

BMJ Open Cluster-randomised controlled trial of Stroke 1-2-0 education programme to reduce stroke prehospital delay in China: a study protocol

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ABSTRACT

Introduction Stroke is the leading cause of death and disability in China. The median time of stroke pre-hospital delay is more than 15 hours, mainly due to the lack of awareness on stroke symptoms and calling emergency services. We developed Stroke 1-2-0 recognition tool in China, by adapting Face, Arm, Speech and Time. Our preliminary findings suggested that Stroke 1-2-0 can improve public's knowledge of the stroke symptoms, but its impact on the prehospital delay is still unclear. Furthermore, these findings were mainly obtained from Shanghai, one of the largest metropolises in China. However, more than half of population in China lives in the rural area. Given the striking disparities in socioeconomic status and quality of stroke care across the nation, a multicentre trial is warranted.

Methods and analysis Stroke 1-2-0 education programme will adopt a multicentre, cluster-randomised controlled design. We aimed to recruit 32 communities from 16 counties across China. Each county includes two communities having more than 100 000 residents. The two communities sampled in the same county will be randomly assigned to receive either Stroke 1-2-0 education programme or usual care. The primary objective of this study is to evaluate the impact of Stroke 1-2-0 public education programme in reducing stroke prehospital delay among adults residing in the community, compared with the usual care. The intervention will be implemented for 1 year. The primary outcomes are the symptom onset to hospital arrival time ('onset-to-door time', ODT) and 3-hour hospital arriving rate. We will use an intention-to-treat approach. A linear mixed model will be used to control for potential cluster effects.

Ethics and dissemination This study is approved by the Shanghai Minhang District Central Hospital Institutional Review Board (Shanghai, China). The findings will be disseminated via peer-reviewed publications and conference presentations.

Trial registration number ChiCTR2000040782.

INTRODUCTION

As the leading cause of death globally, stroke has been prioritised by WHO and the United Nations (UN) in their efforts to reduce the burden of non-communicable diseases.¹ In China, stroke is the first common cause of

Strengths and limitations of this study

- This is the first randomised controlled trial to examine the Stroke 1-2-0 education programme in reducing stroke prehospital delay compared with the usual care in China.
- Patients and publics were involved in the development of intervention, which will be delivered via multiple ways, such as offline education, posters, websites and social media platforms.
- The trial aimed to recruit over 1 million participants and is powered to detect small effects.
- The trial will be carried out in 16 different counties across China with different levels of economic development, to maximise generalisability.
- The main limitation of this study is the potential imbalance between communities at baseline.

death, it caused 149 fatalities per 100 000 population in 2017.² With over 2 million incident cases annually, stroke is also the leading cause of long-term disability and associated with the highest disability-adjusted life-years loss in China.³ Approximately, 40% of patients with stroke suffer severe disability such as hemiplegia.⁴

Rapid management of stroke, which requires early recognition of stroke symptoms, is fundamental in reducing morbidity, mortality and disability.⁵ Based on the current treatment guidelines,^{6 7} intravenous thrombolysis (within 4.5 hours) and mechanical thrombectomy (within 6 hours) are considered as the most effective medical treatments for acute ischaemic stroke (AIS) during the ultraearly period of time after the onset. However, a recent study using the stroke registry data from 62 Chinese hospitals reported that the median of the symptom onset to hospital arrival time ('onset-to-door time', ODT) for AIS patients was 15 hours, with a range of 2.8–21.0 hours⁸. Based on the data from 132 urban hospitals, only 21.5%

patients with AIS arrived to an emergency department (ED) within the 3-hour treatment window.⁹ The prehospital delay—the delay from symptom onset to hospital presentation—was substantial greater than that reported from the developed countries.¹⁰

The prehospital delay was largely attributed to the lack of knowledge about stroke signs and symptoms.^{11–14} In light of the implementation of the Reducing Million New Disable Project,^{15 16} which was administered by the National Health Commission, there has been a concerted effort to reduce stroke-related disability and mortality through multifacet strategies, such as general public education, primary and secondary prevention, and in-hospital management. The Reducing Million New Disable project aimed to reduce the number of newly disabled stroke patients by 1 million by 2030.^{15 16} Improved outcomes after stroke requires not only the appropriate treatment in the hospital, but also more effective public education and greater awareness of individuals at risk.

