the second 24-hour urine collection and repeat the process. During the 24-hour urine collection period, the participants will be asked to take spare urine containers with them when they go to school or work. Spare collection equipment will also be available in the schools, in case children forget to bring them. In the case that the participant misses one or more urine voids or spillage occurs, the participant will be asked to do a further 24-hour urine collection. The 24-hour urine collections will be made either at weekdays or at weekends. For each

1  
2  
3 participant, the 24-hour urines will be collected on the same days of the week for baseline  
4  
5 and for follow-up at the end of the trial.  
6

7  
8 We will measure urine volume, sodium, potassium and creatinine. Ion-selective electrode  
9  
10 method will be used for sodium and potassium analysis and enzymatic method for creatinine  
11  
12 assay. 24-hour urinary creatinine together with urine volume will be used to determine if the  
13  
14 collection is likely to be complete. The biochemist who performs the measurements of  
15  
16 urinary electrolytes will not be told which group the participant is allocated.  
17

18  
19 In addition to 24-hour urine collection, we will measure BP and heart rate using a validated  
20  
21 automatic machine with the appropriate size of cuff. Three readings will be taken in the right  
22  
23 arm at 1-2-minute intervals at sitting position after the participant has had 10 minutes' rest in  
24  
25 a quiet room. Body weight, height and waist circumference will also be measured. Survey on  
26  
27 Knowledge, Attitude and Practice (KAP) related to salt will be completed via questionnaire.  
28  
29

## 30 31 **Data collection, management and analysis**

### 32 33 *Data collection*

34  
35 Our study will have two major data outputs. One is the “App Data” generated automatically  
36  
37 when the AppSalt platform is used by the families in intervention group to support salt  
38  
39 reduction. The App Data include information on demographic characteristics, eating habits,  
40  
41 amount and sources of salt in the diet, as well as information (or App logs) on the use of  
42  
43 AppSalt. The other data output is the “RCT Data” which is generated by both intervention  
44  
45 and control groups during the RCT. The RCT Data will be collected through a specially  
46  
47 designed mobile device based electronic data capture system (mEDC) by well-trained field  
48  
49 investigators. The mEDC has been validated and widely used in other clinical trials<sup>26</sup> with  
50  
51 more advantages on process and quality control compared with traditional EDC. The RCT  
52  
53 data include information on demographics, social-economic information, KAP, measurement  
54  
55 of height, weight, waist circumference, BP, heart rate, 24-hour urine volume and electrolytes,  
56  
57  
58  
59  
60

1  
2  
3 as well as information on costs for all the components of intervention conducted through the  
4  
5 AppSalt programme.  
6  
7

### 8 ***Data management***

9  
10 All cleaned and locked datasets together with the study design, questionnaire, code list and  
11  
12 definition of database and variables will be stored with a unique ID number attached but no  
13  
14 personal identifiers, in The George Institute China (TGI), following an established standard  
15  
16 operating procedure for data security. To guarantee the data security, the mobile app  
17  
18 developer (i.e. the IT team at Beihang University) must follow the “Mobile Application  
19  
20 Information Service Regulation” issued by the Cyberspace Administration of China in 2016.  
21  
22 Although personal data are accessible to app developer, disclosure of such information is  
23  
24 prohibited. In addition to the development and maintenance of the AppSalt and mEDC, IT  
25  
26 team will also provide data management service during the study to guarantee the safety,  
27  
28 integrity and proper use of the data collected through AppSalt and mEDC.  
29  
30  
31  
32  
33

### 34 ***Statistical Analysis***

35  
36 Data analyses will be performed according to the intention-to-treat approach. The effect of  
37  
38 the intervention on the outcomes will be tested using linear mixed models with participants  
39  
40 nested within family units and families nested within schools. We will include group  
41  
42 (intervention, control), time (baseline, end of trial), and time×group interaction, with the  
43  
44 time×group interaction term indicating differential change by group from baseline to the end  
45  
46 of the trial. We will adjust for the stratification variables at randomization and potential  
47  
48 confounding variables. Various sensitivity analyses will be carried out to examine the  
49  
50 robustness of the conclusions of the primary analysis. Results will be reported as mean, SD,  
51  
52 SE, and 95% confidence interval where appropriate. All analyses will be two sided and  
53  
54 P<0.05 is considered significant. SAS will be used for the analyses.  
55  
56  
57  
58  
59  
60

