

Assessing a WeChat-based integrative family intervention (WIFI) for schizophrenia: protocol for a type 2 hybrid effectiveness-implementation stepped-wedge cluster randomized trial

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Study protocol

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Abstract

Background

Schizophrenia is a persistent and debilitating mental illness, whose prognosis depends largely on supportive care and systematic treatment. In 2016, the Chinese government instituted a Reward Policy to financially support family caregiving of serious mental illness, including schizophrenia. However, family caregivers are still faced with many other challenges, such as lack of knowledge about serious mental illness, skills specific to family caregiving, social support, and other resources to assist with caring for a family member with schizophrenia. How to support family caregiving in an accessible, affordable, feasible and cost-effective way remains unresolved. The wide spread use of WeChat provides a promising and cost-effective medium for health intervention delivery. The current study aims to assess a WeChat-based integrative family intervention (WIFI) embedded in the Reward Policy to support family caregiving of schizophrenia.

Methods

We will conduct a type 2 hybrid effectiveness-implementation study to test both the effect of and the implementation process of the WIFI program. The program will include three core components: 1) psycho-education through WeChat Official Account (WOA), 2) peer support through WeChat chat group, and 3) professional support through WeChat video chat. A rigorous stepped wedge cluster randomized trial will be used to evaluate the implementation, effectiveness, and cost of the WIFI program. The WIFI program will be implemented in 12 communities affiliated with the Changsha psychiatric hospital through the free medicine delivery process in the 686 Program. The 12 communities will be randomized to one of four fixed sequences every two months during an 8-month intervention period in four clusters of 3 communities each. All clusters will receive the usual financial benefit of the Reward Policy as the control condition, and then successively and in random order, will cross over to the WIFI intervention at 2-month intervals until the study ends. Outcomes will be assessed for both family caregivers and the family member with schizophrenia. Family caregivers will be assessed for their knowledge and skills about caregiving, social support and coping, perceived stigma, caregiver burden, family functioning, positive feelings, and psychological distress. Schizophrenia individuals will be assessed for their symptoms and functioning, quality of life, recovery and rehospitalization. Cost data such as costs of the intervention, health care utilization, and costs associated with lost productivity will also be collected. In addition, we will collect process data including fidelity and quality of program implementation as well as users' attitudes will also be collected. Treatment effects will be estimated using generalized linear maximum likelihood mixed modeling (GLMM) with clusters as a random effect and time as a fixed effect. Cost-effectiveness analysis will be performed from the societal perspective using incremental cost effectiveness ratios (ICERs). Qualitative analysis will use the grounded theory approach and immersion-crystallization process. All statistical analyses will be conducted according to the intention-to-treat principle.

Discussion

This is the first hybrid effectiveness-implementation study to test a WeChat-based mHealth intervention to support family caregiving of schizophrenia in China. The innovative study will contribute to the development of a more cost-effective and evidence-based family management model in the community for schizophrenia individuals. If found to be effective, the intervention could potentially be integrated into current national policy to support family caregiving. The intervention could also be adapted for use with other populations with a persistent and disabling condition.

Contributions To The Literature

- This study proposes a WeChat-based integrative family intervention (WIFI) that is accessible, affordable, feasible and cost-effective.
- This study will evaluate both the effectiveness and implementation strategy of the WIFI program using a type 2 hybrid effectiveness-implementation stepped-wedge clustered randomized trial.
- This study provides a model for family management and care of schizophrenia individuals that can be integrated into current national policy.

Background

Schizophrenia and family caregiving

Globally, schizophrenia is a debilitating, persistent psychiatric disorder affecting over 21 million people [1, 2] and contributing to 60% increased premature deaths among people living with schizophrenia (PLWS) compared to general population [3]. The most recent global burden of disease (GBD) study in 2016 shows that schizophrenia contributes 13.4 million years of life lived with disability to the burden of disease globally [2]. The prognosis of schizophrenia depends largely on integrated mental health and social care services in community-based settings, which has been listed by the World Health Organization (WHO) as one of the four major objectives in its Mental Health Action Plan 2013 – 2020 [3]. Among the multiple initiatives proposed by the WHO [3], strengthening the active involvement and support of family caregivers in caring for PLWS stand out as a most sustainable and cost-effective solution to addressing the worldwide treatment gap in resource-poor settings. Recent years has seen a global shift in the responsibility of care from the hospital setting to families [4] such that the economic value of informal family caregiving now greatly exceeds spending through formal health care systems. Recently, the Chinese government has recognized the value of family caregiving by instituting the Reward Policy (described below) to support family caregivers financially [5], however, this policy is an exception globally [6].

The Reward Policy and challenges

In China, there are over 7.16 million PLWS [7] and over 90% of them live with and depend on their families for care [8]. Family caregiving often requires a range of support that extends across physical, psychological, emotional, social and financial domains [9]. The essential roles of family caregivers in the

care of schizophrenia have been increasingly recognized in China's mental health policy. In 2016, the Chinese government instituted a Reward Policy to encourage family involvement in care of people with serious mental illness. According to the Reward Policy, a monthly subsidy equal to the local poverty line allowance (currently at least 200 RMB) is paid to each family based on good management and care of the family member with serious mental illness, including schizophrenia [5, 10].