In response to improving public's knowledge of stroke symptoms in China, we developed Stroke 1-2-0 in 2016,¹⁷ by adapting Face, Arm, Speech and Time (FAST), which was one of the most popular and effective stroke recognition tools.^{18 19} Despite FAST been adopted in China for many years,²⁰ its effects on improving awareness of stroke signs and calling ambulance is still very poor due to linguistic barriers.²¹ The English word 'FAST' is relatively difficult to remember for Chinese people, especially for the elderly. In Stroke 1-2-0, 1 is for 'First, look for an uneven face, '2 for' Second, examine for arm weakness', and 0 for 'Zero (absence of) clear speech'. If a stroke sign is suspected or identified through the above-mentioned three-step procedure, the emergency number 120 should be dialled.

Preliminary data

Stroke 1-2-0 has been highly recognised by the health-care providers,²¹ and demonstrated promising results in our pilot studies as described below. To understand the public acceptance of Stroke 1-2-0, we conducted a Stroke 1-2-0 education programme in a junior middle school and a senior high school in Shanghai. A total of 625 students participated in the training programme.²² All participants agreed that Stroke 1-2-0 was a much easier tool to remember than FAST. On the completion of one-session training, almost all the students (96.4%) remembered the meaning of Stroke 1-2-0 as compared with 7.3% from the baseline. More importantly, Stroke 1-2-0 improved community physician's knowledge of early stroke symptoms. In a survey conducted among 435 community physicians in three provinces,²³ 88.5% participants would transfer patients with early stroke symptoms to the nearest hospital specialised in stroke care by emergency medical service. 96.3% of community physicians considered that Stroke 1-2-0 was the most suitable stroke educational tool for Chinese, because it's potential on eliminating the language barrier for general publics. Additionally, we piloted Stroke 1-2-0 educational campaign in

China in 2017.²⁴ Based on the survey prior to and after the educational campaign, the knowledge on the therapeutic window for thrombolytic therapy increased from 6.5% in 2016 to 32.8% in 2018.²⁴ However, more than half of the survey respondents are physicians or healthcare providers, the general population's knowledge on the stroke symptoms is still lacking. To understand the potential effect of Stroke 1-2-0 on reducing pre-hospital delay among patients with stroke, we retrospectively reviewed the electronic medical records of stroke patients who admitted to ED between 2017 and 2018, and found that the introduction of Stroke 1-2-0 substantially shortened the time between symptom onset and presentation to the hospital.

In summary, the preliminary findings suggested that Stroke 1-2-0 can improve public's knowledge of the stroke symptoms, but its impact on the prehospital delay is still unclear. Furthermore, these findings were mainly obtained from Shanghai, one of the largest metropolises in China. However, more than half of population in China lives in the rural area. Given the striking disparities in socioeconomic status and quality of stroke care across the nation, a multicentre trial is warranted.

Objectives

The primary objective of this study is to evaluate the impact of Stroke 1-2-0 public educational campaign in reducing prehospital delay among adults residing in the community, compared with the usual care. The secondary objective is to determine whether Stroke 1-2-0 education programme can improve individual's knowledge of stroke symptoms and intravenous thrombolysis rate of stroke patients and leads to a better prognosis.

METHODS AND ANALYSIS

The protocol of the study strictly followed the Standard Protocol Items: Recommendations for Interventional Trials statement.^{25 26}

Study design and settings

This study is a multicentre, cluster-randomised controlled trial. We did not employ a stepped-wedge design due to the feasibility constraints. A cluster is defined as the community managed by the structural leader group in each community. To accommodate the social and economic variations within the country, this study aims to recruit 32 communities from 16 counties. Each county includes two communities, which will be randomly assigned to intervention and control group. Participants in the control group will only receive usual care (annual education session), while those in the intervention group will receive the Stroke 1-2-0 education programme in addition to the usual care. The intervention will be implemented for 1 year, and the study will continue with a 1-year follow-up for data collection in the hospitals of each community. [Figure 1](#) is the study flow chart.

