


# BMJ Open Effects of Message Framing and Time Discounting on Health Communication for Optimum Cardiovascular Disease and Stroke Prevention (EMT-OCSP): a protocol for a pragmatic, multicentre, observer-blinded, 12-month randomised controlled study

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## ABSTRACT

**Introduction** Primary prevention of cardiovascular disease (CVD) and stroke often fails due to poor adherence among patients to evidence-based prevention recommendations. The proper formatting of messages portraying CVD and stroke risks and interventional benefits may promote individuals' perception and motivation, adherence to healthy plans and eventual success in achieving risk control. The main objective of this study is to determine whether risk and intervention communication strategies (gain-framed vs loss-framed and long-term vs short-term contexts) and potential interaction thereof have different effects on the optimisation of adherence to clinical preventive management for the endpoint of CVD risk reduction among subjects with at least one CVD risk factor.

**Methods and analysis** This trial is designed as a 2×2 factorial, observer-blinded multicentre randomised controlled study with four parallel groups. Trial participants are aged 45–80 years and have at least one CVD risk factor. Based on sample size calculations for primary outcome, we plan to enrol 15 000 participants. Data collection will occur at baseline, 6 months and 1 year after randomisation. The primary outcomes are changes in the estimated 10-year CVD risk, estimated lifetime CVD risk and estimated CVD-free life expectancy from baseline to the 1-year follow-up.

**Ethics and dissemination** This study received approval from the Ethical Committee of West China Hospital, Sichuan University and will be disseminated via peer-reviewed publications and conference presentations.

**Trial registration number** NCT04450888.

## INTRODUCTION

Primary prevention of cardiovascular disease (CVD) and stroke often fails due to poor

## Strengths and limitations of this study

- We aim to conduct a well-designed randomised controlled trial with large sample size to provide evidence that the pattern of a risk communication-related message is an important consideration in promoting cardiovascular disease (CVD) prevention behaviour.
- These messaging strategies, taking advantage of human cognitive bias, can be leveraged as cost-effective tactics for CVD risk communication to improve prevention and produce better outcomes.
- Follow-up for this study is limited to 12 months due to study budget and timeframe. Ideally longer term follow-up would be preferable to allow for the the clinical endpoints, such as myocardial infarction, stroke and mortality (all-cause and CVD-specific), to be assessed.

patient adherence to evidence-based recommendations and interventions, and poor motivation to engage in healthy behaviour, despite evidence that lifestyle changes and pharmacological therapy effectively modify risk factors.<sup>1–4</sup> Poor adherence is multifactorial, with large contributions from physicians' poor communication about CVD risks and individuals' inaccurate perceptions.<sup>5</sup> Many proposed means of improving adherence are insufficiently effective.<sup>5–7</sup>

The current approach to CVD risk communication usually centres on total CVD risk scores;<sup>8</sup> however, many people incorrectly

interpret statistical information, and poor comprehension likely limits their ability to make healthier choices.<sup>9–11</sup> Appropriate message design may promote individuals' perception and motivation, adherence to health plans and successful CVD risk control,<sup>12–15</sup> but this depends on many factors (eg, age; risk, socioeconomic and educational levels; personality and psychological characteristics).<sup>16</sup> CVD risk communication could be improved by intuitively visualising life expectancy changes or disease-free survival losses/gains.<sup>17–19</sup>

Considering people's tendency to overweigh losses relative to gains,<sup>20</sup> loss-framed health messages may be more likely to motivate healthy behaviour.<sup>20–21</sup> However, health behaviour findings on framing impacts are inconsistent, and effects may depend on the behaviour in question.<sup>22–25</sup> In addition, people tend to discount future (long-term/lifetime) effects, responding more to immediate (short-term) costs and benefits (time discounting or time preference), especially as they age, although this tendency varies among individuals.<sup>12–16–26–34</sup> Time preference/discounting is the most common cognitive bias affecting intentions to engage in actual behaviour, and it may fluctuate asymmetrically for gains versus losses.<sup>35–37</sup> Health behaviour researchers have sought to identify the contexts in which gain/loss-framed health messages are most likely to motivate healthy behaviour.<sup>23–24</sup> Moreover, several small trials have investigated the combined effects of message framing and time discounting in the promotion of smoking and drinking cessation.<sup>38–40</sup> Their findings have not produced consistent conclusions, due in part to limitations (ie, small samples, immediate measures of attitudes toward health behaviours or intentions to engage in behaviours as primary outcomes of interest). Few studies have examined actual behavioural changes,<sup>23</sup> which enable better characterisation of the circumstances under which cognitive deviation is likely to make practical differences in health promotion, and the identification of contexts in which health message shaping is likely to maximally affect healthy behaviour.

The use of smartphone applications (apps) for disease prevention is growing. It enhances CVD risk communication and intervention delivery, and increases access to effective CVD prevention.<sup>41–44</sup> Although preliminary trials have documented benefits of app use among people with CVD, high-quality data are limited and long-term outcome data are not available.<sup>44–45</sup> Rigorous evidence for the clinical validity of mobile healthcare is lacking, raising questions such as which app components are likely to facilitate behavioural changes and enable individuals to adhere to medical advice.<sup>41–44</sup>

Recently, a competing risk-adjusted lifetime-perspective model for CVD (LIFE-CVD) was developed and validated to aid survival gain calculation for primary CVD prevention and individuals' understanding of risks and interventions.<sup>19–46</sup> The model has three types of input data (demographic characteristics, existing and anticipated risk factors) and provides generic formulas for CVD risk, life expectancy and survival gain calculation according to

individuals' ethnic backgrounds, facilitating the intuitive framing of health communication.<sup>17</sup> Gain-framed and loss-framed communications can be created by setting different reference points (actual and ideal CVD-free life expectancy, respectively),<sup>47–48</sup> and short-term and long-term interventional benefits can be represented graphically.