Three years after its implementation, the Reward Policy has helped alleviate financial burden for caregiving families. However, family caregivers are still faced with other challenges during the process of caregiving, such as insufficient knowledge and skills in providing appropriate care to PLWS, social isolation due to stigma, stress from caregiving, family conflict on task-sharing, and lack of self-care due to overwhelming caregiving responsibilities [4, 11, 12]. As a result, family caregivers experience a considerable level of burden which not only impact detrimentally their own health and well-being, but also lead to poor prognosis in PLWS due to impaired quality of care. These challenges have stimulated a focus beyond simply identifying caregiver burden to also developing effective family interventions to reduce this burden and improve care [13].

Family intervention programs

To date, several family intervention programs have been developed and tested, with three elements identified as most promising and feasible: 1) psycho-education to families to increase knowledge about schizophrenia and strengthen related caregiving skills; 2) peer-support for both family caregivers and PLWS where they can share experiences and feelings, exchange information, and provide mutual emotional support; and 3) professional support to family caregivers that troubleshoots specific problems and provides private, targeted guidance to address specific [13-18]. Thus far, an integrative application of all three intervention components has been limited in China due to their low accessibility and high cost, and evidence on their combined use and effectiveness to support family caregivers and PLWS is lacking. An innovative, affordable, and cost-effective platform that integrates all three of these intervention components thus represents a pressing need in the scientific literature and also for national health care policy.

WeChat use in China

WeChat is the most common social media platform in China with over one billion monthly active users of all ages [19]. 93% of urban users log into WeChat every day [20]. WeChat features diverse platforms such as Moments, Chat group and WeChat Official Account (WOA) and boasts of multiple powerful functions including voice and text messaging, voice and video calls, photo sharing, payment and games. Due to its wide range of platforms and functions, WeChat has been dubbed China's 'app for everything' and characterized as "4A" (Anybody, Anytime, Anywhere, Anything)[21, 22]. The seamless infiltration of WeChat into every aspect of human life suggests a promising and cost-effective medium for health intervention delivery. A growing number of WeChat-based health intervention programs have been developed for patients with various health conditions, with robust evidence showing their acceptability, feasibility and efficacy [23-27]. Specifically, WeChat-based health interventions have been found to cost

less, improve treatment adherence, have fewer complications, increase rates of follow-up, require less intervention time, and improve patient satisfaction [23-27]. Thus, we hypothesize that a WeChat-based Integrative Family Intervention (WIFI) program that includes the three elements noted above (psycho-education, peer support, professional support) will be an accessible and cost-effective approach to improve outcomes of both PLWS and family caregivers.

Theoretical framework for the proposed study

The theory underlying the proposed study is depicted in Figure 1 below. As shown, consistent with the literature, three components are included in the WIFI program to provide education and support to families – psycho-education, peer support, and professional support. WeChat will provide access for caregivers and PLWS to each of these intervention components. Psycho-education and supports will increase knowledge and skills as well as social supports (peer and professional) and coping to reduce perceived stigma and caregiver burden. In addition, these components are expected to enhance family functioning and positive feelings such that emotional distress will be reduced. Finally, these effects are hypothesized to reduce caregiving costs. For the PLWS, these components are expected to enhance the overall quality of care in the community, which is hypothesized to reduce PLWS symptoms and enhance functioning, increase quality of life and recovery, and decrease rehospitalization, thus reducing overall health care costs.

This paper describes the protocol of a study designed to assess the impact of a WeChat-based Integrative Family Intervention (WIFI) program fully aligned with the Reward Policy for families caring for people living with schizophrenia (PLWS), compared to the Reward Policy alone. Specific aims include: (1) Compare the effect of WIFI program + the Reward Policy with the Reward Policy alone on caregiving and the health outcomes of family caregivers and PLWS, such as caregiving knowledge and skills, social support and coping, caregiver burden, family functioning, positive feelings, and psychological distress of caregivers, as well as symptoms, functioning, and recovery of PLWS. (2) Compare the total costs of the WIFI program + the Reward Policy with the Reward Policy alone including: the program itself, health care utilization of the PLWS and family caregiver, and production loss of the family caregiver. (3) Conduct a process evaluation of the WIFI program to assess fidelity and quality of program implementation as well as users' attitudes towards the program. To simultaneously assess intervention effectiveness and implementation strategies using mixed methods in "real life" healthcare settings, we used a hybrid type II effectiveness-implementation design by stepped-wedge clustered randomized trial [28] .

Methods

Setting

The study will be conducted in the Changsha psychiatric hospital (also named The Ninth hospital of Changsha). Established in 1952 and affiliated to Changsha civil affairs bureau, Changsha psychiatric hospital bears the responsibility of prevention, treatment and rehabilitation for all residents with mental illness in Changsha City. The hospital not only provides out-patient and in-patient healthcare, but also

extends its services to community-based mental healthcare for its 12 affiliated communities, including the “686 program” and the Reward Policy implementation. The “686 Program” is China's largest demonstration project in mental health service aimed at integrating hospital and community services for serious mental illness, with the following services provided: patient registration and initial assessment, free medication and regular follow-up in the community, management of community emergencies, and free emergency hospitalization [29, 30]. In Changsha psychiatric hospital, a medical team composed of 3 psychiatrists and 4 nurses are responsible for the “686 program” and circulate around the 12 communities each month to deliver free medicine for over 1000 registered clients who they know very well after long-term visits. The Reward Policy is a newly issued policy to encourage family care of people with serious mental illness, with a current 200 RMB/month offered to each family registered under the 686 Program by the Changsha psychiatric hospital.