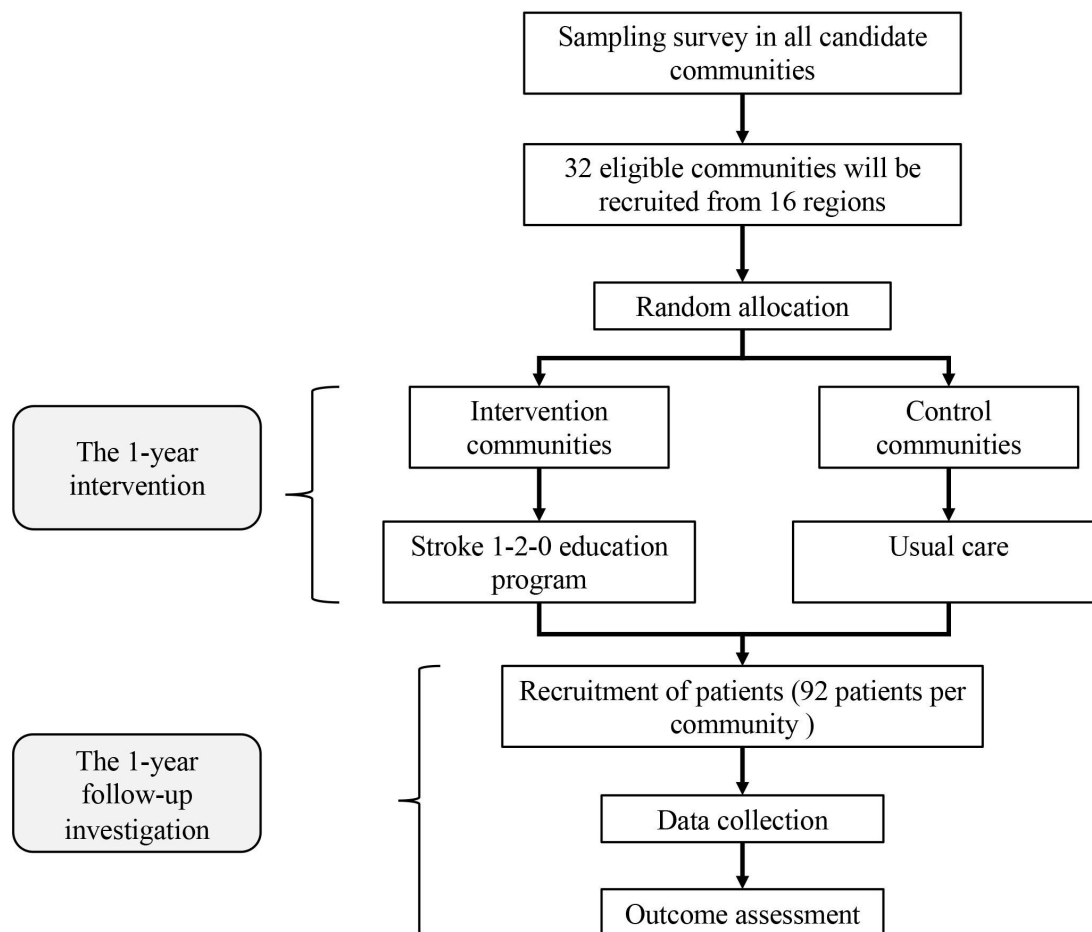


Figure 1 Study flow chart.

Patient and public involvement

There was collaboration with patients and public who worked as active partners in the design of the intervention of this study. The major activities include: (1) patient consultation prior to the design of the intervention; (2) the education tool and training materials were developed by the intervention development group consisting of physicians, community workers, patients and researchers; (3) patient and public provided feedbacks on the intervention programmes.

Recruitment

Recruitment will occur first at the cluster (community) level and then the patient level.

