Supplementary Appendix

A Village Doctor-led Mobile Health Intervention for Cardiovascular Risk Reduction in Rural China: Cluster Randomised Controlled Trial

CONTENTS

APPENDIX 1:

STUDY PROTOCOL

Strategy for Cardiovascular Disease Prevention through Tailored Health **M**anagement and Its Effectiveness **A**ssessment through a cluster **R**andomized **T**rial in Individuals with **E**levated **R**isk (SMARTER)

The study is funded by:

National Clinical Research Center for Cardiovascular Diseases, China

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Note: Everything described in this protocol is consistent with what is registered with ClinicalTrials.gov NCT05645640

Contents

1. BACKGROUND

Cardiovascular disease (CVD) is a major public health issue in China. Approximately 4 million deaths are attributed to CVD each year, accounting for 40% of total mortality in the population.[1] However, with social change and economic development, aging of population and accelerated urbanization,[2,3] incidence of CVD is steadily increasing,[4] posing tremendous burden on both individuals and society. [5,6]

In 2014, the China Health Evaluation And risk Reduction through nationwide Teamwork (ChinaHEART) project was launched as a nationwide public health initiative aimed at screening and managing individuals at elevated risk for CVD, supported by the Ministry of Finance and the National Health Commission of China (formerly known as the National Health and Family Planning Commission). As of April 2022, the project had reached 353 urban districts and rural counties across 31 provinces, screened 4.4 million residents, identified and managed 1.42 million high-risk individuals, and achieved a follow-up totalling 3.47 million person-years.

However, prior investigations showed that the management of risk factors in high-risk individuals was suboptimal. Multiple risk factors were prevalent and often clustered together.[3,7] Among high-risk subjects, 23.3% exhibited concurrent high blood pressure, elevated fasting glucose levels, and dyslipidaemia. Additionally, 30% of high-risk individuals were smokers, 18% were alcoholics, and 23% were classified as overweight and obese.[7] At the same time, challenges persisted in the routine follow-up of high-risk individuals, including low response rates to follow-up, poor medication adherence, delayed updates of health information, monotonous intervention strategies, and a lack of personalized health management plans. These issues were particularly pronounced in rural areas, where the quality of care was often hindered by the inadequate education and qualifications of the healthcare workforce.[8] The traditional health management model fails to meet the needs of high-risk populations. Therefore, it is crucial to integrate new models and technologies to develop an effective, feasible, and sustainable strategy for the prevention of

cardiovascular disease in these high-risk groups.

Family doctor contract service (FDCS) is a reform of primary healthcare service that launched in 2016.[9] After years of promotion, FDCS makes great progress in coverage - serving at least 30% of general population and 60% of priority population including the elderly, pregnant women, children, individuals with disabilities, those with chronic diseases, and people with mental illnesses.[10-12] Compared with usual care models, FDCS extends healthcare treatment beyond conventional clinical settings into the community, offering advantages such as long-term care, continuity, comprehensiveness, convenience.[13] Recent studies have shown that interventions led by family doctors were remarkably effective in management of blood pressure[14] and metabolic syndrome [15] in communities. However, effectiveness of similar family doctor-led interventions in broader application scenarios still needs to be verified.

In the meantime, with the rapid development of information industry, smartphones and novel wearable devices such as smart bands have emerged overnight. These new technologies and products have gained popularity as tools for chronic disease management by their superior features.[16] As a medium for health education, short message service (SMS) via smartphones is convenient, efficient and cost-effective. It can provide personalized and precise health education tailored to each population group, without relying on the time and energy of health practitioners. Compared with the traditional model of health education in communities, this approach offers various advantages. Researchers have developed such smart tools for chronic disease prevention, which have been applied to management of hypertension,[17,18] coronary heart disease,[19] and diabetes.[20,21] On the other hand, smart bands, in conjunction with corresponding health management mobile phone applications (APPs), can simultaneously perform several functions, including step counting, sedentary reminder, sleep evaluation, heart rate tracking, and blood oxygen saturation monitoring. Their immediacy, convenience, and intelligence significantly enhance follow-up management for targeted populations. Smart bands have been used as a tool for health management in patients with obesity,[22] cancers,[23] atrial

fibrillation[24] and other chronic diseases. Regarding the management of cardiovascular risks, a research team in Australia developed a smartphone-based customized intervention strategy, which proved effective in reducing the number of risk factors associated with cardiovascular disease, particularly in enhancing physical activity. [25] Additionally, a research group in Turkey created a comprehensive intervention package that incorporated smartphones and smart bands, demonstrating effectiveness in lowering the 10-year risk score for cardiovascular disease and improving quality of life.[26] However, these studies were usually limited by small sample sizes or restricted outcome measures, resulting in a weak level of evidence.

The Strategy for Cardiovascular Disease Prevention through Tailored Health Management and Its Effectiveness Assessment through a Cluster Randomised Trial in Individuals with Elevated Risk (SMARTER) study aims to develop a series of intervention strategies for the primary prevention of cardiovascular disease through tailored health management led by village doctors, and to assess its effectiveness through a cluster randomized trial in individuals with elevated risk.

2. OBJECTIVES

2.1 Objectives

The objective of the SMARTER study is to develop a series of effective, feasible, and sustainable health management strategies led by village doctors in rural China, and assess their effectiveness of these strategies in reducing the 10-year risk for developing atherosclerotic cardiovascular disease (ASCVD) and in managing cardiovascular risk factors in individuals with elevated risk over a 12-month period.

2.2 Assumptions

The null hypothesis to be tested is that the village doctor-led tailored health management will have no effect on 10-year ASCVD risk and risk factor control in individuals with elevated risk.

3. METHODS

3.1 Study Design

An open-labelled, cluster-randomised controlled trial.

3.2 Participants

3.2.1 Participant Selection

The study will be conducted in at least 120 villages, aiming to recruit approximately 35 participants from each village and follow them for 12 months.

3.2.1.1 Provinces and autonomous regions, counties and villages

Provinces and autonomous regions – The study choose 5 provinces and autonomous regions that are willing to participate (Henan Province, Shandong Province, Liaoning Province, Ningxia Hui Autonomous Region, Jiangxi Province).

Counties – At least 12 counties will be selected from the collaborating provinces and autonomous regions to provide diversity in geographic distribution, socioeconomic development, and lifestyle patterns.

Villages – At least 120 villages will be selected from the counties based on their population size and stability, as well as the capacity of village clinics and the qualifications of village doctors. The eligibility criteria for villages will be as follows:

(1) having a village clinic that stocked common cardiovascular drugs;

(2) having at least one certificated village doctor who has technical school education or above and is willing to participate in the study;

(3) being at least 2 km away from other participating villages.

3.2.1.2 Inclusion Criteria

Individuals will be considered eligible if they meet all the following criteria:

(1) aged 35 or above;

(2) 10-year risk of ASCVD ≥10% based on the Prediction for ASCVD Risk in China (China-PAR) model;

(3) owning a smartphone and being able to use applications (apps);

(4) contracting with the local village doctor for family doctor service;

(5) being willing to participate and sign the informed consent.

3.2.1.3 Exclusion Criteria

Individuals will be excluded if they meet any of the following conditions:

(1) a history of myocardial infarction (MI), stroke, heart failure, severe arrhythmia, or having received percutaneous coronary intervention (PCI) or coronary artery by-pass grafting operation (CABG);

(2) severe illnesses, such as cancer, severe hepatic or renal dysfunction;

(3) pregnant or lactational women, or those planning to conceive in 12 months;

(4) cognitive impairments, communication issues, or limitations in activities.

3.2.2 Randomisation and Blinding

The group assignment will be conducted by a central randomisation system based on minimisation algorithm. The villages will serve as the units of randomisation. The assignment will be stratified by county, and will be conducted after all participants within each county have been recruited and baseline survey data have been collected. Factors to be balanced between the comparison groups include participants' age, systolic blood pressure, and 10-year risk of ASCVD, as well as the education attainment of the village doctor. Random numbers will be generated by an independent statistician using a computer. To enhance unpredictability in the allocation process, a random element of 0.9 will be introduced.

Due to the nature of the cluster design and the intervention programme, the village doctors and the study participants will be aware of their group allocation. However, the allocation will be concealed from the study statisticians.

3.2.3 Intervention and Control

3.2.3.1 Control

Participants in the control group will receive usual care by the village doctors.

Village doctors bear multiple responsibilities in practice. Their routine work includes providing generalist care and implementing the National Basic Public Health Services Program. These public health services include vaccination, health education; child health management; maternal health care; elderly health management; traditional Chinese medicine; reporting of infectious diseases and public health emergencies; and management for hypertension, type 2 diabetes, psychosis, and tuberculosis. These can be considered as usual care in a broad sense.

3.2.3.2 Intervention

Participants in the intervention group will receive a village doctor-led tailored health management program based on mHealth technologies. The multifaceted strategy is involved with all tagetes of the American Heart Association's Life's Essential 8,[27] and includes five components:

(1) Assessing risk factors to identify individualized intervention targets

At baseline survey, the research staff will conduct standardized interview and measurements to collect detailed information about each participant's existing risk factors (i.e., hypertension, diabetes, dyslipidaemia, obesity, smoking, alcohol use, physical inactivity, unhealthy diet, sleep deprivation) and medication adherence (Table 1). Village doctors then will be empowered to use this information to guide tailored health promotion for each participant. Participants' risk portrait will be updated based on the remeasurements at each follow-up visit.