No study to date has investigated the effects of message framing and time discounting on CVD prevention adherence with a focus on long-term persistence of healthy behavioural changes. Large-scale randomised controlled trials (RCTs) assessing the effects of cognitive deviation in CVD risk communication on individuals' risk perceptions, health motivation and sustained healthy behaviour changes, as well as on major clinical outcomes, should be prioritised. Considering that physician-patient risk communication time is commonly limited, clarity regarding the most effective messaging strategies for general and specific populations is valuable. The combined application of the LIFE-CVD model, a cognitive bias-based messaging strategy and a health communication app may optimise primary CVD prevention in target populations.

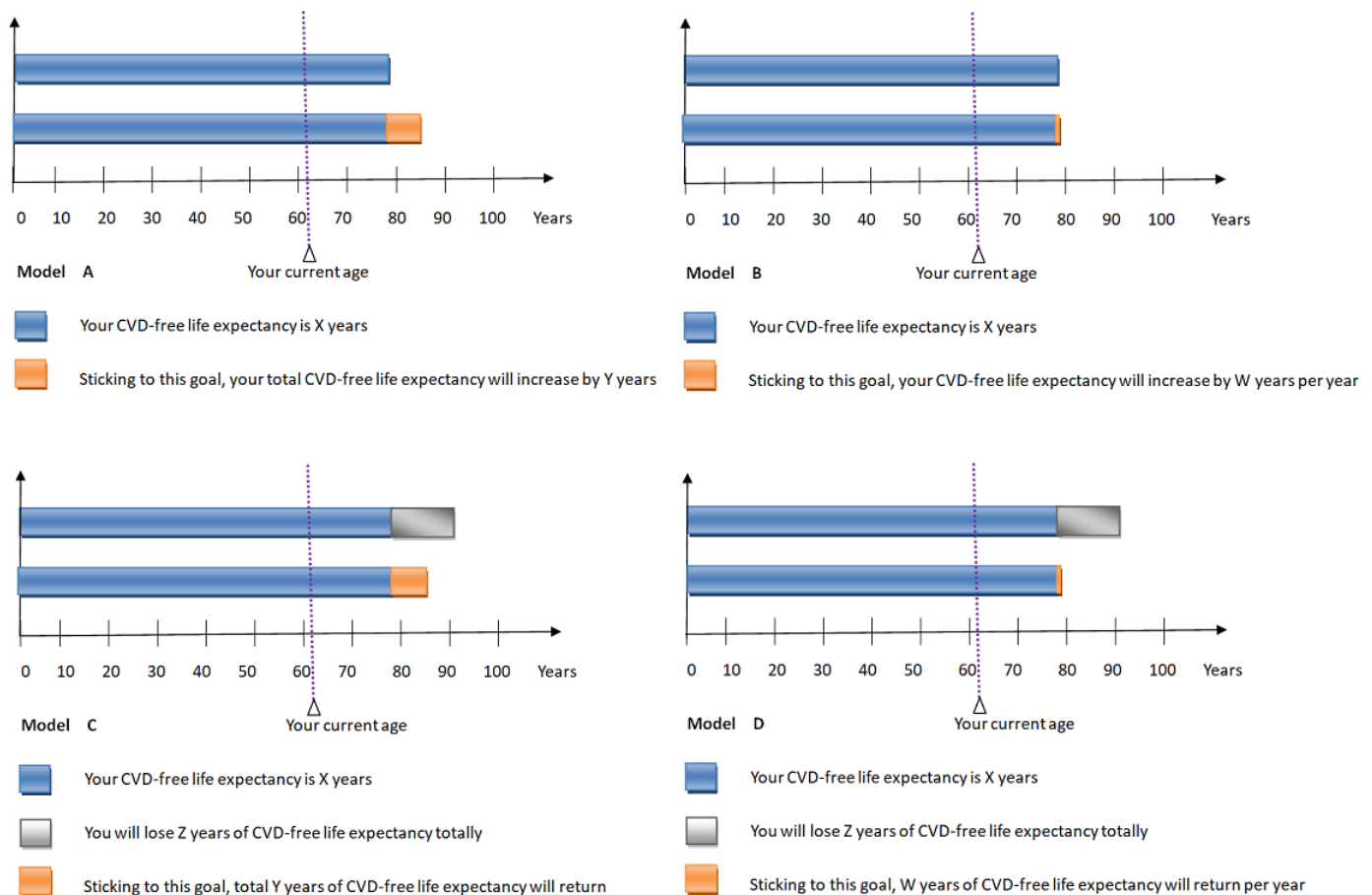
## OBJECTIVE

In the Effects of Message Framing and Time Discounting on Health Communication for Optimum Cardiovascular Disease and Stroke Prevention (EMT-OCSP) Study, we aim to determine whether risk/intervention communication strategies (gain-framed vs loss-framed, long-term vs short-term) and potential interaction thereof have different effects on the optimisation of primary prevention adherence among subjects with at least one CVD risk factor using a smartphone app based on the LIFE-CVD model. We have developed and pre-tested the 'Health Keeper' (HK) app (under the China National Key Research and Development Project), based on the LIFE-CVD model (figure 1), and will employ it in this study. Strategic message design, taking advantage of cognitive bias, will be used to maximise participants' uptake and engagement in primary prevention, and the outcomes of interventions will be evaluated according to participants' sex, age, risk level, socioeconomic status and psychological characteristics. Evidence of variation in preventive effectiveness (CVD risk reduction) among study groups, regardless of the effect size, will indicate the importance of messaging strategy leveraging.

