

# BMJ Open Protocol of a multicenter, single-blind, randomised, parallel controlled feeding trial evaluating the effect of a Chinese Healthy Heart (CHH) diet in lowering blood pressure and other cardiovascular risk factors

Wuxiang Xie <sup>1</sup>, Yanfang Wang,<sup>2</sup> Jianqin Sun,<sup>3</sup> Guo Zeng,<sup>4</sup> Huilian Zhu,<sup>5</sup> Zhenquan Yang,<sup>6</sup> Pei Gao <sup>7</sup>, Jing Yang,<sup>8</sup> Lin Feng,<sup>1</sup> Pao-Hwa Lin,<sup>9</sup> Ming Li,<sup>10</sup> Jianguo Xu,<sup>8</sup> Junshi Chen,<sup>11</sup> Yangfeng Wu<sup>1,7</sup>

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For numbered affiliations see end of article.

## Correspondence to

Dr Yanfang Wang;  
pucui\_wangyf1225@bjmu.edu.cn

## ABSTRACT

**Introduction** Unhealthy diet has been identified as the number one attributor of total mortality in China, accounting for more than 20% of total deaths. Although the Dietary Approach to Stop Hypertension (DASH) and Mediterranean diets have been proven beneficial in managing cardiovascular risk factors in Western countries, whether healthy diets with similar cardiovascular benefits can be developed that are consistent with Chinese food culture remains unknown.

**Methods/design** The Diet, Exercise and Cardiovascular Health (DECIDE)-Diet trial is a multicentre, single-blind, randomised controlled feeding trial to evaluate the effect of the Chinese Healthy Heart (CHH) diet, in comparison with the Chinese usual diet, in lowering cardiovascular risk factors among community residents with the increased cardiovascular risk. A total of 360 adults aged between 25 and 75 years old and with systolic blood pressure between 130 and 159 mm Hg will be recruited from four centres located in four areas representing four major Chinese cuisines: Beijing, Shanghai, Guangzhou and Chengdu. After 1 week of run-in period with local usual diet, the compliant participants will be randomised to the intervention group with the CHH diet or the control group with the usual local diet, on a 1:1 ratio, for 4 weeks. Body weight of study participants will be maintained during the entire study period. The primary outcome is the change in SBP from the baseline to the end of the study. DECIDE-Diet trial will be the first randomised controlled feeding trial to evaluate the effect of a CHH diet in lowering cardiovascular risk factors. This trial will provide compelling evidence on the CHH diet in effect of improving cardiovascular health among Chinese food consumers all around the world.

**Ethics and dissemination** This trial adheres to the Declaration of Helsinki and guidelines of Good Clinical Practice. Signed informed consent will be obtained from all participants. The trial has been approved by the Peking University Institutional Review Board (approval number: IRB00001052-18094). The results will be disseminated

## Strengths and limitations of this study

- This trial will be the first randomised controlled feeding trial to evaluate the effect of a Chinese Healthy Heart (CHH) diet in lowering cardiovascular risk factors.
- The CHH diet includes different versions according to four major Chinese cuisines to ensure the preference by local people.
- We will investigate the effect of the CHH diet on gut microbiome in this trial and the results might provide additional information linking the healthy diet and health outcomes.
- The food nutrients in the CHH diet will be calculated according to the China Food Consumption Table, instead of using chemical analyses of the whole dishes.

through academic conferences and publications in international peer-reviewed journals.

**Trial registration number** ClinicalTrials.gov Registry (NCT03882645); Pre-results.

## INTRODUCTION

Cardiovascular disease (CVD), including ischaemic heart disease and stroke, remains the leading cause of death worldwide, but its mortality has declined in high-income countries.<sup>1</sup> In contrast, the cardiovascular burden in China has increased rapidly since 1980s, as a consequence of rapid changes in lifestyle, environment and population ageing.<sup>2,3</sup> Among these changes, dietary changes might be one of the biggest changes and one of the biggest drivers to the increase in the burden of CVD in China. Data from the China National Nutrition Surveys showed that the

average consumption of pork among Chinese residents increased from 37.1 g/day to 64.3 g/day, and dietary energy from fat increased from 22.5% to 33.1% from 1992 to 2012.<sup>4</sup> Conversely, Chinese people are eating much less grains and vegetables during the same time period.<sup>4</sup> Such dramatic changes in the food pattern have been confirmed in multiple studies.<sup>5,6</sup> According to the Global Burden of Diseases (GBD) study 2013, the unhealthy diet and high systolic blood pressure (SBP) ranked the top 1 and 2 risk factors leading to total death and the loss of disability-adjusted life-years (DALYs).<sup>7</sup> More recently, the GBD study reported that dietary risk factors accounted for 11 million deaths and 255 million DALYs worldwide in 2017.<sup>8</sup> Among the world's 20 most populated countries, China ranked the first on the age-standardised rates of diet-related CVD deaths.<sup>8</sup> Clearly, China needs to develop effective dietary strategies to improve the health status of its people.