(2) Setting gradual goals based on doctor-participant communication

In a shared decision-making process, each participant will be engaged in an in-depth discussion with his/her village doctor on their risk portrait at baseline. After fully

communication, they will create a checklist of seven health promotion goals for blood pressure, blood glucose, and blood lipid control, as well as weight loss, smoking cessation, alcohol reduction, and daily step count. The coordinating centre established a principle for the formulation of health promotion goals; however, adjustments based on specific circumstances are permitted (Table 2). These goals will be evaluated at each subsequent follow-up visit, and updated based on their accomplishment.

(3) Providing targeted health promotion short messages and videos

The coordinating centre organized a multidisciplinary team comprising cardiologists, psychologists, public health specialists, and patients to develop a pool of health education short videos for this study. These short videos, lasting less than three minutes for each, present educational content on physical exercise, healthy eating, smoking cessation, alcohol reduction, healthy sleep, and medication adherence, which are tailored for individuals with various combinations of risk factors, based on the latest recommendations from CVD prevention guidelines and behavioural change techniques. Village doctors will receive push notifications about several new short videos through the SMARTER WeChat mini program every Monday, Wednesday, and Friday, and they are supposed to browse and forward the short videos on specific topics to local participants with relevant conditions. The coordinating centre will track the participants' viewing statistics and feedback to the village doctors.

(4) Conducting health monitoring and providing periodical feedback

A smart band (HUAWEI Band 4, Huawei Technologies Co., Ltd., Dongguan, China) is provided to each participant in the intervention group to help monitor their health data, including step count, heart rate, and sleep patterns. These data are expected to be uploaded 2 to 3 times per week. The study also encourages participants to their self-measured blood pressure and glucose levels monthly, by responding to text messages from the coordinating centre. Weekly health monitoring reports for each participant will be automatically generated and sent to the village doctors to enhance communication with participants regarding their progress in risk mitigation.

(5) Motivating to reduce risk based on gamification

With an automatic algorithm, the participants will be provided a report detailing their progress in achieving seven individualized risk mitigation targets at each during follow-up visits. This report will be presented in a visual format, featuring a virtual golden egg to symbolize achieving the target and a virtual bomb to represent failing to meet the target. Based on the number of virtual golden eggs received, participants could redeem gifts from the village doctors in real life.

3.2.4 Follow Up

The study will last for 12 months, with four follow up visits (at each 3 months).

Table 1. Study follow-up visits

	Baseline	**Follow-up visits, months**			
Time schedule	0	3rd month	6th month	9th month	12th month
Registration	√				
Inclusion/Exclusion	√				
Informed consent	√				
Risk assessment	√	√	√	√	√
Questionnaire Interview	√	√	√	√	√
Physical examination	√	√	√	√	√
Fingertip blood test	√	√	√	√	√
Outcome evaluation					√

3.3 Outcomes

3.3.1 Primary Outcomes

Mean changes in the 10-year risk of ASCVD based on the China-PAR risk prediction model from baseline to 12 months.

3.3.2 Secondary Outcomes

(1) Mean changes in lifetime risk of ASCVD based on the China-PAR risk prediction model from baseline to 12 months;

(2) Mean changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP)

from baseline to 12 months;

(3) Mean changes in fasting blood glucose (FBG) from baseline to 12 months;

(4) Mean changes in non-HDL cholesterol (non-HDL-C) from baseline to 12 months;

(5) Changes in proportion of overweight and obesity from baseline to 12 months;

(6) Changes in proportion of daily smoking from baseline to 12 months;

(7) Changes in proportion of insufficient physical activity (<3000 MET-min/wk) from baseline to 12 months;

3.3.3 Exploratory Outcomes

(1) Medication adherence (changes in proportion of subjects who report taking the full dose of prescribed medications ≥ 6 days per week among all necessary subjects from baseline to 12 months);

(2) Major adverse cardiovascular events (MACEs), including occurrence of cardiovascular deaths, MI, stroke, or cardiovascular hospitalization.

4. STATISTICAL CONSIDERATION

4.1 Sample Size and Statistic Power

The sample size for the proposed trial is calculated based on the primary outcome. The overall minimum sample size is 4200 participants in 120 villages (60 villages in each comparison group, and 35 participants in each village), which will provide a statistical power of 90% with a two-sided significance level of 0.05 to detect an 1.0% absolute difference in the 12-month change of 10-year risk of ASCVD between the intervention and control groups. The calculation assumes a standard deviation (SD) of 6.0% for both the intervention and control groups at baseline, an intra-cluster correlation coefficient (ICC) of 0.04, and allow a loss of follow-up of 10%.

4.2 Statistic Analysis Plan

All analyses will be conducted according to the intention-to-treat principle. Detailed

information will be provided in the Statistical Analysis Plan.

5. DATA MANAGEMENT

5.1 Data Collection

The participants basic information, including demographic information, socioeconomic status (SES), and medical history will be collected at baseline survey. And information of study outcomes (for participants in both intervention and control groups) will be collected at baseline and each follow-up visits at 3th month, 6th month, 9th month, and 12th month.

These data will be collected in three ways:

(1) standardized electronic questionnaire interview (basic information, lifestyle behaviours, and medication use);

(2) physical examination (blood pressure, height, weight, waist circumference, grip strength, walking speed, and vital capacity);

(3) fingertip blood sample collection (fast test for blood glucose and lipid).

Regarding assessment of the metabolic risk factors, to be more specific, blood pressure will be measured twice on the right upper arm using a standard sphygmomanometer (Omron HEM-7121, Omron Corporation, Japan) after 5 minutes of rest in the sitting position. Blood glucose and blood lipid will be tested by the rapid blood glucose analyser (BeneCheck BK6-20 M Multi-Monitoring System, Suzhou Pu Chun Tang Biotechnology, China) and the fast photochemical lipid analyser (CardioChek PA Analyzer; Polymer Technology Systems, USA), respectively. Body mass index (BMI) will be calculated as body weight in kilograms divided by the squared value of height in meters, with obesity is defined as a BMI≥28.0 kg/m^2.

For assessment of lifestyle behaviours, smoking status (never, former, or current smokers) and frequency will be inquired in the questionnaire. Daily smoking is defined as self-reported consuming tobacco products every day. Regarding physical activity, we will ask the participants about the time they spend on four types of

physical activity (occupational, commuting, domestic, and leisure-time) in details, and overall physical activity level is quantified by multiplying the metabolic equivalent tasks (METs) value for each by time spent on that per day. According to studies of the global burden of disease (GBD), an overall physical activity of less than 3000 MET-min per week is considered as insufficient physical activity. Leisure-time activity, as the focused part that could be intervened in the trial, we will ask the participants about typical types of leisure-time activity at different intensity (swimming/running/aerobic exercise/ rope skipping as vigorous- intensity activity; ball games/hiking/brisk walking/gymnastics/folk dancing/Tai-Chi or qigong as moderate-intensity activity), frequency, and exercise time per week. Participants performing<150 minutes of moderate-intensity aerobic activities or <75 minutes of vigorous-intensity aerobic activities per week will be considered as having insufficient leisure-time activity.

5.2 Data Management

All the data in this study are processed through a specially developed software system that includes functions such as data verification, logical jumps, and data tracing. Data transfers are encrypted, and all information will be stored securely. Each access to the data system requires a unique username and password. Research staff will be granted access to specific datasets and the ability to perform certain functions in accordance with their roles in the study. The dataset to be analysed for the study will be curated by the data manager at the national coordinating centre and provided to the statisticians. The data transfer process will ensure the anonymity of the subjects. All data will be stored on a computer that is not connected to the Internet, thereby preventing any potential data leaks.

6. CONFIDENTIALITY PRINCIPLE

All the data in this study will be stored at the national coordinating centre and will be kept strictly confidential. The research platform will employ information encryption technologies, set identity and authorization controls, and establish different levels of

permissions for research staff. Data desensitization techniques will be utilized to de-identify personal information, protect individual privacy, ensure information security, and facilitate the collection, extraction, and analysis of data in the background. All data will be securely stored as the foundational material for the research and will not be used for any other purposes. Access to the relevant research data will be limited to researchers, related research authorities, and ethics committees. The identities and any other personal information of the participants will remain confidential and will not be disclosed in any research report. Third parties must obtain authorization from the primary investigator before gaining access to the data for academic use and analysis. The data and analysis results of this study may be published or disclosed in print or electronic formats in domestic or international medical journals or open media. However, the investigator will maintain the confidentiality of the study subjects' identities and ensure that their personal information remains protected in accordance with legal requirements.

7. QUALITY CONTROL

The study will conduct two phases of quality control measures: quality control before the project begins and quality control during project implementation. Prior to the project's launch, the national coordinating centre will assemble a committee of experts to develop the project's technical scheme, operational manuals, questionnaires, research document lists, and provincial on-site implementation plans, ensuring scientific rigor and operational feasibility. The national coordinating centre is responsible for supervising and ensuring quality control during the training of village doctors and the selection of research subjects. Throughout the implementation of the project, quality control is maintained through various methods, including on-site inspections and centralized data monitoring. This oversight encompasses all processes, including project preparation, management of materials and equipment, selection of research subjects, intervention, follow-up, and safety reporting in the

participating villages.

7.1 On-site Inspections

The national coordinating centre will establish a working group to perform quality control checks for all participating villages during the implementation process through on-site inspections. Every on-site inspection must be documented in a report, which will be recorded and filed by designated research staff. Any issues identified during the inspections should be addressed promptly, and retraining should be conducted for the local research team and village doctors if necessary. For villages where quality problems are detected, additional inspections will be organized according to the established timeline.