## METHODS AND ANALYSES

### Study design and setting

The EMT-OCSP trial is designed as a 2×2 factorial, observer-blinded multicentre RCT with four parallel groups. It will be integrated with the National Basic Public Health Service Program (NBPHSP) in China,<sup>49–51</sup> initiated in 2009. NBPHSP activities include the full spectrum of population-based essential health services for all



**Figure 1** LIFE-CVD models. (A) Model A: total cardiovascular disease (CVD)-free life expectancy gain in one's remaining life. (B) Model B: average CVD-free life expectancy gain per year. (C) Model C: total CVD-free life expectancy loss that can be reclaimed in one's remaining life. (D) Model D: average CVD-free life expectancy loss that can be reclaimed per year. Blue, estimated CVD-free life expectancy; orange, CVD-free years gained by the adoption of preventive strategies (eg, smoking cessation, systolic blood pressure and low-density lipoprotein cholesterol reduction); grey, shortened life expectancy relative to ideal risk factor levels.

urban and rural inhabitants. For the EMT-OCSP Study, we will use data from 32 rural and 24 urban primary healthcare centres. The study has been registered at the trial registration.

The HK app was developed at West China Hospital, Sichuan, China, with stroke neurologists and software developers following a user-centred, evidence-based approach. Based on the LIFE-CVD model, it enables the calculation of 10-year and lifetime CVD risks, and risk-adjusted gains/losses in life expectancy.<sup>19</sup> The app has physician and patient portals, and is compatible with Apple and Android systems.

Participants register and are given user IDs based on their cell phone numbers; they must accept the terms and conditions of app use and confirm that they have read the brief explanatory introduction. Participants then input profile data (birthdate, sex, ethnicity, height and weight (the body mass index is then calculated), total and high-density lipoprotein (HDL) cholesterol levels (the non-HDL cholesterol level is then calculated) and systolic blood pressure (BP); pull-down options and definitions are provided when applicable), which the participants

and their physicians check for accuracy before submission. Referential data rules, valid values, range checks and consistency checks for the input data will be pre-set according to the LIFE-CVD model and stored in the software. After submission, these data (birthdate, sex, ethnicity and height) are locked and cannot be modified at will to avoid cross-use and contamination. Any necessary data modification will require physician approval.

Users then click 'next' to view their estimated baseline CVD risk and CVD-free life expectancy in their randomly assigned format; these results will be saved. The app's main screen shows estimated CVD-free life expectancy (represented as a thermometer) with a brief explanation (figure 1). Participants will be required to click the 'I want to be better' button to set personal optimal values (eg, for BP and cholesterol; the app limits values to reasonable ranges) and interventional goals (to achieve motivation, these must be better than baseline, eg, lower systolic BP and cholesterol level). Possible gains derived from anticipated lifestyle and pharmacological interventions, which may decrease with age and increase with risk-factor burden, are displayed with brief text descriptions,

permitting intuitive comparison of baseline and optimised CVD-free years (figure 1; models A and C, larger later outcomes; models B and D, smaller sooner outcomes). The optimised CVD-free life expectancy is saved until the next calculation. The user can click a reset button to return to baseline, with a pop-up ‘see what doctor says’ link. In this section, individuals receive brief individually tailored pictorial recommendations (eg, to quit smoking, control weight or attain a target BP) according to current primary prevention guidelines. This information is sent simultaneously to corresponding physicians’ mobile terminals.

Individuals are required to use the app for this game-like estimation/desired goal setting, and accept the motivations for optimised goals, one to three times per month (thereafter, the app locks the estimation function to prevent cross-use). Unless the task has been completed, each participant will receive three reminders in the last week of each month (on Monday, Tuesday and Wednesday; two alarms with text messages sent automatically at 19:00, and a physician phone call). The software will record failure to complete this task as a truancy on the user’s activity calendar.

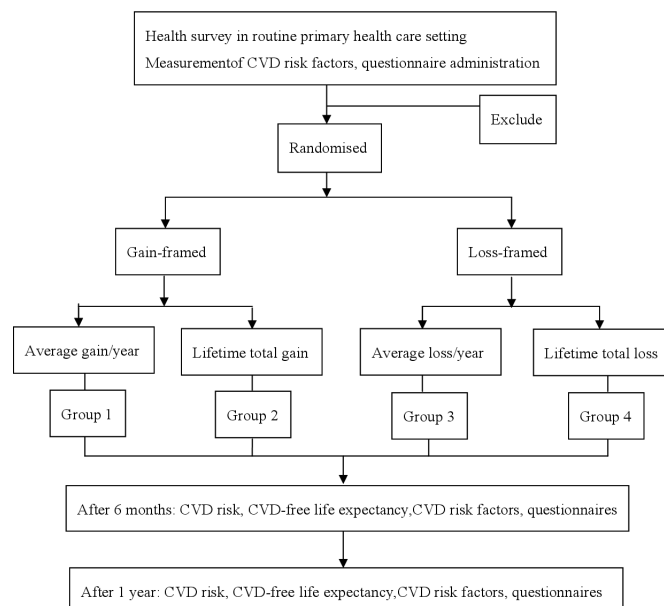
The physician portal provides access to data for an average of 100 patients per physician. The community physicians will uniformly apply pooled cohort equations (PCEs) for risk assessment to guide decision making for primary prevention<sup>52 53</sup>; to avoid misunderstanding and with recognition of potential inaccuracy,<sup>54</sup> PCE results will not be presented in the HK app.

### Participants

Participants will be aged 45–80 years, personally own and use a smartphone (Apple or Android platform) with Internet access, and have at least one of the following CVD risk factors: history of CVD at age <60 years in a first-degree relative, smoking, diabetes, hypertension and low-density lipoprotein (LDL) cholesterol  $\geq 4.5$  mmol/L. Participants with histories of CVD, heart failure or chronic kidney disease (estimated glomerular filtration rate  $< 30$  mL/min/1.73 m<sup>2</sup>); those with terminal malignancy at baseline and those with severe psychological or mental disorders will be excluded. Violation of the study protocol, including inadequate informed consent; enrollment of subjects not meeting the inclusion/exclusion criteria; improper breaking of the blinding; multiple visits missed or outside permissible windows; inadequate record-keeping; intentional deviation from the protocol; repeated non-compliance by the subject; and falsification, and participation in another clinical study during follow-up will prompt exclusion.