### ***Economic evaluation and process evaluation***

1  
2  
3 Economic evaluations will be carried out from health sector perspective to compare the m-  
4 Health strategy with usual care and it will entail two components: a trial-based economic  
5 evaluation and a modelled economic evaluation of long-term costs and outcomes.  
6  
7

8  
9  
10 Intervention costs will include those in running the programme but exclude any research and  
11 development costs. The trial-based economic evaluation will be assessed initially in terms of  
12 incremental cost per unit reduction in salt intake and systolic BP. The modelled economic  
13 evaluation with discounting will examine the cost, survival, quality of life over lifetime, via  
14 capturing various health states (including death and CVD events) to estimate incremental cost  
15 per life year saved and cost per Quality-Adjusted Life Year (QALY) gained. The transition  
16 probabilities across health states and costs attached to various health states will be based on  
17 literatures and the long-term effects of the reduction in salt intake or systolic BP will be  
18 derived from the trial findings and/or literatures of disease progression. Sensitivity analyses  
19 will be carried out to estimate uncertainty about the primary findings associated with varying  
20 key parameters.  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35

36 Mixed-method process evaluations will be conducted during and at the end of the study using  
37 data from AppSalt, key informant interviews with researchers and teachers, and focus groups  
38 interviews with participants. This will help understand the barriers and facilitators of the  
39 intervention as well as the acceptance and effect of the AppSalt programme.  
40  
41  
42  
43  
44

#### 45 **Project status and timelines**

46  
47 Recruitment of schools and participants started in September 2018. Baseline assessments  
48 were carried out between September and December 2018. As the intervention duration is one  
49 year, the final follow-up assessments will be carried out between September and December  
50 2019.  
51  
52  
53  
54  
55

#### 56 **Expected outcome and potential impact**

57  
58 The study will provide a novel, feasible and effective approach to achieving a sustainable  
59  
60

1  
2  
3 reduction in salt intake in both children and adults. The use of AppSalt platform in delivering  
4 health education lessons is particularly advantageous over the traditional school education  
5 method in terms of reducing the burden on teaching staff. Furthermore, our study covers a  
6 wide range of the population (children and adults, rural and urban, north and south), the  
7 results should therefore be generally applicable to the whole Chinese population. If the  
8 programme is implemented and sustained across China, it will reduce population salt intake  
9 and thereby prevent hundreds of thousands of strokes, heart attacks and heart failure each  
10 year, and lead to major cost-savings to individuals, their families and the health service.  
11 Although our study will be carried out in China, the AppSalt programme could potentially be  
12 adapted by many other countries. Additionally, our model on salt reduction could possibly be  
13 adapted for other dietary and lifestyle changes to prevent CVD and other non-communicable  
14 diseases, which will have major public health implications.

### 31 **Patient and Public Involvement**

32 During the development of the study protocol, we had 2 round-table meetings with 6 head-  
33 teachers from 3 different cities and several telephone meetings with teachers and children's  
34 parents to gain their opinion, particularly on the feasibility of carrying out the study in school  
35 settings and how to incorporate the intervention programme into the school curriculum.

36 During the study, school teachers will assign and check children's homework. Both teachers  
37 and head-teachers will be informed of the study progress by monthly communication via  
38 newsletters, WeChat and website. Upon completion of the study, we will disseminate the  
39 results to head-teachers, teachers, children and their parents. We will also discuss with them  
40 and other stakeholders on how to translate research findings into practice.

### 55 **ETHICS AND DISSEMINATION**

56 The study has been approved by Queen Mary Research Ethics Committee in the UK  
57 (QMERC2018/13) and Peking University IRB in China (IRB00001052-18051). Written  
58  
59  
60

1  
2  
3 consent will be obtained from all participants according to well-established practices. For  
4  
5 children, participant assent and parental written consent will be obtained. All participants will  
6  
7 be free to discontinue their participation at any time with no explanation required.  
8  
9

10 The findings of this study will be disseminated widely through conference presentations,  
11  
12 peer-reviewed publications, press release and social media. Furthermore, the results will be  
13  
14 disseminated worldwide through World Action on Salt and Health<sup>27</sup> which is a global non-  
15  
16 profit organisation with 600 members from 100 countries with the mission to improve the  
17  
18 health of populations by reducing salt intake.  
19  
20  
21  
22  
23