Studies have demonstrated that the high intake of sodium and low intake of whole grains and fruits are the leading dietary risk factors for deaths and DALYs worldwide.<sup>8</sup> Several healthy diets with low-sodium, high fruits/vegetables and fibres, such as the DASH diet and the Mediterranean diet, have been proven to lower blood pressure, lipids, glucose and the risk of CVD with randomised controlled trials (RCTs).<sup>9–13</sup> However, these diets have not been tested within Chinese food culture. China has one-fifth of the world's total population and Chinese food is popular around the world. A healthy diet that fits into Chinese food culture and well received by Chinese people and is affordable and effective in improving CVD health could bear great significance in prevention and control of CVD in China, in overseas Chinese communities and people who like Chinese food globally. The development and evidence in health benefit gained on such a diet has the potential to impact a large segment of people globally.

To develop effective lifestyle interventions for prevention and control of CVD in China, the Diet, Exercise and Cardiovascular Health (DECIDE) programme was initiated in 2016. As one of the five independent DECIDE projects, the DECIDE-Diet trial aims to develop a tasty, affordable and healthy Chinese diet—the Chinese Healthy Heart (CHH) diet—that could improve CVD health. Specifically, the primary aim of the study is to determine the effect of the CHH diet in reducing SBP, compared with the usual Chinese diet. The secondary aims of the study are: (1) to evaluate the effect of the CHH diet in lowering diastolic blood pressure (DBP), blood glucose, serum lipids and estimated 10-year risk of CVD; (2) to understand whether the intervention effects would be modified by the types of Chinese cuisines; (3) to compare the participants' preference of the CHH diet with that of the usual Chinese diet and (4) to explore the possible impact of the CHH diet on the gut microbial community, including microbial composition and abundance. Recent studies have reported that gut microbiome might play a key role in linking the healthy dietary intakes with CVD risk reduction.<sup>14,15</sup> But the causal relationships between

dietary intakes, gut microbial community and CVD risk factors have not been rigorously studied in randomised controlled studies.

## METHODS

### Study design

The DECIDE-Diet trial is a four-centre, single-blind, randomised controlled feeding trial among community residents with the increased risk of CVD. Eligible participants, 90 from each centre, will be recruited from four centres in four geographical locations representing four different styles of Chinese cuisines (Cantonese, Szechuan, Huaiyang and Shandong). Participants will be randomised with stratification by the centre in a 1:1 ratio into intervention and control, after 1 week of a run-in period on the local usual diet. The intervention group will receive the CHH diet and the control group will receive the local usual diet. Both diets will be prepared by cooks hired by the study, according to the menus and recipes developed by the study nutritionists. Both diets will use food materials available on the local markets at the season and will be provided free of charge. The interventions will last for 4 weeks, and both groups will be followed up on the same time schedules for all outcome measurements. [Figure 1](#) shows the flowchart of the study participants.