Community recruitment

We will promote our project via a variety of ways, such as direct contact with local health agencies and/or hospital alliance, advertisement on social media platforms and sharing information by collaborators. The candidate communities will be provided with a full description of the study. If they agree to participate, we will collect information on demographics, socioeconomics, and risk factors of stroke on the community level. Selection criteria for communities are: (1) the cluster (community) has more than 100 000 residents; (2) the communities

sampled in the same county have a distance of at least 20 km to minimise the risk for spillover effects from cross-contamination; (3) the communities sampled in the same county have similar demographic characteristics (eg, age distribution, gender ratio, etc), socioeconomic levels (eg, income, education, etc), and risk factors of stroke (eg, prevalence of hypertension), to ensure the balance of baseline characteristics and (4) the hospital alliance serves over 90% stroke patients from the sampled community, and has the capability to perform >20 cases of intravenous thrombolysis treatment per year. The hospital alliance will be formed by the hospitals in the selected community.

Patients recruitment

Residents with a diagnosis of AIS that was confirmed in any hospital of each hospital alliance will be recruited. The risks and benefits of participation will be fully explained before patients sign the informed consent. During the study period, for residents with an incident AIS will be continuously followed up.

Randomisation and blinding

We will use simple randomisation method and employ a non-inferiority framework. The selected clusters (communities) will be randomly assigned in a 1:1 ratio to either

Table 1 Description of the intervention package implemented in the Stroke 1-2-0 education programme

Content	Frequency and duration	Person responsible
Health education session and free clinics: key messages will include the risk factors of stroke, the three stroke recognition actions of Stroke 1-2-0, and the action of triggering the medical emergency system in a timely manner.	The 60 min of on-site PowerPoint-based Stroke 1-2-0 health education lecture and free clinics will be provided by a community physician once a month.	Trained community physician
Offline educational materials: health education messages will be spread through the stroke 1-2-0 posters and brochures describing our Stroke 1-2-0 strategy, and a 1 min educational video about how to recognise stroke and act immediately to dial 1-2-0.	The stroke 1-2-0 posters will be posted at eye-catching places in hospitals and resident area of communities for 1 year; the stroke 1-2-0 brochures will be delivered to residents every weekend; 1 min Stroke 1-2-0 educational video will be rolling aired in the community for 1 year.	Trained community physician and local project coordinator
Online educational materials: website (www.stroke120.org) and social media platform (Chinastroke120, www.wechat.com) describing our Stroke 1-2-0 strategy will be delivered to residents.	The stroke-related information (paper, songs, movies, short videos, etc) will be released in website and social media once a month.	Trained project staff

the intervention or control group by random sequences generated by STATA V.15.0 (StataCorp). Randomisation will be conducted by an independent statistician who will not be involved in outcome assessments. All researchers who perform outcome assessment and data analysis will be blinded to group allocations.

Intervention

We adapted the Stroke 1-2-0 education programme that was previously piloted with a community in Shanghai, China. The intervention includes three major components: (1) education session and free clinics will be provided regularly in each community to improve awareness of Stroke 1-2-0 recognition tool and knowledge on the early sign of stroke, because residents would like to gain health-related information from their primary physicians; (2) offline educational materials, including posters and brochures reflecting the Stroke 1-2-0, will be distributed in the community for at least 1 year. Educational video about how to recognise stroke and act immediately to dial 1-2-0 will be aired in the community,²⁷ this intervention component will be delivered because it will provide a supportive community environment; (3) online educational materials including website (www.stroke120.org) and social media platform (Chinastroke120, www.wechat.com), will be promoted for the residents in the selected community, we included this intervention component because accessing to information via internet or social media platforms is very popular in China. Table 1 summarises the detailed information of intervention.

Intervention fidelity

Since community involvement is an important element of successful intervention, we will recruit one member of hospital alliance to serve as the project coordinator in each community. Local project coordinators will work with the research team to schedule education session and distribute education materials (eg, posters, video clips, etc). To ensure the intervention is replicable across

different communities, we developed standard procedures for local project coordinators and community physicians who will deliver the intervention. The manual describes in detail the intervention components. The physicians who will provide education session will be trained.

We will use a multidimensional approach to assess intervention fidelity, that is the extent to which the intervention is delivered as planned. The education session will be recorded to ensure that the community physicians conduct the intervention in accordance with the manual. If the community physicians do not follow the protocol, we will contact the local communities and provide additional training for the physicians. We will also provide continuous training for local project coordinator and physicians. The distribution of education materials (eg, posters, brochures) will be recorded by making photographs. We will also record the visitor counts to our WeChat public platform and websites. The airing time of video will be also recorded.