24 **Authors' contributions:** FJH and PZ conceived the project and contribute equally to the  
25 work. FJH, PZ, YLi and RL designed the study and oversaw the conceptualisation and  
26 development of the app. PZ, YLi, RL, FC, YZ, WZ, DL, HC, TW, JY, JL and SZ facilitates  
27 Patient and Public Involvement and were responsible for setting up the study in each site.  
28 YLiu and RL are leading the development and maintenance of the app. XL and CW  
29 contributed to sample size calculation and analysis plan. All authors contributed to the  
30 development of the intervention and evaluation. FJH wrote the first draft of the manuscript,  
31 and PZ, YLi, RL, CW and GAM revised the draft. All authors contributed to the refinement  
32 of the study protocol and approved the final manuscript.  
33  
34  
35  
36

37 **Funding statement:** This work is supported by the National Institute of Health Research  
38 using Official Development Assistance (ODA) funding (16/136/77). The views expressed in  
39 this publication are those of the authors and not necessarily those of the NHS, the National  
40 Institute for Health Research or the Department of Health.  
41  
42  
43

44 **Competing interests:** FJH is a member of Consensus Action on Salt & Health (CASH) and  
45 World Action on Salt & Health (WASH). Both CASH and WASH are non-profit charitable  
46 organisations and FJH does not receive any financial support from CASH or WASH. GAM is  
47 Chairman of Blood Pressure UK (BPUK), Chairman of CASH and Chairman of WASH.  
48 BPUK, CASH and WASH are non-profit charitable organisations. GAM does not receive any  
49 financial support from any of these organisations. Other authors declare no competing  
50 interests.  
51  
52  
53

54 **Acknowledgement:** We would like to thank the head-teachers, teachers and parents who  
55 shared their opinion on the development of the intervention programme.  
56  
57

58 **Word Count:** 4076 words.  
59  
60

## References

1. Lawes CM, Vander Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. *Lancet* 2008;371:1513-8.
2. World Health Report 2002: Reducing risks, promoting healthy life. Geneva, Switzerland: World Health Organisation, 2002. [www.who.int/whr/2002](http://www.who.int/whr/2002).
3. He FJ, MacGregor GA. Reducing population salt intake worldwide: from evidence to implementation. *Prog Cardiovasc Dis* 2010;52:363-82.
4. He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *BMJ* 2013;346:f1325.
5. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. *Hypertension* 2006;48:861-9.
6. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ* 2013;346:f1326.
7. He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. *Lancet* 2011;378:380-2.
8. He FJ, Campbell NR, Ma Y, et al. Errors in estimating usual sodium intake by the Kawasaki formula alter its relationship with mortality: implications for public health. *International Journal of Epidemiology* 2018;47:1784-95.
9. Asaria P, Chisholm D, Mathers C, et al. Chronic disease prevention: health effects and financial costs of strategies to reduce salt intake and control tobacco use. *Lancet* 2007;370:2044-53.
10. WHO issues new guidance on dietary salt and potassium, 31 January 2013. [http://www.who.int/mediacentre/news/notes/2013/salt\\_potassium\\_20130131/en/](http://www.who.int/mediacentre/news/notes/2013/salt_potassium_20130131/en/) (Accessed 30 January 2017).
11. Trieu K, Neal B, Hawkes C, et al. Salt Reduction Initiatives around the World - A Systematic Review of Progress towards the Global Target. *PLoS One* 2015;10:e0130247.
12. He FJ, Pombo-Rodrigues S, MacGregor GA. Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease mortality. *BMJ Open* 2014;4:e004549.
13. He FJ, Wu Y, Feng XX, et al. School based education programme to reduce salt intake in children and their families (School-EduSalt): cluster randomised controlled trial. *BMJ* 2015;350:h770.
14. Zhou BF, Stamler J, Dennis B, et al. Nutrient intakes of middle-aged men and women in China, Japan, United Kingdom, and United States in the late 1990s: the INTERMAP study. *J Hum Hypertens* 2003;17:623-30.
15. Zhang JY, Yan LX, Tang JL, et al. Estimating daily salt intake based on 24 h urinary sodium excretion in adults aged 18-69 years in Shandong, China. *BMJ Open* 2014;4:e005089.
16. Zhang L, Zhao F, Zhang P, et al. A pilot study to validate a standardized one-week salt estimation method evaluating salt intake and its sources for family members in China. *Nutrients* 2015;7:751-63.