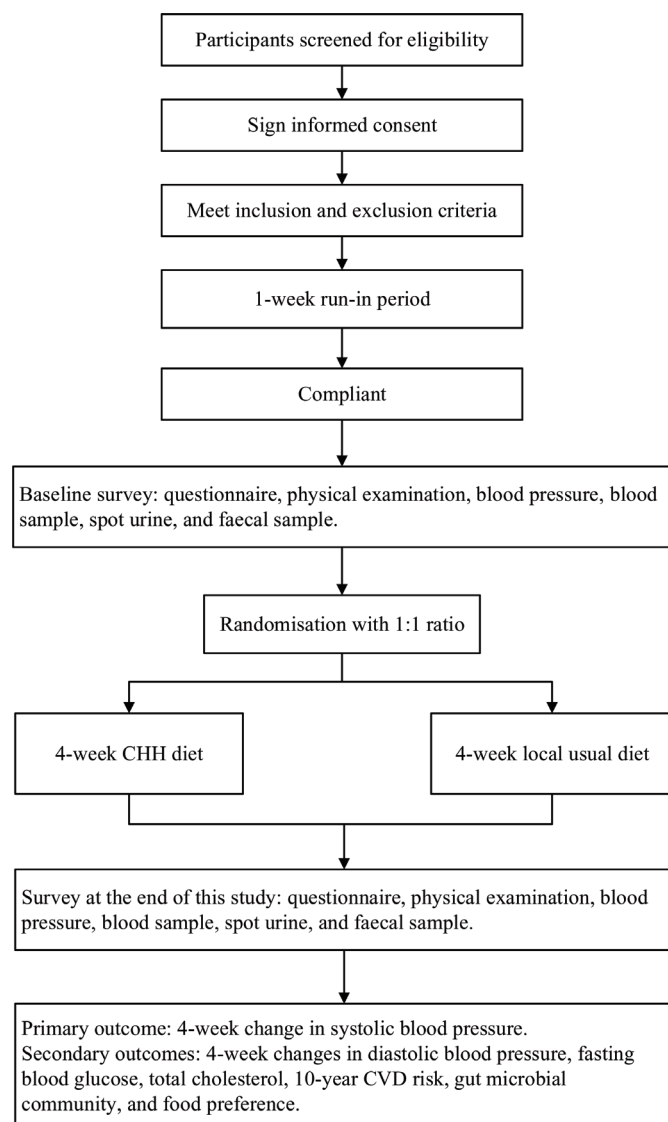
### Participant recruitment

Four cities selected as the study sites representing four typical Chinese cuisines are Beijing (Shandong cuisine), Shanghai (Huaiyang cuisine), Guangzhou (Cantonese cuisine) and Chengdu (Szechuan cuisine). Inclusion of different cuisines increases the acceptability of the CHH diet in local residents and demonstrates the generalisability of the CHH diet.

Men and women aged between 25 and 75 years old, living in the target communities for at least 6 months prior of the study, with SBP between 130 and 159 mm Hg are eligible for this trial. [Boxes 1 and 2](#) list the details of inclusion and exclusion criteria. Potential participants will complete two screening visits for eligibility before entering the run-in phase. At the first screening visit, a trained lay recruiter will screen the potential participants using a simple questionnaire. At the second screening visit, a trained research staff will confirm the eligibility by measuring blood pressure and checking every inclusion and exclusion criteria.

### Run-in period

Only participants that passed the second screening will be invited to participate in the 1-week run-in phase during which all participants will be provided with the usual local diet. During the run-in period, amounts of food consumed will be measured daily to assess the total energy, salt and cooking oil intake. Participants will be asked, on a daily basis, of food preference, in particular the saltiness, and adjustments will be made to best fit their preferred taste. The total energy and nutrients composition, amount of



**Figure 1** The flowchart of the Diet, ExerCISE and Cardiovascular hEalth (DECIDE)-Diet trial. CHH, Chinese Healthy Heart; CVD, cardiovascular disease.

salt and cooking oil used daily during the run-in phase will be kept unchanged during the rest of the study period in the control group.

## Box 1 Inclusion criteria

- ▶ Men and women aged 25–75 years old.
- ▶ Living in the study communities for the past 6 months and having no plan to move or travel in the next 3 months.
- ▶ Having a mean systolic blood pressure in 130–159 mm Hg, regardless of medication use.
- ▶ Agreed to keep the current medications and dosages unchanged throughout the study.
- ▶ Promised to follow the study diets for 5 weeks and eat at least 18 study meals per week.
- ▶ Able to have at least one meal per day taken on site.
- ▶ Signed informed consent.

## Box 2 Exclusion criteria

- ▶ Fasting blood glucose  $\geq 10.0$  mmol/L.
- ▶ Total cholesterol  $\geq 7.2$  mmol/L.
- ▶ The number of total oral medications for antihypertensive, hypoglycemic or lipid-lowering  $> 2$  for the past 3 months.
- ▶ Any changes in dose and/or type of oral medication for antihypertensive, hypoglycemic or lipid-lowering in the past 3 months.
- ▶ Insulin injection within 1 month.
- ▶ Unable or unwilling to change diet for any reason (such as vegetarians).
- ▶ Relatives of researchers or study administrators.
- ▶ Already having family members in this study.
- ▶ Alcohol consumption  $\geq 8$  drinks per week for women,  $\geq 15$  drinks per week for men.
- ▶ Body mass index  $\geq 30$  kg/m<sup>2</sup> or currently losing weight.
- ▶ Acute cardiovascular and cerebrovascular events within the past 6 months.
- ▶ A history of chronic kidney disease, intestinal irritation or asthma.
- ▶ Current or planned pregnancy prior to the end of study, or breast feeding.
- ▶ Other serious chronic disease thought to interfere with the effect of the diet or with participation, such as tumour, chronic heart failure, severe depression or other mental disorders, immobilisation or unable to move freely.
- ▶ Allergy of common food (eg, eggs, seafood, peanuts, etc).
- ▶ On special diet due to medical needs.
- ▶ Acute diseases such as upper respiratory tract infection, fever and severe diarrhoea.
- ▶ Deafness, dementia and inability to communicate.