Design

This study uses a pragmatic type II hybrid effectiveness implementation design [28] to evaluate both effectiveness and implementation strategy of the WIFI program. See Additional file 1 for the CONSORT checklist and additional file 2 for the SPIRIT checklist. We will conduct a multi-center prospective controlled trial, using a step-wedged design, comparing the WIFI program integrated into the Reward Policy (=intervention group) and the Reward Policy alone (=control group) in family caregiving of PLWS.

In a stepped-wedge cluster-randomized trial (SWCRT), all clusters randomly and sequentially are crossed over from control to intervention over a number of time periods [31]. All clusters serve as a control group at the beginning of the study and end up in the intervention group at the end of the study. Compared to the traditional randomized controlled trial and parallel cluster studies, SWCRT enjoys unique ethical benefits since all clusters will ultimately receive the assumingly beneficial intervention at the end of the study [32]. In addition, SWCRT enables analyses of any temporal effects of the intervention since each cluster acts as its own control and also allows for estimation of both between- and within-cluster effects of the intervention due to the repeated measurements [32]. As a result, a SWCRT design achieves greater statistical power with smaller sample sizes and is more cost-effective than parallel group designs.

In the proposed study, a WIFI program will be implemented sequentially across an 8-month intervention period in the 12 communities by the Changsha psychiatric hospital. A total of 20 families will be recruited from each community, leading to a total sample of 240 families. Allocation will be determined by an external statistician using a computer-generated random number sequence. Each number will be secretly and securely stored in a sealed envelope by the external statistician until the intervention starts. The first author (YY) will generate the allocation sequence, the medical team will work on enrolling participants, and the second author (TXL) will assign participants to interventions. The 12 communities will be randomized into 4 groups based on geographic distance and number of PLWS to reduce the risk of contamination and group size inequality. After allocation, each group will be randomized to one of four fixed sequences every two months during an 8-month intervention period (Table 2 and figure 1). All communities will receive the usual financial benefit of the Reward Policy as the control condition before

the intervention, and then successively and in random order, will cross over to the WIFI intervention at 2-month intervals until the study ends.

Participants and recruitment

Recruitment is estimated to start in March 2020. The study aims at recruiting 240 PLWS families from 12 communities affiliated to the Changsha Psychiatric Hospital through the “686 program”. Within each community, 20 eligible PLWS will be randomly selected from the registry name list by a statistician, leading to a sampling frame of 240 PLWS families. Each family will be approached and invited to participate in the study during the monthly medicine delivery by the medical team from the Changsha Psychiatric Hospital. The medical team have been providing mental health services including free anti-psychotic medicine delivery for the communities for a long time and thus know very well about each family of PLWS, which greatly facilitates our participants recruitment and retention. Detailed information about the research will be provided both orally and in written format to interested families by the medical team. All families will be fully informed of the study risk and benefits, and their right to drop out of the study any time. Families agreeing to participate in the study will be invited to scan a WeChat barcode of the research program so that they can be allocated to receive the intervention in the future.

Participants of the study will include both PLWS and their family members. Inclusion criteria for participating PLWS are: 1) being registered in the “686 Program”; 2) fulfilling the Chinese Classification of Mental Disorders-3 (CCMD-3) or the International Classification of Diseases-10 (ICD-10) criteria for schizophrenia; 3) living with at least one family member; and 4) able to use a smartphone and WeChat to read and communicate. Inclusion criteria for participating family members are: 1) joining the Reward Policy and receiving a subsidy for family care; 2) living with a PLWS for at least the past two years; 3) involved with caregiving activities of PLWS; 4) able to use a smartphone and WeChat to read and communicate; and 5) at least one family member having a smartphone with WeChat app installed.

Blinding

PLWS, family caregivers, medical team and researchers cannot be blinded for the allocated treatment. The program team conducting the intervention will not be involved in assessing any of the outcomes. The analyses of the data by the researcher will be blinded.

Intervention

Control group: participants in the control group will receive the usual financial benefits of the Reward Policy and receive payment from the Changsha psychiatric hospital. However, they will not have access to the WIFI program since they cannot scan the WeChat barcode for the research.

Intervention group: participants in the intervention group will receive the usual financial benefits of the Reward Policy as well as the WIFI program which will include three key components: psycho-education through WOA publications, peer-support through a WeChat chat group, and professional support through WeChat private chat and video call, as shown in Table 2.

Contamination

Since randomization is performed at the community level, using the step-wedged design, the risk of contamination between the control and intervention group is very low. Also, since the intervention is delivered through WeChat and each participant scans the special WeChat account of the research program to obtain access to the WIFI program, it is unlikely that participants in the control group will receive the intervention during the control stage. Even if participants in the control group learn about the WeChat account of the research program, they will not be able to add it because the research team will recognize each participant and decline any request from the control group until their allotted sequence to join the intervention. Thus, intervention contamination will be avoided.

Outcomes

Effect Measures

The effect of the intervention will be assessed at the individual level for both family caregivers and PLWS.