17. Anderson CA, Appel LJ, Okuda N, 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;110:736-45.
18. Burke LE, Ma J, Azar KM, et al. Current science on consumer use of mobile health for cardiovascular disease prevention: a scientific statement from the American Heart Association. *Circulation* 2015;132:1157-213.
19. Payne HE, Moxley VB, MacDonald E. Health Behavior Theory in Physical Activity Game Apps: A Content Analysis. *JMIR Serious Games* 2015;3:e4.
20. CNNIC. The 42nd Statistical Report on the Development of China's Internet Network, 10 August 2018. [https://cnnic.net.cn/gywm/xwzx/rdxw/20172017\\_7047/201808/t20180820\\_70486.htm](https://cnnic.net.cn/gywm/xwzx/rdxw/20172017_7047/201808/t20180820_70486.htm) (Accessed 1 Nov 2018).
21. Tian M, Ajay V, Dunzhu D, et al. A Cluster-Randomized Controlled Trial of a Simplified Multifaceted Management Program for Individuals at High Cardiovascular Risk (SimCard Trial) in Rural Tibet, China, and Haryana, India. *Circulation* 2015;132:815-24.
22. Zhang L, Zhao F, Zhang P, et al. A pilot study to validate a standardized one-week salt estimation method evaluating salt intake and its sources for family members in China. *Nutrients* 2015;7:751-63.
23. Zhang L, Zhao F, Zhang P, et al. A pilot study to validate a standardized one-week salt estimation method evaluating salt intake and its sources for family members in China. *Nutrients* 2015;7:751-63.
24. Dunford E, Trevena H, Goodsell C, et al. FoodSwitch: a mobile phone app to enable consumers to make healthier food choices and crowdsourcing of national food composition data. *JMIR mHealth and uHealth* 2014;2:e37.
25. McLean R. Measuring population sodium intake: a review of methods. *Nutrients* 2014;6:4651-62.
26. Zhang J, Sun L, Liu Y, et al. Mobile Device-Based Electronic Data Capture System Used in a Clinical Randomized Controlled Trial: Advantages and Challenges. *J Med Internet Res* 2017;19:e66.
27. World Action on Salt and Health. <http://www.worldactiononsalt.com>

1  
2  
3 **Figure Legends**  
4  
5

6  
7 **Figure 1.** AppSalt core procedures and modules.  
8  
9

10 **Figure 2.** Appsalt trial design. BP: Blood Pressure.  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

Enseignement Supérieur (ABES) .  
Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

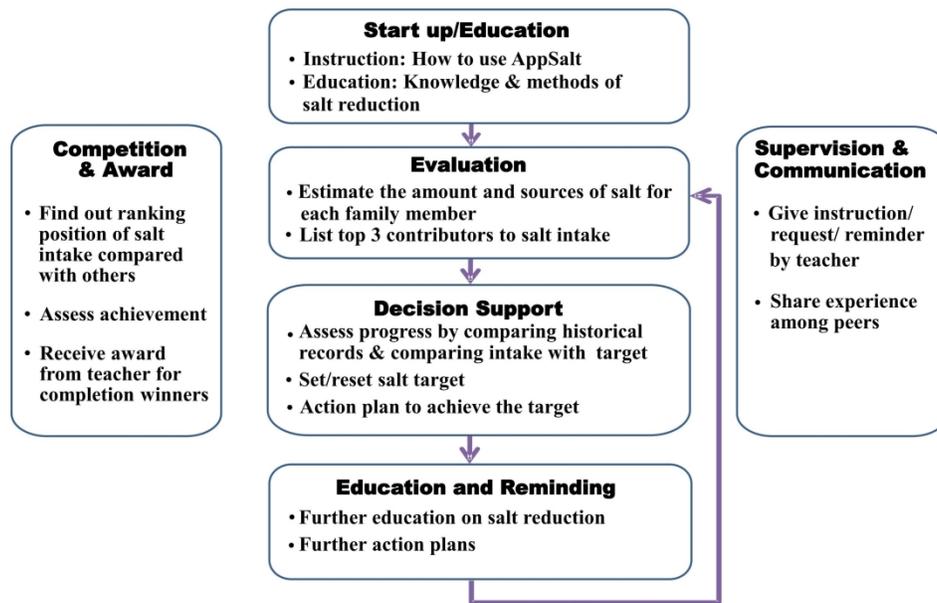


Figure 1 AppSalt core procedures and modules.