The total energy intake level of each participant will be maintained for all individuals in both groups throughout the study to avoid significant weight changes. At the end of the run-in phase, the participants will be assessed again for their eligibility to the study and adherence to the study protocol. Any participant who failed to consume three or more study meals for any reason during the week and any participant with mean SBP measured on three occasions (08:00–10:00, 14:00–16:00 and 18:00–20:00), 3 readings for each, within 24 hours and with an average reading of  $< 130$  or  $\geq 160$  mm Hg will be excluded from further participating the trial.

## Randomisation

Participants who pass the run-in phase and complete the baseline data collection on the last 2 days of the run-in will be randomly assigned in a 1:1 ratio to the intervention and control group. We will use a centrally concealed randomisation procedure stratified by study sites and batches of study participants. We assume that each study site needs to implement the trial in multiple batches of participants for the reason of feasibility. However, the multiple batches may introduce possible variances in foods and blood pressure by seasons. Thus, the randomisation stratified by batches of participants and study sites is considered necessary. A statistician centrally based at the study coordinating centre in Peking University Clinical Research Institute will be responsible for generating

the random allocation sequence using SAS V.9.4 (SAS Institute).

### Blinding

Due to the nature of the dietary intervention, it is impractical to blind the cook, dietitian and the study staff who are responsible for preparing the foods and taking all measurements of the diets. However, staffs conducting the outcome assessments will be blinded to the allocation of intervention assignments. In addition, every effort is made to blind the study participants in their intervention assignment. First, they will not be told of their group assignment. Second, the two groups will consume their meals in separate rooms. Third, the same dishes using similar food materials will be used for both groups at the same meal. For example, both groups will have Kung Pao Chicken at the same meal, but the one for the intervention group will be the healthy version and the one for control will be the regular version. In some occasions, foods that look-alike but contain different nutrients may be used.

### Intervention

Both intervention and control diets will be prepared in the study kitchen at each centre and then delivered to the dining rooms and distributed to each study participant. Standardised energy foods, with energy level ranging from 80 kcal to 200 kcal each, will be used to provide additional energy for the study participants when needed to assist with maintenance of body weight. The participants will be generally required to eat all their meals on-site during the entire study period. Less than 20% of the study meals are allowed to be taken home to eat with

investigators permission each week when the participants are unable to consume on-site. In these cases, the photos of the remaining foods need to be taken and submitted to the study staff for assessment. Overall, the study participants should consume at least the lunch meal on-site each day and should have more than 80% of the study meals consumed on-site each week. Otherwise, the participant is considered non-compliant according to the study protocol.

China has a unique blend of culturally and geographically diverse regional cuisines. To maximise the generalisability and acceptability of the diet, four different versions of the CHH diet have been developed according to the four major Chinese cuisines: Shandong cuisine (north of China), Huaiyang cuisine (east of China), Cantonese cuisine (south of China) and Szechuan cuisine (south-west of China). All four versions of the CHH diet share the same nutrient targets (table 1). The healthy version dishes menu was based on a survey of local residents on the most common and popular local foods, and to ensure the preference of flavour by the participants.

The recipes of the CHH diet (intervention diet) were designed by the research team consisted of medical researchers, physician, nutritionists, registered dietitian and chefs of each study centre, according to the nutrient composition targets of the CHH diet. See table 1 for specific targets of each nutrient and the strategies to achieve these targets. The nutrients composition of a usual Chinese diet in urban China<sup>16</sup> are also listed in table 1 for comparison. According to the nutrient targets, the resultant CHH diet will increase intakes of nuts, seeds and beans or bean product to 200 g/week, fruits to 150 g/

**Table 1** The nutrients composition of a usual Chinese diet in urban China and the CHH diet, and strategies to achieve the CHH diet's nutrients' targets

Nutrients	Usual diet in urban China	CHH diet	Strategies to achieve the CHH diet's target
Energy (kcal)	2053	Individualised	Averaged intake assessed during run-in
Fat (% of total kcal)	33	25–27	Reducing the use of cooking oil by changing cooking method, for example, replacing deep frying with steaming and use low-fat or non-fat dairy products
Saturated	–	6	
Monounsaturated	–	12	
Polyunsaturated	–	8	
Carbohydrates (% of total kcal)	55	55–60	Increasing whole grains and limiting the use of monosaccharide
Protein (% of total kcal)	13.5	17–19	Increasing intake of protein from lean meat, beans and milk
Fibre (g/day)	11	30	Increasing use of foods with higher dietary fibre
Sodium (mg/day)	5859	3000	Using less salt in cooking and replacing regular salt with salt substitute
Potassium (mg/day)	1660	3700	Increasing use of food that contain high amount of potassium and use of salt substitute
Magnesium (mg/day)	–	500	Using food that contain high amount of magnesium
Calcium (mg/day)	412	1200	Increasing use of dairy products, lean meat and beans

CHH, Chinese Healthy Heart.