For family caregivers, the outcomes will include knowledge and skills about caregiving (Knowledge and Skill of Caregiving for Schizophrenia, KSCS, self-developed), social support (Multi-dimensional Scale of Perceived Social Support, MSPSS) [33], coping (Simplified Coping Style Questionnaire, SCSQ) [34], perceived stigma (Perceived Devaluation and Discrimination Scale, PDD) [35], caregiver burden (Zarit Burden Interview, ZBI) [36], family functioning (Family Adaptation, Partnership, Growth, Affection and Resolve Index scale, APGAR) [37, 38], positive feelings (Caregiving Rewarding Feelings, CRF) [39], perceived stress (Perceived Stress Scale, PSS) [40], depression (Patient Health Questionnaire-9, PHQ-9) [41] and anxiety (Generalized Anxiety Disorder Scale-7, GAD-7) [42].

For PLWS, the outcomes will include clinical symptoms (Brief Psychiatric Rating Scale, BPRS) [43] and overall functioning (Global Assessment of Functioning, GAF) [44], which will both be rated by psychiatrists. Other outcomes will include: self-reported quality of life (The World Health Organization Quality of life brief scale, WHOQOL-BREF) [45], recovery (Recovery Assessment Scale, RAS) [46], rehospitalization, depression (Patient Health Questionnaire-9, PHQ-9) [41] and anxiety (Generalized Anxiety Disorder Scale-7, GAD-7) [42].

Potential Confounding Factors

At baseline, we will also collect information about potential confounding factors by adjusting for the following: (1) Sociodemographic data such as age, gender, education and occupation; (2) Clinical data, such as diagnosis type of schizophrenia, length of illness, and length of caregiving; and (3) WeChat use intensity as assessed by the WeChat Use Intensity Questionnaire (WUIQ) [47, 48].

Cost measures

Costs will be measured from a societal perspective and consist of at least the following three levels: (1) costs of the intervention, (2) health care utilization, and (3) costs associated with lost productivity. All of the costs will be converted to the year 2019 using consumer price indices.

The intervention costs pertain to implementation and operation of the WIFI program. A bottom-up approach will be used to assess the intervention costs which may include but not limited to: (1) training of the psychiatrists, researchers, and other project team members; and (2) the WeChat intervention (WOA fee, administrator time, consultation fee of the psychiatrists, etc.).

The health care utilization costs pertain to medical care for both PLWS and family caregivers. A monthly cost diary will be used to retrospectively track medical expenses incurred by the PLWS and family caregivers, which may include but not limited to: (1) visits to health care professionals in primary or secondary care; (2) hospitalization; (3) visits to alternative medicine therapists; (4) medication; and (5) other non-medical expenses incurred by medical care such as transportation, food and lodging. Health care utilization costs will be estimated by China guideline prices that are supplemented by population-based estimates in the literature.

The costs associated with productivity loss will be assessed at both the PLWS and caregiver level. For both PLWS and caregivers, costs include absenteeism due to sick leave, which will be assessed by monthly sick leave calendars. The human capital approach will be used to calculate the costs of losses to production due to sickness or caregiving (net number of days on leave during follow-up, multiplied by the daily wage of the worker if employed or equivalent values if unemployed).

Process measures

A process evaluation will be conducted to evaluate the implementation process of the intervention to understand potential factors related to implementation that may be associated with observed outcomes. The evaluation includes fidelity and quality of WIFI implementation, as well as users' attitudes towards the program, which will be evaluated separately for PLWS, their family members, and psychiatrists. After completion of the intervention in each randomized community, both quantitative and qualitative process data will be collected from survey samples of PLWS and family members to assess their awareness of and responsiveness to the WIFI program.

Quantitative data will be directly collected through the WeChat backstage management system and include information about families' use of and engagement with the WIFI program. For psycho-education data, we will collect information on views/downloads/shares of WOA publications. For peer-support data, we will collect information on chatting topics, number of messages sent, and active users of the WeChat chat group through chatting records. For profession support, we will collect information on help-seeking behaviors of family, number of consultations, problems addressed by psychiatrists, and so on.

Qualitative information will include responses by PLWS and family members to questions about how they felt about their WIFI program experience, such as attitudes, beliefs, and feedback about the program.

In addition, we will survey the psychiatrists to assess their exposure to and experience with each element of the WIFI program, and to find both facilitators and barriers of program implementation at the provider level. All this information will help the research team gain insight into the feasibility and replicability of the program.

Data collection and management

Data are collected from PLWS, their family members and psychiatrists at baseline (Month 1-2), and at 4, 6, 8, and 10 months. All participants will be invited through WeChat to complete Sojump surveys. The questionnaire was produced, distributed, and collected with the online survey tool Sojump (<http://www.sojump.com>), a professional online survey tool that provides a series of services including questionnaire design and distribution, data collection and analysis. Each family will be reimbursed with money for participation each time, conditional on completion of both the PLWS questionnaire (about 20 minutes to complete) and caregiver questionnaire (about 45 minutes to complete). The reimbursement will increase by 25% for each repeated measurement in order to incentivize retainment and increase intervention adherence, that is, RMB35 (equal to USD \$5) for the baseline measurement, followed by RMB44 (\$6.25), RMB55 (\$7.81), RMB69 (\$9.77), and RMB86 (\$12.21) for the next 4 measurements. A family will be reimbursed with a total of RMB289 (about \$41) for completion of all five measurements. The money will be sent directly to one designated family member through the WeChat money transfer function. Double entry method will be adopted to input data, with range for data values preset to avoid any wrong input. All data will be safely stored in a disk and managed by a special data specialist. Table 3 provides an overview of all outcome measures and assessment instruments used in this trial.