### Enrolment

The research nurses will contact potentially eligible participants identified from the NBPHSP database, explaining the trial and ascertaining interest. Interested patients will be evaluated at their primary healthcare centres; those eligible for EMT-OCSP participation will



**Figure 2** Flow of the study. CVD, cardiovascular disease.

be invited to participate during NBPHSP-related visits. The research nurses will send invitations for baseline visits with available appointment times by message, and register all forms documenting NBPHSP baseline visits. Reasons for individuals’ refusal to participate in the study will be documented.

### Randomisation

Using a computer-generated randomisation schedule with permuted blocks of random sizes, study participants will be assigned to groups A–D (figure 1), representing different CVD-free life expectancy formats, and receive corresponding smartphone app upgrade packages. Random numbers will be generated prior to the study by a computerised random number generator. Block sizes will not be disclosed until primary endpoint analysis. Randomisation will be requested by the staff member responsible for recruitment and clinical interviewing from the Clinical Trial Coordinating Centre. The intervention does not permit participant or provider allocation blinding, but providers will be instructed to not disclose allocation status at follow-up assessments. Staff responsible for data collection and analysis will be blinded to group allocation. At randomisation, participants will be assigned unique identification codes.

### Procedure

The study flow, schedule and activities are presented in figures 2 and 3 and table 1, respectively. The same 12-month outcome schedule will be used for all randomised participants, regardless of intervention completion/discontinuation, except for the adherence assessment. The study will be closed on 21 January 2022. Data collection will be finalised in January 2022, or on completion of all 1-year visits.

Study-related primary healthcare centre visits will be conducted using motivational interviewing methodology,

	2020	2021	2021	2022
	7–12	1–6	7–12	1
Baseline				
6-month follow-up				
1-year follow-up				
Interview				

**Figure 3** Study schedule.

with the aim of promoting health and CVD prevention. A pictorial depiction of the LIFE-CVD model will be used to facilitate individuals' understanding of how their lifestyles and drug therapies are linked to CVD risk. Participants will be blinded to study hypotheses and theories underlying which interventions are considered to be active.

At baseline visits, in addition to health assessment, participants will install and test the HK app, register and link their app accounts for this study. Following standardised, simplified procedures, community physicians will teach participants how to use the app calculator and communicate about calculation results using the 'teach-back' method, providing additional information when needed. Family members will be permitted to attend baseline visits.

Participants will use the HK app to set goals, receive performance feedback and self-monitor primary CVD prevention. Physicians at primary healthcare centres will routinely manage participants according to primary CVD prevention guidelines.<sup>52 53</sup> They will aim to provide accurate, accessible and understandable CVD-related information and confirm participants' understanding of calculation results and conceptualisation of CVD-free life expectancy as dynamic, modifiable by lifestyle changes and pharmacological treatment. Participants will also be given written guidance on CVD-free life expectancy calculation. The intervention will be regarded as low intensity if fewer than 6 monthly CVD-free life expectancy calculations per year, or fewer than three calculations in the

first 6 months, are completed. Using the app, research nurses will periodically inform healthcare centre staff and participants about CVD prevention, the current trial status and plans for the next phase, and acknowledge their support. At 9 months, participants will receive a message with information about the study proceedings and a reminder about the 1-year follow-up visit, irrespective of participation status at the 6-month follow-up, provided that they have not been excluded or withdrawn consent.

At recruitment and 6 months, physicians will indicate the importance of following study guidelines (including once-monthly calculation) and contacting physicians with potentially study-related problems, and explain the app's purpose, use and updating, what to do in the event of smartphone/app loss/damage and monthly task counts and study visits. Participants will be asked whether they are having problems with app use. At follow-up sessions, reasons for task non-completion and simple strategies for enhancing adherence (eg, linking calculation to normal routines) will be discussed briefly.

Follow-up assessments and interviews will be conducted at 6 and 12 months after randomisation, within a 28-day window extending from 7 days before to 21 days after the due date. Research nurses will prompt the healthcare centres to invite participants and conduct the 6-month and 12-month examinations (ie, risk factor measurement and questionnaire administration) at the local primary healthcare centres. When appropriate, participants will receive recommendations for additional follow-up visits and/or referrals to community physicians for pharmacological treatment according to CVD prevention guidelines. Cross-group contamination will be assessed at 1 year (have you talked to other participants about your LIFE-CVD model, and if yes was your attitude changed? Are you aware of the model of a participant in another group, or vice versa?). Research nurses will send assessment results to the research centre. All participants will be informed about these results.

**Table 1** Study activities

Activity	Baseline	6 months	1 year
Informed consent provision	X		
Clinical risk markers measurement	X	X	X
Lifestyle habits assessment	X	X	X
Demographic, socioeconomic and psychosocial factors assessment	X		
Psychological questionnaires	X	X	X
Self-rated health, risk of CVD and health-specific self-efficacy	X	X	X
Interviews with community physicians	X		
Interviews with study participants	X		X
Pharmacological treatment	X	X	X
Interviews, contamination assessment			X

CVD, cardiovascular disease.

## Endpoints

The primary endpoints are changes in the estimated 10-year CVD risk, estimated lifetime CVD risk and estimated CVD-free life expectancy from baseline to the 1-year follow-up, based on the levels of total, HDL and LDL cholesterol; systolic BP; body mass index; history of diabetes mellitus and/or early (age <60 years) parental myocardial infarction; antithrombotic therapy and high BP treatment; diabetes; smoking habit and age. Secondary endpoints are changes in CVD risk factors (BP and serum cholesterol, LDL, non-HDL, triglycerides and fasting glucose levels); lifestyle factors (physical activity, tobacco use, alcohol use and dietary habits); pharmacological treatments for hypertension, dyslipidaemia and diabetes; and anti-thrombotic drug prescriptions after 1 year.