7.2 Central Data Monitoring

All real-time data generated by the participating villages during the implementation of the project shall be uploaded to the national coordinating centre. The national coordinating centre is responsible for evaluating the quality of the uploaded data from the research sites. The results of the data quality evaluation will be utilized to inform subsequent on-site inspections and training for research staff. If any issues arise with the data, the underlying causes should be identified and rectified promptly.

8. ETHICAL PRINCIPLE

8.1 Ethical Review

This study will be conducted in accordance with the requirements of the Declaration of Helsinki and relevant national regulations in China. The research protocol complies with applicable laws and regulations and will receive approval from the Ethics Committee prior to implementation. Throughout the research process, the investigators will strictly adhere to the research protocol and standardized operating procedures. If any necessary changes are required to the research plan or informed consent during the study, they must be resubmitted to the Ethics Committee for

review and approval before implementation.

8.2 Informed Consent

Before enrolling each research subject in this study, the researcher staff must provide the subject or their legal representative with a complete, comprehensive, and easy-to-understand informed consent document, along with an explanation approved by the Ethics Committee, in written form. The researcher must also allow sufficient time for the subject or their legal representative to consider whether to participate in the study. Subjects or their legal representatives may only enter the study after signing the informed consent. During the study period, if new safety information leads to significant changes in the risk/benefit assessment, the subject or their legal representative should be provided with all updated information, and a new informed consent form must be signed.

8.3 Risk Minimisation

In the study, the cardiovascular health surveys, physical examinations, and lab tests for the study participants, will be conducted by trained research staff, which will not pose any risk to the participants. In the questionnaire interview, participants may choose not to answer any questions they prefer to skip. Fingertip blood collection may cause mild pain and subcutaneous bruising; if discomfort arises, participants can seek on-site medical assistance. During the study, the village doctors will provide the participants with guidance on lifestyle modification or medication recommendations that do not introduce additional health risks. If participants have any questions about the study, professional staff will be available to address them. Participants have the right to decline participation or withdraw from the study at any stage without any impact on their medical rights. All the data in this study will be stored at the national coordinating centre and will be kept strictly confidential, and all research staff will receive training in data security. Health monitoring data in the intervention group, such as the step counts and heart rate collected by smart bands, will be uploaded to the Huawei Research Platform and subsequently transferred to the research database.

All research staff, as well as inspectors from relevant government departments or academic management bodies, must obtain authorization from the primary investigators to access the database, which is password-protected. Strict security measures will be implemented to prevent unauthorized personnel from accessing the personal information of study participants, and no staff member shall disclose this information to external parties. The identities and any other personal information of the participants will remain confidential and will not be disclosed in any research report. All expenses incurred for the examination items in this study will be covered by the research sponsor, and participants will not be required to pay any costs. However, the study does not cover treatment expenses incurred by participants for personal medical reasons, transportation subsidies, or any other forms of compensation or remuneration.

8.4 Safety Issues

The interventions in this study do not involve any new drugs or invasive procedures and do not pose risks beyond those associated with routine clinical care. Furthermore, these interventions may help reduce disease risks. Therefore, no special safety monitoring is required for this study. Nevertheless, the study will document all deaths, hospitalizations, and other significant medical events that may be defined as serious adverse events. In addition to monitoring serious adverse events, participants will be asked at each follow-up visit whether they have experienced symptoms of low blood pressure, hypoglycaemia, or sports-related injuries.

8.5 Competing Interest

None.

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TABLES

Table 2. Cardiovascular risk factors to be assessed in the SMARTER study

Risk factors	Indicators	Warning criteria
10-year risk of ASCVD	Risk (value)	≥10%
	Risk (stratification)	High-risk
1. Hypertension	SBP	≥130 mmHg
	DBP	≥80 mmHg
2. Diabetes	FBG	≥6.1 mmol/L
3. Dyslipidaemia	TC	≥5.2 mmol/L
	Non-HDL-C	≥3.4 mmol/L
4. Obesity	BMI	Overweight: ≥24 kg/m^2, Obesity: ≥28 kg/m^2
	Bodyweight	According to the BMI criteria
	Waist circumstance	Males: ≥90 cm, Females: ≥85 cm
5. Smoking	Daily smoking amount	＞0
	Heaviness of Smoking Index (HSI)	Heavy dependence
6. Alcohol use	Daily consumption of pure alcohol	≥15g (on average)
7. Physical activity	Total physical activity	<3000 MET-min/wk
	Exercise intensity	No exercise
	Weekly exercise time	Moderate-intensity aerobic activities<150 minutes, or vigorous-intensity aerobic activities<75 minutes
8. Unhealthy diet	Fruit	Less than everyday
	Fresh vegetables	Less than everyday
	Whole grains	Less than everyday
	Bean and bean food	Less than four days per week
	Red meat	Everyday
9. Sleep deprivation	Sleep duration	<6 hours/day (on average)
10. Medication adherence	Self-reported adherence	Intermittent or absent use of medications

Table 3. Principles for Establishing Individualized Health Promotion Goals

Risk factors	Targets	Principles
Hypertension	SBP/DBP	Age<80: <130/80 mmHg; Age≥80: <150/90 mmHg (recommended; allow for adjustment according to the circumstances)
Diabetes	FBG	Participants without a diagnosis of DM: <6.1 mmol/L; DM patients: <7.0 mmol/L
Dyslipidaemia	Non-HDL-C	Age<75, no diagnosis of DM: <3.4 mmol/L; Age<75, DM patients: <2.6 mmol/L; Age ≥75: lipid lowering target should be set under guidance of the physicians in higher-level hospitals
Obesity	Weight loss	BMI<28 kg/m^2: with a body weight at BMI 24 as the target weight, setting the weight loss goal to be achieved in four stages during follow-up; BMI≥28 kg/m^2: setting a 15% of the current body weight as the bodyweight loss goal to be achieved in four stages during follow-up
Smoking	Smoking cessation	Never smokers: no smoking; Current smokers: quitting smoking
Alcohol use	Alcohol reduction	Never drinkers or non-weekly drinkers: no alcohol; Weekly drinkers: limiting the frequency and consumption of alcohol (pure alcohol should not exceed 15g per day on average)
Physical activity	Daily step count; Exercise frequency	Age<60: the daily step count should reach 8000-10000 per exercise day; Age≥60: the daily step count should reach 6000-8000 per exercise day; At the first 6 months of the study, it is recommended to exercise at least 3 days per week; at the last 6 months, competent participants are recommended to exercise 5 days per week

APPENDIX 2:

STATISTICAL ANALYSIS PLAN

Strategy for Cardiovascular Disease Prevention through Tailored Health **M**anagement and Its Effectiveness **A**ssessment through a cluster **R**andomized **T**rial in Individuals with **E**levated **R**isk (SMARTER)

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Contents

1. INTRODUCTION

This Statistical Analysis Plan (SAP) outlines the main statistical analyses to be conducted on the data collected in the Strategy for Cardiovascular Disease Prevention through Tailored Health Management and Its Effectiveness Assessment through a Cluster Randomised Trial in Individuals with Elevated Risk (SMARTER) study, in accordance with the study protocol. It provides an overview of the study, summarizes the key variables that will be analysed, and describes the statistical methods that will be employed in the analyses. The results reported in the papers should follow the methodologies set out here.

The analyses as planned in the SAP will be performed after the completion of the trial. All procedures should be conducted by qualified statisticians, ensuring the integrity and accuracy of the data and the fidelity to the SAP. Any deviations from the SAP should be described and justified in the final report of the trial.

2. STUDY OBJECTIVE

2.1 Objectives

The objective of the SMARTER study is to develop a series of effective, feasible, and sustainable health management strategies led by village doctors in rural China, and assess their effectiveness of these strategies in reducing the 10-year risk for developing atherosclerotic cardiovascular disease (ASCVD) and in managing cardiovascular risk factors in individuals with elevated risk over a 12-month period.

2.2 Assumptions

The null hypothesis to be tested is that the village doctor-led tailored health management will have no effect on 10-year ASCVD risk and risk factor control in individuals with elevated risk.

3. METHODS

3.1 Study Design

The SMARTER study was an open-labelled, cluster-randomized controlled trial. A total of 4533 participants in 127 villages (clusters) were enrolled from five provinces and autonomous regions across China and randomly assigned in a 1:1 ratio to the intervention group and control. Participants in the intervention group received the village doctor-led multifaceted mobile health interventions, and the control group received usual care. Participants in both groups will be followed for 12 months and received follow-up visits every three months, specifically at the 3rd, 6th, 9th, and 12th months. The primary outcome of the study is the mean change in 10-year risk of ASCVD from baseline to 12 months, and the secondary outcomes are the changes in metabolic and lifestyle risk factors from baseline to 12 months.

3.2 Study Population

3.2.1 Inclusion Criteria for villages

(1) having a village clinic that stocked common cardiovascular drugs;

(2) having at least one certificated village doctor who has technical school education or above and is willing to participate in the study;

(3) being at least 2 km away from other participating villages.

3.2.2 Inclusion Criteria for Participants

Individuals were considered eligible if they met all the following criteria:

(1) aged 35 or above;

(2) 10-year risk of ASCVD ≥10% based on the Prediction for ASCVD Risk in China (China-PAR) model;

(3) owning a smartphone and being able to use applications (apps);

(4) contracting with the local village doctor for family doctor service;

(5) being willing to participate and sign the informed consent.

3.2.3 Exclusion Criteria for Participants

Individuals were excluded if they met any of the following conditions:

(1) a history of myocardial infarction (MI), stroke, heart failure, severe arrhythmia, or having received percutaneous coronary intervention (PCI) or coronary artery by-pass grafting operation (CABG);

(2) severe illnesses, such as cancer, severe hepatic or renal dysfunction;

(3) pregnant or lactational women, or those planning to conceive in 12 months;

(4) cognitive impairments, communication issues, or limitations in activities.