Statistical Analysis

We will use mixed-methods analysis on both qualitative and quantitative data collected during each step of the WIFI program. For qualitative data, a grounded theory approach[49] and immersion-crystallization process [50] will be used to assess process implementation and gain deep insight into feasibility and replicability of the WIFI program. For quantitative data, descriptive analysis will be conducted to describe characteristics of participants during the control and intervention periods. Continuous variables will be described by the mean \pm standard deviation, or by median (Interquartile range) depending on the shape of the distribution. Categorical variables will be described by number and percentages in each category. For two-group comparisons, student-t test or non-parametric tests will be conducted for continuous variables, while chi-squared test or a Fisher's exact test will be conducted for categorical variables. Multiple imputation will be adopted to deal with missing values.

Treatment effects (WIFI vs control) will be estimated using generalized linear maximum modeling (GLMM) with clusters as a random effect and time as a fixed effect. All of the available measurements (2 months, 4 months, 6 months, 8 months, 10 months) will be used, with the baseline values of each outcome as a covariate. This analysis will take into account the within-cluster and between-cluster correlation, as well as any evolution of the intervention effect over time. Statistical analyses will be

performed at the individual level and according to the intention-to-treat principle, which will be compared to the per-protocol analyses. Additionally, extra costs of the WIFI program will be evaluated.

Power analyses

To illustrate power for both caregiver and PLWS analyses, we can use a baseline ZBI score of 45 for caregivers and a baseline GAF score of 42 for PLWS observed by the research team in a previous cross-sectional study conducted with caregivers and PLWS in Hunan province. Using a SWCRT with 12 communities over five time periods or steps (baseline and four intervention steps), a sample size of 20 families per communities (240 families in total) will be sufficient to detect a clinically important decrease in caregiver burden as assessed by the Zarit Burden Inventory score from a baseline of 45 to 30, assuming an intra-cluster correlation of 0.05, with 90% power at a 5% significance level, and 20% dropout ratio [50]. Similarly, the power for PLWS analyses also reaches 90% with the same sample size for a GAF score to increase from 42 to 56, with the same assumptions.

Cost-effectiveness analyses

A cost-effectiveness analysis will be performed from the societal perspective according to the intention-to-treat approach, with missing data imputed using multiple imputation [51]. Confidence intervals (95%) will be obtained by bias corrected and accelerated bootstrapping. The incremental cost effectiveness ratios (ICERs) will be calculated by dividing the differences in mean total costs between both groups, by the difference in mean effects between both groups (e.g., ZBI score of caregiver, BPRS and GAF score of PLWS). The incremental cost utility ratio will be calculated by dividing the incremental costs by the difference in the quality adjusted life years assessed with EQ-5D between both treatment groups. These ratios will be graphically presented in a cost-effectiveness plane [52].

Data Monitoring and Evaluation

In order to ensure the smooth progress of the intervention and protect participants welfare, a data monitoring committee (DMC) will be established. The DMC is composed of administrative staff from both the hospital and its 12 affiliated community health centers, who are independent from the sponsor and have no competing interests. Their main responsibility is to monitor the study progress and deal with any adverse event during the study process, which will be reported by the medical team to the PI and then to the DMC. Every month, the DMC will hold a study meeting to summarize study progress, trouble shoot problems, and deal with any adverse event happened during the study. The DMC also has the right to terminate the intervention when it deems huge risk to participants.

Ethical consideration

The study protocol was reviewed and approved by the Institutional review board of Xiangya School of Public Health Central South University (No.: XYGW-2019-029). All procedures are in accordance with the Declaration of Helsinki. The WIFI program has been registered as a clinical trial (Current Controlled Trials NCT03751111). Any modifications (eg, changes to eligibility criteria, outcomes, analyses) to the study

protocol should be reported to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) immediately. The medical team will approach participants to fully inform them of the study aims and contents and acquire written informed consent from participants before recruitment. The medical team must recommend the WIFI program for each PLWS and their family who come for free medicine, without any biased selection based on personal preference. Participants' participation or refusal will not affect their medicine acquirement and following medical or nursing care. In order to protect participant confidentiality, personal information of participants will be collected only once during baseline data collection and then de-identified with newly generated numbers instead of name, age, etc. after the trial. The de-identified data will only be shared or reported aggregately instead of individually. All data are securely and secretly stored in a disk and managed by a special data specialist. Only the PI and her research team has access to the final trial datasets.

Knowledge dissemination

Trial results will be communicated to participants, healthcare professionals, the public, and other relevant groups through papers in peer reviewed journals (4-6 international and 2-4 national), a PhD thesis and a Master thesis, presentation at 1 national and 1 international conference. Authorship should follow the ICMJE recommendation for authorship based on the criteria of: substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content; and final approval of the version to be published. The full protocol, participant-level dataset, and statistical code are available from the first author and corresponding author on reasonable request.

Discussion

Using a stepped wedge cluster randomized trial (SWCRT) design, this proposed study will develop a WeChat-based integrative family intervention (WIFI) program fully aligned with the Reward Policy and test its effectiveness. Expected results and products will include: (1) Significant improvement in outcomes for both PLWS and their family due to WIFI program participation. (2) Stronger impact for WIFI combined with Reward Policy than Reward Policy alone. (3) Development of a cost-effective, replicable family management model for schizophrenia that can be integrated into the current national Reward Policy.