## Examinations and measurements

From the baseline questionnaire, data on age, sex, civil status, education, family histories of premature CVD and diabetes, and systolic and diastolic BP will be recorded. Socioeconomic status will be classified according to the per-capita disposable income of urban households (by quintile) and highest attained educational level.

The following data will be collected: self-reported lifestyle data (tobacco use; alcohol use (Alcohol Use Disorders Identification Test)<sup>55</sup>; physical activity and time spent sitting; dietary habit (daily fruit, root, legume and vegetable consumption); health; diabetes and BP and lipid-lowering pharmacological treatments), physical measurements (height (in cm), weight (in kg), systolic and diastolic BP (in mm Hg)) and blood examination findings (serum total, HDL and LDL cholesterol, triglycerides and fasting glucose levels (in mmol/L), determined using standard biochemical methods). Height and weight will be measured with subjects barefoot in light clothing using calibrated scales and stadiometers. Systolic and diastolic BP will be measured two times with a calibrated digital gauge (2 mm precision) after 5 min rest with subjects seated; mean values will be recorded. Blood samples will be collected after overnight fasts and sent to the clinical chemistry departments of the nearest local hospitals.

Data on prescriptions for antithrombotic medications and those used to treat hypertension, dyslipidaemia and diabetes will be retrieved from the digital medical records of community hospitals. Purchases of pharmacological products from community hospitals, registered in participants' medical insurance records, will also be recorded.

Psychological variables will be used as moderators/mediators of intervention effects on primary and secondary outcomes, and as outcomes at 1 year. At baseline and 1 year, participants' health literacy, coping strategies (using the Brief Coping Orientation to Problems Experienced Instrument), general self-efficacy, anxiety and depression (using the Hospital Anxiety and Depression Scale), and optimism/pessimism (using the Life Orientation Test) will be measured. At baseline and follow-up visits, participants will be asked to self-rate their health (five alternatives), CVD risk and health-specific

self-efficacy (ability to reduce CVD risk through preventive actions) using a visual analogue scale (0–10).

## Training and certification

Before participant recruitment, community physicians and key personnel at participating sites will be trained and certified. Personnel at each centre will be trained centrally, and training session content will be standardised and presented by members of the study's executive team. The beta version of the HK app, operating instructions, forms, training manuals and other materials will be provided. The training session will cover trial overview; participant recruitment, eligibility and exclusion criteria; participant visit procedures; app-based data entry; data collection; physician–patient health communication requirements (standardised trial introduction, app use instruction, education and counselling for adherence, uniform and reproducible elicitation and explanation of information from the app and data discrepancy management) and general information about obtaining high-quality research data, intervention providers' responsibilities, workflow and strategies to minimise communication bias and cross-group contamination. The providers should meet well-defined performance criteria, assessed by observation during role play with standardised mock participants.

## Pilot study

A 1-month pilot study was performed in 2019 to test the original HK app with 200 participants from a district far from the study region, with different socioeconomic statuses and at least one CVD risk factor. The study organisation worked well, and its protocols and procedures were developed further and showed good feasibility. Two per cent cross-group contamination was detected. Life expectancy and CVD risk information was calibrated according to participants' experiences and suggestions, obtained through questionnaires and interviews. Community physicians' experiences, derived in part from discussions of the results with participants, were also considered. Based on these findings, and as we expect <20% contamination in the EMT-OCSP Study, we chose to use an individually randomised design rather than a clustering method.<sup>56</sup>

## Sample size calculation

The sample size needed to detect clinically significant between-group differences in baseline–1-year changes in primary outcome variables, with sufficient power and considering 20% drop-out, was determined to be 15 000 (table 2). We used a power threshold of 0.9 and significance level of 0.05. Calculation was based on SD of CVD-free life expectancy, CVD risk and conventional risk factors derived from the China National Stroke Screening Survey and the best available data so far.<sup>1 17</sup>

## Statistical analyses

Data management and statistical analyses will be performed using SPSS software (V.20.0; SPSS).

**Table 2** Sample size calculation data

Variable	Precision	Power	SD	Relevant change at population level	Sample size per group	Minimum detectable change threshold
CVD-free life expectancy (months)	0.05	0.9	22	4	3750	0.921
CVD risk	0.05	0.9	3%	0.5%	3750	0.126%
Systolic BP (mm Hg)	0.05	0.9	20	2	3750	0.873
Serum cholesterol (mmol/L)	0.05	0.9	1	0.5	3750	0.042
LDL (mmol/L)	0.05	0.9	1	0.5	3750	0.042

BP, blood pressure; CVD, cardiovascular disease; LDL, low-density lipoprotein.

Analyses will include data from all study participants. Data from individuals who do not consent to participation (sex, age, socioeconomic status, clinical CVD risk factors and lifestyle factors) will be included in selection bias analysis.

The baseline demographic and clinical characteristics of the four parallel groups will be compared. Continuous variables (represented as means and SDs) will be compared using analysis of variance (ANOVA) and categorical variables (represented by frequencies and percentages) will be compared using  $\chi^2$  tests. Wilcoxon test will be used if necessary.

Primary and secondary outcomes will be evaluated according to intention-to-treat methodology. The 2×2 factorial design ANOVA will be used to assess effects of message framing and time discounting and interactions between them due to both independent variables having two levels. Differences in changes of primary outcomes from baseline to 1-year follow-up will be analysed with regression methods to identify predictors of the changes in the endpoints. In subgroup analyses, we will estimate the intervention's effects on primary outcomes for different age groups, sexes, CVD risk levels, socioeconomic status and interventional intensities. We will also perform Bonferroni correction for multiple comparisons in our analysis and sensitivity analyses to assess the robustness of trial results obtained with different methods of handling missing data.

### Patient and public involvement

No patient involved.