3.3 Randomisation and Blinding

The group assignment was conducted by a central randomisation system based on minimisation algorithm. The villages served as the units of randomisation. The assignment was stratified by county, and was conducted after all participants within each county had been recruited and baseline survey data had been collected. Factors that were balanced between the comparison groups include participants' age, systolic blood pressure, and 10-year risk of ASCVD, as well as the education attainment of the village doctor. Random numbers were generated by an independent statistician using a computer. A random element of 0.9 were introduced to enhance unpredictability in the allocation process.

Due to the nature of the cluster design and the intervention programme, the village doctors and the study participants were aware of their group allocation. However, the allocation will be concealed from the study statisticians.

3.4 Intervention and Control

3.4.1 Control

Participants in the control group received usual care by the village doctors.

Village doctors bear multiple responsibilities in practice. Their routine work

includes providing generalist care and implementing the National Basic Public Health Services Program. These public health services include vaccination, health education; child health management; maternal health care; elderly health management; traditional Chinese medicine; reporting of infectious diseases and public health emergencies; and management for hypertension, type 2 diabetes, psychosis, and tuberculosis. These can be considered as usual care in a broad sense.

3.4.2 Intervention

Participants in the intervention group received a village doctor-led tailored health management program based on mHealth technologies. The multifaceted strategy is involved with all tagetes of the American Heart Association's Life's Essential 8, and includes five components:

(1) Assessing risk factors to identify individualized intervention targets

At baseline survey, the research staff conducted standardized interview and measurements to collect detailed information about each participant’s existing risk factors (i.e., hypertension, diabetes, dyslipidaemia, obesity, smoking, alcohol use, physical inactivity, unhealthy diet, sleep deprivation) and medication adherence. Village doctors then were empowered to use this information to guide tailored health promotion for each participant. Participants’ risk portrait was updated based on the remeasurements at each follow-up visit.

(2) Setting gradual goals based on doctor-participant communication

In a shared decision-making process, each participant was engaged in an in-depth discussion with his/her village doctor on their risk portrait at baseline. After fully communication, they created a checklist of seven health promotion goals for blood pressure, blood glucose, and blood lipid control, as well as weight loss, smoking cessation, alcohol reduction, and daily step count. The coordinating centre established a principle for the formulation of health promotion goals. These goals were evaluated at each subsequent follow-up visit, and updated based on their accomplishment.

(3) Providing targeted health promotion short messages and videos

The coordinating centre organized a multidisciplinary team comprising cardiologists, psychologists, public health specialists, and patients to develop a pool of health education short videos for this study. These short videos, lasting less than three minutes for each, presented educational content on physical exercise, healthy eating, smoking cessation, alcohol reduction, healthy sleep, and medication adherence, which were tailored for individuals with various combinations of risk factors, based on the latest recommendations from CVD prevention guidelines and behavioural change techniques. Village doctors received push notifications about several new short videos through the SMARTER WeChat mini program every Monday, Wednesday, and Friday, and they browsed and forwarded the short videos on specific topics to local participants with relevant conditions. The coordinating centre tracked the participants' viewing statistics and provided feedback to the village doctors.

(4) Conducting health monitoring and providing periodical feedback

A smart band (HUAWEI Band 4, Huawei Technologies Co., Ltd., Dongguan, China) was provided to each participant in the intervention group to help monitor their health data, including step count, heart rate, and sleep patterns. These data were uploaded 2 to 3 times per week. The study also encouraged participants to their self-measured blood pressure and glucose levels monthly, by responding to text messages from the coordinating centre. Weekly health monitoring reports for each participant were automatically generated and sent to the village doctors to enhance communication with participants regarding their progress in risk mitigation.

(5) Motivating to reduce risk based on gamification

With an automatic algorithm, the participants were provided a report detailing their progress in achieving seven individualized risk mitigation targets at each during follow-up visits. This report was presented in a visual format, featuring a virtual golden egg to symbolize achieving the target and a virtual bomb to represent failing to meet the target. Based on the number of virtual golden eggs received, participants could redeem gifts from the village doctors in real life.

3.5 Outcome Measures

3.5.1 Primary Outcomes

Mean changes in the 10-year risk of ASCVD based on the China-PAR risk prediction model from baseline to 12 months.

3.5.2 Secondary Outcomes

(1) Mean changes in lifetime risk of ASCVD based on the China-PAR risk prediction model from baseline to 12 months;

(2) Mean changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) from baseline to 12 months;

(3) Mean changes in fasting blood glucose (FBG) from baseline to 12 months;

(4) Mean changes in non-HDL cholesterol (non-HDL-C) from baseline to 12 months;

(5) Changes in proportion of overweight and obesity from baseline to 12 months;

(6) Changes in proportion of daily smoking from baseline to 12 months;

(7) Changes in proportion of insufficient physical activity (<3000 MET-min/wk) from baseline to 12 months;

3.6 Outcome Evaluation

The information of study outcomes (for participants in both intervention and control groups) was collected at baseline and each follow-up visits at 3th month, 6th month, 9th month, and 12th month. All the data collection was conducted using standardized equipment and following uniform operational protocols. These data were collected in three ways: (1) standardized electronic questionnaire interview; (2) physical examination; (3) fingertip blood sample collection.

The primary outcome, 10-year risk of ASCVD, was calculated by the China-PAR prediction model based on age, sex, geographic region (northern/southern China), urbanity, waist circumference, systolic blood pressure (SBP), use of antihypertensive

medication, presence of diabetes, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), smoking status, and family history of ASCVD.

Regarding assessment of the metabolic risk factors, to be more specific, blood pressure was measured twice on the right upper arm using a standard sphygmomanometer (Omron HEM-7121, Omron Corporation, Japan) after 5 minutes of rest in the sitting position. Blood glucose and blood lipid were tested by the rapid blood glucose analyser (BeneCheck BK6-20 M Multi-Monitoring System, Suzhou Pu Chun Tang Biotechnology, China) and the fast photochemical lipid analyser (CardioChek PA Analyzer; Polymer Technology Systems, USA), respectively. Body mass index (BMI) was calculated as body weight in kilograms divided by the squared value of height in meters, with obesity was defined as a BMI≥28.0 kg/m^2.

For assessment of lifestyle behaviours factors, smoking status (never, former, or current smokers) and frequency were inquired in the questionnaire. Daily smoking was defined as self-reported consuming tobacco products every day. Regarding physical activity, we asked the participants about the time they spent on four types of physical activity (occupational, commuting, domestic, and leisure-time) in details, and overall physical activity level was quantified by multiplying the metabolic equivalent tasks (METs) value for each by time spent on that per day. According to studies of the global burden of disease (GBD), an overall physical activity of less than 3000 MET-min per week was considered as insufficient physical activity. Leisure-time activity, as the focused part that could be intervened in the trial, we asked the participants about typical types of leisure-time activity at different intensity (swimming/running/aerobic exercise/ rope skipping as vigorous- intensity activity; ball games/hiking/brisk walking/gymnastics/folk dancing/Tai-Chi or qigong as moderate-intensity activity), frequency, and exercise time per week. Participants performing <150 minutes of moderate-intensity aerobic activities or <75 minutes of vigorous-intensity aerobic activities per week will be considered as having insufficient leisure-time activity.

3. SAMPLE SIZE

The sample size for the proposed trial was calculated based on the primary outcome. At the time of the study design, we calculated a minimum sample size of 4200 participants in 120 villages (60 villages in each comparison group, and 35 participants in each village), which would provide a statistical power of 90% with a two-sided significance level of 0.05 to detect an 1.0% absolute difference in the 12-month change of 10-year risk of ASCVD between the intervention and control groups. The calculation assumed a standard deviation (SD) of 6.0% for both the intervention and control groups at baseline, an intra-cluster correlation coefficient (ICC) of 0.04, and allowed a loss of follow-up of 10%.

To compensate for the risk of entire-village withdrawing, the study screened more villages at enrolment. At last, a total of 4533 participants from 127 villages were included. With an actual ICC of 0.06, the statistical power finally achieved was 88%.

5. STATISTICAL CONSIDERATION

5.1 Statistical Analysis Principle

The analysis will be based on the intent-to-treat (ITT) principle. For all study outcomes, the comparison will be conducted in all randomized participants based on their randomisation group results. All comparisons will be two-sided and statistical significance is defined as $P<0.05$.

5.2 Participation and Withdrawal Data

All participants who sign informed consent and attend baseline assessment will be included in the study analysis. The flow of participants through the study will be graphically displayed using a CONSORT diagram. The study will outline the dataset, number and proportions of participants who withdrawal and lost-to-follow-up, including (but not limited to):

Number of patients screened;

Number and proportions of patients in the intervention and control group;

Number and proportions of patients that do not meet the inclusion criteria;

Number and proportions of patients that complete the trial;

Number and proportions of patients that drop out of the trial.

5.3 Handling of Missing Data and Outliers

When data are missing, we will report the number of observations and assess the presence of specific missingness patterns. The analysis will be performed on the complete-case records without any imputation (i.e. the participant has a missing value for a variable required for a model will be excluded from that analysis).

Due to the rigorous data query during the whole process of data collection in the trial, outliers will be not determined in the primary statistical analysis.

5.4 Statistical Analysis Software

The analyses will be performed using SAS 9.4 (SAS Institute lnc., Cary, NC, USA).