The study enjoys some unique advantages and innovations as follows: First, the WIFI program recruits the whole family of PLWS as our intervention target, which may produce more far-reaching positive effect than interventions targeted at PLWS alone, or caregivers alone. In Asian countries like China, family cohesion and harmony are the core of its family-oriented culture. Intervention targeted at the family not only directly improves the well-being of each member, but also improves family dynamic, which in turn, will also promote each member's well-being. Second, the WIFI program is based on the most widely used social media in China-WeChat, which is accessible, affordable, feasible and cost-effective. Compared to traditional on-site intervention, the WeChat-based intervention provides both synchronous and asynchronous communication that can serve a broad range of respondents who would otherwise not be

recruited due to time restraints and geographical constraints. Third, the WIFI program provides the most comprehensive intervention by integrating all three key components of family intervention that have been internationally recognized: psycho-education, peer support, and private/professional support. Each component has its unique effect in improving the health outcome of PLWS and their family and compensates with each other to maximize their benefits to the family. Fourth, the step-wedge design enjoys ethical advantages by ensuring all participants receive the intervention, as well as statistical advantages by generating more sound and robust scientific evidence than traditional randomized cluster trial. Fifth, the WIFI program recruit a medical team composed of both clinical psychiatrists and psychiatric nurses into the research team to work as both intervention implementers and data collectors. The medical team have long close relationship with the community and are well accepted by PLWS and their family, which greatly increase participant recruitment rate. In addition, the medical team know well about each PLWS and can make more accurate assessment on the symptoms and function of PLWS, which further increase the reliability and validity of the WIFI program.

In conclusion, this innovative study will contribute to the development of a more cost-effective and evidence-based family management model in the community for PLWS. The proposed study is among the first innovations to develop and test a WeChat-based mHealth intervention to support family caregiving of schizophrenia in China. If found to be effective, the intervention could potentially be integrated into current national policy to support family caregiving. The intervention could also be adapted for use with other populations with a persistent and disabling condition.

Abbreviations

4A

Anybody, Anytime, Anywhere, Anything

APGAR

Family Adaptation, Partnership, Growth, Affection and Resolve Index scale

BPRS

The Brief Psychiatric Rating Scale

CCMD-3

Chinese Classification of Mental Disorders-3

CM

Cluster Communities

CRF

Caregiving Rewarding Feelings

EQ-5D

EuroQol-5D

GAD-7

Generalized Anxiety Disorder Scale-7

GAF

Global Assessment of Functioning

GBD
Global Burden of Disease
GLMM
Generalized Linear Mixed Modeling
ICD-10
International Classification of Diseases-10
ICER
Incremental Cost Effectiveness Ratio
KSCS
Knowledge and Skill of Caregiving for Schizophrenia
M
Month.
MSPSS
Multi-dimensional Scale of Perceived Social Support
PDD
Perceived Devaluation and Discrimination
PLWS
People Living with Schizophrenia
PSS
Perceived Stress Scale
PHQ-9
Patient Health Questionnaire-9
RAS
Recovery Assessment Scale
RMB
Ren Min Bi
SCSQ
The Simplified Coping Style Questionnaire
SWCRT
Stepped-Wedge Cluster-Randomized Trial
USD
United States Dollars
WHO
World Health Organization
WIFI
WeChat-based Integrative Family Intervention
WOA
WeChat Official Account
WUIQ
WeChat Use Intensity Questionnaire

Declarations

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Competing interests

The authors declare that they have no competing interests.

Authors' contributions:

All authors have made substantial contributions to the study conception and design, data collection and analysis, as well as to the development and editing of the manuscript. The principal investigator, YY led the initial study design, while JKT and SYX substantially revised and updated the research question and study design prior to initiating the project. YY was responsible for obtaining ethics approval and acquiring financial support. YY, TXL and SYX provided essential input on executing the research in partnership with Changsha psychiatric Hospital and its twelve affiliated communities. YY, TXL, JKT and SYX developed the WIFI program. YY, YLL, and QRL developed detailed evaluation methods based on the original research plan. TXL, SJX, YLL, QRL, XX, MY, XPG contributed to data collection, XX, MY, and XPG assisted with methodology and statistical analytic planning for qualitative part, while TXL, SJX, YLL, and QRL assisted with methodology and statistical analytic planning for quantitative part. YY drafted the publication with contributions from all authors. All authors are contributing to the conduct of the study and have read and approved the final manuscript for publication.

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Ethics approval and consent to participate

The Institutional review board of Xiangya School of Public Health Central South University (No.: XYGW-2019-029) has approved and regulates the ethical execution of this research.

Availability of Data and Materials

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Consent for publication

Not applicable.

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Tables

Table 1. Design of the four-stage SWCRT

CM/M	Baseline (M ₁₋₂)	Step 1 (M ₃₋₄)	Step 2 (M ₅₋₆)	Step 3 (M ₇₋₈)	Step 4 (M ₉₋₁₀)
CM ₁₋₃	C	WIFI	WIFI	WIFI	WIFI
CM ₄₋₆	C	C	WIFI	WIFI	WIFI
CM ₇₋₉	C	C	C	WIFI	WIFI
CM ₁₀₋₁₂	C	C	C	C	WIFI

C: Control - Reward Policy alone. WIFI: WeChat-based Integrative Family Intervention. M=Month. CM=Cluster communities. No. of clusters = 12. No. of groups = 4. No. of clusters per group =3. Step length = 2 months. No. of participants per step = 20.