## ETHICS AND DISSEMINATION

### Funding and approval

The EMT-OCSP Study is supported by the China National Key Research and Development Project (2018YFC1311406). Funding covers only meetings and organisational costs. This funding source had no role in the study design and will have no role in study execution, data analysis or interpretation or the decision to publish results.

The study application was submitted to the institutional review board of West China Hospital in 2019. Approval

to conduct study activities and informed consent forms will be obtained from the regional ethics committee overseeing the participating healthcare centres, and attached to the application to the regional ethics board. The study will be conducted according to ethical principles based on the Helsinki Declaration, good clinical practice (GCP), national regulatory mandatory instructions and this protocol.

### Informed consent and anonymity

Participants (or representatives) will be required to provide informed consent after receipt of written and oral study information and before any study procedure is performed. The informed consent form will describe study monitoring procedures and the handling of access to national registry data and participants' medical records. Subjects will be informed verbally and in writing that participation is voluntary and can be withdrawn at any time, with no consequence for ordinary healthcare. District nurses will provide written confirmation that study information has been provided, and will collect informed consent forms and send them to the research nurses. Participant anonymity will be maintained through transcript masking and restriction of raw data access to the study team.

### Fear-arousing communication

As with all screening targeting healthy populations, the presentation of CVD risk profiles is of concern. The app's intuitive presentation of CVD-free life expectancy may generate more anxiety than would being informed of risk marker increases. The risk messages were confirmed in the pilot study to be easily understandable and accurately interpreted. Any negative reaction (eg, anxiety) that they generate will be addressed with individualised supportive counselling from research nurses. Participants may communicate questions to research nurses at any time.

We expect that effective risk communication will increase CVD prevention guideline compliance. We do not consider this to be ethically problematic, as message shaping has not been demonstrated to improve prognoses among CVD-free subjects, and as all communication will follow current guidelines. The study will not compromise participants' receipt of healthcare. On invitation

to NBPHSP participation, individuals are informed that health screening will be combined with advice and description of measures to improve long-term health. The EMT-OCSP Study will adhere fully to all intentions of the NBPHSP. The expected improvements in risk stratification and communication outweigh any potential negative effect of the study.

### Individualisation and contamination control

As phone numbers in China can be registered only under users' real names and identification card numbers, HK app user IDs will be unique login credentials corresponding to individual mobile devices. The activities permitted for individual users will be regulated by these credentials, preventing unauthorised access to or loss of participant data. If a participant's mobile phone is lost or broken, he/she will need to apply for a new account through the community physician to the research centre.

Although the intervention will be housed on individuals' smartphones, the EMT-OCSP Study is likely susceptible to contamination.<sup>57</sup> App messages cannot be fully blinded, and friends randomised to different study groups are likely to discuss app results. To minimise contamination, we will educate physicians in contamination avoidance; instruct participants to not transfer, share or exchange intervention content; prevent cross-use through app design; separate different groups' follow-up schedules; measure contamination at the individual level to permit analytical control and increase the sample size to compensate.<sup>56-58</sup> If necessary, we will use contamination-adjusted intention-to-treat analysis, which employs instrumental variables analysis.<sup>59</sup>

### Protocol modification

Any significant protocol modification (eg, of eligibility criteria, sample size, outcomes assessed or analyses) will require formal approval by the EMT-OCSP research group and the institutional review board prior to implementation. Minor corrections/clarifications that do not affect study conduct will be approved by the research group and documented in memoranda.

### Data storage and access

All data will be entered into the password-protected EMT-OCSP research database at the Clinical Research Centre of West China Hospital, Sichuan University, managed by a trained database manager. Different security levels (password access) may be granted to groups and individuals. To enable external data linkage, participants' identification numbers will be retained in the database. The data manager will log study data in access files on computers used solely for this purpose, and import these files, consent forms and case report forms into the database. All records with participant ID numbers linked to other identifying information will be stored in a separate, locked file in an area with limited access. Identifying information will be redacted from data dispersed to team members. The core coordinating centres will have access

only to their own data. The principal investigator will have direct access to datasets from her own site, and to data from other sites by request.

The key code will be retained for a maximum of 3 years. Participant files will be stored for 3 years after study completion. All personal data will be processed in accordance with the Cybersecurity Law of People's Republic of China, and will be available annually and free of charge to study participants, who can request error correction. Participants' study information will not be released outside of the study without their written permission.

### Prevention of missing data

We will seek to follow participants for the entire study period, regardless of intervention modification/discontinuation, to enable follow-up data collection and prevent missing data. The pilot study helped to identify and address potential problems to minimise missing data. The study's executive team will set a priori targets for the acceptable level of missing data, and on-site data collection will be monitored and reported monthly. Reasons for non-adherence (eg, intervention discontinuation due to harms vs inefficacy) and non-retention (ie, consent withdrawal or loss to follow-up) will be recorded.

### Data monitoring and quality assurance

In addition to app-based manual and automatic data checks, data quality and completeness will be ensured by monthly visual validation at the data coordinating centre (DCC) and regular on-site monitoring (at least once per participating site). Errors will be recorded in data query reports sent to data managers at core coordinating centres. The managers will check the original sources for inconsistency, check other sources to determine the correction required and correct the errors. DCC monitors will review source documents as needed to assess the completeness and accuracy of app data (patient initials, birthdate, sex, written informed consent provision, eligibility criteria fulfilment, randomisation date and intervention assignment).

Through visits and electronic monitoring, the DCC will audit overall data quality and completeness and send monthly reports by email with information on missing data and missed visits. Personnel at the core coordinating centre and participating sites will review these reports for accuracy and report any discrepancies to the DCC.

A qualified external monitor from the Clinical Trial Unit of West China Hospital, Sichuan University, will ensure that the data are reliable, accurate and complete; participants' safety and rights are protected; and the study is conducted in accordance with current protocols and study agreements, as well as GCP and all applicable government requirements. The principal investigator has approved the monitor's direct access to relevant documentation and will ensure co-investigators' and departments' cooperation with monitoring. He will be notified of corrective/preventive measures for any violation or negligence.