6. STATISTICAL ANALYSES

6.1 Baseline Characteristics

Descriptive statistics will be used to summarize the baseline characteristics of the whole cohort of the study participants and by study groups: continuous variables will be presented as mean and standard deviation, or medians, interquartile range, minimum and maximum, and categorical variables as frequencies and percentages.

T-test/Wilcoxon rank sum test will be used to compare continuous variables between the intervention and control group. The Chi-square test/Fisher exact test will be used to compare the categorical variables between the two groups.

6.2 Adherence to Intervention

The adherence to village doctor-led health management strategies in the intervention group was monitored using an automated system since the first follow-up visit (at 3 months). Thet study will report monthly data of the short video view rate, smart band wearing rate, and daily step target achieving rate.

Satisfaction of the intervention participants with the health education short videos was inquired at each stage follow-up visits. We will report the proportion of participants who believed the short videos were relevant to their health conditions, the proportion of participants who believed the short videos were rather useful, and the proportion of participants who expressed willingness continue receiving short videos of the trial after the study was ended.

6.3 Analysis of Primary Outcomes

The primary outcome of the trial is the mean changes in 10-year risk of ASCVD based on the China-PAR model from baseline to the 12 months. Linear mixed effects model will be used to compare the primary outcome between the intervention group and the control group. The dependent variable is the change in 10-year risk of ASCVD of the participants from baseline to the 12-month, and the independent variable is the study group. Villages will be adjusted in the model as a random effect. The net difference between the two groups was assessed by the model, with multivariable adjustment by baseline covariates including age, sex, education, occupation, annual household income, marital status, and social medical insurance.

6.4 Analysis of Secondary Outcomes

The secondary outcomes included mean changes in the levels of lifetime risk of ASCVD based on the China-PAR model, SBP, DBP, FBG, and non-HDL-C, as well as changes in the proportions of obesity, daily smoking, and insufficient physical activity, from baseline to the 12 months. The assessment of secondary outcomes of continuous variables will be analysed using linear mixed effects models, same as the analysis method of primary outcome, and the categorical variables will be analysed using the generalised linear mixed effects models. Villages will be adjusted in the

models as a random effect. The net differences between the two groups were assessed by the models, with multivariable adjustment by baseline covariates including age, sex, education, occupation, annual household income, marital status, and social medical insurance.

6.5 Subgroup Analyses

Potential interactions will be explored for the primary outcome by subgroups of age, sex, education, occupation, annual household income, and tertile of baseline 10-year risk of ASCVD, with a statistical significance level of 0.05 (two-sided).

6.6 Opportunities for Adding Unanticipated Assessments

If evidence emerges from other studies to suggest that additional assessments would be of high research value then the statistical analysis plan may be amended to include them (either in all participants or in subsets of sufficient size). Given the controlled nature of the trial, comparisons between the randomized groups of outcomes assessed in this way (i.e., without a baseline assessment) can still provide a reliable unbiased result of the intervention effects.

Reference

None.

APPENDIX 3:

SUPPLEMENTARY TABLES AND FIGURES

List of the SMARTER Collaborative Group Members

Study Coordinating Center

Fuwai Hospital, Chinese Academy of Medical Sciences, Beijing/Shenzhen, China:
Xi Li, Xingyi Zhang, Siming Wang, Xingyu Zhou, Yajie Tang, Chaoqun Wu, Jianlan Cui, Yang Yang, Chunying Lin, Yi Wu, Haibo Zhang

Subcenter: Henan Province

Henan Provincial Center for Disease Control and Prevention, Zhengzhou, China: Lei Fan, Hanxue Zhang, Minjie Qi
Fangcheng County Center for Disease Control and Prevention, Nanyang, China: Pu Li, Jingying Ma, Hao Jia
Wugang City Center for Disease Control and Prevention, Pingdingshan, China: Qinglan Liu, Xinke Yin
Wugang Hospital of Traditional Chinese Medicine, Pingdingshan, China: Guanghe Cai
Qixian Center for Disease Control and Prevention, Hebi, China: Ruilai Wang, Yanhui Li, Xiaoyi Luo
Neihuang County Center for Disease Control and Prevention, Anyang, China: Yanlong Wang, Yongjuan Wu
Mashang Township Central Health Center, Neihuang County, Anyang, Henan, China: Quanbo Li
Queshan County Center for Disease Control and Prevention, Zhumadian, China: Gencheng Fang, Huiyong Liu
Zhongmu County Center for Disease Control and Prevention, Zhengzhou, China: Fei Shang, Fuke Qiao, Yuting Liu

Subcenter: Shandong Province

Shandong Center for Disease Control and Prevention, Jinan, China: Chunxiao Xu, Xiaolei Guo, Xiaohui Xu
Yishui County Center for Disease Control and Prevention, Linyi, China: Weixia Wang, Dengqiang Yang, Jiangbao Zhang
Jinxiang County Center for Disease Control and Prevention, Jining, China: Xiaoxue Liu, Chenlan Liu, Xianhui Wu
Rushan City Center for Disease Control and Prevention, Weihai, China: Yuewei Zou, Like Li, Yujia Zhang
Shanxian County Center for Disease Control and Prevention, Heze, China: Haizhou Zhao, Guangying Shao

Subcenter: Liaoning Province

Liaoning Provincial Center for Disease Control and Prevention, Shenyang, China: Liying Xing, Li Jing, Han Yan
Lingyuan City Center for Disease Control and Prevention, Chaoyang, China: Zhenli Ma, Wulan Liang

Subcenter: Ningxia Hui Autonomous Region

Ningxia Center for Disease Control and Prevention, Yinchuan, China: Shaoning Ma, He Yuan, Hui Juan, Haihong Wang
Helan County Center for Disease Control and Prevention, Yinchuan, China: Chunning Sheng, Hairong Chen

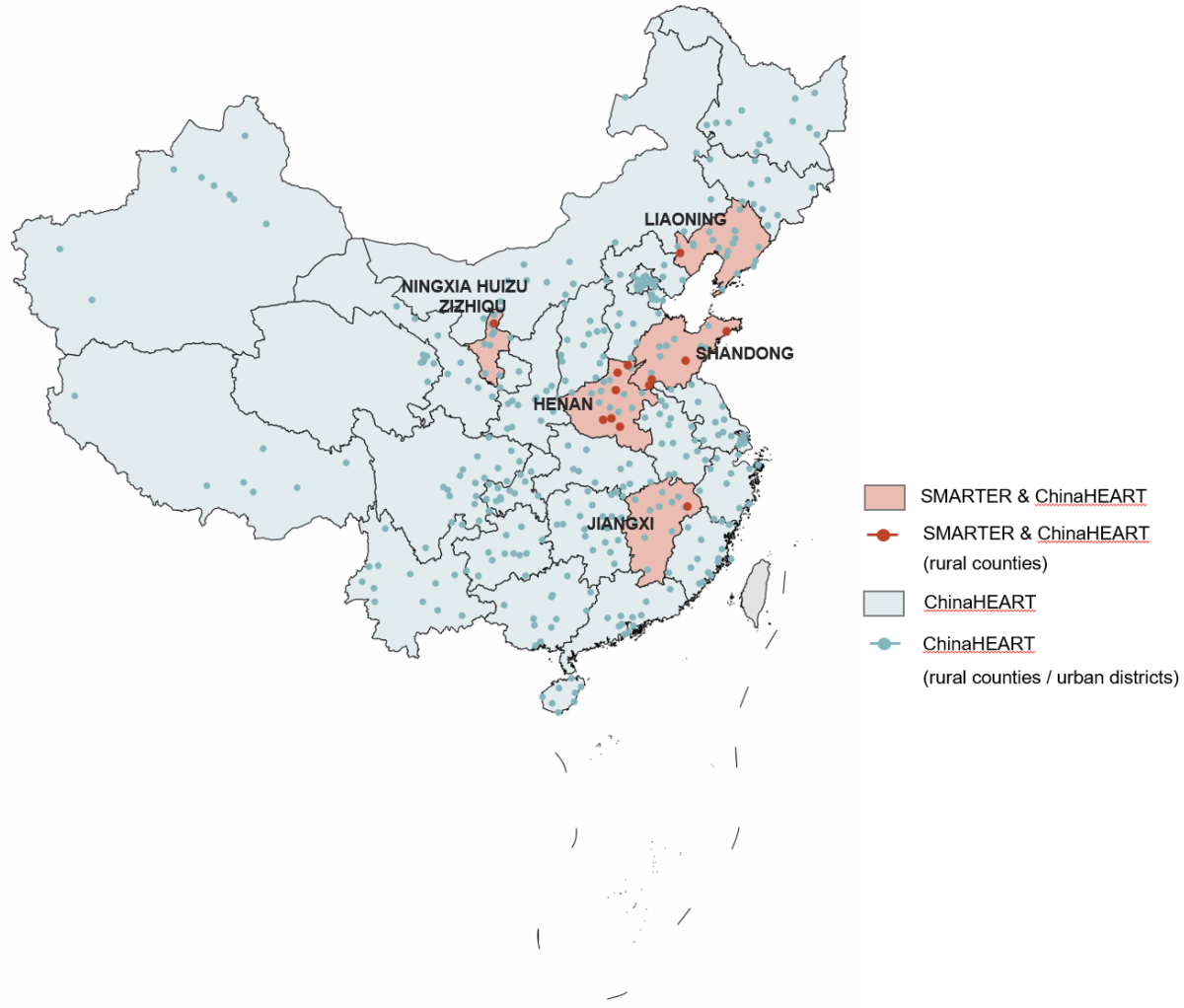
Subcenter: Jiangxi Province

Jiangxi Provincial Center for Disease Control and Prevention, Nanchang, China: Yan Xu, Wei Yan
Hengfeng County People's Hospital, Shangrao, China: Mei Li