Table 2. Contents of the WIFI program

Components	Format	Frequency	Leader	Possible Contents/Topics
Psycho-education	WeChat official account publications	Weekly	Psychiatrists and researchers	What is schizophrenia? What causes schizophrenia? How is schizophrenia treated? What can be done to promote recovery in schizophrenia? What are the early signs of relapse? What support do families need? How can feelings of stigma be addressed?
Peer-support	WeChat chat group of PLWS	Daily	PLWS volunteer	Introduce self and tell your story, identify a specific problem encountered to discuss with the group, discuss skills and techniques used to cope with challenging situations, share feelings and resources, organize off-line activities for support and stress reduction, such as hiking, dinner, group meetings, etc.
	WeChat chat group of caregivers	Daily	Caregiver volunteer	
Professional support	Private WeChat chat & video call	Monthly	Psychiatrists	Evaluation of PLWS symptoms & function; update on medication & treatment; troubleshoot specific problems; provide consultation, guidance and assistance, etc.

Table 3. Assessment of study outcomes

Outcome measures	M₁₋₂	M₃₋₄	M₅₋₆	M₇₋₈	M₉₋₁₀	Figures
Caregivers						
Knowledge and skill (KSCS)	✓	✓	✓	✓	✓	
Social support (MSPSS)	✓	✓	✓	✓	✓	
Coping (SCSQ)	✓	✓	✓	✓	✓	
Perceived stigma (PDD)	✓	✓	✓	✓	✓	
Caregiver burden (ZBI)	✓	✓	✓	✓	✓	
Family functioning (APGAR)	✓	✓	✓	✓	✓	
Positive feelings (CRF)	✓	✓	✓	✓	✓	
Perceived stress (PSS)	✓	✓	✓	✓	✓	
Depression (PHQ-9)	✓	✓	✓	✓	✓	
Anxiety (GAD-7)	✓	✓	✓	✓	✓	
PLWS						
Symptoms (BPRS)	✓	✓	✓	✓	✓	
Functioning (GAF)	✓	✓	✓	✓	✓	
Quality of life (WHOQOL-BREF)	✓	✓	✓	✓	✓	
Recovery (RAS)	✓	✓	✓	✓	✓	
Rehospitalization	✓	✓	✓	✓	✓	
Depression (PHQ-9)	✓	✓	✓	✓	✓	
Anxiety (GAD-7)	✓	✓	✓	✓	✓	
Potential confounding factors						
Social demographic variables	✓					
Clinical variables	✓					
WeChat use intensity (WUIQ)	✓					
Cost						
WIFI program (bottom-up approach)	✓	✓	✓	✓	✓	
Health care utilization (cost dairy)	✓	✓	✓	✓	✓	
Productivity loss (sick leave calendar)	✓	✓	✓	✓	✓	
Process						
Fidelity (quantitative)						✓
Quality (quantitative)						✓
Attitudes (qualitative)						✓