**Table 2** An example of 1-day menu of Shandong cuisine

	Chinese Healthy Heart diet	Control diet
Breakfast	Steamed twisted roll mixed with vegetable	Steamed twisted roll
	Millet congee	Millet congee
	Boiled egg	Boiled egg
	Boiled Mung bean sprout in sauce with nuts	Boiled soybean sprouts in sauce
Lunch	Steamed rice with oats	Stir fried rice with meat and bean
	Stir fried cabbage with vermicelli	Stir fried cabbage with bean starch noodle
	Stewed tofu with shrimp and radish	Seaweed and egg soup
	Banana (half)	
Dinner	Skim milk	
	Steamed bun mixed with corn meal	Steamed bun stuffed with round pork and celery
	Rice congee with red bean	Rice congee
	Stir fried enoki mushroom with bell pepper and dried bean curd	Stir fried mushroom with bell pepper and dried bean curd
	Yoghurt	Steamed twisted roll

day and vegetables to 300g/day. A sample 1-day menu of Shandong cuisine is shown in [table 2](#).

The CHH diet was designed to be easily adopted so that it can be applied in a variety of settings. Specifically, the CHH diet consists of a set of menus that include 2 weeks of non-repeating and exchangeable meals for breakfast, lunch and dinner. With fixed recipes and standard cooking procedures, this diet can be easily learnt and used by professional cooks and even individuals at home. The flavour and preference of each main dish had been tested before it is incorporated into the CHH diet, to ensure the acceptability by the study participants.

The control group will receive the local usual diet with the same 4-week menus as the CHH diet, but the targets of major nutrients, salt and cooking oil will be kept the same as that in the run-in phase.

### Measurements and data collection

The formal baseline data collection should be performed on the last 2 days of the run-in phase, which includes a questionnaire interview on demography (age, sex, occupation, education, marital status, household income and health insurance), lifestyle and health behaviours (smoking, drinking, physical activity and dietary habits), history of diseases (stroke, myocardial infarction, angina, atrial fibrillation, heart failure, chronic kidney disease, chronic obstructive pulmonary disease and cancer), medication use (antihypertensive drugs, antidiabetic drugs and lipid-lowering drugs), food preference, physical examinations (blood pressure, height, weight and pulse rate), fasting blood tests (fasting blood glucose, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and serum potassium), spot urine tests (sodium and potassium excretion) and faecal sample tests on the gut microbial community.

The questionnaire has been developed by the study team employing standard questions from previous

studies. For assessment of food preference, participants will be asked at end of each week to rate their preference of the previous week's meals on a visual analogue scale ranging from 0 to 10 (10 represents 'preferred the most'). We will further request more specific information about the foods if someone's scale is less than 7. Meanwhile, we will also regularly collect their comments about the food during this trial on site.

### Methods of physical measurements

We will use Omron HEM-7136 blood pressure monitor to measure SBP, DBP and pulse rate. Blood pressure will be taken three times within 24 hours at baseline and at the end of this trial: one in the morning between 08:00 and 10:00, one in the afternoon between 14:00 and 16:00 and one in the evening between 18:00 and 20:00, respectively. In each time, three readings should be taken with at least 1-minute intervals. The average of the nine SBP readings will be used in our analysis. We will use the Tanita HD-366 digital weight scale to measure body weight. We will stick a Hoehchstmass-99202 tape measure vertically to a vertical wall and a trigonometric ruler to measure height.

### Blood and spot urine samples collection and tests

The blood sample of participants from the four centres will be collected in their fasting state by the qualified nurses. The over-night urine sample of each participant will be collected to estimate population mean levels of sodium excretion which reflects dietary sodium intake using Kawasaki's formula.<sup>17</sup> Participants will be carefully instructed on how to accurately collect spot urine by research staff. Centrifuged serum samples and urine samples will be frozen and transported to Beijing through the complete cold chain and measured in the central laboratory, Lawke Health Laboratory in Beijing. Analysis of fasting blood glucose (using the hexokinase method), total cholesterol, low-density lipoprotein cholesterol,

high-density lipoprotein cholesterol (using the enzymatic colourimetric assay) and triglycerides (using the colourimetric assay), serum potassium and urinary sodium and potassium (using the Ion selective electrode (ISE) method) will be carried out on a Roche Cobas c501 automatic biochemistry analyzer.