Technical Support Group

Fuwai Hospital, Chinese Academy of Medical Sciences, Beijing, China: Binbin Jin, Haiyang Li
Liangma Boxin Data Technology Co., Ltd., Beijing, China: Xiaowei Han, Chengzhi Huang
HUAWEI Device Co., Ltd., Dongguan, China: Jie Zhou, Hang Liu, Teng Xu, Jiahui Peng

Fig S1. Distribution of project sites in the SMARTER and the ChinaHEART



Selection of Project Sites

The provinces and autonomous regions, counties, and villages included in the SMARTER study were chosen from an established collaborative network associated with ChinaHEART, a nationwide government-funded public health project in China. From September 2014 to December 2024, ChinaHEART encompassed 155 urban districts and 229 rural counties across all 31 provinces in Chinese mainland, based on their heterogeneity in geographic distribution, demographic structure, and disease patterns. This project enrolled over 5.5 million local residents for cardiovascular risk screening. To assess whether the village doctor-led mobile health intervention strategy could be generalized across areas with varying environmental conditions and lifestyle patterns, 13 counties were selected from five geographically dispersed provinces and autonomous regions to enhance diversity in exposure to risk factors, with participating villages were chosen based on uniform eligibility criteria.

Fig S2. Average daily step count and self-report physical activity levels

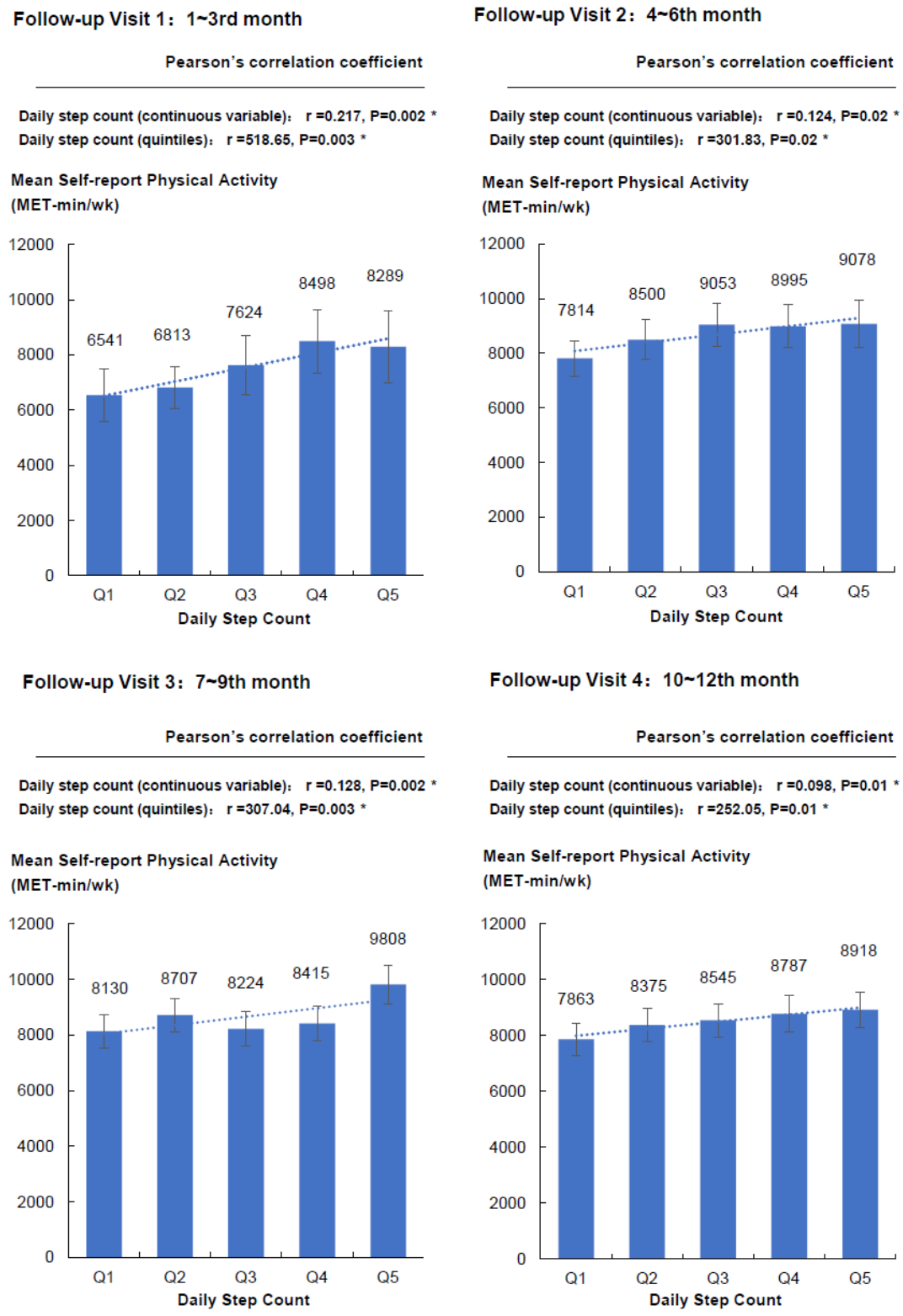


Fig S3. Features of the SMARTER WeChat mini program

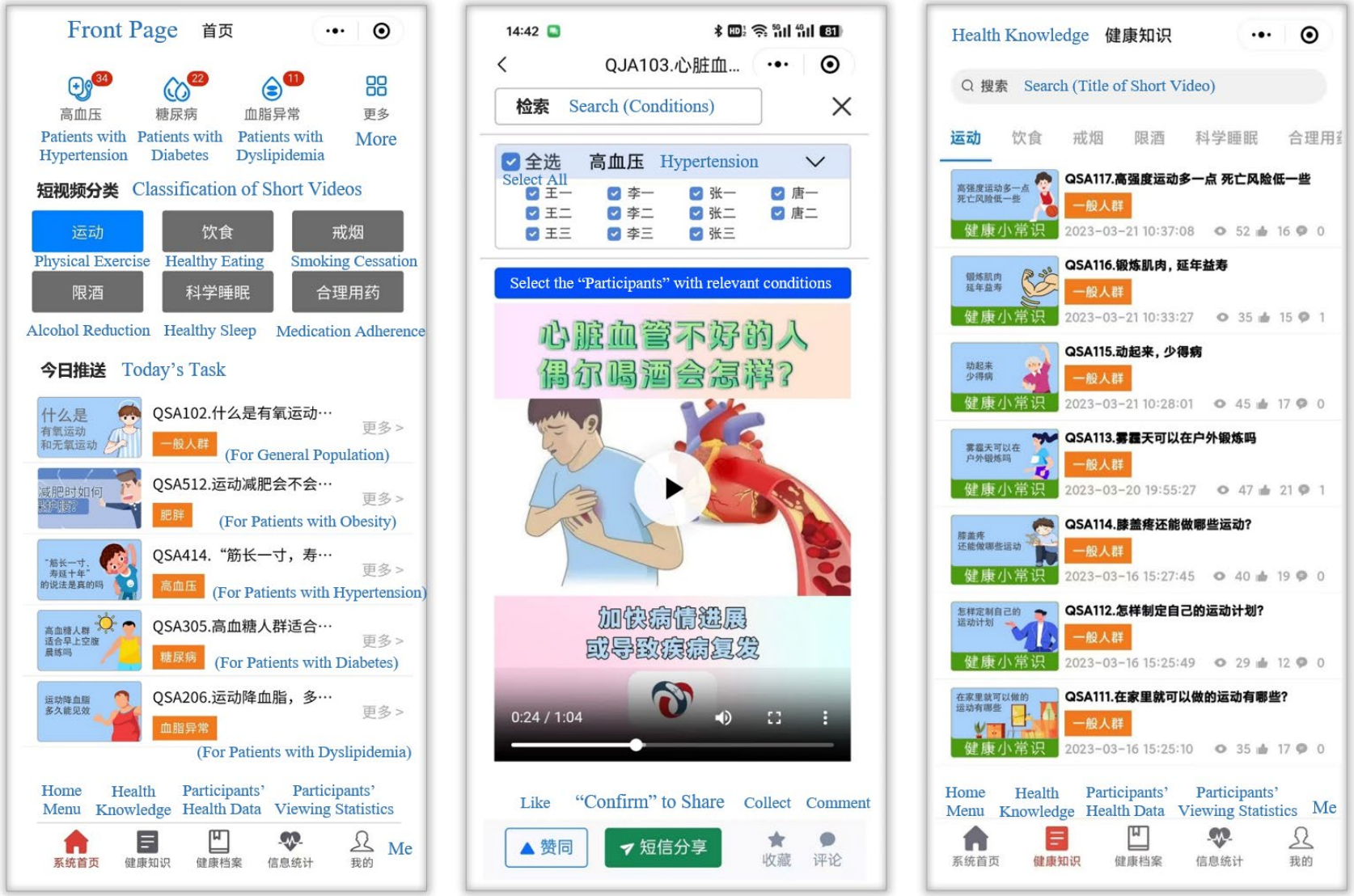


Table S1. Adherence statistics for targeted health education short videos

Months	Number of short videos successfully forwarded	Number of short videos unwatched	Number of short videos viewed	Proportion of short videos viewed
3	44693	28811	15882	35.5%
4	50446	26526	23920	47.4%
5	47989	25244	22745	47.4%
6	50229	20062	30167	60.1%
7	49521	15356	34165	69.0%
8	49750	11070	38680	77.7%
9	49116	6933	42183	85.9%
10	53404	7038	46366	86.8%
11	45404	7804	37600	82.8%
12	49834	8792	41042	82.4%