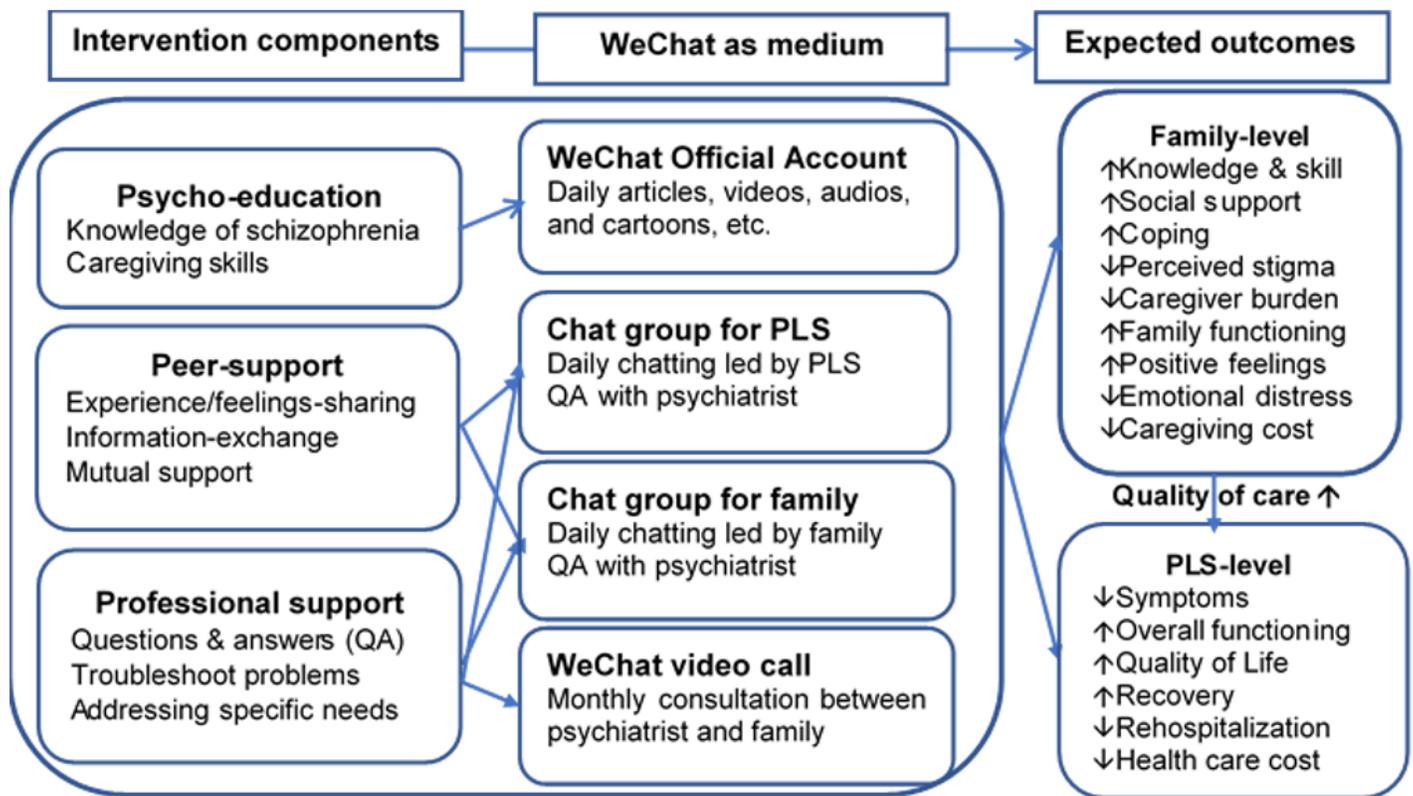


Figure 1

Theoretical framework for the proposed study

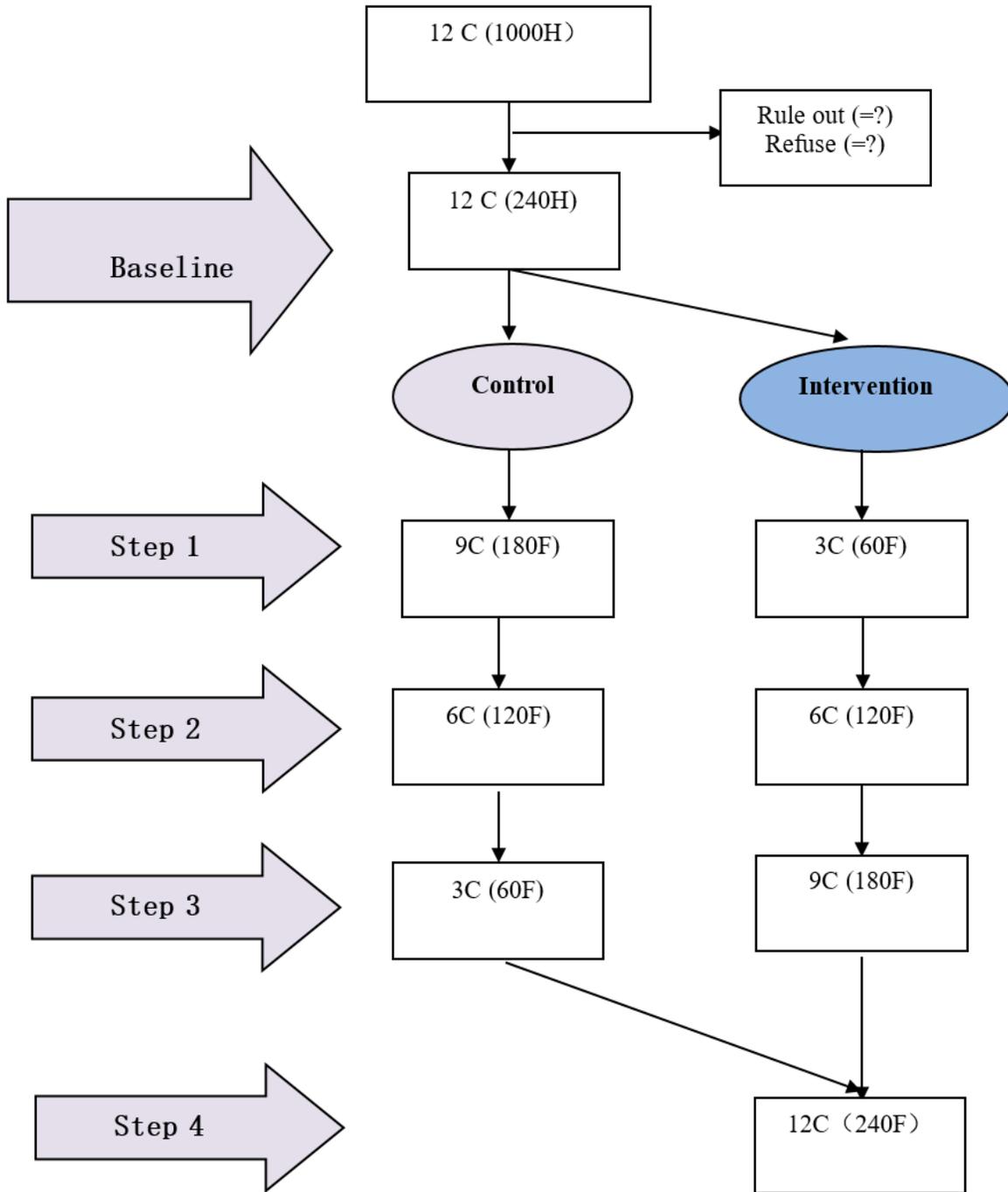


Figure 2

Flowchart for participant recruitment and allocation

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