### Faecal sample collection and tests

Stool collection supplies, including sampling bowl, gloves and faecal collection tube, will be given to participants, with verbal instructions delivered and written instructions distributed on how to collect and deliver the faecal sample to the research centre. Once the participant defecates the next morning, an approximate 50-gram faeces sample per person will be collected into sterile faecal collection tubes (40 mL), and placed in icebox immediately for storage, and then transporting to the central laboratory in Beijing. Faecal DNA will be extracted from each sample using the QIAamp Fast DNA Stool Mini Kit (QIAGEN, cat. 51604). To investigate the microbial community, shotgun metagenomic and amplicon sequencing strategies will be used.

### Dietary intake of foods and nutrients

First, for each food/dish, raw food materials will be weighted after cleaning and before cooking. Then, before the food serviced to the study participants, it will also be measured and recorded. After each meal, the leftover from each participant will be weighed and recorded as well. The daily average total energy and dietary nutrients taken by each participant can be calculated using the China Food Composition (second edition, volume 1).<sup>18</sup>

When weighing the leftover is not applicable, the proportion of leftovers will be estimated by the visual observation method by the trained staff. The mean difference of the estimated from the weighted proportion was 0.5% (95% CI -1.1% to 2.1%) for on-site visual

observation and -0.4% (95% CI -1.9% to 1.0%) for photo visual observation (observing photos of leftovers), respectively. The intraobserver correlation coefficient (ICC) of the estimated proportion of leftover for onsite visual observation with weighing ranged from 0.714 to 0.960 and the ICC of the estimated proportion of leftover for photo visual observation ranged from 0.756 to 0.959.

We will also collect self-reported information before every meal on foods that are taken by the participants but not provided by the study.

### Follow-up schedules

The same questionnaire interview and physical examinations will be repeated at the end of the trial with the same methods by staffs blinded to the interventions. In addition, blood pressure, body weight and food preference will be assessed weekly during the trial. If a participant's weight changes more than 2 kg from baseline, we will adjust his/her energy intake right away in order to stabilise weight. The medication use will be monitored, and participants will be reminded to take their prescribed medication daily unless their physicians require to change. The schedule of measurements and visits of this trial has been summarised in [table 3](#).

### Data management

A web-based data management system (DMS) will be used to facilitate data collection and central management during the whole process of the trial. Data will be subjected to a full set of web-based DMS validation checks and additional manual data checking procedures to assure the quality of data entry. Access to stored information is restricted to authorised personnel only. Paper forms with participant-identifiable information are held in secure, locked filing cabinets within a restricted area of

**Table 3** The schedule of measurements and visits of this trial

	Screening	Run-in*	Follow-up (weeks)			
			1	2	3	4
Signed informed consent	√					
Eligibility confirmation	√	√				
Questionnaire interview	√	√				√
Dietary record†		√	√	√	√	√
Food preference assessment		√	√	√	√	√
Height	√					
Weight	√	√	√	√	√	√
Blood pressure and pulse rate	√	√	√	√	√	√
Blood sample		√				√
Spot urine		√				√
Faecal sample		√				√
Reasons for withdrawal		√	√	√	√	√

\*Baseline data are collected on the last 2 days of the run-in period.

†Dietary data will be collected on the daily basis.

each site. Trial documentation and data will be archived for at least 5 years after the completion of the trial.

## Outcomes

The primary outcome is the change in SBP from baseline to the end of the study. The mean of nine readings will be used for the calculation of the changes in each participant. The secondary outcomes include a change in DBP, fasting blood glucose, total cholesterol, 10-year CVD risk, gut microbial community and food preference from baseline to the end of study. The 10-year CVD risk will be calculated according to 10-year risk prediction models for ischaemic CVD derived from the USA-PRC (The People's Republic of China) Collaborative Study of Cardiovascular Epidemiology cohort.<sup>19</sup>

## Sample size

According to the findings from the DASH diet that successfully reduced SBP by 5.5 mm Hg in 8 weeks,<sup>9</sup> we conservatively assumed that the CHH diet will reduce SBP by 3.0 mm Hg in comparison with the control diet in 4 weeks. And we further assumed the SD of SBP change will be 8 mm Hg in the control group according to our previous studies.<sup>19 20</sup> To have 90% power with a type I error rate of 5% to detect the assumed effect size, we would need 165 participants in each arm. Assuming that 10% of study participants will be lost by the end of the study, we will recruit a total of 360 participants (90 from each centre).