## Research data requests

Researchers affiliated with the EMT-OCSP Study will have access to an internal webpage listing available aggregated datasets and variables; they will not have access to individual data or the original database. External researchers collaborating with at least one steering group member may submit standardised applications for data via this webpage. On steering group approval, the data manager will export anonymised aggregated data to authorised researchers.

## Publication policy

The scientific integrity of the trial requires that data from all participating sites be analysed study-wide. Individual centres are not expected to report solely on data collected on site. A publications committee will approve all papers and abstracts based on study data before submission. The study results will be released to participating physicians and patients, and to the medical community.

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## REFERENCES

- 1 Wu S, Wu B, Liu M, *et al*. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol* 2019;18:394–405.
- 2 Zhao D, Liu J, Wang M, *et al*. Epidemiology of cardiovascular disease in China: current features and implications. *Nat Rev Cardiol* 2019;16:203–12.
- 3 Kones R. Molecular sources of residual cardiovascular risk, clinical signals, and innovative solutions: relationship with subclinical disease, undertreatment, and poor adherence: implications of new evidence upon optimizing cardiovascular patient outcomes. *Vasc Health Risk Manag* 2013;9:617–70.
- 4 Riekert KA, Ockene JK, Pbert L. *The Handbook of health behavior change*. New York: Springer Publishing Company, 2013.
- 5 Kones R, Rumana U, Morales-Salinas A. Confronting the most challenging risk factor: non-adherence. *The Lancet* 2019;393:105–6.
- 6 Salinas AM, Kones R. Barriers to global action plan for the prevention and control of noncommunicable diseases: proposal modifications to the voluntary targets. *J Prev Med* 2018;03:1.
- 7 Nieuwlaat R, Wilczynski N, Navarro T. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2014;11:CD000011.
- 8 Neuner-Jehle S, Senn O, Wegwarth O, *et al*. How do family physicians communicate about cardiovascular risk? frequencies and determinants of different communication formats. *BMC Fam Pract* 2011;12:15.
- 9 Lipkus IM, Samsa G, Rimer BK. General performance on a numeracy scale among highly educated samples. *Med Decis Making* 2001;21:37–44.
- 10 Damman OC, Bogaerts NMM, van den Haak MJ, *et al*. How lay people understand and make sense of personalized disease risk information. *Health Expect* 2017;20:973–83.
- 11 Mohd Azahar NMZ, Krishnapillai ADS, Zaini NH, *et al*. Risk perception of cardiovascular diseases among individuals with hypertension in rural Malaysia. *Heart Asia* 2017;9:e010864.
- 12 Volpp KG, Asch DA, Galvin R, *et al*. Redesigning employee health incentives — lessons from behavioral economics. *N Engl J Med* 2011;365:388–90.
- 13 Halvorsen PA, Wisløff TF, Støvring H, *et al*. Therapeutic decisions by number needed to treat and survival gains: a cross-sectional survey of lipid-lowering drug recommendations. *Br J Gen Pract* 2011;61:e477–83.
- 14 Edwards A, Elwyn G, Covey J, *et al*. Presenting risk information—a review of the effects of "framing" and other manipulations on patient outcomes. *J Health Commun* 2001;6:61–82.
- 15 Levin IP, Schneider SL, Gaeth GJ. All frames are not created equal: a typology and critical analysis of framing effects. *Organ Behav Hum Decis Process* 1998;76:149–88.
- 16 Board JBS, JBS3 Board. Joint British societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart* 2014;100 Suppl 2:ii1–67.
- 17 Berkelmans GFN, Gudbjörnsdóttir S, Visseren FLJ, *et al*. Prediction of individual life-years gained without cardiovascular events from lipid, blood pressure, glucose, and aspirin treatment based on data of more than 500 000 patients with Type 2 diabetes mellitus. *Eur Heart J* 2019;40:2899–906.
- 18 Jaspers NEM, Ridker PM, Dorresteijn JAN, *et al*. The prediction of therapy-benefit for individual cardiovascular disease prevention: rationale, implications, and implementation. *Curr Opin Lipidol* 2018;29:436–44.
- 19 Jaspers NEM, Blaha MJ, Matsushita K, *et al*. Prediction of individualized lifetime benefit from cholesterol lowering, blood pressure lowering, antithrombotic therapy, and smoking cessation in apparently healthy people. *Eur Heart J* 2020;41:1190–9.
- 20 Schwartz A, Goldberg J, Hazen G. Prospect theory, reference points, and health decisions. *Judgment and Decision Making* 2008;3:174–80.
- 21 Rothman AJ, Salovey P. Shaping perceptions to motivate healthy behavior: the role of message framing. *Psychol Bull* 1997;121:3–19.
- 22 Rothman AJ, Bartels RD, Wlaschin J, *et al*. The strategic use of gain- and loss-framed messages to promote healthy behavior: how theory can inform practice. *J Commun* 2006;56:S202–20.