278x181mm (300 x 300 DPI)

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

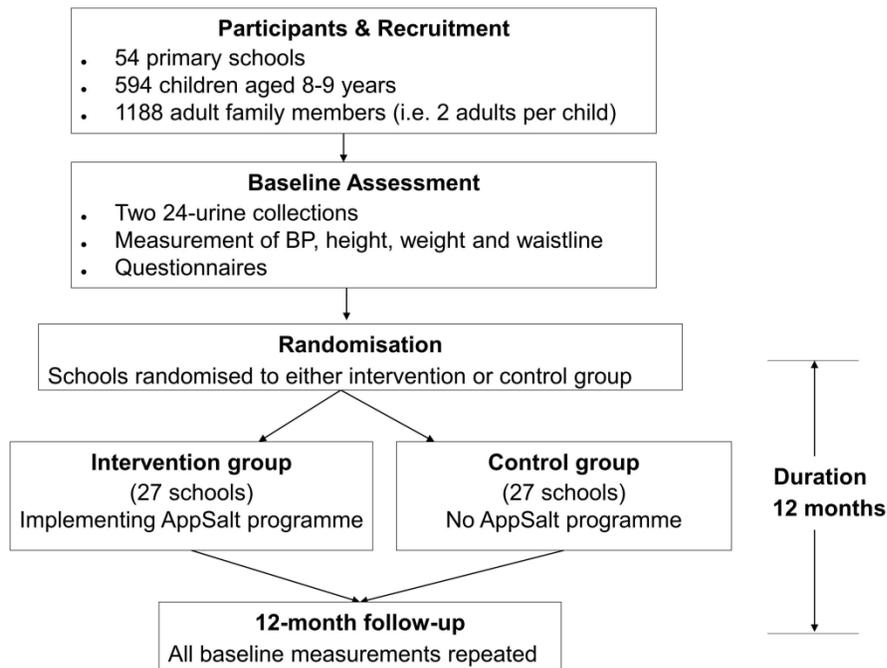


Figure 2 Appsalt trial design. BP: Blood Pressure.

277x189mm (300 x 300 DPI)



SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents\*

Section/item	Item No	Description
<b>Administrative information</b>		
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym <b>An app-based programme to reinforce and maintain lower salt intake (AppSalt) in schoolchildren and their families in China Protocol of a cluster randomised controlled trial</b>
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry <b>ChiCTR1800017553</b>
	2b	All items from the World Health Organization Trial Registration Data Set <b>Yes</b>
Protocol version	3	Date and version identifier <b>N/A</b>
Funding	4	Sources and types of financial, material, and other support <b>Page 17</b>
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors <b>Page 17</b>
	5b	Name and contact information for the trial sponsor <b>Queen Mary University of London</b>
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities <b>None</b>
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) <b>N/A</b>

## Introduction

- Background and rationale
- 6a Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention  
**Page 4-5**
- 6b Explanation for choice of comparators  
**Page 11-13**
- Objectives
- 7 Specific objectives or hypotheses  
**Page 9**
- Trial design
- 8 Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)  
**Page 8-11**

## Methods: Participants, interventions, and outcomes

- Study setting
- 9 Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained  
**Page 8-9**
- Eligibility criteria
- 10 Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)  
**Page 8-9**
- Interventions
- 11a Interventions for each group with sufficient detail to allow replication, including how and when they will be administered  
**Page 9-11**
- 11b Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)  
**N/A**
- 11c Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)  
**Page 10-11**
- 11d Relevant concomitant care and interventions that are permitted or prohibited during the trial  
**N/A**

1			
2	Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended
3			<b>Page 11-13</b>
4			
5			
6			
7			
8			
9			
10			
11	Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)
12			<b>Page 15</b>
13			
14			
15			
16			
17	Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations
18			<b>Page 11</b>
19			
20			
21			
22			
23	Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size
24			<b>Page 8</b>
25			
26			

### Methods: Assignment of interventions (for controlled trials)

#### Allocation:

27			
28			
29			
30			
31	Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions
32			<b>Page 8-9</b>
33			
34			
35			
36			
37			
38			
39			
40			
41	Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned
42			<b>Page 8-9</b>
43			
44			
45			
46			
47	Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions
48			<b>Page 9</b>
49			
50			
51			
52	Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how
53			<b>Page 13</b>
54			
55			
56			
57			
58			
59			
60			

- 1  
2  
3  
4  
5  
6  
7
- 17b If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial  
N/A

8  
9

### Methods: Data collection, management, and analysis

- 10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60
- Data collection methods 18a Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol  
**Page 13-14**
- 18b Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols  
**Page 7-8**
- Data management 19 Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol  
**Page 13-14**
- Statistical methods 20a Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol  
**Page 14**
- 20b Methods for any additional analyses (eg, subgroup and adjusted analyses)  
**Page 14**
- 20c Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)  
**Page 14**
- ### Methods: Monitoring
- Data monitoring 21a Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed  
**N/A**