## Statistical analysis

The primary analyses will follow the intention-to-treat principle and will be conducted among participants who have been randomised and also completed the final follow-up. The linear regression will be used to estimate the absolute differences between two groups in both primary and secondary outcomes, reported as least squares means after adjusting for centres. The differences in baseline variables between groups will be evaluated by using a t-test, Wilcoxon rank test or  $\chi^2$  test. Sensitivity analyses will be performed to adjust for the imbalanced baseline variables if existed and to repeat the analyses with imputed missing values due to the lost to follow-ups. We will adopt the multiple imputation, chained-equations method to impute the missing values of primary and secondary outcomes if participants are lost to the follow-up at the end of this study. Variables used to impute the missing values of each outcome will include participants' available values of this outcome (such as baseline values and weekly measurements) and other variables which are associated with this outcome. We will create 20 imputed data sets for each outcome and the mean value of this outcome will be used in our analysis. Per-protocol analyses will be conducted among population, including those who will consume more than 80% of study meals and completed the final follow-up. Subgroup analyses will be performed to identify potential modifiers of the intervention effect, including the type of Chinese cuisine,

gender, age, baseline multi-morbidity, medications use, blood pressure, glucose, total cholesterol and estimated a 10-year risk of ischaemic CVD.

## Patient and public involvement

No patients or public were involved in the design, conduct, reporting or dissemination of this research study.

## Ethical and dissemination

This trial adheres to the Declaration of Helsinki and guidelines of good clinical practice. Signed informed consent will be obtained from all participants. Participant data in the DMS will be protected by password and only available to users designated by the study with appropriate authorisation levels. De-identified data will be used for statistical analysis. The current trial has been approved by the Peking University Institutional Review Board (approval number: IRB00001052-18094) and registered in ClinicalTrials.gov.

The results of this trial will be disseminated through academic conferences and publications in international peer-reviewed journals.

## Quality control

The quality control team was established before the initiation of this study. All the researchers participating in this study must attend the technical training and pass the examination organised by the coordinating centre, including study protocol, informed consent, case report form, standard operating procedures of participants' data collections and collection and preservation methods of biological samples.

All biological samples will be tested in our central laboratories located in Beijing. The biochemist who performs the measurements will be blinded to the participant's randomisation allocation. In addition, 10% of urine and blood samples will be taken as split samples to control the quality of laboratory test results. On-site and on-line monitoring for data verification will be used. Each site will have at least two on-site monitoring visits, one at the beginning of the trial and one at the end of the trial, to ensure the implementation of the study according to the protocol and standard operating procedures. During the study, an appointed staff in the coordinating centre will monitor the delivery of the target nutrients of the study diet, changes of body weight and medications of each participant in both two groups based on the data in the DMS. The quality control team will convene executive committee teleconferencing for quality control if necessary.

## Current status

The first participant was enrolled on 22 March 2019.

## DISCUSSION

To the best of our knowledge, the DECIDE-Diet trial will be the first randomised controlled feeding trial to evaluate the effect of a healthy Chinese diet in reducing



blood pressure and improving the CVD risk factor profile among community-based individuals with the increased risk of CVD. Previous RCTs in Western populations have demonstrated that healthy diets such as the DASH diet and the Mediterranean diet could reduce the CVD risk by reducing CVD risk factors.<sup>9,10</sup> The meta-analysis that pooled data of 1917 participants from 20 trials found that the DASH diet was associated with a significant decrease in SBP (−5.2 mm Hg), DBP (−2.6 mm Hg), total cholesterol (−0.20 mmol/L) and low-density lipoprotein cholesterol (−0.10 mmol/L). These changes predicted a 13% reduction in the 10-year Framingham CVD risk.<sup>21</sup>

Taken the evidences from the previous studies on healthy diets in the Western populations, the DASH diet in particular,<sup>9</sup> we developed the CHH diet with similar nutrients profile, including energy proportions from fat, protein and carbohydrate, as well as the amount of sodium, potassium, fibre, vegetables and fruits, in order to achieve similar CVD benefit observed in previous research. The major difference of the CHH diet from the Western healthy diets is that it was developed with common local Chinese food items and cooking methods to ensure its wide acceptability.<sup>22</sup>