- 23 Gallagher KM, Updegraff JA. Health message framing effects on attitudes, intentions, and behavior: a meta-analytic review. *Ann Behav Med* 2012;43:101–16.
- 24 Akl EA, Oxman AD, Herrin J. Framing of health information messages. *Cochrane Database Syst Rev* 2011;12:CD006777.
- 25 Seo K, Dillard JP, Shen F. The effects of message framing and visual image on persuasion. *Commun Q* 2013;61:564–83.
- 26 Dorrestein JAN, Kaasenbrood L, Cook NR, et al. How to translate clinical trial results into gain in healthy life expectancy for individual patients. *BMJ* 2016;352:i1548.
- 27 Story GW, Vlaev I, Seymour B, et al. Does temporal discounting explain unhealthy behavior? A systematic review and reinforcement learning perspective. *Front Behav Neurosci* 2014;8:76.
- 28 Hong K-S. Disability-adjusted life years analysis: implications for stroke research. *J Clin Neurol* 2011;7:109–14.
- 29 Lebeau G, Consoli SM, Le Bouc R, et al. Delay discounting of gains and losses, glycemic control and therapeutic adherence in type 2 diabetes. *Behav Processes* 2016;132:42–8.
- 30 Ikeda S, Kato HK, Ohtake F. *Behavioral economics of preferences, choices, and happiness*. Japan: Springer Verlag, 2016.
- 31 Amasino DR, Sullivan NJ, Kranton RE, et al. Amount and time exert independent influences on intertemporal choice. *Nat Hum Behav* 2019;3:383–92.
- 32 Read D, Frederick S, Scholten M. Drift: an analysis of outcome framing in intertemporal choice. *J Exp Psychol* 2013;39:573–88.
- 33 Stillwell DJ, Tunney RJ. Effects of measurement methods on the relationship between smoking and delay reward discounting. *Addiction* 2012;107:1003–12.
- 34 Chapman GB. Time preferences for the very long term. *Acta Psychologica* 2001;108:95–116.
- 35 Matjasko JL, Cawley JH, Baker-Goering MM, et al. Applying behavioral economics to public health policy: illustrative examples and promising directions. *Am J Prev Med* 2016;50:S13–19.
- 36 Holyoak KJ, Morrison RG. *The Cambridge handbook of thinking and reasoning*. Cambridge: Cambridge University Press, 2005.
- 37 Berndsen M, van der Pligt J. Time is on my side: optimism in intertemporal choice. *Acta Psychologica* 2001;108:173–86.
- 38 Mollen S, Engelen S, Kessels LTE, et al. Short and sweet: the persuasive effects of message framing and temporal context in antismoking warning labels. *J Health Commun* 2017;22:20–8.
- 39 Bernstein MH, Wood MD, Erickson LR. The effectiveness of message framing and temporal context on college student alcohol use and problems: a selective e-mail intervention. *Alcohol and Alcoholism* 2016;51:106–16.
- 40 Churchill S, Pavey L, Jessop D, et al. Persuading people to drink less alcohol: the role of message framing, temporal focus and autonomy. *Alcohol and Alcoholism* 2016;51:727–33.
- 41 Morgan J. The power of the APP: can mobile-technology save lives? *Lancet Neurol* 2016;15:668.
- 42 Sim I. Mobile devices and health. *N Engl J Med* 2019;381:956–68.
- 43 Feigin VL, Norrving B, Mensah GA. Primary prevention of cardiovascular disease through population-wide motivational strategies: insights from using smartphones in stroke prevention. *BMJ Glob Health* 2017;2:e000306.
- 44 Neubeck L, Lowres N, Benjamin EJ, et al. The mobile revolution—using smartphone apps to prevent cardiovascular disease. *Nat Rev Cardiol* 2015;12:350–60.
- 45 Palmer MJ, Barnard S, Perel P. Mobile phone-based interventions for improving adherence to medication prescribed for the primary prevention of cardiovascular disease in adults. *Cochrane Database Syst Rev* 2018;6:CD012675.
- 46 Rossello X, Dorrestein JAN, Janssen A, et al. Risk prediction tools in cardiovascular disease prevention: a report from the ESC prevention of CVD programme led by the European association of preventive cardiology (EAPC) in collaboration with the acute cardiovascular care association (ACCA) and the association of cardiovascular nursing and allied professions (ACNAP). *Eur J Prev Cardiol* 2019;26:1534–44.
- 47 Cooney MT, Vartiainen E, Laatikainen T, et al. Cardiovascular risk age: concepts and practicalities. *Heart* 2012;98:941–6.
- 48 Piepoli MF, Hoes AW, Agewall S. 2016 European guidelines on cardiovascular disease prevention in clinical practice: the Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* 2016;37:2315–81.
- 49 Wang L, Wang Z, Ma Q, et al. The development and reform of public health in China from 1949 to 2019. *Global Health* 2019;15:45.
- 50 Meng Q, Mills A, Wang L, et al. What can we learn from China's health system reform? *BMJ* 2019;365:12349.
- 51 Li X, Krumholz HM, Yip W, et al. Quality of primary health care in China: challenges and recommendations. *The Lancet* 2020;395:1802–12.
- 52 Goff DC, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American heart association Task force on practice guidelines. *J Am Coll Cardiol* 2014;63:2935–59.
- 53 Wenger NK. Prevention of cardiovascular disease: highlights for the clinician of the 2013 American College of Cardiology/American heart association guidelines. *Clin Cardiol* 2014;37:239–51.
- 54 Lloyd-Jones DM, Huffman MD, Karmali KN, et al. Estimating longitudinal risks and benefits from cardiovascular preventive therapies among Medicare patients: the million hearts longitudinal ASCVD risk assessment tool: a special report from the American heart association and American College of cardiology. *Circulation* 2017;135:e793–813.
- 55 UpToDate. Calculator: alcohol consumption screening audit questionnaire in adults (patient education), 2019. Available: <https://www.uptodate.com/contents/calculator-alcohol-consumption-screening-audit-questionnaire-in-adults-patient-education>
- 56 Torgerson DJ. Contamination in trials: is cluster randomisation the answer? *BMJ* 2001;322:355–7.
- 57 Keogh-Brown MR, Bachmann MO, Shepstone L, et al. Contamination in trials of educational interventions. *Health Technol Assess* 2007;11:iii, ix-107.
- 58 Sharma S, Jensen MP, Moseley GL, et al. Results of a feasibility randomised clinical trial on pain education for low back pain in Nepal: the pain education in Nepal-Low back pain (PEN-LBP) feasibility trial. *BMJ Open* 2019;9:e026874.
- 59 Sussman JB, Hayward RA. An IV for the RCT: using instrumental variables to adjust for treatment contamination in randomised controlled trials. *BMJ* 2010;340:c2073.