1		21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial
2			<b>N/A</b>
3			
4			
5			
6			
7	Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct
8			<b>N/A</b>
9			
10			
11			
12			
13	Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor
14			<b>N/A</b>
15			
16			
17			
18			
19	<b>Ethics and dissemination</b>		
20			
21	Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval
22			<b>Page 16-17</b>
23			
24			
25	Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)
26			<b>Page 16-17</b>
27			
28			
29			
30			
31			
32	Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)
33			<b>Page 16-17</b>
34			
35			
36			
37		26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable
38			<b>N/A</b>
39			
40			
41	Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial
42			<b>Page 13-14</b>
43			
44			
45			
46			
47	Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site
48			<b>Page 17</b>
49			
50			
51	Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators
52			<b>Page 13-14</b>
53			
54			
55			
56			
57			
58			
59			
60			

1			
2	Ancillary and	30	Provisions, if any, for ancillary and post-trial care, and for
3	post-trial care		compensation to those who suffer harm from trial participation
4			<b>N/A</b>
5			
6	Dissemination	31a	Plans for investigators and sponsor to communicate trial results to
7	policy		participants, healthcare professionals, the public, and other relevant
8			groups (eg, via publication, reporting in results databases, or other
9			data sharing arrangements), including any publication restrictions
10			<b>Page 16-17</b>
11			
12			
13		31b	Authorship eligibility guidelines and any intended use of professional
14			writers
15			<b>N/A</b>
16			
17			
18		31c	Plans, if any, for granting public access to the full protocol, participant-
19			level dataset, and statistical code
20			<b>N/A</b>
21			
22			
23	<b>Appendices</b>		
24	Informed consent	32	Model consent form and other related documentation given to
25	materials		participants and authorised surrogates
26			<b>Available Upon Request</b>
27			
28			
29	Biological	33	Plans for collection, laboratory evaluation, and storage of biological
30	specimens		specimens for genetic or molecular analysis in the current trial and for
31			future use in ancillary studies, if applicable
32			<b>N/A</b>
33			

---

\*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "[Attribution-NonCommercial-NoDerivs 3.0 Unported](https://creativecommons.org/licenses/by-nc-nd/3.0/)" license.



## CONSORT 2010 checklist of information to include when reporting a randomised trial\*

Section/Topic	Item No	Checklist item	Reported on page No
<b>Title and abstract</b>			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance, see CONSORT for abstracts)	2-3
<b>Introduction</b>			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	9
<b>Methods</b>			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6-10
	3b	Important changes to methods after trial commencement (such as eligibility criteria) with reasons	Not applicable
Participants	4a	Eligibility criteria for participants	8-9
	4b	Settings and locations where the data were collected	8-9
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	9-11
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	11-13
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Not applicable
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Not applicable
<b>Randomisation:</b>			
Sequence generation	8a	Method used to generate the random allocation sequence	9
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	9
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	9

1	Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	9
2				
3	Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	13
4				
5		11b	If relevant, description of the similarity of interventions	Not applicable
6				
7	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	14
8		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	14
9				
10	<b>Results</b>			
11	Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Not applicable
12				
13		13b	For each group, losses and exclusions after randomisation, together with reasons	Not applicable
14	Recruitment	14a	Dates defining the periods of recruitment and follow-up	Not applicable
15				
16		14b	Why the trial ended or was stopped	Not applicable
17	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Not applicable
18	Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Not applicable
19				
20				
21	Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Not applicable
22				
23		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Not applicable
24	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Not applicable
25				
26				
27	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Not applicable
28				
29	<b>Discussion</b>			
30	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	3
31	Generalisability	21	Generalisability (external validity, applicability) of the trial findings	15-16
32	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	15-16
33				
34	<b>Other information</b>			
35	Registration	23	Registration number and name of trial registry	2
36	Protocol	24	Where the full trial protocol can be accessed, if available	Not applicable
37	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	17
38				
39				
40				
41				
42				
43	CONSORT 2010 checklist			
44				
45				
46				

1 \*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also  
2 recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials.  
3 Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see [www.consort-statement.org](http://www.consort-statement.org).  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42

For peer review only

BMJ Open: first published as 10.1136/bmjopen-2018-027793 on 3 July 2019. Downloaded from <http://bmjopen.bmj.com/> on June 12, 2025 at Agence Bibliographique de l'Enseignement Supérieur (ABES).  
Including for uses related to text and data mining, AI training, and similar technologies.