Control group

The communities allocated to the control group will not receive any of the Stroke 1-2-0 intervention components. Instead, they will receive usual care, which is the unified education session offered by local health agencies on World Stroke Day. The session will only be offered once per year.

Outcome measures

The primary outcome measures are the ODT time and 3-hour hospital arriving rate. A 3-hour hospital arriving rate is calculated as the proportion of patients who arrive at hospital within 3 hours after onset.

The secondary outcome measures include the intravenous thrombolysis rate and the change in the knowledge level of stroke symptoms²⁴ and Modified Rankin Scale score²⁸ prior to and after the intervention. Intravenous thrombolysis rate is the proportion of patients receiving

intravenous thrombolysis. The knowledge level will be measured using the questionnaire we developed previously.²⁴ The questionnaire is presented in online supplemental table S1.

Sample size estimation

Based on the data from the China National Stroke Registry study⁹ and our preliminary data, we assumed that the 3-hour hospital arriving rate would be 20% in the control group and 28% in the intervention components of Stroke 1-2-0 education programme in the intervention group. We assumed that the intraclass correlation coefficient would be 0.02^{29 30} and the rate of drop-out would be 5% for the sample size calculation in our study. We aimed to recruit a total of 2944 ischaemic stroke patients from 32 communities with an average cluster size of 92 patients per community. This sample size will provide 85% power with $\alpha=0.05$ to detect a mean difference of 8% in the change in the 3-hour hospital arriving rate between groups after the intervention lasting 1 year. The report of stroke burden in China indicated that the incidence of stroke is 276.75 per 100 000,³¹ and the sample size of participants in each community will be 35 000. Therefore, the total sample size of participants in the present study will be 1 120 000 across 32 communities.

Data collection and management

The data collection procedure will be the same for both intervention and control groups. All study data collection will be performed or supervised by trained project staff.

Questionnaire

We will collect data on the demographics, socioeconomic, stroke-related risk factors for all selected communities. The knowledge of stroke symptoms will be evaluated by using validated instrument we developed previously.²⁴ The questionnaire is shown in online supplemental table S1. All questionnaire that completed by residents will be locked in cabinet.

Clinical data

We designed a data management system to collect clinical data of every new ischaemic stroke case in the selected communities. The hospital alliance will upload electronic medical records to our data management system if patients agreed to participate and signed informed consents. Only designated personnel from the hospital alliances will have the access to the password-protected data.

Statistical analyses

Baseline characteristics at both the community and individual levels will be reported by using descriptive statistics. Continuous variables will be presented as mean \pm SD or median (IQR) and categorical variables will be expressed as frequency (percentage). Comparisons of means of continuous variables (normal distribution) and in medians of continuous variables (skewed distribution) will be analysed by using Student's t-test and Wilcoxon

rank-sum test, respectively. Comparisons of rates for categorical variables will be performed by using the χ^2 test. The 95% CIs and associated p values will be calculated.

The primary analyses will use an intention-to-treat approach using data from all participants as they were randomised. Generalised linear mixed models will be used to compare the primary and secondary outcomes, to adjust for the clustering effect and baseline characteristics. Statistical analyses will be performed using STATA V.15.0. All statistical tests will be two-sided at the 5% level of significance.

ETHICS AND DISSEMINATION

Ethics approval

This trial has obtained ethical approval from the Shanghai Minhang District Central Hospital Institutional Review Board, Shanghai, China (ID number: 039-01K). The trial has commenced in July 2020 and currently recruiting participants.

Informed consent

Informed consent will be obtained from participants for the enrollment of them into the study. The clinical researcher will tell participants the details of the trial, including the purpose the study, the benefit and risk of the participants, and the voluntary nature of their participation. Participants have the right to withdraw from the trial at any time at any stage of the trial without affecting their medical rights and interests.

Dissemination

The study findings will be disseminated in national and international conferences, and peer-reviewed publications.

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