The menus of the CHH diet also incorporated feedback from surveys of local residents. Comparing to the Western diet, the Chinese diet is special in many aspects. First, Chinese usually prefer well cooked and hot meals, but Westerners are used to have raw and cool foods.<sup>23,24</sup> Second, Chinese do not use table salt but salt has a critical role in the Chinese diet. Chinese cooks often cite “A good cook has a handful of salt”, and that might be a reason why the salt intake level is so high in China.<sup>22</sup> Third, there are more varieties of cooking methods for the Chinese diet. In addition to boiling, frying, roasting and baking, Chinese uses stewing, braising, steaming, sauteing, pickling and so on.<sup>25</sup> Fourth, the ingredients or seasonings are significantly different between Chinese and Western diets.<sup>24</sup> A lot of ingredients or seasonings are commonly used in Chinese cuisine, such as soy sauce, black or yellow bean sauce, monosodium glutamate, ginger, spring onion, garlic, mint, coriander, white pepper, and Chinese red pepper, which are rarely used in Western dietary. Meanwhile, cheese, butter, cream or milk are hardly found in the traditional Chinese diet. Fifth, unlike the Western diet serves sweet desserts often after every meal, the Chinese diet includes sweet dishes but usually only for festivals or banquets treating guests.<sup>23</sup> Last, Chinese often diet together sharing their dishes.<sup>22</sup> These differences between Chinese and Western diets indicate the significance of developing a healthy diet for Chinese, who account for one-fifth of the world’s total population.

Beside the commonalities, Chinese living in different parts of China had their own specialties in foods, tastes and ways of cooking, namely different cuisines. Thus, the CHH diet includes different versions according to the major Chinese cuisines to ensure its acceptability in different regions. Similarly, since the local usual diet may vary from centre to centre, the control diet was prepared

according to the average local nutrients intake but adjusted according to the participants’ preference of the food taste during the run-in period, to better reflect their usual diet. Regardless, different cuisines versions of the CHH diet follow the same targets of nutrients (table 1). The four major cuisines are estimated to cover over 80% of China’s total population.<sup>26</sup>

In addition to the consideration on the acceptability of the CHH diet, we also considered the affordability of the diet which is important to its scalability. The CHH diet was developed with a daily total cost of ¥30–50 RMB (US\$4–7) per person using local commonly available food materials. The price is affordable for the wage-earning class in the cities where the study will be conducted. With this consideration, the menus and recipes of the CHH diet will be possible to be accepted by the common people and generate the real impact from the public health point of view.

Although previous trials proved that dietary intervention could improve cardiovascular health, the mechanisms that links the intervention and outcomes are still unclear. Recently, several studies reported that gut microbiome might play a key role linking dietary intervention and CVD risk reduction.<sup>27–29</sup> However, none of them used the RCT design and thus could establish the causal relationship. Thus, we will investigate the effect of the CHH diet on gut microbiome in this trial and the results will enhance understanding the role of gut microbiome in the links between healthy diets and health outcomes.

In summary, this trial is the first randomised controlled feeding trial to rigorously investigate the effects of a healthy Chinese diet (the CHH diet) on cardiovascular health among community living individuals. This trial is designed with considerations including not only the health effect of the CHH diet, but also its acceptability, feasibility and affordability. Findings from this trial have a great potential in impacting the cardiovascular health of many individuals.

#### Author affiliations

<sup>1</sup>Peking University Clinical Research Institute, Peking University First Hospital, Beijing, China

<sup>2</sup>Peking University Clinical Research Institute, Peking University Health Science Center, Beijing, China

<sup>3</sup>Clinical Nutrition Center, Huadong Hospital affiliated to Fudan University, Shanghai, China

<sup>4</sup>Department of Nutrition, Food Safety and Toxicology, West China School of Public Health and West China Fourth Hospital, Sichuan University, Chengdu, China

<sup>5</sup>Department of Nutrition, School of Public Health, Sun Yat-sen University, Guangzhou, China

<sup>6</sup>College of Tourism and Culinary Science, Yangzhou University, Yangzhou, China

<sup>7</sup>Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, China

<sup>8</sup>State Key Laboratory of Infectious Disease Prevention and Control, National Institute for Communicable Disease Control and Prevention, China CDC, Beijing, China

<sup>9</sup>Department of Medicine, Nephrology Division, Duke University Medical Center, Durham, North Carolina, USA

<sup>10</sup>Society of Health Risk Assessment & Control, Chinese Preventive Medicine Association, Beijing, China



<sup>11</sup>Key Laboratory of Food Safety Risk Assessment of Ministry of Health, National Center for Food Safety Risk Assessment, Beijing, China

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#### ORCID iDs

Wuxiang Xie <http://orcid.org/0000-0001-7527-1022>

Pei Gao <http://orcid.org/0000-0001-8649-1290>

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