Table S2. Satisfaction statistics for targeted health education short videos

Follow-up visit	Numbers of respondents	Question: Do you think the short videos are relevant to your health conditions? Answer: YES	Question: Do you think the short videos are useful? Answer: YES	Question: Would you like to continue to receive short videos after the study ends? Answer: YES
3rd month	**2268**	**98.9%** (2244)	**98.6%** (2236)	**N/A**
6th month	**2265**	**98.9%** (2239)	**98.9%** (2240)	**N/A**
9th month	**2268**	**98.9%** (2242)	**98.6%** (2237)	**N/A**
12th month	**2284**	**N/A**	**N/A**	**87.6%** (2000)
Total		**98.9%** (6725/6801)	**98.7%** (6713/6801)	**87.6%** (2000/2284)

Table S3. Adherence statistics for health monitoring using smart bands

(a) Smart band wearing statistics

Months	Total number (person-week)	Wearing⩾3 days per week		Wearing ≥5 days per week	
		Number (person-week)	Proportion	Number (person-week)	Proportion
3	8824	5064	57.4%	4314	48.9%
4	8824	6067	68.8%	5455	61.8%
5	8824	6063	68.7%	5482	62.1%
6	8824	6680	75.7%	5929	67.2%
7	11030	8794	79.7%	7860	71.3%
8	8824	7614	86.3%	6814	77.2%
9	11030	10040	91.0%	9168	83.1%
10	8824	8070	91.5%	7474	84.7%
11	8824	7515	85.2%	6760	76.6%
12	11030	9614	87.2%	8725	79.1%

(b) Daily step target achieving statistics

Months	Total number (person-week)	Target achieved ≥3 days per week		Target achieved ≥5 days per week	
		Number (person-week)	Proportion	Number (person-week)	Proportion
3	8824	3152	35.7%	1814	20.6%
4	8824	3383	38.3%	2013	22.8%
5	8824	3145	35.6%	1839	20.8%
6	8824	3755	42.6%	2240	25.4%
7	11030	5817	52.7%	3684	33.4%
8	8824	5266	59.7%	3661	41.5%
9	11030	6525	59.2%	4492	40.7%
10	8824	5403	61.2%	3773	42.8%
11	8824	5036	57.1%	3416	38.7%
12	11030	7006	63.5%	4997	45.3%

Table S4. Awareness and treatment of hypertension, diabetes, and dyslipidaemia

Group	Awareness at baseline	Treatment				
		Baseline	3rd month	6th month	9th month	12th month
Hypertension (n=4390)						
Intervention (n=2234)	**88.3%** (1973/2234)	**41.4%** (924/2234)	**64.5%** (1423/2207)	**68.8%** (1517/2205)	**71.5%** (1579/2208)	**74.8%** (1663/2222)
Control (n=2156)	**89.1%** (1921/2156)	**41.6%** (896/2156)	**55.0%** (1178/2142)	**60.5%** (1302/2151)	**63.2%** (1357/2147)	**65.4%** (1403/2144)
Diabetes (n=2262)						
Intervention (n=1131)	**66.1%** (748/1131)	**27.6%** (312/1131)	**39.8%** (446/1120)	**44.7%** (500/1119)	**46.0%** (516/1121)	**47.3%** (532/1125)
Control (n=1131)	**63.8%** (721/1131)	**27.6%** (312/1131)	**34.5%** (387/1123)	**37.7%** (425/1128)	**39.4%** (444/1126)	**41.0%** (461/1125)
Dyslipidaemia (n=2479)						
Intervention (n=1207)	**N/A**	**12.7%** (153/1207)	**18.8%** (225/1195)	**22.0%** (262/1192)	**25.0%** (298/1192)	**28.7%** (345/1201)
Control (n=1272)	**N/A**	**15.9%** (202/1272)	**18.5%** (234/1265)	**19.3%** (245/1270)	**21.1%** (268/1268)	**20.7%** (262/1266)

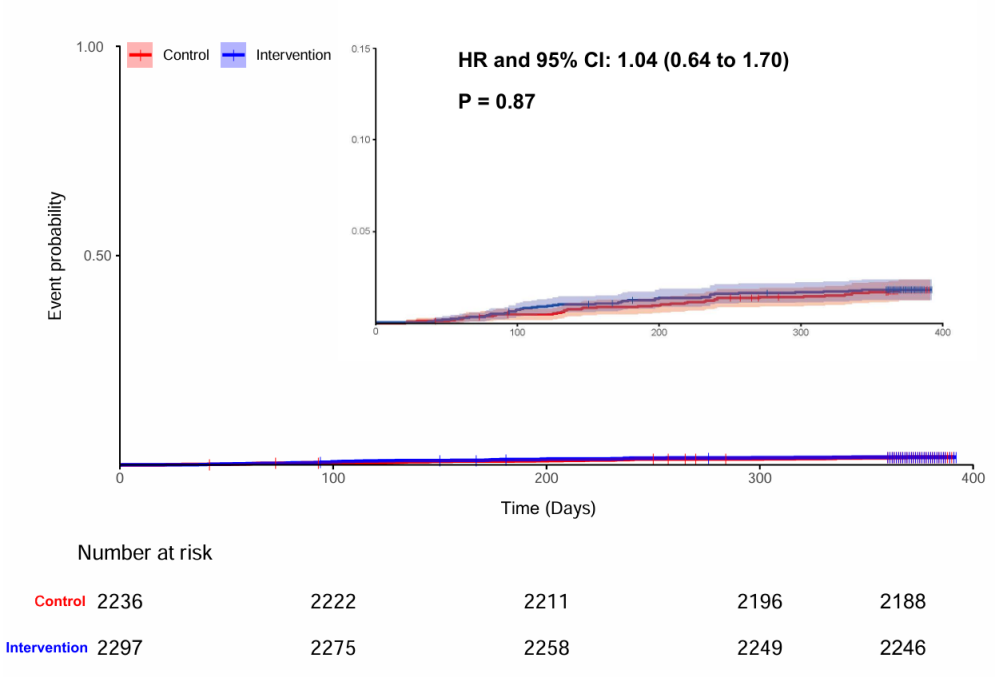
* Based on the baseline data, the three conditions were defined as follows: (1) Hypertension was defined as an average SBP≥140 mmHg, or an average DBP≥90 mmHg, or a self-reported history of hypertension, or in the use of antihypertensive medications; (2) Diabetes was defined as a FBG≥7 mmol/L, or a self-reported history of diabetes, or in the use of antidiabetic medications; (3) Dyslipidaemia was defined as TC≥6.2 mmol/L, or LDL-C≥4.1 mmol/L, or TG≥2.3 mmol/L, or HDL-C<1.0 mmol/L, or in the use of lipid-lowering medications.

Table S5. Exploratory Outcome: Medication adherence

Group	Baseline	3rd months	6th months	9th months	12 months	Net Group Difference (OR, 95%CI)
Intervention	**45.1%** (1031/2287)	**64.7%** (1462/2258)	**71.2%** (1606/2256)	**76.2%** (1721/2259)	**80.7%** (1835/2275)	**1.99 (1.46 to 2.71) P<0.001***
Control	**44.8%** (992/2212)	**58.9%** (1295/2197)	**63.2%** (1395/2207)	**67.2%** (1480/2203)	**70.7%** (1556/2200)	
(Mean change) Intervention: 35.6% (33.5% to 37.8%), Control: 25.9% (23.8% to 27.9%)						

* Medication adherence was defined as taking the full dose of prescribed medications≥6 days per week among all participants with hypertension, diabetes, or dyslipidaemia. The net group difference was adjusted for clustering effects by villages (as random effect), four minimisation factors, age, sex, education, occupation, annual household income, marriage status, social medical insurance, and baseline level of the outcome.

Fig S4. Exploratory Outcome: MACEs



* The HR and 95%CI of MACEs were estimated by Cox frailty model with adjustment of clustering effects by villages (as random effect), four minimisation factors, age, sex, education, occupation, annual household income, marriage status, and social medical insurance.

Table S6 (a). Primary and secondary research outcomes (sensitivity analysis: excluding participants with MACEs)

	Intervention (n=2246)			Control (n=2188)			Net Group Difference (95%CI)	P value
	Baseline	12-month	Change (95%CI)	Baseline	12-month	Change (95%CI)		
Primary outcome								
10-year risk of ASCVD, %	18.0 (7.1)	11.7 (5.8)	-6.3 (-6.5 to -6.0)	17.7 (6.8)	13.5 (6.9)	-4.2 (-4.5 to -3.9)	-1.88 (-2.57 to -1.19)	<0.001
Secondary outcomes								
Lifetime risk of ASCVD, % *	49.9 (15.4)	34.0 (12.7)	-15.9 (-16.4 to -15.3)	49.4 (15.8)	38.4 (14.8)	-11.0 (-11.5 to -10.4)	-4.59 (-6.23 to -2.96)	<0.001
Systolic blood pressure, mmHg	157.7 (16.2)	134.4 (12.1)	-23.2 (-23.9 to -22.5)	157.0 (16.1)	141.9 (16.1)	-15.0 (-15.8 to -14.3)	-7.70 (-9.38 to -6.02)	<0.001
Diastolic blood pressure, mmHg	93.4 (11.0)	82.5 (8.0)	-10.9 (-11.3 to -10.4)	92.6 (10.7)	85.8 (9.8)	-6.8 (-7.2 to -6.4)	-3.63 (-4.70 to -2.55)	<0.001
Fasting blood glucose, mmol/L	7.2 (2.7)	6.3 (1.6)	-0.9 (-1.0 to -0.8)	7.1 (2.5)	6.6 (1.8)	-0.5 (-0.6 to -0.4)	-0.29 (-0.51 to -0.07)	0.009
Non-HDL-C, mmol/L	3.4 (1.2)	3.0 (1.1)	-0.4 (-0.4 to -0.3)	3.4 (1.3)	3.1 (1.1)	-0.3 (-0.4 to -0.3)	-0.06 (-0.19 to 0.08)	0.43
Obesity	869 (38.7%)	784 (34.9%)	-3.8% (-5.0% to -2.6%)	842 (38.5%)	792 (36.2%)	-2.3% (-3.5% to -1.1%)	0.83 (0.65 to 1.05)	0.13
Daily smoking	515 (22.9%)	449 (20.0%)	-2.9% (-4.0% to -1.9%)	473 (21.6%)	462 (21.1%)	-0.5% (-1.5% to 0.4%)	0.61 (0.43 to 0.85)	0.004
Insufficient physical activity (<3000 MET-min/wk)	315 (14.0%)	247 (11.0%)	-3.0% (-4.6% to -1.5%)	309 (14.1%)	337 (15.4%)	1.3% (-0.3% to 2.8%)	0.63 (0.42 to 0.94)	0.03
Insufficient leisure-time activity (<150/75 min/wk)	1541 (68.6%)	1040 (46.3%)	-22.3% (-24.7% to -19.9%)	1420 (64.9%)	1372 (62.7%)	-2.2% (-4.5% to 0.1%)	0.38 (0.24 to 0.59)	<0.001

* Data were mean (SD), n (%), mean (95%CI) or OR (95%CI) unless otherwise stated.

All net group difference was adjusted for clustering effects by villages (as random effect), four minimisation factors, age, sex, education, occupation, annual household income, marriage status, social medical insurance, and baseline level of the outcome.

Table S6 (b). Subgroup results of the primary outcome (sensitivity analysis: excluding participants with MACEs)

Subgroup	Intervention (n=2246)		Control (n=2188)		Net Group Difference (95%CI)	P value	P-inter
	Number	Changes (95%CI)	Number	Changes (95%CI)			
Age, year							0.73
<60	1352	-7.0 (-7.3 to -6.6)	1301	-5.2 (-5.6 to -4.9)	-1.86 (-2.57 to -1.16)	<0.001	
≥60	894	-5.2 (-5.6 to -4.8)	887	-2.7 (-3.1 to -2.3)	-1.82 (-2.63 to -1.01)	<0.001	
Sex							0.03
Male	1130	-7.2 (-7.6 to -6.7)	1062	-4.6 (-5.0 to -4.2)	-2.20 (-3.05 to -1.36)	<0.001	
Female	1116	-5.4 (-5.7 to -5.1)	1126	-3.8 (-4.1 to -3.5)	-1.55 (-2.20 to -0.90)	<0.001	
Education							0.74
Below high school	1755	-6.0 (-6.3 to -5.7)	1749	-4.1 (-4.4 to -3.9)	-1.83 (-2.54 to -1.12)	<0.001	
High school and above	491	-7.3 (-7.9 to -6.7)	439	-4.4 (-5.0 to -3.7)	-2.11 (-3.03 to -1.20)	<0.001	
Occupation							0.03
Farmer	1535	-6.1 (-6.4 to -5.8)	1465	-4.4 (-4.7 to -4.0)	-1.63 (-2.41 to -0.85)	<0.001	
Non-farmer	711	-6.6 (-7.1 to -6.1)	723	-3.8 (-4.3 to -3.4)	-2.60 (-3.37 to -1.83)	<0.001	
Annual household income, yuan							0.02
<10 000	358	-5.1 (-5.8 to -4.5)	347	-2.4 (-3.1 to -1.8)	-2.76 (-3.90 to -1.63)	<0.001	
≥10 000	1888	-6.5 (-6.8 to -6.2)	1841	-4.5 (-4.8 to -4.2)	-1.72 (-2.40 to -1.03)	<0.001	
10-year risk of ASCVD, %							<0.001
<16	1128	-3.5 (-3.7 to -3.3)	1128	-2.3 (-2.6 to -2.0)	-1.14 (-1.76 to -0.52)	<0.001	
≥16	1118	-9.0 (-9.5 to -8.6)	1060	-6.2 (-6.6 to -5.8)	-2.57 (-3.42 to -1.72)	<0.001	

APPENDIX 4:

ANALYSIS CODE FOR THE STUDY

```
* Compare Baseline Characteristics;
* continuous variables;
proc means data=smarter_data mean std;
var IS_age SBP0 DBP0 GLU0 NHDL0 waist0 BMI0 risk0 risk_lifetime_0;
by group;
run;

* categorical variables;
proc freq data=smarter_data;
tables male pd_education pd_labor pd_income pd_married pd_insure smk_daily_0
PA_lt3000_0;
by group;
run;

* Evaluation of Research Outcomes;

data fu4_data; set smarter_data; if risk4^=.; run;
proc means data=fu4_data n mean std;
var risk0 risk4 risk_lifetime_0 risk_lifetime_4 SBP0 SBP4 DBP0 DBP4 GLU0 GLU4
NHDL0 NHDL4;
by group;
run;
proc freq data=fu4_data;
tables obesity_0 obesity_4 smk_daily_0 smk_daily_4 PA_lt3000_0 PA_lt3000_4 LTPA0
LTPA4;
by group;
run;
proc means data=fu4_data n mean clm;
var risk4_change risk_lifetime4_change SBP4_change DBP4_change GLU4_change
NHDL4_change;
by group;
run;
```

```
* model for continuous variables (eg.10-y ASCVD risk);

proc glimmix data=fu4_data;
class village_id group(ref='2') male education_high_above Last_year_income_lt_10k
occupation_farmer marriage_yes insure_yes vc_risk_grp vc_sbp_grp vc_age_grp
doctor_college_above;
model risk4_change=group risk0 IS_age male education_high_above
Last_year_income_lt_10k occupation_farmer marriage_yes insure_yes vc_risk_grp
vc_sbp_grp vc_age_grp doctor_college_above
/solution dist=normal link=identity ddfm=bw cl ;
random int/subject=village_id type=un;
run;

* model for categorical variables (eg.smk_daily);

proc glimmix data=fu4_data;
class village_id group(ref='2') male education_high_above Last_year_income_lt_10k
occupation_farmer marriage_yes insure_yes smk_daily_0 vc_risk_grp vc_sbp_grp
vc_age_grp doctor_college_above;
model smk_daily_4(event="1") =group smk_daily_0 IS_age male education_high_above
Last_year_income_lt_10k occupation_farmer marriage_yes insure_yes vc_risk_grp
vc_sbp_grp vc_age_grp doctor_college_above/solution dist=binary link=logit ddfm=bw cl;
random int/solution subject=village_id type=un;
ods output ParameterEstimates=Coefficients_smk;
run;

data coefficients_smk;
set coefficients_smk;
if effect~='Intercept' then do;
PA_OR=exp(Estimate);
PA_OR_L=exp(Estimate-1.96*stderr);
PA_OR_U=exp(Estimate+1.96*stderr);
PA_OR_95CI=compress(put(PA_OR,4.2))||"("||compress(put(PA_OR_L,4.2))||","||compress(p
ut(PA_OR_U,4.2))||")";
end;
run;
```

```
* Subgroup Analysis;
* eg.sex: male/female;

data male; set fu4_data; if male=1; run;
data female; set fu4_data; if male=0; run;

proc means data=male n mean clm;
var risk4_change;
by group;
run;

proc glimmix data=male;
class village_id group(ref='2') education_high_above occupation_farmer
Last_year_income_lt_10k marriage_yes insure_yes vc_risk_grp vc_sbp_grp vc_age_grp
doctor_college_above;
model risk4_change=group risk0 IS_age education_high_above occupation_farmer
Last_year_income_lt_10k marriage_yes insure_yes vc_risk_grp vc_sbp_grp vc_age_grp
doctor_college_above/solution dist=normal link=identity ddfm=bw cl ;
random int/subject=village_id type=un;
run;

proc means data=female n mean clm;
var risk4_change;
by group;
run;

proc glimmix data=female;
class village_id group(ref='2') education_high_above occupation_farmer
Last_year_income_lt_10k marriage_yes insure_yes vc_risk_grp vc_sbp_grp vc_age_grp
doctor_college_above;
model risk4_change=group risk0 IS_age education_high_above occupation_farmer
Last_year_income_lt_10k marriage_yes insure_yes vc_risk_grp vc_sbp_grp vc_age_grp
doctor_college_above/solution dist=normal link=identity ddfm=bw cl ;
random int/subject=village_id type=un;
run;
```

```
* test for interaction;

proc glimmix data=fu4_data;
class village_id group(ref='2') male education_high_above occupation_farmer
Last_year_income_lt_10k marriage_yes insure_yes vc_risk_grp vc_sbp_grp vc_age_grp
doctor_college_above;
model risk4_change=group risk0 IS_age male male*group education_high_above
occupation_farmer Last_year_income_lt_10k marriage_yes insure_yes vc_risk_grp
vc_sbp_grp vc_age_grp doctor_college_above
/solution dist=normal link=identity ddfm=bw cl ;
random int/subject=village_id type=un;
run;
```